7·8/2003

ISSN 0009-4293

CHIMIA

www.chimia.ch

FALL MEETING 2003
HERBSTVERSAMMLUNG 2003
ASSEMBLÉE D'AUTOMNE 2003

SCHWEIZERISCHE CHEMISCHE GESELLSCHAFT
SOCIETE SUISSE DE CHIMIE
SWISS CHEMICAL SOCIETY

CHIMIA 2003, VOLUME 57, NUMBER 7/8/03, PAGES 367–482// CHIMIAD 57(7/8) 367–482 (2003)

CHIMIA 2003, 57, No. 7/8

CHIMIA

www.chimia.ch

International Journal for Chemistry
and
Official Membership Journal
of the Swiss Chemical Society (SCS)
and its Divisions

Internationale Zeitschrift für Chemie
und
Offizielles Publikationsorgan
der Schweizerischen Chemischen Gesellschaft (SCG)
und ihrer Divisionen

Divisions	Divisionen	
Chemical Research	Chemische Forschung	www.swiss-chem-soc.ch/dcr
Medicinal Chemistry	Medizinische Chemie	www.swiss-chem-soc.ch/dmc
Industrial Chemistry	Industrielle Chemie	www.swiss-chem-soc.ch/dic
Analytical Chemistry	Analytische Chemie	www.swiss-chem-soc.ch/dac

Associated Society Members		Kollektivmitgliedgesellschaften	
GSASA	Swiss Soc. of Public Health and Hospital Pharmacists	GSASA	Ges. Schweiz. Amts- und Spitalapotheker
PGS	Polymer Group of Switzerland	PGS	Polymer-Gruppe der Schweiz
SACC	Swiss Association of Computational Chemistry	SACC	Schweiz. Arbeitsgemeinschaft für Computerchemie
SGLUC	Swiss Soc. of Food and Environmental Chemistry	SGLUC	Schweiz. Ges. für Lebensmittel- und Umweltchemie
SGMS	Swiss Group for Mass Spectrometry	SGMS	Schweiz. Gruppe für Massenspektrometrie
SGPP	Swiss Soc. of Photochemistry and Photophysics	SGPP	Schweiz. Ges. für Photochemie und Photophysik
SVC	Swiss Chemical Engineers FH Association	SVC	Schweizerischer Verband diplomierter Chemiker FH
VSN	Swiss Association of Science Teachers	VSN	Verein Schweiz. Naturwissenschaftslehrerinnen und -lehrer

Editor/Redaktor
Prof. Camille Ganter
Laboratorium für Organische Chemie
ETH Hönggerberg, CH–8093 Zürich
Tel.: +41 1 632 29 00, Fax: +41 1 633 12 87
E-Mail: ganter@org.chem.ethz.ch

Frequency: Monthly
Erscheinungsweise: Monatlich

Annual Subscription 2003 (VAT included)
Jahresabonnement 2003 (inkl. MWSt)

Switzerland/Schweiz	CHF	220.–
Foreign Countries/Ausland	CHF	270.–
Air Mail Surcharge/Luftpostzuschlag	CHF	80.–

Single Issue/Einzelheft

Switzerland/Schweiz	CHF	30.–
Foreign Countries/Ausland	CHF	35.–

For members of the SCS subscription to CHIMIA is included in the membership fee.
Für Mitglieder der SCG ist das CHIMIA-Abonnement im Mitgliedsbeitrag inbegriffen.

Member and Subscriber Services
Adress- und Abonnement-Verwaltung
Swiss Chemical Society
Schweizerische Chemische Gesellschaft
Bärenplatz 2, CH–3011 Bern
Tel.: +41 31 310 40 90, Fax: +41 31 312 16 78
E-Mail: info@swiss-chem-soc.ch
www.swiss-chem-soc.ch

Head Office of the Swiss Chemical Society
Geschäftsstelle der Schweizerischen Chemischen Gesellschaft
Dr. M. Straub
Bärenplatz 2, CH–3011 Bern
Tel.: +41 31 310 40 90, Fax: +41 31 312 16 78
E-Mail: info@swiss-chem-soc.ch
www.swiss-chem-soc.ch

Technical Editor/Technische Redaktion
Dr. Gillian Harvey
Postfach
CH–8028 Zürich
Tel.: +41 1 262 65 46, Fax: +41 1 262 65 46
E-Mail: chimia.tr@bluewin.ch

Design and Production
Gestaltung und Herstellung
Werner Druck AG
Kanonengasse 32
Postfach, CH–4001 Basel
Tel.: +41 61 270 15 15, Fax: +41 61 270 15 16
ISDN: +41 61 283 08 51
E-Mail: werner@wernerdruck.ch
www.wernerdruck.ch

Advertisements and CHIMIA-Report
Anzeigenregie und CHIMIA-Report
Kretz AG, General Wille-Strasse 147, Postfach
CH–8706 Feldmeilen
Tel.: +41 1 925 50 60, Fax: +41 1 925 50 77
E-Mail: chimia.annoncen@kretzag.ch
www.kretzag.ch

Printing and Mailing/Druck und Versand
Birkhäuser+GBC AG, Römerstrasse 54
CH–4153 Reinach

CONTENTS
INHALT
SOMMAIRE

SCS Fall Meeting 2003
SCG Herbstversammlung 2003
SSC Assemblée d'automne 2003

CHIMIA 2003, 57, No. 7/8

EDITORIAL

Invitation to Attend the Fall Meeting of the Swiss Chemical Society in Lausanne, on Thursday, October 9th, 2003

On behalf of the Swiss Chemical Society (SCS) and the local Organizing Committee, it is our pleasure to invite you to attend the 2003 Fall Meeting of the SCS. Following the tradition of alternating universities to host this event, it is now Lausanne's turn, and we will do our best at the EPFL to offer you an interesting meeting.

The Fall Meeting of the SCS is the largest annual event in Switzerland where graduate chemistry students, post-docs, and chemists of all levels have the opportunity to present results they have achieved in their research projects. It provides the opportunity for all generations of scientists to exchange ideas, often generating the seeds for new projects and collaborations. As in past meetings, there will be a jury to select the best poster presentations and oral contributions in each session, for which prizes will be awarded.

The following pages of CHIMIA display 345 abstracts of scientific contributions that will be presented at the meeting. These abstracts demonstrate the diversity and outstanding creativity of chemists in Switzerland, both in academic institutions as well as in industry. Much of this research is at the exciting frontiers between chemistry and several other disciplines such as physics, materials science, biology and the life sciences and demonstrates the multifaceted aspects of chemistry.

For the second time, the 'Swiss Young Chemists' Committee' (JCFch) is taking part in the meeting with an initiative to provide information about job perspectives through contacts and workshops with people already working in the industry.

We hope that this exciting program interests you, and we encourage you to come to Lausanne and participate – it is this very thing that will make the 2003 Fall Meeting of the Swiss Chemical Society a grand success. We look forward to seeing you there.

Prof. Martin Quack
Chairman
Division Chemical Research

Prof. Tom Rizzo
Chairman
Local Organizing Committee

CHIMIA **2003**, *57*, No. 7/8

Chimia 57 (2003) 368–470

ISSN 0009–4293

SCHWEIZERISCHE CHEMISCHE GESELLSCHAFT

SOCIETE SUISSE DE CHIMIE

SWISS CHEMICAL SOCIETY

DIVISIONS	DIVISIONEN	DIVISIONS
ANALYTICAL CHEMISTRY	ANALYTISCHE CHEMIE	CHIMIE ANALYTIQUE
CHEMICAL RESEARCH	CHEMISCHE FORSCHUNG	RECHERCHE CHIMIQUE
MEDICINAL CHEMISTRY	MEDIZINISCHE CHEMIE	CHIMIE THERAPEUTIQUE

Fall Meeting 2003
Herbstversammlung 2003
Assemblée d'automne 2003

Thursday, October 9th, 2003
Donnerstag, 9. Oktober 2003
Jeudi, 9 Octobre 2003

Lausanne

Ecole Polytechnique Fédérale
Centre Est-1st Floor

CHIMIA 2003, 57, No. 7/8

Organizing Committee

Prof. T. Rizzo (Chairman) – EPF Lausanne
Dr. W. Froestl – Novartis Pharma AG, Basel
Dr. J.-L. Marendaz – EPF Lausanne
Prof. P.S. Pregosin – ETH Zürich
Prof. K. Severin – EPF Lausanne
Prof. J.-L. Veuthey – University of Geneva
Prof. C.A. Daul – University of Fribourg
Prof. K. Johnsson – EPF Lausanne
M.F. Menges – Young Chemists' Committee
Prof. M. Quack – ETH Zürich
Dr. D. Stahl – EPF Lausanne (Co-Chairman)
Dr. R. Wenger – Wenger Chemtech, Riehen

Secretary

Christina Zamanos Epremian, École Polytechnique Fédérale de Lausanne, Institut de chimie moléculaire et biologique, Secrétariat, EPFL - BCH 3305, CH–1015 Lausanne
Tel: +41 21 693 93 15, Fax: +41 21 693 93 05, E-Mail: christina.zamanosepremian@epfl.ch

Information

No registration for SCS members is required for participation in the meeting, coffee breaks, and lunch, all of which are free of charge. Please don't forget to carry your membership card, which will be required at the entrance to the meeting.

Non-members of the SCS will be asked to pay a SFr. 50.– entrance fee, which will allow access to the conferences, poster sessions, lunch, and coffee breaks.

Students who are members of the SCS can request reimbursement of their travel expenses on the basis of the train ticket to Lausanne and return (2nd class, 1/2 fare) by sending to the SCS central office a filled-in reimbursement form available at the registration desk of the meeting along with their train ticket. For members coming from abroad travel expenses within Switzerland are reimbursed (2nd class, 1/2 fare).

Lunch: Sandwiches, drinks, and coffee will be offered by the SCS in the vicinity of the poster session. A cafeteria and a restaurant are located in the vicinity of the conference rooms.

Coffee Breaks: Coffee and drinks will be available until 10.00 and a coffee break is organized from 16.30 to 17.00 before the award presentations.

Transportation

By train: When traveling from Basel (BS), Bern (BE), Fribourg (FR), and Zürich (ZH) do not leave the train in Lausanne (for the train times listed below), but continue until Renens (next stop after Lausanne). From Geneva (GE) leave the train in Renens (one stop before Lausanne). From the Renens train station, take the tram (TSOL) to the EPFL campus (Tram stop UNIL/Sorge, one stop after EPFL main stop). Unfortunately this does not apply for people coming from Neuchâtel (NE). They should stop in Lausanne, then take the underground from Lausanne train station to Place du Flon and then the tram (TSOL) to UNIL-Sorge. See the enclosed map that shows the path from the tram stop (UNIL-Sorge) to the entrance of the Bâtiment des Services (BS).

Train Timetable

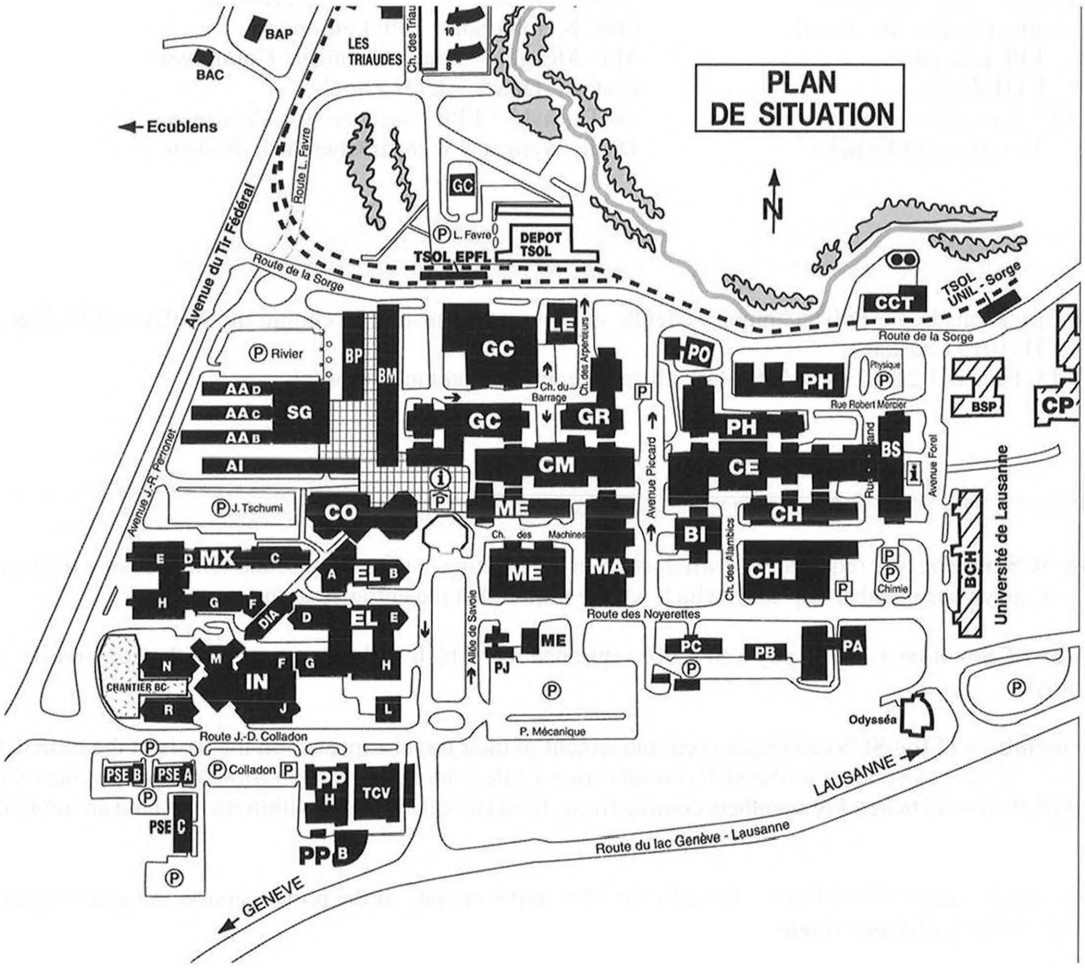
Train from	Departure	Arrival Renens/**Lausanne**	Departure Renens/**Lausanne**	Arrival	Train to
BS	7.02	9.45	17.48*/**18.27**	20.35	BS
BE	8.22	9.45	17.48*/**18.06**	19.13	BE
FR	8.43	9.45	17.48*/**18.06**	18.50	FR
GE	8.34	9.13	17.46	18.26	GE
NE	7.52	**8.33**	17.48*/**18.08**	19.02	NE
ZH	7.07	9.45	17.48*/**18.06**	20.26	ZH

* change train in Lausanne

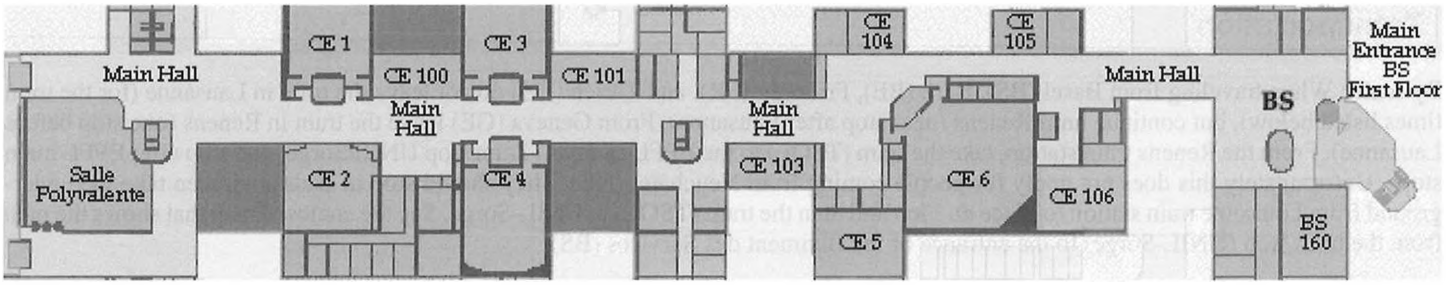
By car: Follow Lausanne-Sud, exit UNIL-EPFL, then turn to the right at the signpost EPFL/UNIL. Limited parking facilities will be available at the 'Parking Mécanique' (see map). People who would like to have a daily parking ticket (SFr. 5.–) are kindly invited to make a request in advance to Mme Christina Zamanos Epremian (address:*vide supra)*. It will be sent in due course and should be paid by the applicant at the registration desk of the meeting.

CHIMIA 2003, 57, No. 7/8

The EPFL Campus



The meeting will be held on the first floor of the Bâtiment des Services (BS) and of the Centre Est (CE). You are kindly requested to enter exclusively via the main entrance of the BS (first floor). The nearest tram stop is TSOL UNIL-Sorge (upper right corner on the map)



CE1 and CE3: Organic Chemistry
CE2: Computational Chemistry
CE4: Analytical Chemistry
CE5: Physical Chemistry
CE6: Opening Ceremony, Inorganic and Coordination Chemistry
CE106 and BS160: Medicinal Chemistry
Salle Polyvalente: *Contact**chemists.ch***
Main Hall and rooms CE100, CE101, CE103: Poster Sessions

Program of the Fall Meeting 2003

10.00–10.50 **Opening Ceremony**
EPFL-Centre Est, 1st Floor: Auditorium CE 6

Presentation of the Werner Prize Laureates for 2003
Prof. ***André Merbach***

Lectures of the Werner Prize Laureates 2003

Prof. ***Kay Severin***
Laboratoire de Chimie Supramoléculaire, ICMB, EPFL, Lausanne
'Synthesis of Catalysts and Receptors by Self-Assembly and Combinatorial Chemistry'
Abstract 1

Prof. ***Thomas C. Brunold***
Department of Chemistry, University of Wisconsin, Madison, USA
'Spectroscopic and Computational Insights into Coenzyme B_{12} Function'
Abstract 2

11.00–16.20 Analytical Chemistry

11.00–11.30 **General Assembly of the Members**
EPFL-Centre Est, 1st Floor: Auditorium CE 4

11.30–13.10 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 4
Abstracts 3–7

13.10–14.30 **Lunch and Poster Session**
Main Hall of EPFL-Centre Est and Room CE 101
Abstracts 14–57

14.30–16.20 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 4
Abstracts 8–13

11.00–16.20 Medicinal Chemistry

11.00–11.20 **General Assembly of the Members**
EPFL-Centre Est, 1st Floor: Auditorium CE 106

Session One
11.20–12.40 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 106
Abstracts 58–61

Session Two
11.20–12.40 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium BS 160
Abstracts 69–72

13.00–14.30 **Lunch and Poster Session**
Main Hall of EPFL-Centre Est
Abstracts 80–88

Session One
14.30–16.20 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 106
Abstracts 62–68

Session Two
14.30–16.20 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium BS 160
Abstracts 73–79

11.00–16.30 Chemical Research

11.00–11.15 **General Assembly of the Members**
EPFL-Centre Est, 1st Floor: Auditorium CE 6

11.15–16.30 Inorganic and Coordination Chemistry

11.15–13.15 **Minisymposium**
EPFL-Centre Est, 1st Floor: Auditorium CE 6
Abstracts 89–91

13.15–15.30 **Lunch and Poster Session**
Main Hall of EPFL-Centre Est and Room CE 103
Abstracts 92, 99–177

15.30–16.40 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 6
Abstracts 92–98

11.00–16.30 Organic Chemistry

Session One
11.15–12.45 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 1
Abstracts 178–183

12.45–13.00 **Short Poster Presentations**
Abstracts 206–212

Session Two
11.15–12.45 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 3
Abstracts 192–197

12.45–13.00 **Short Poster Presentations**
Abstracts 213–219

13.00–14.00 **Lunch and Poster Session**
Main Hall of EPFL-Centre Est and Room CE 100
Abstracts 206–271

Session One
14.30–16.30 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 1
Abstracts 184–191

Session Two
14.30–16.30 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 3
Abstracts 198–205

11.10–16.30 Physical Chemistry

11.10–12.45 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 5
Abstracts 272–277

12.45-13.00 **Short Poster Presentations**
Abstracts 286–290

13.00–14.30 **Lunch and Poster Session**
Main Hall of EPFL-Centre Est
Abstracts 286–321

14.30–16.30 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 5
Abstracts 278–285

11.15–15.45 Computational Chemistry

11.15–12.30 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 2
Abstracts 322–326

12.40–12.45 **Short Poster Presentation**
EPFL-Centre Est, 1st Floor: Auditorium CE 2
Abstract 332

13.00–14.30 **Lunch and Poster Session**
Main Hall of EPFL-Centre Est
Abstracts: 332–345

14.30–15.45 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 2
Abstracts 327–331

10.00–16.00 *contact**chemists**.ch*

The Swiss Young Chemists' Committee's Careers Fair
EPFL-Centre Est, Salle Polyvalente

11.15–11.20 **Welcoming Remarks for** *contact**chemists**.ch*
EPFL-Centre Est, Salle Polyvalente

11.20–16.00 **Company Presentations**
EPFL-Centre Est, Salle Polyvalente

16.30–17.00 Coffee Break

17.00–17.15 Awards for the Best Oral and Poster Presentations
EPFL-Centre Est: Auditorium CE 6

Analytical Chemistry:
2 poster and 1 oral presentations
Jury: *W. Giger, J.-L. Veuthey*

Medicinal Chemistry:
1 poster and 2 oral presentations
Jury: *K.-H. Altmann, P. Floersheim, W. Froestl, H.P. Märki*

Inorganic and Coordination Chemistry:
3 poster and 1 oral presentations
Jury: *P. Dyson, P.S. Pregosin, K. Severin*

Organic Chemistry:
2 poster and 2 oral presentations
Jury: *S. Matile, J.-L. Reymond, S. Pitsch, K. Johnsson, S. Gerber-Lemaire*

Physical Chemistry:
2 poster and 1 oral presentations
Jury: *M. Chergui, M. Quack, T. Rizzo*

Computational Chemistry:
1 poster and 1 oral presentations
Jury: *C.A. Daul, U. Röthlisberger*

DETAILED PROGRAM

Analytical Chemistry

11.00–11.30 General Assembly of the Members
EPFL-Centre Est, 1st Floor: Auditorium CE4

11.30–13.05 Lectures
EPFL-Centre Est, 1st Floor: Auditorium CE4
Abstracts 3–7
Chairperson: *W. Giger*

11.30–12.05 Plenary Lecture
M.-C. Hennion, *V. Pichon, F. Chapuis, P. Andrieux*
Department Environment and Analytical Chemistry, Ecole Supérieure de Physique et de Chimie de Paris, 10 Rue Vauquelin, 75005 Paris, France
'A New Generation of Selective Solid-phase Extraction Sorbents'
Abstract 3

12.05–12.20 ***Y. Ilias,*** *P. Mathieu, S. Rudaz, P. Christen, J.-L. Veuthey*
University of Geneva, School of Pharmacy, Laboratory of Pharmaceutical Analytical Chemistry, 20 Boulevard d'Yvoy, CH-1211 Geneva 4
'Analysis of Cannabis Material by Headspace Solid-Phase Microextraction Combined with Gas Chromatography-Mass Spectrometry'
Abstract 4

12.20–12.35 ***M. Tzouros,*** *S. Bienz, L. Bigler*
University of Zürich, Winterthurerstrasse 190, CH-8057 Zürich
'Tandem-Mass Spectrometry as a Key Tool for the Structure Elucidation of Spermidine Alkaloids'
Abstract 5

12.35–12.50 ***B. Hattendorf,*** *D. Günther*
ETH Zürich, Laboratory of Inorganic Chemistry, CH-8093 Zürich
'Suppression of Cell-generated Polyatomic Ions in Reaction Cell ICP-MS'
Abstract 6

12.50–13.05 ***K. Wojciechowski,*** *P. Salaun, J. Buffle*
Analytical and Biophysical Environmental Chemistry (CABE), Chimie Analytique minérale et Appliquée, Sciences II, 30 Quai E. Ansermet, CH-1211 Genève 4
'Metal Ion Speciation with PLM'
Abstract 7

13.05–13.10 **Short Poster Presentations**
R. Althaus, N. Parthasarathy
Abstracts 14–15

13.10–14.30 **Lunch and Poster Session**
Main Hall of EPFL- Centre Est and Room CE 101
Abstracts 14–57

14.30–16.20 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE4
Abstracts 8–13
Chairperson: *J.-L. Veuthey*

14.30–15.05 **Keynote lecture**
M.J.-F. Suter, *A.C. Alder, W. Giger, E.M. Golet, C.S. McArdell, E. Molnar, V.J. Nesatyy, R. Schönenberger*
'Modern Analytical Tools for Environmental Risk Assessment'
Abstract 8

15.05–15.20 ***L. Emmenegger***[a], *J. Poulleau*[b]
[a]EMPA, Ueberlandstrasse 129, CH-8600 Dübendorf
[b]INERIS, BP 2, F-60550 Verneuil en Halatte, France
'Uncertainty of NO_x and SO_2 Emission Measurements'
Abstract 9

15.20–15.35 ***D. Ferri***[a], *H.-J. Brunnert*[b], *M. Luft*[b], *M. Boese*[b]
[a]Bruker Optics GmbH, Industriestrasse 26, CH-8117 Fällanden
[b]Bruker Optik GmbH, Rudolf-Planck-Strasse 27, D-76275 Ettlingen, Germany
'Temperature Induced Conformational Changes in Proteins Monitored by FT-IR Spectroscopy'
Abstract 10

15.35–15.50 ***C. Roussel,*** *L. Dayon, T.C. Rohner, H. Jensen, H.H. Girault*
Laboratoire d'Electrochimie Physique et Analytique, EPFL, CH-1015 Lausanne
'On-line Electrochemical Tagging of Free Cysteine by Electrogenerated Benzoquinones during Nanospray Ionisation for Mass Spectrometry in Protein Analysis'
Abstract 11

15.50–16.05 ***R. Houriet,*** *A. Ferrari, E. Gallucci, O. Zinger*
Institut des matériaux, EPFL, CH-1015 Lausanne
'Chemical Mapping of Microstructured Samples by Microanalysis and Infra-Red Imaging Techniques'
Abstract 12

16.05–16.20 ***G.K. Belin***[a,b], *O.F. Gülaçar*[a]
[a]University of Geneva, CH-1211 Geneva
[b]Technical University of Istanbul, 34469 Istanbul, Turkey
'Separation of Chlorins and Carotenoids in Capillary Electrokinetic Chromatography'
Abstract 13

16.30–17.00 Coffee Break

17.00-17.15 Awards for the best oral and poster presentations

Medicinal Chemistry

11.00–11.20 **General Assembly of the Members**
EPFL-Centre Est, 1st Floor: Auditorium CE 106
Report of the President and the Treasurer on the year 2002

Session One
11.20–12.40 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 106
Abstracts 58–61
Chairperson: *W. Froestl*

11.20–11.40 *M. Nettekoven,* ***A. Alanine***
F. Hoffmann-La Roche, Basel
'Enhancing the Hit to Lead Generation Process: A Case Study with Aryl-[1,2,4]-Triazolo-[1,5a]-Pyridine Derivatives as Adenosine-2a Receptor Antagonists'
Abstract 58

11.40–12.00 ***R.D. Norcross,*** *A. Alanine, G.J. Kilpatrick, J.-L. Moreau, S.M. Poli*
F. Hoffmann-La Roche AG, Basel
'Development of 2-Amino-Pyrimidines as Selective Adenosine hA2a Receptor Antagonists'
Abstract 59

12.00–12.20 ***P. Furet***
Novartis Pharma AG/ Oncology Research, Basel
'Structure-Based Approaches to the Discovery of Protein Kinase Inhibitors'
Abstract 60

12.20–12.40 ***P.W. Manley,*** *G. Bold, J. Brüggen, G. Fendrich, P. Furet, J. Mestan, T. Meyer, B. Meyhack, C. Schnell, W. Stark, A. Strauss, J. Wood*
Novartis Institutes of Biomedical Research, Basel
'2-[(4-Pyridinylmethyl)amino]-N-[3-(trifluor-omethyl)phenyl]benzamide: A Novel, Antiangiogenic VEGF Receptor Kinase Inhibitor'
Abstract 61

12.45–13.00 **Short Poster Presentations**
EPFL-Centre Est, 1st Floor: Auditorium CE 106
G. Francese, S. Marti, S.V. Shelke, O. Turpin
Abstracts 80–83

13.00–14.30 **Lunch and Poster Session**
Main Hall of EPFL-Centre Est
Abstracts 80–88

14.00–16.20 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 106
Abstracts 62–68
Chairperson: *H.P. Märki*

14.00–14.20 ***D. Barron*,*** *C. Terreaux, K. Hostettmann*
School of Pharmacy, University of Lausanne
*Present address:
Nestlé Research Center, Lausanne
'Synthesis of Isoprenoid Flavonoids, Potential Phytoestrogens and Modulators of the Activity of ATP-Transporters'
Abstract 62

14.20–14.40 ***A. Freund-Renard[a],*** *F. Boato[a], U. Kienzl[a], K. Moehle[a], M. Mueller[b], E. Peduzzi[b], R. Zurbriggen[c], G. Pluschke[b], J.A. Robinson[a]*
[a]Institute of Organic Chemistry, University of Zurich
[b]Tropical Institute, Basel
and [c]Pevion-Biotech, Bern
'A Virosome-Peptide Mimetic Approach to Synthetic Vaccine Design: Synthesis, Conformation and Recognition of Malaria Epitope Mimetic'
Abstract 63

14.40–15.00 ***D. Orain,*** *G. Koch, R. Giger*
Novartis Institutes of Biomedical Research, Combinatorial Chemistry Unit, Basel
'New Heterocyclic Scaffolds for Combinatorial Chemistry'
Abstract 64

15.00–15.20 ***K. Malagu,*** *J. Hinrichs, J. Zimmermann*
Novartis Institutes of Biomedical Research, Combinatorial Chemistry Unit, Basel
'Macrocycles Containing ß-Amino Acids and a Biaryl Moiety'
Abstract 65

15.20–15.40 ***G. Gao,*** *O. Schwardt, S. Shelke, T. Visekruna, B. Ernst*
Institute of Molecular Pharmacy, Pharmacenter of the University of Basel
'Chemical and Chemo-enzymatic Synthesis of Antagonists of Myelin Associated Glycoprotein for Conformational and SAR Studies'
Abstract 66

15.40–16.00 ***F. Popowycz,*** *S. Gerber-Lemaire, E. Rodriguez-Garcia, C. Schutz, P. Vogel*
Laboratory of Glycochemistry and Asymmetric Synthesis, EPF Lausanne
'Design of Selective and Competitive α-Mannosidases Inhibitors'
Abstract 67

16.00–16.20 ***R. Fasan,*** *R.L.A. Dias, K. Moehle, J.A. Robinson*
Institute of Organic Chemistry, University of Zürich
'Towards the Development of Potent Mdm2 Inhibitors'
Abstract 68

16.30–17.00 Coffee Break

17.00–17.15 Awards for the best oral and poster presentations

Session Two
11.20–12.40 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium BS 160
Abstracts 69–72
Chairperson: *P. Floersheim*

11.20–11.40 *L. Alig, D. Banner, K. Groebke Zbinden, K. Hilpert, H. Kühne,* ***U. Obst Sander,*** *M. Stahl, H.-P. Wessel*
F. Hoffmann-La Roche, Basel
'Factor VIIa Inhibitors as Novel Anticoagulants'
Abstract 69

11.40–12.00 *S. Kritter, S. Weber, P. Weiss, M. Boehringer, M. Hennig,* ***J.-U. Peters***
F. Hoffmann-La Roche, Basel
'Aminomethylpyrimidines as Novel DPP-IV Inhibitors'
Abstract 70

12.00–12.20 ***T. Ritchie,*** *E. Dziadulewicz, A. Culshaw, W. Müller, C. Snell, G. Burgess, M. Brown, P. Ganju, M. Webb*
Novartis Institute for Medical Sciences, London, UK
'Potent, Selective and Orally Active Non-peptide Bradykinin B1 Receptor Antagonists to Treat Chronic Inflammatory Pain'
Abstract 71

12.20–12.40 ***I. Lewis,*** *W. Bauer, R. Albert, N. Chandramouli, J. Pless, G. Weckbecker, C. Bruns*

Novartis Pharma
Transplantation Research, Basel
'The Superior Therapeutic Potential of SOM230 Originates from Unique Structural Elements'
Abstract 72

12.45–13.00 **Short Poster Presentations**
EPFL-Centre Est, 1st Floor: Auditorium CE 106
G. Francese, S. Marti, S. Shelke, O. Turpin
Abstracts 80–83

13.00–14.30 **Lunch and Poster Session**
Main Hall of EPFL-Centre Est
Abstracts 80–88

14.00–16.20 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium BS 160
Abstracts 73–79
Chairperson: *K.-H. Altmann*

14.00–14.20 ***R. Waelchli**, B. Bollbuck, T. Buhl, C. Bruns, J. Eder, R. Feifel, R. Hersperger, P. Janser, L. Revesz, H.-G. Zerwes, A. Schlapbach*
Novartis Institute for Biomedical Research, Basel
'Design and Preparation of 2-Benzamido-pyrimidines as IKK Inhibitors'
Abstract 73

14.20–14.40 *D. Adams[b], J.M. Bentley[b], M.J. Bickerdike[b], I.A. Cliffe[b], C.T. Dourish[b], C.S. Malcolm[b], J. Davidson[b], G. Kennett[b], A.R. Knight[b], A. Misra[b], A. Bénardeau[a], A. Bourson[a], P. Coassolo[a], P. Hebeisen[a], P. Mattei[a], J. Mizrahi[a], M. Muller[a], P. Pflieger[a], R.H.P. Porter[a], S. Roever[a], S. Taylor, P.Verry[a], **H. Richter**[a]*
[a]F. Hoffmann- La Roche, Basel
[b]Vernalis Research Ltd, Wokingham, UK
'Highly Potent and Selective 5-HT_{2C} Receptor Agonists Based on the Pyrazino[1,2-a]indole Scaffold'
Abstract 74

14.40–15.00 *M. Lerch, B. Christen, **O. Zerbe***
Institute of Organic Chemistry, University of Zürich
'Are Peptides from the NPY Family of Neurohormones Recognized From Their Membrane-bound State?'
Abstract 75

15.00–15.20 *V. Zoete[a,b], M. Meuwly[a], **M. Karplus**[b]*
[a]Chemistry Department, University of Basel
[b]Université Louis Pasteur, Strasbourg, France
'Investigation of Glucose Binding Sites on Insulin'
Abstract 76

15.20–15.40 ***B. Cutting**[a], A. Strauss[a], G. Fendrich[a], P.W. Manley[b], W. Jahnke[a]*
[a]Novartis Pharma AG and
[b]Novartis Pharma AG – Oncology Research, Basel
'Biomolecular NMR Tools to Accelerate Investigations of Protein-Ligand Complexes'
Abstract 77

15.40–16.00 ***D. Kaufmann**, P. Fünfschilling, U. Beutler, W. Zaugg, O. Lohse*
Novartis Pharma AG, Chemical and Analytical Development, Basel
'New Synthetic Routes for Oxcarbazepine'
Abstract 78

16.00–16.20 *U. Pivk, P. Kastenmeyer, N. Godinot, A. Rytz, C. Yeretzian, **K. Bortlik***
Nestlé Research Center, Lausanne
'Impact of Saliva Composition on Umami Taste Perception'
Abstract 79

16.30–17.00 **Coffee Break**

17.00–17.15 **Awards for the best oral and poster presentations**

Chemical Research

11.00–11.15 **General Assembly of the Members**
EPFL-Centre Est, 1st Floor: Auditorium CE 6

Inorganic and Coordination Chemistry

11.15–13.15 **Minisymposium**
EPFL-Centre Est, 1st Floor: Auditorium CE 6
Chairperson: *P.S. Pregosin*

11.15–11.55 **Prof. *Y. Bertini***
Magnetic Resonance Center CERM, University of Florence, Italy
'Perspectives in Inorganic Structural Genomics'
Abstract 89

11.55–12.35 **Prof. *R. van Eldik***
Institute for Inorganic Chemistry, University of Erlangen, Nürnberg, Egerlandstrasse 1, 91058 Erlangen, Germany
'To Be or not to Be NO? A Mechanistic Approach'
Abstract 90

12.35–13.15 **Prof. *M.J. Rosseinsky***
Department of Chemistry, The University of Liverpool, Liverpool, UK L697ZD
'New Chemistry of Oxides and Microporous Materials'
Abstract 91

13.00–15.45 **Lunch and Poster Session**
Main Hall of EPFL-Centre Est and Room CE 103

Abstracts 92, 99–177
Chairpersons: *J.-C. Bünzli, C. Piguet, T. Ward*
A: Catalysis Abstracts: 99–116
B: Solid State Abstracts: 117–126
C: Bioinorganic Abstracts: 127–146
D: Fundamental aspects Abstracts: 92, 147–177

15.30–16.40 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 6
Abstracts 92–98
Chairperson: *P. Dyson*

15.30–15.40 ***R. Frantz,*** S. Constant, G. Berrardinelli, J. Lacour
Département de Chimie Organique, Université de Genève, CH-1211 Genève 4
'Fluorinated "TRISPHAT" Anions. Chiral NMR Probes for Detailed Asymmetric Ion Pairing Studies'
Abstract 92

15.40–15.50 ***P. Kurz,*** *B. Spingler, R. Alberto*
Institute of Inorganic Chemistry, University of Zürich, Winterthurerstr. 190, CH-8057 Zürich
'Cyano-Carbonyl Complexes of Technetium(I) and Rhenium(I)'
Abstract 93

15.50–16.00 ***A. Cecchetto,*** *G.D. Pirngruber, R. Prins*
Institute for Chemical and Bioengineering, ETH Zürich, CH-8093 Zürich
'Synthesis and Characterization of New Bidentate Pd(II) Complex Anchored by Covalent Bond into MCM41'
Abstract 94

16.00–16.10 ***F. Zobi,*** *B. Spingler, P. Kurz, R. Alberto*
Institute of Inorganic Chemistry, University of Zürich, Winterthurerstr. 190, CH-8057 Zürich
'Head-to-Head (HH) and Head-to-Tail (HT) Conformers of cis-bis Purine Ligands Bound to the $[Re(CO)_3]^+$ Core'
Abstract 95

16.10–16.20 ***R.K.O. Sigel***[a], *A.G. Palmer*[b], *A.M. Pyle*[c]
[a]Institute of Inorganic Chemistry, University of Zürich, Winterthurerstrasse 190, 8057 Zürich
[b]Department of Biochemistry, Columbia University, New York, USA
[c]Department of Molecular Biophysics & Biochemistry, Yale University, New Haven, USA
'Metal Ion Binding to the Catalytic Center of a Group II Intron Ribozyme'
Abstract 96

16.20–16.30 ***B. Knobloch***[a], *W. Linert*[b], *H. Sigel*[a]
[a]Department of Chemistry, University, Spitalstrasse 51, CH-4056 Basel
[b]Institute of Applied Synthetic Chemistry, Technical University, A-1060 Vienna, Austria
'Metal Ion Complex Stabilities in Aqueous Solution of N3-deprotonated Uridine and of Related Nucleosides'
Abstract 97

16.30–16.40 ***E. Martínez Viviente,*** *P.S. Pregosin*
Laboratory of Inorganic Chemistry, ETH, HCI, Hönggerberg, CH-8093 Zürich
'PGSE Diffusion Studies on Organometallic and Organic Compounds'
Abstract 98

16.30–17.00 Coffee Break

17.00–17.15 Awards for the best oral and poster presentations

Organic Chemistry

Session One
11.15–12.45 **Lectures**
EPFL-Centre Est, 1st Floor:
Auditorium CE 1
Abstracts 178–183
Chairperson: *S. Matile*

11.15–11.30 ***S. Gerber-Lemaire,*** *P. Vogel*
Laboratory of Glycochemistry and Asymmetric Synthesis, EPF Lausanne
'An Expeditive Asymmetric and Non-Iterative Synthesis of Long-Chain Polyols'
Abstract 178

11.30–11.45 ***T. Schultz,*** *A. Pfaltz*
Department of Chemistry, University of Basel
'Heck Reactions with Homogeneous Palladium Catalysts: Synthesis of Novel Complexes and Mechanistic Investigations'
Abstract 179

11.45–12.00 ***L. Bouchez,*** *S.R. Dubbaka, M. Turks, P. Vogel*
Laboratory of Glycochemistry and Asymmetric Synthesis, EPF Lausanne
'Sulfur Dioxide Mediated One-Pot Synthesis of Polyfunctional Sulfones, Sulfonic Esters and Sulfonamides'
Abstract 180

12.00–12.15 ***T. Holzer,*** *H.C. Kolb, K.B. Sharpless*
The Scripps Research Institute, Department of Chemistry, California, USA
'Synthesis of a New Inhibitor Library for the Lethal Factor of the B. Anthracis Toxin'
Abstract 181

12.15–12.30 ***M. Turks,*** *P. Vogel*
Laboratory of Glycochemistry and Asymmetric Synthesis, EPF Lausanne
'Umpolung of 1,3-Dioxy-1,3-dienes by Sulfur Dioxide and its Application in Polypropionate Synthesis'
Abstract 182

12.30–12.45 *P. Müller, **Y. Allenbach, F. Lacrampe***
Department of Organic Chemistry, University of Geneva
'Enantioselective Metallocarbene Reactions of Silicon containing Diazo-compounds by Chiral Dirhodium(II) Catalysts'
Abstract 183

12.45–13.00 **Short Poster Presentations**
S. Sergeyev, A. Ghanem, P. Panchaud, R. Piccardi, X. Salom-Roig, P. Schär, C. Craita
Abstract 206–212

13.00–14.30 **Lunch and Poster Session**
Main Hall of EPFL-Centre Est and Room CE 100
Abstracts 206–272

14.30–16.30 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 1
Abstracts 184–191
Chairperson: *S. Gerber-Lemaire*

14.30–14.45 ***F. Menges,** A. Pfaltz*
Department of Chemistry, University of Basel
'Chiral P,N-Ligands for the Iridium Catalyzed Asymmetric Hydrogenation'
Abstract 184

14.45–15.00 ***M. Nold,** H. Wennemers*
Department of Chemistry, University of Basel, St. Johanns-Ring 19, CH-4056 Basel
'Sequence Dependent Peptide Cleavage under Fenton Conditions'
Abstract 185

15.00–15.15 *E.P. Kündig, **T. Lomberget,** C. Poulard, R. Bragg*
Department of Organic Chemistry, University of Geneva
'Desymmetrization of (Naphtho-quinone)$Cr(CO)_3$: A New Entry to Planar Chiral Complexes'
Abstract186

15.15–15.30 *G. Frater[a,b], A. Goeke[b], **M. Lovchik[a]***
[a]Institute of Organic Chemistry, University of Zurich
[b]Givaudan Schweiz AG - Duebendorf
'Studies on the Enantioselective Alkylation of Phenols'
Abstract 187

15.30–15.45 ***D. Markovic,** P. Vogel*
Laboratory of Glycochemistry and Asymmetric Synthesis, EPF Lausanne
'Mechanism of the Isomerisation of Alkenes Induced by Polysufones'
Abstract 188

15.45–16.00 ***M. Nagel[a],** T. Lippert[b]*
[a]Swiss Federal Laboratories for Materials Testing and Research (EMPA)
[b]Institute – Material Group, Villigen PSI
'Polymeric Materials Designed for Laser Ablation Lithography (LAL) Based on Photosensitive Triazene Containing Building Blocks'
Abstract 189

16.00–16.15 ***C. Corminboeuf[a],** T. Heine[b], J. Weber[a]*
[a]Department of Physical Chemistry, University of Geneva
[b]Institut für 'Physikalische Chemie, Technische Universität Dresden, Germany
'A New Analysis Tool for Stability and Aromaticity of Rings'
Abstract 190

16.15–16.30 ***G. Rüedi,** H.-J. Hansen*
Institute of Organic Chemistry, University of Zurich
'Designed Bond Fission in High Temperature Chemistry: Novel Ring Expansions, Ring Openings, and Ring Contractions'
Abstract 191

16.30–17.00 Coffee Break

17.00–17.15 Awards for the best oral and poster presentations

Session Two
11.15–12.45 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 3
Abstracts 192–197
Chairperson: *J.-L. Reymond*

11.15–11.30 ***N. Sordé,** S. Matile*
Institute of Organic Chemistry, University of Geneva
'Enzyme Screening with Synthetic Multifunctional Pore Sensors'
Abstract 192

11.30–11.45 ***S. Gendreizig,** K. Johnsson*
Laboratory of Protein Engineering, EPF Lausanne
'Induced Dimerization of Fusion Proteins in vivo by Covalent Labeling'
Abstract 193

11.45–12.00 ***L.C.J. Gillet,** O.D. Schaerer*
Institute for Molecular Cancer Research, Uni. Zurich
'Preparation of Oligomers Containing 8-(N-Acetyl-aminofluorene)-2'-deoxyguanosine Adducts Using a New 'Ultramild' DNA Synthesis'
Abstract 194

12.00–12.15 ***N. Amiot,** S. Saigne, B. Giese*
Department of Organic Chemistry, University of Basel
'A New Assay to Investigate Electron Transfer into DNA Based on the UV Properties of a New Non-natural Nucleoside'
Abstract 195

12.15–12.30 ***J.-P. Goddard,*** *J.-L. Reymond*
Departement für Chemie und Biochemie, Laboratorium für Kristallographie, Universität Bern
'HTS Profiling of Lipases and Esterases'
Abstract 196

12.20–12.45 ***P. Tafelmeyer,*** *K. Johnsson*
Laboratory of Protein Engineering, EPF Lausanne
'Development of a New Reporter System for Monitoring Protein-Protein Interactions in Living Cells'
Abstract 197

12.45–13.00 Short Poster Presentations
F. Perret, M. Peretolchin, P. Krattiger, A. Clouet, O. Renaudet, A. Zumbühl
Abstracts 213–218

13.00–14.30 Lunch and Poster Session
Main Hall of EPFL-Centre Est and Room CE 100
Abstracts 206–271

14.30–16.30 Lectures
EPFL-Centre Est, 1st Floor: Auditorium CE 3
Abstracts 198–205
Chairperson: *S. Pitsch*

14.30–14.45 ***G. Mathis,*** *R. Schütz, J. Hunziker*
Departement für Chemie und Biochemie, Laboratorium für Kristallographie, Universität Bern
'Towards a DNA-Like Duplex Without Hydrogen Bonds'
Abstract 198

14.45–15.00 ***M. Kindermann,*** *N. George, N. Johnsson, K. Johnsson*
Laboratory of Protein Engineering, Lausanne
'Covalent and Selective Immobilization of Fusion Proteins'
Abstract 199

15.00–15.15 ***D. Lagnoux,*** *J.-L. Reymond*
Departement für Chemie und Biochemie, Laboratorium für Kristallographie, Universität Bern
'Synthesis of Colchicine Dendrimer Derivatives'
Abstract 200

15.15–15.30 ***K. Gademann,*** *Y. Bethuel*
Laboratorium für Organische Chemie, ETH Zürich
'The Cyanobaterial Siderophore Anachelin – Synthetic, Structural and Mechanistic Studies'
Abstract 201

15.30–15.45 ***M.J. Stöckli,*** *P. Rüedi*
Organisch-chemisches Institut der Universität Zürich
'Optically Active Deuterated Dioxaphosphadecalins as Inhibitors of ∂-Chymotrypsin: ^{31}P-NMR Evidence of Covalent Bond Formation'
Abstract 202

15.45–16.00 *D. Banfi,* ***L. Patiny***
Laboratory of Biomimetic and Peptide Chemistry, EPFL Lausanne
'Storing and Retrieving In-House Chemical Information from a Web Browser'
Abstract 203

16.00–16.15 ***D. Jeannerat***
Department of Organic Chemistry, University of Geneva
'High resolution in Heteronuclear NMR experiments'
Abstract 204

16.15–16.30 ***F. Heirtzler***[a], *S.I.G. Dias*[a], *I. Prokes*[b], *P. Cragg*[c]
[a]Chemical Laboratory, University of Kent, UK
[b]Department of Chemistry, University of Exeter, UK
[c]School of Pharmacy and Biomolecular Sciences, University of Brighton, UK
'Towards Double-Decker, Metallo-organic Supramolecular Mesogens'
Abstract 205

16.30–17.00 Coffee Break

17.00–17.15 Awards for the best oral and poster presentations

Physical Chemistry

11.15–12.45 Lectures
EPFL-Centre Est, 1st Floor: Auditorium CE 5
Abstracts 272–277
Chairperson: *T. Rizzo*

11.15–11.30 ***D. Brühwiler,*** *H. Frei*
Physical Biosciences Division, Lawrence Berkeley National Laboratory, University of California, Berkeley, CA 94720, USA
'Coordination Chemistry at the Silica Surface: Towards New Materials for Photochemical Applications'
Abstract 272

11.30–11.45 ***D. Tonti***[a], *J. Liu*[a], *C. Bonati*[a], *M. Mohammed*[a], *A. Chemseddine*[b], *M. Chergui*[a]
[a]Institut de Physique de la Matière Condensée, Université de Lausanne, CH-1015, Lausanne
[b]Department for Solar Energy Research, Hahn-Meitner-Institut Berlin, D-14109 Berlin, Germany
'On the Surface Properties of Chemically Prepared CdSe Nanocrystals'
Abstract 273

11.45–12.00 ***R.D. Beck,*** *T.T. Dang, P. Maroni, D. Papageorgopoulos, T.R. Rizzo*
Laboratoire de Chimie Physique Moléculaire, Ecole Polytechnqiue Fédérale de Lausanne, CH-1015 Lausanne
'Probing and Controlling Gas/Surface Chemistry by Pulsed Laser Radiation'
Abstract 274

12.00–12.15 ***A. Callegari,*** *D. Tonti, A. Al Salman, L. Bonacina, F. Chaussard, F. van Mourik, M. Chergui*
Institut de Physique de la Matière Condensée, Université de Lausanne, CH-1015, Lausanne
'Photochemical Growth and Vibrational Coherences of Silver Nanoplates'
Abstract 275

12.15–12.30 ***C. Tanner,*** *C. Manca, S. Leutwyler*
Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, CH-3012 Bern
'Excited-State Proton Transfer with an Energy Selective Threshold'
Abstract 276

12.30–12.45 ***S. Huber,*** *G. Calzaferri*
Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, CH-3012 Bern
'Energy Transfer from Photonic Zeolite Antenna Crystals to Bulk Silicon'
Abstract 277

12.45–13.00 **Short Poster Presentations**
C. Manca, S. Lammers, N. Fatin-Rouge, N. Fatin-Rouge, G. Pirngruber
Abstracts 286–290

13.00–14.30 **Lunch and Poster Session**
Main Hall of EPFL-Centre Est
Abstracts 286–321

14.30–16.30 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 5
Abstracts 278–285
Chairperson: *M. Chergui*

14.30–14.45 ***A. Devaux,*** *C. Minkowski, G. Calzaferri*
Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, 3012 Bern
'Electronic and Vibrational Spectra of Fluorenone in Zeolite L'
Abstract 278

14.45–15.00 ***A. Abraham[a],*** *J.A. van Bokhoven[a], S.B. Hong[b], R. Prins[a]*
[a]Institute for Chemical and Bioengineering, Swiss Federal Institute of Technology (ETHZ), CH-8093 Zürich
[b]Division of Chemical Engineering, Hanbat National University, Taejon 305-719, Korea
'Distribution of Aluminium in Zeolite Beta'
Abstract 279

15.00–15.15 ***A. Urakawa,*** *R. Wirz, T. Bürgi, A. Baiker*
Institute for Chemical and Bioengineering, Swiss Federal Institute of Technology (ETHZ), CH-8093 Zürich
'ATR-IR Modulation Excitation Spectroscopy: Application to Diffusion and Heterogeneous Catalysis'
Abstract 280

15.15–15.30 ***M. Luechinger,*** *G.D. Pirngruber, R. Prins*
Institute for Chemical and Bioengineering, Swiss Federal Institute of Technology (ETHZ), CH-8093 Zürich
'Swelling of Templating Micelles with Substituted Aromatic Compounds'
Abstract 281

15.30–15.45 ***S.M. Benito,*** *P. Broz, C. Saw, H. Heider, P. Hunziker, W. Meier*
Department of Chemistry, University of Basel, Klingelbergstrasse 80, CH-4056 Basel
'Selective Targeting of Cells with Functionalized ABA Triblock Copolymer Nanocontainers'
Abstract 282

15.45–16.00 ***O. Nicolet,*** *E. Vauthey*
Department of Physical Chemistry, University of Geneva, CH-1211 Geneva
'Heavy Atom Effect on the Charge Recombination Dynamics of Geminate Ion Pairs'
Abstract 283

16.00–16.15 ***T. Skalicky,*** *N. Zimmermann, M. Allan*
Department of Chemistry, University of Fribourg, CH-1700 Fribourg
'Properties of the π^* and σ^* States of the Pyrrole, Thiophene, and Phenol Anion Determined by Electron Impact Spectroscopy'
Abstract 284

16.15–16.30 ***T. Makarov,*** *H. Paul, E. Bagryanskaya*
Institute of Physical Chemistry, University of Zürich, CH-8057 Zürich
'Electron Spin Relaxation in Benzoyl and Acyl Type Radicals'
Abstract 285

16.30–17.00 Coffee Break

17.00–17.15 Awards for the best oral and poster presentations

Computational Chemistry

11.15–12.30 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 2
Abstracts 322–326
Chairperson: *U. Röthlisberger*

11.15–11.30 ***M. Meyer,*** *S. Glaus, G. Calzaferri*
University of Bern, Freiestrasse 3, 3012 Bern

'Basic Terms of Band Structures – Introduction by Means of an Interactive Mathcad Course'
Abstract 322

11.30–11.45 ***C. Rauzy,*** *M. Sahnoun, C.A. Daul*
Département de Chimie, CH-1700 Fribourg
'A DFT Study of Mixed Valent Hexacyano Mn(II/III) Cluster'
Abstract 323

11.45–12.00 ***M. Sulpizi***[a], *P.Carloni*[b], *U. Röthlisberger*[a]
[a]Lab. of Comp. Chem. and Biochemistry, Federal Institute of Technology (EPFL), CH-1015 Lausanne
[b]SISSA, International School for Advanced Studies, 34103 Trieste, Italy
'A Hybrid Time-Dependent Density Functional/ Molecular Mechanics Investigation of Aminocoumarins in Solution'
Abstract 324

12.00–12.15 ***B. Kirchner***
Institute of Physical Chemistry, University of Zürich, CH-8057 Zürich
'A C_{2v} Symmetrical Barbaralane'
Abstract 325

12.15–12.30 ***D. Bas***[a], *C. Herse*[b], *J. Lacour*[b], *P.-Y. Morgantini*[a], *J. Weber*[a], *T. Wesolowski*[a]
Department of Physical Chemistry[a] and Organic Chemistry[b], University of Geneva, 30 Quai Ernest Ansermet, CH-1211 Geneva 4
'Theoretical and Experimental Study of the Racemisation of a [4]Heterohelicenium Cation'
Abstract 326

12.40–12.45 **Short Poster Presentation**
EPFL-Centre Est, 1st Floor: Auditorium CE 2
M. Meuwly
Abstract 332

13.00–14.30 **Lunch and Poster Session**
Main Hall of EPFL-Centre Est
Abstracts: 332–345

14.30–15.45 **Lectures**
EPFL-Centre Est, 1st Floor: Auditorium CE 2
Abstracts 327–331
Chairperson: *C.A. Daul*

14.30–14.45 ***R. Nutt,*** *M. Meuwly*
University of Basel, Klingelbergstrasse 80, CH-4056 Basel
'Theoretical Investigation of Infrared Spectra and Pocket Dynamics of Photodissociated Carbonmonoxy Myoglobin'
Abstract 327

14.45–15.00 ***U.F. Roehrig,*** *U. Röthlisberger*
Lab. of Comp. Chem. and Biochemistry, Federal Institute of Technology (EPFL), CH-1015 Lausanne
'QM/MM Molecular Dynamics Study of the Absorption and the Fluorescence Spectra of Acetone in Water'
Abstract 328

15.00–15.15 ***I. Tavernelli,*** *U. Röthlisberger*
Lab. of Comp. Chem. and Biochemistry, Federal Institute of Technology (EPFL), CH-1015 Lausanne
'Models for Time Dependent Density Functional Theory in Chemistry and Biochemistry'
Abstract 329

15.15–15.30 ***L. Guidoni,*** *U. Röthlisberger*
Lab. of Comp. Chem. and Biochemistry, Federal Institute of Technology (EPFL), CH-1015 Lausanne
'Driving Chemical Reactions via Biases of Molecular Orbital'
Abstract 330

15.30–15.45 ***O.A. von Lilienfeld-Toal***[a], *L. Guidoni*[a], *P. Cummins*[b], *J.E. Gready*[b], *U. Röthlisberger*[a]
[a]Lab. of Comp. Chem. and Biochemistry, Federal Institute of Technology (EPFL), CH-1015 Lausanne
[b]Computational Proteomics and Therapy Design Group, John Curtin School of Medical Research, Australian national University, Canberra ACT 2601, Australia
'Ab initio QM/MM Calculations of Dihydrofolate Reductase'
Abstract 331

16.30–17.00 Coffee Break

17.00–17.15 Awards for the best oral and poster presentations

*contact***chemists.ch**

10.00–16.00 *contact**chemists.ch***
The Swiss Young Chemists' Committee's Careers Fair
EPFL-Centre Est, Salle Polyvalente

11.15–11.20 **Welcoming Remarks for** *contact**chemists.ch***
EPFL-Centre Est, Salle Polyvalente

11.20–16.00 **Company Presentations**
EPFL-Centre Est, Salle Polyvalente

11.20–12.05 **F. Hoffmann-La Roche**
12.15–13.00 **Ciba SC**
13.15–14.00 **Workshop: *'How to Apply' by Baer Management Consulting***
14.15–15.00 **Novartis**
15.15–16.00 **Ares Serono**

Awards for the Best Oral and Poster Presentations

17.00–17.15 *EPFL-Centre Est: Auditorium CE 6*
Chairperson: *T. Rizzo*

CHIMIA 2003, 57, No. 7/8

Inorganic and Coordination Chemistry **1**

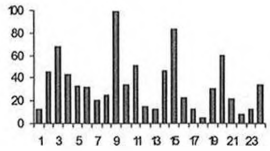
Synthesis of Catalysts and Receptors by Self-Assembly and Combinatorial Chemistry

Kay Severin

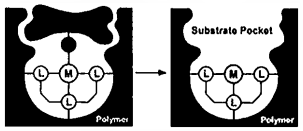
Institut de Chimie Moléculaire et Biologique
École Polytechnique Fédérale de Lausanne, 1015 Lausanne, Suisse

New strategies for the development of catalysts and receptors will be discussed. In particular, the following topics will be addressed:

1) Combinatorial catalysis with bimetallic complexes



2) Biomimetic catalysis by molecular imprinting



3) Self-assembled chemosensors

Selected references: 1) K. Polborn, K. Severin, *Chem. Eur. J.* **2000**, *6*, 4604; 2) H. Piotrowski, K. Polborn, G. Hilt, K. Severin, *J. Am. Chem. Soc.* **2001**, *123*, 2699; 3) K. Severin, *Chem. Eur. J.* **2002**, *8*, 1514; 4) M.-L. Lehaire, R. Scopelliti, H. Piotrowski, K. Severin, *Angew. Chem. Int. Ed.* **2002**, *41*, 1419; Z. Grote, R. Scopelliti, K. Severin, *Angew. Chem. Int. Ed.* **2003**, in press.

Inorganic and Coordination Chemistry **2**

Spectroscopic and Computational Insights into Coenzyme B_{12} Function

Thomas C. Brunold

University of Wisconsin, 1101 University Avenue, Madison, Wisconsin 53703, United States

Enzymes that rely on coenzyme B_{12} (the biologically active form of vitamin B_{12}) for their catalytic activity achieve an ~10^{12}-fold acceleration for the homolytic cleavage rate of the cofactor's Co–C bond to produce Co^{2+}-cobalamin and an organic radical centered on the 5'-carbon of the adenosyl (Ado) moiety [1]. We explore the mechanism for this exalted rate enhancement using electronic absorption, circular dichroism, magnetic circular dichroism, and resonance Raman spectroscopic techniques in conjunction with time-dependent density functional theory calculations to generate experimentally-validated electronic-structure descriptions for the free and enzyme-bound cofactor. This combination of experimental and theoretical methods has permitted us to develop a simple model that explains why the lower axial ligand (corresponding to the tethered base 5,6-dimethylbenzimidizole in the free cofactor) does not appreciably modulate the nature of the Co–C bond [2]. Our studies reveal further that enzymatic Co–C bond activation does not involve corrin ring deformation and/or electronic perturbations induced by the lower axial ligand; rather, a mechanism invoking stabilization of the Co–C bond cleavage products (i.e., the Co^{2+}-cobalamin/Ado$^{\bullet}$ radical pair) is shown to be more plausible [3].

[1] Banerjee, R. *Biochemistry* **2001**, *40*, 6191-6198.
[2] Stich, T. A.; Brooks, A. J.; Buan, N. R.; Brunold, T. C. *J. Am. Chem. Soc.* **2003**, *125*, 5897-5914.
[3] Brooks, A. J.; Vlasie, M.; Banerjee, R.; Brunold, T. C., submitted for publication.

Analytical Chemistry **3**

A new generation of selective solid-phase extraction sorbents

Marie-Claire Hennion, Valérie Pichon, Florence Chapuis and Pierre Andrieux

Dpt Environment and Analytical Chemistry, Ecole Supérieure de Physique et de Chimie de Paris, 10 rue Vauquelin, 75005 Paris, France

Despite the advance in the development of highly sensitive analytical instrumentation for the final determination of analytes in complex matrices, a pre-treatment step is still required. Classical solid-phase extraction (SPE) sorbents such as n-alkylsilicas, polymer s and carbons suffer from a lack of selectivity. The co-extraction of other analytes and matrix interferences occurs when analytes are at a trace level and interferences at a higher concentration.

Tailor-made selectivity for a group of structurally related contaminants can be obtained using sorbents involving molecular recognition mechanisms. A first biological approach consists in developing antibodies against a target molecule, which are further immobilized onto silica. The main parameters affecting extraction recoveries (sample volume, sorbent capacity, ionic strength and nature of added pH buffers, residual organic solvents...) are presented. Several examples illustrate the highly selective extraction of contaminants in complex samples (industrial effluents, sludges, etc.). A second approach consists in the development of molecurlaly-imprinted polymers (MIP). Their selectivity is based on hydrogen interactions between the analytes and the MIP. Their direct use in aqueous samples involves two steps. Some examples will illustrate the high selectivity obtained after optimisation of the extraction conditions.

Another selective material is based on receptor affinity that offers the possibility of specific concentration compounds having a biological activity. A receptor-based extraction sorbent has been produced for estrogens using a chimeric protein containing ligand binding domain of human estrogens receptor. Applications to the trace-analysis of estrogenic-like analytes in environmental samples will be presented.

Analytical Chemistry **4**

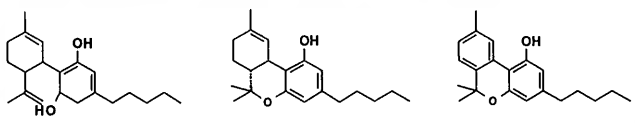
Analysis of *cannabis* material by headspace solid-phase microextraction combined with gas chromatography-mass spectrometry

Y. Ilias, P. Mathieu, S. Rudaz, P. Christen, J.-L. Veuthey

University of Geneva, School of Pharmacy, Laboratory of Pharmaceutical Analytical Chemistry, 20, Boulevard d'Yvoy, 1211 Geneva 4, Switzerland

Solid-phase microextraction (SPME) is a solvent-free sampling and sample preparation technique that can be used for a broad range of analytes. It presents a fast, sensitive and low cost approach for laboratory and field work and can be easily integrated with analytical instrumentation into an automation process.

The aim of this work is to describe the application of SPME in the headspace mode combined with gas chromatography-mass spectrometry (GC-MS) to the extraction and analysis of cannabinoids in *cannabis*. Analyses were performed on the whole plant material (marijuana) without any preliminary sample preparation. In order to optimize the method, the influence of several experimental parameters on the extraction of cannabidiol (CBD, ***a***), Δ^9-tetrahydrocannabinol (Δ^9-THC, ***b***) and cannabinol (CBN, ***c***) was studied. The experimental parameters were fiber type, equilibrium time, exposure time and temperature, desorption time and influence of water.



a ***b*** ***c***

Finally, the method was applied to trace chromatographic profiles of plants from different geographical origins.

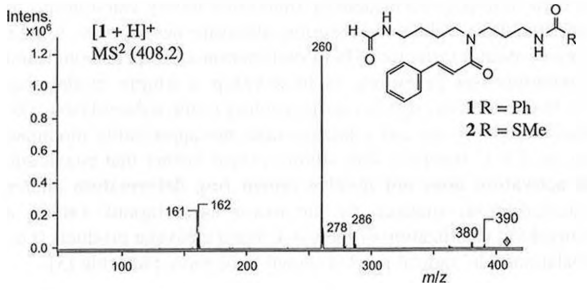
Analytical Chemistry **5**

Tandem-Mass Spectrometry as a Key Tool for the Structure Elucidation of Spermidine Alkaloids

Manuel Tzouros, Stefan Bienz, Laurent Bigler*

University of Zürich, Winterthurerstr. 190, CH-8057 Zürich, Switzerland

Tandem-mass spectrometry proved to be a powerful tool for the structure elucidation of polyamine derivatives isolated from several natural sources [1]. Collision induced dissociation (CID) spectra are particularly informative for the polyamine sequence allowing to differenciate between regioisomers [2]. This technique, combined with NMR spectroscopy, allowed us to structurally characterize the two novel spermidine alkaloids **1** and **2** isolated from *Chisocheton weinlandii* (Meliaceae).



The structures were deduced by detailed analysis of the tandem MS data and fragmentation paths and were confirmed by comparison with synthetic samples.

[1] S. Chesnov, L. Bigler, M. Hesse, *Eur. J. Mass Spectrom.* **2002**, *8*, 1.
[2] N. Manov, M. Tzouros, S. Chesnov, L. Bigler, S. Bienz, *Helv. Chim. Acta*, **2002**, *85*, 2827.

Analytical Chemistry **6**

Suppression of cell-generated polyatomic ions in reaction cell ICP-MS

Bodo Hattendorf, Detlef Günther

ETH Zürich, Laboratory for Inorganic Chemistry
ETH Hönggerberg, CH-8093 Zürich

Inductively coupled plasma mass spectrometry (ICP-MS) is widely used for elemental and isotopic analysis. Multipole ion guides have recently been introduced into commercial ICP-MS instrumentation to serve as a reaction volume to carry out ion-molecule reactions for the suppression of spectral interferences [1]. Provided that a reaction scheme of high selectivity is available, it allows the separation of analyte and interfering ions, where the required mass resolving power exceeds that of other instrumental approaches like sector field MS, e.g.:

$^{40}Ar^+ + NH_3 \rightarrow {}^{40}Ar + NH_3^+$ fast
$^{40}Ca^+ + NH_3 \rightarrow {}^{40}Ca + NH_3^+$ not observed

A mass resolution $m/\Delta m > 190000$ is required to separate $^{40}Ar^+$ from $^{40}Ca^+$.

Depending on the gas and also its purity, however, analyte ions may also react and form stable ("secondary") polyatomic ions, which lead to additional interferences.
Kinetic energy discrimination (KED) between the primary and secondary ions and selective removal of the precursors by adjusting the bandpass transmission of a quadrupole ion guide (BT) were evaluated in order to minimize the abundance of these secondary ions in the mass spectrum. It is found that KED and BT are similarly effective in removing the product ions, while the BT approach retains a significantly higher primary ion transmission, hence better elemental sensitivity, especially when the relative mass difference between precursor and reaction product is small.

[1] D. R. Bandura, V. I. Baranov, S. D. Tanner, *Fresenius J. Anal. Chem.* **2001**, 370, 618

Analytical Chemistry **7**

Metal Ion Speciation with PLM

K. Wojciechowski, P. Salaun, J. Buffle

Analytical and Biophysical Environmental Chemistry (CABE)
Chimie Analytique Minérale et Applique, Sciences II
30 quai E. Ansermet, CH-1211 Genève 4, Suisse

From the environmental point of view the most important fraction of metallic species in water are free metal ions, and its labile or lipophilic complexes. The research in CABE focuses on the development of different types of sensors selective to these bioavailable fractions of metal species. Permeation Liquid Membranes (PLM) containing artificial carriers, due to their resemblance to the biological membranes, are very good model systems to study the transport of metal ions as a function of their speciation in an aqeous solution.

We have shown that by changing different parameters in the PLM system it is possible to vary the so called permeability criterion (π) and thus to obtain different speciation information. In short words, the flux through the PLM might be proportional to the concentration of either free metal ions ($\pi<<1$) or all labile hydrophilic species ($\pi>>1$). An easy way of changing π parameter is by varying the diffusion layer thickness in the source solution of PLM. A flow minicell produced by microtechnology, integrating the PLM system with a microvoltammetric detection will be described and analytical results of the metal ion speciation will be presented for $Cu^{2+}$and Pb^{2+}.

Besides the diffusion layer thickness, other experimental variables may influence the π parameter, e.g. membrane thickness, carrier concentration and its nature. The former two parameters are also very interesting from the mechanistic point of view, since different carriers in the membrane might operate according to different mechanisms. Recently we started the mechanistic studies of the metal ion transport through the PLM membrane, and ion transfer through the aqueous/membrane interface. Especially the exact role of azacrown ether (1,10-didodecyl-1,10-diaza-18-crown-6) and the fatty acid (lauric or palmitic acid) is investigated with respect to their surface activity and complexing properties towards transported metal ions.

Analytical Chemistry **8**

Modern analytical tools for environmental risk assessment

Marc J.-F. Suter, Alfredo C. Alder, Walter Giger, Eva M. Golet, Christa S. McArdell, Eva Molnar, Victor J. Nesatyy, René Schönenberger

Swiss Federal Institute for Environmental Science and Technology, EAWAG, Ueberlandstr. 133, 8600 Duebendorf, Switzerland

The challenge facing environmental analytical chemists is among others the need to quantify target analytes at down to ng/L-levels in complex matrices. This requires sophisticated tools for enrichment and determination.
Today there is an increasing concern regarding pharmaceuticals and xeno-estrogens being released into the aquatic environment through various pathways. There is for instance the potential risk of generating antibiotic resistant bacterial strains through discharge of antibiotics, as observed in fish-farm sediments. Measurements in the Glatt valley watershed revealed concentrations of up to 75 ng/L for one macrolide antibiotic, and also showed that elimination along a 36 km stretch of the Glatt River was insignificant, indicating a potential environmental risk [1].
Considerable research is focused on the effect of environmental hormones on aquatic organisms. Already 0.1 ng/L of ethinylestradiol, the active component in the contraceptive pill, affected male rainbow trout. This indicats the need for selective enrichment, since these concentrations are at best equal to published limits of quantitation (LOQ). Mass flux calculations for estimating discharge of estrogens through wastewater treatment plants allow identifying potential hot-spots, even if predicted concentrations are below LOQs. Furthermore, the potential risk of less potent environmental hormones can be evaluated using mass spectrometric techniques based on H/D exchange [3]. This approach will be useful for regulators, faced with the need to screen the universe of chemicals for endocrine disrupting activity.

[1] McArdell, C.S., Molnar, E., Suter, M.J.-F., Giger, W., **2003**, submitted to *Environ. Toxicol. Chem*
[3] Powell, K.D., Fitzgerald, M.C., *Anal. Chem.* **2001**, *73*, 3300.

Analytical Chemistry **9**

Uncertainty of NOx and SO_2 Emission Measurements

Lukas Emmenegger* and Jean Poulleau*

*EMPA, Ueberlandstrasse 129, 8600 Dübendorf, Switzerland
*INERIS, BP 2, 60550 Verneuil en Halatte

The reporting of analytical results shall include some quantitative indication of its quality. General principles for this quality assessment are outlined in the ISO Guide to the Expression of Uncertainty in Measurement (GUM). For accredited laboratories, the ISO 17025 specifically asks to take into account all uncertainty components which are of importance in a given situation.
Validation of standards developed for emission measurements by the Comité Européen de Normalisation (CEN) typically includes two basic approaches to determine uncertainty: (i) uncertainty budgets according to GUM and (ii) in-field comparison between laboratories. The first concept is primarily useful to determine the main uncertainty factors, while field tests provide data on repeatability and reproducibility, based on procedures outlined by ISO 5725-2.
The prEN standards for NO_x and SO_2 emission measurements, which will be available by the end of this year, are thorough examples for the theoretical-, laboratory- and field evaluation of measurement uncertainty. SO_2 is determined by a manual method which consists of its absorption in a H_2O_2 solution and subsequent laboratory analysis. The uncertainty of this method is dominated by the laboratory analysis. This leads to a relatively simple system with very consistent results considering repeatability, reproducibility and uncertainty budgets. The NO_x standard is an automated method based on chemiluminescence of NO after oxidation by ozone. International field tests and uncertainty budgets done by various experts are not very consistent. This is largely due to difficulties in obtaining reliable performance characteristics to set up uncertainty budgets, that are valid over a large concentration range.

Analytical Chemistry **10**

Temperature Induced Conformational Changes in Proteins Monitored by FT-IR Spectroscopy

Davide Ferri§, Hans-Josef Brunnert, Martin Luft and Matthias Boese*
§ Bruker Optics GmbH, Industriestrasse 26, CH-8117 Fällanden
Bruker Optik GmbH, Rudolf-Planck-Strasse 27, D-76275 Ettlingen

FT-IR spectroscopy has been used efficiently to probe protein-protein and protein-ligand interactions for more than a decade [1]. Besides the determination of the secondary structure of proteins in aqueous solutions, FT-IR spectroscopy sensitively detects conformational changes, induced for example by ligand binding and changes in temperature or pH.

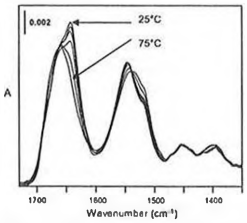


Figure 1: Temperature induced unfolding of RNase A. 10°C steps; 15 mg/ml in 60 mM phosphate buffer, pH 7.

The suitability of a new developed IR cell [2] for analysing proteins in aqueous solutions and overcoming the strong absorption of water is proved here by following the temperature induced unfolding/folding process of RNase A in solution. Unfolding was observed at *ca.* 55°C (Figure 1) in the 1500-1700 cm^{-1} spectral range and was found to be fully reversible. The conformational changes in the secondary structure of RNase A could also be monitored quantitatively in solution as a function of temperature by using a protein database, built on proteins with known X-ray structure, and a PLS algorithm. A decrease of the β-sheet content was clearly observed again at *ca.* 55°C with this experimental approach. The β-sheet content dropped of about 50% from 25°C to 65°C as monitored by taking the absorbance of the amide I band at 1641 cm^{-1}. A similar though irreversible unfolding process was also found for lysozyme, which started aggregating at *ca.* 55°C.

[1] H. Fabian and C.P. Schultz, in *Encyclopedia of Analytical Chemistry*, Ed. R.A. Meyers, John Wiley & Sons, **2000**. p. 5579.
[2] M. Luft and M. Boese, *Bioforum International*, **2002**, *6(4)*, 182.

Analytical Chemistry **11**

On-line Electrochemical Tagging of Free Cysteine by Electrogenerated Benzoquinones during Nanospray Ionisation for Mass Spectrometry in Protein Analysis

C. Roussel, L. Dayon, T.C. Rohner, H. Jensen and H.H. Girault*

Laboratoire d'Electrochimie Physique et Analytique, EPFL, CH-1015 Lausanne, Switzerland

A nanospray interface with an integrated electrode [1] coupled to a mass spectrometer (MS) has been used to generate benzoquinone which reacts with cysteine residues of polypeptides *via* a 1,4-Michael addition [2,3]. This tool is useful to quantify cysteine residues present in biomacromolecules and leads to a simplified proteins analysis. Different hydroquinones like hydroquinone, 2-methoxyhydroquinone, 2-methylhydroquinone, methyl 2,5-dihydroxybenzoate and 2-nitrohydroquinone were tested in order to improve the tagging reaction. The behaviour of the different hydroquinones were studied in the presence of L-cysteine by electrochemical methods. The 1,4-Michael addition kinetic was determined using cyclic voltammetry performed in the spray medium ($MeOH/H_2O/AcOH$ 50/49/1). Digital simulations were used to extract the kinetic constants and the final tagging efficiency was studied by MS using the nanospray interface. The electrochemical investigations have shown that the reactivity of the hydroquinones follows the electronic effect of each substituent. The MS analyses have revealed that 2-methoxyhydroquinone (though it presents the smaller kinetic constant) leads to a good tagging yield. This was explained by the higher ionisation efficiency of the L-cysteine-2-methoxyhydroquinone adduct compared to the ones obtained with the other hydroquinones. It was observed, using several peptides as well as β-Lactoglobulin A (a protein present in bovine milk) that this kind of reaction is an appropriate tool for protein structure studies. The selectivity of the tagging reaction against L-cysteine was also studied and was found to be total. In conclusion, this newly developed tool has been found to be highly selective and efficient to study protein structures on-line.

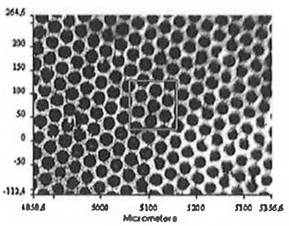
[1] T.C. Rohner, J.S. Rossier, H.H. Girault, *Analytical Chemistry* **2001**, 73, 5353-5357.
[2] T.C. Rohner, J.S. Rossier, H.H. Girault, *Electrochemistry Communications* **2002**, 4, 695-700.
[3] C. Roussel, T.C. Rohner, H. Jensen, H.H. Girault, *Chem .Phys. Chem.* **2003**, 4 (2), 200-206.

Analytical Chemistry **12**

Chemical mapping of microstructured samples by microanalysis and infra-red imaging techniques

Raymond Houriet, Annie Ferrari, Emmanuel Gallucci, Olivier Zinger
Institut des Matériaux EPFL, CH-1015 Lausanne

In the course of our projects aiming at improved reconstruction of the bone tissues following hip surgery, we have investigated the use of microstructured titanium substrates prepared by electrochemical micromachining. The coating of theses substrates with calcium phosphate used a laser atomisation deposition process which forms a highly porous film that favours subsequent trapping of co-added materials such as proteins.



microstructured titanium with 30 µm diameter spherical alveoli

The prepared specimen were examined by scanning electron microscopy in order to check the homogeneity of the calcium phosphate coating while microanalysis provided the mapping of the elemental analysis.
Imaging infra-red spectroscopy was used to obtain molecular information on the samples. Although the lateral resolution of the technique is limited to about 6 µm, specific information could be obtained. Firstly, the calcium phosphate distribution could be established, then possible phase changes occurring in the sample could be monitored and finally the occurrence of added proteins could be traced.
In this paper, we shall describe the issues related to the adhesion of the prosthesis to the bone tissue. The performances and limitations of the analytical techniques used in this study will also be discussed.

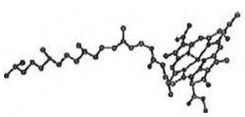
Analytical Chemistry **13**

Separation of Chlorins and Carotenoids in Capillary Electrokinetic Chromatography

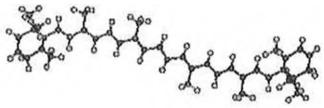
Gamze Kavran Belin[1,2,*], O. Fazil Gülaçar[1]

[1] University of Geneva, CH-1211 Geneva, Switzerland
[2] Technical University of Istanbul, 34469, Istanbul, Turkey

Nowadays, among all modern analyses techniques, capillary electrophoresis (CE) became more popular and widely used technique because of its easy usage, small amount of sample and chemical requirements and short analyses times with efficient peak resolutions and reproducubilities. Since the first introduction of MEKC by Terabe and co-workers [1], this method was used especially for neutral solutes. The separation mechanism in MEKC is based on differential partitioning between aqueous and micellar pseudo-stationary phases. In organic-rich media, surfactants lack the capability of aggregating to form micelles [2] and this CE technique is called as capillary electrokinetic chromatography (EKC). In this work, separation of chlorins (**1a**) and carotenoids (**1b**) was performed by using cationic surfactants in EKC.



1a



1b

For the solubilities and selectivities of analytes, tetrahydrofuran (THF) was used as organic modifier. The effects of additive concentration and structure, voltage and analyte-additive interactions were investigated.

[1] S.Terabe, K.Otsuka, K.Ichikawa, A.Tsuchiya, T.Ando, *Anal.Chem.* **1984**, 56, 111.
[2] M.T.Bowser, A.R.Kranack, D.D.Y.Chen, *Trends Anal.Chem.* **1998**,17, 424.

Analytical Chemistry **14**

Ion-Molecule Reaction Mass Spectrometry for Trace Analysis of Gas Standards

R. Althaus, H.-P. Haerri, L. Mounier

Swiss Federal Office of Metrology and Accreditation, metas
Lindenweg 50, CH-3003 Bern-Wabern

For the calibration of gas immissions instruments and the production of gas standards with low amount of substance fractions of analytes **[1]**, trace amounts of foreign gases may contribute substantially to the combined measurement uncertainty. With ion-molecule reaction mass spectrometry (IMR-MS) **[2]** substances are selectively ionised with high sensitivity according to their ionisation potentials thus distinguishing isotopes with similar atomic masses but chemically different.

The instrument was adapted such that the inlet pressure can be below ambient and the flow as low as 70 ml/min allowing to measure gases from various sources. The pressure regulation of the inlets was made independent of the high vacuum system, increasing the sensitivity and making the MS more reliable. Besides Kr and Xe as ionisation gases CF_3I, I_2 and Hg were tested for analytes with low IP's (10 eV) **[3]**.

By mixing calibration gases with pure buffer gases (dilution) the characteristics of the MS like response, selectivity, limit of detection and quantification were determined for CO, CO_2, CH_4 and C_3H_8 under various operation parameters. Various zero gas generators used in calibration and field gas immission instruments were investigated and it was found that the gas composition varied substantially depending on the construction of the generators and the condition of the elements. The NO to NO_2 ratios from standards made by dynamic volumetric mixing were compared with mixtures from bottles.

[1] D.W. Zickert, M. Quintilii, Proceedings10th Intl. Metrology Congress, St. Louis, F, (2001).
[2] H.-P. Haerri, B. Niederhauser, J.-F. Perrochet, D. Zickert, Chimia **2001**, 55, No. 7/8 p. 592.
[3] D. Bassi, P. Tosi, and R. Schlögl; J. Vacuum Sci. Tech. **A16** (1998) 114.

Analytical Chemistry **15**

Permeation liquid membrane device as an analytical tool for trace metal speciation studies in natural waters

Nalini Parthasarathy, Michel Pelletier and Jacques Buffle

University of Geneva, Department of Analytical Chemistry, Sciences II, 30 Quai Ernest-Ansermet, CH-1211 Geneva 4, Switzerland

Metal ions in particular Cu, Pb, Cd and Zn exist in various chemical forms in natural waters. Their toxicity and bioavailability to organisms depend on the specific forms in which they exist, in particular the free metal ions is the most toxic form. These species exist at levels below the detection limits of most analytical instrumental speciation techniques and their determination still remains a challenging problem to chemists. One way of achieving this is the use of emerging analytical tools such as carrier assisted metal transport through permeation liquid membrane (PLM), based on liquid-liquid extraction principles. The attractive features of PLM are simultaneous extraction, back extraction and preconcentration of the metals. PLM utilizing species selective carrier 1,10 didecyl 18 crown6 ether for Cu, Pb, Cd and Zn has been designed. The capability of this PLM for trace metal speciation studies and the role of lipophilic organo - Cu(II) complexes in the transport of Cu(II) across PLM will be presented in this poster. In addition, simple models to describe the metal transport across PLM and application of PLM to speciation of Cu and Pb in natural waters will also be presented. The limit of detection of this method is ca. 10 pmol/L.

[1] J. Buffle, N. Parthasarathy, N.K. Djane and L. Mattiasson in *In Situ Monitoring of Aquatic Systems*, **2000**, *chap. 10*, Ed. J. Buffle and G. Horvai, John Wiley, Chichester
[2] N. Parthasarathy and J. Buffle, *Anal. Chim. Acta* **1994**, *284*, 649

Analytical Chemistry **16**

HMBC-RELAY: A Combined NMR Technique for the Differentiation of Simultaneously Detected $^2J_{CH}$ and $^nJ_{CH}$ Connectivities

Thomas Sprang and Peter Bigler

Department of Chemistry and Biochemistry, University of Berne, Freiestrasse 3, CH-3012 Bern, Switzerland

2D ^{13}C-^1H heteronuclear correlation spectroscopy detecting $^1J_{CH}$ and $^nJ_{CH}$ coupling connectivities using techniques such as HSQC and HMBC respectively has proved to be very successful for unraveling molecular structures. The reliable differentiation between $^2J_{CH}$ and the residual $^nJ_{CH}$ connectivities however would certainly facilitate the analysis of HMBC spectra.

We present a new pulse sequence that detects simultaneously $^nJ_{CH}$ and $^2J_{CH}$ connectivities and that allows the two types of interactions to be disentangled by a simple add/subtract procedure. As a result we obtain two subspectra, one showing all kinds of $^nJ_{CH}$ connectivities – the "HMBC"-spectrum – and one showing the $^2J_{CH}$ connectivities of protonated carbons.

In contrast to the previously published $^2J/^nJ$ experiment [1], this sequence detects the $^2J_{CH}$ connectivities via a CHH-RELAY pathway taking advantage of corresponding ^1H-^1H homonuclear couplings. This improves the sensitivity of the $^2J_{CH}$ subspectrum in general and allows $^2J_{CH}$ connectivities to be detected even for $^2J_{CH}$ coupling constants close or equal to zero.

Corresponding spectra of strychnine obtained with this new technique will be shown.

[1] T. Sprang and P. Bigler, *Magn. Reson.Chem.*, **2003**, 41, 177-182.Authors Names,

Analytical Chemistry **17**

Surface Topology Probing of Proteins by Noncovalent Receptors and MALDI Mass Spectrometry

Sebastian D. Friess and Renato Zenobi

Department of Chemistry and Applied Biosciences, Swiss Federal Institute of Technology ETH, 8093 ETH Hönggerberg

We have recently introduced a novel method to probe biomolecular struture via noncovalent complexation with recognition tags [1-3]: sulfonic acid receptors selectively form noncovalent complexes with arginines. Structural information can be derived, because only accessible residues on the exposed surface of a biomolecule are complexed and hence detected.
In the present work, we report an experimental study where calculated surface accessibility parameters are correlated with new mass spectromeric data of proteins such as ribonuclease A, lysozyme, myoglobin, adenylate kinase, aldolase, and albumin; a broad mass range up to 66 kD is covered. The noncovalent complexes are all analyzed by MALDI mass spectrometry. Using a non-acidic matrix, a special multilayer sample preparation and low laser power, the desorption/ionization becomes sufficiently gentle to transfer the intact noncovalent assemblies into the gas phase. The sulfonic acid receptor for arginine is chosen upon its selectivity and mass: 2.5-naphthalene disulfonate, 2.6-anthraquinone disulfonate, 1.3.7.9-pyrene tetrasulfonate, and related compounds allow adducts to be (at least partially) mass resolved. In high molecular weight systems (e.g. aldolase, 39 kD), individual receptor adducts are no longer resolved and the overall peak position and width have to be interpreted. Preliminary results on such pattern recognition strategies are presented. Correlating surface accessibility obtained from computational methods with mass spectrometric data allows to relate gas-phase measurements of solution-phase protein structure to NMR and X-ray data, adressing one of the primary issues in biochemistry.

[1] S. D. Friess, R. Zenobi, *J. Am. Soc. Mass Spectrom.* **2001**, *12*, 810.
[2] S. D. Friess, J. M. Daniel, R. Hartmann, R. Zenobi, *Int. J. Mass Spectrom.* **2002**, *219*, 269.
[3] S. D. Friess, R. Zenobi, *Proceedings of the 50th ASMS conference* **2002**, Orlando / FL.

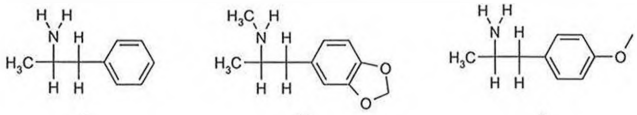
Analytical Chemistry **18**

Detection and identification of amphetamine derivatives using a novel sheath liquid capillary electrophoresis-mass spectrometer interface

Pascal Bernet[1], Martin Schär[1], Stefan Berger[2]

[1] University of Applied Sciences Berne, HTA Burgdorf, Department of Chemistry, Pestalozzistr. 20, 3400 Burgdorf, Switzerland
[2] ReseaChem GmbH, Pestalozzistrasse 16, 3400 Burgdorf, Switzerland

The importance of the analysis of amphetamine **1** and its derivatives is widely recognized for toxicological, clinical and forensic purposes [1]. In particular, the analysis of so-called designer drugs like Ecstasy (3,4-methylendioxymethamphetamine **2**) has become an important topic.



1 **2** **3**

Due to the similar structure of the amphetamine derivatives, the identification by hyphenated techniques such as capillary electrophoresis (CE) coupled to electrospray mass spectrometry (MS) is a prerequisite to identify and quantitate possibly harmful substances in Ecstasy pills like parameth-oxyamphetamine **3**.

A novel sheath liquid CE-MS interface [2] has been developed and used for the analysis of Ecstasy pills. Further, the in-source dissociation of amphetamines has been investigated.

[1] a) W. Thormann, J. Caslavska, A. Ramseier, *Electrophoresis* **1998**, *19*, 2956; b) L. Geiser, S. Cherkaoui, J.-L. Veuthey, *J. Chromatogr. A*, **2000**, *895*, 111.
[2] See poster: M. Schär, D. Blaser, P. Bernet, "Development of a robust capillary electrophoresis-mass spectrometer interface with a floating sheath liquid feed".

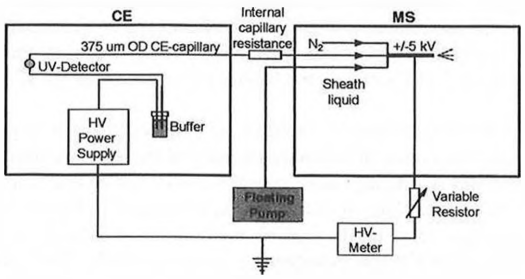
Analytical Chemistry **19**

Development of a robust capillary electrophoresis-mass spectrometer interface with a floating sheath liquid feed

Martin Schär, Dominik Blaser, Pascal Bernet

University of Applied Sciences Berne, HTA Burgdorf, Department of Chemistry, Pestalozzistr. 20, 3400 Burgdorf, Switzerland

The on-line combination of capillary electrophoresis (CE) with mass spectrometry (MS) has attracted major attention for the in depth analysis of peptids and proteins [1]. However, CE-MS coupling is not straightforward. We present a novel sheath liquid CE-MS interface, which is robust and allows to use both hyphenated techiques, liquid chromatography-mass spectrometry (LC-MS) and CE-MS, alternatively on the same mass spectrometer. The two separation techniques can be switched within minutes.



The necessary sheath liquid is delivered by a pump which floats on the ion sprayer potential of the MS, avoiding any current flow towards ground. To obtain a stable ion spray, only the CE-power supply is used for both the CE and the sprayer tip voltage. The sole parameter which has to be adjusted if the CE conditions are changed is the variable resistor.

[1] C. Neusüss, M. Pelzing, M. Macht, *Electrophoresis* **2002**, *23*, 3149.

Analytical Chemistry **20**

Stereoselectivity of Methadone Metabolism assessed by Single CYP450 Enzymes and Capillary Electrophoresis

Francine Prost, Wolfgang Thormann
Department of Clinical Pharmacology, University of Bern
Murtenstrasse 35, CH-3010 Bern, Switzerland.

Drug metabolism studies can be performed in vivo after drug intake and following its fate via analysis of the temporal drug and metabolite concentrations in body fluids and tissues. Alternatively, in vitro systems which mimic hepatic functions are important tools in the field of pharmacological and toxicological research. The methadone (MET) to 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP) conversion obtained after incubation of methadone with microsomes containing single human cytochromes that were prepared from baculovirus-infected insect cells containing a human CYP450 expressed gene (CYP2D6, CYP3A4, CYP2C9, CYP2C19, CYP1A2 SUPERSOMES™) was investigated using a chiral capillary electrophoresis assay. MET and EDDP enantiomers were determined in a pH 2.3 phosphate buffer containing 2 mM heptakis (2,6-di-O-methyl)-β-cyclodextrin and 10 % methanol. Incubation of racemic and non-racemic MET with CYP3A4 revealed no stereoselectivity for the MET to EDDP conversion, whereas no EDDP formation was observed with CYP1A2. CYP2C9 and CYP2C19 provided enhanced formation of R-EDDP and CYP2D6 incubation resulted in the preferential conversion to S-EDDP. Investigations using racemic MET and human liver microsomes revealed a modest stereoselectivity with a S/R EDDP ratio > 1 which is similar to the in vivo findings in urine. Chiral capillary electrophoresis is demonstrated to be a simple and effective tool for the assessment of drug metabolism in vitro.

This work was supported by the Swiss National Science Foundation.

Analytical Chemistry **21**

Identification of Oxycodone Metabolites in Human Urine by Capillary Electrophoresis - Electrospray Ionization Ion Trap Mass Spectrometry

Andrea Baldacci, Jitka Caslavska, Anita B. Wey, Wolfgang Thormann
Department of Clinical Pharmacology, University of Bern, Murtenstrasse 35, CH-3010 Bern, Switzerland.

Oxycodone (OCOD) is a semisynthetic opioid that carries an OH group at position 14 and is otherwise structurally related to other opioids, including dihydrocodeine, codeine and morphine. It is a strong opioid analgesic and is used for the management of moderate to severe mainly postoperative or cancer related pain. The metabolism of OCOD is largely unknown [1]. Using capillary electrophoresis with an aqueous pH 9 ammonium acetate buffer coupled to electrospray ionization ion trap mass spectrometry ($CE-MS^n$), OCOD and its metabolites oxymorphone, noroxycodone, noroxymorphone, 6oxycodol, nor6oxycodol and oxycodone-N-oxide could be identified in solid-phase extracts of unhydrolized and hydrolyzed urines that were collected after ingestion of OCOD (up to 80 mg daily). $CE-MS^2$, $CE-MS^3$ and $CE-MS^4$ data are shown to represent effective approaches to identify drug metabolites in human urine. Furthermore, experimental data were found to compare well with fragmentation simulation employing the HighChem Mass Frontier software.

This work was supported partly by Mundipharma Medical Company, Basel, Switzerland and by the Swiss National Science Foundation.

[1] A.B. Wey, W. Thormann, *J. Chromatogr. B* **2002**, *770*, 191.

Analytical Chemistry **22**

Production and utilization of multiply charged ions in MALDI.

Vladimir Frankevich, Juan Zhang, and Renato Zenobi.

Department of Chemistry, Swiss Federal Institute of Technology, ETH Hönggerberg, CH-8093 Zürich, Switzerland.

The formation of multiply charged ions and the origin of ion fragments in matrix-assisted laser desorption/ionization (MALDI) mass spectrometry are currently subject to active studies. In the present work we investigate the influence of free electrons on ion fragmentation and multiply charged ion formation.

Experiments were performed on a 4.7 tesla Fourier transform ion cyclotron resonance (FTICR) mass spectrometer utilizing an internal MALDI source and an open FTICR trap. For laser desorption, a Nd:YAG laser (Continuum, Minilite ML-10, USA) with a 5 ns pulse duration at 355 nm was employed. The temporal evolution of the laser heated MALDI sample was measured via detection of the black body radiation on the nanosecond timescale by infrared InGaAs-PIN photodiod (Hamamatsu, model G8376-03)

In preliminary experiments we have shown that multiply charged ions are present in a MALDI plume but are usually neutralized to charge state +1 by reactions with electrons and anions. It is shown that formation of multiply charged ions is directly related to the ability to limit the number of electrons in a plume. Suppression of the electron emission can be achieved by using "electron free" MALDI using a non-metallic MALDI target to suppress photoelectrons from the metal, low laser pulse energy, and a high IP matrix to prevent multiphoton ionization of the matrix which also releases electrons. Ion fragmentation is considerably reduced in "electron free" MALDI. The correlation between MALDI ion fragmentation and multiply charged ions yield is discussed. We conclude that the electrons do play a significant role in analyte fragmentation.

Analytical Chemistry **23**

Combining Fluorescence Spectroscopy and FT-ICR MS to study the trapped and mass-selected biomolecular ions in gas phase

Xianwen Guan, Vladimir Frankevich, and Renato Zenobi

Department of Chemistry, Swiss Federal Institute of Technology, ETH Hoenggerberg, CH-8093 Zurich, Switzerland

Fluorescence spectroscopy is a very sensitive and selective technique. Fluorescence Resonance Energy Transfer (FRET) is a very effective method to obtain conformational information of biomolecules in solution. FT-ICR MS is a versatile technique, which provides high mass accuracy and high mass resolution. Combining these two techniques together will be very useful for studying intramolecular conformational structure of biomolecules and their intermolecular interaction in the gas phase.

An open cylindrical cell has been constructed for laser induced fluorescence determination of trapped and mass-selected ions by FT-ICR MS. The FT-ICR MS is equipped with a 4.7 T magnet and an internal MALDI source. The new design is based on detection perpendicular rather than parallel to the laser beam. The fluorescence signal is transported by an optical fiber from vacuum to a detector outside. The experimental parameters for the newly designed device were optimized with Rhodamine 6G ions as the test samples, such as the trapping potentials, the pressure of N_2 for cooling ions, the localization of excitation laser, and excitation laser power. It is found that the background signal has been decreased greatly.

GFP is one of the most widely studied and exploited proteins in biochemistry and cell biology. GFP is a rather small protein with a molecular weight of roughly 27kDa. Its fluorescence can be used as an indicator for the formation of the 11 _-sheet barrel-like structure. Thus it is suitable candidate for the investigation of biomolecular conformation changes in gas phase by this technique. The optimization of experimental conditions for detection of GFP by MALDI was performed on TOF-MS in order to get relevant information for the formation of GFP ions in gas phase. Further investigations with GFP are on the way.

Analytical Chemistry **24**

Determination of Short-Chain Polychlorinated Paraffins in North Sea Sediments

Jana Hüttig and Michael Oehme

University of Basel, Neuhausstr. 31, CH-4057 Basel, Switzerland

Polychlorinated paraffins (CPs) are chlorination products of n-alkane mixtures (chain length C_{10-30}) produced since the early 1930s. They are used mainly as additives for sealants, metal cutting oil, plasticizers and flame retardants. After the ban of polychlorinated biphenyls in the 1980s, CPs are used as a substitute in various application fields and production has amounted to more than 300 000 tons per year[1]. CPs are persistent in the environment, and first studies detected them in a wide variety of environmental samples. Short-chain CPs (C_{10-13}) are highly toxic to aquatic organisms, and a risk assessment indicated a significant risk to the aquatic compartment[2]. Therefore, the German government decided to stop the use of short-chain CPs in metal working and leather industry in summer 2003[3].

The analysis of CPs consisting of probably several thousands of single compounds is very demanding and mainly carried out by high resolution mass spectrometry (MS). Currently, only very few studies have been carried on the occurrence of this class of compound in sediments[4]. The aim of this work is to develop a less costly analysis method and to generate a general survey of short-chain CP concentrations in sediments in the North Sea. Details about method development and optimization will be given based low resolution MS in the negative ion chemical ionisation mode. Moreover, results of investigated North Sea sediments are presented.

[1] Coelhan, M, Saraci, M, Parlar, H; *Chemosphere*. **2000**, *40*, 685-689.
[2] EU Risk Assessment; *C10-13 Chloro Alkanes*. Ispra, **1999**.
[3] Umweltbundesamt; *Umwelt*. **2003**, *2*, 120.
[4] de Boer, J; *J. Chromatogr. A*. **1999**, *843*, 179-198.

Analytical Chemistry **25**

Determination of Short Chain Polychlorinated n-Alkanes in Biota

Margot Reth and Michael Oehme

Organic Analytical Chemistry, University of Basel, Neuhausstr. 31, 4057 Basel, Switzerland

Short chain polychlorinated n-alkanes (sPCAs) are classified as persistent, very toxic to aquatic organisms and carcinogenic for rats. Because of their wide application, their large-volume production and their wide distribution in the environment, the determination of sPCAs gained increasing attention in recent years. However, the complex composition of sPCA mixtures (thousands of congeners) complicates their analysis so that it is mainly carried out by high-resolution mass spectrometry (MS) [1].

A new analytical method has been developed for sPCA determination in fish samples. The clean-up procedure comprised fat elimination by adsorption chromatography on silica gel impregnated with concentrated H_2SO_4 followed by separation from other organochlorines on florisil. High-resolution gas chromatography combined with electron capture negative ionization low-resolution MS was applied for the sPCA detection.

This method allowed a complete separation of sPCAs from polychlorinated biphenyls and toxaphenes. sPCA recoveries were between 70-90%. The linear range of the detection method was 1-100 ng and the limit of detection 1 ng of technical sPCA mixture at a signal-to-noise ratio of 3:1. sPCA levels determined in liver of North Sea dab and cod from the North Sea and Baltic Sea ranged between 90-287 ng/g of wet weight. Details of the developed method, the determined total sPCA amount and the obtained congener and homologue pattern will be presented.

[1] OSPAR Commission, Ospar Background Document on Short Chain Chlorinated Paraffins, **2001**, 141, http://www.ospar.org.

Analytical Chemistry **26**

On-line electrochemical tagging of cysteine by hydroquinones during nanospray ionisation for mass spectrometry in protein analysis

L. Dayon, C. Roussel, T.C. Rohner H. Jensen, H.H. Girault*

Laboratoire d'Electrochimie Physique et Analytique, EPFL, CH-1015 Lausanne, Switzerland

A nanospray interface with an integrated electrode [1] coupled to a mass spectrometer has been used to electrogenerate (1,4)-benzoquinone from (1,4)-hydroquinone which reacts with free cysteine *via* a 1,4-Michael addition [2, 3]. The tool has revealed itself very useful to quantify cysteine in biomolecules. To optimise the tagging reaction coupled with MS detection, 2-methoxyhydroquinone, 2-methylhydroquinone, methyl 2,5-dihydroxybenzoate and 2-nitrohydroquinone were first studied in the presence of L-cysteine: kinetic behaviours of the coupled chemical reaction were determined by cyclic voltammetry and digital simulations. The final tagging efficiency was studied by MS. Methyl 2,5-dihydroxybenzoate gave the best results whereas 2-nitrohydroquinone was abandoned (inadequate tendency to polymerise). Unexpectedly, 2-methoxyhydroquinone, though its small kinetic constant, gave good results in MS experiments (high ionisation efficiency of the adduct formed). Several peptides containing up to three cysteines residues were investigated in the tagging experiment. The spectrum of β-Lactoglobuline A infused in the presence of the hydroquinones showed the native distributions of peaks for the protein and a shifted distribution corresponding to the adduct formation with the free cysteine.

[1] T.C. Rohner, J.S. Rossier, H.H. Girault, *Anal. Chem.* **2001**, 73, 5353-5357
[2] T.C. Rohner, J.S. Rossier, H.H. Girault, *Electrochem. Commun.* **2002**, 4, 695-700
[3] C. Roussel, T.C. Rohner, H. Jensen, H.H. Girault, *Chem. Phys. Chem.* **2003**, 4, 200-206

Analytical Chemistry **27**

Quantification of Polychlorinated *n*-Alkanes by Ion Trap EI-MS/MS

Zdenek Zencak and Michael Oehme

Organic Analytical Chemistry, University of Basel, Neuhausstr. 31, 4057 Basel, Switzerland.

Polychlorinated n-alkanes (PCAs) are complex technical mixtures with a chlorination degree between 30 and 70% and a linear chain length of C_{10}-C_{13} (short chain PCAs or sPCAs), C_{14}-C_{17} (medium chain PCAs or mPCAs) or $C_{>17}$ (long chain PCAs or lPCAs). Due to their wide use PCAs can be found in aquatic and terrestrial food webs in rural and remote areas [1].

The detection method of choice for PCAs is electron capture negative ionization mass spectrometry (MS). However, the determination of the total PCA concentration with this method is highly time-consuming.

This work presents the development of a method for the determination of PCAs in biota based on electron ionization (EI) MS. EI of PCAs results in a strong fragmentation and little specific fragment ions at low *m/z*. However, among them, fragment ions could be identified common to all PCAs independent from chlorine substitution and chain length. The low specificity of these ions could be compensated by the application of ion trap tandem mass spectrometry (MS/MS). Two fragmentations (*m/z* 91 to 53 and *m/z* 102 to 65) were selected and gave good linearity (R^2>0.998, 6 measuring points between 2 to 100 ng technical sPCA mixture) and detection limits of 5 ng or 1 ng of technical PCA mixture, respectively. The analysis of spiked fish oil samples recovered the added amount within an uncertainty of 20 %. Analysis of fish liver samples (North Sea dab and cod from the Norh Sea and Baltic Sea) showed PCA concentrations in the range of 210-1450 ng/g wet weight (literature values for fish 100-1700 ng/g wet weight [2]).

[1] D. C. G. Muir, *et al.*, Chlorinated Paraffins, The Handbook of Environmental Chemistry, **2000**, Springer-Verlag: Berlin, 3, 203.
[2] A. Borgen, *et al.*, Organohalogen Compd., **2001**, 52, 75.

Analytical Chemistry **28**

Quantitative Analysis of PAHs in water in the low ng/l range with Two-Step Laser Mass Spectroscopy

Christian Emmenegger, Markus Kalberer, Renato Zenobi*

Department of Chemistry, Swiss Federal Institute of Technology Hönggerberg, Wolfgang-Pauli-Str. 10, CH-8093 Zürich, Switzerland

Polycyclic aromatic compounds (PAHs) are of major concern in all environmental compartments due to their mutagenic and carcinogenic properties. Two-Step Laser Mass Spectrometry (L2MS) is a sensitive and selective method to measure PAHs in complex solid matrices [1][2]. In most previous studies L2MS has been used for qualitative or semi-quantitative analyses.

Here a quantitative method for analyzing PAHs in water at the ng/l level is presented. PAHs are extracted from a 30 ml water sample with a solid PVC membrane, which is then directly measured by L2MS without further treatment. Detection limits are in the low ng/l range (2-125 ng/l) for skeletal 3-6-ring PAHs.

In a first application samples from the different stages of a wastewater treatment plant at EAWAG (Swiss Federal Institute for Environmental Science and Technology), Dübendorf, were measured, showing that microbial activities efficiently decrease PAH concentrations by 75-90 %.

[1] Dale, M.J.; Jones, A.C.; Pollard, S.J.T.; Langridge-Smith, P.R.R. *Environ. Sci. Technol.* **1993**, *27*, 1693-1596.
[2] Kalberer, M.; Morrical, B.D.; Sax, M.; Zenobi, R. *Anal. Chem.* **2002**, *74*, 3492-3497.

Analytical Chemistry **29**

LC–ESI, APCI, APPI- MS-MS Analysis of Phytotoxins and Phytoalexins involved in Vine Resistance and Diseases

J.B. Jean-Denis, E. Abou-Mansour; R. Tabacchi

Institut de Chimie, Université de Neuchâtel, Av de Bellevaux 51 CH-2007 Neuchâtel

Downy mildew is a grapevine disease caused by *Plasmopara viticola*. Stilbene derivatives, like resveratrol and viniferin isomers, are phytoalexins produced in the infected grapevine plants and play a major role in the defense against pathogens[1].
Eutypine, sterehirsutinal and diverse naphatelnones are phytotoxins produced by fungal pathogens, *Eutypa lata, Stereum hirsutum, Phaeoacreminum* sp. responsible for eutypiosis and esca of wood grapevine disease[2].
As these metabolites, *in vivo*, are present in too low concentrations, mass spectrometry is the most powerful analytical tool for the detection of these substances in small biological samples.
This work describes the MS detection method of these compounds by direct flow injection or liquid chromatography. Three ionisation interfaces were used and compared: electrospray ionisation (ESI), atmospheric pressure chemical ionisation (APCI) and photoionization (APPI). Hence, detection limits of stilbene derivatives and eutypine derivatives were established for each ionisation method.

[1] O. Jeandet, R. Bessis, M. Sbaghi, P Meunier, *J. Phytopathol. 143*, **1995,** 135
[2] R. Tabacchi, A. Fkyerat, C. Poliart, G.-M. Dubin, *Phytopathol. Mediterr 39*, **2000,** 156

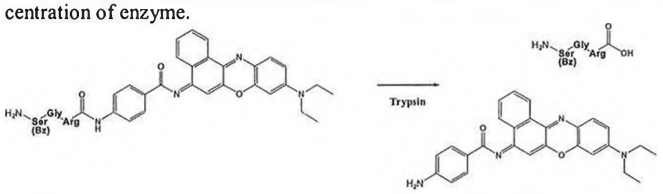
Analytical Chemistry **30**

Long-wavelength chromogenic substrates for an absorption-based assay for serine proteases

Victor Ramos, Gleb Zhylyak, Daniel Citterio, Ursula E. Spichiger-Keller

Center for Chemical Sensors, ETH Technopark, CH-8005 Zürich

The majority of commercially available chromogenic substrates are based on *p*-nitroanilides systems (λ_{max} = 300 nm). These substrates release *p*-nitroanilin (λ_{max} = 385 nm) when treated with the appropriate protease. Since the biological background in this range of the spectrum is severely interfering, this methodology has undoubted restrictions. Therefore, peptide substrates labeled with chromophores, which absorb at higher wavelengths, are currently developed.
Novel Dyes, absorbing in the red region of the visible electromagnetic spectrum, were synthesized. Specific peptide sequences labeled with the dyes allow detection of serine proteases activity with high selectivity, at low concentration of enzyme.



Cleavage of substrates labeled with nileblue derivatives at physiological pH was observed during this study both in solution and on an optical chip.
The substrates show an absorbance maximum at 660 nm and are supposed to show no spectral interference with constituents of blood samples or absorbing molecules from blood cells or blood plasma itself. Therefore, they are very attractive for rapid diagnosis of cancer diseases, for Point-of-Care-Testing and high throughput screening of drugs. The approach combines an integrated optical microchip with highly selective enzyme substrates in order to measure the enzyme activity.

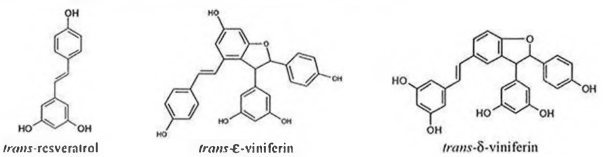
Analytical Chemistry **31**

Identification of δ-Viniferin, a resveratrol dehydrodimer biosynthesised by grapevine plants

R. Pezet [a], J.B. Jean-Denis [b], H. Richter [a], C. Perret [b] and R. Tabacchi [b]

[a] Swiss Federal Research Station for Plant Production, Changins, CH-1260 Nyon 1, Switzerland.
[b] Institute of Chemistry, University of Neuchatel, av de Bellevaux 51, CH-2000 Neuchatel, Switzerland.

Downy Mildew, caused by *Plasmopara viticola*, is a well known grapevine disease damaging vineyard all around the world. We know that stressed grapevine plant generates ε-viniferin, a resveratrol dehydrodimer, and other resveratrol derivatives [1]. A ε-viniferin isomer was only characterized as a phytoalexin mimic produced *in vitro* by the oxidative dimerization [2,3,4] of resveratrol by plant peroxidases or *Botrytis cinerea* laccases [5]. This compound was identified in grapevine leaves, either infected by *P. viticola* or UV-C treated. Hence, we demonstrated that a new resveratrol dehydrodimer, called δ-viniferin, is produced *in vivo* by the grapevine plants. δ-viniferin was characterized by an optimized and sensitive LC-MS method using an electrospray ionisation source.



[1] Kortekamp A. *et al., J. Plant Dis. Prot.*, **1998**, 105, 475.
[2] Breuil A.C. *et al. Tetrahedron Lett.*, **1998**, 39, 537.
[3] Cichewicz R.H. *et al., J. Natur. Prod.*, **2000**, 63, 29.
[4] Douillet-Breuil A.C. *et al., J. Agric. Food Chem.*, **1999**, 47, 4456.
[5] Pedreno M.A. *et al., Plant Peroxydases: Biochemistry and physiology* by Obinger C. *et al.*, University of Geneva, **1996**, 338.

Analytical Chemistry **32**

Analysis of Peptides Modified by Lipid Oxidation Products by ESI-MS/MS and Immunoaffinity ESI-MS/MS

François Fenaille[1], Jean-Claude Tabet[2] and Philippe A. Guy[1]

[1]Department of Quality and Safety Assurance, Nestlé Research Center, Nestec Ltd., Vers-Chez-les-Blanc, 1000 Lausanne 26, Switzerland.
[2]Laboratoire de Chimie Structurale Organique et Biologique, University Pierre & Marie Curie, 4 Place Jussieu, 75252 Paris cedex 05, France.

Among the numerous low molecular aldehydes generated upon lipid oxidation, 4-hydroxy-2-nonenal (HNE) has received particular attention because it can readily react with nucleophilic amino acids (mainly *via* a Michael addition mechanism), causing numerous diseases [1]. Analytical methodologies using either amino acid analysis [2] or western blot [3] have been developed to analyze HNE-modified proteins. However, despite a relative simplicity, such techniques could be, under certain conditions, not "artifact-free", specific or sensitive enough to enable the characterization of HNE adducts. Bolgar and Gaskell developed a methodology using tandem mass spectrometry (MS) to specifically characterize HNE-modified histidine residues in a model protein [4]. To analyze simultaneously different HNE-modified amino acids in a protein mixture, we have developed an immuno-affinity enrichment step prior to MS characterization, approach that has also been extended to carbonylated peptides enrichment [5]. In the present work, we have compared the use of a tandem MS approach (precursor ion scanning) with another one combining affinity enrichment followed by MS analysis to characterize some (lipid oxidation products)-modified peptides.

[1] K. Uchida, *Prog. Lipid Res.* **2003**, *42*, 418.
[2] K. Uchida et al., *Biochemistry* **1994**, *33*, 12487.
[3] K. Uchida, E.R. Stadtman, *Proc. Natl. Acad. Sci. USA* **1993**, *90*, 8742.
[4] M.S. Bolgar, S.J. Gaskell, *Anal. Chem.* **1996**, *68*, 2325.
[5] F. Fenaille, J.C. Tabet, P.A. Guy, *Anal. Chem.* **2002**, *74*, 6298.

Analytical Chemistry **33**

Analytical challenge applying LC-MS to perfluoroalkylated compounds analysis

Ingrid Langlois[1], Michael Oehme[1], Urs Berger[2], Roland Kallenborn[2], Einar Jensen[3]

[1]Organic Analytical Chemistry, University of Basel, Switzerland
[2]Norwegian Institute for Air Research, Tromsø, Norway
[3]Institute for Pharmacy, University of Tromsø, Norway

Perfluoroalkylated substances (PFAs) is used as acronym for a group of perfluorinated chemicals applied in textile and paper protection, fire-fighting foam and insecticide formulations. Perfluorooctane sulfonate (PFOS) has recently gained considerable attention due to its detection in human blood[1] and its ubiquitous presence in the environment on a global scale[2]. This resulted in a phase-out of PFOS and replacement by other PFAs with longer chains or fluorotelomer alcohols (FTOHs). This requires the development of analytical methods for these compounds classes as well.

So far, LC-MS was the most useful analytical tool for characterizing compositions of PFAs products as well as concentrations in the environment. The aim of this work was to explore the benefits and limitations of three different mass spectrometric techniques for identification and quantification. Time of flight, ion trap and triple quadrupole instruments were evaluated concerning fragmentation patterns, ionisation behavior, selectivity and linearity for five PFAs and three FTOHs. Fragmentation efficiency was studied for the ionisation modes electrospray ionisation (ESI) and atmospheric pressure chemical ionisation (APCI) using the negative ion mode. Moreover, commercial solutions of PFOS are mixtures of isomers and by-products. They provide an additional challenge concerning structure elucidation and quantification. Therefore, details about composition of technical mixtures will also be given.

[1] Olsen, GW, Hansen, KJ, Stevenson, LA, Burris, JM, Mandel, JH; *Environ. Sci. Technol.* **1999**, *37*, 888-891.
[2] Giesy, JP, Kannan, K; *Environ. Sci. Technol.* **2001**, *35*, 1339-1342.

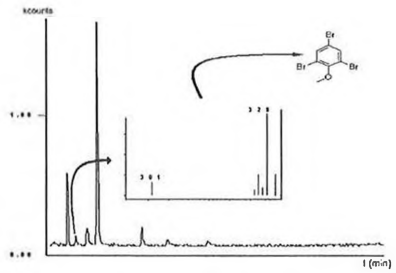
Analytical Chemistry **34**

Mustiness in Wine Bottled Without Cork ? TBA at ng/l Level Traced by GC/MSMS

Urban Frey, Pascal Jacquemettaz

University of Applied Sciences, HEVs, Rte du Rawyl 64, CH-1950 Sion

Mustiness, also called cork taint, in wine has different sources. Most often, in wine bottles closed with natural cork, it is TCA (trichloroanisole),[1] which is the responsible molecule at a ng/l level. To overcome this problem some wine producers use screw caps. But even with this, the problem is not completely solved.



We observed that in musty tainted wine, the flaw was due to TBA (tribromoanisole).[2] The odour threshold is about 50 ng/l in white wine. The fast analysis of TBA was achieved with a preconcentration step using SPME followed by GC/MSMS detection. (LOD = 2 ng/l)

[1] H Tanner, C. Zannier, H.R. Buser, *Schweizerische Zeitschrift für Obst- und Weinbau.* **1981**, *117*, 97-103.
[2] F.B. Whitfield, J.L. Hill, K.J. Shaw, *J. Agric. Food Chem.* **1997**, *45*, 889-893. (and refs therein)

Analytical Chemistry **35**

A study on the interlaboratory influence on column evaluation

Stella C., Rudaz S., Veuthey J.-L.[1]

Laboratory of Pharmaceutical Analytical Chemistry-School of Pharmacy-University of Geneva, Geneva, CH

The popularity of reversed-phase liquid chromatography (RPLC) has increased to the point where it is used in almost 70% of all LC separations. Therefore, manufacturers are continuously improving and introducing new HPLC phases, in particular for the analysis of basic compounds. Selecting the appropriate stationary phase for a specific separation is an important parameter in the development of LC methods. In order to characterize and evaluate the relative chromatographic performances of stationary phases, a series of chromatographic tests are proposed in the literature. In a previous work, a chromatographic test for the characterization of base deactivated columns was developed. The aim of the present study was to evaluate the reproducibility of the chromatographic data between different laboratories (n = 6) following the same analytical procedure. With this aim, all the work was carried out using two chromatographic supports. Furthermore, the phase mobile preparation was carefully specified and the test solutions prepared by the same operator. Some neutral compounds were also injected in this study to evaluate the extra-column volume. In addition, the influence of the column thermoregulation system on the chromatographic data was studied. Thanks to this study, it could be demonstrated that, for the same support, the interlaboratory variability (between six laboratories) was quite low and even better than the inter-batch variability (n = 3) obtained in the same laboratory. This suggested that chromatographic performance of columns tested in different laboratories can be compared with the same chromatographic test.

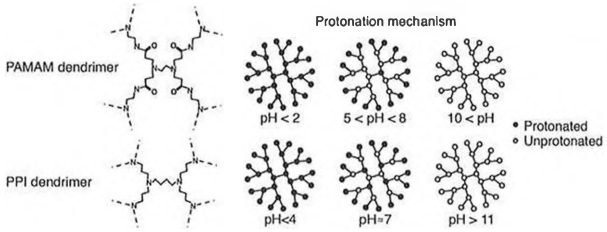
Analytical Chemistry **36**

Resolution of Microscopic Protonation Equilibria for Poly(amidoamine) and Poly(propyleneimine) Dendrimers

Dusko Cakara, Jörg Kleimann, Michal Borkovec

Colloid and Surface Chemistry Laboratory, CHIAM, University of Geneva 30, Qaui Ernest Ansermet, 1211 Geneva, Switzerland

Constant ionic strength potentiometric titrations of six different generations of poly(amidoamine) (PAMAM) dendrimers were performed at different levels of added KCl. From the resulting titration curves, microscopic protonation constants were obtained by means of a non-linear least squares method. The regularity in the molecular structure allows us to model these constants in terms of a simple site-binding model, and deduce the precise microscopic speciation at each stage of the titration (i.e. protonation mechanism). Further, we compare the titration curves and the corresponding protonation mechanisms of poly(amidoamine) and poly(propyleneimine) (PPI) dendrimers (see figure). In spite of their chemical similarity, their protonation behavior turns out to be significantly different. While the intermediate protonation state for PAMAM dendrimers is featured with the outer rim and a core site protonated, for PPI dendrimers the protonated sites are found in alternating shells. We explain this difference by electrostatic repulsion between the neighboring protonated sites, which decreases with an increasing chain length between them, and thus for the PAMAM dendrimers is significantly lower than for the PPI dendrimers.



Analytical Chemistry **37**

Amperometric Biosensor for Taste of Tomato Paste

Gleb Zhylyak, Rasa Pauliukaite, Daniel Citterio and Ursula Spichiger

Centre for Chemical Sensors and Information Technology, ETH Technopark, Technoparkstrasse 1, CH – 8005, Zürich, Switzerland

Glutamic acid or monosodium glutamate (MSG) gives food enjoyable taste – Umami. Some kinds of vegetables such as corn and ripe tomato have quit a high amount of MSG (130-140 mg per 100 g of vegetable). Nevertheless, MSG is added to the tomato foods, e.g. tomato paste, sauces, juice, and other products for their seasoning. Since MSG causes some allergic reactions such as tension in stomach, headache, pain in neck and shoulders, tachycardia, and etc. known as "Chinese Restaurant Syndrome", it is relevant to qualify the taste of tomato food. Our aim was to develop an amperometric biosensor for monitoring the *L*-glutamate concentration in different kinds of tomato products.*

Biosensor is constructed from mediating paste, where conductive organic complex salt – tetrathiafulvalene and 7,7,8,8-tetracyanoquinodimethane – serves as a mediator - electron transferor, carbon paste with silicon oil [1], and *L*-Glutamate Oxidase (GLOD) from *Streptomycis* sp. cross-linked on the surface of the paste electrode. Taste biosensor should meet the goals of high selectivity (working at an applied potential < 100 mV), sensitivity, negligible leaching of enzyme and mediator, response in the range between 0.25-2 mM of *L*-glutamate, and lifetime at least 10 days. Since GLOD is active only in neutral medium, and pH of tomato foods is 3.3-4.5. Consequently, the tomato paste samples have to be diluted and buffered to pH 7. The biosensor developed complies with goals, and results obtained with biosensor are comparable to standard reference method.

1. U. Korell, U.E. Spichiger. *Electroanalysis*, **1994**, *6*, 305.

* This work is based on the basis of the Innovative Functional Materials and Associated Technologies for the Development of New Improved Chemical Sensors (MICS), EU-Project No. GR01-2øøø-25288.

Analytical Chemistry **38**

Capillary Electrophoresis – Mass Spectrometry for the Analysis of a Pharmaceutical Formulation

Geiser L. ; Schappler J. ; Rudaz S. ; Veuthey J.-L.

Laboratory of Pharmaceutical Analytical Chemistry, School of Pharmacy

University of Geneva, Bd d'Yvoy 20, 1211 Geneva 4, Switzerland

Despite the wide application range of UV detectors, capillary electrophoresis (CE) coupled to UV exhibits a lack of sensitivity in the quantification of some compounds present at low concentration or with low UV absorbance. Hence, the use of a mass spectrometer (MS) in the selected ion monitoring (SIM) mode may expand CE potential for quantification, due to its great selectivity and sensitivity. The coupling of CE-MS with an electrospray ionisation technique (ESI) is generally used for qualitative applications. However, only few quantitative results have been reported by CE-ESI-MS.

First, some important ESI criteria were studied to ensure stable conditions and improve CE-ESI-MS quantitative performances. Investigated parameters were sheath liquid composition, nebulizing gas pressure and position of the CE capillary outlet.

Afterwards, quantitative performances achieved by CE-ESI-MS were compared to those obtained by CE-UV. For this purpose, a pharmaceutical formulation was selected with lidocaine as active principle, and validations were carried out according to SFSTP requirements [1]. Using an internal standard (procaine), an intermediate precision of about 5% was achieved by CE-ESI-MS.

Finally, a multiple injection procedure was developed to reduce the analysis time per sample and it was successfully applied to both CE-UV and CE-MS methods. The validation results achieved by the multiple injection were identical to those obtained with classical injection, but afforded a reduction of the analysis time by a factor of 2.5.

[1] J. Caporal-Gautier, J.M. Nivet, S.T.P. Pharma pratiques, 2 (4), 205-226, (1992)

Analytical Chemistry **39**

A finite element simulation study of surface adsorption in microfluidics systems

Andrea Lionello, Jacques Josserand, Henrik Jensen, Hubert Girault*

Laboratoire d'Electrochimie Physique et Analytique, EPFL, 1015 Lausanne, Switzerland

The kinetics of adsorption of a component onto the walls of a microchannel has been studied using finite element simulations. The model takes in account the diffusion coefficient, the initial concentration, the rate of adsorption and desorption of the adsorbate and the initial concentration of active sites present on the surface and enables to study the time evolution of the surface concentration and bulk concentration of the adsorbate. Calibration has been done for diffusion control adsorption in the cases of a linear adsorption isotherm [1] and for a Langmuir isotherm [2].

Comparison with experimental data from confocal microscopy measurements of the kinetics of adsorption of a fluorescent labelled IgG antibody on the walls of a PET channel has been performed; in this way it has been possible to reveal data such as bulk concentration, not easily accessible in other ways for such systems. The model provides a useful mean to obtain the optimal parameters (adsorption time, initial concentration of primary antibody and analyte, dimensions of the system) for the development of a fast ELISA test.

[1] P. Delahay, I. Trachtenberg, *J. Am. Chem. Soc.* **1957**, *75*, 2355.
[2] W. H. Reinmuth, *J. Phys. Chem.-US.* **1961**, *65*, 473.

Analytical Chemistry **40**

Protonation of Acidic Latex Particles in the Presence of an Adsorbed Basic Polyeletrolyte

Dusko Cakara, Claire Chassagne, Michal Borkovec

Colloid and Surface Chemistry Laboratory, CHIAM, University of Geneva

30, Quai Ernest Ansermet, 1211 Geneva, Switzerland

Mixtures of acidic latex particles and basic polyelectrolytes were investigated by means of potentiometric titrations at different ionic strengths and polyelectrolyte/latex dosages. The surface charge of the bare particles as a function of pH could be analyzed in terms of a well-established model that includes dissociation of the surface functional groups. When polyelectrolyte is added, the experimental titration curves at different ionic strengths are showing charge reversal at the same pH value, which depends on the amount of the adsorbed polyelectrolyte. This behavior could be predicted with an extension of the surface model by considering two types of charged surface groups: one corresponding to the functional groups of the particle, the other one corresponding to the functional groups of the adsorbed polyelectrolyte, evenly spread onto the surface.

Analytical Chemistry **41**

Development and Validation of a LCMS method for benzimidazoles in meat and meat products

Markus Zehringer and Mathias Stöckli

State-Laboratory Basel-City, Kannenfeldstr. 2, 4012 Basel

Benzimidazoles are antiparasitic drugs which are used against gastrointestinal parasites in cattle, swine an chickens. Residues of antiparasitics may occur in food derived from animals treated with such drugs. For toxicological reasons benzimidazoles can only be applied for therapeutical use. Maximum residue levels are established in Swiss Legislation for different matrices such as meat, liver or kidney ranging from 0.01 up to 1 mg/kg [1].
Due to the polar structure of the analytes reversed phase liquid chromatography with photodiode array detection (LC/DAD) is the method of choice [2-4]. On the basis of several published methods we developed a routine method with mass spectrometric detection. With this routine method it is possible to quantify and verify residues of albendazol, dimetridazol, fenbendazol, flubendazol, levamisol, mebendazol, oxyfendazol, oxybendazol, parendazol, thiabendazol and triclabendazol in meat and meat products.
The meat sample is minced and extracted with methanol. The extract is passed through a solid phase cartridge (extrelute) and eluted with dichloromethane/n-hexane. The eluate is evaporated to dryness and resolved with methanol. The methanolic solution is extracted with n-hexane to remove fat and then injected into the LC/MS. The analyses are performed with an LC coupled with an ion trap mass spectrometer. The analytes are separated on an inertsil ODS 3 100 x 3 mm RP column and analysed in full scan mode from m/z 100 – 500 after positive, atmospheric pressure chemical ionisation (APCI). For verification the extracts are measured in ms-ms-mode. Detection limits are 0.01 mg/kg for most of the analytes. Recovery studies are carried out for meat at residue levels from 0.1 to 0.01 mg/kg. Test samples at the level of 0.1 mg/kg showed recoveries between 65 and 105 % and between 41 and 131 % for 0.01 mg/kg. Total method uncertainty on the basis of a propabilitiy of 99 % (2σ) is estimated from 23 % (oxybendazol) up to 64 % (albendazol).

[1] Eid. Departement des Innern: Verordnung über Fremd- und Inhaltsstoffe in Lebensmitteln, *Liste 3* **1995**, rev. **2002**.
[2] Aerts, Rene M. L. et. al., *J. Assoc. Off. Anal. chem.* **1991**, *74*, 46 – 55
[3] Long, Austin .r. et. al., *J. Assoc. Off. Anal. chem.* **1989**, 72, 739 – 741
[4] Eid. Departement des Innern: *Schweizerisches Lebensmittelbuch*, **1999**, Kapitel 55

Analytical Chemistry **42**

Combination of FIA-ES/TOF-MS LC-ES/MS, LC-APCI/MS and GC-MS for a comprehensive metabolomic study of *Arabidopis thaliana* submitted to a pathosystem.

A. Thiocone[a], S.C. Mende[a], E.E. Farmer[b], J.-L. Wolfender[a]*

[a]Institut de Pharmacognosie et Phytochimie, Université de Lausanne, BEP, CH-1015 Lausanne, [b]Laboratoire d'Expression Génétique, Université de Lausanne, BB, CH-1015 Lausanne

Response to stress in plants is the result of complex signal transduction which depends, in part, on low molecular mass regulators and which is not yet completely understood [1]. In order to detect and identify new signalling molecules, a non-targeted differential metabolite profiling approach (metabolomics) has been developed using *A. thaliana* as a model organism. The array of metabolites produced by this plant was analysed by a combination of direct FIA-ES-TOF/MS of the crude extracts, for a rapid prescreening, followed by comprehensive LC-APCI/MS, LC-ES/MS and GC/MS profiling of the stress induced metabolites. Various chemometric methods for the deconvolution of the complex sets of MS data such as background noise reduction, peak alignment and systematic single ion traces comparison were developed. In a preliminary phase, general stress induction methods such as wounding were used and, besides known wound-inducible compounds, a series of unknown metabolites were detected. In a second phase *A. thaliana* was challenged with the bacterial pathogen (*Pseudomonas syringae pv tomato*, Pst). Less metabolome modifications were recorded in the pathosystem than in the wound response but defence compounds that are systematically induced, independently from sample to sample variations, could be efficiently evidenced following this approach. An assessment of the defence signalling potential of these latter molecules by checking their ability to activate defence genes is foreseen.

[1] E.E. Farmer, E. Alméras. V Krishnamurthy, *Curr. Opin. Plant Biol.* **2003**, 6, *in press*.

Analytical Chemistry **43**

Polymer nanosprays for sample preparation in proteomics

Niels Lion[1], Jean-Olivier Gellon[1], Joël S. Rossier[2], Hubert H. Girault[1]

[1]Laboratoire d'Electrochimie Physique et Analytique, Ecole Polytechnique Fédérale de Lausanne, CH-1015 Lausanne
[2] DiagnoSwiss SA, c/o CIMO, rue de l'Ile au Bois, CH-1870 Monthey

Electrospray Ionization Mass Spectrometry (ESI-MS) has become over the last 15 years a central analytical technology for peptide and protein characterization and identification. The advent of proteomics has pushed the trend towards the development of high-throuput technologies for sample preparation and delivery to the mass spectrometer. We present herein the addition of a sample preparation functionality to polymer nanosprays developed in the laboratory [1-2]. A piece of polyvinylidene fluoride membrane is placed at the inlet of the nanospray, and used as a solid-phase for sample desalting and solvent exchange: first analytes in aqueous buffers are flown through the membrane in which they are retained through hydrophobic interactions. Salts are then washed out with water, and the spraying solution is applied. Analytes are therefore eluted from the membrane and sprayed to the mass spectrometer at the same time. This scheme has been characterized with model compounds [3], as well as in the presence of different cosolvents used in protein sample preparation (chaotropes for protein solubilization and reducers for disulfide bridge reduction) [4]. Moreover, tryptic peptide digests of proteins isolated by 2D-gel electrophoresis were successfully analyzed, avoiding the need for manual sample desalting, which shows the interest of functionality integration on microsystems for proteomics.

[1] Rohner TC, Rossier JS, Girault HH, *Anal. Chem.*, **2000**, *73*, 5353.
[2] Gobry V, van Oostrum J, Matinelli M, Rohner T, Rossier JS, Girault HH, *Proteomics*, **2002**, 2, 405.
[3] Lion N, Gobry V, Jensen H, Rossier JS, Girault HH, *Electrophoresis*, **2002**, 23, 3583.
[4] Lion N, Gellon JO, Jensen H, Girault HH, *J. Chrom. A*, **2003**, *in press*

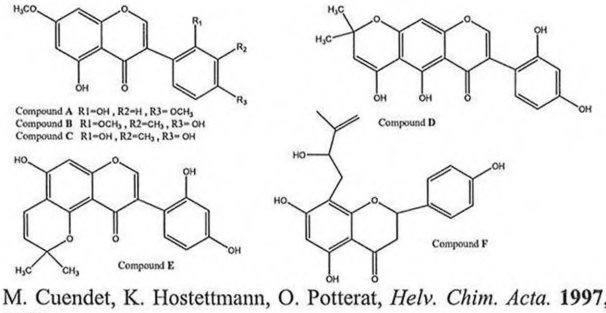
Analytical Chemistry **44**

Isolation of new flavonoids from *Eriophorum scheuchzeri* Hoppe (Cyperaceae)

M. Maver, E.F. Queiroz, J.-L. Wolfender, K. Hostettmann*

Institut de Pharmacognosie et Phytochimie, Université de Lausanne, BEP, CH-1015 Lausanne

In the course of our studies on alpine plants, the CH_2Cl_2 extract of *Eriophorum scheuchzeri* Hoppe was investigated. The targeted isolation of the compounds exhibiting radical scavenging proprieties towards the DPPH radical [1] lead to the isolation of two already known antioxidant constituents, a methoxyflavone (tricine) [2], a methoxyisoflavone (cajanin) and six new flavonoids: isoflavones **A, B, C,** isopyranoflavones **D, E,** and flavanone **F**. Compounds **C, D, E, F** also showed antifungal activities against *Cladosporium cucumerinum*, and *Candida Albicans* on TLC bioautography. Based on this investigation, the LC/UV/MS analysis enable a survey of the chemical constituents of two related species *E. angustifolium* Honck and *E. latifolium* Hoppe.



[1] M. Cuendet, K. Hostettmann, O. Potterat, *Helv. Chim. Acta.* **1997**, *80*, 1144.

45

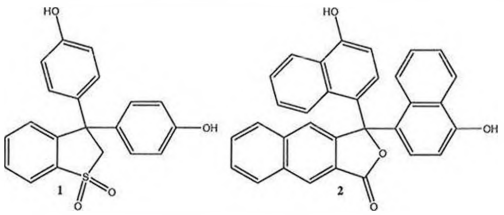
Analytical Chemistry

Optical Sensor for CO_2

Rita Cannas, Gleb Zhylyak, Tomas Nezel, Ursula Spichiger

CCS-ETH Technopark, Technoparkstrasse 1, 8005 Zürich, Switzerland

The development of optical sensors for detection of gases, ions, and molecules of physiological and biological importance has now become a well-established field of research. One gas of particular interest is CO_2 as its quantitative detection is important in such fields as medical monitoring and food packaging.
The use of an optical sensor was first introduced by Mills and coworkers [1]. The optical sensor is constituted by a plastic film which utilise a pH sensitive hydrophilic indicator dye, phenol red **1**, combined with a phase-transfer agent, Q^+OH^-, to form an ion pair, Q^+D^-, which can be dissolved in a hydrophobic, plasticised polymer
In order to find a correlation between the structure and the activity of the dye we studied several commercial dyes, containing different functional groups.



We found that the best result was obtained with naphtholphthalein, **2**, which demonstrated sufficient sensitivity to CO_2, reversibility and stability for more than a month and was practically inert to the humidity.
We also investigated the mechanism of the interaction between the dye and the carbon dioxide, with a modified ATR FT-IR spectrometer.

[1] Mills, A.; Lepre, A.; Wild, L. *Sensors and Actuators B* **1997**, 419.

46

Analytical Chemistry

CHEMICAL COMPOSITION OF SECONDARY ORGANIC AEROSOL FROM AROMATIC COMPOUNDS PRODUCED IN A SMOG CHAMBER

M. Sax[1,2], M. Kalberer[1], R. Zenobi[1], D. Paulsen[2,1], U. Baltensperger[2]

[1]Department of Chemistry and Applied Biology, ETH Zürich, 8093 Zürich, Switzerland.
[2]Paul Scherrer Institut, 5232 Villigen-PSI, Switzerland

Upon photooxidation, reaction products of aromatic hydrocarbons form secondary organic aerosol (SOA). In this study we performed experiments with 1,3,5-trimethylbenzene (1,3,5-TMB) in a smog chamber (a 27 m^3 bag made out of Teflon™) to study the formation and composition of SOA. We report the results of an investigation with different NO_x-concentrations and different aromatic hydrocarbon concentrations upon irradiation with light similar to the solar spectrum. For detailed chemical analysis, the aerosol and gas phases were separated and collected with a filter- polyurethane foam (PUF)-line [1, 2]. The extracts are measured with GC-MS to give information on a molecular level. Simultanously, we sampled the particle phase on ZnSe and steel plates, respectively, with a cascade impactor at a flow rate of 10.7 L min^{-1}. The ZnSe plates are transparent to IR light and were therefore used to study the functional groups present in the aerosol with IR spectroscopy. Over the course of a 24h reaction time we observed a shift in the associated OH-band as well as an increase in the C=O signal at 1730cm^{-1}. The signals at 1650 and 1280cm^{-1} indicate O-NO_2 groups, that decrease in time. The steel plates were used for laser desorption ionization mass spectrometry (LDI-MS) experiments to gain information about high molecular weight compounds. We consistently observed peaks up to *m/z* 400 indicating polymerization reactions.

[1] L.A. Gundel, V.C. Lee, K.R.R. Mahanama, R.K. Stevens, J.M. Daisey, *Atmos. Environ.* **1995**, *29*, 1719.
[2] R.L. Maddalena, T.E. McKone, N.Y. Kado, *Atmos. Environ.* **1998**, *32*, 2497.

47

Analytical Chemistry

Infinite enantiomeric resolution of selected basic compounds in capillary electrophoresis

S. Rudaz[1], E. Calleri[2], L Geiser[1], J. Prat[1], JL. Veuthey[1]

[1]Laboratory of Pharmaceutical Analytical Chemistry, School of Pharmacy, University of Geneva, 20 Bd D'Yvoy, 1211 Geneva, Switzerland

[2]Department of Pharmaceutical Chemistry, University of Pavia, Via Taramelli 12, I-27100 Pavia, Italy

The enantioseparation of selected basic compounds namely, methadone, venlafaxine, fluoxetine and tramadol was studied using highly sulfated gamma cyclodextrin (HS-γ-CD) as chiral selector. The baseline separation of these compounds was achieved in reverse polarity mode. Because CD are not suitable for ESI-MS, this mode was not compatible with the use of mass spectrometry detection. Separation optimisation was carried out in normal polarity mode with the partial-filling technique. Stereoselective resolutions were obtained at low concentration of HS-γ-CD, demonstrating the high resolution power of this chiral selector towards basic compounds. When increasing the chiral selector concentration, one enantiomer only was detected achieving an infinite enantioselectivity. In fact, a CD concentration was determined for each analyte where one enantiomer still migrated cationically while the other migrated anionically. This phenomenon, theoretically predicted by the CHARM model developed by Vigh et al., was investigated by pressure-assisted experiments. For all analytes, experimental conditions allowed to reach an infinite chiral resolution.

48

Analytical Chemistry

Coupling GC-MS with PTR-MS for unambiguous chemical characterization of on-line PTR-MS spectra

Chahan Yeretzian[1*], Christian Lindinger[1,2], Philippe Pollien[1], Santo Ali[1], Tilmann Märk[2]

[1] Nestlé Research Center, Vers-chez-les-Blanc, 1000-Lausanne, Switzerland
[2] Institute of Ion Physics, University of Innsbruck, A-6020 Austria

This work introduces a significant technical extension of Proton-Transfer-Reaction Mass-Spectrometry (PTR-MS) [1-6]. Coupling gas chromatographic (GC) neutral separation with simultaneous detection by PTR-MS and Electron-Impact-MS, makes an unambiguous chemical interpretation of complex PTR-MS spectra feasible. In order to exploit the full potential of the coupling, the PTR-MS was upgraded with the recently introduced Fast Drift Tube (FDT). Here a detailed discussion of selected technical aspects will be given, focusing in particular on critical modifications of the PTR-MS, the GC EI-MS and the automatic thermal desorber (ATD) necessary to operate

[1] Lindinger, W.; Hirber, J.; Paretzke, H. *Int. Journal of Mass Spec. and Ion Processes* **1993**, *129*, 79-88.
[2] Yeretzian, C.; Jordan, A.; Lindinger, W. *Int.J.Mass Spec.* **2003**, *223-224*, 115-39.
[3] Karl, T.; Yeretzian, C.; Jordan, A.; Lindinger, W. *Int.J.Mass Spec.* **2003**, *223-224*, 383-95.
[4] Yeretzian, C.; Jordan, A.; Badoud, R.; Lindinger, W. *Eur.Food Res.Technol.* **2002**, *214*, 92-104.
[5] Karl, T.; Prazeller, P.; Mayr, D.; Jordan, A.; Rieder, J.; Fall, R.; Lindinger, W. *J.Appl.Physiol.* **2001**, *91*, 762-70.
[6] Lindinger, W.; Hansel, A.; Jordan, A. Chemical Society Reviews 1998, 27, 347-54.

Analytical Chemistry **49**

Characterization of humic-like substances in atmospheric aerosols by Laser Desorption / Ionization Mass Spectrometry and Size Exclusion Chromatography

V. Sambourova, M. Kalberer and R. Zenobi

D-CHAB, ETH Zürich, 8093 Zürich, Switzerland.

The presence of macromolecules in atmospheric aerosols was first reported in 1960 [1]. Later the term Humic-Like Substances (HULIS) was suggested for these compounds [2]. HULIS may be an important fraction of the organic aerosol mass. The chemical nature of these macromolecules is poorly however understood. Also, quantitative methods for analyzig HULIS are not well established. Thus the aim of this work is to investigate in detail the properties of these macromolecules in urban aerosols and to develop a quantitative method for HULIS.
Urban aerosols were sampled in downtown Zurich. Airborne particulate matter was collected on quartz fiber filters using a high volume sampling system. Day-time and night-time samples were collected separately during one month. Laser Desorption/Ionization Mass Spectrometry (LDI) and Size Exclusion Chromatography (SEC) were employed to characterize HULIS.
Filter extracts (aqueous, methanol, tetrahydrofuran, toluene, basic extracts) were analysed using SEC. Chromatograms from the ambient aerosol samples were compared with humic acid standards. LDI spectra of the aerosols show three main regions with higher peak intentsities (i.e., m/z < 250, m/z 1000-2000, m/z 3000-4000).These results correspond well with the SEC measurements. Different extracts (unpolar, polar solvents) from filters were fractionated by SEC and investigated by MALDI spectrometry to compare these two techniques.

[1] Went, F.W., *Nature.* **1960**, 187, 641-643.
[2] Havers, N., Burba, P., Lambert, J., Klockow, D., *J. of Atmos. Chem.* **1998**, 29, 45-54.

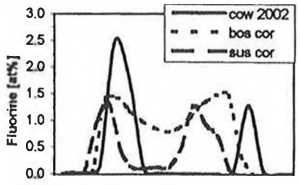
Analytical Chemistry **50**

Examination of Fluorine Diffusion Processes in Archaeological Bones and Artificial Doping

Annina Gaschen[*], *Urs Krähenbühl*[*], *Max Döbeli*[#]

[*]*Department of Chemistry and Biochemistry, University of Berne, CH-3012 Berne, Switzerland,* [#]*Paul Scherrer Institute, IPP HPK H32, c/o ETH-Hönggerberg, CH-8093 Zurich, Switzerland*

In humid soil hydroxyl-apatite ($Ca_5(PO_4)_3OH$), the main component of bone and teeth substance, is transformed into the hardly soluble and very stable fluorine-apatite ($Ca_5(PO_4)_3F$). So fluorine will be enriched in bones buried in humid soils by adsorption and diffusion from the outer bone surface and from the marrow cavity towards the bulk of the structure. The fact that under stable environmental conditions the fluorine-uptake leads to an u-shaped concentration profile suggested the idea of using fluorine diffusion for dating[1,3]. Taking into account the mathematical theory of diffusion, the profile itself carries the information on the duration of this process.
The fluorine profile was determined by proton induced gamma emission (PIGE-NRA) with a scanning milliprobe beam using the nuclear reaction $^{19}F(p,\alpha\gamma)^{16}O$.
This investigation brings into focus the interaction and the dependency of fluorine accumulation on bone diagenesis[2]. Site-specific parameters, especially water conditions and dry periods in soils can strongly affect the diffusion-process and make it very difficult to understand the uptake of halogens. So attempts to develop a fluorine dating method are not straightforward and need further careful investigation of bone and environmental parameters.



Archaeological bones (~3760 b.c.) can show either advanced (bos cor) or undeveloped (sus cor) profile shapes. For comparison an artificially doped fresh sample (cow 2002). Bone surface (left), marrow cavity (right).

[1] C. Kottler et al., Nucl. Instr. and Meth. in Physics Research B 188 (2002) 61-66
[2] R.E.M. Hedges, A.R. Millard, J. of Arch. Sci. (1995) **22**, 201-209
[3] G. E. Coote, Nucl. Instr. and Meth. B66 (1992) 191-204

Analytical Chemistry **51**

Use of monolithic supports for the direct injection of drugs and metabolites in plasma

S. Souverain, S. Rudaz, J.-L. Veuthey
Laboratory of Pharmaceutical Analytical Chemistry, School of pharmacy, University of Geneva, 20 Bd d'Yvoy, 1211 Geneva, Switzerland.

Liquid chromatography coupled to mass spectrometry (LC/MS) with an on-line sample extraction raises a great interest for the rapid analysis of compounds from biological matrices. Among extraction supports compatible with a direct injection of blood samples, restricted access media (RAM) [1] and large size particles (LPS) [2] sorbents are the most commonly used. The latter, which tolerate the direct and repetitive injection of biological matrices, allow the simplication and the speeding-up of the sample preparation step. These sorbents retain selectively small analytes while high molecular weight compounds, suchs as proteins, are excluded. Exclusion is mainly due to the particular chemistry of the stationary phase or to the high flow rate applied for RAM and LPS sorbents, respectively.
Recently, monolithic columns have been commercialized to improve chromatographic performances. Thank to their high porosity (c.a. 80%), these columns allow a fast separation at high flow rate without generating excessive back-pressure [3]. Furthermore, the absence of frits at column extremities are advantageous to consider monolithic support as a suitable tool for the rapid direct injection of biofluids [4].
In this work, monolithic supports are evaluated for the direct injection of plasma samples which contain various drugs and their metabolites. A rapid and sensitive method was developed with a short monolithic column (Chromolith Flash column 25 x 4.6 mm I.D.) as extraction and enrichment support coupled to an octadecyl microbore analytical column. The method permits the simultaneous analysis, including extraction and chromatographic separation, of three drugs and their primary metabolites (namely fluoxetine and norfluoxetine, methadone and EDDP, flunitrazepam and norflunitrazepam) in less than 10 min. The method developed exhibited great selectivity and sensitivity. Indeed, for all investigated compounds, the limits of quantification (LOQ) were estimated in the $ng.mL^{-1}$ range for an injection volume of 50 µL. The method developed was also successfully applied to real clinical cases.

[1] K.-S. Boos, A. Rudolphi LC-GC, 15, 602-611 (1997).
[2] C. J. Oberhauser *et al.* LC-GC, 18, 716-724 (2000).
[3] N. Tanaka et al. J. High Resol. Chromatogr. 23, 111-116 (2000)
[4] R. Plumb *et al.* Rapid Commun. Mass Spectrom., 15, 986-993 (2001)

Analytical Chemistry **52**

Development of a long travel sample stage for µ-XRF – profiling of large samples

Beat Aeschlimann, Markus Küpfer, Detlef Günther

ETH Zürich, Laboratory for Inorganic Chemistry
ETH Hönggerberg, CH-8093 Zürich

Recent results have shown that X-ray fluorescence with a spatial resolution of 50 µm (µ-XRF) is well suited to determine the elemental distribution of major and minor elements in a wide range of samples [1]. In order to allow large samples to be analyzed without cutting, a long-travel sample stage was constructed, which can hold samples of up to 1000 mm length and 150 mm width.
The current version uses the original sample stage for computer-controlled sample targeting and positioning, which has an operating distance of 100 mm. Thus, the sample needs to be moved along a graduated bar after each run to cover the entire sample length. Indicators, placed on the sample surface are used to determine the start- and endpoint of each run.
The source/detector unit is removed from its original position and placed over the long-travel stage for analysis.
Future modifications will include full computer control over a new 1200 mm sample stage to allow automated analysis of an entire sample.
This poster will present the design of the system and first results obtained on sediment samples.

[1] G. H. Haug, D. Günther, L. C. Peterson, D. M. Sigman, K. A. Hughen, B. Aeschlimann, *Science* **2003**, 299, 1731

53

Analytical Chemistry

Effect of different matrices on transport and ionization in LA-ICP-MS

Ivana Bindzarova, Detlef Günther

ETH Zürich, Laboratory for Inorganic Chemistry
ETH Hönggerberg, CH-8093 Zürich

Laser ablation inductively coupled plasma (LA-ICP-MS) has become a versatile analytical tool for direct solid samples analysis and bulk analysis. Despite several achievements in development, there is still a requirement for instrumental improvement. Namely, its applicability in elemental analysis is often limited by matrix effects as elemental fractionation at the ablation spot, transport efficiency to the ICP, atomization efficiency of particles, total ionization efficiency of atoms in the ICP and space charge effects, which have to be taken all into account when performing laser ablation analysis.
The size of laser-induced particles affects the vaporization and ionization efficiency to certain extent in the ICP [1]. In this study different powder samples (CaO, CuO, SiO_2, TiN, TiC, V_2O_5, ZnO) and their mixtures were investigated to determine the influence of different matrices on the abovementioned matrix effects. A 266nm Nd:YAG laser was used for ablation, and the response of given analytes in the plasma was measured. In addition, the particles size distribution was manipulated by a separation device, which allows effective particle separation and removal using centrifugal forces in a thin, coiled tube [1].
This work presents the influence of different matrix compositions as well as particles size distributions, produced during laser ablation, and their effect on ionization efficiencies in the ICP.

[1] M. Guillong, H. R. Kuhn, D. Günther, *Spectrochim. Acta, Part B* **2003**, 58, 211.

54

Analytical Chemistry

Electrospray ionization mass spectrometry for the determination of binding constants for metal ion binding to peptides

Arno Wortmann, Francesco Rossi, Gerald Lelais, Renato Zenobi

Swiss Federal Institute of Technology Zürich, Wolfgang-Pauli-Str. 10, CH-8093 Zürich

Electrospray ionization mass spectrometry is a soft ionization method for the intact transfer of large molecules like proteins and even noncovalent complexes into the gas phase [1]. Hence, strategies were developed to determine binding constants of noncovalent assemblies [2].
Mass spectrometry has the advantages of very low sample consumption, no need for labeling the target and the possibility of simultaneously monitoring binding properties for more than one species.
Here we present a strategy to determine binding constants for metal ion binding to peptidic molecules, based on solution parameters. As model compounds we used beta-peptides [3] with the ability to bind zinc with high affinity and specificity. Different control experiments were designed to prove the specifity of the zinc-binding and to exclude artifacts.

[1] J. A. Loo, *Mass Spectrometry Reviews*, **1997**, 16, 1-23
[2] J. M. Daniel, S. D. Friess, S. Rajagopalan, S. Wendt, R. Zenobi, *International Journal of Mass Spectrometry*, **2002**, 216, 1-27
[3] D. Seebach, J.L. Matthews, *Chemical Communications*, **1997**, 2015-2022

55

Analytical Chemistry

Open-path spectroscopic detection of trace gases with quantum-cascade lasers: Potential and challenges

R. Jiménez, M. Taslakov, V. Simeonov, B. Calpini and H. van den Bergh

Air Pollution Laboratory (LPAS), EPFL, CH-1015 Lausanne, Switzerland

Finite volume atmospheric models are the only scientifically relevant pollution abatement decision-making tools at the present time. Their averaged description of the atmosphere entails validation measurements of similar spatial resolution. Current open-path (OP) spectroscopic monitoring techniques (DOAS, OP-FTIR, TDLAS) provide such measurements but attain only a limited number of species and have several intrinsic limitations [1]. The advent of the quantum-cascade laser (QCL) in 1994 [2], and its rapid development thereafter, offers to open-path absorption spectroscopy a promising doorway to the mid-IR.

QCL trace gas detection has been already successfully demonstrated in multipass cells operated at low pressure for sensitivity improvement. These measurements are nevertheless local and require sample manipulation. Our research aims at developing non-contact, long atmospheric path trace gas detection systems. Operation at atmospheric pressure is nevertheless disadvantageous due to line broadening.

We have recently demonstrated ozone measurements at room pressure with a ~9.6 μm, single mode (~0.13 cm^{-1} FWHM), pulsed-operated DFB QCL [1]. Concentrations were retrieved by differential absorption, a method that appears particularly well suited for open path applications. Preliminary measurements over a 460 m open-air path showing no photon limitation are encouraging. Several QCL instrumental aspects, including baseline, linewidth, wavelength scanning and detection limits are discussed.

[1] R. Jiménez, M. Taslakov, V. Simeonov et al, *Appl. Phys. B* **2003**, submitted.
[2] J. Faist, F. Capasso, D.L. Sivco et al, *Science* **1994**, 264, 553.

56

Analytical Chemistry

Multi Physical-Chemical Profiler for Real-time Continuous In situ Monitoring of Specific Fractions of Trace Metals and Master Variables

Mary-Lou Tercier-Waeber[1*], Fabio Confalonieri[2], Antonio Sina[2], Flavio Graziottin[2], Jacques Buffle[1]

[1]University of Geneva, 30 Quai E.-Ansermet, 1211 Geneva 4, Switzerland
[2]Idronaut Srl, Via Monte Amiata 10, 20047 Brugherio (MI), Italy

Novel analytical tools allowing real-time monitoring as well as detailed temporal and spatial evolution of the distribution of specific metal species and master variables is of prime interest to better understand the role and the fate of trace metals in coastal aquatic ecosystems [1,2].
The development of a Multi Physical-Chemical Profiler (MPCP) will be presented. The MPCP allows simultaneous in situ, autonomous monitoring of three specific fractions of Cu(II), Pb(II), Cd(II) and Zn(II): i) free metal ion concentrations which is known to be related to biological uptake, ii) the dynamic Me species which are potentially available for organisms, iii) the particulate and colloidal species (total extractable Me concentration minus dynamic fractions) which play important role in transport properties and residence time, as well as master variables (P, T, pH, O_2, conductivity, salinity, redox E and chlorophyll a). It is based on unique gel integrated voltammetric microsensors, a submersible probe with three independent measuring channels, a submersible flow-injection system, integrated conventional physical/chemical sensors. The characteristics of the microsensors and main components of the probe will be summarized. Its environmental utility will be illustrated with examples of in situ applications in various aquatic systems.

[1] *In situ monitoring of aquatic systems; Chemical analysis and speciation.* Buffle J. and Horvai G. (Eds.), IUPAC Series in Analytical and Physical Chemistry of Environmental Systems. Chichester, Wiley, **2000**.
[2] Tercier-Waeber M.-L., Buffle J., Koudelka-Hep M., Graziottin F. in : *Environmental Electrochemistry: Analysis of Trace Element Biogechemitry.* Taillefert M. and Rozan T.F. (Eds.), ACS Symposium Series No. 811, Washington DC, 2002, Ch. 2, pp. 16-39.

Analytical Chemistry **57**

Complexing Gel Integrated Microelectrode Array for Direct Detection of Free Metal Ion Concentrations in Natural Waters

Stéphane Noël, Lin Lin, Mary-Lou Tercier-Waeber*, Jacques Buffle

CABE, University of Geneva, 30 Quai E.-Ansermet, 1211 Geneva 4, Switzerland

Measurements of relevant fractions of trace metals in natural waters are essential to improve our understanding of their behavior and long-term impact [1]. Free metal ions is of particular interest since these species are related to biological uptake. Their reliable detection in aquatic systems is however a challenging task.

A novel Complexing Gel Integrated Microelectrode (CGIME) has been developed to allow simultaneous direct monitoring of free ion concentrations of several metals in natural waters. It is based on the Gel Integrated Microelectrode (GIME) [2] and the Diffusion Gradients in Thin-films (DGT) [3] principles. The surface of an Ir-based microelectrode array is covered with a 2.7 μm thin Microchelex chelating resin which in turn is covered with a 300 μm thick agarose gel. The Hg layers are electrochemically deposited and reoxidized through both layers. During equilibration with the test water, metals accumulate on the Microchelex resin in proportion to the free metal ion concentrations. After equilibration, the sample solution is replaced by an acidified electrolyte solution. The metal accumulated are released by the acid, and immediately measured by the voltammetric microsensor. Laboratory optimization of the key analytical conditions and on-field applications in sea water will be shown.

[1] *In situ monitoring of aquatic systems; Chemical analysis and speciation.* Buffle J. and Horvai G. (Eds.), IUPAC Series in Analytical and Physical Chemistry of Environmental Systems. Chichester, Wiley, **2000**.
[2] C. Belmont-Hébert C., M.-L. Tercier, J. Buffle, G.C. Fiaccabrino, M. Koudelka-Hep, *Anal. Chem.* **1998**, *70*, 2949.
[3] H. Zhang H., W. Davison, *Anal. Chem.* **1995**, *67*, 3391.

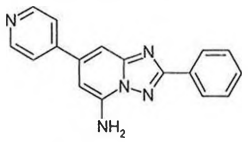
Medicinal Chemistry **58**

Enhancing the Hit to Lead Generation Process: a Case Study with Aryl-[1,2,4]-Triazolo-[1,5-a]-Pyridine Derivatives as Adenosine-2a Receptor Antagonists

Matthias Nettekoven and Alexander Alanine*

F. Hoffmann-La Roche, Grenzacher Str. 124, CH-4070 Basel, Switzerland.

The hit to lead generation process is an increasingly complex and critical one as it strongly influences the success potential of further optimization to a drug development candidate [1]. Recent advances in hit-to-lead tools, processes and the lead generation approach at Roche will be described. This will be illustrated by following the course of screening hit (compound **1**), through the various hit-to-lead exploration activities.



(1) hA2a, K_i=154 nM

The importance of the synthetic assembly strategy [2] [3] and its impact on structure activity relationship (SAR) exploration will be highlighted as well as the critical role of key physiochemical and drug-like properties, in the context of an increasingly multi-dimensional optimization (MDO) process.

[1] Alanine, A.; Nettekoven, M.; Roberts, E.; Thomas, A. W.; *Combin. Chem. & High Throughput Screen.*, **2003**, *6(1)*, 51-66.
[2] Nettekoven, M.; *Synlett* **2001**, *(12)*, 1917-1920.
[3] Brodbeck, B.; Pullmann, B.; Schmitt, S.; Nettekoven, M.; *Tetrahedron. Letts.* **2003**, *44(8)*, 1675-1678.

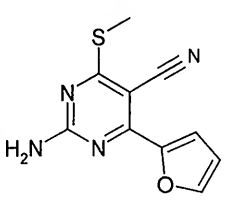
Medicinal Chemistry **59**

Development of 2-Amino-Pyrimidines as Selective Adenosine hA_{2a} Receptor Antagonists

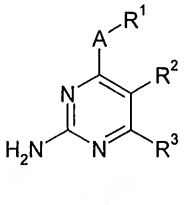
Roger D. Norcross,* Alex Alanine, Gavin J. Kilpatrick, Jean-Luc Moreau, Sonia M. Poli

F. Hoffmann-La Roche AG, CH-4070 Basel, Switzerland

Antagonists of the human adenosine A_{2a} receptor show potential as therapeutic agents in the treatment of a number of disorders of the central nervous system, such as Parkinson's Disease [1]. A random screen of the Roche compound library led to the identification of several 2-amino-5-cyano-pyrimidines – as exemplified by RO-19-2712 (**1**) – possessing moderate binding affinity at the hA_{2a} receptor but lacking selectivity *vs* the other adenosine receptor sub-types. Systematic investigation of the structure-activity relationships (SAR) guided the optimization of this class to provide compounds (**2**) having significantly enhanced binding affinity at the A_{2a} receptor ($K_i \leq 1$ nM) and improved selectivity (100-1000 fold) *vs* the hA_1 receptor [2]. Many of these compounds displayed A_{2a} antagonistic activity in animal behavioural models.



1



2

[1] S. Hess, *Expert Opinion on Therapeutic Patents* **2001**, *11*, 1533.
[2] E. M. Borroni, G. Huber-Trottmann, G. J. Kilpatrick, R. D. Norcross, *PCT International Patent Application* WO0162233 (**2001**).

Medicinal Chemistry **60**

Structure-Based Approaches to the Discovery of Protein Kinase Inhibitors

Pascal Furet

Novartis Pharma AG/Oncology Research WKL-136.P.12, CH-4002 Basel Switzerland

Protein kinases form a large superfamily of homologous proteins accounting for about 1.7 % of all human genes with 518 members. These enzymes catalyze protein phosphorylation, one of the basic mechanisms of regulation of cellular processes. Thus, protein kinases play a key role in such important aspects of cell biology as signal transduction, cell cycle control and apoptosis to name a few. It is therefore no wonder that protein kinases are currently very popular therapeutic targets in the pharmaceutical industry. This is especially true in oncology.

The first protein kinase inhibitors were identified by screening a decade ago. From that time, the intense activity of structural biologists in this field has produced more than 100 crystal structures of protein kinase domains (apo-or ligated enzymes). Concomitantly, a lot of knowledge has been gained in the structure-activity relationships of protein kinase inhibitors. The combined information has provided us with a deep insight into the structural determinants of kinase inhibition by small molecules binding to the ATP (co-factor) pocket.

We will present and illustrate how this knowledge can be exploited for the discovery of new kinase inhibitors.

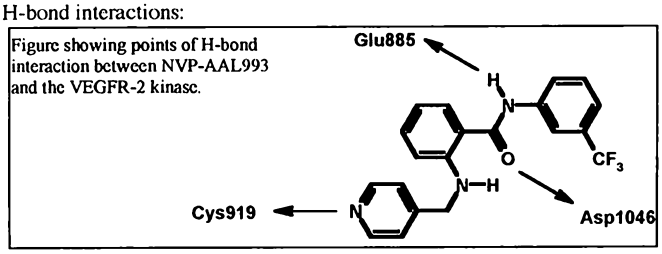
Medicinal Chemistry **61**

2-[(4-Pyridinylmethyl)amino]-*N*-[3-(trifluoromethyl)phenyl]benzamide: A novel, antiangiogenic VEGF receptor kinase inhibitor

P. W. Manley, G. Bold, J. Brüggen, G. Fendrich, P. Furet, J. Mestan, T. Meyer, B. Meyhack, C. Schnell, W. Stark, A Strauss, J. Wood.

Novartis Institutes for Biomedical Research, Basel, Switzerland.

Targeting the vascular endothelial growth factor receptor (VEGFR) kinases, VEGFR-1 (Flt-1), VEGFR-2 (KDR) and VEGFR-3 (Flt-4), provide attractive strategies for inhibiting vasculogenesis, angiogenesis and lymphangiogenesis. The anthranilamide, NVP-AAL993 (ZK 260255), potently and selectively inhibits recombinant VEGFR-1 (IC_{50} 130 nM), VEGFR-2 (IC_{50} 23 nM) and VEGFR-3 (IC_{50} 18 nM) kinases. The selectivity of this molecule is probably due to it interacting with an inactive conformation of theVEGFR-2 kinase. The X-ray crystal structure of a complex with the diphosphorylated VEGFR-2 kinase domain revealed three H-bond interactions:



When administered orally once daily for 5 days, NVP-AAL993 exhibits dose-dependent, antiangiogenic activity against VEGF-stimulated vascularisation in a growth factor implant model in mice (ED_{50} 7 mg/kg). It also exhibited anti-tumour (ED_{50} ≈ 50 mg/kg/day) and anti-metastatic efficacy (ED_{50} 25 mg/kg/day) in a mouse orthotopic model of melanoma, following once daily oral administration for 14 days.
This is an attractive profile for oral anti-angiogenic therapy for the treatment of cancer.

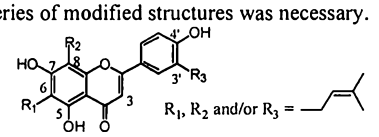
Medicinal Chemistry **62**

Synthesis of isoprenoid flavonoids, potential phytoestrogens and modulators of the activity of ATP-transporters

Denis Barron,* Christian Terreaux, Kurt Hostettmann

School of Pharmacy, University of Lausanne, CH-1015 Lausanne
*Present addess: Nestlé Research Center, CH-1000 Lausanne 26

Isoprenoid flavonoids are natural products of restricted occurrence in the plant kingdom [1]. Recently, significant biological activities have been demonstrated for these compounds, of which their phytoestrogenic properties [2] and their ability to inhibit the ABC transporter P-glycoprotein [3] are the most important. For Structure-Activity Relationship studies, the availability of series of modified structures was necessary.



We have developed regioselective syntheses of *C*-isoprenoid flavonoids, based on the sigmatropic rearrangements of their *O*-isoprenoid precursors. From the evaluation of their effects, the structural requirements for their biological activities have been deduced.

[1] D. Barron, R.K. Ibrahim, *Phytochemistry* **1996**, *43*, 921.
[2] M. Kitaoka, H. Kadokawa, M. Sugano, K. Ichikawa, M. Taki, S. Takaichi, Y. Iijima, S. Tsutsumi, M. Boriboon, T. Akiyama, *Planta Medica* **1998**, *64*, 511.
[3] G. Comte, J.B. Daskiewicz, C. Bayet, G. Conseil, A. Viornery-Vanier, C. Dumontet, A. Di Pietro, D. Barron, *J. Med. Chem.* **2001**, *44*, 763.

Medicinal Chemistry **63**

A VIROSOME-PEPTIDE MIMETIC APPROACH TO SYNTHETIC VACCINE DESIGN : SYNTHESIS, CONFORMATION AND RECOGNITION OF A MALARIA EPITOPE MIMETIC

Annabelle Freund-Renard[1], Francesca Boato[1], Ursula Kienzl[1], Kerstin Moehle[1], Markus Mueller[2], Elisabetta Peduzzi[2], Rinaldo Zurbriggen[3], Gerd Pluschke[2] and John A. Robinson[1]
[1]Institute of Organic Chemistry, University of Zurich, 8057-Zurich; [2]Swiss Tropical Institute[2], 4002-Basel; and [3]Pevion-Biotech, 3018-Bern, Switzerland.

We describe here an approach to synthetic vaccine design and optimisation which involves using peptidomimetics delivered to the immune system on the surface of immunopotentiating reconstituted influenza virosomes (IRIVs).[1-4] To illustrate the approach, we describe here studies on epitope mimetics of regions of surface proteins from *P. falciparum* sporozoites and merozoites. Cyclic peptidomimetics were prepared, linked to a phospolipid, and incorporated into IRIVs for immunizations. The mimetics are presented in a native-like conformation on the surface of the virus-like particles. Several rounds of optimization led to mimetics that elicit strong humoral immune response in mice, that bind sporozoites and merozoites, and show inhibitory activity in vitro. This approach could be useful for the design of new combination vaccines, e.g. targeted against multiple antigens and developmental stages of *P. falciparum*, or indeed against other infectious agents.

[1] R. Glück, *Vaccine* **1999**, *17*, 1782.
[2] R. Moreno, L. Jiang, K. Moehle, R. Zurbriggen, R. Glück, J. A. Robinson, G. Pluschke, *ChemBioChem* **2001**, *2*, 838.
[3] B. Pfeifer, E. Peduzzi, K. Moehle, R. Zurbriggen, R. Glück, G. Pluschke and J. A. Robinson, *Angew. Chem. Int. Ed.* 2003, in press.
[4] M. S. Mueller, A. Renard, F. Boato, D. Vogel, M. Naegeli, R. Zurbriggen, J. A. Robinson, and G. Pluschke, *Infect. Immunity* 2003, in press.

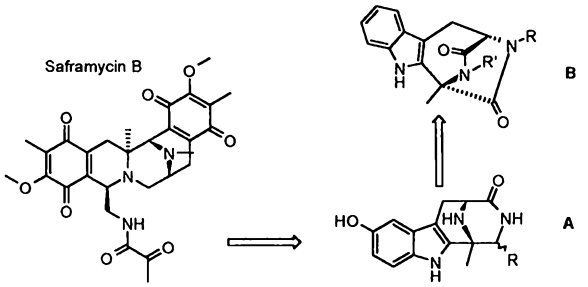
Medicinal Chemistry **64**

New Heterocyclic Scaffolds for Combinatorial Chemistry

David Orain, Guido Koch*, Rudolf Giger*

Novartis Institutes for Biomedical Research, Combinatorial Chemistry Unit
Postfach, CH-4002 Basel, Switzerland

In the process of identifying novel scaffolds for combinatorial library generation, one possible approach is to use the diversity pool of natural products as a guideline. Following this approach, the 3,9–diazabicyclo [3.3.1]non-6-ene core structure of the Saframycin family was investigated.



Initially, the synthesis of 3,9–diazabicyclo[3.3.1]non-6-en-2-one scaffold **A** [1] was completed in solution. A sequential Dakin-West/Pictet-Spengler reaction was developed for the key steps of the synthesis. Then, solid-phase chemistry of scaffold **A** was elaborated. Modifications of the building blocks and synthesis route led to alternative polycyclic products (e.g diazabicyclo[3.3.1]nonendione scaffold **B** [2]). Scope and limitations of solution and solid-phase routes will be discussed.

[1] D. Orain, R. Canova, M. Dattilo, E. Kloppner, R. Denay, G. Koch, R. Giger, *Synlett* **2002**, 1443. D. Orain, G. Koch, R. Giger, *Chimia* to be published.
[2] D. Orain, R. Denay, G. Koch, R. Giger, *Org. Lett.* **2002**, *4(26)*, 4709.

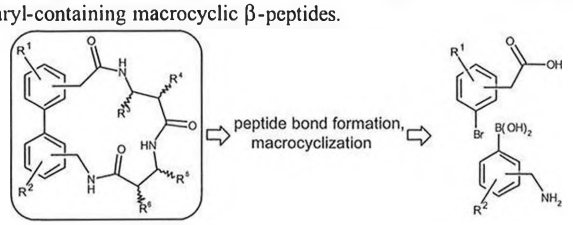
Medicinal Chemistry **65**

Macrocycles Containing β-Amino Acids and a Biaryl Moiety

Karine Malagu, Jürgen Hinrichs, Jürg Zimmermann*

Novartis Institutes for Biomedical Research, Combinatorial Chemistry Unit Postfach, CH-4002 Basel, Switzerland

To overcome the limitations of α-peptidic structures like low bioavailability and easy proteolysis, we were interested in peptido-mimetic macrocycles containing β-amino acids. Whereas the tripeptide can mimic a β-turn [1], the biaryl part (with the appropriate substitution pattern) should be capable of acting like a α-helix [2]. These *protein-mimetic* structures with their two binding elements to discover ligands with high affinity and specificity for a broad range of protein targets are ideally suited for combinatorial chemistry. Here we report the development of a solid-phase protocol for the synthesis of biaryl-containing macrocyclic β-peptides.



β-peptidic macrocycle with different ring sizes

biaryl coupling

We have evaluated the scope and limitations of the macrocyclization step on a number of linear precursors of various chain lengths in solution. The synthesis of the required new biaryls has proven to be robust and can be applied to gram scale. In order to speed up the production of a library of 200 compounds, the synthesis has been transferred to solid-phase.

[1] K. Gademann, T. Kimmerlin, D. Hoyer, D. Seebach, *J. Med. Chem.* **2001**, *44*, 2460-2468.
[2] E. Jacoby, *Bioorg. Med. Chem.* **2002**, *12*, 891-893.

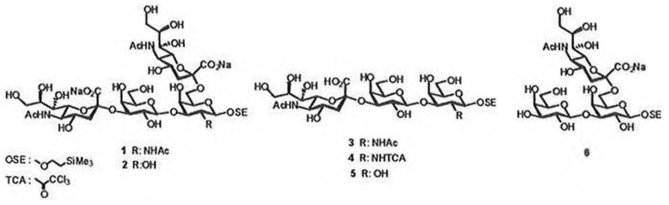
Medicinal Chemistry **66**

Chemical and Chemo-enzymatic Synthesis of Antagonists of Myelin Associated Glycoprotein for Conformational and SAR Studies

Ganpan Gao, Oliver Schwardt, Sachin Shelke, Tamara Visekruna and Beat Ernst*

Institute of Molecular Pharmacy, Pharmacenter of the University of Basel Klingelbergstrasse 50, CH-4056 Basel, Switzerland

Myelin associated glycoprotein (MAG), the only siglec of the mammalian central nervous system (CNS), inhibits the neurite outgrowth of mature nerve cells, the main problem in reconnecting severed nerves of the CNS, e.g. in quadriplegic[1].
Ganglioside GQ1bα is the most potent MAG antagonist identified so far[2]. Because of its structural complexity, GQ1bα is not suited for a therapeutic application. Our aim is to simplify and modify its structure and at the same time retain or even improve the bioaffinity.
To establish a SAR for GQ1bα, the following partial structures **1-6** and mimetics thereof have been synthesized by chemical and chemo-enzymatic methods. They have been investigated by trNOEs, STD-NMR and bioaffinity assays, the results from which are utilized for the design of conformationally improved structures.



[1] L. McKerracher, S. David, D.L. Jackson, V. Kottis, R.J. Dunn, P.E. Braun, *Neuron* **1994**, *13*, 805-811.
[2] L.S. Yang, C.B. Zeller, N.L. Shaper, M. Kiso, A. Hasegawa, R. E. Shapiro, R.L. Schnaar, *Proc. Natl. Acad. Sci. USA*, **1996**, *93*, 814-818.

Medicinal Chemistry **67**

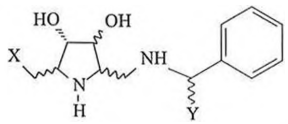
Design of selective and competitive α-mannosidases inhibitors

Florence Popowycz, Sandrine Gerber-Lemaire, Eliazar Rodríguez-García, Catherine Schütz and Pierre Vogel

ICMB, Swiss Federal Institute of Technology, BCH, 1015 Lausanne, Switzerland, Florence.Popowycz@epfl.ch

The specific inhibition of *N*-linked glycoprotein-processing α-mannosidases may provide a useful anti-cancer strategy. Clinical trials have shown that swainsonine, a natural α-mannosidase inhibitor that contains a 4-amino-4-deoxy-mannofuranoside moiety reduces solid tumor and hematological malignancies. Simpler synthetic analogues have also potent inhibitory activities.
Here, we report the structure-activity relationship study that led us to the discovery of a new family of α-mannosidases inhibitors. [1] Chemical modifications on the pyrrolidine ring and on the lateral side chains have been performed to enhance the biological activity.

Inhibitories activities :
α-mannosidase (*jack bean*)
K_i = 0.14 μM-10 μM
Competitive inhibition



Moreover, a combinatorial approach developped in the laboratory will be used further to screen quickly diamines on a large range of glycosidases. [2]

[1]. Popowycz, F.; Gerber-Lemaire, S.; Rodriguez-García, E.; Schütz, C.; Vogel, P. *Helvetica Chimica Acta*. **2003**, *under press,* Popowycz, F.; Gerber-Lemaire, S.; Demange, R.; Rodriguez-García, E.; Carmona Asenjo, A.T.; Robina, I.; Vogel, P. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2489
[2] Gerber-Lemaire, S.; Popowycz, F.; Rodriguez-García, E.; Carmona Asenjo,A.T.; Robina, I.; Vogel, P. *ChemBioChem* **2002**, *5*, 466.

Medicinal Chemistry **68**

Towards the development of potent Mdm2 inhibitors

Rudi Fasan, Ricardo L. A. Dias, Kerstin Moehle, John A. Robinson

University of Zürich, Winterthurerstr. 190, CH-8057 Zürich, Switzerland

Many strategies have been envisioned and undertaken over the last few years to induce tumor-suppressor activity of p53 [1]. A recent approach relies on inhibition of Mdm2 protein [2]. Main goal of present work was to determine whether small cyclic peptides could effectively mimic binding site of p53 to Mdm2. To achieve this aim, a series of p53 mimetics were designed and synthesized. Binding to target protein has been investigated and characterized by NMR and SPR. Potent Mdm2-inhibitors may find a practical application as potential anticancer drugs.
Additionally, the use of cyclic peptides to modify Mdm2-p53 interaction represents also a novel challenge in the field of functional mimicry. In this regards, Mdm2 protein comes up as an ideal target for validating this methodology.

[1] Hupp T.R., Lane D.P., Ball K.L., *Biochem. J.*, **2000**, *352*, 1-17.
[2] Chene P., *Nature Review Cancer*, **2003**, *3(2)*, 102-9.

Medicinal Chemistry **69**

Factor VIIa Inhibitors as Novel Anticoagulants

L. Alig, D. Banner, K. Groebke Zbinden, K. Hilpert, H. Kühne, U.Obst Sander, M. Stahl, H.-P. Wessel

F. Hoffmann-La Roche, CH-4070 Basel, Switzerland

Deep vein thrombosis, pulmonary embolism, stroke and myocardial infarction represent major causes for morbidity and mortality. Therefore substantial efforts have been directed at finding novel small molecule anticoagulants for prevention and treatment of thromboembolism. Due to their selective influence on the extrinsic pathway of the coagulation cascade, inhibitors of the tissue factor/factor VIIa complex should be able to interfere with thrombotic events without prolonging bleeding time and therefore should have an optimal efficacy/safety profile [1].
Lead structures which inhibit the serine protease factor VIIa with submicromolar activity were generated by a biased combinatorial approach. Guided by X-ray analysis and molecular modeling, factor VIIa inhibitors with low nanomolar affinity and good selectivity against other serine proteases were designed. Plasma activity was achieved by reduction of molecular weight and by modulation of physicochemical properties such as solubility and lipophilicity. A prodrug approach was used to render the inhibitors bioavailable.

[1] J. Himber, C.J. Refino, L. Burcklen, S. Roux, D. Kirchhofer, *Thromb. Haemost.* **2001**, *85*, 475.

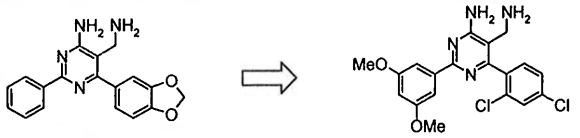
Medicinal Chemistry **70**

Aminomethylpyrimidines as Novel DPP-IV Inhibitors

Stephane Kritter, Silja Weber, Peter Weiss, Markus Boehringer, Michael Hennig, Jens-Uwe Peters

F. Hoffmann-La Roche Ltd, CH4070 Basel, Switzerland

The enzyme dipeptidyl peptidase IV (DPP-IV) [1] cleaves and inactivates glucagon-like peptide 1 (GLP-1) [2], which is one of the most important stimulators of insulin production [3]. Inhibition of DPP-IV should increase the level of endogenous GLP-1 and thus should increase insulin secretion. An improved insulin production would moderate hyperglycaemia in patients suffering from type 2 diabetes mellitus (T2DM). Consequently, DPP-IV inhibition has been proposed as a new treatment for T2DM [4]. We identified **1** as a relatively weak inhibitor of DPP-IV in a high-throughput screen. Optimization of aromatic substituents by high-throughput chemistry led to **2** with a 100000fold increased inhibitory activity. The observed SAR could be rationalized by an X-ray analysis of **2** bound to DPP-IV.



1
IC_{50} (DPP-IV) = 10μM

2
IC_{50} (DPP-IV) = 0.0001μM

[1] Yaron A., Naider F. *Crit. Rev. Biochem. Mol.* **1993**, *28*, 31 – 81.
[2] Mentlein R., Gallwitz B., Schmidt W. E. *Eur. J. Biochem.* **1993**, *214 (3)*, 829 – 835.
[3] Holst J. J. Glucagon-like peptide 1 (GLP-1): *Trends Endocrinol. Metab.* **1999**, *10(6)*, 229 – 235.
[4] Holst, J. J., Deacon, C. F. *Diabetes* **1998**, *47*, 1663 – 1670.

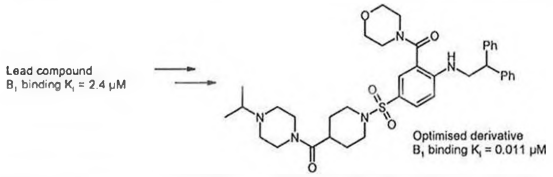
Medicinal Chemistry **71**

Potent, selective and orally active non-peptide bradykinin B_1 receptor antagonists to treat chronic inflammatory pain.

Tim Ritchie, Ed Dziadulewicz, Andrew Culshaw, Werner Müller, Christopher Snell, Gillian Burgess, Michael Brown, Pam Ganju, Michael Webb.

Novartis Institute for Medical Sciences, 5 Gower Place, London WC1E 6BS, United Kingdom.

The bradykinin B_1 receptor is a GPCR that is upregulated after tissue injury and inflammation, and activation of this receptor is thought to play an important role in the maintenance of persistent inflammatory hyperalgesia[1].
This paper describes the medicinal chemistry involved in the optimization of a micromolar lead molecule to afford subnanomolar affinity antagonists at the human B_1 receptor. Further optimization to improve oral bioavailability in the compound series produced analogues with 20-40% oral bioavailability in rats and dogs.
The optimized B_1 antagonists were selective for the human form of the receptor, so it was not possible to test these derivatives *in vivo* using wild type rodent models. Therefore a transgenic mouse was generated, which expressed the human B_1 receptor in place of the mouse receptor. Using these animals, the B_1 antagonists were shown to be effective at reversing established inflammatory mechanical hyperalgesia with a similar potency and efficacy to COX inhibitors.



[1] Couture, R.; Harrison, M.; Vianna, R. M.; Cloutier, F. *Eur. J. Pharmacol.* **2001**, *429*, 161 – 176.

Medicinal Chemistry **72**

The Superior Therapeutic Potential of SOM230 Originates From Unique Structural Elements

Ian Lewis*, Wilfried Bauer, Rainer Albert, Nagarajan Chandramouli, Janos Pless, Gisbert Weckbecker and Christian Bruns

Novartis Pharma Transplantation Research Department, Basel, CH-4002, Switzerland

A rational approach has successfully lead to the discovery of SOM230, a novel, stable cyclohexapeptide somatostatin analogue which exhibits unique binding to human somatostatin receptors (sst1-5) and consequently superior pharmacological properties. This approach has been based on transposing functional groups from SRIF-14 into reduced size, stable cyclohexapeptide templates. Incorporation of $Tyr(Bzl)^5$, mimicking Phe^6, Phe^7, Thr^{10} and Phe^{11} of SRIF-14 in combination with (2S,4R)-(4-OCO-NH-CH_2-CH_2-NH_2)-Pro^1, a novel optimised basic extension, mimicking Lys^4 of SRIF-14 in the cyclohexapeptide template was pivotal to the discovery of the unique binding of SOM230 to SRIF receptor subtypes. SOM230 exhibits higher efficacy in lowering Growth Hormone and Insulin-Like Growth Factor-1, longer duration of action than SMS 201-995 and lowers IGF-1 cross-species. Phase I and Phase II clinical studies are underway to determine the inhibitory profile of SOM230 in man.

[1] Ian Lewis, Wilfried Bauer, Rainer Albert, Nagarajan Chandramouli, Janos Pless, Günter Engel, Gisbert Weckbecker and Christian Bruns, Peptides: The Wave of the Future: Proceedings of the 17th American/2nd International Peptide Symposium, Editors Richard Houghten and Michal Lebl, pp718 – 720, 2001.

[2] Bruns, C; Lewis, I; Briner, U; Meno-Tetang, G; and Weckbecker, G. European Journal of Endocrinology, **2002**, 146, 707-716.

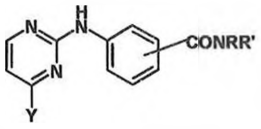
Medicinal Chemistry **73**

Design and Preparation of 2-Benzamido-pyrimidines as IKK Inhibitors

Rudolf Waelchli, Birgit Bollbuck, Thomas Buhl, Christian Bruns, Joerg Eder, Roland Feifel, Rene Hersperger, Philipp Janser, Laszlo Revesz, Hans-Guenter Zerwes and Achim Schlapbach

Novartis Institute for Biomedical Research, Lichtstrasse, 4002 Basel, Switzerland

Tumor necrosis factor α (TNFα) and interleukin 1β (IL-1β) are potent pro-inflammatory cytokines, which have been implicated in a number of pathological conditions. Many of their biological effects are mediated by nuclear factor kappa B (NF-κB). In non-stimulated cells this transcription factor is sequestered in the cytoplasm by a member of the inhibitor kappa B (IκB) family. After stimulation with TNFα or IL-1β, IκB is phosphorylated by the specific IκB kinases (IKK-1 and IKK-2) on two N-terminated serine residues. Following phosphorylation IκB is degraded and the released NF-κB translocates to the nucleus where it activates a variety of inflammatory genes such as other cytokines, adhesion molecules or cyclooxygenase 2. The analysis of single knockout mice for IKK-1 and IKK-2 has established that NF-κB activation by pro-inflammatory cytokines is highly dependent on IKK-2. Thus inhibitors of IKK-2 should be efficient modulators of the NF-κB pathway and should find use in a number of inflammatory conditions like rheumatoid arthritis or asthma.
In our presentation we will report on our efforts to identify, optimize and profile selective, low-molecular weight inhibitors of IKK-2.



"2- Benzamido-pyrimidines"

Medicinal Chemistry **74**

Highly potent and selective 5-HT_{2C} receptor agonists based on the pyrazino[1,2-a]indole scaffold

D. Adams,[†] J. M. Bentley,[†] M. J. Bickerdike,[†] I. A. Cliffe,[†] C. T. Dourish,[†] C. S. Malcolm,[†] J. Davidson,[†] G. Kennett,[†] A. R. Knight,[†] A. Misra,[†] A. Bénardeau,[‡] A. Bourson,[‡] P. Coassolo,[‡] P. Hebeisen,[‡] P. Mattei,[‡] J. Mizrahi,[‡] M. Muller,[‡*] P. Pflieger,[‡] R. H. P. Porter,[‡] S. Roever,[‡] S. Taylor,[‡] P. Verry[‡] and H. Richter[‡]

F. Hoffmann-La Roche Ltd, Discovery Research, 4070 Basel, Switzerland;[‡] Vernalis Research Ltd, Oakdene Court, 613 Reading Road, Wokingham, RG41 5UA, UK.[†]

Research in the field of serotoninergics (5-HT) has generated a wealth of therapeutic agents e.g. the SSRIs (5-HT uptake inhibitors) for depression, 5-$HT_{1B/1D}$ receptor agonists for treating migraine, anxiolytic 5-HT_{1A} receptor partial agonists and 5-HT_3 receptor antagonists for chemotherapy induced emesis. More recently there is an increasing body of evidence supporting the important role of the 5-HT_{2C} receptor in appetite control.
5-HT_2 receptor agonists and partial agonists based on the tetrahydropyrazino-[1,2-a]indole[1] and hexahydropyrazino[1,2-a]indole[2] scaffold have been discovered by researchers from Roche and Vernalis, respectively. Using these as our starting point for optimization, we obtained highly potent and selective 5-HT_{2C} receptor agonists by systematic variation.
The compounds were efficiently synthesized from simple indole precursors by using newly developed chiral N-*Boc*-protected 5-methyl-1,2,3-oxathiazolidine-2,2-dioxide alkylating agents for the key step.
The synthesis and SAR data of prototypical compounds will be discussed.[3]

[1] Boes M. CNS-Active pyrazinoindoles and their preparation, compositions, and use. EP 572863 A1.
[2] Adams DR, Bentley JM, Davidson J, Duncton MAJ, Porter RHP. Preparation of hexahydropyrazino[1,2-a]indoles as 5-HT2 receptor ligands. WO 0044753 A1.
[3] Bentley JM, Hebeisen P, Muller M, Richter H, Roever S, Mattei P. Taylor S. Preparation of 1,2,3,4,10,10a-hexahydro-1H-pyrazino[1,2-a]indoles and analogs and 5-HT receptor agonists for treatment of CNS diseases, cardiovascular disorders, gastrointestinal disorders, and obesity. WO 0210169 A1.

Medicinal Chemistry **75**

Are peptides from the NPY family of neurohormones recognized from their membrane-bound state ?

M. Lerch, B. Christen, O. Zerbe
Institute of Organic Chemistry, University of Zürich, CH-8057 Zürich

For binding of ligands of the neuropeptide Y family of hormones to their membrane-bound receptors the membrane compartment theory by Schwyzer *et al.* has been postulated[1]. In his model, ligands bind to the membrane prior to receptor binding and hence it is the membrane-bound conformation that is recognized.
Recently, we have characterized structure and dynamics of a number of peptides from the NPY family or mutants thereof both when free in solution and when bound to the membrane-mimicking dodecylphosphocholine (DPC) micelles by NMR spectroscopy. In particular, we were interested in ligands displaying similar receptor subtype selectivities but different conformational properties or in ligands with very different subtype selectivies but similar conformational properties in the two environments in order to yield indirect evidence in favor or against a membrane-bound receptor binding pathway.
Our investigations comprise porcine NPY[2] and peptide YY (PYY) as well as bovine pancreatic polypeptide (bPP) [3]. Moreover, results of the two chimera [$^{19-23}$hPP]-pNPY and [$^{19-23}$pNPY]-hPP, two peptides with dramatically altered receptor subtype specificities with respect to their parent peptides [4], are presented.
The structural and dynamical data indicate common features of the peptides in their membrane-bound and in their solution state which strongly favor the membrane-bound receptor recognition pathway. Moreover, a general scenario for receptor binding of peptides from the NPY family is presented that considers membrane biophysics.

[1] Schwyzer R. (1995), *Biopolymers*, **37**, 5-16.
[2] Bader, R., Bettio, A., Beck-Sickinger, A.G. , Zerbe, O. (2001), *J. Mol. Biol.*, **305**, 307-329.
[3] Lerch, M., Gafner, V., Bader, R., Christen, G., Folkers, G., Zerbe, O. (2002) *J. Mol. Biol.*, **322**, 1117-1133.
[4] Cabrele, C., Wieland, H. A., Langer, M., Stidsen, C. E., Beck-Sickinger, A. G. (2001), *Peptides*, **22**, 365-378.

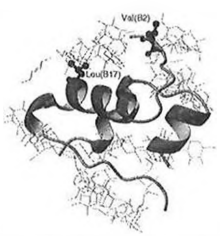
Medicinal Chemistry **76**

Investigation of glucose binding sites on insulin

Vincent ZOETE[1,2], Markus MEUWLY[1,*] and Martin KARPLUS[2,*]

[1]Chemistry Department, University of Basel, Klingelbergstrasse 80, CH-4056 Basel, Switzerland. [2]Laboratoire de Chimie Biophysique, ISIS, Université Louis Pasteur, 4 rue Blaise Pascal, 67000 Strasbourg, France.

Possible insulin binding sites for D-glucose have been investigated theoretically[1] using two different docking programs for small molecules: Multiple Copy Simultaneous Search (MCSS[2]) and Solvation Energy for Exhaustive Docking (SEED)[3]. Scoring functions emphasizing non-polar interactions gave a preferential binding site at a location inferred from experiment.[4] The D-glucose is stable in the binding pocket found by the docking programs during molecular dynamics simulations of 500 ps, and motions of the bound glucose are correlated with the motions of the insulin side chains that are in contact with it and with larger scale insulin motions. The relevance of the theoretical results to medicinal chemistry is discussed in view of the role of insulin-D-glucose complexes in insulin function, including insulin activation.



The positions of the 50 best glucose replicas obtained with MCSS.[2] The score ranges from -1.3 kcal/mol (green) to -3.5 kcal/mol (red).

[1] V. Zoete, M. Meuwly and M. Karplus, *J. Mol. Biol.*, submitted.
[2] A. Miranker and M. Karplus, *Proteins*, **1991**, *11*, 29.
[3] N. Majeux, M. Scarsi, J. Apostokalis, C. Ehrhardt and A. Caflisch, *Proteins*, **1999**, *37*, 88.
[4] M. Falconi, et al., *Int. J. Biol. Macromol.*, **2001**, *29*, 161.

Medicinal Chemistry **77**

Biomolecular NMR Tools to Accelerate Investigations of Protein-Ligand Complexes

Brian Cutting[a], André Strauss[a], Gabriele Fendrich[a], Paul W. Manley[b] & Wolfgang Jahnke[a]

[a]Novartis Pharma AG, Central Technologies and [b]Novartis Pharma AG, Oncology Research, CH-4002 Basel, Switzerland

Understanding of a given proteins biological function is often dependent upon factors occurring through various regions of its structure. Examples include activation at a recognition site located on one domain prior to its catalytic function in another. Although numerous examples exist where small domains have been characterized by NMR, far fewer concern larger more complete constructs. These types of NMR studies are complicated due to, among other concerns, a larger number of peaks appearing in the spectrum.

Herein two independent methods are described with the purpose of aiding mapping the NMR peaks with their corresponding location on the proteins primary sequence. The first involves the preparation of selective amino-acid-type ^{15}N isotope labeling using Baculovirus infected insect cells. Advantages include a reduction in the time required for assignment due to facilitated NMR peak connectivity, financial benefits if uniform isotopic labeling is unnecessary as well as potentially identifying regions of spectral overlap. In addition, it is demonstrated that substitution of a diamagnetic inhibitor with that of its paramagnetic analog can map peaks in the vicinity of the binding site via their enhanced NMR relaxation rates.

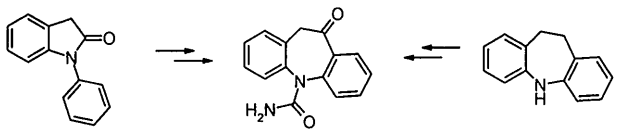
Medicinal Chemistry **78**

New Synthetic Routes for Oxcarbazepine

D. Kaufmann, P. Fünfschilling, U. Beutler, W. Zaugg and O. Lohse

Novartis Pharma AG, Chemical and Analytical Development, CH-4002 Basel, Switzerland

Oxcarbazepine **1** is the active ingredient of Trileptal® an antiepileptic drug. The synthetic routes described in the literature for **1** start from *o*-nitrotoluene or *o*-nitrobenzyl chloride to build first iminodibenzyl **2** which is then further functionalized by a cascade of oxidation and reduction reactions. Our goal was to find novel, simple and straightforward approaches to **1** starting from **3**.



3 1 2

The presentation will focus on the synthesis screening [1], [2] and the ensuing development of a new process for the large scale production of **1** [3],[4].

[1] O. Lohse, U. Beutler, P. Fünfschilling, P. Furet, J. France, D. Kaufmann, G. Penn, W. Zaugg, *Tetrahedron Lett.* **2001**, *42*, 385.
[2] D. Kaufmann, P. Fünfschilling, U. Beutler, P. Hoehn, O. Lohse, W. Zaugg, *Tetrahedron Lett.* in preparation.
[3] P. Fünfschilling, D. Kaufmann, O. Lohse, U. Beutler, W. Zaugg, PCT Int. Appl. WO 0156992, **2001**.
[4] P. Fünfschilling, W. Zaugg, U. Beutler, D. Kaufmann, O. Lohse, U. Onken, J.-P. Mutz, J.-L. Reber *Org. Process Res. Dev.* in preparation.

Medical Chemistry **79**

Impact of saliva composition on Umami taste perception

Urska Pivk, Peter Kastenmeyer, Nicolas Godinot, Andreas Rytz, Chahan Yeretzian, Karlheinz Bortlik

Nestlé Research Center, Vers-chez-les-Blanc, 1000 Lausanne 26, Switzerland

Umami is recognized as a fifth basic taste quality primarily stimulated by L-glutamate and potentiated by sodium chloride and purine nucleotides such as inosine 5'-monophosphate (IMP) [1]. Previous work has shown a close relationship between the level of secreted sodium in saliva and the perception threshold of tasters for saltiness [2]. We expected a similar impact of salivary L-glutamate concentration on Umami taste perception. 20 young and healthy volunteers of both genders were selected to participate in a taste threshold evaluation for sodium chloride and mono sodium glutamate. The saliva of the same subjects, collected just before the sensorial evaluation, was analysed by Atomic Absorption Spectroscopy and HPLC for sodium, amino acid and nucleotide concentration. Both, the inter-individual differences and correlation between saliva composition and Umami taste perception will be discussed.

[1] B.P. Halpern, *Chem. Senses* **2002**, *27*, 845.
[2] Fujimora et al., *Am. J. Physiol.* **1990**, *295*, R931.

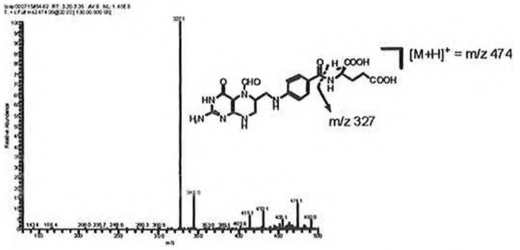
Medicinal Chemistry **80**

LC-MS characterisation and synthesis of trace impurities contained in Folic Acid derivatives

Giancarlo Francese[1*], Federica Corana[2], Fabrizio Marazza[1]

[1] R&D Division, Cerbios-Pharma SA, via Pian Scairolo 6, CH-6917 Barbengo, Switzerland; E-mail: francese@cerbios.ch
[2] Centro Grandi Strumenti, Cascina Cravino, via Bassi 21, I-27100 Pavia, Italy

Monitoring impurities in API (Active Pharmaceutical Ingredients) is important to ensure safety and efficacy: guidelines have been issued to this effect by the International Conference on Harmonization (ICH) [1]. Trace level impurities in API can be structurally related to the drug substance, as in the case of intermediates, degradation products or synthetic by-products. In the present work we describe the characterisation through LC-MS/MS of a group of trace impurities generated during the industrial synthesis of Folic Acid derivatives. In order to definitively demonstrate the hypothesized structure of these impurities, we have designed an efficient synthetic approach to produce such molecules.



[1] International Conference on Harmonisation Quality Guideline. "Impurities in New Drug Substance" Q3A(R) 7 February 2002.

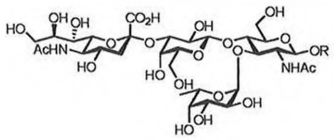
Medicinal Chemistry **81**

Synthesis of a Macrocyclic E-selectin Antagonist

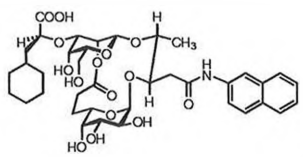
Sébastien Marti, Beat Ernst*

Institute of Molecular Pharmacy, Pharmacenter of the University of Basel, Klingelbergstrasse 50, CH-4056 Basel, Switzerland

Selectins are involved in the orderly migration of leukocytes from blood vessels to sites of inflammation. Although extravasation of leukocytes represents an essential defense mechanism against infection, excessive or inappropriate leukocyte accumulation results in injury to host tissues.



1



2

Physiological selectin ligands contain a common tetrasaccharide epitope, called sialyl Lewis^x (**1**) [1] that serves as lead structure in our search for E-selectin antagonists.

With the sLe^x analog **2** we explored the role of the spatial orientation of the pharmacophores in the bioactive conformation [2]. The rigid macrocyclic core is thought to provide the basis for enhanced bioactivity due to a potentially high pre-organization of the functional groups involved in binding [3].

[1] J.C. Paulson et al. *Science* **1990**, 250, 1130; M. Bevilacqua et al. *Science* **1990**, 250, 1132.
[2] H.C. Kolb, B. Ernst, *Chem. Eur. J.* **1997**, *3*, 1571.
[3] H.C. Kolb, *Bioorg. Med. Chem. Lett.* **1997**, 7, 2629.

Medicinal Chemistry **82**

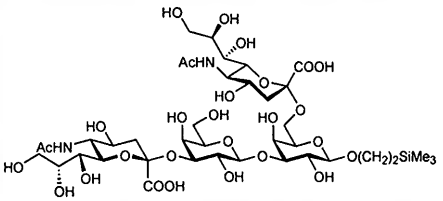
Exploring the Carbohydrate Binding Site of MAG

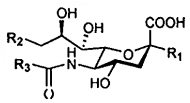
Sachin. V. Shelke, Oliver Schwardt, Ganpan Gao and Beat Ernst*

Institute of Molecular Pharmacy, University of Basel, Klingelbergstrasse-50 CH-4056 Basel, Switzerland

Myelin associated glycoprotein (MAG) is a transmembrane protein in the central nervous system which has drawn a lot of attention because of its role as inhibitor of axonal regeneration[1].

The functional groups of sialylated glycans contributing to the recognition of MAG have been identified using a series of synthetic monosaccharides[2] and oligosaccharides[3]. Thus, the 8- and 9-hydroxyl group as well as the substituent at the 5-position of terminal sialic acid contribute significantly to the binding to all siglecs investigated so far.





Based on this information, we synthesized several sialic acid derivatives, which showed high affinity for MAG. In addition, the interaction of a selected ligand with MAG was studied by STD-NMR.

1. M.T. Filbin, *Curr. Opin. Neurobiol.* **1995**, *5*, 588-595.
2. S. Kelm, R. Brossmer, H.J. Gross, K. Strenge, R. Schauer, *Eur. J. Biochem.* **1998**, *255*, 663-672.
3. K. Strenge, R. Schauer, N. Bovin, A. Hasegawa, H. Ishida, M. Kiso, S. Kelm, *Eur. J. Biochem.* **1998**, *258*, 677-685.

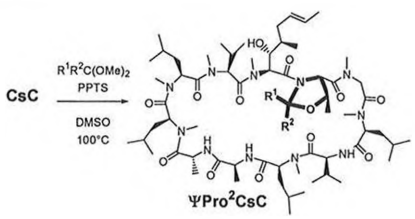
Medicinal Chemistry **83**

Pseudo-proline as reversible solubilizing group : an application to cyclosporin C

Olivier Turpin, Luc Patiny, and Manfred Mutter

Institute of Molecular and Biological Chemistry (ICMB), EPFL, CH-1015 Lausanne, Switzerland

Our laboratory has developed a new class of proline mimics, referred as pseudo-prolines (ΨPro), for enhancing the conformational effects of Pro. A striking feature of 2-C-dialkylated pseudo-prolines is the induction of cis amide bonds prior to the pseudo-proline unit[1].
In this poster we present the direct and selective insertion of pseudo-proline (ΨPro) systems into cyclosporin C (CsC) featuring different 2-C-substituents at the oxazolidine ring. The presence of this 5-membered ring not only exerts drastic effects upon the backbone conformation but also allows the introduction of solubilizing groups at the 2-C position converting cyclosporin to a water soluble derivative. Moreover this group is readily cleaved under conditions similar to the digestive tract



[1] (a) Nefzi, A., Schenk, K., Mutter, M. *Protein and Peptide Letters*, **1**, 66 (1994). (b) Wöhr, T., Mutter, M. *Tetrahedron Lett.*, **36**, 3847 (1995). (c) Keller, M., Wöhr, T.; Dumy, P., Patiny, L., Mutter, M. *Chem. Eur. J.*, **6**, 4358 (2000).

Medicinal Chemistry **84**

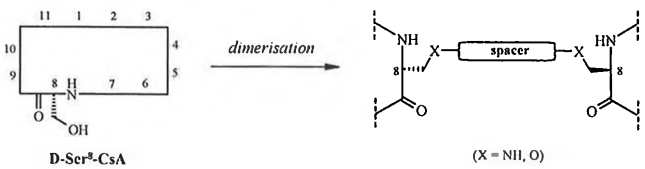
Dimers of cyclosporin A analogues as potential HIV-I inhibitors

Arnaud Hamel, Olivier Turpin, Jaime Lage, Annelis Carrupt, Luc Patiny, and Manfred Mutter

Institute of Molecular and Biomolecular Chemistry (ICMB), EPFL, CH-1015 Lausanne, Switzerland.

Cyclosporin A (CsA) is a well-known cyclic undecapeptide from the fungus *Tolypocladium Inflatum Gams* with a large range of biological activities. Since the discovery of its immunosuppressive activity, it has been widely used to prevent rejection of transplanted organs. More recently, the finding of potential anti-HIV I activity of CsA raised interest for the design of CsA-derived compounds devoid of immunosuppressive activity.

Based on the X-ray structure of CsA bound to its receptor proteins and structure-activity relationship studies concerning the inhibition pathway, position 8 of CsA represents a sensitive target for the design of non-immunosuppressive compounds retaining anti-HIV activity. With this goal in mind, we present here the first results on the dimerisation of [D-Ser]^8-CsA with various linkers yielding to C2 symmetric molecules easily characterized by NMR spectroscopy. The new cyclosporin dimers obtained in good yields show high affinity in cyclophilin A binding studies. This finding, together with their lack of immunosuppression, represents an excellent base for the further tuning of their pharmacokinetical and anti-HIV I profiles.



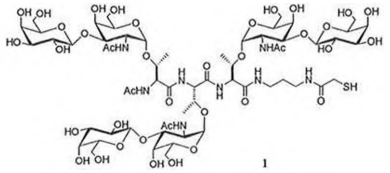
Medicinal Chemistry **85**

Towards the Synthesis of Anticancer Vaccine

Loay Awad, Jens Riedner and Pierre Vogel*

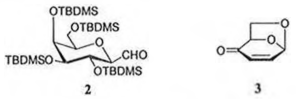
EPFL, Institut de Chimie Moléculaire et Biologique, CH-1015 Lausanne, Switzerland

The Thomsen-Friedenreich antigen (T antigen) is a cancer-associated disaccharide and plays an important role in tumor cell-cell recognition. The great potential of clustered antigen motifs such as **1** for antitumor vaccines has been demonstrated[1].



1

C-linked disaccharide analogues offer an increased stability towards hydrolysis as required for vaccines based on disaccharides. We wish to present here the extension of our previous efforts [2]. towards the synthesis of C-disaccharide analogues of the T antigen based on a Baylis-Hillman type of condensation between the D-galactose derived aldehyde **2** and isolevoglucosenone **3**.



2 **3**

[1] S. D. Kuduk, J. B. Schwarz, X.-T. Chen, P. W. Glunz, D. Sames, G. Ragupathi, P. O. Livingston, S. J. Danishefsky, *J. Am. Chem. Soc.* **1998**, *120*, 12474.
[2] Y.-H. Zhu, P. Vogel, *Synlett* **2001**, 79.

Medicinal Chemistry **86**

Assessment of the therapeutic potential of ^{99m}Tc

Nikos Agorastos, Pascal Haefliger, Roger Alberto

University of Zürich, Winterthurerstr. 190, 8057 Zürich, Switzerland

Due to its γ-emission energy of 140 keV and its convenient half-life of six hours, ^{99m}Tc is widely used for imaging applications. However, this radionuclide also emits an average of four Auger and Coster-Kronig electrons per decay, carrying a total energy of 899 eV. The ability of Auger emitting radionuclides to induce DNA double stand breaks (DSBs) when located in the close proximity of the cell nucleus, and thus to have a cytotoxic effect, has already been shown for other nuclides. This phenomenon has however, up to our knowledge, never been demonstrated experimentally for ^{99m}Tc. The goal of the present study is to establish the therapeutic potential of ^{99m}Tc by measuring its ability to induce DSBs in DNA when located in its close proximity.

A molecule containing a DNA intercalator, pyrene, a tridentate triamine ligand system and a $[M(CO)_3]^+$ (M = ^{99m}Tc, Re) moiety **(1)** was synthesized. The intercalation constant of the positively charged Re complex **1** in DNA was determined by UV/VIS titration with increasing amounts of calf-thymus DNA and subsequent fitting of the data obtained by the McGhee and von Hippel method. In order to determine the ability of ^{99m}Tc to induce DSBs in DNA when located in its close proximity, we incubated supercoiled plasmid DNA (phiX174) with the ^{99m}Tc complex **1**. Subsequent agarose gel electrophoresis allowed then the determination of the amount of DSBs induced.

Compound **1** was found to readily intercalate into DNA with an intercalation constant $K = 1*10^6\ M^{-1}$. The *in vitro* incubation during 48 hours of plasmid DNA with 30 equivalents of the DNA-intercalating ^{99m}Tc complex **1** induced one DNA DSB in 13% of the plasmids. Incubation with the same amount of the non-intercalating $[^{99m}Tc(CO)_3(diethylenetriamine)]^+$ complex induced one DNA DSB in less than 1% of the plasmids. This proves that ^{99m}Tc can, if brought close enough to the DNA of targeted cells, be considered as a potential radiotherapeutic nuclide.

Further derivatization of compound **1** with cancer-targeting and cell-internalizing biomolecules is in progress. This will allow us to determine the cytotoxic effect of such systems on living cells.

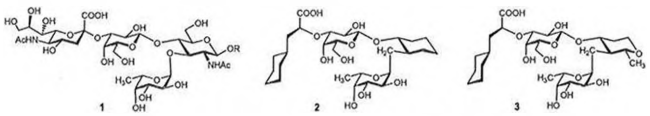
Medicinal Chemistry **87**

Synthesis of *C*-glycosidic E-Selectin Antagonists

Christian Müller, Beat Ernst*

Institute of Molecular Pharmacy, Pharmacenter of the University of Basel, Klingelbergstrasse 50, CH-4056 Basel, Switzerland

The migration of neutrophiles from the intravascular space to sites of inflammation or tissue injury is mediated by the interaction of cell adhesion molecules (E-, P- and L-selectin) with their physiological ligands containing the common tetrasaccharide epitope sialyl Lewis X (sLe^X) **1** [1]. Mimetics of the tetrasaccharide showed up to 60-fold stronger binding affinity to E-selectin in comparison to the natural ligand [2].



1 **2** **3**

Here we report the synthesis of the *C*-glycosidic sLe^X mimetics **2** and **3**, where the Glc*N*Ac-moiety is replaced by a cyclohexane or a tetrahydropyrane ring system and neuraminic acid is replaced by *(S)*-cyclohexyllactic acid [3]. Key step of both syntheses is the stereospecific radical coupling of 2,3,4-tri-*O*-benzoylfucosylbromide with an α-methyleneketone [4].
Conformational issues and biological affinities will be discussed.

[1] a) J.C. Paulson et al., *Science* **1990**, 250, 1130;
b) M. Bevilacqua et al., *Science* **1990**, 250, 1132.
[2] B. Ernst, Z. Dragic, S. Marti, C. Müller, B. Wagner, W. Jahnke, J.L. Magnani, K.E. Norman, R. Oehrlein, T. Peters, H. C. Kolb, *Chimia* **2001**, 55, 268.
[3] H. C. Kolb, B. Ernst, *Chem. Eur. J.* **1997**, 3, 1571.
[4] B. Giese, T. Witzel, *Angew. Chem.* **1986**, 98, 459.

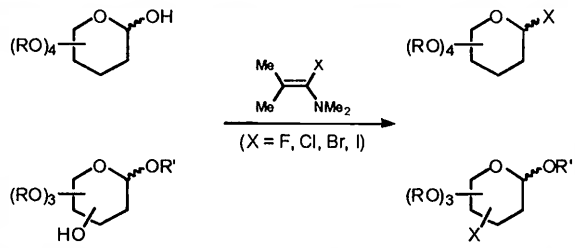
Medicinal Chemistry **88**

Selective Halogenation of Carbohydrates Using Haloenamines

Oliver Schwardt, Bea Wagner, Beat Ernst*

Institute of Molecular Pharmacy, Pharmacenter of the University of Basel Klingelbergstrasse 50, CH-4056 Basel, Switzerland

Haloenamines are useful reagents for the preparation of acyl halides [1] and have been used for the halogenation of primary, secondary and tertiary alcohols under neutral conditions [2]. The haloenamines can be prepared in large scale [3] and are stable if stored under argon at room temperature.



Here we report on the replacement of the anomeric as well as all other hydroxyl groups of various carbohydrates by a fluorine, chlorine, bromine or iodine atom under neutral conditions using haloenamines.

[1] a) A. Devos, J. Remion, A.-M. Frisque-Hesbain, A. Colens, L. Ghosez, *J. Chem. Soc., Chem. Commun.* **1979**, 1180. b) U. Schmidt, M. Kroner, U. Beutler, *Synthesis* **1988**, 475.
[2] a) B. Ernst, B. Wagner, *Helv. Chim. Acta* **1989**, *72*, 165. b) F. Munyemana, A.-M. Frisque-Hesbain, A. Colens, L. Ghosez, *Tetrahedron Lett.* **1989**, *30*, 3077.
[3] B. Haveaux, A. Dekoker, M. Rens, A.R. Sidani, J. Toye, L. Ghosez, *Org. Synth.* **1979**, *59*, 26.

Inorganic and coordination chemistry **89**

Perspectives in Inorganic Structural Genomics

Ivano Bertini

Magnetic Resonance Center CERM, University of Florence, Italy

Genome sequencing projects have provided a wealth of data, and most notably the primary sequences of all the proteins that a given organism can produce. This information must match with our knowledge that a number of metal ions are essential for life. Three-dimensional structural information is necessary to unravel at atomic level the mechanisms by which a protein carries out its function, and can often be very useful to predict at least gross functional features even in the absence of biochemical data. An exhaustive structural characterization of the proteins encoded in the genomes is thus highly desirable. In order to enhance the functional insights provided by genome-scale structural determination, we have prioritized our research to target specific processes of the cell, i.e. those responsible for controlling metal homeostasis. Results obtained by the Magnetic Resonance Center of the University of Florence on the proteins involved in the homeostasis of copper are presented. An overview of their relevance to the understanding of molecular function and cellular processes is also given.

Inorganic and Coordination Chemistry **90**

To be or not to be NO? A mechanistic approach

Rudi van Eldik

Institute for Inorganic Chemistry, University of Erlangen-Nürnberg, Egerlandstr. 1, 91058 Erlangen, Germany.

The interaction of NO with metal complexes of biological and environmental interest has received much attention from many researchers in different areas [1]. In many cases little is known about the detailed reaction mechanisms underlying this interaction, since it involves a combination of ligand substitution and electron transfer reactions. We have undertaken comprehensive thermodynamic and kinetic studies on the interaction of NO with aquacobalamin [2], reduced cobalamin [3], metmyoglobin [4] hexaaquairon(II) [5] and a series of polyaminecarboxylate complexes of iron(II) [6,7]. In these studies a combination of stopped-flow, flash photolysis and pulse radiolysis techniques were employed to measure the rate and activation parameters ($\Delta H^{\neq}$, $\Delta S^{\neq}$ and $\Delta V^{\neq}$) for the 'on' and 'off' reactions. The activation parameters were used to construct energy and volume profiles for the binding and release of NO, from which detailed mechanistic insight could be gained. More recently, we have studied a few systems in which the binding of NO to the metal centre is not the rate-determining step [8,9]. An overview of our recent mechanistic findings will be presented.

[1]. Williams, R.J.P. *Chem. Soc. Rev.*, **1996**, *25*, 77.
[2]. Wolak, M. *et al.*, *Inorg. Chem.*, **2000**, *39*, 2018.
[3]. Wolak, M.; Zahl, A.; Schneppensieper, T.; Stochel, G.; van Eldik, R. *J. Am. Chem. Soc.*, **2001**, *123*, 9780.
[4]. Laverman, L.E. *et al.*, *J. Am. Chem. Soc.*, **2001**, *123*, 285.
[5]. Wanat, A. *et al.*, *Inorg. Chem.*, **2002**, *41*, 4.
[6]. Finkler, S. *et al.*, *Eur. J. Inorg. Chem.*, **2001**, 491.
[7]. Schneppensieper, T. *et al.*, *Inorg. Chem.*, **2002**, *41*, 2565.
[8]. Roncaroli, F.; Olabe, J.; van Eldik, R. *Inorg. Chem.*, **2002**, *41*, 5417.
[9]. Czap, A.; van Eldik, R. *Dalton Trans.*, **2003**, 665.

Inorganic and Coordination Chemistry **91**

New Chemistry of Oxides and Microporous Materials

M.J. Rosseinsky

Department of Chemistry, The University of Liverpool, Liverpool, UK L69 7ZD

Solid state chemistry has long been regarded as a high-temperature subject, because of the diffusion limitations in bringing reactants together in the solid state. Such reaction conditions lead predominantly to a chemistry of thermodynamically stable materials. This talk will address two distinct areas of solid state synthesis where progress in kinetically controlled chemistry is being made.

Transition metal oxides display a very broad chemistry associated with oxygen removal (deintercalation). However, until recently kinetic limitations associated with the traditional gaseous and metal getter reducing agents have prevented the potential diversity of this chemistry being exploited. We have developed electropositive metal hydrides such as NaH and CaH_2 as reagents for low temperature (<150°C in some cases) transformations of metal oxides. The most unusual aspect of this reactivity is the synthesis of a transition metal oxide hydride, $LaSrCoO_3H_{0.7}$. This compound has an extended $CoOH_{0.7}$ two-dimensional sheet and displays magnetic properties which indicate that the hydride anion is at least as effective in propagating magnetic exchange interactions as the oxide anion.

There has recently been considerable interest in exploiting the coordination of multidentate ligands to isolated or polynuclear transition metal centres to systematically assemble open-framework structures in a chemically predictable manner. This section of the talk will concentrate on the introduction of functionality in such metal-organic frameworks that is difficult to confer on zeolites, as the strength of the Si-O bond will always make zeolites preferable for high temperature applications. In particular, the preparation of permanently porous chiral open framework materials will be discussed.

Inorganic and Coordination Chemistry **92**

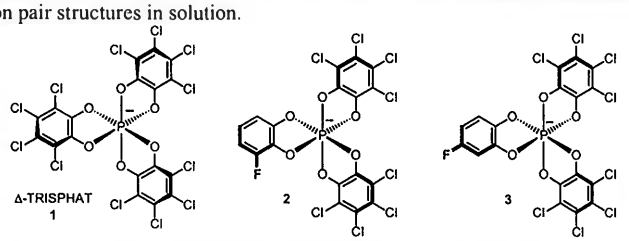
Fluorinated "TRISPHAT" Anions. Chiral NMR probes for detailed asymmetric ion pairing studies.

Richard Frantz, Samuel Constant, Gérald Bernardinelli and Jérôme Lacour*

Département de Chimie Organique, Université de Genève CH-1211 Genève 4

Ion pairing is essential phenomena, which has been strongly studied and reviewed [1]. Until recently, detailed structural analysis of ion pairs in solution was elusive but much progress has been made by the use of ^{19}F, ^{1}H HOESY and PGSE NMR experiments [2].

Recently readily prepared and resolved chiral TRISPHAT anion (**1**) was shown to be an effective NMR chiral shift, resolving and asymmetry-inducing agent for metal tris(diimine) complexes [3]. Herein we report the synthesis and the resolution of fluorinated "TRISPHAT" anions (**2** and **3**) which are NMR probes for detailed ion pairing studies; their use as chiral counterions allowing a precise determination of some preferred asymmetric ion pair structures in solution.



[1] A. Loupy, B. Tchoubar, *Salt Effects in Organic and Organometallic Chemistry*, VCH, Weinheim, Germany, **1992**.
[2] (a) A. Macchioni, *Eur. J. Inorg. Chem.* **2003**, 195-205. (b) M. Valentini, H. Rüegger, P. S. Pregosin, *Helv. Chim. Acta*. **2001**, *84*, 2833-2853.
[3] D. Monchaud, J. J. Jodry, D. Pomeranc, V. Heitz, J.-C. Chambron, J.-P. Sauvage, J. Lacour, *Angew. Chem. Int. Ed.* **2002**, *41*, 2317-2319.

Inorganic and Coordination Chemistry **93**

Cyano-Carbonyl complexes of Technetium(I) and Rhenium(I)

Philipp Kurz, Bernhard Spingler, and Roger Alberto

Institute of Inorganic Chemistry, University of Zürich, Winterthurerstr. 190, CH - 8057 Zürich, Switzerland

The isoelectronic ligands carbon monoxide and cyanide are two of the most fundamental ligands in inorganic chemistry. The good σ-donor cyanide is able to stabilize the complexation of π–acceptors like CO. Additionally cyanide can act as a linear μ-cyano bridging unit between two metal centers. [1]

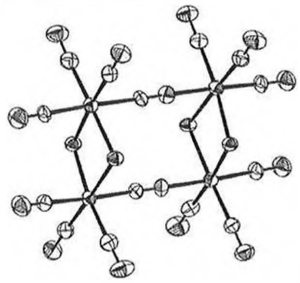


Fig.:Crystal structure of **1**.

We will demonstrate these particular properties of the cyanide ligand in a study of the reactions of cyanide with Re(I) and Tc(I) carbonyls. By variation of the reaction conditions it was possible to synthesize mononuclear complexes $[M(CO)_3(CN)_3]^{2-}$ (M= Re, Tc), mixed-ligand mononuclear complexes $[M(CO)_3(CN)(L)]$ (L= bidentate nitrogen ligand), binuclear rods $[(CO)_3(L)Re(\mu\text{-}CN)Re(L)(CO)_3]^+$, and even the tetranuclear complex $[(CO)_3(\mu\text{-}OH)Re(\mu\text{-}CN)Re(\mu\text{-}OH)(CO)_3]_2^{2-}$ **1**.
These compounds are beautiful models to study structures and bonding of carbonyl and cyanide group 7 transition metal complexes.

[1] Dunbar, Heintz, *Progr.Inorg.Chem.* **1997**, *45*, 283.

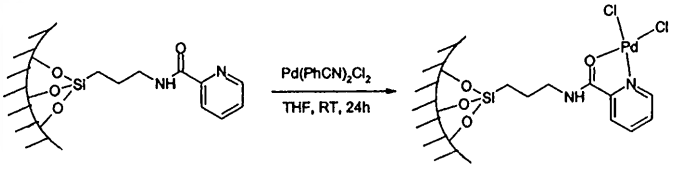
Inorganic and Coordination Chemistry **94**

Synthesis and characterization of new bidentate Pd(II) complex anchored by covalent bond into MCM41

Andrea Cecchetto, Gerhard D. Pirngruber, Roel Prins

Institute for Chemical and Bioengineering, ETH Zürich, CH-8093 Zürich, Switzerland

The ordered mesoporous silica MCM41 was covalently grafted with N-(pyridine-2-carbonyl)-3-aminopropyltrimethoxysilane. The organo-functionalised material was suspended in THF solution of bis(benzonitrile)dichloro palladium(II) complex to form the respective metal complex.



The complexation was confirmed by FT-IR and ^{13}C-NMR spectroscopy, AAS and elementar analysis. The ligand coordinated through its oxygen and nitrogen atom. Our present efforts are concentrated on the establishment of the catalytic behaviour in hydrocarboxylation reaction [1].

[1] Kausik Mukhopadhyay, Bibhas R. Sarkar, and Raghunath V. Chaudhari, J. Am. Chem. Soc. **2002**, 124, 9692-9693.

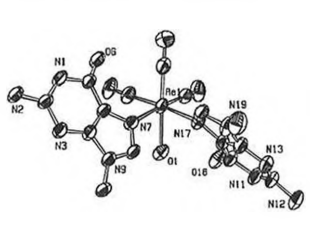
Inorganic and Coordination Chemistry **95**

Head-to-Head (HH) and Head-to-Tail (HT) Conformers of cis-bis Purine Ligands Bound to the $[Re(CO)_3]^+$ Core

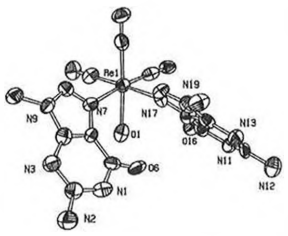
Fabio Zobi, Bernhard Spingler, Philipp Kurz and Roger Alberto

Institute of Inorganic Chemistry, University of Zurich, Winterthurerstr. 190, CH-8057 Zurich, Switzerland

Rhenium tricarbonyl complexes have been reported to suppress the growth of tumor cell lines. Coordination to N7 in purine bases in a fashion similar to cisplatin was anticipated to be a possible mode of action for some of these complexes. We have recently shown that the $[Re(CO)_3]^+$ core can binds two purine bases in a *cis* fashion. The bases were shown by X-ray crystallography to be in a HT conformation around the metal core.
Here we present structural evidence that neither hydrogen bonding interactions nor steric factors are important in determining the orientation of the purine ligands bound to $[Re(CO)_3]^+$.



HT Conformer



HH Conformer

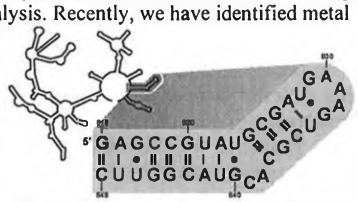
Inorganic and Coordination Chemistry **96**

Metal ion binding to the catalytic center of a group II intron ribozyme

Roland K. O. Sigel[1], Arthur G. Palmer[2], Anna Marie Pyle[3,4]

[1]Institute of Inorganic Chemistry, University of Zürich, Winterthurerstrasse 190, 8057 Zürich, Switzerland; Department of Biochemistry, Columbia University, New York, USA; [3]Department of Molecular Biophysics & Biochemistry, Yale University, New Haven, USA; [4]Howard Hughes Medical Institute

Group II introns are naturally occurring, autocatalytic self-splicing RNAs. These large molecular machines require divalent metal ions for folding, substrate binding and chemical catalysis. Recently, we have identified metal ion binding sites by site specific hydrolysis of the RNA by different kinds of bound lanthanide(III) and Mg(II) ions. Strong metal ion binding sites were located in catalytically essential regions such as domain 5 (D5) (see also highlighted sequence in the Scheme above) and its cognate tertiary interactions partners of a ribozyme construct derived from the *S. cerevisiae* group II intron ai5γ.[1,2]



Based on the solution structure of the 34-nucleotide long hairpin D5,[3] we now determined the Mg(II) affinities to several catalytically important nucleotides in this hairpin by NOESY titration studies. The affinity constant of one of the stronger Mg(II) binding sites is in the order of $\log K = 2.5 \pm 0.1$ and is found in the minor groove of the unpaired nucleobases connecting the two helices, possibly inducing a conformational change within this molecule. Numerous functional groups of the nucleotides in this region are crucial for the reaction catalyzed by these ribozymes.

Financial support by the Swiss National Science Foundation (PP002--68733) and the Swiss Academy of Natural Sciences is gratefully acknowledged. Part of this work was carried out at the Department of Biochemistry, Columbia University, New York.

[1] Sigel R. K. O., Vaidya A., & Pyle A. M., *Nature Struct. Biol.* **2000** 7, 1111
[2] Sigel R. K. O., & Pyle A. M., *Met. Ions. Biol. Syst.* **2003** 40, 477.
[3] Sigel R. K. O., Butcher S. E., Palmer A. G., & Pyle A. M. submitted.

Inorganic and Coordination Chemistry **97**

Metal Ion Complex Stabilities in Aqueous Solution of N3-deprotonated Uridine and of Related Nucleosides

Bernd Knobloch,[a] Wolfgang Linert,[b] Helmut Sigel[a],*

[a]Dept. of Chem. (IC), University, Spitalstr. 51, 4056 Basel, Switzerland; [b]Inst. of Appl. Synth. Chemistry, Tech. University, A-1060 Vienna, Austria

The nucleoside uridine (Urd) is an important component of nucleotides and of RNA, while in DNA it is replaced by thymidine (dThd) [1]. Since metal ions (M^{2+}) are important in this context and because their affinities towards pyrimidines, especially towards uridine [2] and thymidine, have hardly been investigated, we studied now their binding properties. To obtain also information about the stability determining factors two synthetic derivatives, FUrd and CldUrd, were included. These nucleosides (Ns) are deprotonated at their (N3)H sites with pK_a = 7.55 ± 0.02 (FUrd), 7.90 ± 0.01 (CldUrd), 9.19 ± 0.02 (Urd) and 9.67 ± 0.02 (dThd) to give the $(Ns–H)^-$ species (pot. pH titrations; aq. sol.; 25 °C; I = 0.1 M, $NaNO_3$). For the $Cd(Ns–H)^+$ complexes we obtained the stability constants log $K^{M}_{M(Ns-H)}$ = 2.59 ± 0.05, 2.70 ± 0.03, 3.15 ± 0.04 and 3.43 ± 0.05 with $(FUrd–H)^-$, $(CldUrd–H)^-$, $(Urd–H)^-$ and $(dThd–H)^-$, respectively. Hence, there is a clear dependence of the stability on the pK_a of the ligand.

	R	R'
FUrd	F	OH
CldUrd	Cl	H
Urd	H	OH
dThd	Me	H

Supp. by Swiss Nat. Sci. Found. and Swiss Fed. Off. for Educ. & Sci. (COST D20).

[1] *Metal Ions in Biological Systems*, Vol. 32: *Interactions of Metal Ions with Nucleotides, Nucleic Acids, and Their Constituents*; Eds: A. Sigel, H. Sigel; Dekker, New York & Basel, **1996**, pp. 1-678.
[2] B. Knobloch, C. P. Da Costa, W. Linert, H. Sigel, *Inorg. Chem. Commun.* **2003**, 6, 90.

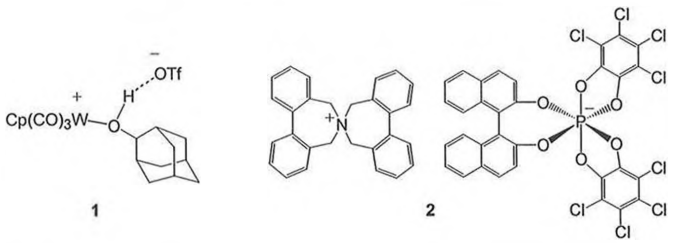
Inorganic and Coordination Chemistry **98**

PGSE Diffusion Studies on Organometallic and Organic Compounds

Eloísa Martínez Viviente, Paul S. Pregosin

Laboratory of Inorganic Chemistry. ETH, HCI, Hönggerberg. CH-8093. Zürich. Switzerland

Pulsed Gradient Spin Echo (PGSE) diffusion studies allow a separate determination of the diffusion coefficients for cation and anion in ionic compounds, thus affording insight into the inter-ionic interactions [1]. We have applied this technique to several organometallic and organic salts. For the cationic alcohol complex **1** [2], a strong hydrogen bond could be demonstrated. For the spirobi(dibenzazepinium) BINPHAT salt **2** [3], the induction of chirality from the anion onto the cation [3] has been shown to be related to a different degree of ion pairing in the two diastereomeric salts. Diffusion measurements on unstable or fluxional products were carried out at low temperature, with special precautions to avoid convection effects.



[1] E. Martínez-Viviente, H. Rüegger, P. S. Pregosin, J. L. Serrano. *Organometallics*, **2002**, 21, 5841. E. Martínez-Viviente, P. S. Pregosin. *Inorg. Chem.* **2002**, 42, 2209.
[2] J.-S. Song, D. J. Szalda, R. M. Bullock. *Organometallics*, **2001**, *20*, 3337.
[3] L. Vial, J. Lacour, *Org. Lett.* **2002**, *4*, 3939.

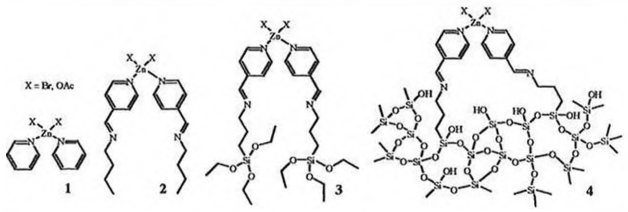
Inorganic Chemistry **99**

Immobilized Catalysts for CO_2-Fixation

Michael Ramin, Jan-Dierk Grunwaldt, Alfons Baiker*

Institute for Chemical and Bioengineering, Swiss Federal Institute of Technology, ETH Hönggerberg HCI, CH-8093 Zürich, Switzerland

Heterogeneous catalysts for the synthesis of cyclic carbonates from ethylene oxide and CO_2 have been reported in literature [1]. However there are no efficient heterogeneous catalysts for the reaction with propylene oxide and larger epoxides up to now. Our approach to receive an efficient heterogeneous catalyst is to combine the advantage of a homogenous catalyst system and the chemical anchoring of the corresponding metal complex on a silica support. Starting from homogeneous zinc-pyridine-complexes - known as good catalysts for CO_2-fixation in the synthesis of propylene carbonate [2] [3] - a series of catalysts (compounds **1** – **4**) is synthesized. At 140 °C and 4.5 MPa, good propylene carbonate yields with compounds **1** – **3** as homogeneous catalysts were achieved and first experiments with the heterogeneous counterpart (compound **4**) gave promising catalytic results.



[1] M. Tu, R.J. Davis, *J. Catal.* **2001**, *199*, 85.
[2] H.S. Kim, J.J. Kim, B.G. Lee, O.S. Jung, H.G. Jang, S.O. Kang, *Angew. Chem., Int. Ed.* **2000**, *39*, 4096.
[3] H.S. Kim, J.J. Kim, H.N. Kwon, M.J. Chung, B.G. Lee, H.G. Jang, *J. Catal.* **2002**, *205*, 226.

Inorganic and Coordination Chemistry **100**

Carbonate Reduction in Pressurised RTIL/Aqueous Systems

C. Andy Ohlin, Gábor Laurenczy

EPFL, ICMB, CH-1015 Lausanne, Switzerland

The reduction of carbonates has been studied in pressurised systems comprising of an ionic liquid containing a catalyst, and an aqueous phase, in which the reactant and the product are confined.

$$H_2 + CO_2 \xrightarrow{\text{Catalyst}} HCOOH$$

The reduction of CO_2/carbonate salts by H_2 is a reaction of high potential importance (see equation), providing a possible alternative C1 source of hydrocarbons. Work has previously been conducted on the reaction of inorganic carbonate salts in aqueous single-phase systems, as well as on the reduction of carbon dioxide in the presence of amines in $scCO_2$ or organic solvents. [1-2]

Five water-immiscible ionic liquids have been investigated, of which [bmim][Tf_2N] was found to have the most desirable properties. Under 90 bar of H_2 and 10 bar of CO_2, $RuCl_2(PPh_3)_4$ catalysed the conversion of a 1M $NaHCO_3$ with a TOF of 454 h^{-1}. Two ruthenium hydride species were detected in the ionic liquid phase and subsequently characterised. Consecutive recycling of the ionic liquid and catalyst deteriorated the catalyst performance. The reasons for this have been investigated. The catalyst lifetime and leaching were determined.

The authors gratefully acknowledge financial support through the following grant: Swiss National Science Foundation, 2000-067976.02 (G.L.).

[1] F. Joó, G. Laurenczy, L. Nádasdi, J. Elek: *Chem. Comm.* **1999**, 971.
[2] (a) Jessop, P.G.; Hsiao, Y.; Ikariya, T.; Noyori, R. *J. Amer. Chem. Soc.* **1994**, *116*, 8851 (b) Kröcher, O.; Köppel, R.A.; Baiker, A. *Chem. Commun.* **1997**, 453-454.

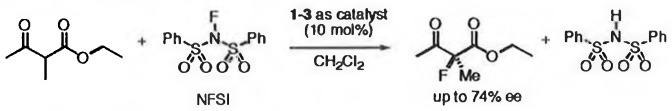
Inorganic Chemistry **101**

Enantioselective Electrophilic Fluorination Catalyzed by Chiral Ruthenium PNNP Complexes

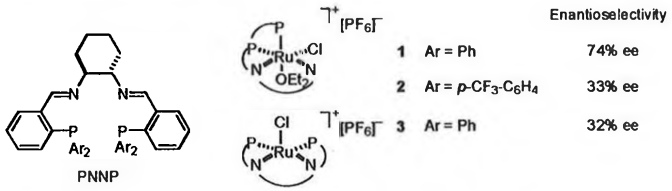
Claus Becker, Christina Dauth, Antonio Togni, Antonio Mezzetti*

Department of Chemistry, ETH Zürich, CH-8093 Zürich, Switzerland

Recently, the first enantioselective fluorination of β-ketoesters catalyzed by a titanium TADDOL complex has been reported from our group [1]. We now find that ruthenium complexes with tetradentate PNNP ligands [2] also catalyze the electrophilic fluorination of β-ketoesters with enantioselectivities of up to 74% ee in the presence of NFSI as electrophilic fluorinating agent:



The enantioselectivity of this reaction strongly depends on the electronic properties of the catalyst, as shown for different ruthenium complexes (**1-3**) and the reference substrate ethyl 2-methylacetoacetate:



		Enantioselectivity
1	Ar = Ph	74% ee
2	Ar = *p*-CF_3-C_6H_4	33% ee
3	Ar = Ph	32% ee

[1] L. Hintermann, A. Togni, *Angew. Chem.* **2000**, *39*, 4359.
[2] S. Bachmann, M. Furler, A. Mezzetti, *Organometallics* **2001**, *20*, 2102.

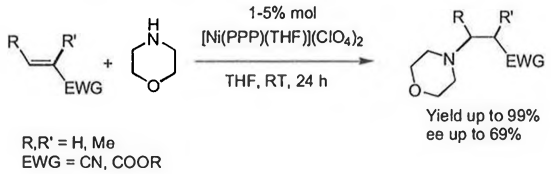
Inorganic and Coordination Chemistry **102**

Ni(II)-PPP Complexes: From the Hydroamination of Activated Olefins to the Synthesis of ß-Aminoacids

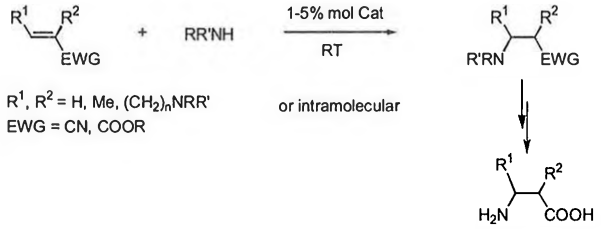
Luca Fadini and Antonio Togni

Department of Chemistry, Swiss Federal Institute of Technology, ETH Hönggerberg, CH - 8093 Zürich, Switzerland

We have recently reported the first asymmetric hydroamination of olefins bearing electronwithdrawing groups catalyzed by Ni(II)-complexes [1], containing tridentate ferrocenyl ligands [2].



The intermediate hydroamination products have been exploited for the preparation of ß-aminoacids.



[1] L. Fadini, A. Togni, *Chemical Comunications* , 2003, 31
[2] P. Barbaro, C. Bianchini, A. Togni, *Organometallics* , 1997, **16**, 3004

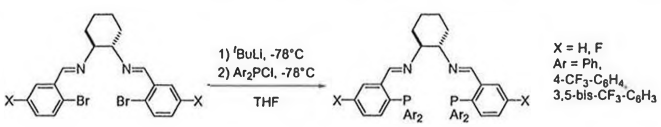
Inorganic and Coordination Chemistry **103**

Synthesis of New Electron-deficient PNNP Ruthenium Complexes for the Asymmetric Cyclopropanation of Olefins.

Cristina Bonaccorsi, Francesco Santoro, Stephan Bachmann and Antonio Mezzetti

Department of Chemistry, Swiss Federal Institute of Technology, ETH Hönggerberg, CH-8093 Zürich, Switzerland

We recently reported that cationic ruthenium complexes of the type $[RuCl(L)(\mathbf{1a})]^+$ (L = OEt_2, **2a**, L = OH_2, **3a**), where **1a** is a CF_3-substituted PNNP ligand, catalyze the asymmetric cyclopropanation of styrene by decomposition of ethyl diazoacetate with higher *cis*- and enantio-selectivities than their analogues containing the unsubstituted ligand **1b**.[1,2] Thus, in the case of the complexes $[RuCl(OH_2)(\mathbf{1a})]$BArF (**3a**BArF), and $[RuCl(OH_2)(\mathbf{1b})]$BArF (**3b**BArF), we observed a significant increase both in the *cis*-selectivity (98% vs 72%) and in the enantioselectivity (80% vs 64%). In view of these results, we are now performing the electronic tuning of the phenylene PNNP-bridge. For the synthesis of the new and old PNNP ligands, we have discovered a new synthetic pathway, that is simpler then the previously reported one. [3]



The use of the new complexes in the asymmetric cyclopropanation of olefins will be presented.

[1] C. Bonaccorsi, S. Bachmann, A. Mezzetti, *Tetrahedron: Asymmetry* **2003**, *14*, 845-853.
[2] S. Bachmann, A. Mezzetti, *Helv. Chim. Acta* **2001**, *84*, 3063-3073.
[3] J. C. Jeffery, T. B. Rauchfuss, P.A. Tucker, *Inorg. Chem.* **1980**, *19*, 3306-3316.

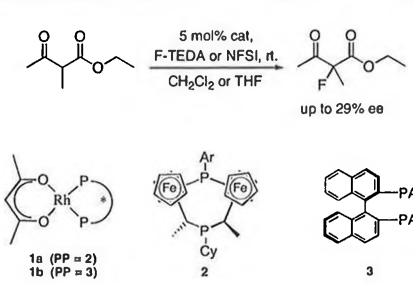
Inorganic and Coordination Chemistry **104**

Electrophilic Fluorination catalyzed by Rh and Ir Complexes

Isabelle Haller, Diego Broggini, Antonio Togni.

Department of Chemistry, Swiss Federal Institute of Technology ETH Hönggerberg, CH - 8093 Zürich, Switzerland

The first catalytic enantioselective fluorination of β-ketoesters using F-TEDA (selecfluor®) as the fluorinating agent and crystalline Ti(TADDOLato) complexes was reported from our group.[1] Recently, Sodeoka described Pd-Biphosphines complexes as catalysts for analogous electrophilic fluorinations.[2] In view of these results, we investigated other late transition metal complexes. We have found that β-ketoesters can be fluorinated using chiral Rh-biphosphines complexes as catalysts.



The use of further Rh and Ir complexes containing different chiral phosphines will be presented.

[1] (a) L. Hintermann, A. Togni, *Angew.Chem.Int.Ed.*, 2000, *39*, 4359. (b) S. Piana, I. Devillers, U. Rothlisberger, *Angew.Chem.Int.Ed.* 2002, **41**, 979.
[2] Y. Hamashima, K. Yagi, H. Takano, L. Tamas, M. Sodeoka, *J.Am.Chem.Soc.*, 2002, *124*; 14530-14531.

CHIMIA 2003, 57, No. 7/8

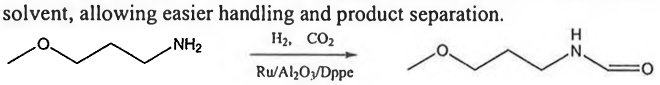
Inorganic Chemistry **105**

Solvent-free synthesis of 3-methoxypropylformamide from amine, hydrogen and carbon dioxide

Markus Rohr, Jan-Dierk Grunwaldt, Alfons Baiker*

Institute for Chemical and Bioengineering, Swiss Federal Institute of Technology, ETH Hönggerberg HCI, CH-8093 Zürich, Switzerland

Several synthetic methods for the formylation of primary and secondary amines to formamides are known [1]. Prominent C_1-building blocks for this purpose are phosgene and carbon monoxide. An interesting alternative would be the use of carbon dioxide both as reactant and solvent, allowing easier handling and product separation.



Using this approach the synthesis of *N,N*-dimethylformamide from carbon dioxide, hydrogen and dimethylamine has been successfully performed previously [2], achieving TOF's up to 360000 h^{-1} with $RuCl_2(dppe)_2$. Motivated by these interesting results we extended the scope of products, including e.g. 3-methoxypropylformamide (see reaction scheme). One technical limitation of the homogeneous process is catalyst separation. This prompted us to search for an efficient heterogeneous catalyst. Ru/Al_2O_3 in the presence of dppe proved to be an interesting catalyst. It showed excellent performance, even after catalyst recycling. However, leaching experiments and UV-VIS spectroscopy revealed the dissolution of some Ru under reaction conditions, indicating that the modified Ru/Al_2O_3 cannot be considered as a truly heterogeneous catalyst.

[1] P. Haynes, L. H. Slaugh, J. F. Kohnle, *Tetrahedron Lett.*, 1970, 365.
[2] O. Kröcher, A. Baiker, *J. Chem. Soc., Chem Commun.*, 1997, 5, 453.

Inorganic and Coordination Chemistry **106**

Formation and reactivity of new water-soluble mixed Ru hydride complexes

Maxime Loy and Gábor Laurenczy

Institut de Chimie Minérale et Biologique, École Polytechnique Fédérale de Lausanne, CH-1015 Lausanne, Switzerland

The fundamental coordination chemistry of the Ru(II) in aqueous solution has been studied with potentially important ligands (phosphines and small gas molecules such as H_2 and CO). New Ru(II) mixed hydride complexes have been identified and investigated with regards to reactivity in aqueous solution, to elucidate the mechanisms of catalytic reductions in water, which is expected to yield new basic insights and a possible outlook on industrial application [1, 2, 3, 4]. These novel, water-soluble ruthenium mixed hydride complexes have been synthesized *in situ* by pressurising an aqueous solution of Ru(II) - TPPTS system [5] with H_2 or CO gases in sapphire NMR tubes. The formation of all these complexes has been followed and characterised by multinuclear NMR spectroscopy (^1H, ^{31}P and ^{17}O). Our study showed that the formation of these complexes highly depend on such factors as concentration, temperature and pressure, *e.g.* the final *trans/cis* complex ratios were found to be temperature dependent.

The Swiss National Science Foundation is thanked for financial support (Grant 2000-067976.02)

[1] A. K. Rappé, *Inorg Chem.* **1986**, 25, 4686-4691
[2] P. Pelikán, R. Boca and M. Magová, *J. of Molecular Catalysis*, **1983**, 19,243-255
[3] M. Hidai and Y. Mizobe, *Topics in Organometallic Chemistry*, **1999**, 3, 227-241.
[4] M. Hernandez and P. Kalck, *J. of Molecular Catalysis A: Chemical*, **1997**, 116, 117-130
[5] J. Kovács, F. Joó and G. Laurenczy, *in preparation.*

Inorganic and Coordination Chemistry **107**

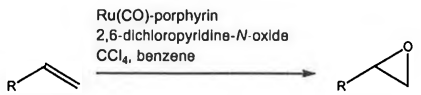
In situ activation of ruthenium prophyrin oxygen transfer catalyst

Estelle Burri, Kay Severin*

Institut de Chimie Moléculaire et Biologique, Ecole Polytechnique Fédérale de Lausanne, BCH, 1015 Lausanne, Switzerland

Ruthenium porphyrin catalysts have been widely employed in oxygen transfer reactions with 2,6-dichloropyridine-*N*-oxide as the oxidant. Usually, ruthenium carbonyl complexes are used as catalyst precursors.

We were able to significantly enhance the oxygen transfer reaction by addition of CCl_4 or $CBrCl_3$ to the reaction mixture. The turnover numbers obtained are above 50'000 and the turnover frequencies above 15'000 h^{-1}.



Catalyses with various ruthenium porphyrin complexes and substrates are now under investigation.

[1] E. Burri, K. Severin, submitted.

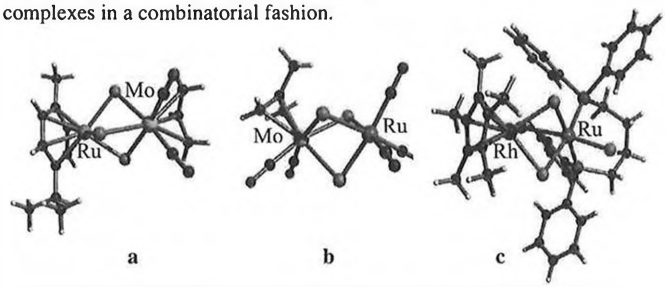
Inorganic Chemistry **108**

Combinatorial Synthesis of Bimetallic Complexes

Sébastien Gauthier, Rosario Scopelliti, Kay Severin*

Institut de Chimie Moléculaire et Biologique, Ecole Polytechnique Fédérale de Lausanne, BCH, 1015 Lausanne, Switzerland

During the last decades tremendous efforts have been made to synthesize structurally defined polynuclear complexes. The motivation behind these efforts were often potential applications of such compounds as catalysts and reagents in organic chemistry. New methods for the synthesis of bimetallic complexes, in which two different fragments are connected by three halogeno-bridges are reported. The reactions are general, fast and give rise to structurally defined products in quantitative yields [1, 2]. Therefore, they are ideally suited to generate a library of homo and heterobimetallic complexes in a combinatorial fashion.



Selected members of this library were synthesized and comprehensively characterized including single crystal X-ray analyses for 15 new bimetallic compounds including the complexes $[(cymene)Ru(\mu\text{-}Cl)_3Mo(CO)_2(\eta^3\text{-}C_3H_5)]$, $[Ru(CO)_3(\mu\text{-}Cl)_3Mo(\eta^3\text{-}C_3H_4)(CH_3))(CO)_2]$ and $[(Cp^*)Rh(\mu\text{-}Cl)_3Ru(dppb)Cl]$ (**a, b, c**).

[1] K. Severin, *Chem. Eur. J.* **2002**, *8*, 1515 and references cited.
[2] S. Gauthier, L. Quebatte, R. Scopelliti, K. Severin, submitted

Inorganic and Coordination Chemistry **109**

The Role of Support in Lean DeNO$_x$ Catalysis

M. Piacentini, M.Maciejewski, T. Bürgi and A. Baiker*

Institute for Chemical and Bioengineering, ETH-Hönggerberg, HCI, CH-8093 Zurich, Switzerland

Activity of lean DeNO$_x$ catalysts containing Ba components as a NO$_x$ trapping agent is related to the reactivity of the stored NO$_x$ species and CO_2. Species too strongly adsorbed will not react easily. Supports could play a primary role in the activity of the catalysts influencing the different stability of $BaCO_3$ and $Ba(NO_x)_2$. FTIR and Pulse Thermal Analysis (Pulse TA) [1] were performed on Pt(1 wt%) /Ba(17 wt%) supported on γ-Al_2O_3, SiO_2 and ZrO_2 catalysts to investigate the influence of the supports on adsorption of NO$_x$ and CO_2 at different temperatures and related formation of surface and bulk $BaCO_3$ and $Ba(NO_x)_2$ species. It has been found that γ-Al_2O_3 plays a major role in adsorbing both CO_2 and NO$_x$ species in an active form and in influencing the thermal stability of corresponding barium salts $BaCO_3$ and $Ba(NO_3)_2$. This finding may explain the higher activity of γ-Al_2O_3 supported catalysts in NO$_x$ storage reduction reactions.

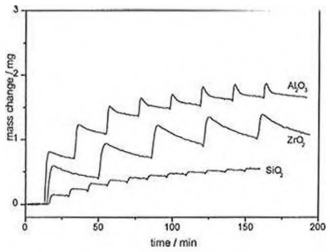


Fig.1 Pulses of NO in 5% O_2 / He atmosphere at 300°C on Pt/Ba supported on Al_2O_3, SiO_2 and ZrO_2.

1. M. Maciejewski, C. A. Müller, R. Tschan, W. D. Emmerich and A. Baiker, Thermochim. Acta 295 (1997)

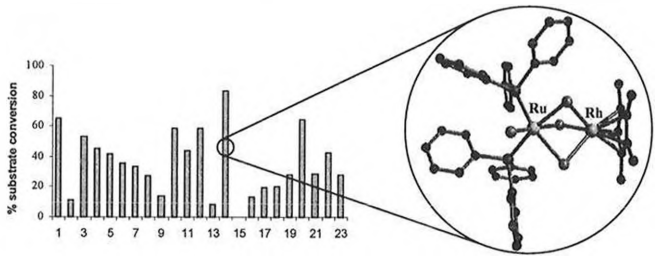
Inorganic and Coordination Chemistry **110**

New catalysts for the Kharasch reaction by fast screening of homo- and heterobimetallic complexes

Laurent Québatte, Rosario Scopelliti and Kay Severin*

Institut de Chimie Moléculaire et Biologique, Ecole Polytechnique Fédérale de Lausanne, BCH , CH-1015 Lausanne, Switzerland

High throughput screening methods are increasingly being used for the discovery of new homogeneous catalysts. So far, this method has not been applied to heterobimetallic catalysts, probably due to the difficulty to obtain a large pool of structurally defined complexes. Recently we have shown that bimetallic complexes, in which two different metal fragments are connected by halogeno-bridges, can easily be synthesized using metathesis reactions. [1]



Various Pd(II), Pt(II), Rh(I), Rh(III), Ir(I), Ir(III), Ru(II) and Ru(IV) bimetallic complexes have been tested in a parallel screening for their catalytic activity in atom transfer radical addition. As benchmark reaction we have employed the Kharasch addition of CCl_4 to styrene. A Ru-Rh complex showing remarkable activity and stability has been identified.

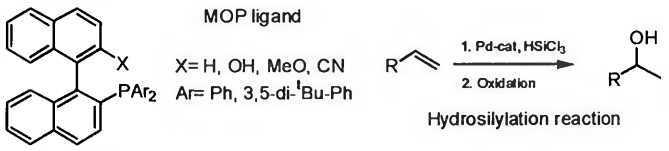
[1] K. Severin, *Chem. Eur. J.* **2002**, *8*, (7), 1514-1518.

Inorganic and Coordination Chemistry **111**

Monodentate phosphine ligands with a binaphthyl backbone: Coordination chemistry with Palladium and enantioselective hydrosilylation reaction

Pascal Dotta and Paul S. Pregosin
Laboratorium für Anorganische Chemie, ETH Zürich
CH - 8093 Zürich, Switzerland

The MOP ligand system, introduced by Hayashi, was shown to be a highly efficient chiral ligand for palladium catalyzed hydrosilylation of olefins [1]. It is known, that introducing alkyl groups in 3,5-positions on phenyl groups of tertiary chiral bidentate phosphines can lead to a significant increase in enantioselectivity in asymmetric catalysis [2].



To expand this principle to a monodentate ligand system, 4 different MOP ligands (X= H, OH, MeO, CN) bearing 3,5-Di-^{t}Bu-phenyl groups on the phosphorous were synthesized. In the asymmetric hydrosilylation of different olefins improved enantioselectivities were obtained in several cases compared to the results with the corresponding phenyl substituted analogues. The influence of the X substituent in 2' position on the reaction rate of the catalysis as well as on the enantioselectivity was partially rationalised by comparing the coordination behavior of the different MOP ligands in some Palladium complexes.

[1] T. Hayashi, *Acc. Chem. Res* , **2000**, *33*, 354.
[2] P.Dotta, A.Magistrato, U.Röthlisberger, P.S. Pregosin, *Organometallics*, **2002**, *21*, 3033

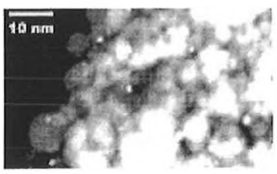
Physical Chemistry **112**

Flame Made Au and Ag catalysts for Selective CO Oxidation

S. Hannemann[a], J.-D. Grunwaldt[a], W.J. Stark[a,b], S.E. Pratsinis[b], A. Baiker*[a]

[a]Institute for Chemical and Bioenginering, ETH-Hönggerberg, CH-8093 Zürich
[b]Institute for Particle Technology, ETH-Zentrum, CH-8092 Zürich

Selective CO oxidation in the presence of H_2 is an important step in PEM fuel cells, since CO poisons the anode catalyst. During the past years, CO oxidation over Au nano particles (< 5 nm) has gained considerable interest and different preparation methods are known[1,2]. In this work, flame synthesis was used to prepare monometallic and bimetallic gold and gold-silver nanoparticles[3] with 0.1 to 1wt% of each noble metal (see Figure).
The materials were tested with respect to selective oxidation of CO in the presence of H_2 (0.5% O_2, 0.5% CO, 5% H_2 in Ar). Maximum rates of 0.4 mmol CO $\cdot g_{Au}^{-1} \cdot s^{-1}$ (0.1% Au on TiO_2) correspond to typical values reported in literature.
Important issues in bimetallic catalysts are not only particle size, but also the proof of alloying EXAFS spectra in the fluorescence mode (Ag K and Au L_3-edges) seem to be suitable to characterize the nano Au and Ag particles concerning alloy formation. Apart from this technique, also Electron Spectroscopic Imaging indicated that Ag-Au alloying takes place particularly in smaller particles.



TEM picture of flame-made 1% Au-1% Ag/TiO_2

[1] M. Haruta, M. Date, *Appl. Catal. A* **2001**, *222*, 427.
[2] J. D. Grunwaldt, C. Kiener, C. Wogerbauer, A. Baiker, *J. Catal.* **1999**, *181*, 223.
[3] W. J. Stark, S. E. Pratsinis, A. Baiker, *Chimia* **2002**, *56*, 485.

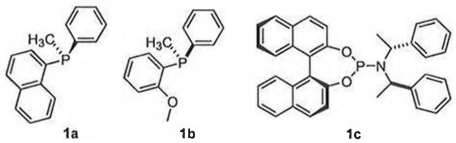
Inorganic Chemistry **113**

Controlling Absolute Configuration at Stereogenic Ruthenium with Monodentate Chiral P-Ligands: Application in Asymmetric Catalysis

Dominik Huber, Evert Wipplinger, Antonio Mezzetti*

Department of Chemistry, ETH Zürich, CH-8093 Zürich, Switzerland

Following our investigation of five-coordinate ruthenium(II) complexes as catalysts for asymmetric cyclopropanation [1], epoxidation [2], and fluorination [3], we try now to exploit the chiral monodentate phosphorus ligands **1a-1b**, **1c** [4] (P*) to control the stereochemistry of the addition of a sixth ligand (e. g. carbene) to the corresponding 16-electron complexes [RuCl(*p*-cymene)(P*)], which can be prepared from $[RuCl_2(p\text{-cymene})]_2$ and P*, followed by Cl abstraction.



1a **1b** **1c**

Although phosphines **1a** and **1b** are not bulky enough to stabilize five-coordinate species, the corresponding $[RuCl_2(p\text{-cymene})(P^*)]$ catalyze the fluorination of PhMeCHBr with TlF upon activation with $TlPF_6$. The newly prepared $[RuCl_2(p\text{-cymene})(\mathbf{1c})]$ reacts with $TlPF_6$ to give a cyclopropanation catalyst that showed low activity and selectivity with styrene and N_2CHCO_2Et (16% yield after 20 h; 57:43 trans:cis; ee ≤ 4%).

[1] S. Bachmann, M. Furler, A. Mezzetti *Organometallics* **2001**, *20*, 2102.
[2] R. M. Stoop, S. Bachmann, M. Valentini, A. Mezzetti *Organometallics* **2000**, *19*, 4117.
[3] P. Barthazy, A. Togni, A. Mezzetti *Organometallics* **2001**, *20*, 3472.
[4] L. A. Arnold, R. Imbos, A. Mandoli, A. H. M. de Vries, R. Naasz, B. L. Feringa *Tetrahedron* **2000**, *56*, 2865.

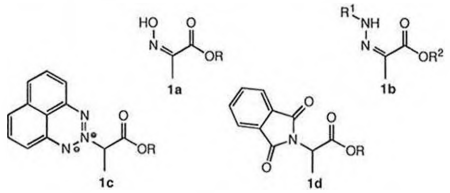
Inorganic Chemistry **114**

Enantioselective Electrophilic Fluorination Towards α-fluoro-α-amino acid derivatives?

Dominique P. Huber, Antonio Togni*

Department of Chemistry, ETH Zürich, CH-8093 Zürich, Switzerland

Recently, the first enantioselective fluorination of β-ketoesters catalyzed by a titanium TADDOL complex has been reported from our group [1].
Also other substrates, such as diketones, β-ketothioesters, β-ketophosphonates etc., have been fluorinated with moderate to good enantiomeric excess [2].
The question now was whether it was possible to fluorinate substrates which could be regarded as precursors for α-fluoro-α-aminoacids. For this purpose substrates containing a unit isoelectronic to a 1,3-dicarbonyl fragment (**1a-c**), as well as a N-protected alanine ester (**1d**) were studied.



1a **1b** **1c** **1d**

[1] L. Hintermann, A. Togni, *Angew. Chem.* **2000**, *39*, 4359.
[2] To be published.

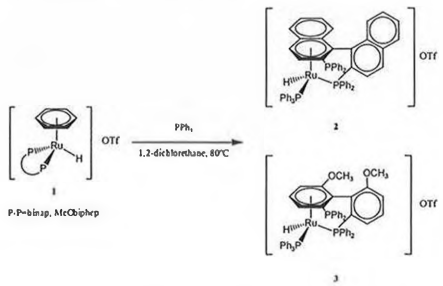
Inorganic and Coordination Chemistry **115**

Novel Ru(II) complexes containing Binap and MeOBiphep as 8e donor

René Hermatschweiler, Paul S. Pregosin

ETH Zürich, ETH Hönggerberg, CH-8093 Zürich, Switzerland

The synthesis and reactivity of Ruthenium hydride complexes with an η^6-arene ligand represents a subject of interest. In our group, complexes of type **1** have recently been prepared through a new synthetic method [1].



The reaction of **1** (P-P=binap, MeObiphep) with PPh_3 affords the unexpected complexes **2** and **3**. After loss of the η^6-benzene, the Ru-cation generated, chooses to stabilize itself by coordinating the proximate naphthyl ring at the expense of one of the two phosphorous donors. Both complexes have been characterized by 2D-NMR and **2** by X-ray crystallography.

Complexes **2** and **3** were tested as potential catalysts for transfer-hydrogenation of acetophenone. The Binap complex was shown to be faster than the MeObiphep complex. The simple arene compound **1** was not active.

[1] T. J. Geldbach, P. S. Pregosin, *Helv. Chim. Acta*, **2002**, 85, 3937.

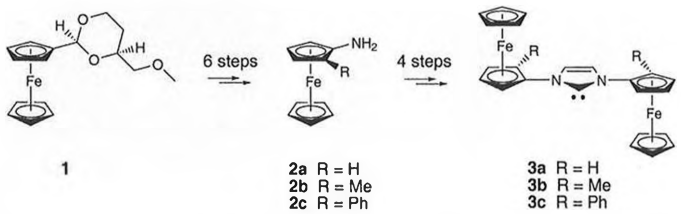
Inorganic and Coordination Chemistry **116**

Synthetic Approaches to C_2-Symmetrical, Planar-Chiral, *N*-Ferrocenyl-Substituted *N*-Heterocyclic Carbene Ligands

Andreas Bertogg, Antonio Togni*

Departement of Chemistry, Swiss Federal Institute of Technology, ETH Hönggerberg, CH-8093 Zürich, Switzerland

N-Heterocyclic carbenes (NHC's) [1] are becoming ubiquitous ligands in organometallic chemistry and homogeneous catalysis [2]. Recently, achiral imidazolium salts based on the structure of NHC **3a** and corresponding silver complexes were reported [3].



1 **2a** R = H, **2b** R = Me, **2c** R = Ph **3a** R = H, **3b** R = Me, **3c** R = Ph

On the way towards planar-chiral, *N*-ferrocenyl substituted NHC's we synthesised **2a** and **2b**, in the latter case starting from the known chiral acetal **1** [4]. A new synthetic strategy led to the formation of **3a** and was applied to the synthesis of **3b** and **3c**. Preliminary coordination chemistry using the target compounds **3a-b** will be presented.

[1] A.J. Arduengo, R.L. Harlow, M. Kline, *J. Am. Chem. Soc.* **1991**, *113*, 361.
[2] D. Bourissou, O. Guerret, F. P. Gabbaï, G. Bertrand, *Chem. Rev.* **2000**, *100*, 39.
[3] B. Bildstein *et al.*, *Organometallics* **1999**, *18*, 4325.
[4] O. Riant, O. Samuel, T. Flessner, S. Taudien, H.B. Kagan, *J. Org. Chem.* **1997**, *62*, 6733.

Inorganic and coordination chemistry **117**

New soft magnetical carbon nanostructures from thermal decomposition of metallocenes.

A.Ivantchenko, F.Krumeich, R.Nesper.

ETH-Hönggerberg, Wolfgang-Pauli Str10, 8093 Zürich, Switzerland

Large quantities of aligned carbon nanotubes bundles can be produced by pyrolysis of ferrocene on metal catalyst [1]. Upon mild heat treatments, the ferritin structure is carbonized into quasi-spherical graphitic shells with encapsulated metal particles [2]. Here, we describe preparation of magnetical carbon nanostructures from thermal decomposition of ferrocene and titanocene chloride. Metallocenes were used of ca. 99% and high purity. The solid precursor was introduced in a hot reactor with corundum or steel crucible. The main variables in the experiments were the pyrolysis temperature (700-1050°C) and additional agents ($FeCl_2$, $FeCl_3$, $CoCl_2$, $NiCl_2$, LiCl). Salt melts are believed to support homogeneity in reaction and high concentration of metal particles. The products were examined with TEM, HRTEM, X-Ray powder diffraction and C,H-elemental analyses. Magnetization measurements were carried out by using a physical property magnetization system (PPMS). Powder diffraction patterns contain peaks of the typical graphite interlayer distance (002), iron and iron carbide (Fe_3C_4, cementite). There is an optimal temperature range at which iron peaks have a maximum intensity. The products have saturation magnetization maximum about 50emu/g. The highest remanence magnetization found so far is 10emu/g. On TEM images particles are encapsulated in a dense carbon material. A size histogram was constructed after examining over 200 of these particles. Electron microscopy micrographs of samples after long acid behaviors showed large amount of carbon nanotubes with encapsulated iron and iron carbide.

[1] C.N.R.Rao, R.Sen, B.C.Satishkumar, *Chem.Commun.*, **1998**, 1525.
[2] C.C.Tsang, J.Qiu, P.J.F.Harris, *Chem.Phys.Lett.* **2000**, 322, 553.

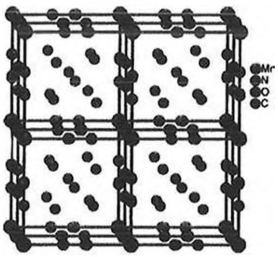
Inorganic and Coordination Chemistry **118**

Structure and Magnetic Properties of a Mixed-Valence Mn-Prussian-Blue Phase

Christina Ambrus[a], Patrick Franz[a], Cédérick Rauzy[b], Claude Daul[b], Andreas Hauser[c], Lukas Keller[d] and Silvio Decurtins[a]

[a] Departement für Chemie und Biochemie, Universität Bern, Freiestrasse 3, CH-3012 Bern, Switzerland; [b] Département de Chimie, Université de Fribourg-Pérolles, CH-1700 Fribourg, Switzerland; [c] Département de Chimie Physique, Université de Genève, 30 Quai E.Ansermet, CH-1211 Genève, Switzerland; [d] Paul-Scherrer Institut, CH-5232 Villigen PSI, Switzerland

The single crystal structure of the mixed-valence Mn-Prussian-Blue phase has been obtained by X-ray diffraction [1]. Combined with theoretical calculations it results, that within the μ-CN brigded system the N-coordinated manganese ion could be assigned to the high-spin manganese(II), whereas the low-spin manganese(III) ion is C-coordinated. Magnetic measurements show a cooperative magnetic ordering below 35 K for this compound. As revealed by elastic neutron scattering experiments, this ordering corresponds to an antiferromagnetic arrangement of the high-spin manganese(II) and the low-spin manganese(III) moments.



[1] P. Franz, L. Keller, H. Stoeckli-Evans, A. Hauser, H. B. Bürgi, S. Decurtins, *Europ. J. of Chem.*, in preparation

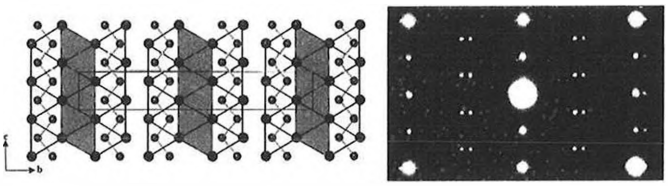
Inorganic and Coordination Chemistry **119**

Ordering Phenomena in $YbSi_x$ (x≈1.4)

F. Krumeich, C. Kubata, M. Wörle, and R. Nesper

Laboratory of Inorganic Chemistry, ETH Zürich, CH-8093 Zürich, Switzerland

According to XRD results, the novel phase $YbSi_{1.4}$ [1,2] crystallizes with orthorhombic symmetry (space group: *Cmcm*; a = 4.159(1), b = 23.510(5), c = 3.775(1) Å). The structure (left figure) contains trigonal Yb_6 prisms that are fully occupied by Si forming zigzag chains along the c-axis. Residual electron density intensity that was detected in the other Yb_6 prisms can be explained by a partial occupancy of this Si site.



In electron diffraction patterns, there are additional reflections in the b*c* plane which indicate that the length of the c-axis is doubled. Moreover, a splitting of these reflection has been observed in the ED patterns of most crystals (right figure). This indicates the presence of a modulated superstructure. The modulation, which has a period of about 5 nm, can also be detected by high-resolution transmission electron microscopy. According to the experimental knowledge at hand, this modulation is due to an ordering in the sublattice of partially occupied Si positions.

[1] C. Kubata, F. Krumeich, M. Wörle, R. Nesper, *Chimia* **2002**, *56*, 395.
[2] C. Kubata, F. Krumeich, M. Wörle, R. Nesper, *Z. Anorg. Allg. Chem.* **2002**, *628*, 2201.

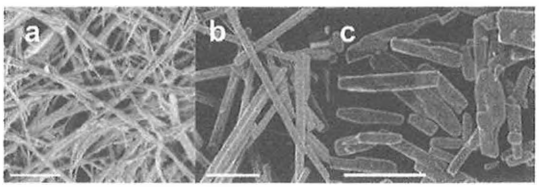
Inorganic and Coordination Chemistry **120**

Nanoscopic Design of Molybdenum Oxides

A. Michailovski, G. R. Patzke, and R. Nesper

Laboratory of Inorganic Chemistry,
ETH Hönggerberg, HCI, CH-8093 Zürich, Switzerland

Nanostructured materials attract a steadily growing interest due to their properties that often enhance those of the bulk material. Molybdenum oxide nanorods [1] with diameters in the 100 nm range and high aspect ratios are accessible *via* a tunable and efficient one-step solvothermal routine [2, 3].



Scale bar: 1 μm

As a follow-up step, the influence of ionic additives on the morphology of nanoscopic molybdenum oxide particles is investigated. The reaction was tuned by parameter optimization with respect to additive concentration, temperature and reaction time. Both morphology and aspect ratio of the emerging MoO_3 nanoparticles can be tailored by the choice of an appropriate ionic additive within a defined parameter window (100 - 180 °C, >2 d), e.g. 1 M $(CH_3)_4NBr$ (Fig. a), 1 M LiBr (Fig. b) or 1 M $AlCl_3$ (Fig. c) solutions. Altered reaction conditions afford a series of hexagonal alkali- and earth alkali-based molybdates as well as novel compounds.

[1] M. Niederberger, F. Krumeich, H.-J. Muhr, M. Müller, R. Nesper, *J. Mater. Chem.* **2001**, *11*, 1941.
[2] G. R. Patzke, F. Krumeich, R. Nesper, *Angew. Chem. Int. Ed.* **2002**, *41*, 2446.
[3] G. R. Patzke, A. Michailovski, F. Krumeich, R. Nesper, J.-D. Grunwaldt, A. Baiker, *Chem. Mater.*, submitted.

Inorganic and Coordination Chemistry **121**

Eu^{III} luminescence to detect the crystalline-to-mesogenic phase transitions

Stéphane Suárez[a], Olimpia Mamula[a], Daniel Imbert[a], Claude Piguet[b], J.-C. G. Bünzli[a]

[a]Swiss Federal Institute of Technology, Institute of Molecular and Biological Chemistry, CH-1015-Lausanne, Switzerland. stephane.suarez@epfl.ch
[b]University of Geneva, Department of Inorganic, Analytical and Applied Chemistry, 30 quai E. Ansermet, CH-1211 Geneva 4

Lanthanide-containing liquid crystals are of particular interest for the design of new luminescent materials able to emit narrow bands with different colours, such as blue (Eu^{2+}), red (Eu^{3+}) and green (Tb^{3+}) [1]. Diaza-18-crown-6 ethers being known to form stable complexes with lanthanides [2], we have synthesized the pro-mesogenic ligand L. The europium and terbium nitrate complexes obtained with this new ligand exhibit stable and reversible liquid-crystalline phases between 85 and 198 °C. High-resolution laser-excited luminescence has been used to probe the Eu^{3+} ion environment. Moreover, we show that the phase transitions may be detected by monitoring both luminescence intensity and lifetime *vs* temperature. Plots of ln (τ_{obs}/τ_{295K}) and ln (I_{obs}/I_{295K}) versus the inverse of the absolute temperature are indeed sigmoid and demonstrate that the phase transitions intrinsically affect the luminescence parameters, allowing a precise determination of the temperature at which these transitions occur [3].

[1] K. Binnemans and C. Görller-Walrand, *Chem. Rev.* 2002, **102**, 2303.
[2] J.-C. G.Bünzli in *Rare Earths*, Sastri, B., Ed.; Elsevier Science B.V.: Amsterdam, 2003.
[3] S. Suárez, O. Mamula, D. Imbert, C. Piguet, J.-C. G. Bünzli, *Chem. Comm.*, 2003, 1226-1227.

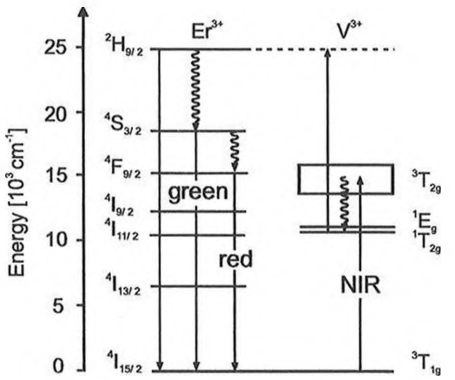
Inorganic Chemistry **122**

Cooperative Upconversion in $K_2NaScF_6:Er^{3+};V^{3+}$

Christine Reinhard, Karl Krämer, Hans U. Güdel*

Departement für Chemie und Biochemie, Universität Bern, Freiestrasse 3, CH-3000 Bern 9, Switzerland

A single crystal of K_2NaScF_6 codoped with Er^{3+} and V^{3+} was synthesized and studied by high-resolution optical spectroscopy. The principal objective is the search for a material containing a broad-band absorber in the near-infrared (NIR), i.e. V^{3+}, to sensitize the NIR to visible upconversion of Er^{3+}.



In $K_2NaScF_6:Er^{3+};V^{3+}$ NIR excitation over the whole V^{3+} $^3T_{2g}$ absorption band at 15 K leads to strong V^{3+} and Er^{3+} infrared emission and to weak Er^{3+} $^2H_{9/2}$, green $^4S_{3/2}$ and red $^2F_{9/2}$ upconversion emission, see Figure. At 15 K broad-band excitation between 12000 cm^{-1} and 14500 cm^{-1} roughly doubles the visible light output in an Er^{3+} and V^{3+} codoped crystal of K_2NaScF_6 compared to doping solely with Er^{3+}.

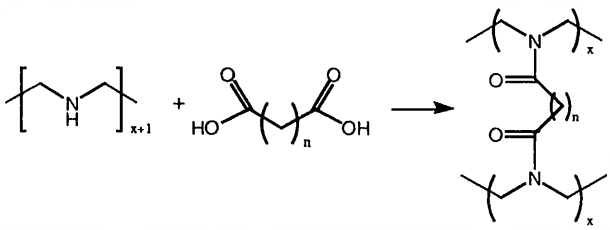
Inorganic and Coordination Chemistry **123**

Synthesis of new hydrogels by cross-linking LPEI with aliphatic dicarboxilic acids

Andriy Shkilnyy, Carl-Wilhelm Schlaepfer

University of Fribourg, Ch. du Musée 9, CH-1700 Fribourg, Switzerland

Polyelectrolyte gels were prepared by cross-linking linear poly(ethylenimine) (LPEI) with heptanedioic (n=5) and dodecanedioic (n=10) acids.



The reactions are carried out in bulk. The temperature necessary for the cross-linking reaction is determinated by TG and DSC experiments. The degree of cross-linking is varied changing the concentrations of the cross-linker. The products are investigated by elemental analysis and IR-spectroscopy. The swelling properties of the gels are investigated under different condition and related to the composition of the gel. The protonation and deprotonotation process followed by potentiometry allowed the determination number of the active sites and the understanding how the pH influences the properties of gel. Absorption of small species is studied as a function of the pH.

[1] Schlaepfer, C.W.; Spuck, J. Abstract: *Chimia* **1998**, *52*, 467.
[2] Schlaepfer, C. W.; Najla Ben Ameur, J. Abstract: *Chimia* **2002**, *56*, 385.

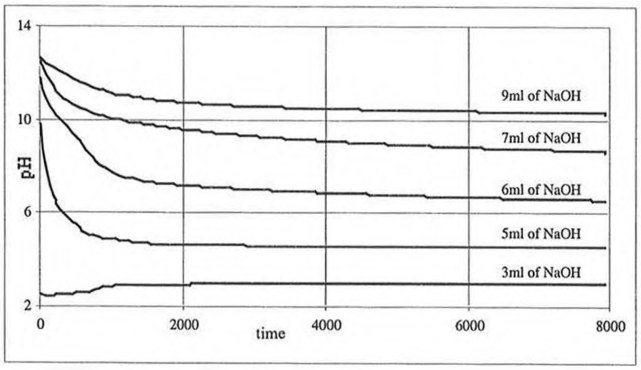
Inorganic and Coordination Chemistry **124**

Chemical characterization of hydrogels obtained by crosslinking LPEI with 1,4 butanediol-diglycidyl-ether

Najla Ben Ameur, Carl-Wilhelm Schläpfer

Université de Fribourg, Ch. du Musée 9, CH-1700 Fribourg, Suisse

Hydrogels obtained by crosslinking LPEI with 1,4 butanediol-diglycidyl-ether are weak polybases and good ligands binding for transition metal ion. Investigation of the protonation-deprotonation process by titration provides a key for the understanding of the pH dependent properties of the gel.
Deprotonation of gel in Cu^{2+} solution shows that the complexation of Cu^{2+} by the gel is reversible within the investigated region of pH. Rate constants for the deprotonation of these gel complexes with different concentrations of Cu^{2+} are determined; the value of these constants are larger than for gels without Cu^{2+}.



pH Change in suspensions of complexes of the gel with Cu^{2+} (N:Cu^{2+} =1:7) after addition of NaOH (0,5 M)

[1] Schläpfer, C.W.; Spuck, J. *Abstract: Chimia* **1998**, *52*, 467.
[2] Kokufuta, E.; Suzuki, H.; Yoshida, R.;Yamada, K.; Hirata, M.; Kaneko, F. *Langmuir* , **1997**,*14*, 788-795.

Inorganic and Coordination Chemistry **125**

Synthesis and Structural Investigation of $Eu_4Li_2Ge_6$

Qinxing Xie, Reinhard Nesper*

Inorg. Chem. Lab., ETH Hönggerberg, 8093 Zürich, Switzerland

$Eu_4Li_2Ge_6$ was synthesized from a mixture of pure elements at stoichiometric amounts via direct heating method in argon atmosphere. The structure (Fig. 1) was solved and refined in orthorhombic space group Pnnm (No. 58) with a = 10.968(2), b = 11.687(2), c = 4.5482(7) Å, V = 583.0 Å^3, Z = 2, R_{gt} = 0.036, wR_{ref} (F^2) = 0.0824. $Eu_4Li_2Ge_6$ is isostructural to $Ca_4Li_2Tt_6$ (Tt = Si, Ge) [1] and α-$Sr_4Li_2Ge_6$ [2] crystallizing in a layered structure. The Zintl anion is one dimensional infinite chain in $(tttctc)_n$ conformation. $Eu_4Li_2Ge_6$ can be formulated as $(Eu^{2+})_4(Li^+)_2[Ge_6]^{10-}$ according to the Zintl-Klemm Concept [3], each Zintl anion has a delocalized π system.

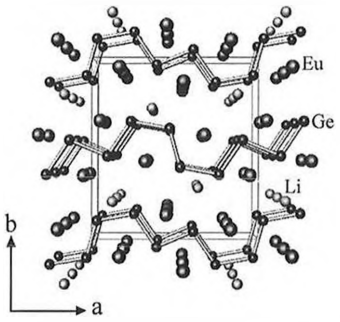


Fig. 1 Perspective view [001] of the crystal structure of $Eu_4Li_2Ge_6$

[1] W. Müller, H. Schäfer, A. Weiss, *Z. Naturforsch.* **1971**, *26b*, 5.
[2] Q. Xie, R. Nesper, 9th European Conference on Solid State Chemistry **2003**, submitted.
[3] E. Zintl, *Angew. Chem.* **1939**, *52*, 1; W.Klemm, *Proc. Chem. Soc.* London, **1958**, 329; R. Nesper, *Prog. Solid State Chem.* **1990**, *20*, 1.

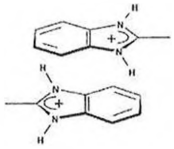
Inorganic and Coordination Chemistry **126**

Protonated Benzimidazoles as Synthons for Crystal Engineering

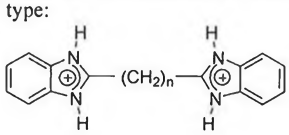
Simon Verdan, Craig J. Matthews, Xavier Melich, Ludovic Grémaud, Gérald Bernardinelli, Alan F. Williams

Department of Inorganic, Analytical and Applied Chemistry, University of Geneva, 30 quai Ernest Ansermet, CH 1211 Geneva 4, Switzerland

Crystal engineering seeks the planned synthesis of extended molecular structures. Desiraju [1] has introduced the notion of the supramolecular synthon, an interaction between two functionalities on neighbouring molecules which occurs in a regular and predictable manner, and which may thus be used to link molecules in a solid in a rational manner. We have previously shown [2] that protonated benzimidazoles stack in the solid state as shown below:



We report here a number of crystal structures containing benzimidazole cations of the general type:



and show that they lead to a series of layered structures in which the crystal is held together by benzimidazole stacking and hydrogen bonding to anions.

[1] G. R. Desiraju, *Angew. Chem. Int. Ed. Engl.*, **1995**, *34*, 2311.
[2] C. J. Matthews, V. Broughton, G. Bernardinelli, X. Melich, G. Brand, A. C. Willis, and A. F. Williams, *New J. Chem.*, **2003**, *27*, 354.

Inorganic and Coordination Chemistry **127**

Peroxynitrite Scavenging by Myoglobin and Hemoglobin

Shivashankar Kalinga and Susanna Herold

Institute of Inorganic Chemistry, ETH Hönggerberg, 8093 Zürich, Switzerland

Peroxynitrite, produced *in vivo* by the diffusion controlled reaction between NO$^\bullet$ and $O_2^{\bullet-}$, is capable to nitrate and oxidize various biomolecules. Metal proteins are believed to be among the major targets for peroxynitrite. We have recently shown that myoglobin (Mb) and hemoglobin (Hb) can scavenge this toxic compound efficiently [1]. Here we present stopped-flow spectroscopic studies of the reaction of peroxynitrite with the iron(III) forms of Mb and Hb (metMb and metHb). Our data show that metMb and metHb catalyze the decay of peroxynitrite. The catalytic rate constants are in the order of magnitude of 10^4 M^{-1} s^{-1}. Analysis of the nitrogen-containing products by ion-chromatography shows that the yield of nitrate increases with increasing amounts of these proteins. In addition, we have determined the yield of 3-nitrotyrosine, the biomarker for the peroxynitrite *in vivo*, in Mb and Hb after treatment with peroxynitrite. HPLC chromatography after acid hydrolysis shows that the iron(III) forms of Mb and Hb are nitrated slightly less than the corresponding oxygenated forms. Possible mechanisms for this catalytic reaction will be discussed.

[1] S. Herold , S. Kalinga and M. Mehl *Biochemistry* **2002**, *41*, 13460.

Inorganic and Coordination Chemistry **128**

Mechanistic Studies of the Reaction Between Peroxynitrite and Oxyhemoglobin

Francesca Boccini and Susanna Herold

Laboratorium für Anorganische Chemie; Eidgenössische Technische Hochschule, ETH Hönggerberg, CH-8093 Zürich, Switzerland

Peroxynitrite ($ONOO^-$/ONOOH) is formed *in vivo* by the diffusion-controlled reaction between superoxide and nitrogen monoxide. In living cells one of the most important targets for peroxynitrite is carbon dioxide, which reacts rapidly with $ONOO^-$ to produce 1-carboxylato-2-nitrosodioxidane ($ONOOCO_2^-$). Both, this adduct and peroxynitrite, are able to damage DNA, to hydroxylate or nitrate aromatic compounds, and to oxidize thiols. In addition, we have recently shown that peroxynitrite can oxidize myoglobin and hemoglobin to their iron(III) forms [1]. In this work, we present stopped-flow spectroscopic studies of the reaction between peroxynitrite and oxyhemoglobin in the absence and presence of carbon dioxide. In analogy to oxymyoglobin [1,2], this reaction proceeds in two steps:

(1) $HbFeO_2 + ONOOH \rightarrow HbFe^{IV}{=}O + ...$

(2) $HbFe^{IV}{=}O + ONOOH \rightarrow HbFe^{III} + ...$

We found that at 20 °C and pH 7.4 the rate constants for the first and the second step are (3.28±0.08) × 10^4 M^{-1} s^{-1} and (3.3±0.4) × 10^4 M^{-1} s^{-1}, respectively. Under similar conditions, in the presence of 1.2 mM of carbon dioxide, the two values are (14±3) × 10^4 M^{-1} s^{-1} and (2.3±0.6) × 10^4 M^{-1} s^{-1}. The mechanism of the two reaction steps is complex. Possible hypotheses will be discussed.

[1] M. Exner and S. Herold, *Chem. Res. Toxicol.* **2000**, *13*, 287–293.
[2] S. Herold, M. Exner and F. Boccini, *Chem. Res. Toxicol.* **2003**, *16*, 390–402.

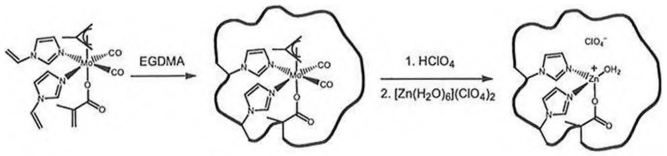
Inorganic and Coordination Chemistry **129**

Can the active site of an enzyme exchange its peptide frame for a polymer?

Alexander Schiller, Rosario Scopelliti, Kay Severin*

Institut de Chimie Moléculaire et Biologique, Ecole Polytechnique Fédérale de Lausanne, BCH, 1015 Lausanne, Switzerland

A common structural motif in active sites has been found in proteins like mononuclear zinc hydrolyzing (e.g. Carboxypeptidase A) and non-heme iron oxygen activating enzymes (e.g. Extradiol cleaving catechol dioxygenase): the 2-histidine-1-carboxylate facial triad (N,N,O). [1] Zinc and iron complexes with N,N,O-donor ligands, used as enzyme mimics, tend to aggregate. [2] Nature has solved this problem by generating a peptide frame around the active site. In contrast, polymers with structurally defined metal-binding N,N,O facial triads are synthesized with the protocol of molecular imprinting and exposed to simple test reactions to confirm them also as functional models.



Complex **1** is co-polymerized with an excess of EGDMA. The Mo template in **P1** is subsequently cleaved off by acid and a zinc complex is generated by addition of $[Zn(H_2O)_6](ClO_4)_2$. 4-Nitrophenylacetate is used to show a catalytic activity of **P2** significantly higher than the background.

[1] L. Que Jr., *Nature Struct. Biol.* **2000**, *7*, 182.
[2] A. Beck, B. Weibert, N. Burzlaff, *Eur. J. Inorg. Chem.* **2001**, 521.

Inorganic and Coordination Chemistry **130**

Artifactual Generation of S-Nitroso-Hemoglobin from the Reaction Between Oxyhemoglobin and Nitrogen Monoxide

Gabriele Röck and Susanna Herold

Institute of Inorganic Chemistry, ETH Hönggerberg, 8093 Zürich, Switzerland.

Nitrogen monoxide (NO•), generated from the endothelial isoform of nitric oxide synthase, plays an important role for the control of vascular tone and blood flow. When oxyhemoglobin (oxyHb) is allowed to react with NO• *in vitro*, in addition to the generation of methemoglobin and nitrate, mixing artifacts lead to the partial nitrosation of the cysteine residue β93, and the formation of the so-called S-nitroso-hemoglobin (SNO-Hb). It is argued that *in vivo* NO• may be transported within the cardiovascular system in the stabilized form of SNO-Hb.

We have recently shown that *in vitro* the yield of SNO-Hb depends on the mixing procedure, on the amount of NO• added, and on the volumetric ratio of the NO• and oxyHb solutions mixed [1]. Here we present the results of anion chromatographic analysis of the nitrogen-containing products of the *in vitro* reaction between oxyHb and NO•. Our data show that there is a good correlation between the yield of nitrite and that of SNO-Hb.

As inorganic phosphate is known to catalyze the concurrent hydrolysis of N_2O_3 to nitrite, we varied the concentration of the phosphate buffer in the range 1–100 mM, to find out whether N_2O_3 is involved in the formation of SNO-Hb. We observed that the SNO-Hb yields obtained in 1 mM phosphate buffer are higher than those generated in 10 and 100 mM phosphate buffer. Taken together, our data show that if a bolus of an NO• solution is mixed with an air saturated oxyHb solution, high local concentrations of NO• and O_2 may lead to generation of N_2O_3 and thus artifactual formation of SNO-Hb.

[1] S. Herold and G. Röck, *J. Biol. Chem.* **2003**, *278*, 6623.

Inorganic and Coordination Chemistry **131**

The Mechanism of S-Nitrosothiol Decomposition Catalysed by Iron (II)

Alina A. Papina, Anatoly F. Vanin and Willem H. Koppenol.

ETH Hönggerberg, Wolfgang-Pauli-Str. 10, CH-8093 Zurich, Switzerland

In the last decade it has been recognised that nitrogen monoxide (NO) is involved in a large number of physiological processes (Nobel Prize, 1999). A relatively short life-time of free NO *in vivo* suggests that it might be stabilised by incorporation into a carrier molecule and released on demand. *S*-nitrosothiols (RSNOs) and dinitrosyl–iron complexes (DNICs) have been proposed to transport and store NO [1]. It has long been known that the DNICs $[(L^-)_2Fe^I(NO^+)_2]^+$ are formed from the reaction of Fe(II) with NO in the presence of low molecular weight ligands such as thiols (L^-=*RS*$^-$) [2]. It has recently been shown that Fe(II) can decompose RSNOs with concomitant formation of stable DNICs [3] by a yet unresolved mechanism.

In this work we present optical and EPR spectroscopic evidence that this reaction does not include preliminary NO release from RSNO, but rather a direct reaction of RSNOs with Fe(II). Two RSNO molecules react consecutively with Fe(II) and a mononitrosyl–iron complex (MNIC) is detected as short-lived intermediate in this system. The formation of DNIC has been found to be first order in Fe(II) and second order in RSNO. The line of evidence points to existence of an equilibrium:

$$\text{DNIC} \rightleftharpoons Fe^{2+}+NO+RSNO+RS^-$$

In conclusion, this work shows that in the presence of thiols DNIC and RSNO are interconvertible stable forms of NO. It is plausible that the NO-like biological activity of RS-NO is at least partly mediated by the formation of DNIC.

[1] Vanin, A. F., *Biochemistry (Moscow)* **1998**, *63*, 782.
[2] Vanin, A. F., *Biokhimia* **1967**, *32*, 228.
[3] Williams, D. L. H. *Chem. Commun.* **1996**, *1*, 1085

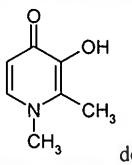
Inorganic and Coordination Chemistry **132**

Iron and Radical Reactions

M. Merkofer, R. Kissner, A. Vanin, W.H. Koppenol

Laboratorium für Anorganische Chemie der ETH Zürich, ETH Hönggerberg, CH-8093 Zürich, Switzerland

High concentrations of iron, as in hereditary hemochromatosis, causes organ damage, first in the liver and later in the heart and the joints. Redox cycling of iron is considered essential to its toxicity. Reduction of a low molecular weight Fe(III)-complex by, for instance, ascorbate followed by oxidation of the Fe(II)-complex by H_2O_2 yields the reactive HO• radical (the Fenton Reaction). Iron chelators are widely employed to protect cells against iron overload. After chelation, for instance by deferiprone or desferrioxamine the complex should be redox-inert. The redox activity of low-molecular weight complexes may also be inhibited by complexation with NO•.



deferiprone

We found that the reduction potential of the Fe(III)-/Fe(II)-deferiprone complex is –0.50 V, too low to be reduced *in vivo*. Binding of nitrogen monoxide to an Fe(II)dithiocarbamate complex reduced the rate constant of the oxidation by H_2O_2 from ca. 10^4 $M^{-1}s^{-1}$ to ~10 $M^{-1}s^{-1}$.

Complexation of iron that either shifts the reduction potential to far below –0.33 V (dioxygen/superoxide) or to far above +0.32 V (HO•, H_2O/H_2O_2) is essential to limit Fenton reactivity. Furthermore, as the oxidation by hydrogen peroxide is an inner-sphere reaction, blocking access by complexation of "open" sites with NO• should also be beneficial. In this study both the lowering of reduction potential and limiting access has been shown to be effective.

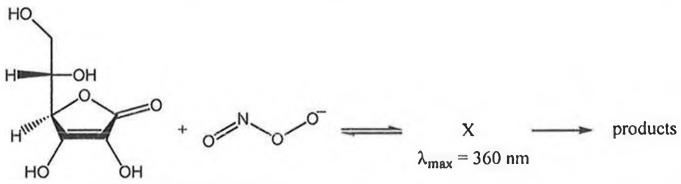
Inorganic and Coordination Chemistry **133**

The Reaction of Peroxynitrite Anion with Vitamin C

Ch. R. Kurz, R. Kissner, W.H. Koppenol

Laboratorium für Anorganische Chemie der ETH Zürich, ETH Hönggerberg, CH-8093 Zürich, Switzerland

Peroxynitrite, formed *in vivo* from the diffusion-controlled reaction of $NO^{\bullet}$ with $O_2^{\bullet-}$, has been shown to be harmful [1,2]. Vitamin C acts as an antioxidant, radical scavenger and re-reducing compound. Thus, it is of interest to investigate the mechanism of the reaction between peroxynitrite and vitamin C. We have recently shown that peroxynitrous acid reacts fast with vitamin C [3]. For peroxynitrite anion, the deprotonated form which is also present at neutral pH, it is unknown how it reacts with vitamin C. Therefore we are investigating the mechanism of thus reaction:



Our preliminary results show that there is an intermediate (X). Currently we are trying do determine the nature of this intermediate.

[1] T. Nauser, W.H. Koppenol, *J. Phys. Chem. A.* **2002**, *106*, 4086.
[2] J.S. Beckman, W.H. Koppenol, *Am. J. Physiol. Cell Physiol.* **1996**, *271*, 1424.
[3] Ch.R. Kurz, R. Kissner, T. Nauser, D. Perrin, W.H. Koppenol, *Free Radical. Biol. Med.* submitted.

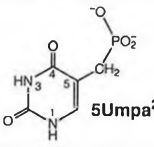
Inorganic and Coordination Chemistry **134**

Intramolecular Equilibria in Metal Ion Complexes formed with 5-Uracilmethylphosphonate ($5Umpa^{2-}$) in Aqueous Solution

Rolf Griesser,[a] Cristóbal F. Moreno-Luque,[a] Justyn Ochocki,[b] Helmut Sigel[a]

[a]Dept. of Chem. (IC), University, Spitalstr. 51, CH-4056 Basel, Switzerland
[b]Fac. of Pharm., Bioinorg. Chem., Med. University, PL-90151 Łódź, Poland

Recently we have studied the acid-base properties of 5-uracilmethylphosphonate [1] since this compound shows promising pharmaceutical properties. Because metal ions are usually involved in the biological action of phosphonate derivatives [2] we studied now the stability of several M(5Umpa) complexes (where M^{2+}, e.g., Mn^{2+}, Zn^{2+}, Cd^{2+}) (pot. pH titrations; aq. sol.; 25 °C; I = 0.1 M, $NaNO_3$). By application of previously established straight-line plots [3] of log $K^{M}_{M(R\text{-}PO_3)}$ *versus* $pK^{H}_{H(R\text{-}PO_3)}$ (where $R\text{-}PO_3^{2-}$ = simple phosphate monoester or phosphonate ligands with a non-interacting residue R), it is shown that several M(5Umpa) complexes are somewhat more stable than is expected on the basis of the basicity of the phosphonate residue. This observation is indicative of a M^{2+}-nucleobase interaction [4]. Since the only sterically accessible binding site of a phosphonate-coordinated metal ion is the (C4)O unit we attribute the increased stability to the formation of 7-membered chelates. For example, the stability increase observed for Mn(5Umpa) amounts to 0.14 ± 0.06 log units and from this value it follows [4] that 28 ± 10 % of the complex are present as the chelated isomer whereas about 70 % exist in the 'open' form with a phosphonate coordination only. In the upper pH range (N3)H is deprotonated and M(5Umpa–H)$^-$ species form which may then further give rise to binuclear $M_2(5Umpa–H)^+$ complexes.



Supported by the Swiss Nat. Science Foundation, the Swiss Fed. Off. for Educ. & Science. (COST D20), and the Medical University of Łódź.

[1] C. F. Moreno-Luque, E. Freisinger, B. Costisella, R. Griesser, J. Ochocki, B. Lippert, H. Sigel, *JCS Perkin Trans. 2*, **2001**, 2005-2011.
[2] E. De Clercq, *Collect. Czech. Chem. Commun.* **1998**, *63*, 480-506.
[3] H. Sigel, B. Song, *Met. Ions Biol. Syst.* **1996**, *32*, 135-205.
[4] R. B. Martin, H. Sigel, *Comments Inorg. Chem.* **1988**, *6*, 285-314.

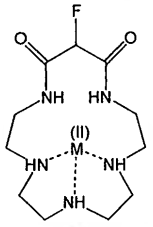
Inorganic and Coordination Chemistry **135**

New Macroazacyclic Ligands as Scaffolds for Dinuclear Metal Complexes

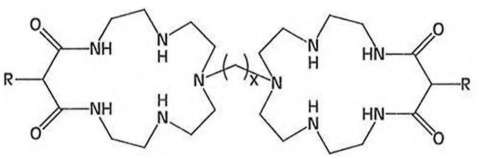
Chiara Da Pieve, Bernhard Spingler*

University of Zürich, Winterthurerstr. 190, CH-8057 Zürich, Switzerland

Macrocyclic metal complexes have been prepared as model compounds for metalloproteins to promote RNA or DNA hydrolysis [1]. Metal complexes such as **1** (M = Ni^{2+}) have been shown to recognise and induce B- to Z-DNA transition of poly d(G-C) [2].
The ligand of **1** has been synthesised following the literature [3] and its complexation behaviour towards various divalent transition metal ions has been explored.
The synthesis of the dinuclear ligand **2** and the interactions of its metal complexes with DNA and RNA will be presented.



1



2

[1] A. Sreedhara, J. A. Cowan, *J. Biol. Inorg. Chem.* **2001**, *6*, 337-347.
[2] H. C. Shih, N. Tang, C. J. Burrows, S. E. Rokita, *J. Am. Chem. Soc.* **1998**, *120*, 3284-3288.
[3] C. C. Cheng, S. E. Rokita, C. J. Burrows, *Angew. Chem.* **1993**, *105*, 290-292.

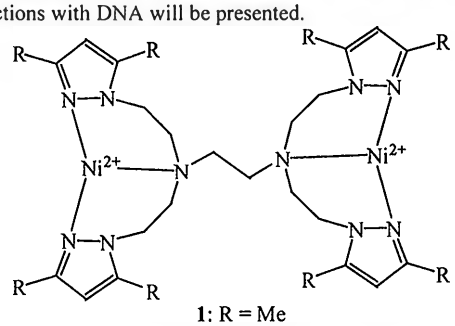
Inorganic and Coordination Chemistry **136**

On the route to Z-DNA recognition by dinuclear nickel complexes

Bernhard Spingler

University of Zürich, Winterthurerstr. 190, CH-8057 Zürich, Switzerland

Recently the known [1] dinickel complex **1** was successfully tested for its ability to transform poly d(GC) from the right-handed to the left-handed form [2]. Becasue the replacement of methyl groups by hydrogen atoms might improve the coordination of **1** to N7 of guanine, the new non-methylated derivative **2** was synthesized. The characterization of **2** as well as its interactions with DNA will be presented.



1: R = Me

2: R = H

Support by the university of Zürich and the Swiss National Science Foundation is gratefully acknowledged.

[1] Veldman, N.; Spek, A. L.; Tabbi, G.; Driessen, W. L.; Reedijk, J. *Acta Cryst.* **1996**, *C52*, 2698.
[2] Spingler, B., Wild, B., manuscript in preparation.

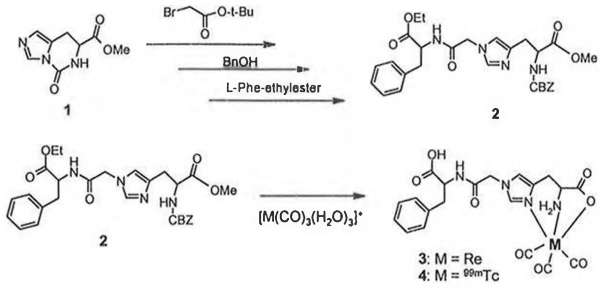
Inorganic and Coordination Chemistry **137**

Development of a Tripodal Histidine Ligand for Radiopharmaceutical Application

Jae Kyoung Pak, Paul Schmutz, and Roger Alberto

Inorganic Chemistry Institute, University of Zurich, Winterthurerstrasse 190, CH-8057 Zurich, Switzerland

Among the many chelators suitable for coordinating to the *fac*-$[M(CO)_3]^+$ moiety (M = ^{99m}Tc, Re), histidine yields neutral hydrophilic complexes, which makes it an excellent choice for the labelling of many bioactive molecules, i.e. peptides, hormones. A new strategy for regiospecific N^{ε}-imidazole derivatization of histidine has been developed. The fully functionalized 1-carboxy-methyl-L-histidine ligand was synthesized from L-histidine methyl ester in a convenient manner.



The modified ligands can be linked to peptides by amide formation and coordinated with metal tricarbonyl complexes, $[M(CO)_3(OH_2)_3]^+$ (M= Re, ^{99m}Tc). As model peptides, the modified histidine ligand as bifunctional ligand was readily coupled with L-Phe and L-Gly-Phe through the N terminus and further complexed with *fac*-$[Re(CO)_3]^+$ or *fac*-$[^{99m}Tc(CO)_3]^+$ in high yield.

Inorganic and Coordination Chemistry **138**

Diastereomeric bioconjugates of Mo(His)(allyl)$(CO)_2$ with amino acids and peptides. Influence of the chirality of the histidine ligand.

Dave R. van Staveren, Thomas Weyhermüller, and Nils-Metzler-Nolte

Max-Planck Institut für Strahlenchemie, Stiftstrasse 34-36
D – 45470 Mülheim/Ruhr, Germany
University of Heidelberg, Im Neuenheimer Feld 364
D – 69120 Heidelberg, Germany

Two sets of diastereomeric compounds of general composition Mo(His-N_{ε}-C_2H_4-CO-AA-PG)(η-allyl)$(CO)_2$ (His = *O*, *N*, N_{δ}-histidinate, AA = amino acid or peptide, OPG = *C*-terminus protecting group) were prepared and investigated by a variety of spectroscopic techniques. The histidine ligand was either of *L* or *D* configuration and the length of the attached biomolecule was varied between 1 and 5 amino acids. This work is a continuation of our ongoing investigation on the properties of molybdenum complexes containing the Mo(η-allyl)$(CO)_2$ moiety [1-5].

Although the compounds are diastereomers, most of them could only be distinguished on the basis of their CD-spectra. Cotton effects owing to the Mo(His)(η-allyl)$(CO)_2$ fragment are observed in the range 300-450 nm. These Cotton effects have a positive or negative sign in the case of *D*-His and *L*-His, respectively. However, in the case of a tethered pentapeptide, the diastereomers could also be discriminated by ^{1}H NMR spectroscopy. For these compounds an ordered structure in solution is anticipated, in which the carboxylate of the coordinated histidine ligand is involved in a hydrogen-bonding interaction.

[1] D. R. van Staveren, T. Weyhermüller, N. Metzler-Nolte, *Organometallics.* **2000**, *19*, 3730-3735.
[2] D. R. van Staveren, E. Bothe, T. Weyhermüller, N. Metzler-Nolte, *Chem. Comm.* **2001**, 131-132.
[3] D. R. van Staveren, E. Bill, E. Bothe, M. Bühl, T. Weyhermüller, N. Metzler-Nolte, *Chem. Eur. J.* **2002**, 8, 1649-1662.
[4] D. R. van Staveren, N. Metzler-Nolte, *Chem. Comm.* **2002**, 1406-1407.
[5] D. R. van Staveren, E. Bothe, N. Metzler-Nolte, *Organometallics.* **2003**, in press.

Inorganic and Coordination Chemistry **139**

Synthesis of Bis-Hisitidine Rhenium Complexes Linked Through the Imidazole Ring

Paul Benny, Roger Alberto

University of Zürich, Wintethurerstr. 190, CH-8057-Zürich, Switzerland

Utilizing the cationic organometallic rhenium (I) tricarbonyl moiety (*fac*-$[Re(CO)_3]^+$) as a protecting group, derivatization of the amino acid histidine can selectively be achieved at the $^{\varepsilon}$N on the imidazole ring.[1] The robust nature of the d^6 organometallic rhenium fragment combined with the stability coordinate bonds of *fac*-$[Re(CO)_3]^+$ with histidine through the carboxylic acid, primary amine ($^{\alpha}$N), and the nitrogen of the imidazole ring ($^{\delta}$N) inhibits alkylation on the coordinated nitrogen donors and preserves the stereogenic center of the L-amino acid. Bis-histidine complexes linked through the $^{\varepsilon}$N are prepared by alkylation of the $^{\varepsilon}$Nitrogen of *fac*-$Re(CO)_3$(Histidine) with a dialkylating linker (i.e. 1,4 dibromobutane) to yield complexes of the type $^{\varepsilon}$N-[*fac*-$Re(CO)_3$(Histidine)]$_2$-1,4Bu. Following the synthesis of the $^{\varepsilon}$N linked bis-histidine rhenium complexes, the *fac*-$[Re(CO)_3]^+$ was deprotected to yield the uncoordinated $^{\varepsilon}$N linked bis-histidine amino acid ligand ready for potential applications with different metal centers.

[1] J.K.Pak, P. Benny, B. Spingler, K. Ortner, R. Alberto, *Chem. Eur. J.*, **2003**, 9, 2053-61.

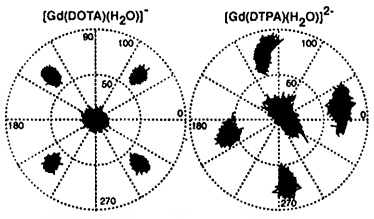
Inorganic and Coordination Chemistry **140**

Molecular Dynamics Simulations of Acyclic and Macrocyclic Gd^{3+} based MRI Contrast Agents: Influence of the Internal Mobility on Water Proton Relaxivity

Fabrice Yerly, Alain Borel, Lothar Helm and André E. Merbach*

École Polytechnique Fédérale de Lausanne, Institut de Chimie Moléculaire et Biologique, CH-1015 Lausanne

The increasing use of contrast agents in magnetic resonance imaging (MRI) for medical diagnosis is due to the ability, called *relaxivity*, of these paramagnetic compounds to increase the relaxation rates of the surrounding water proton spins. A new classical force field for the Gd^{3+} polyaminocarboxylate complexes has recently been published,[1] which allows to study the internal mobility of the chelates.



Direct relationships between the internal mobility and the water proton *relaxivity* are presented, on various Gd^{3+} complexes including macrocyclic cyclen-based and acyclic chelates. We show what properties should be optimized to design more efficient contrast agents.

[1] F. Yerly, K.I. Hardcastle, L. Helm, S. Aime, M. Botta, A. E. Merbach *Chem. Eur. J.*, **2002**, *8*, 1031.

Inorganic and Coordination Chemistry **141**

A new dimeric poly(aminocarboxylate) Gd(III) complex for medical magnetic resonance imaging (MRI)

J. Costa, A.E. Merbach

EPFL, Institut de Chimie Moléculaire et Biologique, Laboratoire de Chimie Inorganique et Bioinorganique, EPFL – BCH, 1015 Lausanne, Switzerland

Gadolinium(III) complexes are currently widely used as medical MRI contrast agents. Relaxivity and fast water exchange are among the important parameters one has to deal with when designing new ligands. A way of increasing the relaxivity of such a complex is to make it heavier whereas a fast water exchange can be reached through poly(aminocarboxylate) DTPA-type ligands.
We therefore synthesized and analysed a new dimeric ligand bearing two TTAHA coordinating units separated by a xylene linker. Stability constants determination of the Gd(III) complex shows that, since the two coordinating units are located *para* on the aromatic moiety, they act independently one to the other. ^{1}H NMRD displays a high relaxivity, as expected by the two TTAHA units[1]. ^{17}O NMR and UV-Vis spectrophotometry have also been performed.

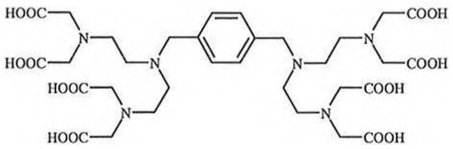


Fig.1 *The new dimeric ligand bearing the two TTAHA coordinating units*

[1] R. Ruloff, R.N. Muller, D. Pubanz, A.E. Merbach, *Inorg. Chim. Acta*, **1998**, *275-276*, 15-23

Inorganic and Coordination Chemistry **142**

Novel oxa-azamacrocyclic ligands for Eu^{II} complexation: towards redox responsive MRI constrast agents

S. Laus, É. Tóth, A.E. Merbach

Institute of Molecular and Biological Chemistry, Swiss Federal Institute of Technology EPFL-CH, CH-1015 Lausanne, Switzerland

The strong paramagnetism and relatively high redox stability of Eu^{II} could make it an ideal paramagnetic probe in bioinorganic chemistry. Eu^{II} has seven unpaired electrons and is isoelectronic with Gd^{III}. In the last two decades, Gd^{III} poly(aminocarboxylate) complexes have been successfully used in medical diagnostics as MRI contrast agents. Eu^{II} being a strong, Eu^{III} a poor relaxing agent, Eu^{III}/Eu^{II} complexes are candidates as MRI contrast agents sensitive to the redox state of the biological environment. Such application requires the stabilization and control of the reduced, Eu^{II} oxidation state. Eu^{III}/Eu^{II} complexes are studied in the perspective of their potential application as redox responsive MRI contrast agents or relaxometric probes. Furthermore, due to the similar size of Sr^{II} and Eu^{II}, another important field of application of stable chelates could be the removal of radioactive Sr from living organisms.
So far the highest redox stability for a Eu^{II} complex was attained with the cryptate ligands 2.2.1 and 2.2.2.[1],[2] The drawback of these ligands is the slow complexation kinetics and, more importantly, the difficulties in introducing functional groups on the ligand in order to fine-tune the coordination properties. For these reasons, we synthesized several oxa-azamacrocyclic ligands having different cavity size, varying number of oxygens in the skeleton and varying number of *N*-carboxymethyl pendant arms.

[1] Gansow, O.A.; Kausar, A.R.; Triplett, K.M.; Weaver, M.J.; Yee, E.L. *J. Am. Chem. Soc.* **1977**, *99*, 7087
[2] Yee, E.L.; Gansow, O.A.; Weaver, M.J. *J. Am. Chem. Soc.* **1980**, *102*, 2278

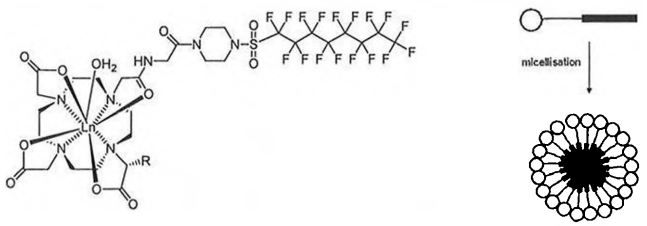
Inorganic and Coordination Chemistry **143**

A perfluoroalkyl surfactant with Ln(III) DO3A-monoamide hydrophilic head (Ln = Y, Gd) : EPR, ^{19}F NMR and ^{1}H NMRD study

Gaëlle M. Nicolle, André E. Merbach

Institute of Molecular and Biological Chemistry, Swiss Federal Institute of Technology EPFL-BCH, CH-1015 Lausanne, Switzerland

Due to the much higher solubility of oxygen in fluorocarbon emulsions, fluorinated materials are widely investigated for *in vivo* oxygen transport for blood substitutes but also for diagnosis and drug delivery [1]. They could be therefore of great interest as specific medical MRI contrast agents.



We report on gadofluorine 8 [2], which is presented above. This surfactant has been investigated by ^{19}F NMR. The water proton relaxivity profiles of the Gd(III) surfactant exhibit the characteristic maximum at MRI fields. EPR spectra recorded for different mole fractions of Gd(III) surfactant *versus* Y(III) surfactant reveal an intramolecular electron interaction between close gadolinium centres. The consequence of the increase of the electron relaxation is addressed for the design of new contrast agents.

[1] J. G. Riess, *Chem. Rev.* **2001**, *101*, 2797.
[2] B. Misselwitz, J. Platzek, B. Radüchel, J. J. Oellinger, H. J.Weinmann, *Magma* **1999**, *8*, 190.

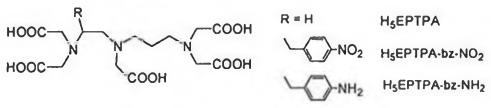
Inorganic and Coordination Chemistry **144**

A Kinetic and Equilibrium Study of Ln^{III}EPTPA Isomers Separated by HPLC

László Burai, Éva Tóth and André E. Merbach

Institut de Chimie Moléculaire et Biologique, Ecole Polytechnique Fédérale de Lausanne, EPFL - BCH, CH-1015 Lausanne, Switzerland
Laszlo.Burai@epfl.ch

The ligand ethylenepropylene-triamine-pentaacetate (EPTPA) has been recently proved to be an ideal chelator of Gd^{III} for the development of high relaxivity, macromolecular contrast agents for Magnetic Resonance Imaging [1]. It ensures a sufficiently high thermodynamic stability of the Gd^{III} complex in order to avoid toxicity. In addition, the water exchange rate, one of the crucial parameters to determine the efficacy of the contrast agents is optimal on the Gd^{III} complex to attain maximum relaxivities, provided the rotation is slowed down.



We have separated the diastereomeric isomers of the different EPTPA-derivative complexes by HPLC. In contrast to DTPA derivatives, there is a remarkable change in the ratio of the two isomers along the lanthanide series. However, this ratio is independent of the nature of the pending groups attached to the amine backbone of the ligand. The two isomers have been studied by different physico-chemical methods. The kinetics of racemization which follows the separation has been found to depend on different factors, such as the pH or the nature of the lanthanide ion. Furthermore, this kinetics provides deeper insight into the formation mechanism of the lanthanide-EPTPA derivatives complexes.

[1] S. Laus, R. Ruloff, É. Tóth, A. E. Merbach *Chem. Eur. J.*, in press.

Inorganic and Coordination Chemistry **145**

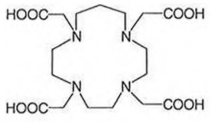
Dissociation and Formation Kinetics of Ln^{III}TRITA Complexes

Edina Balogh and Éva Tóth

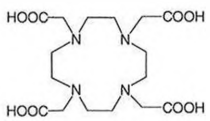
Institut de Chimie Moléculaire et Biologique, Ecole Polytechnique Fédérale de Lausanne, EPFL - BCH, CH-1015 Lausanne, Switzerland
Edina.Balogh@epfl.ch

The 13-membered macrocyclic TRITA has been recently found to possess interesting features for Gd^{III} complexation in the perspective of developing high relaxivity, macromolecular contrast agents for Magnetic Resonance Imaging [1]. The $[Gd(TRITA)(H_2O)]^-$ complex has an optimal water exchange rate to attain maximum proton relaxivities, thus maximum efficiency, provided the rotation of the agent is also optimized (slowed down). In comparison to $[Gd(DOTA)(H_2O)]^-$, a current MRI contrast agent, the thermodynamic stability of $[Gd(TRITA)(H_2O)]^-$ is only slightly diminished and still sufficient to ensure non-toxicity.

In addition to thermodynamic stability, kinetic inertness is another important factor that is related to the in vivo safety of Gd^{III} complexes. We have characterized the kinetic stability by the rates of the exchange reactions that take place between $[Gd(TRITA)(H_2O)]^-$ and Zn^{2+} and Cu^{2+}, the most abundant endogenously available cations. In comparison, we have also studied the exchange with another lanthanide cation, Eu^{3+}. Formation kinetic studies of different lanthanide-TRITA complexes have been also performed.



H_4TRITA



H_4DOTA

[1] R. Ruloff, É. Tóth, R. Tripier, H. Handle, A. E. Merbach, *Chem. Commun.* **2002,** *22,* 2630-2631.

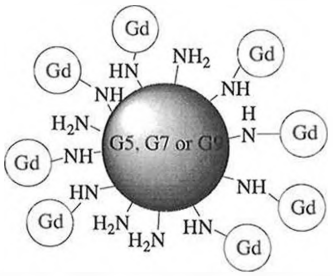
Inorganic and Coordination Chemistry **146**

New high-generation dendrimers with PAMAM and Gd(III) chelates for MRI

Angélique Sour-Carina, Robert Ruloff, Sabrina Laus, Éva Tóth, André E. Merbach

Institut de Chimie Moléculaire et Biologique, Ecole Polytechnique Fédérale de Lausanne, EPFL - BCH, CH-1015 Lausanne, Switzerland
angelique.sour@epfl.ch

Gd(III) chelates attached to high-generation dendrimers are currently investigated as MRI contrast agents. The slow rotation of dendrimers allows increased water proton relaxivities, hence higher efficiency, as compared to low molecular weight Gd(III) complexes [1]. Previous work shows that a raise in relaxivity as the generation increases is limited by the water exchange rate. We now use a Gd(III) complex with a new polyaminocarboxylate ligand which displays a very rapid water exchange rate. This new complex should allow us to observe an increase in relaxivity with higher generations.



We present the synthesis and characterization of these dendrimers. Experimental results for the relaxivity of the three dendrimers will indicate when the water exchange rate limits the relaxivity.

[1] The chemistry of contrast agents in medical magnetic resonance imaging, A.E. Merbach, É. Tóth (Eds), John Wiley & Sons, Chichester, **2001**.

Inorganic and Coordination Chemistry **147**

Structural Studies of Transition Metal Complexes with TTF-type ligands: Probing Their Potential for the Construction of Multifunctional Molecular Assemblies

Shi-Xia Liu,[a] Stefan Dolder,[a] Patrick Franz,[a] Antonia Neels,[b] Helen Stoeckli-Evans,[b] and Silvio Decurtins[a]

[a] Departement für Chemie und Biochemie, Universität Bern, Freiestrasse 3, CH-3012 Bern, Switzerland; [b] Institut de Chimie, Université de Neuchâtel, Avenue Bellevaux 51, CH-2007 Neuchâtel, Switzerland.

An increased interest is devoted to the construction of bifunctional conducting and magnetic molecular materials [1]. Our strategy involves the covalent attachment of metal ion binding groups to TTF derivatives and their linkage into supramolecular systems. Thereby some TTF derivatives functionalised by polypyridines or polypyrazines have been synthesized [2-3]. Chemical oxidation of $Ni(II)Cl_2$ complex produces a mixture of black lustrous crystals with two different crystalline morphologies (for one example, see Fig. 1). Undoubtly, the direct coordination of metal ions to TTF derivatives may constitute a new approach for the achievement of π-*d* interactions in such multifunctional molecular materials.

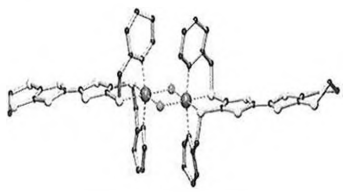


Fig. 1

[1] F. Iwahori, S. Golhen, L. Ouahab *et al.*, *Inorg. Chem.*, **2001**, *40*, 6541.
[2] S-X. Liu, S. Dolder *et al.*, *J. Org. Chem.*, **2002**, *67(9)*, 3160.
[3] S-X. Liu, S. Dolder *et al.*, *Comptes Rendus Chimie*, **2003**, in press.

Inorganic and Coordination Chemistry **148**

The Design of Building Blocks Containing Peripheral Binding Sites Suitable for the Tetramerisation to Phthalocyanines

Claudia Loosli, Marco Haas and Silvio Decurtins

Departement für Chemie und Biochemie, Universität Bern, Freiestrasse 3, 3012 Bern, Switzerland

As a consequence of their wide range of coordination, optical, structural and electronic properties arising from their large π-conjugated systems and their assembling into cofacially-stacked arrays, phthalocyanines have been the subject of intense studies to investigate their applications in the field of liquid crystals, Langmuir-Blodgett films, nonlinear optics, electrochromic devices as well as therapic agents in pharmacology [1].

Since the peripheral substitution of the phthalocyanine skeleton affords new materials with diverse chemical and physical properties, we are currently focusing our interest on the preparation of functionalised phthalocyanine derivatives with additional peripheral binding sites and the design of metal-complexed diimine ligands in order to tetramerise them further to the corresponding phthalocyanines.

A fully conjugated phthalocyanine derivative containing four diimine binding sites has already been prepared in our group [2]. This type of compounds present exciting perspectives for the linkage of a wide range of magnetic, electronic, redox and photo-active components.

[1] N. B. McKeown, Phthalocyanines Materials: Synthesis, Structure and Function, **1988**, Cambridge University Press, Cambridge.
[2] J. Rusanova, M. Pilkington, S. Decurtins, *J. Chem. Soc., Chem. Comm.*, **2002**, 2236-2237.

Inorganic and Coordination Chemistry **149**

Synthesis of Phthalocyanine Precursors with Peripheral Metal-Binding Sites

Marco Haas, Claudia Loosli and Silvio Decurtins

Departement für Chemie und Biochemie, Universität Bern, Freiestrasse 3, CH-3012 Bern, Switzerland

Phthalocyanines display a wide range of interesting physical properties. Most of the applications to-date incorporate non-functionalised phthalocyanines. Only a few examples of novel phthalocyanines that contain peripheral metal-binding sites are known, these include crown ether-substituted phthalocyanines [1], phthalocyanines containing mixed donor macrocycles [2] as well as phthalocyanines with peripheral donor atoms, such as nitrogen [3] or sulfur [4].

It is our aim to synthesise new functionalised phthalocyanine precursors with peripheral metal-binding sites and exploit their coordination chemistry with ruthenium. The next step is to assemble these precursors to novel phthalocyanine materials, which have ruthenium coordinated to their periphery, and study their physical properties.

[1] N. Kobayashi, Y. Nishiyama, *J. Chem. Soc., Chem. Comm.*, **1986**, *19*, 1462.
[2] E. Ağar, S. Şaşmaz, N. Akdemir, I. Keskin, *J. Chem. Soc., Dalton Trans.*, **1997**, *12*, 2087.
[3] J. Rusanova, M. Pilkington, S. Decurtins, *J. Chem. Soc., Chem. Comm.*, **2002**, *19*, 2236.
[4] T. Muto, T. Temma, M. Kimura, K. Hanabusa, H. Shirai, *J. Chem. Soc., Chem. Comm.*, **2000**, *17*, 1649.

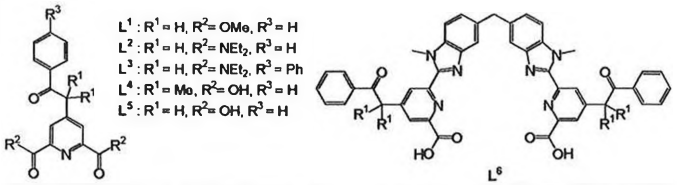
Inorganic and Coordination Chemistry **150**

Lanthanide mono-and bi-metallic luminescent probes from 4-substituted dipicolinic acid derivatives

Anne-Sophie Chauvin, Daniel Imbert, Sandrine Gras and Jean-Claude G. Bünzli.

Institute of Molecular and Biological Chemistry, Swiss Federal Institute of Technology Lausanne, BCH 1405, CH-1015 LAUSANNE (Switzerland)

We are interested by the design of lanthanide-containing luminescent probes for biomedical analyses based on the tris(dipicolinate) framework, the 4 position of the pyridine being substituted by chromophoric groups. Varying the substituent in this position allows one to finely tune the photophysical properties of the resulting complexes with lanthanide ions. Moreover, functional groups may also be introduced in this position for coupling with biological materials. As it has been demonstrated that phenylphenacyl and phenacyl groups grafted onto a calixarene or cyclen framework are very effective in transferring energy onto lanthanide ions, we have undertaken efforts to attach these functional groups in the 4-position of 2,6-pyridinedicarboxamide.[1] Here we discuss the synthesis of these chelating agents, an interesting keto-enol tautomerism depending on the nature of the R^2 substituent, as well as comparative results regarding the thermodynamic and photophysical properties of the $[Ln(L^x)_3]$ (x = 1-5) and $[Ln_2(L^6)_3]$ complexes (Ln = La, Gd, Lu, Eu, Tb).



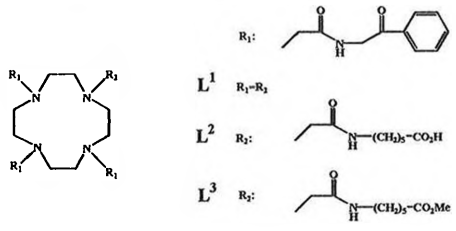
[1] A-S. Chauvin, S. Gras and J.-C. G. Bünzli, *Org. Biomol. Chem*, **2003**, *1*, 737-740 and references therein.

Inorganic and Coordination Chemistry **151**

Asymmetrical Cyclen Derivatives for Biological Applications: Highly Luminescent Lanthanide Chelates

Anne-Claire Ferrand[a], Anjum Dadabhoy[a], Jean-Claude G. Bünzli[a]

Institute of Molecular and Biological Chemistry, Swiss Federal Institute of Technology, CH-1015 Lausanne, Switzerland.



Structural and spectroscopic studies of the cyclen derivative L^1 containing four identical coordinating and chromophoric arms and also of its lanthanide complexes showed promising behaviour towards applications as luminescent molecular probes. Quantitative measurements included the determination of luminescence quantum yields of the Sm(III), Eu(III), Tb(III) and Dy(III) complexes in aqueous solutions; these ions have particular interest in the development of multiplex fluoroimmunoassays[1].
With this in mind, we are currently preparing a series of asymmetric molecules based on the L^1 framework, in the aim of conjugating such complexes to biological materials. The synthesis of such highly functionalised ligands (L^2 and L^3) requires a different approach to that of the symmetrically-substituted parent compound. Solution studies (luminescence, UV titrations) of the new derivatives and their lanthanide complexes are presented.

[1] Zucchi, A.-C. Ferrand, R. Scopelliti, J.-C. G. Bünzli, *Inorg.Chem.* **2002**, *41*, 2459-2465.

Inorganic and Coordination Chemistry **152**

Novel Functionalized BEDT-TTF Derivatives: Synthesis, Properties and Crystal Structures

Stefan Dolder[a], Shi-Xia Liu[a], Antonia Neels[b], Helen Stoeckli-Evans[b], Silvio Decurtins[a]

[a]Departement für Chemie und Biochemie, Universität Bern, Freiestrasse 3, CH - 3012 Bern, Switzerland, e-mail : dolder@iac.unibe.ch; [b]Institut de Chimie, Université de Neuchâtel, Avenue Bellevaux 51, CH-2000 Neuchâtel, Switzerland

Tetrathiafulvalene (TTF) and its analogues have currently attracted interest in the elaboration of multifunctional molecular materials.[1-2] As a consequence, our strategy involves the covalent attachment of metal ion binding groups to bis(ethylenedithio)tetrathiafulvalene (BEDT-TTF) and bis(cyanoethylthio)tetrathiafulvalene (BCET-TTF) derivatives and their linkage into supramolecular systems. With the appropriate choice of metal ions, the resulting system would be expected to show multiple physical properties, such as magnetic effects and electrical conductivity or superconductivity, optical and magnetic properties or spin crossover, in a synergistic way. Here, the synthetic approaches to some symmetrically and asymmetrically functionalized BEDT-TTF derivatives,[3-4] together with an outlook for the use of these systems in the design of new materials are described.

[1] F. Iwahori, et al., *Inorg. Chem.*, **2001**, *40*, 6541
[2] E. Coronado, et al., *Nature*, **2000**, *408(23)*, 447
[3] S-X. Liu, Stefan Dolder, et al., *J. Org. Chem.*, **2002**, *67(9)*, 3160
[4] S-X. Liu, Stefan Dolder, et al. *Comptes Rendus Chimie*, **2003**, in press.

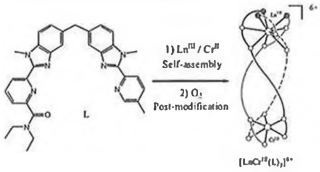
Inorganic and coordination chemistry **153**

Chiral heteobimetalic Cr^{III}-Ln^{III} helicates

Martine Cantuel,[a] Gérald Bernardinelli,[b] Gilles Muller,[c] James P. Riehl[c] and Claude Piguet[a*]

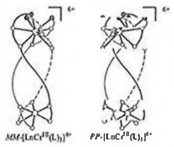
[a] Department of Inorganic Chemistry, University of Geneva,Quai E. Ansermet 30, CH-1211 Geneva 4, Switzerland.
[b] Laboratory of X-ray crystallography, University of Geneva, 1211 Geneva 4, Switzerland.
[c] Department of Chemistry, University of Minnesota Duluth, Minnesota 55812-2496, USA.

Heterobimetallic d-f triple stranded helicates $[LnCr(L)_3]^{6+}$ [1] are well-suited precursors for the preparation of new functional molecular devices. The originality of theses systems lies in their kinetic inertness, obtained by oxidation of the self-assembled helicates $[LnCr(L)_3]^{5+}$. This property allowed us to prepare :



1) A new non-covalent racemic receptor *fac*-$[Cr(L)_3]^{3+}$, whose rigidity and inertness are ensured by Cr^{III} which facially organizes the three tridentate binding units for their complexation to Ln^{III}.

2) Enantiomerically pure lanthanide containing helicates *MM*-$[LnCr(L)_3]^{6+}$ and *PP*-$[LnCr(L)_3]^{6+}$ whose screw directions result from the chromatographic resolution of the two helical enantiomers *M*-$[Cr(L)_3]^{3+}$ and *P*-$[Cr(L)_3]^{3+}$. Recombination with a lanthanide ion preserves chirality in the final helicates which display circularly polarised emission properties.



[1] M. Cantuel, G. Bernardinelli, D. Imbert, J.-C. G Bünzli, G. Hopfgartner and C. Piguet, *J. Chem. Soc., Dalton Trans.*, **2002**, 1929.

Inorganic and Coordination Chemistry **154**

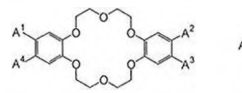
Crown ether-type ligands containing promesogenic arms and their Europium complexes

Olimpia Mamula[a], Stéphane Suárez[a], Claude Piguet[b], Egbert Figgemeyer[c], Jean-Pierre Rivera[b] and Jean-Claude Bünzli*[a]

[a] Institute of Molecular and Biological Chemistry, Swiss Federal Institute of Technology, 1015 Lausanne, Switzerland.
[b] Department of Inorganic, Analytical and Applied Chemistry, Sciences II, University of Geneva, 1211 Geneva 4, Switzerland
[c] Ångström Solar Center , Department of Physical Chemistry, University of Uppsala, 75123 Uppsala, Sweden.

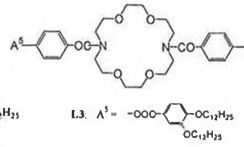
The unique properties of these liquid crystals can be highly diversified by the introduction of lanthanide cations possessing appealing optical and magnetical characteristics.[1]

The ligands presented here possess either a benzo- or aza-crown ether type core, whose cavities are adapted for acting as receptors for Ln(III) cations.[2]



L1: $A^1=A^2=H$; $A^3=A^4=$ -COO-C_6H_4-$OC_{12}H_{25}$

L2: $A^1=A^2=A^3=A^4=$ -NHCO-C_6H_4-$OC_{12}H_{25}$



L3: $A^5=$ -OOO-

To these skeletons, lipophilic arms are anchored in order to induce the suitable mesophases (two, in the case of L1 and L3 and, four in the case of L2).

The factors governing the formation of mesogenic phases in ligands and Eu(III) complexes as well as the characterization of the new compounds by emission spectroscopy, differential scanning calorimetry, thermogravimetry, polarized light microscopy and cyclic voltammetry will be presented.

[1] Binnemans, K., Görler-Walrand, C., *Chem. Rev.* **2002**, *102*, 2303.
[2] Bünzli, J.-C. G. in "*Modern aspects of rare earths and their complexes*" by S. V. Sastri *et al.*, Elsevier Science B.V., in press.

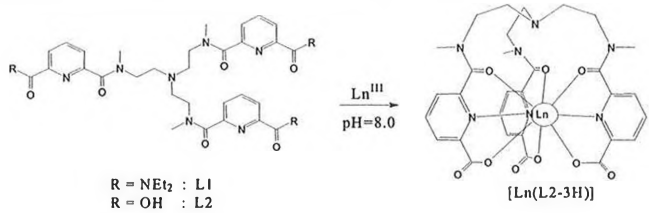
155

Synthesis and Properties of a New Nine-Coordinate Lanthanide Podate Containing Terminal Carboxylate Groups

Jean-Michel Senegas,[a] Gerald Bernardinelli,[b] Daniel Imbert,[c] Jean-Claude G. Bünzli,[c] Pierre-Yves Morgantini,[d] Jacques Weber,[d] and Claude Piguet,[a]

[a] *Department of Inorganic Chemistry, University of Geneva,* Jean-Michel.Senegas@chiam.unige.ch
[b] *Laboratory of X-ray Crystallography, University of Geneva*
[c] *Institute of Molecular and Biological Chemistry, Swiss Federal Institute of Technology*
[d] *Department of Physical Chemistry, University of Geneva*

The hydrolysis of terminal ^{t}butyl-ester groups provides the novel nonadentate podand tris (2-[N-methylcarbamoyl-(6-carboxypyridine-2)-ethyl]amine) L2 which exists as a mixture of slowly interconverting conformers in solution. At pH = 8.0 in water, its deprotonated form $[L2\text{-}3H]^{3-}$ reacts with $Ln(ClO_4)_3$ to give the poorly soluble and stable podates [Ln(L2-3H)]. The isolated complexes $[Ln(L2\text{-}3H)](H_2O)_7$ are isostructural (Ln = Eu, Tb, Lu). High-resolution emission spectroscopy demonstrates that (i) the replacement of terminal carboxamides with carboxylates induces only minor electronic changes for the metallic site, (ii) the solid-state structure is maintained in water and (iii) the metal in the podates is efficiently protected from interactions with solvent molecules. Particular attention is focused on the entropic stabilization provided by the carboxylates and on their influence on the light-conversion processes in Eu(III) and Tb(III) podates.

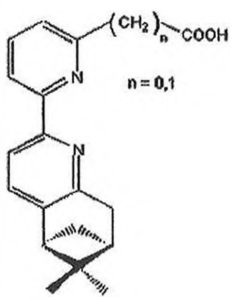


Inorganic and Coordination Chemistry **156**

Diastereoselective synthesis of enantiopure lanthanide complexes: new chiral ligands derived from the pinene-bipyridine moiety

Marco Lama[a] and Olimpia Mamula*[a]

[a] Institute of Molecular and Biological Chemistry, Swiss Federal Institute of Technology, CH-1015-Lausanne, Switzerland.



The stereoselective syntheses of configurationally pure coordination compounds has recently attracted much attention, with many of these compounds already described, having interesting applications *i.e.* enantioselective catalysts and chiral probes.[1] However, in the particular case of generally very labile lanthanide complexes, in which the metal-ligand bonds have virtually no stereochemical rigidity, this task is more challenging.[2] In pursuit of obtaining enantiopure lanthanide (Ln) complexes which represent the first step in the design of more complex supramolecular architectures possessing interesting photo-physical and chiroptical properties, we have set about designing new chiral ligands. The source of our inspiration are the highly successful chirality inducing ligands based around pinene pyridine moiety.[3]

Here we present the multistep synthesis of tridentate acyclic ligands obtained by the functionalization of the 6' position of the (+)-5,6 pinene bipyridine (see Figure) and their complexes with Ln(III) cations. The characterization of the new compounds by a variety of physico-chemical methods including chiroptical spectroscopic techniques will also be discussed.

[1] H.C. Aspinall; *Chem. Rev.*, **2002**, *102*, 1807
[2] A. von Zelewsky, O. Mamula; *J. Chem. Soc., Dalton Trans.*, **2000**, 219
[3] G. Muller, J.-C.G. Bünzli, J. Riehl, D. Suhr, A. von Zelewsky, H. Mürner; *Chem.Comm.*, 2002, 1522

Inorganic and Coordination Chemistry **157**

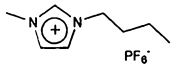
Luminescence and Mesogenic Properties by Doping an Ionic Liquid with Europium(III)

Erwann Guillet, Rosario Scopelliti, and Jean-Claude G. Bünzli*

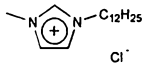
Institute of Molecular and Biological Chemistry, Swiss Federal Institute of Technology, CH-1015 Lausanne, (Switzerland)

In the past years, lanthanide-containing liquid crystals have gained increasing interest due to their potential applications.[1] In addition to their mesogenic behaviour, these compounds may exhibit photo- or electroluminescence and/or magnetic anisotropy from the metal ion.

In order to obtain switchable liquid crystalline materials between the red luminescence of Eu^{III} to the blue luminescence of Eu^{II}, one should be able to stabilise europium in its two different valencies. It has been recently shown[2] that stabilisation of Eu^{II} can be easily achieved in the ionic liquid [Bumim]PF_6. Since one compound of the series, [C_{12}mim]Cl, exhibits SmA phases between -2.8°C and 104.4°C,[3] we have doped this ionic liquid with europium salts and complexes.



[Bumim]PF_6



[C_{12}mim]Cl

These new, highly luminescent, liquid crystals were investigated with respect to their photopysical properties. Mesogenic properties were studied: the inclusion of the lanthanide ion does not affect much the formation of mesogenic phases. We describe the preparation of doped [C_{12}mim]Cl samples and we discuss the influence of both the nature of the doping salts and their concentration on the optical and thermal properties.

[1] K. Binnemans, C. Görller-Walrand, *Chem. Rev.* **2002**, *102*, 2303-2345.
[2] I. Billard, G. Moutiers, A. Labet, A. El Azzi, C. Gaillard, C. Mariet, K. Lützenkirchen, *Inorg. Chem.* **2003**, *42*, 1726-1733.
[3] A. E. Bradley, C. Hardacre, J. D. Holbrey, S. Johnston, S. E. J. McMath, M. Nieuwenhuyzen, *Chem. Mater.* **2002**, *14*, 629-635.

Inorganic and Coordination Chemistry **158**

Hydrogen solubility in Room Temperature Ionic Liquids

C. Andy Ohlin[a] James Vallance[b], Tom Welton[b], Paul J. Dyson[a], Gábor Laurenczy[a]

[a]Institut de Chimie Moléculaire et Biologique, EPFL, CH-1015 Lausanne, Switzerland. [b]Department of Chemistry, Imperial College of Science and Technology, South Kensington, London, SW7 2AY, UK

The solubility of hydrogen gas in twelve room temperature ionic liquids (RTILs) has been studied.

A considerable number of hydrogenation and hydroformylation reactions using ionic liquids as solvents has been reported in the literature [1] and while the solubility of certain gases, in particular CO_2, has been studied [2], the solubility of H_2 has proven more difficult to determine with traditional methods due to its low solubility. In our investigation we have been able to determine the concentration of H_2 in RTILs using high-pressure NMR techniques.

We have found that the solubility of H_2 in the RTILs varies relatively little in 1-alkyl-3-methyl-imidazolium and 1-alkyl-pyridinium type ionic liquids, irrespective of the anion. However, the solubility in one of our chosen ionic liquids was found to be notably higher and the solubility of hydrogen in this ionic liquid was determined at a range of temperatures and pressures.

We have also determined the hydrogen concentration in the same range of ionic liquids containing an organic substrate and conducted hydrogenation reactions in order to correlate the hydrogen solubility with the catalytic turnover frequency.

The Swiss National Science Foundation is thanked for financial support (Grants 2000-067976.02 GL and 21-66918.01 PJD)

[1] a) P.J. Dyson: *Appl. Organomet. Chem.* **2002**, 16(9), 495-500. b) P. Wasserscheid, K. Wilhelm: *Angew. Chemie Int. Ed.* **2000**, 39, 3772-3789
[2] J.L. Anthony, E.J. Maginn, J.F. Brennecke: *J. Phys. Chem. B* **2002**, 106, 7315-7320

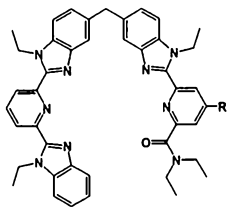
Inorganic and Coordination Chemistry **159**

HHH/HHT Equilibria in Lanthanide Containing Helicates

Thomas B. Jensen, Jean-Claude G. Bünzli

Institute of Molecular and Biological Chemistry, Swiss Federal Institute of Technology Lausanne, BCH 1404, CH-1015 Lausanne, Switzerland

The heteroditopic ligands L^{AB}, NEt_2L^{AB} and L^{AE} self-assemble with lanthanide ions in acetonitrile solution to yield homodimetallic triple-stranded helicates of general formula $[Ln_2L_3]^{6+}$ and with pairs of different lanthanide ions to build heterodimetallic edifices $[LnLn'L_3]^{6+}$ [1].



R = H L^{AB}

R = NEt_2 NEt_2L^{AB}

R = Cl L^{AE}

In order to understand the factors leading to the recognition of lanthanide ions by the ditopic ligands the equilibria between the HHH (*head-head-head*) and HHT (*head-head-tail*) isomers of $[Ln_2L_3]^{6+}$ were studied by variable temperature ^1H NMR. Analysis of the data yielded equilibrium constants as well as ΔH and ΔS values for the equilibria.

The results are rationalised in terms of differences in interactions between ligand strands in the helicates, with subtle differences being responsible for either the HHH or the HHT isomer being predominantly formed.

[1] N. André, R. Scopelliti, G. Hopfgartner, C. Piguet, J.-C. G. Bünzli, *Chem. Commun.* **2002**, 214.

Inorganic and Coordination Chemistry **160**

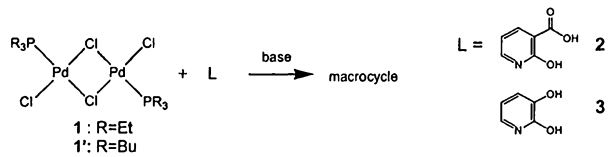
Self-assembly of metallomacrocycles using tridentate ligands

Thomas Brasey, Andrey Buryak, Rosario Scopelliti and Kay Severin*

École Polytechnique Fédérale de Lausanne, 1015 Lausanne, Switzerland

Neutral metallomacrocycles with highly interesting supramolecular properties have already been obtained using Ru^{II}, Rh^{III} and Ir^{III} halfsandwich complexes [1]. In continuation of these studies, Pd^{II} and Re^{I} complexes were investigated.

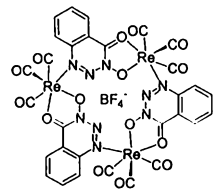
Pd^{II} macrocycles were obtained using the general reaction depicted below:



1 : R=Et
1': R=Bu

2-Hydroxynicotinic acid (**2**) provides a tetramic macrocycle, whereas an octameric one is obtained with 2,3-dihydroxypyridin (**3**).

A Re^{I} trimeric macrocycle (**4**) stabilizing a tris-benzene complex of Ag^+ was obtained by reaction of $[Re(CO)_3Br_3](NEt_4)_2$ with 3-hydroxy-1,2,3-benzotriazine-4(*3H*)-one:



$[Ag(\eta^2\text{-}C_6H_6)_3(OH_2)]^+$ **4**

[1] H. Piotrowsky, G. Hilt, A. Schulz, P. Mayer, K. Polborn, K. Severin, *Chem. Eur. J.* **2001**, *7*, 3196-3208

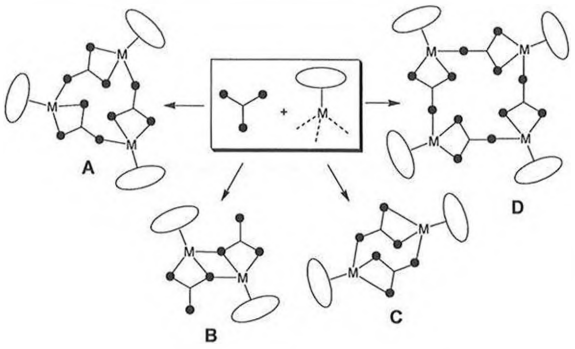
Inorganic and Coordination Chemistry **161**

Self-Assembly of (arene)Ru^{II} and Cp*Rh^{III} Complexes using Tridentate Dianinonic Ligands

Lehaire Marie-Line, Rosario Scopelliti, Kay Severin*

Institut de Chimie Moléculaire et Biologique, Ecole Polytechnique Fédérale de Lausanne, BCH, 1015 Lausanne, Switzerland

Half-sandwich complexes of ruthenium(II) and rhodium(III) are very useful compounds for transition metal based self-assembly processes. Using tridentate dianionic ligands, neutral metallamacrocycles can be formed. Thus, trimeric metallamacrocycles were obtained in excellent yield using 3-hydroxy-2-pyridone in presence of base [1],[2]. Changes in the bridging ligand can give rise to different geometries such as di- (**B** and **C**), tri- (**A**), and tetra- nuclear (**D**) (arene)Ru- and Cp*Rh-complexes.



[1] H. Piotrowski, K. Polborn, G. Hilt, K. Severin, *J. Am. Chem. Soc.* **2001**, *123*, 2699.
[2] H. Piotrowski, G. Hilt, A. Schulz, P. Mayer, K. Polborn, K. Severin, *Chem. Eur. J.* **2001**, *7(15)*, 3196.

Inorganic and Coordination Chemistry **162**

Reactions of $[Pt_3(\mu\text{-}CO)_3(PCy_3)_3]$ with small molecules

Z. Béni[1], R. Scopelliti[1], R.Ros[2], R. Roulet[1]

[1]EPFL, ICMB, BCH, CH - 1015 Lausanne, Switzerland
[2]DPCI, Via Marzolo 9, I-35131 Padova, Italy

Understanding the reactivity of coordinatively unsaturated platinum clusters is essential for evaluating their potential as catalysts or at least catalyst precursors [1,2].

The reaction of iodo-acetonitrile, elementary halogenes and tin-dichloride with the 42 valence electrons $[Pt_3(\mu\text{-}CO)_3(PCy_3)_3]$ cluster complex has been studied with multinuclear NMR, IR and X-ray spectroscopic methods. ICH_2CN reacts with $[Pt_3(\mu\text{-}CO)_3(PCy_3)_3]$ to form the adduct complex $[Pt_3(\mu\text{-}CO)_3(PCy_3)_3I(CH_2CN)]$ **1** by oxidative addition. On the addition of elementary iodine (or bromine) or tin-dichloride, $[Pt_3(\mu\text{-}CO)_2(PCy_3)_3X(\mu\text{-}X)]$ (X=I **2** or Br) or $[Pt_3(\mu\text{-}CO)_2(PCy_3)_3(\mu\text{-}SnCl_2)_2]$ respectively, is initially formed through addition followed by nucleophilic substitution of one CO. Upon addition of further iodo-acetonitrile or halogens or if the temperature is raised, both adducts **1** and **2** break down yielding dinuclear platinum(I) complexes $Pt_2(CO)_2(PCy_3)_2(I)CH_2CN$ and $Pt_2(CO)_2(PCy_3)_2I_2$ and finally, monomeric complexes.
NMR measurements in all cases proved similar stereochemistries in solution and in solid state. The halogen adducts are fluxional, both the two iodide (Br^-) ligands and the bridging CO ligands are in fast exchange on the NMR timescale.

We thank the Swiss National Science Foundation and EPFL for financial support.

[1] A. D. Burows, D. M. P. Mingos *Coord. Chem. Rev.* **1996**, 154, 19.
[2] D. M. P. Mingos, R.W. H.Wardale, *Transition Metal Chem.* **1995**, 10, 441.

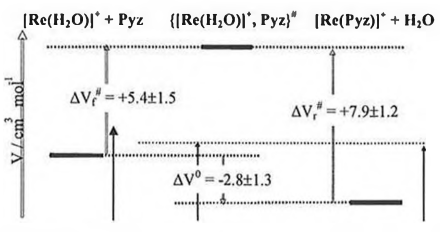
Inorganic and Coordination Chemistry **163**

Mechanistic studies on the half-sandwich complex $[(CO)_3Re^I(H_2O)_3]^+$

Bernadette Ugurtas, Pascal Grundler, Sonia Cayemittes and André E. Merbach*

Institut de Chimie Moléculaire et Biologique, Ecole Polytechnique Fédérale de Lausanne, EPFL-BCH, CH-1015 Lausanne, Switzerland.

In photochemistry and in nuclear medicine, tricarbonyl complexes of Re(I) are key compounds with various potential applications, as is $[(CO)_3Re^I(H_2O)_3]^+$ (**1**), particularly promising for radiotherapy [1]. Kinetic studies of the water exchange on **1** revealed one of the slowest exchange rate for a d^6 complex and positive activation entropy, indicative of a dissociative mechanism [2]. Supporting this result, complex formation kinetics with various ligands showed only a very small increase in *k*, from the harder triflate anion (TFA) to the softer thiourea (TU). However, to assign a mechanism conclusively for complex formation, variable pressure kinetic experiments were conducted with N-donor (Pyz) and S-donor (THT and DMS) ligands.



[1] Alberto, R.; Egli, A.; Abram, U.; Hegetschweiler, K.; Gramlich, V.; Schubiger, P. A. *J. Chem, Soc.; Dalton Trans.* **1994**, 2815.
[2] Salignac, B., Grundler, P. V., Cayemittes, S., Frey, U., Scopelliti, R., Merbach*, A. E., Hedinger, R., Hegetschweiler*, K., Alberto*, R., Prinz, U., Raabe, G., Kölle*, U., Hall, S. *Inorg. Chem*, **2003**, 42, 3516.

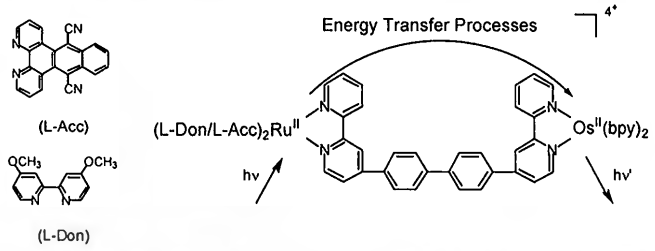
Inorganic and Coordination Chemistry **164**

Photophysical Properties in Bimetallic Ru and/or Os Metal Complexes

Nunzio Salluce and Peter Belser

Department of Inorganic Chemistry, University of Fribourg
CH-1700 Fribourg, E-mail: nunzio.salluce@unifr.ch

The design and the synthesis of artificial systems in which the path of electronic energy can be predetermined is one of the challenges in supramolecular chemistry.
To study the directional energy transfer processes we have modified the Ru(II) sensitizer unit in the heterodinuclear metal complexes by incorporating electron or donor groups on the auxiliary ligands.



Synthesis and photophysical properties (absorption and emission spectra, quantum yields and excited-state lifetimes) of heterodinuclear and homodinuclear complexes will be presented. In the heterodinuclear complexes a quenching of the phosphorescence of the Ru(II) chromophoric unit and a sensitisation of the phosphorescence of the Os(II) chromophoric unit are observed, indicating a fast electronic energy transfer. The rate of these processes depends either on the nature of the auxiliary ligands (donor (L-Don) or acceptor (L-Acc)) and the number of phenylene units used as spacer.

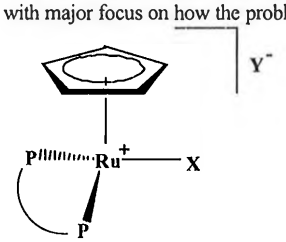
Inorganic and Coordination Chemistry **165**

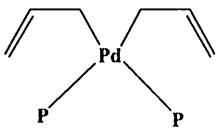
PGSE Diffusion and ^{19}F-^{1}H NOE Spectroscopy: Promising techniques in Organometallic Chemistry.

Anil Kumar Payyadi Govardhan and Paul S. Pregosin

Laboratory of Inorganic Chemistry, ETH Hönggerberg, CH-8093 Zürich Switzerland.

PGSE NMR [1] diffusion is slowly becoming recognized as a useful tool in the field of Organometallic Chemistry. Using this technique, we can elucidate problems related to hydrogen bonding, ion-pairing and molecular volumes [2]. In combination with ^{19}F-^{1}H HOESY, information related to how cations and anions interact in complex salts bcomes available. Application of these techniques to study some of the Ru(II) and Pd(II) Organometallic complexes will be presented with major focus on how the problems(mentioned above) were solved.





X= Acrylonitrile, Acetonitrile, H_2O **P**= MOP

Y= BF_4, BArF

P-P= Binap, Biphop-F

References:

[1] P.Stilbs, *Prog. Nucl. Magn. Reson. Spectrosc.* **1987**, *19*, 1.
[2] Massimiliano Valentini et al, *Helv. Chim. Acta.* **2001**, *84*, 2833.

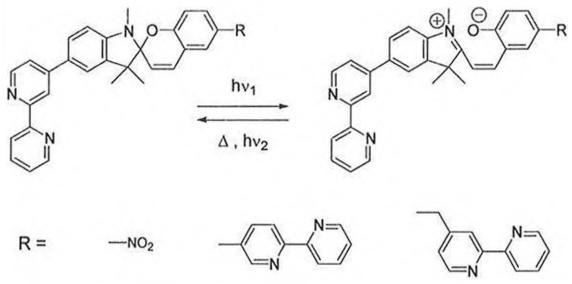
Inorganic and Coordination Chemistry **166**

Metal Complex Formation and Switching Properties of Spiropyrans Linked to Chelating Sites

Biljana Bozic, and Peter Belser

Department of Chemistry, University of Fribourg,
CH-1700 Fribourg, E-mail: Biljana.Bozic@unifr.ch

The photochromic behaviour of spiropyranes (SP) is well known and these compounds have been widely studied due to their applicability in the field of optical filters and optical recording. [1, 2]



We have developed a new series of spiropyrans containing covalently bounded 2,2'-bipyridine co-ordinating sites. Further complexation between the new ligands and photoactive metal centres (Ru(II), Os(II), and Re(I)) extends the molecular structure by the introduction of a chemical bounded photosensitizer.
Irradiations experiments show that no energy transfer occur after irradiation into the ^{1}MLCT band (450 nm) of sensitizer. The metal complex, in the closed form of SP can easily be transferred into the open form by irradiation into the 365 nm band of the SP unit.

[1] Crano, J. C.; Guglielmetti, Eds. *Organic Photochromic and Thermochromic Compounds*; Plenum Publishing: New York, **1998**; Vol. 1; 1999, Vol. 2.
[2] *Photochromism Molecules and Systems*; Eds. H. Dürr, H. Bouas-Laurent, Elsevier, Amsterdam, **1990**.

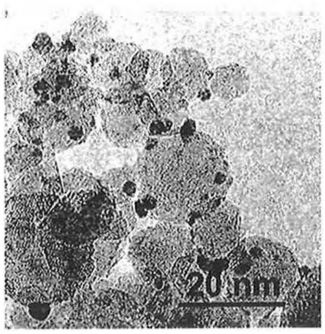
Inorganic Chemistry **167**

Supported noble metal hydrogenation catalysts made by flame synthesis

Reto Strobel[1,2], Wendelin J. Stark[1,2], Lutz Mädler[2], Sotiris E. Pratsinis[2], Alfons Baiker[1*]

[1]ETH Zurich, Laboratory of Technical Chemistry ETH Hoenggerberg, CH-8093 Zuerich, Switzerland
[2]ETH Zurich, Particle Technology Laboratory ETH Zentrum CH-8092 Zuerich, Switzerland

Supported noble metal catalysts are widely used in many applications. Flame synthesis is a one-step process for the production of well dispersed supported platinum or palladium catalysts (Figure). These nanomaterials were chirally modified and tested for enantioselective hydrogenation [1]. Compared with commercially applied catalysts, flame-made Pt/Al_2O_3 showed higher activity at comparable enantioselectivity for the hydrogenation of ethyl pyruvate. This behavior was traced to the very open structure of flame-made materials, facilitating reactant diffusion



HRTEM image of 5 wt% Pt/Al_2O_3 nanoparticles made by flame synthesis.

[1] R. Strobel, W. J. Stark, L. Mädler, S. E. Pratsinis, A. Baiker, *J. Catal.*, **2003**, *213*, 296.

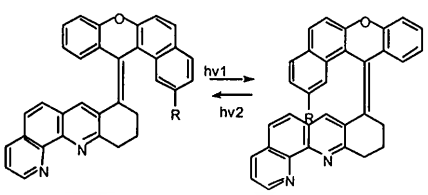
Inorganic and Coordination Chemistry **168**

Towards new chiroptical switches

Silvia Roma and Peter Belser

Department of Inorganic Chemistry, University of Fribourg
CH-1700 Fribourg, E-mail: silvia.roma@unifr.ch

Chiroptical switches are a new class of compounds that are able to found applications in the field of information storage or in liquid crystal displays.
During our investigations, we have synthesized potential dual mode photoswitching ligands. As depicted below, a phenanthroline type ligand and a methoxy-benzo-xantene unit are coupled by a double bond.[1]
These compound, upon irradiation at the appropriate wavelength, undergo a stilbene-like cis-trans photoisomerization. The unique feature of these system is that cis-tran isomerization simultaneously results in change of the helical orientation (M<—>P). Metal complex formation with the binding site of phenanthroline ligand is in progress.
Furthermore thermal rotation barrierrs have to be determined and photochromism has to be tested.



R= O-CH. H

[1] B. L. Feringa, *Acc. Chem Res.*, . **2001**, 34, 501-513.

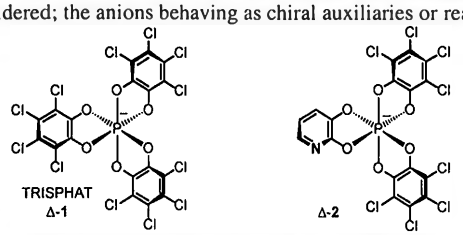
Inorganic and Coordination Chemistry **169**

Synthesis Of A Novel Chiral Hexacoordinated Phosphate Anion Exhibiting Brønsted And Lewis Basic Properties

Samuel Constant, Richard Frantz, Jérôme Lacour *

Département de Chimie Organique, Université de Genève, Switzerland

Cationic transition metal complexes are often chiral and many of their applications, reactions or processes lead to racemic molecular or supramolecular assemblies. To afford instead non-racemic or enantiopure products, an asymmetric ion pairing of the cations with enantiopure anions can be considered; the anions behaving as chiral auxiliaries or reagents.



In Geneva, chiral hexacoordinated phosphate anions have been studied for several years and shown to be efficient NMR chiral shift agents with effective resolving and asymmetric inducing properties such as TRISPHAT **1** [1]. To expand the scope of these anions, we now report the synthesis and the resolution of novel anions (e.g., Λ and Δ **2**) exhibiting Brønsted and Lewis basic properties.

[1] (a) Lacour, J.; Ginglinger, C.; Grivet, C.; Bernardinelli, G. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 608; (b) Lacour, J.; Ginglinger, C.; Torche-Haldimann, S. *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 2377; (c) Lacour, J.; Goujon-Ginglinger, C.; Torche-Haldimann, S. *Angew. Chem. Int. Ed.* **2000**, *39*, 3695; (d) D. Monchaud, J. J. Jodry, D. Pomerac, V. Heitz, J.-C. Chambon, J.-P. Sauvage, J. Lacour., *Angew. Chem. Int. Ed.* **2002**,*41*, 2317.

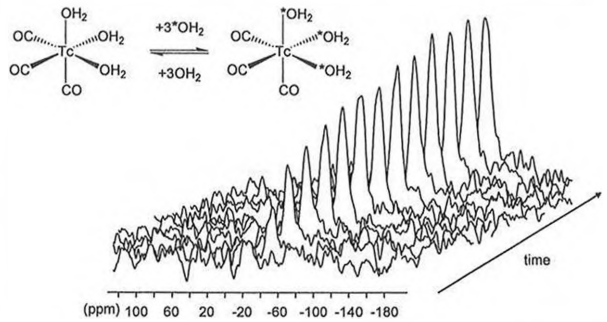
Inorganic and Coordination Chemistry **170**

Water exchange kinetics on $[(CO)_3Tc(H_2O)_3]^+$

Pascal V. Grundler,[a] Roger Alberto,[b] André E. Merbach[a]

[a]Institut de Chimie Moléculaire et Biologique, Ecole Polytechnique Fédérale de Lausanne, EPFL - BCH, CH-1015 Lausanne, Switzerland
[b]Anorganisch-Chemisches Institut, Universität Zürich, Winterthurerstrasse 190, 8057 Zürich, Switzerland
Pascal.Grundler@epfl.ch

The aquaion $[(CO)_3Tc(H_2O)_3]^+$ is currently investigated as a building block for novel radiopharmaceuticals. Although several substitution products are known few kinetic data about these reactions are available.
In order to better understand the reactivity of $[(CO)_3Tc(H_2O)_3]^+$, the water exchange has been studied by ^{17}O NMR using the fast injection technique.



The results of these measurements are discussed and compared with those of the Re analogue $[(CO)_3Re(H_2O)_3]^+$. [1]
R. Schibli and N. Aebischer are thanked for preliminary measurements.
[1] B. Salignac, P.V. Grundler, S. Cayemittes, U. Frey, R. Scopelliti, A.E. Merbach, R. Hedinger, K. Hegetschweiler, R. Alberto, U. Prinz, G. Raabe, U. Kölle, S. Hall, *Inorg. Chem.* **2003**, *42*, 3516-3526.

Inorganic and Coordination Chemistry **171**

Synthesis of the First Molecular Knot with Predetermined Configuration

Laure-Emmanuelle Perret-Aebi and Alexander von Zelewsky

Université de Fribourg, Département de Chimie, Pérolles, 1700 Fribourg, Switzerland

The classical trefoil knot is the prototype of a topologically chiral object [1]. It has been created at the molecular level [2], and recent improvements allow their preparation at a truly preparative scale [3]. The strategy for making knots is based on the three-dimensional template effect of transition metals, which are able to gather and interlace coordination molecular strings prior to the ultimate cyclization step (RCM).
We have prepared the first molecular knot with predetermined configuration using copper (I) and silver (I) as templates. For this purpose we prepared new chiral ligands as precursor [4].

This work is supported by the Swiss National Science Foundation and the CERC3 program.

[1] Frisch, H. L., Wasserman, E. J., *J. Am. Chem. Soc.*, **1961**, 83, 3789-3795.
[2] Dietrich-Buchecker, C. O., Sauvage, J.-P., *Angew. Chem.,Int. Ed.*, **1989**, 28, 1154-1156.
[3] Rapenne, R., Dietrich-Buchecker, C. O., Sauvage, J.-P. *J. Am. Chem. Soc.*, **1996**, 10932-10933.
[4] Perret-Aebi, L.-E., von Zelewsky, A., *Synlett*, **2002**, 5, 773-774.

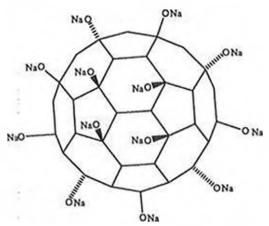
Inorganic and Coordination Chemistry **172**

Deprotonated fullerols - highly water soluble fullerene derivatives

João Bruno Livramento, Éva Tóth, Robert Ruloff, Gabriel González, André E. Merbach

Institut de Chimie Moléculaire et Biologique, Ecole Polytechnique Fédérale de Lausanne, EPFL - BCH, CH-1015 Lausanne, Switzerland
joao.livramento@epfl.ch

Chemically modified fullerenes are currently being investigated for application in the fields of biology and medicine [1]. One important objective of such derivatization is to obtain water soluble fullerenes, enabling their use under biological conditions. We have synthesized highly hydroxylated fullerenes (fullerols) stable in deprotonated form (fullerates) using quaternary ammonium hydroxides as catalysts [2].



The fullerates have been characterized by a series of physico-chemical techniques, such as IR, Karl-Fischer titration, MS, elemental analysis, as well as by ^{13}C, ^{17}O and ^{23}Na NMR. The acid-base behaviour of fullerols in aqueous solution was studied by pH-potentiometry and NMR titration in the absence and in the presence of metal ions.

[1] L.J. Wilson, *Interface*. **1999**, 8, 24.
[2] J. Li, A. Takeuchi, M. Ozawa, X. Li, K. Saigo, K. Kitazawa, *J. Chem. Soc. Chem. Commun.* **1993**, 1784.

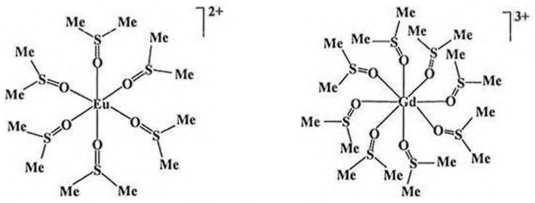
Inorganic and Coordination Chemistry **173**

The first Variable-pressure, -Temperature and -Magnetic Field ^{17}O-NMR Study of the DMSO exchange on $[Eu(DMSO)_6]^{2+}$ and $[Gd(DMSO)_8]^{3+}$

Rémi Dessapt, Gilles Moreau, Lothar Helm and André E. Merbach

Institute of Molecular and Biological Chemistry, Swiss Federal Institute of Technology Lausanne, EPFL-BCH CH-1015 Lausanne, Switzerland

The solvent exchange reaction on a metal ion is often used as a model for the interpretation of substitution reaction mechanisms. Paramagnetic nuclear magnetic resonance spectroscopy has been shown to be an efficient technique to study the very fast solvent exchanges on Eu(II) and Gd(III) [1]. The coordination chemistry of europium(II) ion has received very little interest because of its strong redox instability in aqueous solution, due to its slow oxidation by water protons. The use of non-aqueous solvents like DMSO however allows a better stabilization of the europium divalent ion and we have developed a new route to synthesize the $[Eu(DMSO)_6]^{2+}$ complex.



We report the first variable-pressure (up to 200 MPa), -temperature and -magnetic field ^{17}O-NMR studies of the DMSO exchange on $[Eu(DMSO)_6]^{2+}$ and $[Gd(DMSO)_8]^{3+}$. These studies have been completed by variable-temperature EPR and the first NMRD measurements performed in DMSO.

[1] L. Helm, A. E. Merbach, *Coord. Chem. Rev.*, **1999**, 187, 151.

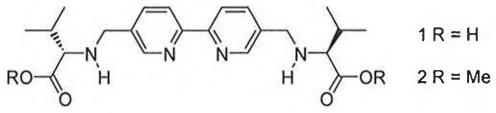
Inorganic and Coordination Chemistry **174**

Bipyridyls substituted by amino acid esters: proton switchable diastereoselectivity, anion binding and combinatorial libraries

Xiao-Juan Yang, Shane G. Telfer, and Alan F. Williams

Department of Inorganic, Analytical and Applied Chemistry, University of Geneva, 30 quai Ernest Ansermet, CH 1211 Geneva 4, Switzerland

We have previously shown that the amino acid substituted bipyridyl **1** shows high diastereoselectivity for metal binding in the bipyridyl site, and that the resulting complex binds chloride ion in solution and in the solid state. [1]



We report here on the chemistry of the methylated ligand **2** which is soluble in non-aqueous solvents. Reaction of **2** with iron(II) or cobalt(II) forms$[M(\mathbf{2})_3]^{2+}$ complexes with no diasteroselectivity, but titration of acid into the solution shows a steady increase in diastereoselectivity as shown by the CD spectrum, reaching a maximum when all the amines are protonated.

The protonated complex binds chloride more strongly than the analogous complex of **1**. Mixtures of cobalt(II), 2,2'-bipyridyl, and **2** in 2: 3: 3 molar ratio form a mixture or library of complexes, but addition of acid generates diastereoselectivity, and chloride favours the formation of $[Co(\mathbf{2}H_2)_3Cl_2]^{8+}$.

[1] Telfer, S.G.; Bernardinelli, G.;Williams, A.F. *Chem. Commun.*, **2001,** 1498; Telfer, S.; Bernardinelli, G.;Williams, A.F. *Dalton Trans.*, **2003**, 435.

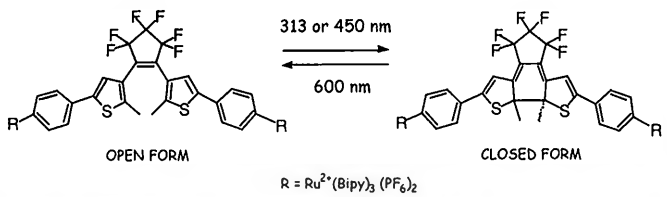
Inorganic Chemistry **175**

Optical Switching Properties of Photochromic Metal Complexes

Vincent Adamo and Peter Belser

Department of Chemistry, University of Fribourg, CH-1700 Fribourg, e-mail: vincent.adamo@unifr.ch

Photochromism species exist in two, differently colored forms that can be reversibly converted to each other by irradiation with UV or visible light. A good photochromic compound will be chemically stable in both forms, their respective absorption spectra will be very different, the photochemical conversion will proceed rapidly and efficiently, that is, with high quantum yields. Dithienylethenes are among the most promising organic photochromic dyes. Their open forms are colorless, whereas the closed isomers show strong absorption in the visible spectral range due to increased electron delocalization.



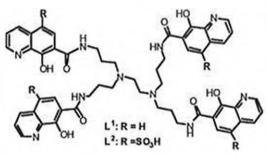
We have investigated effects of metal coordination on spectroscopic and photochemical properties as well as an emergent fluorescence.

Inorganic and Coordination Chemistry **176**

Thermodynamic and photophysical properties of Ln(III) complexes with tetrapodal ligands

Steve Comby, Anne-Sophie Chauvin, Daniel Imbert, Jean-Claude G. Bünzli

Institute of Molecular and Biological Chemistry, Swiss Federal Institute of Technology Lausanne, BCH 1405, CH-1015 Lausanne, Switzerland.



We present new lanthanide-containing chelates which are water soluble at physiological pH. The ligands have been designed to take advantage of the chelating effect of bidentate subunits connected to a *N,N,N',N'*-tetrakis(3-aminopropyl)-1,2-ethanediamine framework. They form stable complexes with Ln(III) ions, the four chromophoric units being coordinated to the metal centre, exploiting the entropic effect generated by the anchor. In the case of $\mathbf{L^2}$ the presence of sulfonate groups allows a high solvatation of the ligand and its chelates in aqueous media, which enlarges the range of possible applications. Furthermore, both ligand $\mathbf{L^1}$ and its complexes are soluble in organic media such as methanol or dichloromethane. We describe here the synthesis of $\mathbf{L^1}$ and $\mathbf{L^2}$, and their complexation reactions in organic and aqueous media, respectively. We focus on the thermodynamic properties of $\mathbf{L^2}$ in water (pK_as of the ligand, stability constants of the complexes), which have been investigated by the use of UV-vis spectrophotometric and potentiometric methods, revealing that $\mathbf{L^2}$ forms only a mono-metallic complex at pH = 7.4 with Ln(III) ions. Luminescence measurements carried out both on the ligands and their complexes reveal the influence of the sulfonate group on the photophysical properties.

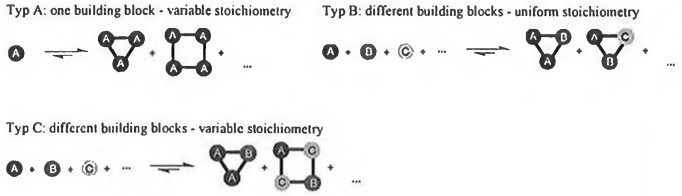
Inorganic and Coordination Chemistry **177**

Adaptive Behavior of Dynamic Combinatorial Libraries Generated by Assembly of Different Building Blocks

Zacharias Grote, Rosario Scopelliti, Kay Severin*

Institut de Chimie Moléculaire et Biologique, Ecole Polytechnique Fédérale de Lausanne, BCH, 1015 Lausanne, Switzerland

Combinatorial libraries in which the individual compounds are connected by dynamic equilibria are able to respond to the environment. If such a system is disturbed by addition of a target molecule (a receptor or a ligand), it will re-equilibrate with the concomitant amplification of compounds, which bind to the target molecule. For dynamic combinatorial libraries (DCLs) obtained by reversible assembly of reactive building blocks, three different types can be distinguished. [1]



In the following we show that DCLs of Type B and C can display a behavior fundamentally different from that of libraries of Type A. Importantly, we will demonstrate that there is no direct correlation between the relative amplification and the thermodynamic stability of the DCL members in such systems.

[1] Z. Grote, R. Scopelliti, K. Severin, *Ang. Chem. Int. Ed.* in press.

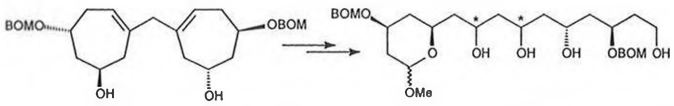
Organic Chemistry **178**

An expeditive asymmetric and non-iterative synthesis of long-chain polyols

Sandrine Gerber-Lemaire and Pierre Vogel

Institute of molecular and biological chemistry, Swiss Federal Institute of Technology, BCH, 1015 Lausanne, Switzerland, Sandrine.Gerber@epfl.ch

A large variety of natural products of biological interest includes polyketides (1,3-polyoxo, 1,3-polyols, aldols),[1] and the search for efficient approaches to this kind of fragments remains an important field of investigation.[2] We have developped an expeditive methodology for the preparation of long-chain polyketides bearing unsymmetrical functions at the terminal positions, based on the ozonolysis of bis-cyclohept-3-en-1,6-diol derivatives followed by the diastereoselective reduction of the resulting β-hydroxy ketones intermediate.[3] Conversion into enantiomerically pure long chain 1,3-polyol subunits can be then easily achieved.



[1] S. Omura, H. Tanaka, *Macrolide Antibiotics: Chemistry, Biology and Practise*, Academic Press: New-York, **1984**; T. I. Richardson, S. D. Rychnovsky, *J. Org. Chem.* **1996**, *61*, 4219; B. H. Lipschutz, B. Ullman, C. Lindsley, S. Recchi, D. J. Buzard, D. Dickson, *J. Org. Chem.* **1998**, *63*, 6092.

[2] For recent proposal, see e.g.: C. J. Sinz, S. D. Rychnovsky, *Angew. Chem. Int. Ed.* **2001**, *40*, 3224; D. J. Kopecky, S. D. Rychnovsky, *J. Am. Chem. Soc.* **2001**, *123*, 8420; S. A. Burova, F. E. McDonald, *J. Am. Chem. Soc.* **2002**, *124*, 8188; C. Schneider, F. Tolksdorf, M. Rehfeuter, *Synlett* **2002**, 2098 and references cited therein.

[3] S. Gerber-Lemaire, P. Vogel *Eur. J. Org. Chem.* **2003**, *in press*.

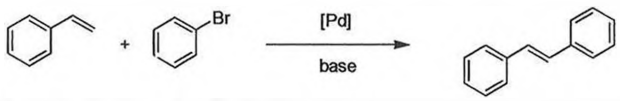
Organic Chemistry **179**

Heck Reactions with Homogeneous Palladium Catalysts: Synthesis of Novel Complexes and Mechanistic Investigations

Thomas Schultz, Andreas Pfaltz*

University of Basel, St.-Johanns Ring 19, CH-4056 Basel, Switzerland

Since its discovery in the early 1970s [1] the Heck reaction became a versatile method in organic synthesis. For industrial applications it is necessary to develop catalysts of higher activity to reduce catalyst loading and to enable the coupling of the cheaper aryl chlorides. Recently palladacycles [2] and bulky alkyl phosphines [3] have been reported to generate highly active catalysts even for the reaction of aryl chlorides. Given its importance it is surprising that significant mechanistic details of the Heck reaction are still unknown. Several attempts have been made to identify key intermediates of the catalytic cycle, [4] and to reveal a kinetic rate law [5].



We synthesized a series of palladium (II) complexes with different chelating bifunctional ligands. These compounds showed high turnover numbers and frequencies applied as catalysts for the coupling of bromobenzene with both styrene and butylacrylate. Their reactivity has been studied under various reaction conditions focusing on the accelerating effect of water. Also kinetic investigations have been performed comparing different catalysts to get a better insight into the mechanism of the Heck reaction.

[1] (a) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581. (b) Heck, R. F.; Nolley, J. P., Jr. *J. Org. Chem.* **1972**, *37*, 2320-2322.
[2] Herrmann, W. A.; Brossmer, C.; Reisinger, C.-P.; Riermeier, T. H.; Öfele, K.; Beller, M. *Chem. Eur. J.* **1997**, *3*, 1357-1364.
[3] Littke, A. F.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 6989-7000.
[4] Brown, J. M.; Hii, K. K. *Angew. Chem., Int. Ed.* **1996**, *35*, 657.
[5] Rosner, T.; Le Bars, J.; Pfaltz, A.; Blackmond, D. G. *J. Am. Chem. Soc.* **2001**, *123*, 1848-1855.

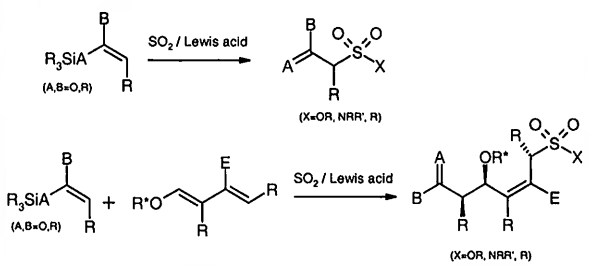
Organic Chemistry **180**

Sulfur Dioxide Mediated One-Pot Synthesis of Polyfunctional Sulfones, Sulfonic Esters and Sulfonamides

Laure Bouchez, Srinivas Reddy Dubbaka, Māris Turks, Pierre Vogel*

ICMB, EPFL, CH-1015 Lausanne-Dorigny, Switzerland

A highly efficient method is presented for three-and four-component reactions to prepare polyfunctional sulfones, sulfonic esters and sulfonamides, in one-pot. The three-component reaction relies on an ene-reaction of silyl enol ethers of esters, ketones and allylsilanes with sulfur dioxide[1]. In the four-component reaction SO_2 undergoes first a hetero-Diels-Alder addition with a 1,3-diene before oxyallylation of silyl enol ethers or allylsilanes [2]. The key intermediate in both reactions is a silyl sulfinate which can react with a wide variety of different electrophiles to provide either polyfunctional sulfones, sulfonic esters or sulfonamides [3]. Since those molecules are well known for their potent biological activities the method should have broad applications in medicinal chemistry.



[1] Bouchez, L.; Vogel, P. *Synthesis* **2002**, *2*, 225.3.
[2] Narkevitch, V.; Megevand, S.; Schenk, K.; Vogel, P. *J.Org.Chem.* **2001**, *66*, 5080.
[3] Bouchez, L.; S. R., Dubbaka; M., Turks; Vogel, P. *in Polyfunctional sulfonamides and sulfonates and process for preparing them* **2003**, EP 03003611.5.

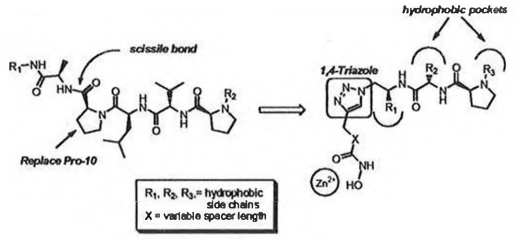
Organic Chemistry **181**

Synthesis of a New Inhibitor Library for the Lethal Factor of the *B. Anthracis* Toxin

Philipp Holzer, Hartmuth C. Kolb, K. Barry Sharpless*

The Scripps Research Institute, Department of Chemistry, BCC-315
10550 North Torrey Pines Road, La Jolla, CA 92037, USA

Bacillus anthracis secretes a tripartite toxin that consists of protective antigen (PA), edema factor (EF) and lethal factor (LF). [1] LF is a metalloproteinase that cleaves mitogen-activated protein kinase kinase 1 and 2 (MAPKK1, MAPKK2) by taking off 7 amino acids from the N terminus of the former and 9 amino acids from the latter. The structure of LF has been determined recently and was an important guide in designing inhibitors. LF is a 776 amino acid protein that contains a zinc cation (Zn^{2+}) binding site. A 40 Å long groove is contiguous with the catalytic center. [2] In a first approach, peptide sequences known to be substrates of LF (MAPKK1 and MAPKK2) were used as starting point to generate a focused inhibitor library in which the scissile bond is replaced with a peptide isostere and a Zn^{2+} binding group. A triazole is used to structurally mimic and replace Pro-10 and a hydroxamate zinc binding group on a variable spacer will replace the catalytic water from the zinc atom.



[1] K.A. Bradley *et al.*, *Nature* **2001**, *414*, 225
[2] A.D. Pannifer *et al.*, *Nature*, **2001**, *414*, 229

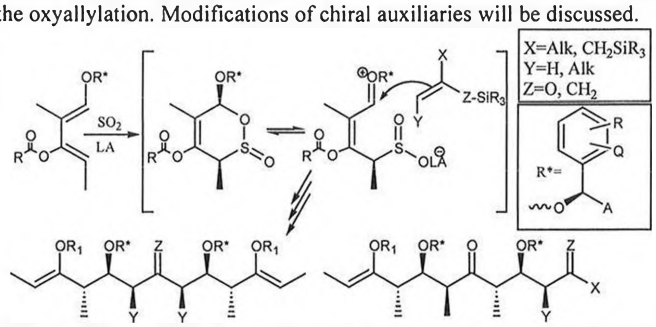
Organic Chemistry **182**

Umpolung of 1,3-Dioxy-1,3-dienes by Sulfur Dioxide and its Application in Polypropionate Synthesis.

Māris Turks, Pierre Vogel*

ICMB, EPFL, CH-1015 Lausanne-Dorigny, Switzerland

Polypropionates are an interesting class of natural compounds with an exceptional profile of biological activity [1]. Our group has shown that simple alkyl-substituted 1,3-dienes can undergo hetero-Diels-Alder reaction with SO_2 giving the corresponding sultines [2]. These cycloadducts can be opened at low temperature in the presence of Lewis acids to hypothetic zwitterionic intermediates, which then can be trapped by nucleophiles. Recently, an asymmetric version of this oxyallylation has been proposed [3]. Here, we would like to report about further development of this method using 1,3-dioxy substituted dienes. For the first time we show that different allylsilanes are also capable to undergo the oxyallylation. Modifications of chiral auxiliaries will be discussed.



[1] Davies-Coleman, M. T.; Garson, M. *J. Nat. Prod. Rep.* **1998**, *15*, 477. Hoffmann, R. W. *Angew. Chem. Int. Ed.* **2000**, *39*, 2054.
[2]. Deguin, B.; Vogel, P. *Tetrahedron Lett.* **1993**, *342*, 6269. Fernandez, T.; Sordo, J. A.; Monnat, F.; Deguin, B.; Vogel, P. *J. Am. Chem. Soc.* **1998**, *120*, 13276.
[3] Narkevitch, V.; Megevand, S.; Schenk, K.; Vogel, P. *J. Org. Chem.* **2001**, *66*, 5080.

Organic Chemistry **183**

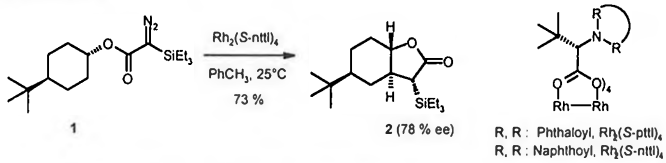
Enantioselective Metallocarbene Reactions of Silicon containing Diazocompounds by Chiral Dirhodium(II) Catalysts

Paul Müller, Yves Allenbach, Fabienne Lacrampe

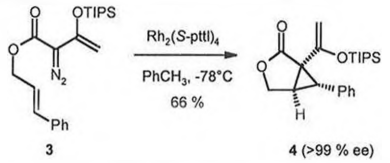
University of Geneva - 30 Quai Ernest-Ansermet
CH-1211 Geneva, Switzerland

Intramolecular C-H insertion and cyclopropanation of carbenes have been studied in enantioselective synthesis.

The catalytic decomposition[1] of the diazo(triethylsilyl) acetate (**1**) by Rh_2(*S*-pttl)$_4$ or Rh_2(*S*-nttl)$_4$[2] affords the silylated lactone **2** with 78 % ee and 73 % yield :



Optically pure bicyclic lactone **4** was obtained by the catalytic intramolecular cyclopropanation of the diazo(triisopropylsilanyloxy) butenoate **3** using Rh_2(S-pttl)$_4$ at –78°C in toluene in 66 % yield :



1 P. Müller, F. Lacrampe, G. Bernardinelli, *Tetrahedron: Asymmetry* **2003**, *14*, 1503-1510.
2 P. Müller, Y. Allenbach, E. Robert, *Tetrahedron: Asymmetry* **2003**, *14*, 779-785.

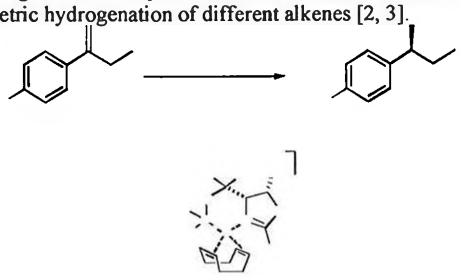
Organic Chemistry **184**

Chiral P,N-Ligands for the Iridium Catalyzed Asymmetric Hydrogenation

Frederik Menges and Andreas Pfaltz*

University of Basel, St. Johanns-Ring 19, CH-4056 Basel, Switzerland

Iridium-complexes of chiral *P,N*-ligands are known to be efficient and highly selective catalysts for the asymmetric hydrogenation [1]. Recently, a new class of phosphinite-oxazoline ligands has been developed in our group. Their modular structure permits to adjust the properties of the corresponding iridium-complexes in order to obtain excellent selectivities in the asymmetric hydrogenation of different alkenes [2, 3].



Now we report our detailed investigations of both, the phosphinite oxazoline ligands and the corresponding iridium-complexes properties as well as the influence of further variations on the backbone.

[1] A. Pfaltz, J. Blankenstein, R. Hilgraf, E. Hörmann, S. McIntyre, F. Menges, M. Schönleber, S. P. Smidt, B. Wüstenberg, N. Zimmermann, *Adv. Synth. Catal.* **2003**, *345*, 33-43.
[2] J. Blankenstein, A. Pfaltz, *Angew. Chem. Int. Ed.* **2001**, *40*, 4445-4447.
[3] F. Menges, A. Pfaltz, *Adv. Synth. Catal.* **2002**, *344*, 40-44.

Organic Chemistry **185**

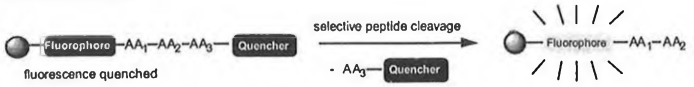
Sequence Dependent Peptide Cleavage under Fenton Conditions

Matthias Nold and Helma Wennemers*

Department of Chemistry, University of Basel,
St. Johanns-Ring 19, CH-4056 Basel

Transition metals play a crucial role in life processes as cofactors of many enzymes. However, they can also cause damage to proteins. Iron for instance is known to catalyze the Fenton reaction that generates highly reactive radicals that can attack proteins leading to either side chain modification or cleavage of peptide bonds.[1,2]

In order to investigate the influence of the amino acid sequence on the extent of metal caused protein damage we synthesized a 29791 membered fluorophore-quencher-peptide-library on solid support with a fluorophore near the bead followed by a combinatorially varied peptide capped by a quencher. Beads carrying peptides that are cleaved by the given reactants will fluoresce.[3]



We will present the synthesis of the fluophore-quencher-library as well as first screening results using Fenton conditions.

[1] Vol. 36 of „Metal Ions in Biological Systems" edited by A. and H. Sigel **1998**.
[2] R.T. Dean, S. Fu, R. Stocker, M.J. Davies, *Biochem. J.* **1997**, *324*, 1-18.
[3] M. Meldal, I. Svendsen, K. Breddam, F.I. Auzanneau, *Proc. Natl. Acad. Sci.* USA **1994**, *91*, 3314.

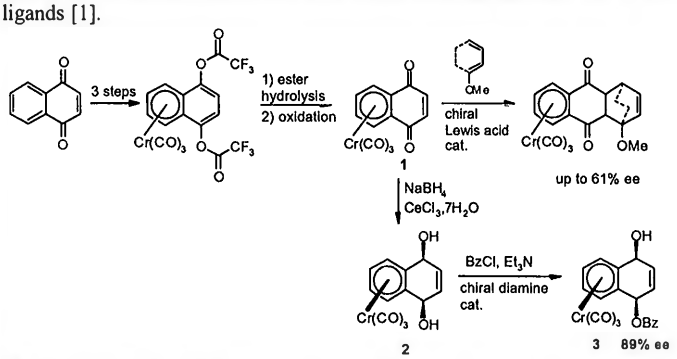
Organic Chemistry **186**

Desymmetrization of (Naphthoquinone)Cr(CO)$_3$: a New Entry to Planar Chiral Complexes

E. Peter Kündig*, Thierry Lomberget, Cyril Poulard, Ryan Bragg

University of Geneva, Dept. of Organic Chemistry
30, quai E. Ansermet, CH-1211 Geneva 4, Switzerland

The obtention of highly enantiomerically enriched compounds is one of the biggest challenge in organic synthesis. Planar chiral (arene)Cr(CO)$_3$ complexes are of interest because of their utility as chiral synthons and chiral ligands [1].



Desymmetrization of the *meso*-complex **1** was achieved by asymmetric Diels-Alder reactions catalyzed by chiral Lewis acids. We also report on the asymmetric acylation of the (1,4-dihydroxynaphthalene)Cr(CO)$_3$ complex **2** catalyzed by a chiral diamine [2] to obtain the monobenzoate **3** in good yield and with high enantiomeric excess.

[1] Kündig, E. P.; Pache, S. H. *Science of Synthesis,* **2003**, *2*, 153
[2] Oriyama, T.; Imai, K.; Sano, T.; Hosoya, T. *Tetrahedron Lett.*, **1998**, *39*, 3529.

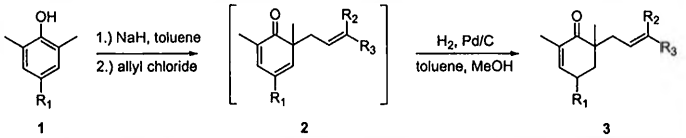
Organic Chemistry **187**

Studies on the Enantioselective Alkylation of Phenols

G. Frater[a,b], A. Goeke[b], M. Lovchik[a]

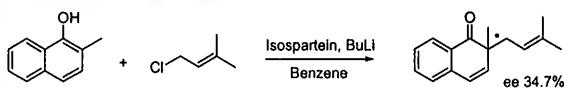
[a]University of Zurich , Winterthurerstrasse 190, 8057 Zurich, Switzerland
[b]Givaudan Schweiz AG, Ueberlandstrasse 138, CH-8600 Duebendorf

Construction of quaternary stereogenic carbon centers in 6-position of cyclohexenones has been subject of numerous research publications over the last decades.[1] In this presentation we report a new effective method to synthesise 6,6-disubstituted cyclohexenones **3**, involving the alkylation of phenols **1** followed by the subsequent selective hydrogenation of the intermediate **2**.[2]



1 2 3

Based on these results, we then studied the effect of replacing NaH with chiral lithium complexes resulting in optical activity of the corresponding 6,6-disubstituted cyclohexadienone **2**. The synthesis of (+)-**6** illustrated below is an example using isospartein as chiral source.[3]



4 5 (+)-6

Several substituted phenols and naphthols were alkylated in the presence of different chiral amines and counter ions. In addition, research on the sterical and electronical effects influencing the selectivity was undertaken.

[1] K. Koga, M. Murakata, *Tetrahedron* **1998**, *54*, 2449
[2] A. Goeke, EP 1213276, priority 5.12.2000 to Givaudan.
[3] D. Hoppe, T. Hense, *Angew. Chem.* **1997**, *109*, 2376

Organic chemistry **188**

MECHANISM OF THE ISOMERISATION OF ALKENES INDUCED BY POLYSULFONES

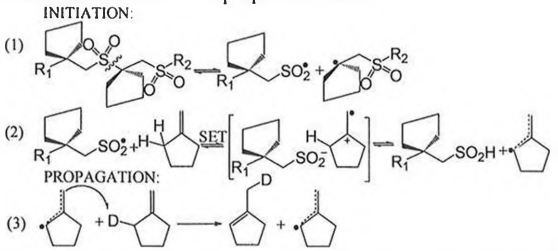
Dean Marković and Pierre Vogel*

ICMB, EPFL; CH-1015 Lausanne-Dorigny, Switzerland

When dissolved in SO_2 methylidenecyclopentane undergo formation of poly(methylidenecyclopentane sulfone) and isomerisation into 1-methylcyclopent-1-ene.

EPR studies of the copolymerisation reaction confirm the presence of sulfonyl and carbon centred radicals. If Bu_3SnH or TEMPO are added to the reaction mixture neither polysulfone nor isomerised olefin are seen. Kinetics of the isomerisation and polymerisation reactions with 1/1.1 mixture of the methylidenecyclopentane and sulfur dioxide confirmed the role of polysulfone in the isomerisation reaction.

Mechanistical studies shows that sulfonyl radicals trapped in the polysulfone can catalyze the isomerisation. It occurs via the intermediary of methylidenecyclopent-2-yl radical (radical chain process (eq. 3.)), as demonstrated by deuterium labelling experiments. This is not the mechanism proposed earlier.[1]



[1] (a) D. Masilamani, M. M. Rogic, *J. Am. Chem. Soc.* **1978**, *100*, 4634; (b) D. Masilamani, M. E. Reuman, M. M. Rogic, *J. Org. Chem.* **1980**, *45*, 4602;

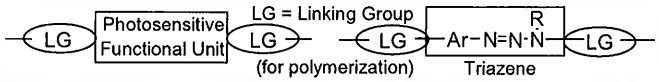
Organic Chemistry **189**

Polymeric Materials Designed for Laser Ablation Lithography (LAL) Based on Photosensitive Triazene Containig Building Blocks

Matthias Nagel,[a] Thomas Lippert*,[b]

[a] Swiss Federal Laboratories for Materials Testing and Research (EMPA) Überlandstrasse 129, CH-8600 Dübendorf, Switzerland; [b] Paul Scherrer Institute, Materials Group, CH-5232 Villigen PSI, Switzerland

Laser ablation lithography (LAL) of designed polymeric resist layers is a promising tool for surface patterning in the area of microtechnology. LAL is a direct dry etching technique and works without a subsequent developing procedure. These ultraphotosensitive resist films have to decompose rapidly and efficiently into gaseous and volatile low molecular mass fragments which are expelled and removed without carbonization upon irradiation with a laser, e.g. a XeCl excimer laser (308 nm) [1].



Polymers with incorporated triazene groups in the backbone proved to have superior ablation characteristics [1][2]. Our synthetic studies are aimed at the further optimization of the film forming properties of the triazene polymer layers and the design of novel tailored materials for the specific requirements, e.g. as dynamic release layer in laser ablation transfer (LAT) experiments where thin layers with a micrometer resolution are transferred. Our concept includes also the synthesis of triazene containing copolymers, based on building blocks which can be combined individually in a copolymerization procedure as a versatile modular assembly system.

[1] T. Lippert, J. T. Dickinson, *Chem. Rev.* **2003**, *103*, 453 – 485.
[2] O. Nuyken, C. Scherer, A. Baindl, A. R. Brenner, U. Dahn, R. Gärtner, S. Kaiser-Röhrich, R. Kollefrath, P. Matusche, B. Voit, *Prog. Polym. Sci.* **1997**, *22*, 93.

Organic Chemistry **190**

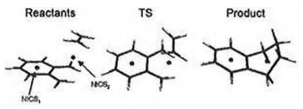
A New Analysis Tool for Stability and Aromaticity of Rings

[a]C.Corminboeuf, [b]T. Heine, [a]J. Weber

[a]Department of Physical Chemistry, University of Geneva, 30 quai Ernest-Ansermet, CH-1211, Genève 4, Switzerland, [b]Institut für Physikalische Chemie, Technische Universität Dresden, D-01062 Dresden, Germany

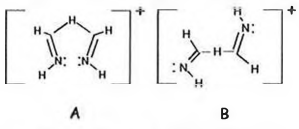
A new analysis of aromaticity based on Nucleus Independent Chemical Shifts (NICS) of molecular orbitals, MO-NICS[1], is applied to a Diels-Alder reaction involving an o-quinodimethane[2], a new family of tetracoordinate planar carbon compounds[3], and a pseudoring.

It is shown that the transition state in a Diels-Alder reaction is stabilized by enhancement of aromaticity of the forming ring, and that the initial cyclohexadiene peripheral ring becomes aromatic in the product.



Possibly stable derivatives of C_5^{2-} containing tetracoordinate planar carbon include triangular rings. MO-NICS analysis shows that the delocalized orbitals around these rings are responsible for the planarity of the tetracoordinate carbon.

The unexpected stability of the pseudoring's isomer A over B was found by high level ab initio calculations[4]. Delocalization of the σ system was suggested to stabilized isomer A. Our analysis give evidence that both σ and π systems are shaped like typical annulene orbitals favorizing the pseudoring shape.



[1] Heine, T.; Corminboeuf, C.; Schleyer, P. v. R.; Seifert, G.; Reviakine, R. Weber, J. *submitted.*
[2] Corminboeuf, C.; Heine, T.; Weber, J. *Org. Lett.* . **2003**, *5*, 1127.
[3] Merino, G.; Mendez-Rojas, M. A.; Vela, A. *J. Am. Chem. Soc.* **2003**, ASAP.
[4] Williams, I.H.; Pain, A.E. *J. Chem. Soc., Chem. Comm.* **1988,** 1368.

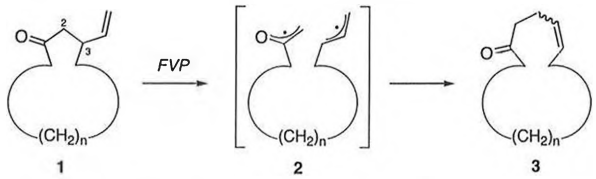
Organic Chemistry **191**

Designed Bond Fission in High Temperature Chemistry: Novel Ring Expansions, Ring Openings, and Ring Contractions

Georg Rüedi and Hans-Jürgen Hansen

University of Zürich, Winterthurerstr. 190, CH-8057 Zürich, Switzerland

Selective cleavage of the weakest single bond in molecules by means of high thermal energy impact can broadly be applied as a useful tool in directed synthetic organic chemistry. Flash vacuum pyrolysis (FVP) of medium and large-ring 3-vinylcycloalkanones **1** effects clean homolysis of the C2–C3 bond. Recombination within the generated diradical intermediate **2** leads to γ,δ-unsaturated cyclic ketones **3** expanded by two carbon atoms. Scope and limitations have been investigated by varying the ring size as well as the vinylic side chain.



FVP conditions, 580 - 620°C, 2 mbar, N_2 flow

Thermal isomerization of appropriately substituted bicyclic monoterpenes, such as camphor and fenchone, results in a regio- and stereoselective ring opening reaction under the formation of α-campholanic and fencholic acid derivatives [1][2]. Subjecting a series of α-substituted cyclododecanones to FVP leads to the corresponding 11membered rings under loss of CO.

[1] G. Rüedi, M. Nagel, H.-J. Hansen, Synlett **2003**, in press.
[2] G. Rüedi, M. Nagel, H.-J. Hansen, *Org. Lett.* **2003**, submitted.

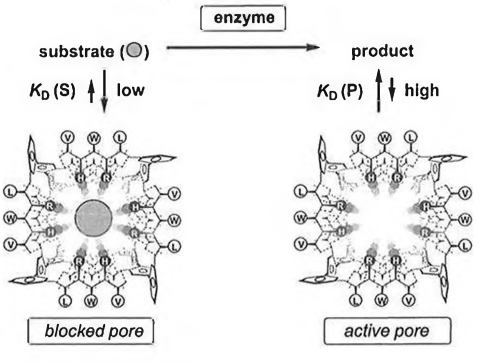
Organic Chemistry **192**

Enzyme Screening with Synthetic Multifunctional Pore Sensors

Nathalie Sordé and Stefan Matile*

University of Geneva, Department of Organic Chemistry
1211 Geneva, Switzerland

Enzyme sensing with synthetic multifunctional pores (SMPs) requires molecular recognition of either substrate or product by the same SMP: If substrates bind better than products, enzyme activity translates into pore activation (below), whereas enzyme activity results in pore inactivation if the SMP recognizes products rather than substrates (not shown) [1]. Here, label-free, "naked-eye" detection of enzymes catalyzing either synthesis or degradation of DNA, RNA, polysaccharides and proteins at work is used to exemplify detectability of many different enzymes with the same SMP sensor. Such usefriendly enzyme screening is attractive for application of SMP sensors in practice



[1] Das, G.; Talukdar, P.; Matile, S. *Science* **2002**, *298*, 1600.

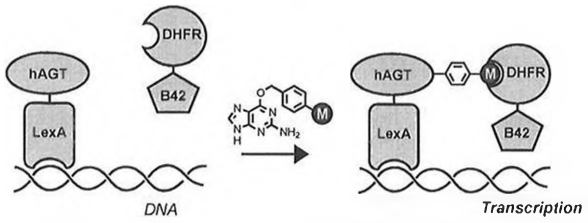
Organic Chemistry **193**

Induced Dimerization of Fusion Proteins in Vivo by Covalent Labeling

Susanne Gendreizig, Kai Johnsson*

Institute of Molecular and Biological Chemistry, Institute of Biomolecular Sciences, EPFL, CH-1015 Lausanne, Switzerland

The specific and covalent labeling of fusion proteins of the human O^6-alkylguanine-DNA alkyltransferase (hAGT) with cell permeable O^6-benzylguanine derivatives enables the investigation and manipulation of a protein of interest *in vivo* [1]. The use of synthetic molecules that can be specifically and covalently bound by hAGT and be recognized simultaneously by another protein through a suitable ligand provides a new approach to induce dimerization of selected proteins *in vivo*.



Such an induced protein dimerization through covalent labeling can be used to trigger selected biological processes as shown here for the formation of a functional transcription factor in *Saccharomyces cerivisiae* [2].

[1] A. Keppler, S. Gendreizig, T. Gronemeyer, H. Pick, H. Vogel, K. Johnsson., *Nat. Biotechnol.* **2003**, *21*, 86.
[2] R. Pollock, T. Clackson, *Curr. Opin. Biotechnol.* **2002**, *13*, 459.

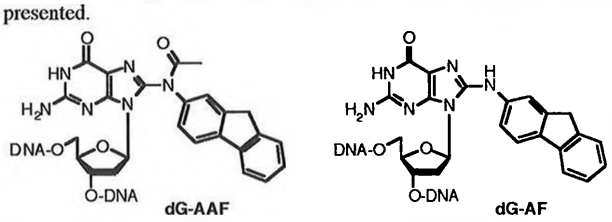
Organic Chemistry **194**

Preparation of oligomers containing 8-(N-acetyl-aminofluorene)-2'-deoxyguanosine adducts using a new "ultramild" DNA synthesis

Ludovic C. J. Gillet, Orlando D. Schärer

Institute of Molecular Cancer Research, University of Zürich, August Forel Str. 7, 8008 Zürich; Switzerland

The synthesis of DNA containing defined site specific damaged bases has long been a limiting step for the study of DNA repair processes. In particular, alkali sensitive DNA adducts are often difficult to prepare by standard oligonucleotide synthesis, since they are unstable to the ammonia treatment required to release the oligomer from the solid support and to remove its different protecting groups. For example, 8-(N-acetyl-aminofluorene)-2'-deoxyguanosine (dG-AAF), an adduct intensively used in the study of mutagenesis, carcinogenesis and DNA repair, gets deacetylated under these conditions to dG-AF, which exhibits very different physicochemical properties and biological effects. We previously described an efficient synthesis of the dG-AAF monomer suitably protected for DNA synthesis [1]. Here we report its incorporation into DNA by solid phase synthesis and the development of new deprotection conditions that lead to oligonucleotides containing either the dG-AAF or the dG-AF adducts. Biochemical studies of the nucleotide excision repair pathway using these modified oligonucleotides will be presented.



[1] Gillet L. C. J.; Schärer O. D. *Org. Lett.* **2002**, *4*, 4205-4208.

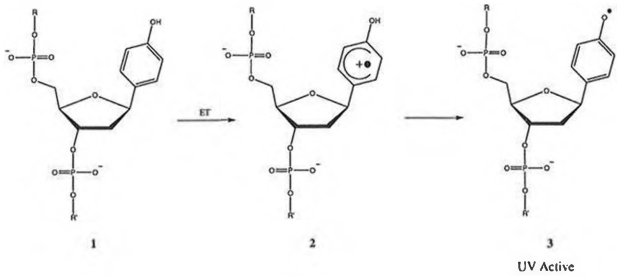
Organic Chemistry **195**

A New Assay To Investigate Electron Transfer Into DNA Based On The UV Properties Of A New Non-Natural Nucleoside

Nicolas Amiot, Stéphanie Saigne, Bernd Giese*

University of Basel, St. Johannsring 19, CH-4056 Basel, Swtzerland

Electron transfer into DNA has been thoroughly studied in the group of Professor Giese [1]. Although the mechanism of electron transfer is now well documented, the electron transfer into DNA is still under investigation to increase its efficiency and to develop its potential applications.
We are currently developing a new assay to replace the somewhat tedious, time-consuming and sometimes limited assays currently used in our group. We plan to use the UV properties of nucleoside **3** to study the electron transfer through a DNA fragment using UV time resolved spectroscopy after a laser irradiation [2].



After achieving the synthesis of the nucleotide precursor used to introduce nucleoside **1** into DNA fragments we are focusing on the development of this new assay.

[1] B. Giese, *Ann. Rev. Biochem.*, **2002**, 71, 51-70
[2] K.H. Bansal, R.W. Fessenden, *Radiat. Res.*, **1976**, 67, 1-8

Organic Chemistry **196**

HTS Profiling of Lipases and Esterases

Jean-Philippe Goddard, J.-L. Reymond*

University of Bern, Freiestrasse 3,CH-3012 Bern

A plethora of enzymes and their mutants have become available over the years from biodiversity mining and directed evolution/mutagenesis studies. Beyond activity screening arises the problem of being able to characterize each enzyme's activity in sufficient details for distinguishing similar enzyme subtypes This can be realized by activity profiling or fingerprinting using substrate arrays.[1]

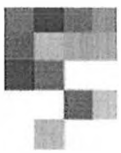


Figure. Activity and Stereoselectivity Profile of a Lipase.

We have developped a set of optically pure substrates for the high-throughput profiling of esterolytic activities of lipases and esterases. Acitivity profiles were analyzed by data clustering and enabled a functional classification of enzymes on the basis of their stereoselectivity and substrate specificity.

[1] D. Wahler, F. Badalassi, P. Crotti, J.-L. Reymond, *Chem. Eur. J.* **2002**, *8*, 3211-3228..

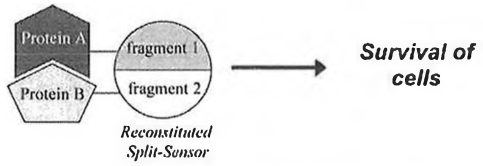
Organic Chemistry **197**

Development of a new reporter system for monitoring protein-protein interactions in living cells

Petra Tafelmeyer, Kai Johnsson *

Institute of Molecular and Biological Chemistry, Institute of Biomolecular Sciences, EPFL, CH-1015 Lausanne, Switzerland

Here, we introduce a new system for the generation of *Split-protein sensors* for the detection of protein-protein interactions *in vivo*. To identify suitable fragmentation sites within a given protein we have devised a combinatorial approach, based on the circular permutation method introduced by Schachmann [1]. Using this approach we were able to identify various suitable fragmentation sites in a yeast enzyme involved in the biosynthesis of an amino acid. Fusing these fragments to interacting proteins A and B then allowed to couple the survival of the yeast to the interaction of the proteins. The system can also be used for the identification of the interaction of membrane proteins, thereby complementing the yeast two-hybrid system [2].



[1] R. Graf, H. K. Schachmann, *PNAS USA* **1996**, *93*, 11591
[2] S. Fields, O. Song, *Nature* **1989**, *340*, 245

Organic Chemistry **198**

TOWARDS A DNA-LIKE DUPLEX WITHOUT HYDROGEN BONDS

Gérald Mathis , Rolf Schütz and Jürg Hunziker*

Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, 3012 Bern, Switzerland

Based on the observation that hydrophobic effects can be exploited in addition to complementary hydrogen bonding to create novel base pairs, we have incorporated the pentafluorophenyl- (F^5) and phenyl-C-deoxyribosides (P) shown below into synthetic oligonucleotides.[1] The inverse quadrupolar moments of the phenyl and pentafluorophenyl residues are expected to lead to edge-to-edge attractive intermolecular forces. The consecutive alternating alignment of pentafluorophenyl and phenyl residues should additionally result in very strong intrastrand π-π-stacking. The more natural base pairs are replaced by this novel pair the higher the thermodynamic stability of the resulting duplex if they are arranged in an alternating fashion. The enzymatic replication of the F^5-P pair in a primer extension reaction with polymerase I (Klenow fragment) is not possible, however.

Fig. 1. The complementary charge distribution in benzene and hexafluorobenzene leads to favourable edge-to-edge (as well as stacking) contacts between these two molecules. This interaction might be exploited in a base pair between pentafluorophenyl- and phenyl-C-deoxyriboside.

[1] G. Mathis, J. Hunziker, *Angew. Chem.* **2002**, *114*, 3335, *Angew. Chem. Int. Ed.* **2002**, *41*, 3203.

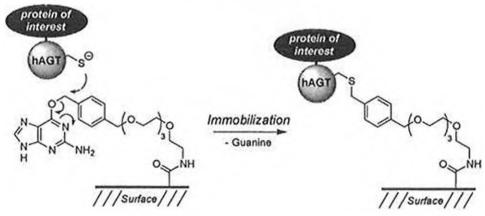
Organic Chemistry **199**

Covalent and selective immobilization of fusion proteins

Maik Kindermann, Nathalie George, Nils Johnsson, Kai Johnsson*

Institute of Molecular and Biological Chemistry, Swiss Federal Institute of Technology, CH-1015 Lausanne, Switzerland.

We report a new and general method for a selective covalent and orientation-controlled immobilization of fusion proteins to various biosensor surfaces suitable to study protein-protein interactions. The strategy is based on the construction of a fusion protein between the protein of interest and the human DNA repair protein O^6-alkylguanine-DNA alkyltransferase (hAGT). This DNA repair protein, which irreversibly transfers the alkyl group from its substrate, O^6-alkylguanine, to one of its cysteine residues accepts also chemically modified O^6- benzylguanine-derivatives as substrates [1].



By covalently linking the O^6-benzylguanine-derivatives to a biosensor surface hAGT fusion proteins covalently immobilize themselves in a highly specific manner [2]. The specificity of the reaction even allows for a selective immobilisation directly out of cell lysates. Both the high specificity as well the covalent nature of the approach makes it an attractive alternative to all currently used immobilization protocols for the constructing of protein microarrays.

[1] A. Keppler, S. Gendreizig, T. Gronemeyer, H. Pick, H. Vogel, K. Johnsson, *Nat Biotechnol* **2003**, *21*, 86-89.
[2] M. Kindermann, N. George, N. Johnsson, K. Johnsson, *J. Am.Chem.Soc* **2003**, in press.

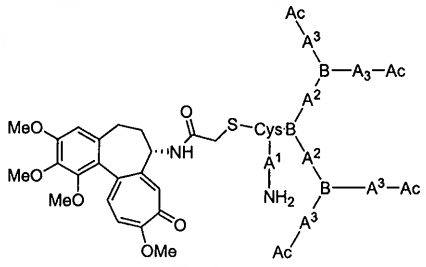
Organic Chemistry **200**

Synthesis of Colchicine Dendrimer Derivatives

David Lagnoux, Jean-Louis Reymond*

University of Chemistry and Biochemistry, Freiestrasse 3, 3012 Berne, Switzerland

Over-expression of the P-glycoprotein multidrug transporter (Pgp) in the plasma membrane is believed to be a major cause of resistance to multiple chemotherapeutic drugs in human cancers. Attachment of chemotherapeutic drugs to dendrimers might make them too large for this efflux pump. Simultaneously, macromolecules such as dendrimers are taken up selectively into cancer cells. Based on a peptide-dendrimer architecture recently reported in our group,[1] we have prepared colchicine-peptide dendrimer conjugates. Colchicine is an antimitotic drug that acts by tubulin binding, but is too toxic for use in chemotherapy.



[1] A. Esposito *et al.*, *Angew. Chem. Int. Ed.* **2003**, *42*, 1381.

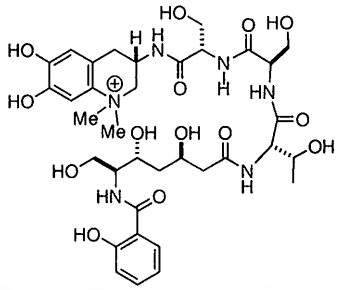
Organic Chemistry **201**

The Cyanobacterial Siderophore Anachelin - Synthetic, Structural and Mechanistic Studies

Karl Gademann* and Yann Bethuel

Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule Zürich, ETH Hönggerberg, CH-8093 Zürich

The Anachelins were recently isolated from the freshwater cyanobacterium *Anabaena cylindrica*[1] and were proposed to act as siderophores facilitating Fe uptake. However, the constitution of the active siderophore, its absolute and relative configuration as well as its mode of action remain unknown. This is the classic stimulus for the total synthesis of these natural products.



Anachelin H

We well present our highly convergent synthetic strategy culminating in the total synthesis of Anachelin H. Moreover, structural and mechanistic aspects of these natural products will be discussed.

[1] H. Beiderbeck, K. Taraz, H. Budzikiewicz, A. E. Walsby, Z. *Naturforsch.* **2000**, *55c*, 681-687; Y. Itou, S. Okada, M. Murakami, *Tetrahedron* **2001**, *57*, 9093-9099.

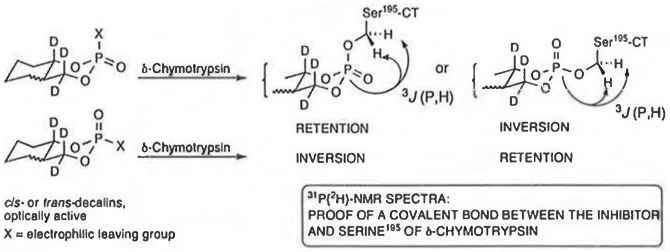
Organic Chemistry **202**

Optically Active Deuterated Dioxaphosphadecalins as Inhibitors of δ-Chymotrypsin: ^{31}P-NMR Evidence of Covalent Bond Formation

Markus J. Stöckli, Peter Rüedi

Organisch-chemisches Institut der Universität Zürich Winterthurerstrasse 190, CH-8057 Zürich

The title compounds (2,4-dioxa-3λ^5-phosphabicyclo[4.4.0]decane-3-ones) are conformationally restricted inhibitors of serine hydrolases (*e.g.* chymotrypsin, acetylcholinesterase). As such they are useful probes for the investigation of the stereochemical pathways of the irreversible inhibition reaction of these enzymes by ^{31}P-NMR spectroscopy [1][2].
In order to prove the covalent nature of the binding interaction between the enzyme and the inhibitor, we have performed inhibition experiments with enantiomerically pure deuterated dioxaphosphadecalins.



The synthesis of the inhibitors, especially the problems connected with the optically active precursors, the determination of the absolute configuration, as well as results of the ^{31}P{^{2}H}-NMR studies will be presented.

[1] W. Ganci, E.J.M. Meier, F. Merckling, G. Przibille, U. Ringeisen, P. Rüedi, *Helv. Chim. Acta* **1997**, *80*, 421; S. Furegati, W. Ganci, G. Przibille, P. Rüedi, *Helv. Chim. Acta* **1998**, *81*, 1127.

[2] M.J. Stöckli, P. Rüedi, *Helv. Chim. Acta* **2001**, *84*, 106.

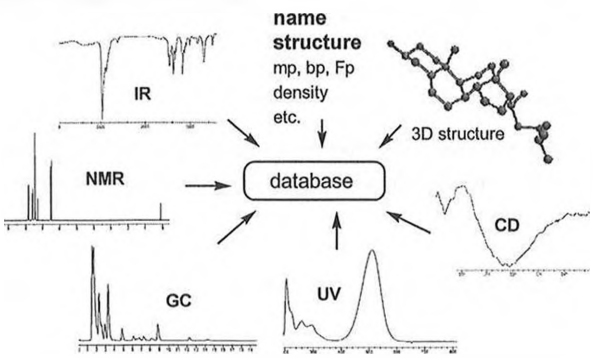
Organic Chemistry **203**

Storing and retrieving in-house chemical information from a Web browser

Damiano Banfi, Luc Patiny

Institute of Molecular and Biological Chemistry (ICMB), EPFL, CH-1015 Lausanne, Switzerland

Various types of chemical information are generated in a research laboratory and their management is a challenging task, especially in an academic environment.
Here we present an evolving database that allows the centralisation of most of this information. Anybody at any time can add new chemicals with their physical characteristics directly from a web browser. Moreover, most of the scientific equipment is connected to the database allowing the automatic storage of NMR spectra, IR spectra, HPLC chromatograms etc.
Providing the tool to store any kind of information to researchers is a first milestone. Even if usual queries are available, we will also present some perspectives in the search possibilities based, for example, on genetic algorithms using a user-friendly interface.



Organic Chemistry **204**

High resolution in Heteronuclear NMR experiments

Damien Jeannerat

University of Geneva, 30 Quai E. Ansermet., CH-1204 Geneva 11, Switzerland

The low resolution in the carbon dimension of two-dimensional NMR experiments can be increased by a factor 10 to 50 using spectral aliasing.[1] This technique allows chemists to avoid difficulties when assigning carbons signals that are resolved in a one-dimensional spectrum but overlap in HSQC. It requires the spectral width of the carbon dimension to be reduced in a controled manner in order to avoid ambiguities in the chemical shift of signals in the alised spectrum. The computer program resolving this task is available on our web site http://rmn.unige.ch/simplealias.[2] It takes as input a list of carbon chemical shifts and a few a other parameters and returns the spectral width insuring the best spread of carbons and the minimal number of increments sufficient to separate all signals. It also provides a table allowing one to determine to what carbon each signal corresponds to. The benefit of this technique is to permit the acquision of high resolution spectra in less acquisition time than using traditional increase of the number of time increments in every cases where the signal-to-noise ratio is not the limiting factor.

[1] Damien Jeannerat, *Magn. Reson. Chem.* **2002**, *41*, 3.
[2] Damien Jeannerat, Submitted.

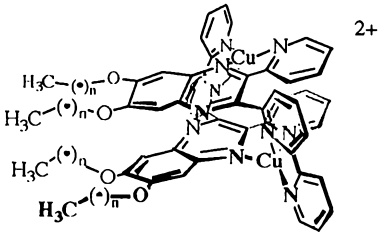
Organic Chemistry **205**

Towards Double-decker, Metallo-organic Supramolecular Mesogens

F. Heirtzler,*// S. I. G. Dias//, I. Prokes,‡ P. Cragg¶

// School of Physical Sciences, University of Kent, Canterbury, CT2 7NH UK; ‡ Department of Chemistry, University of Exeter, UK; ¶ School of Pharmacy and Biomolecular Sciences, University of Brighton, UK

Supramolecular engineering of reversible and directional non-covalent forces can lead to long-range ordering in liquid crystalline materials.[1] *Inter alia*, the introduction of metallo-organic functionality, *e.g.*, redox activity, electrical conductivity, coloration and anisotropy is attractive[2], as is a flat molecular topology for discotic ordering *via* π-stacking interactions.[3]



The preparation and characterisation of hybrid quinoxaline-pyridine ligand systems bearing long-chain alkyl ether groups and their self-assembled, flat dicopper(I) complexes will be discussed.[4] Helically chiral/*meso* stereoisomerism is examined using dynamic NMR spectroscopic methods and semi-empirical calculations on related compounds.

[1] Gulik-Krzywicki, T.; Fouquey, C.; Lehn, J.-M. *Proc. Natl. Acad. Sci. USA* **1993**, *90*, 163.
[2] Even, M.; Heinrich, B.; Guillon, D.; Guldi, D. M.; Prato, M.; Deschenaux, R. *Chem., Eur. J.* **2001**, *7*, 2595; Tschierske, C. *Angew. Chem.-Int. Ed.* **2000**, *39*, 2454; El-ghayoury, A.; Douce, L.; Skoulios, A.; Ziessel, R. *Angew. Chem.-Int. Edit.* **1998**, *37*, 2205.
[3] Farges, J.-P. in *Organic Conductors -Fundamentals and Applications;* Hermann, A.M., Ed.; Marcel Dekker: New York,1994.
[4] Heirtzler, F.; Neuberger, M.; Kulike, K. *J. Chem. Soc., Perkin Trans. 1* **2002**, 809; Dias, S. I. G.; Heirtzler, F. *submitted*, **2003**.

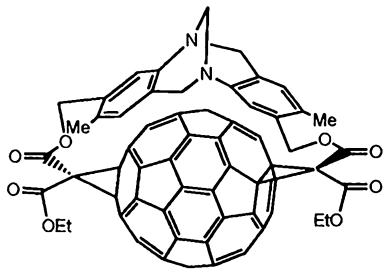
Organic Chemistry **206**

Targeting Inherently Chiral *trans*-2 and *trans*-3 Addukts of C_{60} with *Tröger*'s Base Derivatives

Sergey Sergeyev, François Diederich

ETH Hönggerberg, 8093 Zürich, Switzerland

Tether-directed remote functionalization has been successfully used for the regio- and stereoselective preparation of bis- to hexakis-adducts of buckminsterfullerene C_{60} [1]. In particular, optically active *cis*-3 derivatives have been synthesized stereospecifically by using chiral tethers [2].



However, targeting the inherently chiral C_2-symmetrical *trans*-2 or *trans*-3 adducts with the addends in the opposite hemispheres of C_{60} by this strategy remains unknown. The main challenge is finding a large but conformationally constrained chiral tether. We have used tethered malonates derived from *Tröger*'s base to synthesize new derivatives of C_{60} with excellent regioselectivity by double *Bingel* reaction.

[1] F. Diederich, R. Kessinger, *Acc. Chem. Res.* **1999**, *32*, 537.
[2] R. Kessinger, C. Thilgen, T. Mordasini, F. Diederich, *Helv. Chim. Acta* **2000**, *83*, 3069.

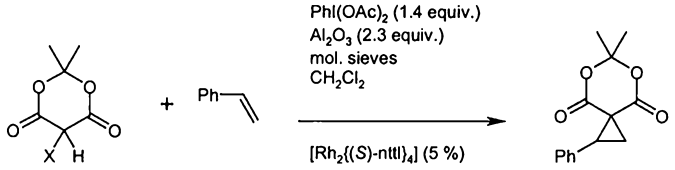
Organic Chemistry **207**

Asymmetric Cyclopropanation of Olefins using a New *in* situ Generated Phenyliodonium Ylide

Paul Müller*, and Ashraf Ghanem

Department of Organic Chemistry, University of Geneva, 30 Quai Ernest Ansermet, CH-1211 Geneva 4, Switzerland

The reaction of diazo compounds with transition metal catalysts affords a metallocarbene which may be transferred to an appropriate substrate. A large number of chiral non-racemic catalysts are available to effect enantioselective carbene transfer. Phenyliodonium ylides react with Rh(II)- or Cu(I)-catalysts to afford the same metallocarbene intermediates and, ultimately, the same products as the corresponding diazo compounds.[1]
We have developed a user-friendly one-pot procedure for olefin cyclopropanation using Meldrum'sacid (**1**) and $PhI(OAc)_2$ for *in* situ generation and decomposition of the ylide **2**.[2] The reaction proceeds well with 5 mol% of catalyst and a 10-fold excess of olefin. The system is compatible with chiral Rh(II)-catalysts. The enantioselectivity for cyclopropanation of styrene with $[Rh_2\{(S)\text{-nttl}\}_4]$ is identical to that obtained with isolated ylide **2**.



(1) P. Müller, C. Boléa, *Helv. Chim. Acta* **2002**, *85*, 483.
(2) P. Müller, Y. Allenbach, E. Robert, *Tetrahedron: Asymmetry* **2003**, *14*, 779.

Organic Chemistry **208**

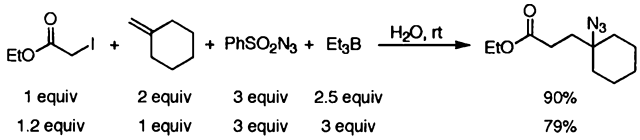
Tin-Free Radical Carboazidation

Philippe Panchaud and Philippe Renaud*

Departement für Chemie und Biochemie, Universität Bern

Freiestrasse 3, 3012 Bern, Switzerland

Recently, we reported a useful procedure for the formation of both C-N and C-C bonds in a single step and its application towards straightforward syntheses of lactams [1,2]. The most efficient version of this procedure uses hexabutylditin as chain transfer reagent. Despite their interesting and well-suited properties for radical chemistry, tin derivatives are not used in the industry since they are very toxic and difficult to remove from the final products. We report here that triethylborane can attractively substitute hexabutylditin.



This tin-free procedure is not only environmentally friendly but it also provides the possibility of running the reaction with an excess of either the alkene or the radical precursor.

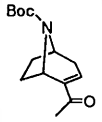
[1] P. Renaud, C. Ollivier and P. Panchaud, *Angew. Chem. Int. Ed.* **2002**, *41*, 3460.
[2] P. Renaud, P. Panchaud and S. Zigmantas, *submitted for publication.*

Organic Chemistry **209**

Total Synthesis of (+)-Ferruginine

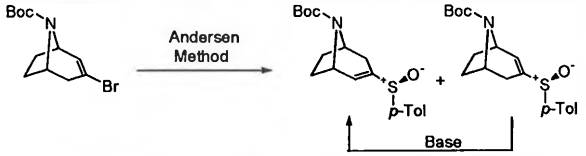
Riccardo Piccardi and Philippe Renaud*
Departement für Chemie und Biochemie, Universität Bern
Freiestrasse 3, 3012 Bern, Switzerland

The tropane alkaloid (+)-ferrugininc has been isolated in 1979 from *Darlingiana Darlingiana* and *Darlingiana Ferruginea* [1, 2]. We report here a concise synthesis of this alkaloid. The key intermediate vinylsulfoxide is



(+)-Ferruginine

readily synthesized in optically pure form *via* the Andersen method. The two different diasteroisomers are easily separated by flash chromatography and the undesired diasteroisomer can be isomerised. Conversion of the α,β-



unsaturated sulfoxide to the (+)-ferruginine was achieved in 6 steps and 4 purifications.

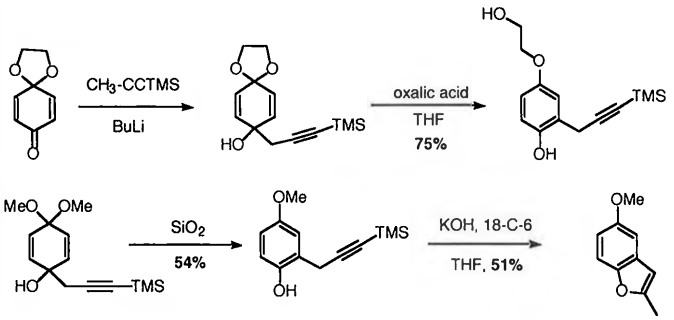
[1] Bick, I. R. C.; Gillard, J.W.; Leow, H.-M. *Aust. J. Chem.* **1979**, *32*, 2537
[2] Bick, I. R. C.; Gillard, J.W.; Leow, H.-M. *Aust. J. Chem.* **1979**, *32*, 2523

Organic Chemistry **210**

Acid-Catalyzed Rearrangement of 4,4-Dialkoxy-1-propargylcyclohexa-2,5-dien-1-ol

Xavier J. Salom-Roig and Philippe Renaud*
Departement für Chemie und Biochemie, Universität Bern
Freiestrasse 3, 3012 Bern, Switzerland

We report here the acid-catalyzed [1,2] migration of propargylic substituents starting from 4,4-dialkoxy-1-propargylcyclohexa-2,5-dien-1-ol. The precursors are easily available via nucleophilic propargylation of 1,4-benzoquinone monoacetals. The mechanism of this rearrangement will be discussed. This procedure can be applyed to the synthesis of substituted benzofurans.



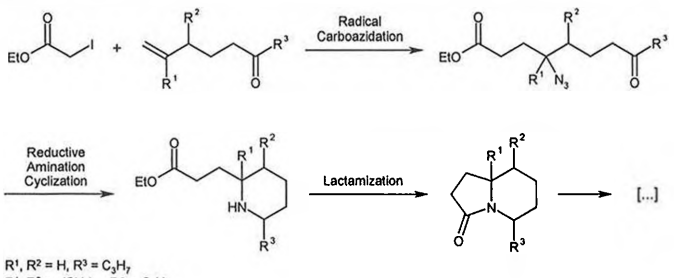
Organic Chemistry **211**

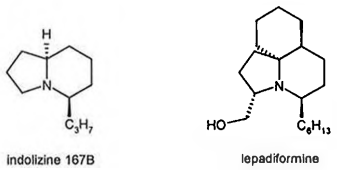
A Short Route to Bi- and Tricyclic Alkaloids

Pascal Schär, Philippe Panchaud and Philippe Renaud*

Universität Bern, Departement für Chemie und Biochemie,
Freiestr. 3, 3012 Bern, Switzerland

Recently, we reported about the radical carboazidation as an efficient tool for the preparation of pyrrolidinone derivatives.[1] Herein we would like to present more examples, where this type of reaction has led to a quick access to the core of alkaloids such as indolizine 167B and lepadiformine.





indolizine 167B lepadiformine

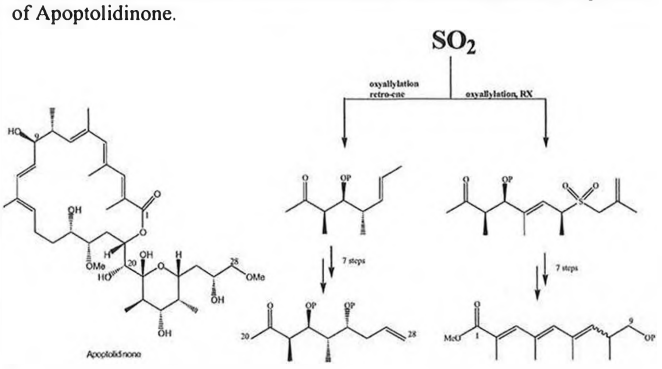
[1] P. Renaud, C. Ollivier, P. Panchaud, *Angew. Chem. Int. Ed.* **2002**, *41*, 3460.

Organic Chemistry **212**

Towards the Synthesis of Apoptolidinone Applying SO_2 Chemistry

Cotinica Craita, Laure Bouchez and Pierre Vogel*
ICMB, EPFL, CH-1015 Lausanne-Dorigny, Switzerland

Here we present a new approach to synthesize the trienic subunit (C_1-C_9) and the fragment C_{20}-C_{28} of Apoptolidinone, the aglycon of Apoptolidin. Apotolidin [1] is a natural product isolated from *Nocardiopsis sp.*, which is capable to induce selectively the apoptosis in tumor cells.
Our strategy is based on the oxyallylation and retro-ene reactions developed in our group [2]. In the presence of a Lewis acid, 1-alkoxy-1,3-dienes can be combined with enoxysilane and sulphur dioxide to generate silyl sulfinate, which could be further transformed either into sulfone or into alkene by retro-ene elimination. Those two building blocks could be afterwards transformed into the corresponding fragments of Apoptolidinone.



[1] K.C. Nicolaou, Y. Li, K. Fylaktakidou, H. Mitchell, H.X Wei, B. Weyershausen, *Angew. Chem. Int. Ed.* **2001**, *40*, 3849.
[2] V. Narkevitch, S. Megevand, K. Schenk, P.Vogel, *J.Org.Chem.* **2001**, *66*, 5080; X.Huang, C. Craita, P.Vogel, unpublished results.

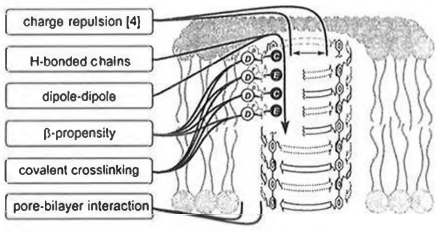
Organic Chemistry **213**

Stabilizing Multifunctional Pores Formed by Rigid-Rod β-Barrels

Florent Perret, Benoît Lambert, Svetlana Litvinchuk, Masamichi Nishihara and Stefan Matile*

University of Geneva, Department of Organic Chemistry
1211 Geneva, Switzerland

Usefulness of synthetic multifunctional pores (SMPs) formed by rigid-rod β-barrels as supramolecular hosts [1], sensors [2] and catalysts [3] is verified experimentally. Current limitations in these applications originate chiefly from the lack of general design strategies for the construction of SMPs with both large interior and high stability. Ongoing studies to overcome this obstacle focus on contributions from amino-acid residues located either at the outer (*B, D, F*) or inner (*C, E*) barrel surface.



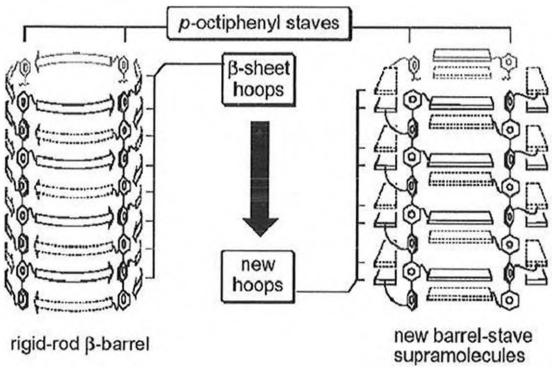
[1] Baudry, Y.; Baumeister, B.; Das, G.; Gerard, D.; Matile, S.; Sakai, N.; Som, A.; Sordé, N.; Talukdar, P. *Chimia* **2002**, *56*, 667.
[2] Das, G.; Talukdar, P.; Matile, S. *Science* **2002**, *298*, 1600.
[3] Sakai, N.; Sordé, N.; Matile, S. *J. Am. Chem. Soc.*, in press.
[4] Baumeister, B.; Som, A.; Das, G.; Sakai, N.; Vilbois, F.; Gerard, D.; Shahi, S. P.; Matile, S. *Helv. Chim. Acta* **2002**, *85*, 2740.

Organic Chemistry **214**

Beyond Rigid-Rod ß-Barrels

Maxim Peretolchin, Yoann Baudry, Dawn Ronan, Muhammad Raza Shah, Pinaki Talukdar and Stefan Matile*
University of Geneva, Department of Organic Chemistry
1211 Geneva, Switzerland

Rigid-rod ß-barrels are barrel-stave supramolecules constructed from *p*-octiphenyl staves and ß-sheet hoops [1]. Their satisfactory multifunctionality stimulated design and synthesis of barrel-stave supramolecules with new rigid-rod staves (not shown) and new hoops (below) to obtain access to new functions. The already completed introduction of push-pull staves to synthesize push-pull ß-barrels that recognize polarized bilayer membranes may exemplify this approach [2,3], studies focusing on other staves and hoops are in progress.



[1] Baudry, Y.; Baumeister, B.; Das, G.; Gerard, D.; Matile, S.; Sakai, N.; Som, A.; Sordé, N.; Talukdar, P. *Chimia* **2002**, *56*, 667.
[2] Sakai, N.; Houdebert, D.; Matile, S. *Chem. Eur. J.* **2003**, *9*, 223.
[3] Sakai, N.; Matile, S. *J. Am. Chem. Soc.* **2002**, *124*, 1184.

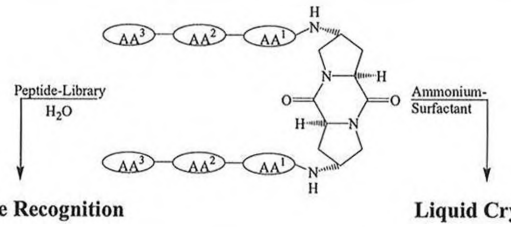
Organic Chemistry **215**

From Aqueous Peptide Receptors to Liquid Crystals

Philipp Krattiger,[a] Charl FJ Faul,[b] Markus Antonietti,[b] Helma Wennemers[a]*

[a] Department of Chemistry, University of Basel, St. Johanns-Ring 19, CH-4056 Basel, Switzerland;
[b] Max Planck Institute for Colloids and Interfaces, D-14424 Potsdam, Germany

We have recently developed the class of two-armed diketopiperazine-receptors that bind short peptides with high selectivity in chloroform.[1] We now show that the same class of receptors is also able to recognize tripeptides in water when polar amino acids are used in the receptor-arms.



The binding selectivities can be modified by complexing the receptors with ammonium surfactants. Interestingly, some of these receptor-surfactant-complexes exhibit liquid-crystalline behaviour.[2]
We will present the results of the binding studies and affinity measurements as well as the properties and x-ray data of the liquid-crystalline materials.

[1] a) H. Wennemers, M. Conza, M. Nold, P. Krattiger, *Chem. Eur. J.* **2001**, *7*, 3342, b) M. Conza, H. Wennemers, *J. Org. Chem.* **2002**, *67*, 2696.
[2] P. Krattiger, C. FJ Faul, M. Antonietti, H. Wennemers, *in preparation*.

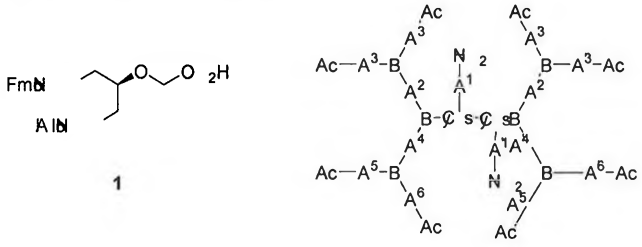
Organic Chemistry **216**

New Catalytic Peptide Dendrimers form an Asymmetric Dendron Extension Strategy

Anthony Clouet, J.-L. Reymond*

University of Bern, Freiestrasse 3,CH-3012 Bern

Rational *de novo* enzyme design, which is one of the main goals of supramolecular chemistry and biochemistry, would require a complete understanding of both protein folding and enzyme catalysis. Our appraoch to *de novo* enzyme design is based on peptide dendrimers incorporating three variable aminoacid positions linked by two diaminoacid linking units. This strategy gives rapid acceses to protein-like globular structures by SPPS, which display enzyme-like catalytic properties.[1] Herein we report the synthesis of asymmetric diaminoacid building block **1**, leading to the dendrimers with differentiated layers as shown.



The synthesis and evaluation of a family of catalytic dendrimers using asymmetrically functionalized layers will be discussed. In particular, these dendrimers exhibits competitive inhibition from transition state analog derivatives.

[1] A. Esposito *et al.*, *Angew. Chem. Int. Ed.* **2003**, *42*, 1381.

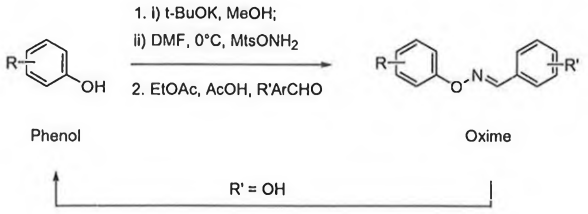
Organic Chemistry **217**

Protease Inhibitors from an Oxime Oligomer Library

Olivier Renaudet, J.-L. Reymond*

University of Bern, Freiestrasse 3,CH-3012 Bern

The exploration of chemical diversity in organic molecules both synthetic and from nature drives drug discovery. Diversity-oriented synthetic strategies focus mostly on di- and multi-component reactions as well as on scaffold assembly from diverse building blocks.[1] Surprisingly, the linear iterative assembly of building blocks as found in peptides has been almost exclusively used to make peptide-like products, all of which contain amide-type bonds which are problematic for their properties. In the present paper we have looked at applying this diversification strategy to assemble new drug-like molecules. We have used the oxime linkage, which is easily formed, to assemble oxime oligomers from a limited set of building blocks. The strategy is validated by the discovery of micromolar protease inhibitors.



[1] a) S. L. Schreiber, *Science*, **2000**, *287*, 1964; b) L. Weber, *Drug Discov. Today*, **2002**, *7*, 143.

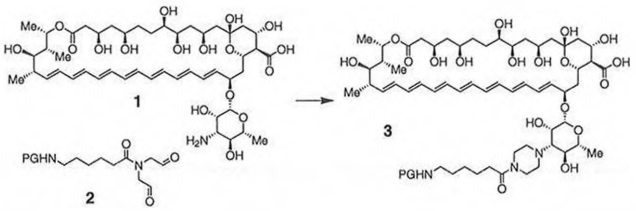
Organic Chemistry **218**

Amphotericin B Conjugates with Preserved Amine Functionality

Andreas Zumbühl, Erick M. Carreira*

ETH Zürich, Wolfgang-Pauli-Strasse, 8093 Zürich

Amphotericin B **1** is an important drug for the treatment of serious systemic fungal infections. Even after 5 decades of research the exact mechanism of action remains unknown [1]. An efficient synthesis of amphotericin B conjugates would allow for the preparation of useful tools for probing this mechanism as well as the creation of molecules with interesting properties.



Our novel bisaldehyde linker **2** readily undergoes double reductive amination with the primary amine of amphotericin B in good yields. Thus we provide a solution to the notorious problem of double alkylation [2] and we also present an amphotericin B conjugate **3** with preserved amine functionality on the mycosamine part. After deprotection the conjugate **3** can be condensed with different reporter groups.

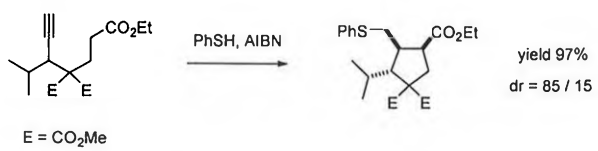
[1] J. Bolard, *Biochim. Biophys. Acta*, **1986**, *864*, 257.
[2] J.-P. Salvi, N. Walchshofer, J. Paris, *Tetrahedron Lett.*, **1994**, *35*, 1181.

Organic Chemistry **219**

Tin-Free Radical Chemistry: Thiophenol Mediated 1,5-Hydrogen Abstraction

Fabrice Dénès, Florent Beaufils, and Philippe Renaud
Departement für Chemie und Biochemie, Universität Bern
Freiestrasse 3, 3012 Bern, Switzerland

Vinylic radicals are know to undergo 1,5-hydrogen shift followed by a 5-*exo*-trig cyclization [1]. In the course of our studies on the diastereoselectivity of this translocation, we were interested in the development of a tin-free procedure to generate the desired vinylic radical. To the best of our knowledge, only one example of thiophenol mediated 1,5-hydrogen abstraction followed by cyclization on the alkenyl moiety has been reported, and in this case the translocation furnished a strongly stabilized radical [2]. We demonstrate here that this procedure is general and often superior to tin hydride mediated reactions. Highly diastereoselective 1,5-hydrogen abstraction have been performed.



1] Feray, L.; Kuznetkov, N.; Renaud, P. in *Radicals in Organic Synthesis*, Renaud, P.; Sibi, M. P. Ed., Wiley-VCH, **2001**, Vol. 2, p. 246.
[2] Burke, S. D.; Jung, K. W. *Tetrahedron Lett.* 1994, 35, 5837.

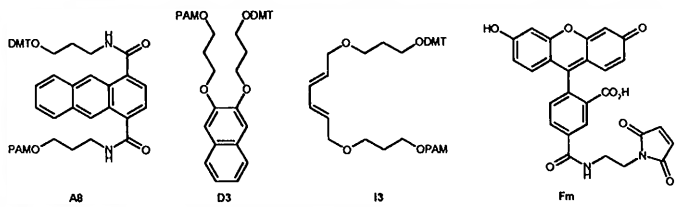
Organic Chemistry **220**

Melting Studies on Diene-Modified Oligonucleotides and their *Diels-Alder* Bioconjugates

Rolf Tona, Robert Häner

University of Bern, Freiestrasse 3, 3012 Bern, Switzerland

Three different diene-building blocks (**A8**, **D3** and **I3**) for automated DNA-Synthesis have been synthesized and successfully incorporated into DNA-Oligonucleotides. These diene-modified oligonucleotides undergo *Diels-Alder* cycloadditions with maleimide-derived dienophiles under very mild conditions.



We used fluoresceine maleimide (**Fm**) for the postsynthetic bioconjugation of our diene-modified oligonucleotides to study the reactivity of the dienes. Furthermore, the influence of the diene-modifications and the *Diels-Alder* bioconjugates on DNA duplex stability was studied by comparison of their melting properties with those of the correspondent unmodified oligonucleotides.

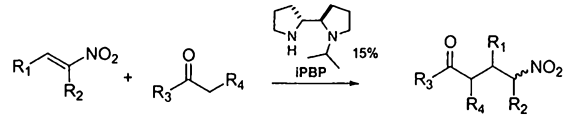
Organic Chemistry **221**

Asymmetric Michael addition catalyzed by N-*i*Pr-2,2'-bipyrrolidine Application in the synthesis of (+) or (-)-Botryodiplodin

Olivier Andrey, Annick Vidonne, Alexandre Alexakis*

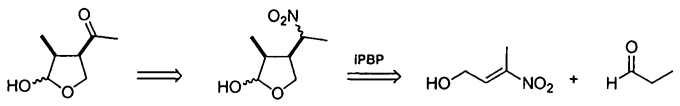
University of Geneva, Quai Ernest Ansermet 30, CH-1211 Geneva

Chiral pyrrolidine derivatives such N-*i*Pr-2,2'-bipyrrolidine **iPBP** catalyze the asymmetric Michael addition of aldehydes or ketones to nitroolefins [1]. The intermediate involved in this reaction is a reactive *in situ* formed enamine obtained from the pyrrolidine moiety and the aldehyde or the ketone. Very high enantioselectivities have been obtained depending of the nitroolefin and the carbonyl compound.



R_1 = aryl or alkyl, R_2 = H or alkyl; R_3 = H or alkyl, R_4 = H, OH or alkyl; dr: up to 95:5, ee: up to 98.5%

This methodology could be applied for the synthesis of Botryodiplodin, a metabolite of *Penicillium roqueforti* which exhibits antibiotic activity. Our retrosynthetic analysis has converged to the addition of propionaldehyde to nitroolefin **1** which could give the intermediate **2** and then the desired Botrodiplodin. This synthesis is actually in development in our laboratory.



Botryodiplodin 2 1

[1] Alexakis, A. ; Andrey, O. *Org. Lett.* **2002**, *4*, 3611.

Organic Chemistry **222**

Oxazoline-imidazolin-2-ylidene Iridium Complexes: Enantioselective Hydrogenation of Unfunctionalized Olefins

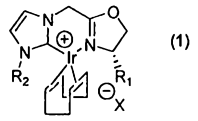
Steve Nanchen and Andreas Pfaltz*

University of Basel, Department of Chemistry, St-Johanns-Ring 19
CH-4056 Basel, Switzerland

Cationic iridium complexes of P,N-ligands have been shown to be efficient homogenous catalysts for the hydrogenation of unfunctionalized olefins. Many variations of the phosphinooxazoline (PHOX) ligand have given rise to a library of catalysts with high activity and enantioselectivity for a large range of alkenes.[1]

Recently, analogues of P,N ligands, where the phosphorus is replaced by a N-heterocyclic carbene have been developed.[2],[3] This new class of ligands, which are versatile and easily accessible, shows interesting catalytic activity in olefin hydrogenations.[3]

Oxazoline-imidazoline-2-ylidene iridium complexes (1) and related structure have been tested for catalytic efficacy. To get a better understanding of these new systems, structural data have been investigated.



(1)

[1] Pfaltz, Andreas; Blankenstein, Joerg; Hilgraf, Robert; Hoermann, Esther; McIntyre, Steven; Menges, Frederik; Schoenleber, Marc; Smidt, Sebastian; Wuestenberg, Bettina; Zimmermann, Nicole; *Adv. Synth. Catal.*; **2003**; *345*(1+2); 33-44.
[2] Herrmann, W. A.; Goossen, L. J.; Spiegler, M.; *Organometallics;* **1998**; *17*(11), 2162-2168.
[3] Perry, M. C.; Powell, M. T.; Cui, X.; Hou, D.-R.; Reibenspies, J. H.; Burgess, K.; *J. Am. Chem. Soc.;* **2003**; *125*(1), 113-123.

Organic Chemistry **223**

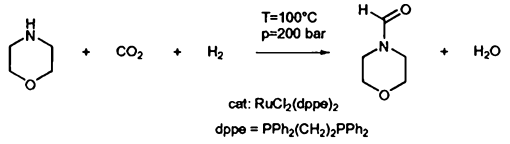
Formylation with Compressed CO_2: Highly Efficient Catalytic Synthesis of *N*-Formylmorpholine

Michael S. Schneider, Leo Schmid, Alfons Baiker

Institute for Chemical and Bioengineering,
ETH Hönggerberg, CH-8093 Zürich

Carbon dioxide fixation has gained considerable attention due to environmental considerations and its large-scale availability at low cost [1]. Replacement of environmentally harmful C_1-building units used in chemical synthesis by non-toxic and easy to handle CO_2 represents an interesting challenge for green chemistry.

We show that formylation of morpholine in compressed CO_2 using a bidentate ruthenium catalyst $RuCl2(dppe)_2$, which has been applied recently in the synthesis of *N,N*-dimethylformamide [2], affords very high *N*-formylmorpholine production rate at almost 100% selectivity. *N*-formylmorpholine is used in large scale amounts in industry for BTX extraction [3].



Video monitoring studies of the reaction mixture during reaction revealed a complex multiphase system including formation of solid carbamate, which strongly influenced the efficiency of the reaction. In-situ infrared spectroscopy gave additional information to unravel the changes in number and composition of the phases.

[1] A. Baiker, Appl. Organometal. Chem., 2000, 14, 751.
[2] O. Kröcher, R.A. Köppel, A. Baiker, Chimia, 1997, 51, 48.
[3] E. Cinelli, S. Noe, G. Paret, Hydrocarbon Process., 1972, 51(4), 141.

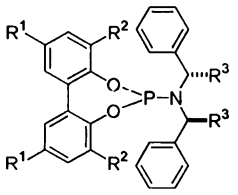
Organic chemistry **224**

Improved Biphenol Phosphoramidite Ligands for the Enantioselective Copper-Catalyzed Conjugate Addition of Dialkyl zincs

Damien Polet, Alexandre Alexakis

Department of Organic Chemistry
University of Geneva, 30 quai Ernest Ansermet, CH-1211 Genève 4,
Switzerland

Phosphoramidite ligands have proved to give high enantioselectivities in copper-catalyzed 1,4-addition of dialkylzinc on a variety of Michael acceptors.[1] In particular biphenol-based ligands such as **L1** seem to be particulary interesting due to their induced atropoisomerism and the possiblity to optimize their structure.[1][2]



L1

This work reports the structural changes in the biphenol core of the ligand (R^1 and R^2), and the influence in enantioselectivity in 1,4-addition. The best ee's reported were obtained for acyclic nitro-olefins.

[1] Alexakis, A.; Benhaim, C. *Eur. J. Org. Chem.* **2002**, 3221-3236.
[2] Alexakis, A.; Rosset, S.; Allamand, J.; March, S.; Guillen, F.; Benhaim, C. *Synlett* **2001**, *9*, 1375-1378.
[3] Alexakis, A.; Benhaim, C.; Rosset, S.; Humam, M. *J. Am. Chem. Soc.* **2002**, *124*, 5262-5263.

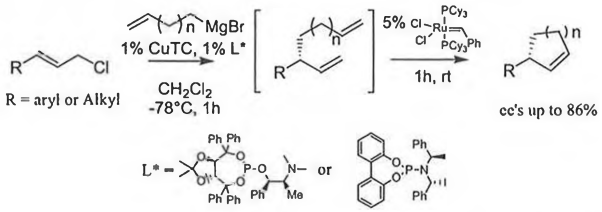
Organic chemistry **225**

Tandem Copper-Catalyzed Enantioselective Allylation-Metathesis

Karine Croset, Alexandre Alexakis

Departement of Organic Chemistry
University of Geneva, 30 quai Ernest Ansermet, CH-1211 Geneva 4, Switzerland
e-mail: *Alexandre.Alexakis@chiorg.unige.ch*

The allylic substitution reaction is a useful organic transformation, if the regio-, stereo- and chemoselectivities could be controlled. This control is usually provided by the type of metal catalyst, by the nucleophile and by the leaving group. We have show that Grignard reagent can afford high enantioselectivity with aryl and alkyl substituted allylic chloride.[1][2]



All the above allylic substitution reactions end up with a terminal vinyl group. This group is usually further transformed in a second step, by cleavage of the double bond or hydroborated and oxidized. Another possibility not yet explored, is the metathesis reaction, particularly if the whole procedure is performed in the same pot. Both intermolecular and intramolecular version were completed without loss of optical purity.[2]

[1] Alexakis, A.; Malan, C.; Lea, L.; Benhaim, C.; Fournioux, X. *Synlett* **2001**, 927.
[2] Alexakis, A.; Croset, K. *Org. Lett.* **2002**, *4*, 4147-4149.

Organic chemistry **226**

Thermodynamic study of a biphenol-based phosphoramidite ligand; link to its applications in asymmetric catalysis

Damien Polet,[1] Clémence Corminboeuf,[2] Jean-François Fuchs,[1] Alfredo Vargas,[2] Jiri Mareda,[1] Jacques Weber,[2] Alexandre Alexakis[1]

[1]Department of Organic Chemistry
[2]Department of Physical Chemistry
University of Geneva, 30 quai Ernest Ansermet, CH-1211 Genève 4, Switzerland

Phosphoramidite ligands with strong ?-accepting properties have been found to be really efficient in terms of regio- and enantioselectivity in 1,4-addition and allylic substitution. In particular biphenol-based ligands of **L1** type seem to be particulary interesting due to their low cost and their induced atropoisomerism.[1][2]

L1

The present work reports a thermodynamic study based on circular dichroism and DFT calculations. The relative stability and the rotation barrier between the two conformers of ligand **L1** have been evaluated in attempt to define a link between efficiency in two organic reactions (1,4-addition and Ir-catalyzed allylic amination) and thermodynamic data. The chameleon-like properties of **L1** is shown, knowing that one conformation of the biphenol reacts in 1,4-addition, whereas the other one seems to be preferred in allylic amination.

[1] Alexakis, A.; Rosset, S.; Allamand, J.; March, S.; Guillen, F.; Benhaim, C. *Synlett* **2001**, *9*, 1375-1378.
[2] Alexakis, A.; Benhaim, C.; Rosset, S.; Humam, M. *J. Am. Chem. Soc.* **2002**, *124*, 5262-5263.

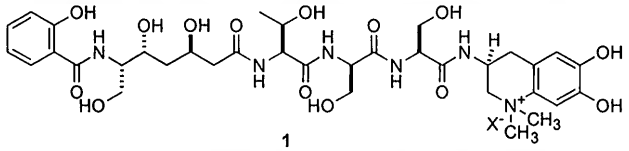
Organic Chemistry **227**

The Total Synthesis of Anachelin H

Yann Bethuel and Karl Gademann*

Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule Zürich, ETH Hönggerberg, CH-8093 Zürich

Iron is an essential nutrient for virtually all forms of life. To overcome its extreme insolubility, many microbes synthesize and excrete powerful iron-selective chelating agents, so-called *siderophores*.
Anachelin H (**1**) was recently isolated from the cyanobacterium *Anabaena cylindrica* and postulated to serve as siderophore.[1] However, both its constitution and the relative and absolute configuration of four stereogenic centers remain unknown as well as its mechanism of action. This provides the classic stimulus for the total synthesis of this natural product.



1

The starting materials in our convergent route are commercially available amino acids like serine, threonine and *L*-DOPA as well as 2,2,6-trimethyl-[1,3]dioxin-4-one. Key steps of our synthesis include the vinylogous *Mukayama*-aldol reaction of the latter to obtain the ε-amino acid, the preparation of the tetrahydroquinoline ring from *L*-DOPA in a short sequence and the selective quaternization of the cyclic *N*-atom.

[1] H. Beiderbeck, K. Taraz, H. Budzikiewicz, A. E. Walsby, *Z. Naturforsch.* **2000**, 55c, 681-687; Y. Itou, S. Okada, M. Murakami, *Tetrahedron* **2001**, 57, 9093-9099.

Organic Chemistry **228**

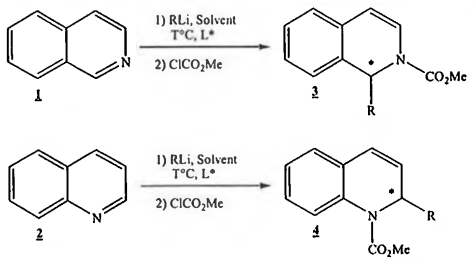
Enantioselective Addition of Organolithium reagents on aza-aromatics

Alexandre Alexakis*, Franck Amiot, Laure Cointeaux

Department of Organic Chemistry, University of Geneva, 30, quai Ernest Ansermet CH-1211 Geneve 4, Switzerland

In nature, alcaloids are of important interest because of their biological and pharmaceutical properties. Then, a large number of methods for the preparation of amine compounds have been described in literature.
Previous work proved that 1,2-dihydro- or 1,4-tetrahydroisoquinoline and 1,2-dihydro- or 1,4-tetrahydroquinoline compounds can be synthesized by nucleophilic addition of Grignard reagents, allylsilylethers or allyltins to isoquinoline **1** and quinoline **2** [1]. Hence, in the presence of a chiral ligand, this reaction can give these amines with good enantiomeric excess.

To the best of our knowledge, there is no example of enantioselective addition of an organolithium reagent to aza-aromatics compounds. We report herein our results which allow to prepare optically enriched compounds 1,2-dihydroisoquinoline **3** [2] and 1,2-dihydroquinoline **4**.



[1] a) R. Yamaguchi *et al.*, *J. Org. Chem.*, **1988**, 53, 3507-3512.
b) R. Yamaguchi *et al.*, *Tetrahedron Lett.*, **2002**, 43, 8871-8874.
[2] A. Alexakis, F. Amiot, *Tetrahedron: Asymmetry*, **2002**, *13*, 2117.

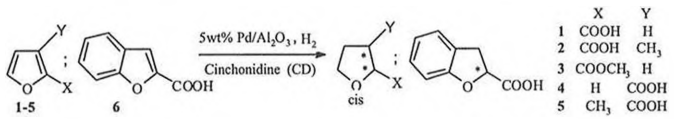
Organic Chemistry **229**

Enantioselective hydrogenation of furan carboxylic acids on cinchona-modified Pd

Mihaela Maris, Thomas Bürgi, Tamas Mallat and Alfons Baiker

Institute for Chemical- and Bioengineering, Swiss Federal Institute of Technology, ETH-Höngerberg HCI, 8093 Zürich, CH

Hydrogenation of aromatic and heteroaromatic compounds is a challenging topic in enantioselective catalysis as most of the reactions are characterized by very poor *ee*'s. Recently, hydrogenation of furan-2-carboxylic acid was attempted with a homogeneous Rh diphosphine catalyst, but only 3% yield and 24% *ee* were obtained in 20 h [1]. Here we show that a heterogeneous catalyst, cinchona-modified Pd, is more active and selective in the enantioselective hydrogenation of furan and benzofuran carboxylic acids.



(*S*)-Tetrahydrofuran-2-carboxylic acid was synthesized in 4 h at r.t. and 30 bar with 95% yield and 32% *ee*. In the hydrogenation of **6** the *ee* went up to 50% at 29% yield.
Hydrogenation of **3**, application of O-methyl-cinchonidine as modifier, and IR measurements revealed that both the quinuclidine N and the OH group of CD are involved in the interaction with the carboxylic group of the reactant during the enantiodifferentiating step on the Pd surface. The mechanistic study has been completed with theoretical calculations.

[1] M. Studer, C. Wedemeyer-Exl, F. Spindler, H.U. Blaser, *Monatsh. Chem.* **2000**, *131*, 1335.

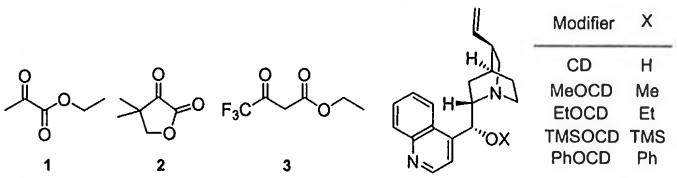
Organic Chemistry **230**

Asymmetric hydrogenation of α–functionalized ketones on Pt/Al_2O_3 modified by ether derivatives of cinchonidine

Simon Diezi, Tamas Mallat, Alfons Baiker*

Institute for Chemical- and Bioengineering, Swiss Federal Institute of Technology, Wolfgang-Pauli-Str. 10, CH-8093 Zürich, Switzerland

The asymmetric hydrogenation of **1-3** was studied on a 5 wt% Pt/Al_2O_3 catalyst in the presence of cinchonidine and some of its O-alkyl derivatives.



In all three hydrogenation reactions, involving a broad range of reaction conditions, the ee decreased with increasing bulkiness of the O-alkyl substituent of CD. When using the bulkiest substituent (PhOCD), sometimes even the opposite enantiomer formed in excess. In the hydrogenation of **2** in toluene at 40 bar CD afforded 79% ee to (*R*)-pantolactone and PhOCD gave 52% ee to (*S*)-pantolactone. Inversion of enantioselectivity with the bulky substituents proved that in the enantiodifferentiating step cinchonidine adsorbs via the quinoline ring lying approximately parallel to the Pt surface. A strong nonlinear effect was observed with cinchonidine – O-phenyl-cinchonidine mixtures, which is attributed to differencies in the adsorption strength and geometry of the modifiers.

Organic Chemistry **231**

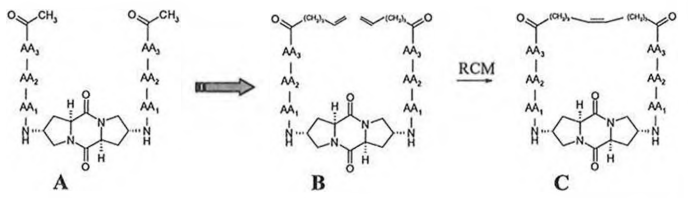
Cyclic Diketopiperazine Receptors via Metathesis

Jessica Grun and Helma Wennemers*

Department of Chemistry, University of Basel, St. Johanns-Ring 19, CH-4056 Basel, Switzerland

Two-armed diketopiperazine receptors of type **A** have proven efficient in binding peptidic substrates as revealed by combinatorial on-bead assays [1]. After this previous work, it was interesting to investigate the influence of cyclisation and thus decreased flexibility on the binding selectivity and affinity properties of the macrocyclized receptors.

For the synthesis of macrocyclic receptors we envisioned a metathesis-reaction for the ring closure. Thus, cyclisation precursors of type **B** were prepared. The metathesis-reaction was realised in the presence of Grubbs catalyst [2] to obtain cyclized diketopiperazine receptors of type **C**.



We will present the synthesis of macrocyclic diketopiperazine receptor as well as their binding properties towards peptides as analyzed in combinatorial on-bead screenings.

[1] (a) H. Wennemers, M. Conza, M. Nold, P. Krattiger, *Chem. Eur. J.*, **2001**, *7*, 3342; (b) M. Conza, H. Wennemers, *J. Org. Chem.*, **2002**, *67*, 2696.
[2] (a) A. Fürstner, K. Langemann, *J. Am. Chem. Soc.*, **1997**, *119*, 9130; (b) S. J. Miller, H. J. Blackwell, R. H. Grubbs, *J. Am. Chem. Soc.*, **1996**, *118*, 9606.

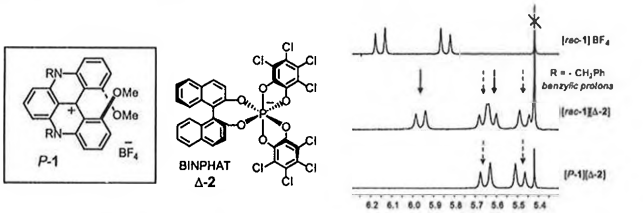
Organic Chemistry **232**

A Highly Configurationally Stable [4]Heterohelicenium Cation.

[a]Christelle Herse, [a]Benoît Laleu, [b]Bo W. Laursen, [a]Jérôme Lacour *

[a]Département de Chimie Organique, Université de Genève, Switzerland
[b]Nano-Science Center, Department of chemistry, Universitetsparken 5, DK-2001 Copenhagen, Denmark

Recently, Laursen and Krebs reported the one-step synthesis of novel cationic dyes of type **1** [1]. We now present results on the resolution and configurational stability of these new cationic [4]helicenium derivatives [2]:



Using hexacoordinated phosphorus-centered BINPHAT anion, an effective resolution procedure was developed affording enantiopure [P-**1**] [Δ-**2**] or [M-**1**] [Λ-**2**] salts. A high barrier to racemization (ΔG =182 kJ/mol) was measured by CSP HPLC and the configuration of **1** was assigned by vibrational circular dichroism.

[1] B.W. Laursen, F.C. Krebs, *Angew. Chem. Int. Ed.* **2000**, *39*, 3432.
[2] C. Herse, D. Bas, F.C. Krebs, T. Bürgi, J. Weber, T. Wesolowski, B.W. Laursen, J. Lacour, *Angew. Chem. Int. Ed.* **2003**, *in press*.
[3] J. Lacour, A. Londez, C. Goujon-Ginglinger, V. Buss, G. Bernardinelli, *Org. Lett.* **2000**, *2*, 4185.

Organic Chemistry **233**

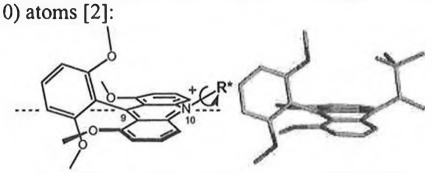
Bent Structure and Stereodynamics of Chiral Acridinium cations.

[a]Benoît Laleu, [a]Christelle Herse, [b]Gérald Bernadinelli, [a]Jérôme Lacour *

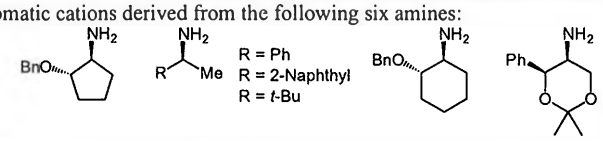
[a]Département de Chimie Organique, Université de Genève, Switzerland

[b]Laboratoire de Cristallographie, Université de Genève, Switzerland

Recently, Laursen and Krebs reported the one-step synthesis of novel acridinium cations by the reaction of primary amines with tris(2,6-dimethoxy)trityl cation [1]. Herein, we show that the introduction of bulky amines leads to (i) a restricted rotation around the C(sp^3)-N(sp^2) bond, (ii) a bending of the aromatic backbone and (iii) "out-of-plane" displacements of C(9) and N(10) atoms [2]:



Variable temperature ^{1}H NMR spectroscopy or X-ray diffraction analyses have allowed the quantification of these phenomena. Rather large differences in barriers to rotation or structural deformations were observed for the aromatic cations derived from the following six amines:



[1] B.W. Laursen, F.C. Krebs, *Angew. Chem. Int. Ed.* **2000**, *39*, 3432.

[2] B. Laleu, C. Herse, B.W. Laursen, G. Bernadinelli, J. Lacour, *J. Org. Chem.* **2003**, *in press*.

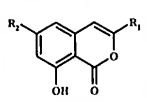
Organic Chemistry **234**

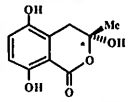
Synthesis of Isocoumarins and 3,4 Dihydroisocoumarins, metabolites of *Ceratocistis fimbriata* sp. fungi

M. Tiouabi and R. Tabacchi
Institut de Chimie, Université de Neuchâtel
51, Avenue de Bellevaux CH-2000 Neuchâtel

Isocoumarins and 3,4 dihydroisocoumarins are important biologically active natural products. They are secondary metabolites of many fungi, bacteria, insects and higher plants and exhibit a wide spectrum of biological activities such as antifungal, antihypertensive, antirheumatic and anticoagulant.
In our investigations on phytotoxins produced by *Ceratocistis fimbriata platani* and *C. f. coffea* fungi responsible for the canker disease of coffee and plane tree, we reported the isolation and structural elucidation by spectroscopic methods of the compounds **a – f** [1, 2], isolated on mg scale.
In order to confirm the phytotoxicity of these natural phytotoxins and to establish the role played by these compounds in the pathogenecity, more specific biotests are necessary. Our objective is the development of an efficient method for the total synthesis of a sufficient amount of these isocoumarins and 3,4 dihydroisocoumarins.

a : R_1= CH_2OH ; R_2= OMe
b : R_1= $CH_2CHOHCH_3$; R_2= OH
c : R_1= CH_2OH ; R_2= OH
d : R_1= Me ; R_2= OMe
e : R_1= Me ; R_2= OH





f

Here, we report the retrosynthetic approach for the total synthesis [3] of these compounds and the synthesis of **d** and **e**.

[1] R. Tabacchi and G. Gremaud, *Phytochem., 42,* **1996**, 1547; G. Gremaud and R. Tabacchi, *Nat. Prod. Lett., 5*, **1994**, 95.
[2] N. Bürki, Thèse, Université de Neuchâtel, **1996**.
[3] C. N. Lewis, J. Staunton, D. C. Sunter, *J. Chem. Soc. Perkin Trans. I*, **1988**, 747.

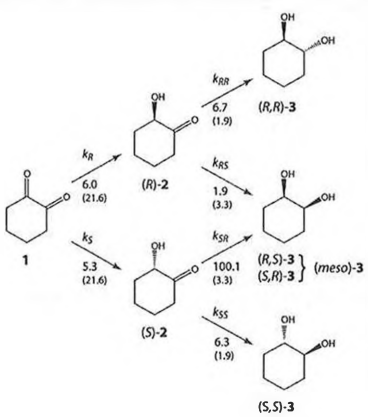
Organic Chemistry **235**

Asymmetric hydrogenation of cyclohexane-1,2-dione over cinchonidine-modified platinum

Otmar J. Sonderegger, Thomas Bürgi, and Alfons Baiker

Institute of Chemical and Bioengineering, ETH Hönggerberg HCI, CH-8093 Zurich, Switzerland

Heterogeneous enantioselective hydrogenation using chirally modified metal catalysts is a promising route for the synthesis of optically pure compounds using a heterogeneous process [1, 2]. The asymmetric hydrogenation of cyclohexane-1,2-dione (**1**) over cinchonidine-modified platinum was investigated. Despite the fact that the first hydrogenation step is close to non-enantioselective, high enantiomeric excess is obtained for the (*R*)-α-hydroxy ketone (**2**) due to kinetic resolution. In the second hydrogenation step one out of the four reactions of the network is substantially accelerated with respect to the others and with respect to the reaction in the absence of modifier, leading to an enantiomeric excess of (1*R*, 2*R*)-*trans*-cyclohexane-1,2-diol (**3**) of over 80%. Comparison with recently reported asymmetric hydrogenation of α-hydroxyethers indicates striking similarities, which hint at alike reactant-modifier interaction in both cases [3].



[1] Y. Orito, S. Imai, S. Niwa, J. *Chem. Soc, Jpn.* **1979**, 1118.
[2] A. Baiker, *J. Mol. Catal. A Chem.* **1997**, *115*, 473.
[3] M. Studer, H.-U.Blaser, S. Burkhardt, *Adv. Synth. Catal.* **2002**, *344*, 511.

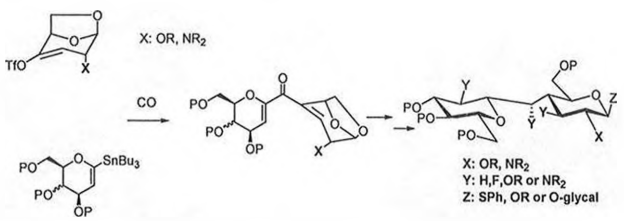
Organic Chemistry **236**

New Approaches towards the Synthesis of *C*-Disaccharides through carbonylative Stille Coupling.

Peter Steunenberg and Pierre Vogel*
Institut de Chimie Moléculaire et Biologique, Ecole Polytechnique Fédérale de Lausanne, BCH, CH-1015 Lausanne-Dorigny, Switzerland

The C-glycoside analogs of O-glycosides have gained interest during the last years through their inherent stability towards hydrolysis. These new compounds are potential inhibitors of glycosyltransferases and glycosidases, [1] which are responsible for the biosynthesis of oligosaccharides, and may become non-hydrolysable mimics of epitopes (artificial vaccines).

Here, we report a new versatile synthetic route for the synthesis of C-disaccharides through carbonylative Stille coupling[2]. The *C*-(1→1) and *C*-(1→4)-disaccharide precursors, formed through coupling, bear cross-conjugated dienone moieties. *C*-dissacharides can then be generated through functionalization of these cross-conjugated dienones. It is also possible to synthesize *C*-dissacharides bearing an amino moiety and fluorinated analogs.



[1] C. Pasquarello, S. Picasso, R. Demange, M. Malissard, E. Berger, P.Vogel. *J. Org. Chem.* **2000**, *65*, 4251
[2] V. Jeanneret, L. Meerpoel, P. Vogel. *Tetrahedron Lett.* **1998**, *38*, 543

CHIMIA 2003, 57, No. 7/8

Organic Chemistry **237**

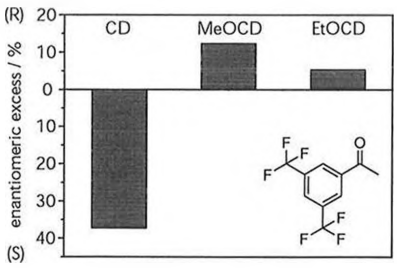
Pt/Cinchona System in the Hydrogenation of Acetophenone Derivatives

R. Hess, T. Mallat and A. Baiker

Institute for Chemical- and Bioengineering, Swiss Federal Institute of Technology, ETH-Hönggerberg, CH-8093 Zurich, Switzerland

Two types of chirally modified metal catalysts are effective in the enantioselective hydrogenation of ketones: the Ni-tartaric acid system for ß-functionalized and unfunctionalized aliphatic ketones, and the Pt-cinchona alkaloid system for α-functionalized (activated) ketones. Here we report the enantioselective hydrogenation of 15 acetophenone derivatives. The results demonstrate the potential of the Pt-cinchona system in the synthesis of chiral aromatic alcohols that are not α-functionalized.

Electron-withdrawing functional groups in the aromatic ring increased the reaction rate and ee compared to those of acetophenone hydrogenation, and the position of the group (o-, m- or p) was also important. 69% ee was obtained in the hydrogenation of 3,5-di-(trifluoromethyl)-acetophenone under ambient conditions after optimization. Addition of cinchonidine (CD) to Pt/Al_2O_3 retarded all hydrogenation reactions - an unusual behaviour for chirally modified Pt.



A mechanistic study revealed that replacing the OH-group of CD by a methoxy- (MeOCD) or ethoxy-group (EtOCD) resulted in the inversion of configuration of the major product (Figure). This behaviour is an indication for two different reaction pathways in which the OH-group and the quinuclidine N of CD, or the latter alone, are involved in the reactant-modifier interaction.

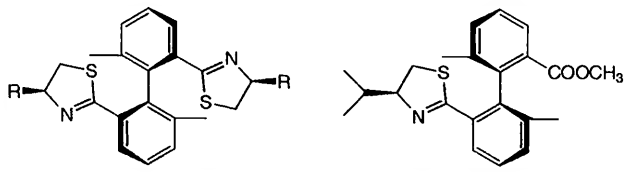
Organic Chemistry **238**

Axially Chiral Mono- and Bis(dihydrothiazoles) as a New Class of Ligands for Catalytic Cyclopropanation

Pierfrancesco Fois, Andreas J. Rippert*

University of Zurich, Winterthurerstr. 190, CH-8057 Zürich, Switzerland

New sulfur-containing ligands have been synthesized, which possess an axially chiral biphenyl as backbone. The chelating moieties of the molecules are constituted either of two dihydrothiazole rings (*N,N* ligands) or of a dihydrooxazole ring and an ester group (*N,O* ligands). The rings bear a chiral bulky substituent at the C(4), which plays a crucial role in the catalytic efficiency of the ligands.



Beside the synthesis of these new ligands, their first applications in asymmetric Cu(I)-catalyzed cyclopropanation reactions are also presented, and their influence on diastereo- and enantioselectivity are reported and discussed.

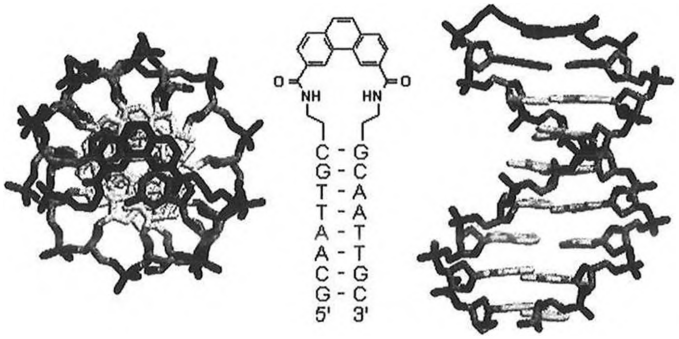
Organic Chemistry **239**

Phenanthrene-derived DNA hairpin mimics

Alfred Stutz, Simon M. Langenegger, and Robert Häner*

Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, CH-3012 Bern. Switzerland

Self-complementary oligodeoxynucleotides containing 3,6-disubstituted phenanthrenes adopt highly stable, hairpin-like structures. The thermodynamic stability of the hairpin mimics depends on the overall length of the phenanthrene building block. Hairpin loops composed of a 3,6-phenanthrene dicarboxamide and ethylene linkers were found to be optimal. The hairpin mimics are more stable than the analogous hairpins containing either a dT_4 or dA_4 tetraloop. Model studies suggest that the thermodynamic stability of the hairpin mimics is primarily due to aromatic stacking of the phenanthrene-3,6-dicarboxamide onto the adjoining base pair of the DNA duplex.



Organic Chemistry **240**

Iterative oxyallylation/retro-ene cascades : a route to 1,3-poyols

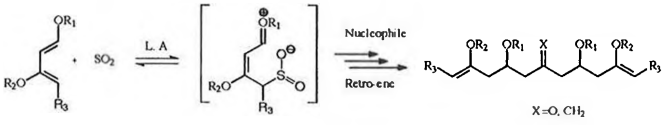
Freddy Fonquerne, Pierre Vogel*

EPFL, Institut de Chimie Moléculaire et Biologique, CH-1015 Lausanne, Switzerland

Polyketides (1,3-polyoxo, 1,3-polyols, aldols) [1] natural products are structurally complex class of compounds. Many of these compounds show important biological activity. A large number of methodologies towards these targets have already been developed. However they require long linear steps and are therefore fastidious.

We wish to report here a rapid and iterative access to 1,3-polyol fragments using a methodology developed in our group [2] based on the quenching of a sultine derived zwitterion intermediate by a suitable nucleophile.

Initial studies of our reaction cascade were carried out with enoxysilanes. This methodology was extended to more elaborated nucleophiles such as bis-allylsilanes giving rise to highly interesting masked 1,3-polyols fragments.



[1] Omura, S.; Tanaka, H. *Macrolide Antibiotics: Chemistry, Biology and Practice; Academic Press, New-York* **1984**, 351.

[2] Narkevitch, V.; Schenk, K.; Vogel, P. *Angew. Chem. Int. Ed.*, **2000**, 39, 1806.

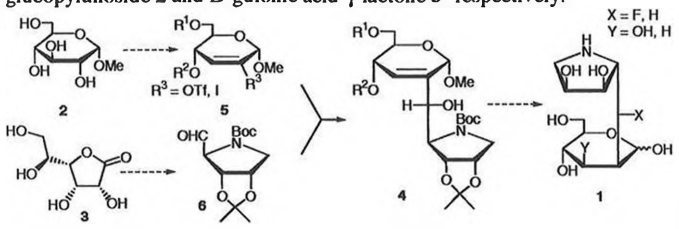
Organic Chemistry **241**

Synthesis of New Glycosidase Inhibitors

Eliazar Rodrfguez-García and Pierre Vogel*

EPFL, Institut de Chimie Moléculaire et Biologique, CH-1015 Lausanne, Switzerland

Nowadays much attention is focused on the synthesis and development of glycosidase inhibitors due to the important role of carbohydrates in biological processes. The chemical and biochemical studies on glycosidase inhibitors may lead to understand the molecular basis of diseases such as diabetes, cancer, AIDS, as well as viral and bacterial-associated diseases, and therefore to their treatment.[1] Our goal is to synthesize a new family of C(1→2)-linked iminodisaccharides **1**, potential inhibitors of glycosidases, starting from the glucose derivative **2** and the γ-lactone **3**. The key step in our approach is the synthesis of **4** by means of the Nozaki-Takai-Hiyama-Kishi coupling[2] between the fragments **5** and **6**. Disaccharide **1** could be synthesized from **4** after carrying out different transformations on the methylene linker and on the double bound, epimerization of C(2) and deprotection. Finally, key building blocks **5** and **6** can be synthesized from methyl-α-D-glucopyranoside **2** and D-gulonic acid-γ-lactone **3**[3] respectively.



[1] (a) Vogel, P. *Chimia* **2000**, *54*, 57. (b) Stütz, A. E. (Ed.): *Iminosugars as Glycosidase Inhibitors: Nojirimycin and Beyond* Wiley-VCH, **1999**.
[2] Navarro, I.; Vogel, P. *Helv. Chim. Acta* **2002**, *85*, 152 and ref. therein.
[3] Fleet, G. W. J.; Son, J. C. *Tetrahedron* **1998**, *44*, 2637.

Organic Chemisry **242**

Raman Optical Activity Measurements - a Tool for the Determination of the Absolute Configuration in Chiral Epoxides

Andreas J. Rippert, Liqiang Li

University of Zurich, Winterthurerstr. 190, CH-8057 Zürich, Switzerland

Jaques Haesler, Werner Hug*

University of Fribourg, Pérolles, CH-1700 Fribourg, Switzerland

The Raman optical activity (ROA) of differently substituted epoxides was measured. The spectra show intriguing similarities in regions characteristic for the epoxide moiety. The interpretation of these characteristc bands in the known epoxides allows to assign the absolute configuration in other epoxides.
The ROA spectra of several epoxides will be presented and the characteristic vibrations will be discussed.

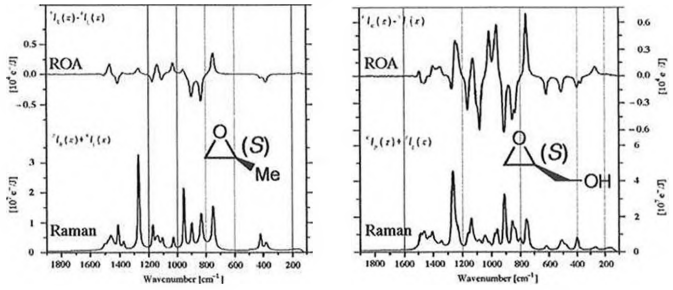


Fig. *Raman and ROA Spectra of* (S)*-Propylene Oxide and* (S)*-Glycidol*

Organic Chemistry **243**

Vibrational Circular Dichroism Measurements of Axially Chiral Biphenyls

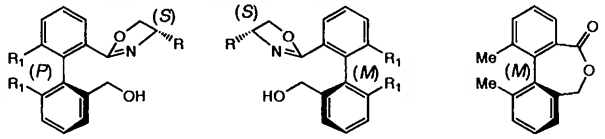
Teresa B. Freedman, Laurence A. Nafie

Syracuse University, 1-014 Center for Science and Technology, 13244-4100 Syracuse, New York, USA

Monica Kalbermatter, Andreas J. Rippert*

University of Zurich, Winterthurerstr. 190, CH-8057 Zürich, Switzerland

Several newly synthesized, axially chiral molecules have been analyzed using vibrational cicular dichroism (VCD). From the derived VCD spectra of the known compounds (*P*)-**1**, (*M*)-**1** and (*M*)-**2** characteristic bands can be assigned to the biphenyl moiety. In our presented poster important vibrations will be outlined and discussed.



(*P*)-**1** (*M*)-**1** (*M*)-**2**

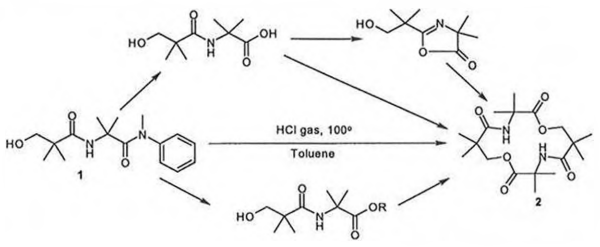
Organic Chemistry **244**

14-Membered Cyclic Depsipeptides by Direct Amide Cyclization

by Boyan Iliev and Heinz Heimgartner

Institute of Organic Chemistry, University of Zurich, Winterthurerstrasse 190, CH-8057 Zurich

The 'direct amide cyclization' method has proved to be an easy synthetic way towards cyclic depsipeptides with potential biological activity [1][2]. When amides of type **1**, obtained easily from of 2*H*-azirin-3-amines and β–hydroxy acids, are subjected to these reaction conditions, an unexpected dimerization occurs, and the 14-membered cyclic depsipeptides of type **2** are obtained and none of the expected 7-membered rings could be detected. Variation of reaction conditions and use of classical lactonization methods lead again to the dimeric structure.



[1] D. Obrecht, H. Heimgartner, *Helv. Chim. Acta* **1984,** *67,* 526.
[2] K. N. Koch, A. Linden, H. Heimgartner, *Tetrahedron* **2001,** *57,* 2311.

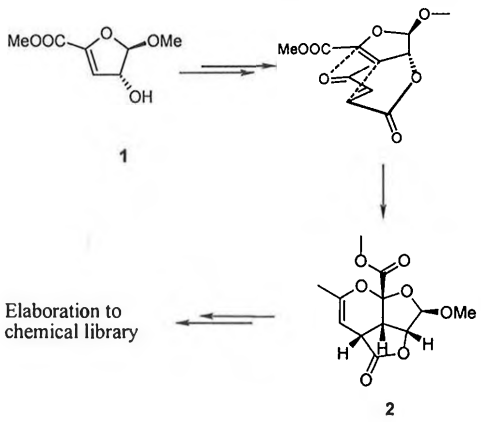
Organic Chemistry **245**

Synthesis of a Natural Product-Like Library

Roland Messer and Robert Häner*

Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, CH-3012 Bern. Switzerland

Tricyclic compounds have been synthesized through an intramolecular Hetero-Diels-Alder cyclisation. Starting point is the dihydrofuranoside **1**. The tricyclic scaffold **2** shows a remarkable structural similarity to a number of natural products containing perhydropyran rings. This led us to explore possibilities of creating combinatorial libraries on the basis of this scaffold. Several ways of derivatisation will be presented. Compounds originating from this diversity oriented synthesis (DOS) approach will be tested for their inhibitory activity in cellular proliferation assays.



Organic Chemistry **246**

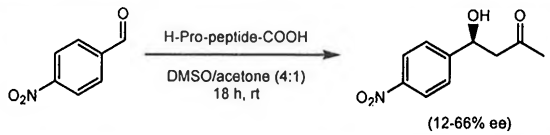
Discovery of new peptide-based catalysts for the direct asymmetric aldol reaction

Jacob Kofoed[1], John Nielsen[2] and Jean-Louis Reymond[1]

[1]Department of Chemistry and Biochemistry, University of Berne, Freiestrasse 3, 3012 Bern, Switzerland

[2]Chemistry Department, The Royal Veterinary and Agricultural University, Thorvaldsensvej 40, 1871 Frederiksberg C, Denmark

Proline is the catalyst of choice for a wide range of aldol-type reactions. Here, we report that peptides containing *N*-terminal proline residues catalyses an aldol reaction between *p*-nitrobenzaldehyde and acetone yielding enantiomeric enriched product. Peptide H-Pro-Glu-Leu-Phe-OH catalyzed the reaction with good activity and moderate enantioselectivity (66% *ee*)[1].



Considered that most modifications on proline, in particular amidation of it's carboxyl side chain[2], are incompatible with catalysis, our discovery opens the way for the preparation of a large family of proline-based aldol catalysts by standard combinatorial peptide synthesis. Such investigations are now in progress.

[1] Kofoed, J., Nielsen, J. Reymond, J.-L. *Bioorg. Med. Chem. Lett.* in press.
[2] List, B., Lerner, R. A., Barbas III, C. F. *J. Am. Chem. Soc.* **2000**, *122*, 2395.

Organic Chemistry **247**

New quaternary alkaloids from the root bark of *Croton cajucara*

Emerson F. Queiroz,[1] Marçal de Queiroz Paulo [2] and Kurt Hostettmann [1]*

[1] Institute of Pharmacognosy and Phytochemistry, University of Lausanne, BEP, CH-1015 Lausanne, Switzerland and [2] Laboratório de Química de Produtos Naturais, Universidade Federal da Paraíba, UFPB, cep 58000, João Pessoa, Paraíba, Brazil.

The aqueous extract of the root bark of *Croton cajucara* (Euphorbiaceae) [1] displays significant radical scavenging activity in a DPPH assay. [2] The crude extract was analysed by LC/UV. LC microfractionation was performed just after LC/UV detection and all peaks collected were submitted to DPPH assay. [3] By this means, radical scavenging activity could be efficiently linked to three of the LC peaks. Information about the nature of the active compounds was provided by LC/UV/MS on-line analysis of the crude extract. The isolation of the active compounds was performed in the first step by centrifugal partition chromatography (CPC). The fractions were monitored by direct DPPH bioautographic assay and active fractions were purified by semi-preparative HPLC. By this means, three new quaternary alkaloids were isolated. The structures of the isolated compounds were elucidated by classical spectroscopic methods including UV, NMR, MS and HR-MS.

[1] M. E. Van Den Berg, In *Plantas Medicinais na Amazônia.* Gráfica Falangola, Bélem, Brazil, **1982**, p.159.
[2] A. Cavin, K. Hostettmann, W. Dyatmyko, O. Potterat, *Planta Med.*, **1998**, *64*, 393-396.
[3] E.F. Queiroz, J.-L. Wolfender, K.K. Atindehou, K. Hostettmann, *J. Chromatogr. A*, **2002**, *974*, 123-134.

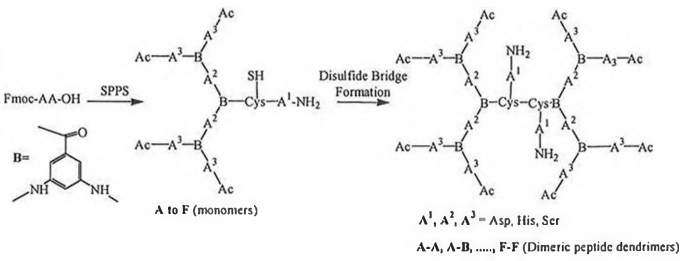
Organic Chemistry **248**

Peptide Dendrimers from 3,5-diaminobenzoic Acid: Synthesis and Esterolytic Activities

Céline Douat-Casassus, Jean-Louis Reymond*

University of Berne Freiestrasse 3 CH-3012 Berne

The aim of *de novo* protein design is to try to mimic the functions of natural enzymes in synthetic assemblies [1]. Recently we published the first synthesis of catalytic peptide dendrimers exhibiting enzyme-like properties for an ester hydrolysis reaction [2]. Herein we present a new family of peptide dendrimers based on 3,5-diaminobenzoic acid as a branching unit. Dendrimers were synthesized by solid phase peptide synthesis following by a disulfide-dimerization strategy. The catalytic triad *Asp, Ser, His* was permutated in each of the 3 positions A^1, A^2 and A^3 resulting in a library of 21 dendrimers.



These dendrimers were screened for esterolytic activities. Two pairs of dendrimers display orthogonal activities on two different classes of ester substrates. Their synthesis, kinetic properties, selectivities, mutagenesis study and structure will be discussed.

[1] Bryson *et al. Science*, **1995**, *270*, 935.
[2] A. Esposito *et al.*, *Angew. Chem. Int. Ed.* **2003**, *42*, 1381

Organic Chemistry **249**

Methylpyrrole tropane alkaloids from the bark of *Erythroxylum vacciniifolium*

B. Zanolari, D. Guilet, A. Marston, E. F. Queiroz and K. Hostettmann*

Institut de Pharmacognosie et Phytochimie, Université de Lausanne, BEP, CH-1015 Lausanne, SWITZERLAND

Nine new tropane alkaloids substituted by a methylpyrrole moiety were isolated from the bark of *Erythroxylum vacciniifolium* Mart. (Erythroxylaceae), a Brazilian endemic plant used in traditional medicine and locally known as *catuaba*.[1] Previous studies reported the isolation and identification of eleven tropane alkaloids (catuabines A to G) from *E. vacciniifolium*.[2, 3] After a dereplication of the alkaloid extract of this species with LC-hyphenated techniques,[4] the isolation and structural characterization of putative new tropane alkaloids was carried out. All compounds were elucidated as tropane-diol or -triol alkaloids esterified by at least one 1-methyl-1*H*-pyrrole-2-carboxylic acid. One of the isolated compounds was identified as a tropane alkaloid *N*-oxide. Their structures were determined by high resolution mass spectrometry and multi-dimensional NMR spectroscopy. The absolute configurations of some tropane products were established by the Mosher method.[5]

[1] D. C. Daly, *Kew Bulletin* **1990**, *45*, 179-194.
[2] E. Graf, W. Lude, *Arch. Pharm. (Weinheim)* **1978**, *311*, 139-152.
[3] B. Zanolari, D. Guilet, A. Marston, E. F. Queiroz, M. de Q. Paulo, K. Hostettmann, *J. Nat. Prod.* **2003**, *66*, 497-502.
[4] B. Zanolari, J.-L. Wolfender, D. Guilet, A. Marston, E. F. Queiroz, M. de Q. Paulo, K. Hostettmann, *J. Chromatogr. A* **2003**, in press.
[5] I. Ohtani, T. Kusumi, Y. Kashman, H. Kakisawa, *J. Am. Chem. Soc.* **1991**, *113*, 4092-4096.

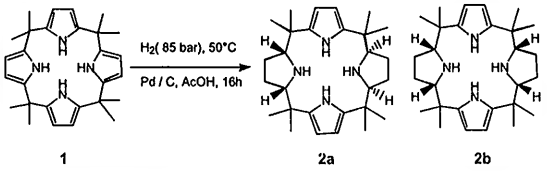
Organic Chemistry **250**

A NEW CLASS OF LIGANDS EASILY OBTAINED BY HYDROGENATION OF CALIX[4]PYRROLE

V. Botomei , M. Schmid , C. Heiss and R. Neier

Institut de Chimie,University of Neuchatel, Av. de Bellevaux 51, CH-2000 Neuchatel, Switzerland

The calix[4]pyrroles (**1**), first synthesized in 1886 by Baeyer, as the result of an acid- catalyzed condensation between acetone and pyrrole, are not very efficient ligands and special conditions have to be applied to obtain metal complexes[1].
The catalytic hydrogenation of calix[4]pyrrole resulted in partially reduced calix[4]pyrroles (**2a** and **2b**), new possible ligands for complexation with metal ions.
Various metal catalysts on different supports have been screened for this reaction. The best results were obtained with a carbon supported palladium catalyst, in acidic medium, under mild reaction conditions (85 bar, 50°C). Ruthenium on carbon also showed activity in this hydrogenation. Scope and limitations of this reaction will be discussed.



References:1. J. Jubb, G. Jacoby, C. Floriani, A. Chiesi-Villa, C. Rizzoli, *Inorg. Chem.*, **1992**, 31, 1306-1308.

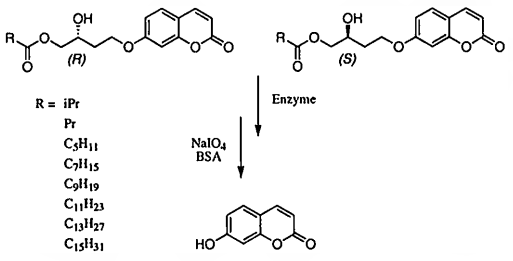
Organic Chemistry **251**

Enantioselective Lipases and Esterases Fingerprints

Johann Grognux and Jean-Louis Reymond

University of Bern, Freiestrasse 3, 3012 Bern, Switzerland

We have recently demonstrated that enzymes can be rapidly evaluated for their reactivities using an array of fluorogenic or chromogenic substrates.[1] Here we consider a particularly well-suited series of aliphatic probes structurally related to the natural lipases substrates that form particularly sensitive probes for these enzymes.[2] In order to go further in the process of differentiation, we introduced chirality as additional feature of enzyme recognition. Fingerprint data on lipases and esterases were generated and analyzed. Visual representation of the global activity fingerprint is presented as arrays of squares with a two-color scale combining stereoslectivity and activity.



[1] a) D. Wahler, F. Baladassi, P. Crotti, J.-L. Reymond, *Angew. Int. Ed. Engl.* **2001**, *40*, 4457. b) D. Wahler, F. Baladassi, P. Crotti, J.-L. Reymond, *Chem. Eur. J.* **2002**, *8*, 3211
[2] E. Nyfeler, J. Grognux, D. Wahler, J.-L. Reymond, submitted.

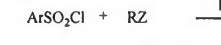
Organic Chemistry **252**

Carbon-Carbon Single and Double Bond Formation from Sulfonyl Halides

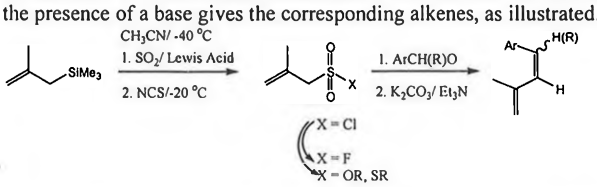
Srinivas Reddy Dubbaka and Pierre Vogel*

ICMB, EPFL; CH-1015 Lausanne-Dorigny, Switzerland.

Palladium catalysts emerged as extremely powerful tools for the construction of carbon-carbon, as well as carbon-heteroatom, bonds[1]. Until recently, nearly all reports of palladium-catalyzed coupling described the use of organic bromides, iodides, and triflates as substrates. Organic chlorides were noticeably uncommon partners among halides because of their dimished reactivity[2]. We report here a novel method for cross-coupling between aryl sulfonyl chlorides and aryl, alkenylboronic acids or arylstananes in the presence of a catalytic amount of palladium(0).



Additionally we wish to report that sulfonyl fluoride[3] or thiosulfonates in the presence of a base gives the corresponding alkenes, as illustrated.



[1] J. Tsuji, *Palladium Reagents and Catalysts, Innovations in Organic Synthesis*, Wiley, New York, **1995**.
[2] L. Brandsma; S.F. Vasilevsky, H.D. Verkruijsse, *Application of Transition Metal Catalysts in Organic Synthesis*, Springer, New York, **1998**, pp. 150, 228-229.
[3] S. Kagabu; K. Hara; J. Takahashi *J. Chem. Soc. Chem. Commun* **1991**, 408.

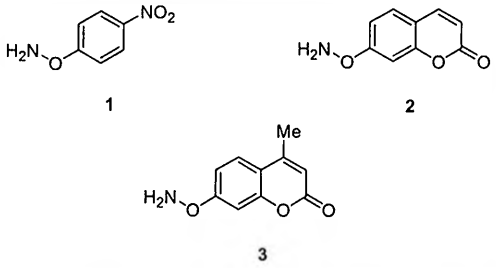
Organic Chemistry **253**

New Chromogenic and Fluorogenic Probes for Aldehydes Based on Oxime Chemistry

Syed Salahuddin, O. Renaudet, J.-L. Reymond*

University of Bern, Freiestrasse 3,CH-3012 Bern

Fluorogenic and chromogenic probes that react selectively form the basis for most detection systems used in either diagnostic applications of high-throughput screening systems.[1] Herein we report the synthesis and properties of oxyamine derivatives of nitrophenol, umbelliferone and 4-methylumbelliferone and their aqueous chemistry.



These unusual oxyamines react with aldehydes and ketones to form the corresponding oximes, which may undergo a Kemp's type elimination reaction leading to the formation of the corresponding phenol. A sensitive detection system for formaldehyde on that basis is presented. Furthermore, a class of oxime derivative was found to undergo catalytic decomposition in the presence of albumins, providing a new class of reactive substrates for catalytic detection of various proteins.

[1] D. Wahler, J.-L. Reymond, *Curr. Opin. Chem. Biol.* **2001**, *5*, 152-158.

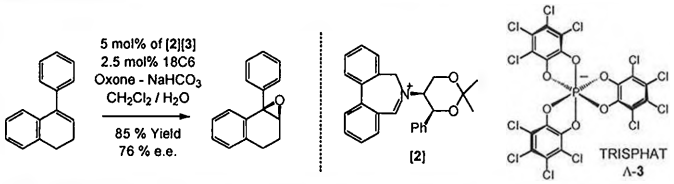
Organic Chemistry **254**

Influence Of Chiral Amines Onto Oxaziridinium-Catalysed Enantioselective Epoxidation

Jérôme Vachon, Claire Marsol, David Monchaud, Jérôme Lacour *

Département de Chimie Organique, Université de Genève, Switzerland

In the early 70's, Lusinchi *et al* reported that iminium species react as oxygen transfer agents with olefins, *via* the *in-situ* formation of oxaziridinium intermediates [1]. Bulman Page *et al* have developed an asymmetric and catalytic process combining a chiral amine and a chiral skeleton although configurationally labile to promote the asymmetric induction [2].



Our laboratory is currently engaged in the synthesis and the use of chiral anions in asymmetric chemistry, such as TRISPHAT anion **3** which was shown to be an asymmetric inducer onto configurationally labile chiral cations [3]. The replacement of the counter-ion BPh_4^- by **3** leads to an improvement of the enantioselectivity of epoxidation reactions due to the use of biphasic conditions (CH_2Cl_2/H_2O) that TRISPHAT allows (figure 1; nb: 41% e.e. with [**2**][BPh_4]). We now explore the influence of different chiral amines on the enantioselectivity, and the results are reported herein.

[1] A. Picot, P. Milliet, X. Lusinchi, *Tetrahedron Lett.*, **1976**, 1573; A. Picot, P. Milliet, X. Lusinchi, *Tetrahedron Lett.*, **1976**, 1577.
[2]. P.C. Bulman Page, G.A. Rassias, D. Barros, A. Ardakani, B. Buckley, D. Bethell, T.A.D. Smith, A.M.Z Slawin, *J. Org. Chem.*, **2001**, *66* (21), 6926.

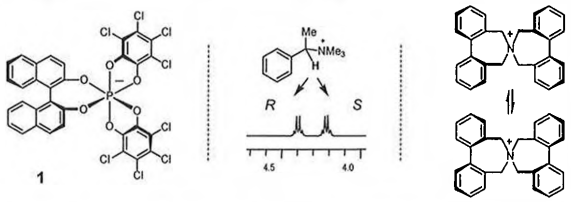
Organic Chemistry **255**

Chiral Quaternary Ammonium Cation Chemistry

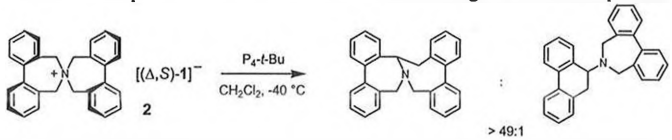
Jérôme Vachon, Laurent Vial, Jérôme Lacour *

Département de Chimie Organique, Université de Genève, Switzerland

Chiral quaternary ammonium cations (or *quats*) have recently received much attention through their use as efficient chiral phase transfer catalysts. Whereas most examples employ cations derived from the chiral pool, recent reports of successful reactions mediated by purely synthetic chiral *quats* raises the question of the enantiomeric purity determination.[1]



In this poster, we show that C_2-Symmetric BINPHAT anion **1** – of configuration controlled by a binol ligand – behaves as an efficient NMR chiral shift agent for *quats*.[2] Combined with configurational labile derivatives, such as cation **2**, an asymmetry-induction occurs (d.e. up to 63%);[3] this further allowing an enantioselective [1,2]-Stevens rearrangement. In addition, mechanistic aspects of this reaction have been investigated and are reported.



[1] T. Ooi, M. Kameda, K. Maruoka, *J. Am. Chem. Soc.* **2003**, *125*, 5139.
[2] J. Lacour, L.Vial, C. Herse, *Org.Lett.* **2002**, *4*, 1351.
[3] L.Vial, J. Lacour, *Org.Lett.* **2002**, *4*, 3939.

Organic Chemistry **256**

HTS Activity Profiling of Glycoside Hydrolases

Renaud Sicard, J.-L. Reymond*

University of Bern, Freiestrasse 3, CH-3012 Bern

A plethora of enzymes and their mutants have become available over the years from biodiversity mining and directed evolution/mutagenesis studies. Beyond activity screening arises the problem of being able to characterize each enzyme's activity in sufficient details for distinguishing similar enzyme subtypes. This can be realized by activity profiling or fingerprinting using substrate arrays.[1] We have focused our attention on the study of glycoside hydrolases, which are used both in industry (paper and food processing) and biomedical research (e.g. viral and tumor therapy targets).

(a) (b)

Figures: Glycoside-fingerprint of β-galactosidase (a) from Saccharomyces fragilis (Sigma G-3782) and α-mannosidase (b) from Jack Beans (Sigma-M-7257)

Herein we report profiling of glycoside hydrolases based on series of selective glycosidase substrates. A new substrate display format was developed which requires only very small amounts of enzyme for each measurements. The application of this method for glycoside-fingerprinting of pure enzymes and microbial preparations will be discussed.

[1] D. Wahler, F. Badalassi, P. Crotti, J.-L. Reymond, *Chem. Eur. J.* **2002**, *8*, 3211-3228..

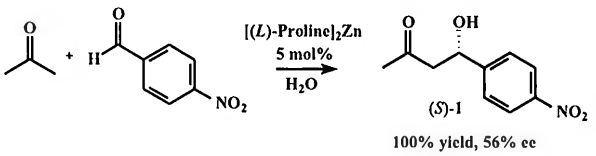
Organic Chemistry **257**

Zn-proline catalyzed direct aldol reaction in aqueous media

Ruben Fernandez-Lopez, Miguel Machuqueiro, Tamis Darbre

Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, Bern, 3012

Zn complexes of proline, lysine and arginine are efficient catalysts for the aldol addition of *p*-nitrobenzaldehyde and acetone in aqueous medium, giving quantitative yields and enantiomeric excesses up to 56% with 5 mol% of the catalyst at room temperature[1]. Alkyl and aryl aldehydes are suitable partner for the reaction. Ketones showed regioselectivity



[1] T. Darbre, M. Machuqueiro, *Chem.Com.* **2003**, *30*, 1090.

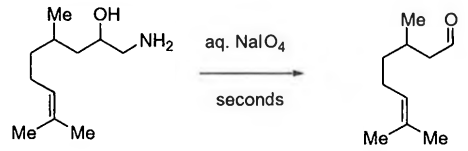
Organic Chemistry **258**

β-Aminoalcohol Properfumes

Yongzheng Yang, Denis Wahler and Jean-Louis Reymond*

University of Bern, Freiestrasse 3, CH-3012 Bern

Over three thousand fragrance ingredients are available today for use in perfumery. Factor such as chemical instability, reactivity, and evanescence, which are intrinsic to many fragrant compouds, however strongly limit the choices for certain applications, in particular when the active ingredients must be stored for some time before being released.[1] Aminoalcohol derivatives of fragrant, volatile aldehydes and ketones were synthesized in a one-pot procedure by sequential cyanohydrin formation with trimethylsilyl cyanide and reduction with lithium aluminium hydride. The aminoalcohols, or acid salts thereof, are non-volatile, stable properfumes. The parent fragrant carbonyls are released by oxidation with sodium periodate, which proceeds quantitatively within seconds in aqueous solution. Examples include aminoalcohol properfumes of citronellal, lilial®, lauryl aldehyde, menthone, benzaldehyde and anisaldehyde.[2]



pro-citronellal
(stable, non-volatile)

citronellal

[1] P. Kraft, J. A. Bajgrowicz, C. Denis, G. Fráter, *Angew. Chem. Int. Ed.* **2000**, *39*, 2980
[2] Y. Yang, D. Wahler, J.-L. Reymond, *Helv. Chim. Acta.*, in press.

Organic Chemistry **259**

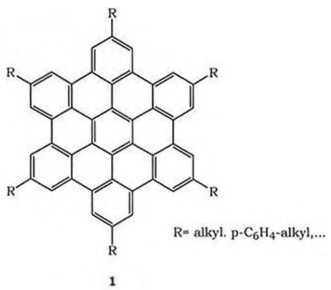
Synthesis and Characterization of Large Self-Assembled Disc-Shaped Supramolecules: Potential Conducting Devices

Alameddine, B.; Jenny, T.A.

University of Fribourg, Chemistry Department, 1700 Fribourg, Switzerland.

Self-assembled organic supramolecules have gained a lot of interest in the last two decades among others in the field of luminescence and electron emission phenomena. Such properties could be applied in the domain of materials for the fabrication of low cost flat panel displays.

The basic idea implies the deposition of large aromatic disc shaped molecules that self assemble by π-π stacking into column like ordered structures on a suitable electrode surface. Improvements of the known hexa-*peri*-benzocoronene (HBC) [1] system (**1**) have been carried out: specially designed side chains are introduced to enhance solubility and stacking properties and to better isolate the stacks from each others to reduce any lateral interaction of those.



1

[1] A. M. Van de Craats, K. Müllen, Y. Geerts, J.D. Brand, *Adv. Mater.* **1998**, *10*, 36.

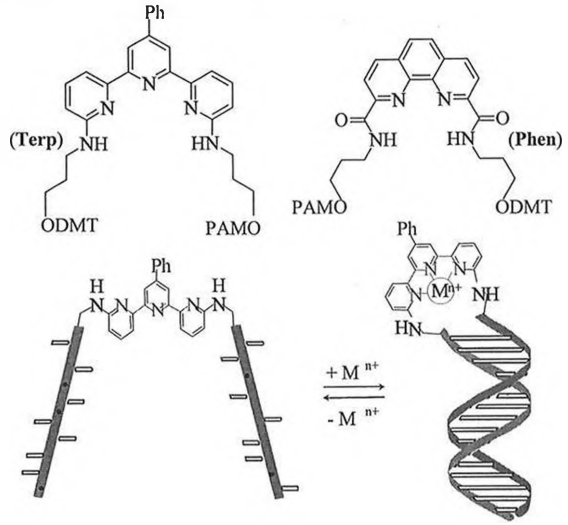
Organic Chemistry **260**

Metal Complexes as Non-Nucleobase Scaffolds for *Hairpin* Mimics.

Gapian Bianké, Robert Häner

University of Bern, Freiestrasse 3, 3012 Bern, Switzerland.

We are interested in the study of modified oligonucleotide hairpins containing terpyridine and phenanthroline-loops, as well as their behaviour under different experimental conditions. Particularly, we are investigating of the hairpin stability as a function of metal concentration. Terpyridine (Terp) and Phenanthroline (Phen) building blocks have been synthesized, incorporated into DNA-oligonucleotides and analysed by thermal denaturation experiments. The results will be shown and discussed in comparison with hairpins containing natural nucleotidic loops.

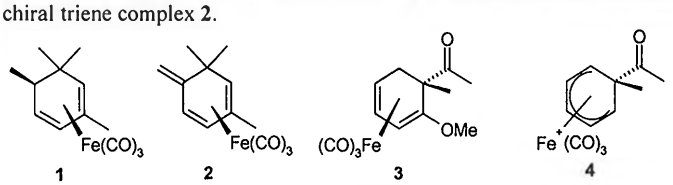


Organic Chemistry **261**

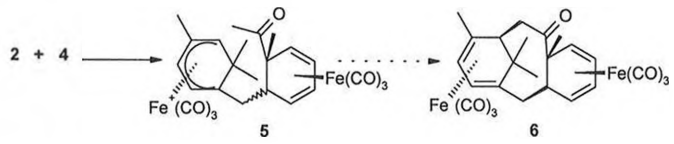
INVESTIGATION OF IRON CARBONYL COMPLEXES FOR TAXANE SKELETON SYNTHESIS

C. Eggertswyler, T.A. Jenny*
Chemistry Department, University of Fribourg, CH-1700 Fribourg, Switzerland

The synthetic potential of olefin iron carbonyl complexes is demonstrated by a new convergent approach in constructing the taxane skeleton.
By an unprecedented oxidation involving the Perrier reagent ($AcCl/AlCl_3$) the optically active cyclohexadiene complex **1**, accessible from (-)-β-pinene in a high yield two step synthesis [1], is transformed to the planar chiral triene complex **2**.



Complex **3**, obtained from 2-methoxyacetophenone, can be ionized with H_2SO_4 to give the cationic complex **4**. Coupling of the nucleophilic iron complex **2** with the electrophilic complex **4** will yield the intermediate **5** which upon treatment with a sterically hindered base gives binuclear complex **6** upon ring closing alkylation.



[1] T.A. Jenny, L. Ma, *Tetrahedron Lett.*, **1991**, 32, 6101

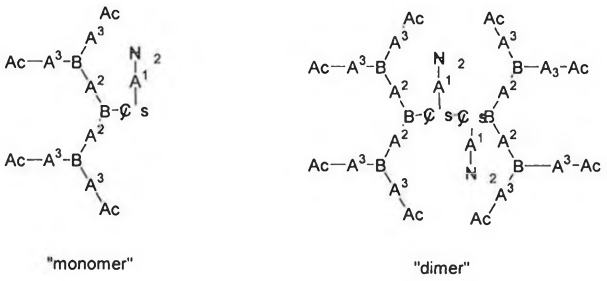
Organic Chemistry **262**

STM-Vizualization of Peptide Dendrimers on Gold(111)

Estelle Delort, Edit Szäcs, Hans Siegenthaler*, Jean-Louis Reymond*

University of Berne Freiestrasse 3CH-3012 Berne

Peptide dendrimers can be rapidly assembled by solid phase peptide synthesis to form enzyme-like structures.[1] Our present efforts are concentrated on the visualization of these peptidic dendrimers by Scanning Tunneling Microscopy. A good control of the immobilization method afforded to visualize from isolated molecules to a densely packed monolayer coverage.



Dendrimers were adsorbed on gold surfaces either as monomers or as dimer. STM analysis was performed either in air or in electrolyte solution, revealing the shape of single dendrimers and ordered layer assemblies.

[1] A. Esposito, E. Delort, D. Lagnoux, F. Djojo, J.-L. Reymond, *Angew. Chem. Int. Ed.* **2003**, *42*, 1381.

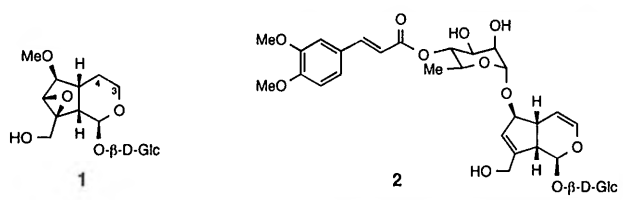
Organic Chemistry **263**

New Iridoid Glycosides from the Roots of *Scrophularia lepidota*

Deniz Tasdemir,[1] Nadide Güner,[2] Ali Dönmez,[3] Ihsan Çalış,[2] Peter Rüedi[1]

[1]Institute of Organic Chemistry, University of Zurich, Winterthurerstrasse 190, CH-8057, Zurich, Switzerland; [2]Department of Pharmacognosy, Hacettepe University, TR-06100, Ankara, Turkey; [3]Department of Biology, Hacettepe University, TR-06532, Ankara, Turkey.

In the flora of Turkey, the genus *Scrophularia* (Scrophulariaceae) is represented by 59 species, 23 of which are endemic [1]. Some *Scrophularia* species are used in the Anatolian folk medicine as diuretic and for the treatment of wounds and hemorrhoids [2]. In continuation of our chemical and biological studies on this genus, we investigated *S. lepidota* BOISS. From the roots of the title plant we isolated two new iridoid glycosides (**1**) and (**2**). Their structures were elucidated by spectroscopic and chemical methods.



3,4-saturated iridoids such as **1** and natural products bearing 3,4-dimethoxycinnamic acid (**2**) are quite rare in nature. The isolation, structure elucidation and the evaluation of biological activities of **1** and **2** will be presented.

[1] S.S. Lall, R.R. Mill, in: *Flora of Turkey and the East Eagean Islands* (P.H. Davis, ed.) Vol. 6, University Press, Edinburgh 1978, p. 603.

[2] T. Baytop, *Therapy with Medicinal Plants in Turkey (Past and Present)*, Nobel Tıp Kitapevleri, Ankara, 1984, p. 422.

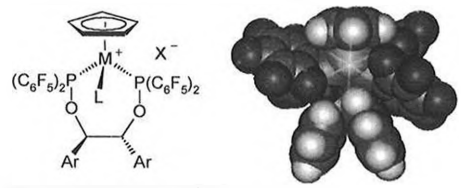
Organic Chemistry **264**

Single Site Ru-Lewis Acids as Catalyst for Asymmetric Cycloaddition Reactions

Gérald Bernardinelli, Anil K. P. Govordhan[⊥], Christophe Saudan, Martial Vallet, Florian Viton, Paul S. Pregosin[⊥], and E. Peter Kündig*

Department of Organic Chemistry, University of Geneva, Switzerland.
Peter.Kundig@chiorg.unige.ch
[⊥] Laboratory of Inorganic Chemistry ETH, Zurich, Switzerland.

The 16-electron half-sandwich complexes of the type CpM(BIPHOP-F)$^+$ (M = Fe, Ru) are efficient catalysts for the asymmetric Diels-Alder reaction between enals and dienes.[1] Counter anion variation shows a large influence on the activity of these Lewis acid.[2] In order to study this effect, PGSE NMR experiments were carried out. In extension of previous studies, we have also modified the hydrobenzoïn derived ligand backbones and here report on the effects on activity and selectivity of the new Lewis acids.



[CpM((R,R)-BIPHOP-F)]$^+X^-$

1. a) Kündig, E. P.; Saudan, C. M.; Bernardinelli, G. *Angew. Chem. Int. Ed.* **1999**, *38*, 1220. b) Kündig, E. P.; Saudan, C. M.; Alézra, V.; Viton, F.; Bernardinelli, G. *Angew. Chem. Int. Ed.* **2001**, *40*, 4481.
2. Kündig, E. P.; Saudan, C. M.; Viton, F. *Adv. Synth. Catal.* **2001**, *343*, 51.

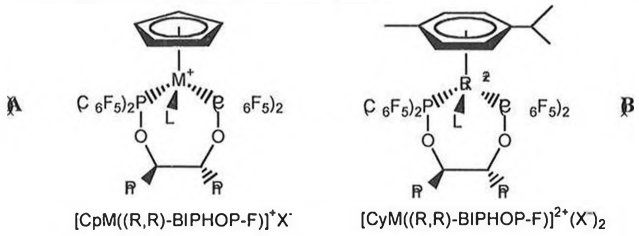
Organic Chemistry **265**

Ru-Lewis Acids as Catalysts for Asymmetric Cycloaddition Reactions

Rodolphe Jazzar, Martial Vallet and E. Peter Kündig*

Départment de Chimie Organique – Sciences II - 30, quai Ernest-Ansermet
CH1211 Genève 4 - Suisse

The 16-electron half-sandwich complexes of the type $[CpM(BIPHOP\text{-}F)]^+$ (M = Fe, Ru) (**A**) are efficient catalysts for the asymmetric Diels-Alder reaction between enals and dienes. Attractive features of this family of Lewis acid catalysts are their straightforward syntheses, well-defined structures and tunable electronic properties. In extension of these DA studies, it has been found that the Fe- and Ru-Lewis acids can also catalyze 1,3-dipolar cycloaddition reactions between nitrones and α,β-unsaturated aldehydes.[1] The weak Lewis acidity of the $[CpRu(BIPHOP\text{-}F)]^+$ systems has so far prevented this class of catalyst from finding larger applications in organic synthesis. We have started to investigate new dicationic $[Ru(arene)(BIPHOP\text{-}F)]^{2+}$ complexes (**B**) in order to access higher Lewis acidity of the metal centre and subsequently improve the activity, the selectivity and the scope of these complexes.



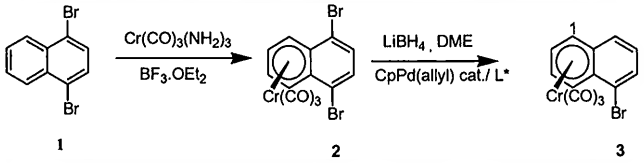
[1] F. Viton, G. Bernardinelli, E. P. Kündig, *J. Am. Chem. Soc.* **2002**, *124*, 4968 and references cited.

Organic Chemistry **266**

Planar Chiral Naphthalene Complexes via Pd-Catalyzed Desymmetrization of a meso-Dibromonaphthalene $Cr(CO)_3$ Complex

Piyali Datta Chaudhuri, E. Peter Kündig*, David House, Gérald Bernardinelli
University of Geneva, 30 Quai E. Ansermet, CH-1211 Geneva-4

In connection with our program on the use of (arene)$Cr(CO)_3$ complexes in asymmetric synthesis, we became interested in the preparation of enantiomerically enriched planar chiral complexes [1]. This contribution reports our new results on the synthesis of planar chiral naphthalene complexes via Pd-catalyzed desymmetrization of a meso-complex [2].
We have found that complexation of 1,4-dihalonaphthalenes to the electrophilic $Cr(CO)_3$ auxiliary provides a single regioisomer in high yield.



Desymmetrization of complex **2** to the mono bromo complex **3** via Pd catalyzed hydrogenolysis will be detailed with a comparison of the efficiency of a number of catalyst precursors / chiral ligand combinations.
Up to 89% *ee* has been obtained by using a monodentate phosphoramidite ligand. The x-ray structure of the major enantiomer (1R-**3**) has been determined. In extension of this study, halide / metal exchange is used to access other planar chiral naphthalene complexes.

[1]. Pape, A. R.; Kaliappan, K. P.; Kündig, E. P. *Chem. Rev.* **2000**, *100*, 2917.
[2]. (a)Uemura, M.; Nishimura, H. *Tetrahedron Lett.* **1993**, *34*, 107.
(b)Gotov, B.; H. G. Schmalz, *Org. Lett.* **2001**, *3*, 1753.

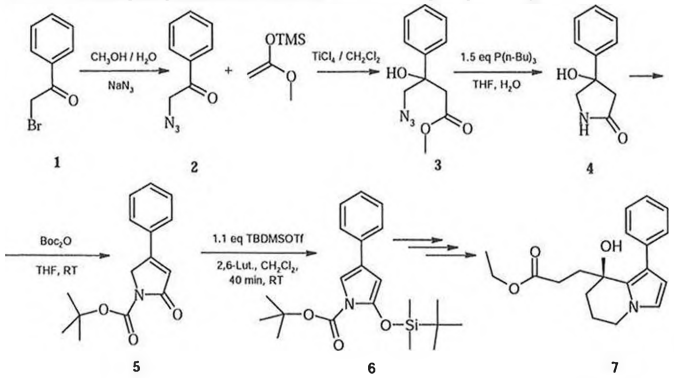
Organic Chemistry **267**

Synthesis of 3-(8-Methyl-1-phenyl-5,6,7,8-tetrahydro-indolizin-8-yl)-propionic acid ethyl ester in view of the synthesis of a model compound of Rhazinilam.

Ana-Maria Buciumas, Olivier Vallat, Reinhard Neier*

University of Neuchâtel, Av. De Bellevaux 51, 2000 Neuchâtel, Switzerland

The Mukayama reaction between **2** and the silyl enol ester of methyl acetate gives compound **3** which is a precursor of the lactam **4**. Transformation of **4** to **6** has been achieved in two steps. To obtain the model compound **7** starting from **6** the following steps have to be achieved: elimination the protected OH group[1,2], subtitution of the Boc group and cyclization.



[1] J. M. Saá, M. Dopico, G. Martorell, A. Garcia-Raso, *J. Org. Chem.*, **1990**, 55, 991.
[2] P. A. Jacobi, R. W. DeSimone, I. Ghosh, J. Guo, S. H. Leung, D. Pippin, *J. Org. Chem.*, **2000**, 65, 8478.

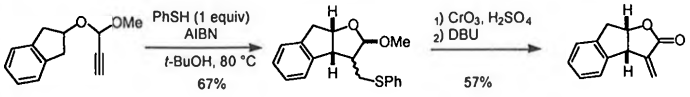
Organic Chemistry **268**

Diastereoselective 1,5-Hydrogen Abstraction Mediated by Thiophenol

Florent Beaufils, Fabrice Dénès and Philippe Renaud

Universität Bern, Departement für Chemie und Biochemie
Freiestrasse 3, CH-3000 Bern 9

Hydrogen atom abstraction is a bond breaking-bond forming process that is frequently encountered in radical reactions.[1] So far, stereoselective hydrogen atom abstractions have been considered as curiosities.[2] In this communication, we report a systematic study of the diastereoselectivity of hydrogen atom abstraction and we demonstrate that it is governed by stereochemical rules similar to the one developed for related cyclization processes.
The stereoselective hydrogen atom abstraction-cyclization cascade is of synthetic interest and may found application for the preparation of diverse polysubstituted tetrahydrofurans. To demonstrate this point, we have prepared α-methylenelactone using a tin-free hydrogen atom abstraction-cyclization process as key step.[3]



[1] L. Feray, N. Kouznetsov, P. Renaud, in *Radicals in Organic Synthesis, Vol. 2* (Eds.: P. Renaud, M. P. Sibi), Wiley-VCH, Weinheim, **2001**, pp. 246.
[2] C. Imboden, F. Villar, P.Renaud, *Organic Letters* **1999**, *1*, 873.
S. Bogen, M. Gulea, L. Fensterbank, M. Malacria, *J. Org. Chem.* **1999**, *64*, 4920.
[3] For a related 1,5-hydrogen abstraction process, see : S. D. Burke, K. W. Jung, *Tetrahedron Lett.* **1994**, *35*, 5837.

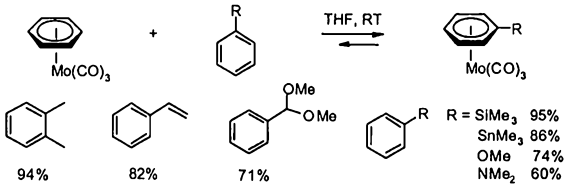
Organic Chemistry **269**

Dearomatization and Arene Exchange Reactions with [(η^6-Benzene)Mo(CO)$_3$] : Difference in Reactivity with Cr

E. Peter Kündig,* Charles-Henry Fabritius, Gabriele Grossheimann, Fabrice Robvieux, Patrick Romanens and Gérald Bernardinelli

University of Geneva, Department of Organic Chemistry
30 Quai Ernest Ansermet, CH-1211 Geneva 4

Complexation of an arene to the electrophilic Cr(CO)$_3$ fragment has been extensively investigated and applied in organic synthesis [1]. Surprisingly no parallel development has taken place with the analogous Mo compounds. M-H and M-C bonds are stronger in Mo than in Cr-complexes and different patterns of reactivity can be expected. This has recently been confirmed in a first example of Mo-mediated arene transformation [2].
Another distinct difference in arene M(CO)$_3$ complexes of Cr and Mo lies in the ease of substitution of the metal-bound arene. Cr complexes, with few exceptions [3], are inert at temperatures below 150 °C whereas Mo complexes are labile at room temperature. We now show that this feature can be used successfully in the synthesis of a range of functionalised complexes. Some examples are shown below and first investigations into their reactivities will be shown in the poster.



[1] A. R. Pape, K. P. Kaliappan, E. P. Kündig, *Chem. Rev.* **2000**, *100*, 2917.
[2] E. P. Kündig, C.-H. Fabritius, G. Grossheimann, F. Robvieux, P. Romanens, G. Bernardinelli, *Angew. Chem. Int. Ed.* **2002**, *41*, 4577.
[3] E. P. Kündig, M. Kondratenko, P. Romanens, *Ang. Chem. Int. Ed.* **1998**, *37*, 3146-3148.

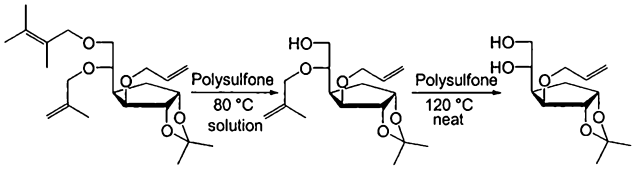
Organic Chemistry **270**

Successive Cleavage of Allylic Ethers by Polysulfone

Dean Marković, Peter Steunenberg and Pierre Vogel*

Laboratory of Glycochemistry and Asymmetric Synthesis, BCH CH-1015 Lausanne- Dorigny

Polysulfones (copolymers of alkene and SO_2) are capable to isomerise alkenes. The process implies the formation of an initial allyl radical, formed by a chain-process involving the hydrogen transfer between the alkene and the intermediate allyl radical. The formation of the latter intermediate is two steep process in which a RSO_2 radical abstracts first an electron from the alkene with formation of an radical cation. In the second steep the latter loses a proton with formation of an allyl radical.
Accordingly, the rate of the polysulfone catalysed alkene isomerisation depends strongly upon its ionisation potential. This fact has been used to invent a new strategy for alcohol, aldehyde, ketone and hemiacetal protections. While allyl ethers are not isomerised with polysulfone, metahallyl ethers are isomerised into the corresponding enol ethers (and then hydrolysed) on heating with polysulfone catalyst. Prenyl ethers and methylprenyl ethers are isomerised much faster. A polyol protected as allyl, metallyl and methylprenyl ethers will be deprotected under neutral conditions by the polysulfone with the following reaction sequence.

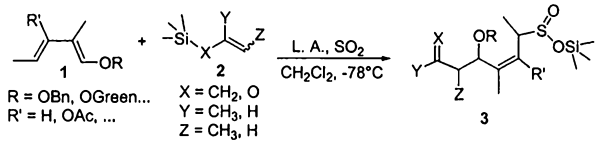


Organic Chemistry **271**

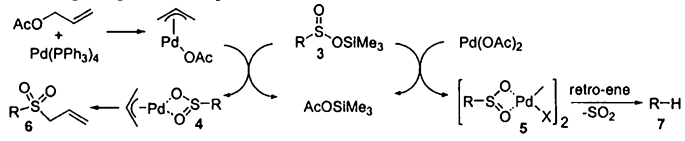
The transmetallation of silyl sulfinates and its application

Xiaogen Huang, Craita Cotinica, Maris Turks, Laure Bouchez, Pierre Vogel*
Institut de chimie moléculaire et biologique de l'Ecole Polytechnique Fédérale de Lausanne, BCH CH-1015 Lausanne- Dorigny

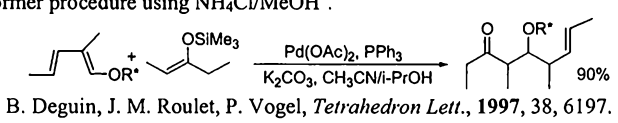
1-Oxy-1,3-dienes **1** reacting with silyl enol ethers or allyl silanes **2** in the presence of SO_2 and Lewis acids as catalysts generate silyl sulfinate intermediates **3**.



Under the catalysis of either $Pd(PPh_3)_4$ or $Pd(OAc)_2$, silyl sulfinates **3** undergo the silicon/palladium transmetallation. The formation of silyl acetate is the driving force of these reactions. When the sulfinyl palladium complexes **4** or **5** are formed, they undergo either reductive elimination to give the allyl sulfones **6**, or elimination of SO_2 in the presence of a proton source giving retro-ene products **7**.



This procedure leads to higher yields of polypropionate fragment than a former procedure using $NH_4Cl/MeOH$[1].



1. B. Deguin, J. M. Roulet, P. Vogel, *Tetrahedron Lett.*, **1997**, 38, 6197.

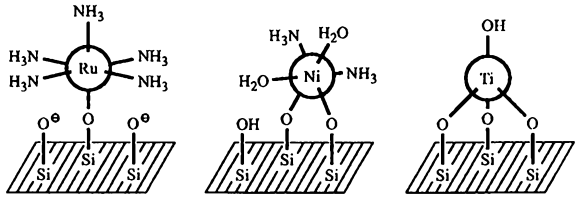
Physical Chemistry **272**

Coordination Chemistry at the Silica Surface: Towards New Materials for Photochemical Applications

Dominik Brühwiler* and Heinz Frei

Physical Biosciences Division, Lawrence Berkeley National Laboratory, University of California, Berkeley, CA 94720

A method is presented which allows the covalent attachment (grafting) of isolated metal centers on mesoporous silica in a pre-selected oxidation state. The structure of Ru(III) and Ni(II) ammines grafted by this method was studied by UV-Vis, FT-IR, and X-ray absorption spectroscopy [1]. Hydrogen bonding between ligands (NH_3 or H_2O) and surface silanol groups was found to play an essential role in determining the reaction pathways and subsequent stabilization of the transition metal complexes.



Grafting of Ni(II) amminc complexes onto mesoporous silica containing isolated Ti(IV) centers [2] resulted in the formation of surface-anchored Ti(IV)-O-Ni(II) groups [1]. Moieties of this kind are of special interest for demanding photochemical applications, such as the reduction of CO_2 using H_2O as electron source and visible light as energy source.

* Current Address: Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, CH-3012 Bern

[1] D. Brühwiler, H. Frei, *J. Phys. Chem. B*, in press.
[2] J. M. Thomas, G. Sankar, *Acc. Chem. Res.* **2001**, *34*, 571.

Physical Chemistry **273**

On the surface properties of chemically prepared CdSe nanocrystals

D. Tonti, J. Liu, C. Bonati, M. Mohammed, A. Chemseddine* and M. Chergui

Institut de Physique de la Matière Condensée, Université de Lausanne, CH-1015 Lausanne, Switzerland
*Department for solar energy research, Hahn-Meitner-Institut Berlin, D-14109-Berlin, Germany

In the last two decades the growing interest in the fundamental properties and in the applications of nanomenter-sized materials stimulated the research of a manifold of synthetic routes to improve control over size, shape, monodispersity, surface and organization. Wet chemical routes are attracting methods due to their technical simplicity and low cost. However, the complexity of the processes involved often leads to a poor reproducibility of the properties the prepared material exhibits.
Semiconductor nanocrystals are interesting for their tunable strong fluorescence. This property, the way it is preserved with time, and under strong illumination, depends in a crucial way on their surface nature and quality.
We prepared organically capped CdSe nanocrystals by different chemical routes, implying different reaction, growth temperature, surfactant molecules, solvent coordination. We characterized the surface by infrared spectroscopy and photoelectron spectroscopy, and correlated it with the static and ultrafast optical properties of the nanocrystals in different solvents.
We proved that taking differently capped samples, by exchanging the ligand for the same amine similar optical properties can be observed.
Based on a more detailed knowledge of the surface and its degradation processes, the most critical aspects of the synthesis and of the storage conditions will be discussed.

Physical Chemistry **274**

Probing and Controlling Gas/Surface Chemistry by Pulsed Laser Radiation

R.D. Beck, T.T. Dang, P. Maroni, D. Papageorgopoulos, T.R. Rizzo

Laboratoire de Chimie Physique Moleculaire (LCPM)
Ecole Polytechnique Fédérale de Lausanne (EPFL)
CH-1015 Lausanne, Switzerland

Laser light is an invaluable tool for detailed experimental studies of chemical reactions. The ability to prepare reagent molecules in specific quantum states and to resolve the quantum state distribution of reaction products using laser radiation has been key to the field of chemical reaction dynamics which studies chemistry at a fundamental microscopic level. Today, state resolved experiments are common for unimolecular and bimolecular reactions in the phase reactions but equivalent measurements for gas/surface reactions have only recently started to appear. This contribution will introduce a new method for the measurement of state resolved gas/surface reactivity and present first results on the dissociative chemisorption of methane on nickel. We use pulsed laser preparation in a molecular beam to measure state resolved sticking coefficients for methane in specific ro-vibrational states on Ni(100) and Ni(111). We find that excitation of the first overtone of the antisymmetric C-H stretch vibration ($2\nu_3$) in CH_4 increases the reactivity by a factor of 10^4-10^2, depending on translational energy. 72 kJ/mol of $2\nu_3$ vibrational energy are on average 80% as efficient in increasing the reactivity as translational energy along the surface normal confirming the importance of C-H stretch motion for the dissociation reaction. C-H bending motion appears to be of lesser importance as judged from the sticking coefficient for a nearly isoenergetic state containing bending motion ($\nu_2+\nu_3+\nu_4$). Comparison with data for CD_3H, excited to the overtone of he unique C-H bond, provides further information about the effect of vibrational energy localization on the gas/surface reactivity.

[1] – M. Schmid, P. Maroni, R.D. Beck and T.R. Rizzo, J. Chem. Phys. **117**, 8603 (2002).

Physical Chemistry **275**

Photochemical Growth and Vibrational Coherences of Silver Nanoplates

A. Callegari, D. Tonti, A. Al Salman, L. Bonacina, F. Chaussard, F. van Mourik and M. Chergui

Institut de Physique de la Matière Condensée, Université de Lausanne, CH.1015 Lausanne, Switzerland

Recent years have witnessed an increasing interest in metal nanoparticles (NPs), due to their fundamental properties and potential applications. In these systems, both size and shape have a profound influence on their physical and chemical properties. We are interested in particular in the effect of these two parameters on the plasmon resonance, which strongly affects the electronic and optical properties.
We have developed a novel photochemical procedure that allows us to grow Ag NPs with controlled and well-defined size and shape. The particles are grown in a water solution starting from smaller (~ 10 nm) spherical particles produced by standard chemical methods. The solution is then exposed to light, which promotes further growth. We have managed to grow triangle and hexagonal shaped NPs in the 50-200 nm size range, with relatively narrow distribution. The size and shape of the final product depend subtly on the wavelength of the light used to drive the growth. The role of light involves at least two different processes: light-induced oxidation of the precursors and plasmon-resonance induced growth of seed metal particle.
The plasmon resonance band of 100 nm wide particles falls in the 800 nm wavelength region, corresponding to the fundamental wavelength of the Ti:Sapphire laser. We have carried out a femtosecond pump-probe transient absorption experiment of these NPs using 800 nm as pump and a white light continuum in the same region as probe. From the observed behavior it can be concluded that excitation of the plasmon resonance generates impulsive heating of the NP in the form of coherent phonons. This leads to periodic changes of the particle size, which change the position of the plasmon band, in an oscillatory fashion.

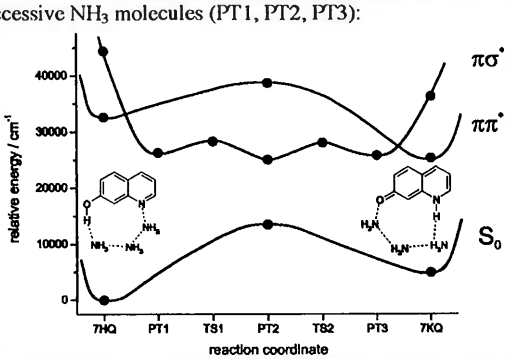
Physical Chemistry **276**

Excited-state proton transfer with an energy selective threshold

Christian Tanner, Carine Manca and Samuel Leutwyler

Department of Chemistry and Biochemistry, University of Berne, Freiestrasse 3, 3012 Bern

The $S_1 \leftarrow S_0$ two-color R2PI spectrum of the 7-hydroxyquinoline-$(NH_3)_3$ cluster rapidly decreases 200 cm^{-1} above the electronic origin, whereupon further vibrational excitations can be monitored in the UV/UV hole-burning spectrum. At the exact energy where the R2PI signal disappears, the excitation spectrum of the fluorescence of the keto tautomer (7KQ) shows the same vibronic band pattern as measured in the hole-burning spectrum, revealing *enol Æ keto* tautomerization in the excited state. CASSCF calculations of the cluster in C_s symmetry predict a proton translocation pathway along successive NH_3 molecules (PT1, PT2, PT3):



The $^1\pi\pi^*$ potential energy surface (PES) is intersected by a low-lying Rydberg-type $^1\pi\sigma^*$ PES [1]. This conical intersection in C_s leads to a very low barrier in C_1 symmetry in agreement with the experiments.

[1] A.L. Sobolewski *et al.*, *Phys. Chem. Chem. Phys.* **2002**, *4*, 1093.

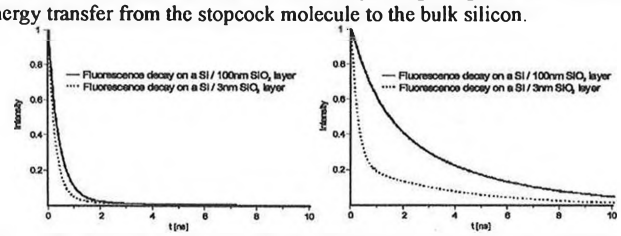
Physical Chemistry **277**

Energy Transfer from photonic zeolite antenna crystals to bulk silicon

Stefan Huber and Gion Calzaferri

Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, CH-3012 Bern, Switzerland

We showed that it is possible to insert various dyes into the channels of zeolite L[1,2]. Due to geometric restrictions of these channels, the dyes are organized in a supramolecular manner. - By modifying the surface of a dye loaded zeolite L crystal with physisorbed or covalently bond stopcock[3] molecules, the harvested excitation energy of a dye loaded zeolite L crystal can be transported to the outside of the crystal.
The photo - physical properties of such crystals are studied on a silicon surface with a thick (> 100 nm) and a thin (~ 3 nm) oxide layer by stationary and time-resolved fluorescence spectroscopy methods. While the fluorescence decay of the dye inside the zeolite remains the same on both surfaces (left figure), the fluorescence decay of the stopcock molecule becomes much faster on the thin oxide layer (right figure). This indicates energy transfer from the stopcock molecule to the bulk silicon.



[1] G. Calzaferri, M. Pauchard, H. Maas, S. Huber, A. Khatyr, T. Schaafsmaa, *J. Mater. Chem.*, **2002**, *12*, p. 1 - 13
[2] G. Calzaferri, S. Huber, H. Maas, C. Minkowski, *Angew. Chem. Int. Ed. (review)* **2003**, in press
[3] H. Maas, G. Calzaferri, *Angew. Chem. Int. Ed.* **2002**,*41*,p.2284-2288

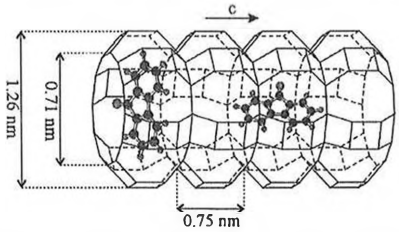
Physical Chemistry **278**

Electronic and Vibrational Spectra of Fluorenone in Zeolite L

André Devaux, Claudia Minkowski, Gion Calzaferri

Department for Chemistry and Biochemistry, University of Bern, Freiestrasse 3, CH-3012 Bern, Switzerland

Fluorenone was inserted into the channels of zeolite L following a method described in [1]. The size, structure, and stability of fluorenone are well suited for studying guest-host properties. Luminescence spectra of fluorenone in different solvents have been studied.[3][4] Here we report FT-IR, Raman, luminescence, and excitation spectra of *fluorenone-zeolite L*. Normal coordinate analysis and molecular orbital calculations were performed to gain a better understanding of the system. Results obtained in a detailed analysis on spherosiloxanes served as a basis for this work.[2] Fluorescence dichroism was studied by means of optical microscopy techniques.



The figure above illustrates two possible orientations of fluorenone molecules in a zeolite channel. The channel diameters correspond to van der Waals radii. The unit cell length is 0.75 nm.

[1] M. Pauchard, A. Devaux, G. Calzaferri, *Chem. Eur. J.* **2000**, *6*, 3456.
[2] C. Marcolli, G. Calzaferri, *J. Phys. Chem. B*, **1997**, *101*, 4925.
[3] K. Yoshihara, D. R. Kearns, *J. Chem. Phys.* **1966**, *45*, 1991.
[4] L. Biczók, T. Bérces, *J. Chem. Phys.* **1988**, *92*, 3842.

Physical Chemistry **279**

Distribution of Aluminium in Zeolite Beta

Anuji Abraham, Jeroen Anton van Bokhoven, #Suk Bong Hong, Roel Prins

Institute for Chemical- and Bioengineering, Swiss Federal Institute of Technology (ETHZ), 8093, Zurich, Switzerland,
#Division of Chemical Engineering, Hanbat National University, Taejon 305-719, Korea.

An important issue in zeolite science is the aluminium distribution over the crystallographic T-sites in the framework. Zeolite Beta has nine crystallographic T-sites [1] and the distribution of aluminium remains unresolved. High-resolution solid- state ^{27}Al Magic-Angle Spinning (MAS) and Triple Quantum (3Q) MAS [2,3] NMR spectroscopic techniques were used to characterize zeolite Beta having different framework Si/Al ratios, obtained by as-synthesis and post-synthesis treatments. Zeolite Beta with varying Si/Al ratios ranging from 8 to 200 were prepared by fluoride synthesis. The as-synthesised zeolites were calcined to obtain H-Beta. By using the quadrupolar parameters extracted from the graphical analysis of the ^{27}Al 3Q-MAS experiment, a quantification of the ^{27}Al MAS experiment is done. Thus, the aluminium distribution over these T-sites is probed. Appearance of a third component is seen in the case of high-silica Beta zeolites, both in the case of as-synthesised and post-synthesized. The distribution of aluminium over the crystallographic T-sites in zeolite Beta is a function of the Si/Al ratio showing the distribution is non-random. Moreover, template affects the average chemical shift of aluminum in different T-sites.

[1] Newsam, J. M.; Treacy, M. M. J.; Koetsier, W. T.; De Gruyter, C. B. *Proc. Royal Soc. of London, A.* **1998**, *420*, 375.
[2] Frydman, L.; Hardwood, J. S. *J. Am. Chem. Soc.* **1995**, *117*, 5367.
[3] Medek, A.; Harwood, J. S.; Frydman, L. *J. Am. Chem. Soc.* **1995**, *117*, 12779.

Physical Chemistry **280**

ATR-IR Modulation Excitation Spectroscopy: Application to diffusion and heterogeneous catalysis

Atsushi Urakawa, Ronny Wirz, Thomas Bürgi, Alfons Baiker

Institute for Chemical and Bioengineering, ETH-Hönggerberg, CH-8093 Zürich, Switzerland

ATR (Attenuated Total Reflection) -IR spectroscopy has been recognised as a valuable tool for studying solid-liquid interfaces relevant in heterogeneous catalysis and biology [1]. Recently, the possibilities and the sensitivity of the ATR technique have been enhanced in combination with MES (Modulation Excitation Spectroscopy) [2,3]. The detection technique in MES, PSD (Phase-Sensitive Detection), can not only improve the signal-to-noise ratio significantly but also give the possibility to separate overlapping signals and to study kinetics of different species.

Diffusion of molecules in a newly designed ATR-IR MES flow-through cell was studied by MES experiments and simulations. The diffusion behaviour of a fast diffusing molecule, acetonitrile, was compared with a slow diffusing molecule, hemoglobin, in water. The effective diffusion layer thickness could be estimated via the 'Diffusion layer model'. On the other hand, the 'Convection-Diffusion model' could well describe the flow behaviour and the diffusion of molecules in the cell. Furthermore, ATR-IR MES applications of catalytic solid-liquid interfaces are presented.

[1] U.P. Fringeli, D. Baurecht, M. Siam, G. Reiter, M. Schwarzott, T. Bürgi, P. Brüesch, *ATR Spectroscopy of Thin Films* in *Handbook of Thin Film Materials; H.S. Nalwa, Ed.* **2001**, *p 191*, vol 2.
[2] U.P. Fringeli, D. Baurecht, H.H. Günthard, *Biophysical Infrared Modulation Spectroscopy* in *Infrared and Raman Spectoroscopy of Biological Materials; H.U. Gremlich, B. Yan, Eds.* **2000**, *p143*.
[3] T. Bürgi, A. Baiker, *J. Phys. Chem. B* **2002**, 106, 10649.

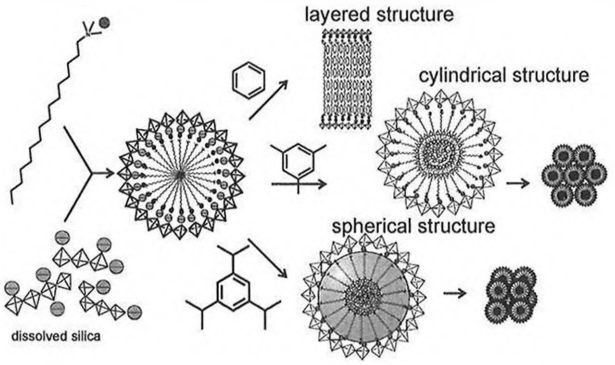
Physical Chemistry **281**

Swelling of templating micelles with substituted aromatic compounds

Marco Luechinger, Gerhard D. Pirngruber, Roel Prins

ETH Zürich, Institute for Chemical and Bioengineering, ETH Hönggerberg HCI, CH-8093 Zürich

Micelles of amphiphilic molecules can be enlarged or swelled by adding apolar organic molecules. We use these micelles as templates for the synthesis of mesoporous silica materials. By varying amount and nature of the swelling agent, size and shape of the pores can be regulated [1]. The materials serve as supports for catalysts and can also be used in chromatography.



The more apolar the swelling agents are, the larger is their tendency to reside in the core of the micelles. This increases the curvature of the micelles. As a consequence layered materials are obtained with benzene, cylindrical pores with mesitylene and spherical pores with triisopropylbenzene.

[1] B. Lindlar, A. Kogelbauer, P.J. Koyman, R. Prins, Microporous Mesoporous Mat. **2001**, 44-45, 89.

Physical Chemistry **282**

Selective targeting of cells with functionalized ABA triblock copolymer Nanocontainers

Samantha M. Benito, Pavel Broz, Cheelong Saw, Harald Heider, Patrick Hunziker and Wolfgang Meier*

Department of Chemistry, University of Basel, Klingelbergstrasse 80, 4056 Basel, Switzerland

Selective targeting of cells is nowadays a current topic of medical research due to the large negative impact of side effects of drugs in organs which are not the primary target of the drug. Therefore, more specific and selective delivery of drugs is desirable. As an alternative to the classical encapsulation with liposomes, more stable structures based on synthetic polymers have been developed recently in our group [1] in which synthetic nanocapsules or nanocontainers are obtained by the self assembly of ABA triblock copolymers [2]. Due to their higher mechanical stability, low protein binding and large choice of chemical modifications, this block copolymer nanocontainers (NC) are ideal candidates for controlled and sustained release of therapeutics. Active targeting can be facilitated when using specific receptors expressed by the target cells. Activated macrophage cells which expressed the scavenger receptor A1 (SRA-1) and SRA-1 transfected COS-7 cells were used as model cell lines. This receptor is responsible for the uptake of highly charged ligands. Therefore, as a model ligand polyguanylic acid (polyG), was used to facilitate the up take of the NCs. Biotinylated NCs were then coupled via avidin to biotinylated polyG ligands to produce active targeting drug delivery complexes. The biocompatibility and toxicity of such NCs was studied via cytotoxicity tests. NC uptake and cell selectivity have been followed via flow cytometry studies and confocal laser microscopy.

[1] C. Nardin, T. Hirt, J. Leukel and W. Meier, *Langmuir*, **2000**, *16*, 1035-1041.
[2] C. Nardin, J. Widmer, M. Winterhalter and W. Meier, *European Physical Journal E: Soft Matter*, **2001**, *4*, 403-410.

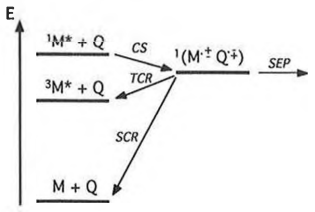
Physical Chemistry **283**

Heavy Atom Effect on the Charge Recombination Dynamics of Geminate Ion Pairs

Olivier Nicolet and Eric Vauthey

Dpt. of Physical Chemistry of the University of Geneva, Switzerland

The influence of a heavy atom on the dynamics of charge recombination (CR) of ions pairs in a polar solvent has been investigated using various ultrafast spectroscopic techniques [1]. Without heavy atom, the only CR pathway is that leading to the neutral ground state. With heavy atom substituted donors, CR to the local triplet state of the excited precursor is observed. Time constant for the triplet CR ranging from 400 ps to less than 10 ps, depending on the heavy atom and on the energy gap between the ion pair and the triplet state, have been measured. This heavy atom effect was observed with ion pair formed upon electron transfer quenching with driving force going from –0.15 eV to –0.6 eV, suggesting that these intermediates are in fact exciplexes.



A new scheme for producing free ions with a relative high yield using this effect and a secondary electron donor will also be presented.

[1] Olivier Nicolet and Eric Vauthey J. Phys. Chem. A (in print)

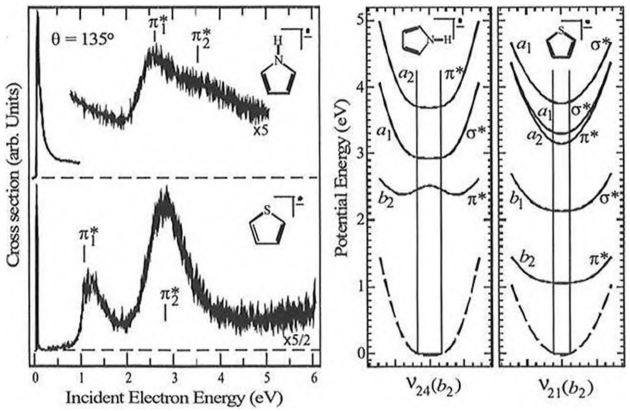
Physical Chemistry **284**

Properties of the π* and σ* States of the Pyrrole, Thiophene and Phenol Anion Determined by Electron Impact Spectroscopy

Tomáš Skalický, Nils Zimmermann and Michael Allan

Department of Chemistry, University of Fribourg, CH-1700 Fribourg

The selectivity of vibrational excitation by electron impact has been used to characterize the negative ion states of pyrrole, thiophene and phenol.



Excitation functions of the lowest energy out-of-plane vibrations and their potential curves are presented here as an example. The potential curves reveal a significant role of vibronic coupling in the electronic states of the pyrrole and thiophene anions which causes their double minimum or makes them very flat. The symmetry (b_2) of the vibrations is appropriate to couple either the (a_1) and (b_2) or (a_2) and (b_1) electronic states. Vibrational structure in the π_1* state of thiophene anion indicates a relatively long lifetime of this state.

Physical Chemistry **285**

Electron Spin Relaxation in Benzoyl and Acyl Type Radicals

Timofei Makarov, Henning Paul, Elena Bagryanskaya*

Institute of Physical-Chemistry, University of Zurich, CH-8057 Zürich, Swizerland

*International Tomography Center SB RAS, Novosibirsk, 630090, Russia

The electron spin-relaxation mechanism and its rate are important parameters, which determine the value of magnetic, isotope and spin effects in photochemical radical reactions, especially in viscous and micellar solutions.

Various conclusions on magnetic field effects and the spin dynamics in radical pairs were drawn assuming negligibly slow electron spin relaxation in benzoyl type radicals [1]. But actually, the relaxation times of these species are not known. Moreover, small acyl radicals are known to relax very fast due to a strong spin-rotation interaction [2].

In this work a sequence of three acyl radicals was investigated (benzoyl, 2,4,6-trimethyl-benzoyl and cyclohexanoyl) by time resolved EPR. Rather short electron spin-lattice relaxation times (100-400 ns) were obtained for benzoyl and 2,4,6-trimethyl-benzoyl radicals from the decay of the integral initial electron polarization to thermal equilibrium at different temperatures and viscosities. The relaxation is induced mainly by the spin-rotation mechanism arising from the internal rotation of the CO group and depends on the barrier of the rotation. The obtained results are explained in the frame of T.E. Bull's theory [3]. The value of the spin-rotation coupling for the internal rotation of the CO group in benzoyl radical has been obtained, $|C_\alpha| = 1670$ MHz.

[1] N.V. Lebedeva, E.G. Bagryanskaya, I.V. Koptyug, R.Z. Sagdeev, *J.Phys.Chem.* A **2001**, *105*, 4640.
[2] H. Paul, *Chem. Phys. Lett.* **1975**, *32*, 472.
[3] T.E. Bull, *J. Chem. Phys.* **1976**, *65*, 4802.

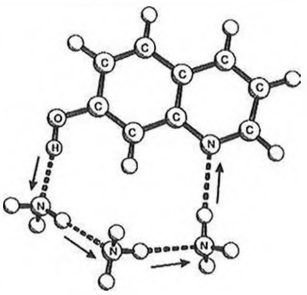
Physical Chemistry **286**

Structure and vibrations of a proton-transferring ammonia wire cluster

Carine Manca, Christian Tanner and Samuel Leutwyler

Department for Chemistry and Biochemistry, University of Bern, Freiestrasse 3, 3012 Bern

Excited state proton transfer (ESPT) reactions are involved in many chemical and biological processes. 7-hydroxyquinoline (7HQ) is a bifunctional hydrogen-bonding molecule acting both as H donor (at the OH group) and as a H acceptor (at the quinolinic N); its acidity and basicity simultaneously increase upon $S_1 \leftarrow S_0$ excitation [1-3]. In the accompanying communication, we show that ESPT occurs at a well-defined excess energy in the S_1 state of $7HQ{\cdot}(NH_3)_3$, the ammonia wire cluster acting as a proton relay:



Here we analyze the inter- and intramolecular vibronic excitations that characterize the Franck-Condon point on the S_1 state potential energy surface, as well as the "early" part of the ESPT reaction. The absorption and fluorescence spectra of $7HQ{\cdot}(NH_3)_3$ and $7HQ{\cdot}(ND_3)_3$ are compared with *ab initio* calculations of vibrational modes in the S_0 and S_1 states.

[1] A. Bach *et al.*, *J. Chem. Phys.* **2000**, *113*, 9032 (and citations therein).
[2] M. Meuwly *et al.*, *J. Am. Chem. Soc.* **2001**, *123*, 11446.
[3] S. Coussan *et al.*, *J. Chem. Phys.* **2003**, *118*, in press.

Physical Chemistry **287**

Proton transfer dynamics using dissociable force fields

Sven Lammers and Markus Meuwly*

University of Basel, Klingelbergstr. 80, 4056 Basel, Switzerland

Proton transfer processes play a fundamental role in chemistry and biology. We investigated the proton transfer dynamics in the protonated ammonia dimer $NH_3\cdots H^+\cdots NH_3$ and the protonated ammonia water dimer $NH_3\cdots H^+\cdots OH_2$ systems. Three-dimensional ab initio potential energy surfaces have been fitted by analytical potential functions in terms of a Legendre expansion and radial strength functions. A force field has been developed to study the intermolecular dynamics of the transfer events by molecular dynamics simulations.

The utility of using force fields that allow to describe bond formation and destruction compared to mixed QM/MM is discussed for systems that have previously been investigated[1,2] by computationally more expensive methods. In particular, the calculation of infrared spectra relevant to vibrational spectroscopy is discussed and the results are compared with experimental investigations[3].

[1] M. Meuwly and K. Karplus, *J. Chem. Phys.*, **2002**, *116*, 2572–2585
[2] M. Meuwly, A. Müller and S. Leutwyler, *Phys. Chem. Chem. Phys* **2003**, in print
[3] D.R. Borst, J.R. Roscioli, D.W. Pratt, G.M. Florio, T.S. Zwier, A.M. Müller and S. Leutwyler, *Chem. Phys.*, **2002**, *283*, 341–354

Physical Chemistry **288**

Diffusion of Polyacrylic Acids In Water and In Agarose Gel

Nicolas Fatin-Rouge, Nathalie Banerji, Jérôme Labille, Jacques Buffle.

Laboratory of Analytical and Biophysical Environmental Chemistry, University Sciences II of Geneva, 30 Quai E. Ansermet, CH-1211 Geneva 4

Polyacrylic acids have been subject to numerous investigations. They are model ligands for natural organic polyacids like fulvic and humic acids, which are expected to play a major role in many physicochemical processes in aquatic systems. The metal ion transport properties of such polyelectrolyte compounds are still under investigation, as separation of chemical and physical contributions remains unclear. On the other hand, agarose films are largely used in aquatic environmental chemistry as protecting layers for metal sensors.

In order to have a better understanding of polyacrylic acids behavior under different physicochemical conditions (ionic strength, pH, concentration, MW), we have investigated their diffusion properties in aqueous solutions and in agarose gels by Fluorescence Correlation Spectroscopy (FCS), thanks to its high sensitivity to measure diffusion coefficients of tracer solutes.

Physical Chemistry **289**

Tracer Diffusion Processes in Agarose Gels

Nicolas Fatin-Rouge, Jacques Buffle.

Laboratory of Analytical and Biophysical Environmental Chemistry, University Sciences II of Geneva, 30 Quai E. Ansermet, CH-1211 Geneva 4.

To investigate the diffusion processes in agarose gel, nanoparticles with size in the range 1 and 140 nm have been tested by means of Fluorescent Correlation Spectroscopy (FCS). The FCS technique is found to be very fruitful for such investigation based on its high sensitivity and selectivity, spatial resolution comparable to the pore size of the gel, and its ability to probe the gel with a wide range of diffusing nanoparticle sizes. The presence of fractal obstacles in gels perturbs the trajectories of diffusing particles, resulting in a general decreasing of the diffusion coefficients as compared to solutions. Previous studies have shown that anomalous diffusion in fractal media is a question of time or length scale and occurs generally at moderate scales. The fractal exponent of diffusion, d_w, which characterizes such behavior may be obtained from FCS measurements in a confocal volume, with dimensions comparable to the characteristic lengths of the gel. The variations of d_w with the reduced particle size give informations about the fractal nature of the porous network and its connectivity as seen by the diffusing particle. An anomalous diffusion has been evidenced on a large scale of diffusing particles' sizes, but changes to entrapped diffusion for particles size comparable to the average gel pore radius.

Physical Chemistry **290**

Active oxygen species formed by interaction of N_2O with iron zeolites

Gerhard D. Pirngruber, Pijus Kanti-Roy, Roel Prins

Institute for Chemical and Bioengineering, ETH Zürich, Wolfgang-Pauli Str. 10, CH-8093 Zürich, Switzerland

The selective oxidation of hydrocarbons to alcohols by insertion of oxygen into the CH-bond, like monooxygenases do, is a difficult task. With O_2, the cheapest and most common oxidant, high selectivities cannot be obtained because of the harsh conditions necessary for O_2-activation. N_2O is an alternative oxidant, which is more costly, but easier to activate. A Russian research group discovered that Fe-ZSM-5 creates a highly active surface oxygen species upon reaction with N_2O. This "α-oxygen" can oxidize benzene to phenol with high selectivity [1]. The behaviour was specific for iron and was only observed after pretreatment of the catalyst in steam and/or vacuum at high temperatures.
We studied the interaction of similar iron-zeolite catalysts (prepared by a different method) with N_2O. Catalysts pretreated at 673 K showed no sign of highly active oxygen species. Yet their activity in N_2O-decomposition increased if they were reduced and reoxidised with N_2O [2]. Thus, incorporation of oxygen from N_2O into the iron cluster increased its activity. Catalysts pretreated at higher temperatures (> 773 K) showed a very high activity during an induction period of 30 to 90 min. After that period activity reached steady state. Methane pulses abruptly stopped the high activity during the induction period, but did not affect the steady-state reaction. This shows that two different oxygen species were involved in the two processes. The oxygen species in the induction period was not inert towards O_2 and, thus, different from α-oxygen.

[1] G.I. Panov, A.S. Kharitonov, V.I. Sobolev, Appl. Catal. A **1993**, 98, 1.
[2] G.D. Pirngruber, J. Catal., in press.

Physical Chemistry **291**

Solvation Dynamics at Nanoparticle Surfaces

A. Tortschanoff[1], F. van Mourik[1], J. Moser[2], S. Steinemann[1], M. Chergui[1]

[1]IPMC, Université de Lausanne, BSP, CH-1015 Lausanne, Switzerland
[2]EPFL, CH-1015 Lausanne, Switzerland

Reactions and dynamics at solid-liquid interfaces are of fundamental importance in chemistry. In our ongoing study we used *femtosecond fluorescence upconversion* to record the fluorescence of chromophores adsorbed on ZrO_2 and TiO_2 surfaces in aqueous solution. This allows to calculate the solvation function $C(t) = \frac{\nu(t)-\nu(\infty)}{\nu(0)-\nu(\infty)}$, where ν(t), ν(0), and ν(∞) represent the maximum of the fluorescence spectrum at times t, zero, and infinity, respectively.

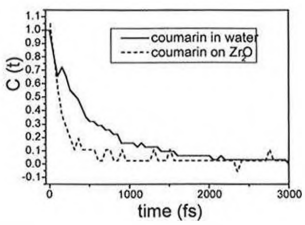


Fig. 1: Solvation function of coumarin 343 in water and adsorbed on ZrO_2

First results confirm the bimodal solvation dynamics in water [1]. The solvation response is much faster for adsorbed dyes, occurring on a sub-picosecond timescale, which is in agreement with previous studies [2].

[1] R. Jimenez, G. R. Fleming, P. V. Kumar and M. Maroncelli, *Nature* **1994**, 369 , 471-473
[2] D. Pant and N. Levinger, *Chem. Phys. Lett.* (1998), 292, 200-206; D. Pant, N. Levinger, *J. Phys. Chem. B* **1999**, 103, 7846-7852

Physical Chemistry **292**

In situ FTIR Investigation of Ethyl Pyruvate Hydrogenation in "Supercritical" Fluids

M.S. Schneider, J.-D. Grunwaldt, T. Bürgi, and A. Baiker

Institute for Chemical and Bioengineering, ETH Hönggerberg, CH-8093 Zürich

The platinum catalysed hydrogenation of ethyl pyruvate (EP) is a prominent and sensitive model reaction for enantioselective hydrogenations in supercritical fluids [1].
With a newly built experimental setup, we can measure *in situ* ATR-FTIR spectra of heterogeneous catalysts under working conditions, monitor the reaction progress by transmission spectroscopy, and simultaneously determine the phase behaviour by digital imaging at high pressures and temperatures [2].
Combining these methods uncovered the influence of the phase behaviour on the reaction performance and provided new insight on the catalytic solid / liquid interface.

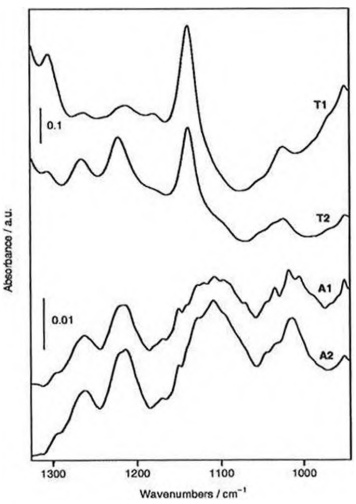


Fig. 1: Comparison of transmission- (marked T) and ATR-FTIR (marked A) spectra of the platinum catalysed hydrogenation of ethyl pyruvate in "supercritical" ethane at the beginning (marked 1) and the end (marked 2) of the reaction.

[1] R. Wandeler et. al., J. Catal. **200**, 377 (2001).
[2] M.S. Schneider et. al., Rev. Sci. Instrum., in press.

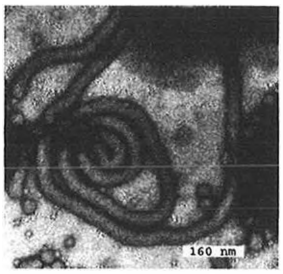
Physical Chemistry **293**

Nanotubes and vesicles from ABA-triblock copolymers : Biomimetic membranes for protein reconstitution

Julie Grumelard, Wolfgang Meier

Department Chemistry, University of Basel, Klingelbergst. 80, CH-4056 Basel, Switzerland

Amphiphilic block copolymers are used to prepare hollow nanotubes (see Fig.), giant vesicles and nanovesicles in aqueous solution. Similar to conventional lipid bilayers the polymer shells mimic biological membranes. Additionally they can be stabilised by cross-linking.



By attaching specific groups to their surface or by inserting membrane proteins (well known for transport or molecular recognition skills) into their shells we control the permeability and the targeting of such containers. Their biocompatibility and stability promise interesting applications in drug delivery or biosensors.

[1] A. Graff, M. Sauer, P. van Gelder and W. Meier; *Proc. Acad. Sci.* **2002**, 99, 5064.
[2] C. Nardin, J. Widmer, M. Winterhalter and W. Meier, *Eur. Phys. J. E* **2001**, 4, 403.

Physical Chemistry **294**

Luminescent Silver Sulfide Clusters

Claudia Leiggener, Dominik Brühwiler, and Gion Calzaferri

Department of Chemistry and Biochemistry, University of Bern, CH-3012 Bern, Switzerland

Silver sulfide particles of different size are synthesized in the cavities of zeolite A by exposing the Ag^+-exchanged dehydrated zeolites to H_2S. The size of the particles is determined by the initial Ag^+-concentration. The two smallest stable particles synthesized by this method are the Ag_2S molecule and the Ag_4S_2 cluster. Both particles show photoluminescence in the visible. The luminescence properties of the samples are studied as a function of the silver sulfide content, of the temperature and of the co-cations. By using the Ca^{2+}-exchanged form of zeolite A it is possible to synthesize silver sulfide-zeolite systems containing only Ag_2S monomers, Ag_2S and Ag_4S_2 in the same zeolite crystal, and mainly Ag_4S_2. After excitation of mixed Ag_2S-Ag_4S_2-zeolites with UV light energy transfer from the excited Ag_2S to Ag_4S_2 most likely occurs. Since the luminescence of Ag_2S and Ag_4S_2 show different temperature dependence over a large temperature range, these systems are potential materials for thermometry.

[1] Dominik Brühwiler, Claudia Leiggener, Stephan Glaus, and Gion Calzaferri, *J. Phys. Chem. B* **2002**, *106*, 3770.
[2] Gion Calzaferri, Claudia Leiggener, Stephan Glaus, David Schürch, and Ken'ichi Kuge, *Chem. Soc. Rev.* **2003**, *32*, 29.

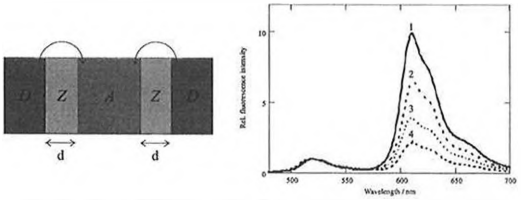
Physical Chemistry **295**

Tuning the Donor-Acceptor Distance in *Dye-Zeolite L* Antenna Systems

Claudia Minkowski and Gion Calzaferri

University of Bern, Freiestrasse 3, 3012 Bern, Switzerland

Zeolite L with its one-dimensional channel structure is a very versatile material to build artificial host-guest antenna systems. These channels can be either filled successively with joint but non-interacting donor dye molecules consecutively followed by acceptor dye molecules, or vice versa. By selectively exciting the donor, Förster energy transfer along the channel axis to the acceptor can be observed.
The energy transfer rate constant from an excited donor *D* to an acceptor *A* in such a *D,A-zeolite L* system depends amongst other things on the donor-acceptor distance d[1]. Therefore, this distance d is one means to control the energy transfer rate. We varied d by placing spacer molecules *Z* of different concentrations between the donor and acceptor molecules.



Left: Organization in a *D,Z,A-zeolite L* crystal. *Right:* Fluorescence spectra (scaled to the same height at the maximum of the donor emission at 520 nm) for four different kind of *D,Z,A-zeolite L* crystals with increasing spacer loadings for 1-4 after specific excitation of the donor at 460 nm[2].

[1] G. Calzaferri, M. Pauchard, H. Maas, S. Huber, A. Kathyr, T. Schaafsma, *J. Mater. Chem.*, **2002**, *12*, 1-13
[2] G. Calzaferri, S. Huber, H. Maas, C. Minkowski, *Angew. Chem.*, **2003**, in press

Physical Chemistry **296**

Liquid Phase Oxidation of Alcohols: Mechanistic Study over Bismuth-Promoted Palladium

Csilla Keresszegi, Jan-Dierk Grunwaldt, Tamas Mallat and Alfons Baiker

Institute for Chemical and Bioengineering, Swiss Federal Institute of Technology, ETH Hönggerberg HCI, CH–8093 Zurich, Switzerland

The aerobic oxidation of alcohols over supported noble metal catalysts offers an environmentally benign route for the synthesis of fine chemicals.[1] Several papers have been published on the promotion of Pt and Pd mainly by Bi and Pb.[2, 3] The origin of the promoting role of metals is, however, still debated, mostly due to the lack of *in situ* studies. Here we propose a new approach to clarify the role of promoters in the reaction mechanism: an *in situ* EXAFS analysis of the oxidation state of metals in Bi-Pd/Al_2O_3 during alcohol oxidation in a continuous-flow fixed-bed reactor.

A special technique was applied to deposit submonolayers of Bi adatoms onto the surface of Pd particles. The XAS studies revealed that both metals in Bi-Pd/Al_2O_3 were reduced to M^0 during dehydrogenation of 1-phenylethanol in He. In oxygen Pd and Bi remained in a reduced state and the catalyst was working with high activity as long as the O_2 supply was rate limiting, indicating a dehydrogenation mechanism. As soon as the rate of O_2 supply exceeded the rate of alcohol dehydrogenation, both Bi and Pd were oxidized concomitantly, leading to catalyst deactivation ("over-oxidation"). There was no sign of higher oxidation state of Bi relative to Pd. The positive influence of Bi adatoms on the reaction rate and selectivity cannot be attributed to (partially) oxidized Bi or to Bi leaching and homogeneous catalysis. Thus, we support the model of site-blocking effect[3] where the beneficial role of Bi is attributed to geometric blocking of the active sites.

[1] Besson, M., and Gallezot, P., *Catal. Today* **2000**, *57*, 127.
[2] Wenkin, M., Ruiz, P., Delmon, B., and Devillers, M., *J. Mol. Catal. A* **2002**, *180*, 141.
[3] Mallat, T., and Baiker, A., *Catal. Today* **1994**, *19*, 247.

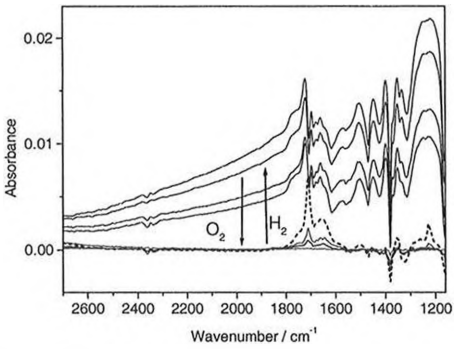
Physical Chemistry **297**

ATR spectroscopy of liquid phase Pd-catalyzed oxidation reactions

Ronny Wirz, Thomas Bürgi, Alfons Baiker

Institute of Chemical- and Bioengineering, ETH-Hönggerberg, HCI, CH-8093 Zürich, Switzerland

Catalyst activity in liquid phase oxidation reactions such as the selective oxidation of alcohols, strongly depends on the oxidation-state and the surface potential, which are difficult to measure for supported catalysts. Attenuated total reflection (ATR) infrared spectroscopy is shown to be a sensitive probe, which can sense simultaneously changes in the oxidation-state of supported Pd as well as adsorbed species and dissolved products.



The Figure shows ATR spectra recorded while flowing alternately hydrogen- and oxygen-saturated 2-propanol over a 5% Pd/TiO_2 catalyst. As hydrogen (oxygen) is admitted the absorbance increases (decreases) over the mid-infrared region due to changes in the optical constants caused by reduction (oxidation) of the catalyst.

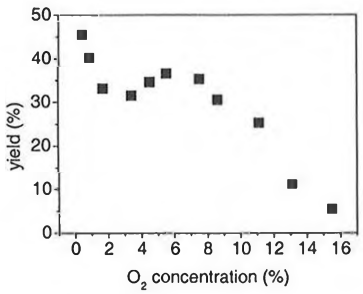
Physical Chemistry **298**

Selective Oxidation of Benzyl Alcohol to Benzaldehyde in "Supercritical" Carbon Dioxide

Matteo Caravati, Jan-Dierk Grunwaldt, Alfons Baiker*

Institute for Chemical and Bioengineering
ETH Hönggerberg, CH-8093 Zürich, Switzerland

"Supercritical" CO_2 is an attractive solvent for water insoluble alcohols oxidation with molecular oxygen. It is a cheap, non-flammable and nontoxic fluid, with tunable solubility for weakly polar alcohols [1]. The oxidation of benzyl alcohol over a commercial 0.5wt%Pd/Al_2O_3 catalyst in $scCO_2$ afforded benzaldehyde with 95% selectivity and a TOF of 1585h^{-1} at 80°C and 150bar. Parameter studies showed a strong dependence of the catalyst activity on temperature and oxygen concentration. Phase behaviour studies indicated that the increase in activity, which resulted in the high TOF, could be traced back to the fact that the reactor was operated under single phase conditions. High pressure *in situ* XAS uncovered that the palladium constituent was mainly in a (reduced) metallic state during alcohol oxidation, and that it was quite easily reduced and re-oxidized at 80°C by the reactants, alcohol and oxygen, respectively [2].



[1] G. Jenzer, M. S. Schneider, R. Wandeler, T. Mallat, A. Baiker, *J. Catal.* **2001**, 199, 141.
[2] J.-D. Grunwaldt, M. Caravati, M. Ramin, A. Baiker, *submitted for publication*.

Physical Chemistry **299**

Aggregates of substituted azacrown ether in organic phase

K. Wojciechowski, J. Buffle

Analytical and Biophysical Environmental Chemistry (CABE)
Department of Analytical Inorganic and Applied Chemistry, Sciences II
30 quai E. Ansermet, CH-1211 Genève 4, Suisse

Crown and azacrown ethers have been extensively used for ion recognition and transport purposes since 1960s. However the interfacial/aggregation properties of the crown ethers attracted relatively little attention so far, despite their usefullness in different extraction processes. One might expect that the presence of lipophilic alkyl chains attached to hydrophilic cyclic oligoether ring drastically increases surfactant properties of such (aza)crown ethers. At the same time their affinity to form aggregates in either aqueous or organic solutions increases. Gokel et al. shown that upon sonication the long alkyl chain (C_4-C_{18}) substituted diaza-18-crown-6 ethers may form micelles/vesicles of up to 450 nm in water [1].

As part of our mechanistic studies on the metal transport through permeation liquid membranes (PLM) we have investigated the aggregation of the carrier used in our PLM membranes: 1,10-didecyl-1,10-diaza-18-crown-6 (22DD) in both aqueous and organic phase. The aggregation during transfer of ions through PLM device might have a great impact on the mechanism of the transport of ions through such a device. Using interfacial tension measurements in toluene-water system we have shown that the 22DD is reasonably surface active, with c.m.c. equal to 0.17 mM. According to Ninham and Israelachvili's empirical formula, 22DD should have poor tendency to form inverted micelles in the organic phase. However in the range of carrier concentrations used for the PLM studies (2-100 mM) different types of inverted micelles exist in toluene, as well as in hexane, as shown by Fluorescence Correlation Spectroscopy (FCS). The former method, combined with Diffusion-Ordered NMR Spectroscopy (DOSY) has also been used to estimate the size of the aggregates in organic phase.

[1] S.L. De Wall, L. J. Barbour, G.W. Gokel, *J. Phys. Org. Chem.* **2001**, *14*, 383
[2] J. Israelachvili, *Intermolecular & Surface Forces. Ch. 17*, Academic Press, **2001**

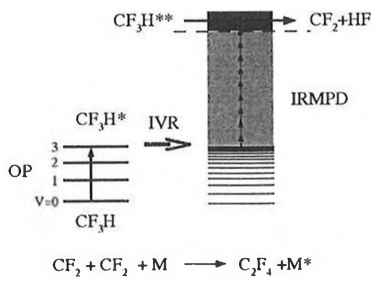
Physical Chemistry **300**

Overtone Preexcitation - Infrared Multiphotone dissociation approach for highly selective laser isotope separation

Mikhail N. Polianski, Oleg V. Boyarkin, Thomas R. Rizzo

Swiss Federal Institute of Technology, 1015 Lausanne, Switzerland

A new highly effective approach to Molecular Laser Isotope Separation (MLIS) - Overtone Preexcitation - Infrared Multiphoton Dissociation (OP-IRMPD) has been developed recently in our laboratory [1,2].



A detailed study of isotopically selective OP-IRMPD of CF_3H molecule (see figure) has been undertaken during the last years resulting in better understanding of the mechanism of the process. Accurate selection of the process parameters based on this understanding (sample pressure and temperature, preexcitation level, laser fluences and experiment timing) has resulted in a significant increase of the process performance.

[1] Monika Kowalzcyk. PhD thesis, Ecole Polytechnique Fédérale de Lausanne, Switzerland **2000**
[2] O. V. Boyarkin, M. Kowalzcyk, and T. R. Rizzo, *J. Chem. Phys.*, **2003**, *118(1)*, 93.

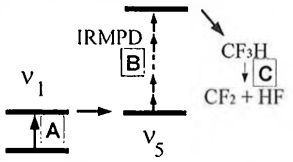
Physical Chemistry **301**

Isotopically selective IRMPD of vibrationally excited CF_3H

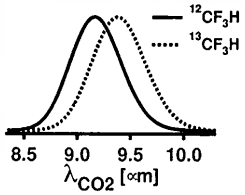
Richard Bossart, Oleg Boyarkin*, Mikhail Polianski, Thomas Rizzo

LCPM, Swiss Federal Institute of Technology, 1015 Lausanne

Infrared laser assisted photofragment spectroscopy (IRLAPS [1]) consists of exciting molecules by direct transition (A) with a first laser, and then by probing them with a CO_2 laser (B) ($\lambda \sim 9 - 10\mu m$) via IR multiple photon dissociation (IRMPD).



The fragments (C) are then detected either by laser induced fluorescence (LIF) or by mass spectrometry (MS). As the IRMPD step has different efficiencies for different isotopic species ($^{12}CF_3H \leftrightarrow {}^{13}CF_3H$), this scheme can be used for Laser Isotope Separation (LIS) [2]. This difference is due to an isotopic shift of the absorption spectra between the two species (see fig); the dissociation efficiencies can further be changed by including a time delay between the two lasershots allowing the molecules to undergo collisional relaxation. We present numerical and experimental studies of both the vibrational relaxation processes between and during the lasershots and also of the IRMPD step for CF_3H molecules pre-excited to $v_{CH} = 3$ ($\tilde{\nu} \approx 8,700cm^{-1}$).



[1] R.D.F. Settle, T.R. Rizzo, *J. Chem. Phys.*, **1992**, *97 (4)*, 2823.
[2] O.V. Boyarkin, M. Kowalczyk, T.R. Rizzo, *J. Chem. Phys.*, **2003**, *118 (1)*, 93.

Physical Chemistry **302**

PAMAM Dendrimers as Model System for the Deposition of Highly-Branched Polycations on Planar Substrate

R. Pericet Cámara, G. Papastavrou, and M. Borkovec

Laboratory of Colloid and Surface Chemistry, Department of Inorganic, Analytical and Applied Chemistry, University of Geneva, 1211 Geneva, Switzerland

The adsorption process of nanoparticles or polyelectrolytes on oppositely charged surfaces is of great importance in many industrial, environmental or biological processes. Simple nm-sized model systems like dendrimers, which allow for a well defined variation of different parameters such as size, charge and chemical composition are especially well suited to further elucidate the main driving forces involved in adsorption kinetics and steady state configurations. First results on the adsorption of high generation Poly(amidoamine) (PAMAM) dendrimers onto mica surfaces are presented. The lateral distributions of PAMAM-dendrimers were obtained by *ex-situ* measurements with Tapping Mode AFM. Besides adsorption kinetics for different bulk concentrations, the influence of ionic strength and dendrimer generation were examined. A preliminary quantitative description in the framework of random sequential adsorption (RSA) model reproduces the experimental data. The main conclusions are as follows. The amount of dendrimers adsorbed is diffusion limited and the surface coverage for long adsorption times does not depend on the dendrimer concentration. Surface coverage and interparticle distance (as determined by the pair-distribution functions) can be regulated by the ionic strength of the solutions.

Physical Chemistry **303**

State resolved methane chemisorption on nickel single crystal surfaces

D.C. Papageorgopoulos, P. Maroni, T.T. Dang, R.D. Beck and T.R. Rizzo

Laboratoire Chimie Physique Moléculaire,
Ecole Polytechnique Fédérale de Lausanne, CH-1015 Lausanne.

The role of vibrational excitation in assisting methane to overcome its relatively high barrier to dissociation on Ni(100) and Ni(111) has been investigated. Methane molecules were excited, by pulsed laser irradiation in a molecular beam, in specific ro-vibrational states prepared via overtone and combination band transitions and their reactivity has been probed by measuring state resolved sticking coefficients on the nickel single crystal. Vibrational energy placed in the first overtone of the antisymmetric C-H stretch (labelled $2\nu_3$) was found to enhance C-H bond scission, with reactivity increasing by a factor of 10000 – 100, depending on translational energy. This corroborates theoretical predictions that the reaction coordinate contains a significant contribution due to C-H stretch motion. On the other hand, the bending motion has not been found to be as effective, as seen from the dissociation probabilities of CH_4 excited in a nearly isoenergetic state containing bending (labelled $\nu_2 + \nu_3 + \nu_4$) Vibrational efficacies for the symmetric (ν_1) and antisymmetric stretch (ν_3) modes are also examined by looking at the reactivity of the $\nu_1+\nu_4$ and $\nu_3+\nu_4$ combination bands respectively and the state specificity for methane dissociation on Ni is discussed.

Physical Chemistry **304**

Femtosecond Time-Resolved Pump-Pump-Probe Studies on Photoinduced Bimolecular Electron Transfer Processes

B. Lang, S. Pagès and E. Vauthey
Department of Physical Chemistry, University of Geneva,
30 quai Ernest Ansermet, CH-1211 Geneva, Switzerland

The structure of the primary product of a bimolecular electron transfer (ET) has to change a lot between the moment of ET and the complete separation into free ions. Different configurations like *contact ion pair* and *loose-* or *solvent-separated ion pair* have been proposed as intermediates [1]. However, since the absorption spectra of these transient species resemble those of the corresponding free ions, these intermediates have not been identified directly so far. In other words, probing the electronic structure of the transients using conventional pump-probe techniques is not sufficient.
Thus, we have implemented a novel experimental set-up using a pump-pump-probe scheme with white light probing. It permits to investigate spectrally resolved ground state recovery and excited state dynamics of the transient species in real time at variable time delays after triggering the ET reaction by a UV pump-pulse. In this contribution we present first measurements on ground and excited state dynamics of the transient radical $Pe^{+\cdot}$ cation in acetonitrile after quenching of Pe in its S1 state by either trans-1,2-dicyanoethylene (fumaronitrile) or 1,4-dicyanobenzene (terephthalonitrile) and tetracyanoethylene.

[1] N. Mataga and H. Miyasaka, Adv. Chem. Phys, (1999), 107, pp 431

Physical Chemistry **305**

Coherence Phenomena in Ultrafast Light-Induced Charge Injection. Beyond Vibrationally Mediated Electron Transfer

Robert Huber,[1] Josef Wachtveitl [2] and Jacques-E. Moser [3]

[1] Lehrstuhl für BioMolekulare Optik, Ludwig-Maximilians-Universität München, Oettingenstr. 67, 80538 München, Germany
[2] Institut für Physikalische und Theoretische Chemie, Goethe Universität Frankfurt, Marie-Curie Str. 11, 60439 Frankfurt am Main, Germany
[3] Institut de Chimie Moléculaire et Biologique, Ecole Polytechnique Fédérale de Lausanne, 1015 Lausanne, Switzerland

Femtosecond transient absorption investigations were carried out on alizarin coupled onto colloidal TiO_2. This surface complex sensitizer/semiconductor system exhibits a superfast electron transfer (ET) with a time constant of ca. 6 fs upon photoexcitation [1]. Oscillatory patterns were observed in the transient signals recorded on the time scale of 100 fs - 1 ps, which indicate that vibrational coherence outlives ET in the reaction products. Detailed Fourier analysis of the oscillatory component and cross-comparison of measurements obtained with various dyes and nonreactive ZrO_2 particles allowed for mode-to-mode assignment of the main frequencies to defined vibrations in the dye ground-state and cation. Because charge separation takes place here much faster than any significant molecular motion, ET causes a fundamentally new regime of vibrational coherence. Experimental evidence was indeed found for the preparation of vibrational wavepackets by the ultrafast ET process itself. All ET theories are based on the assumption that the energies of the donor and the acceptor states are matched by energy fluctuations caused by the surrounding thermal bath. Here we show that the reverse case of coupling between ET and molecular vibrations occurs and that ET is not mediated by molecular oscillations but, on the contrary, generates a coherent superposition of vibrational eigenmodes.

[1] R. Huber, J.-E. Moser, M. Grätzel and J. Wachtveitl, *J. Phys. Chem. B*, **2002**, *106*, 6494-6499.

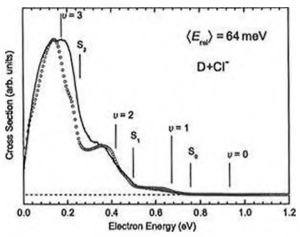
Physical Chemistry **306**

Spectra of electrons detached in associative collisions of Cl^- and Br^- with H and D

S. Živanov, M. Čížek[ϒ], J. Horáček[ϒ] and M. Allan

University of Fribourg, Department of Chemistry, Ch. du Musée 9, CH-1700 Fribourg, Switzerland
[ϒ]Institute of Theoretical Physics, Faculty of Mathematics and Physics, Charles University Prague, v Holešovičkách 2, 1800 Praha 8, Czech Republic

In this work we present data for associative electron detachment in low energy collisions between atomic H and D and halogen anions. Electron spectrum recorded for $D+Cl^-$ collisions for the 0.5 eV laboratory frame ion energy is presented in figure 1.



Two types of the structures appear in the spectra [1]. The first are at rotational onsets for the formation of the product molecules in the different vibrational states that are marked with vertical bars and corresponding value of v. The structures marked by S_i are result of the interchannel coupling effects. With a change of the ion energy positions of the 'S'-steps remain constant but with transfer from ^1H to ^2H it shifts towards higher electron energies.

[1] Živanov S, Allan M, Čížek M, Horáček J, Thiel F A U and Hotop H, *Phys. Rev. Lett.*, **2002**, *89*, 073201.

Physical Chemistry **307**

Fluorescence Correlation Spectroscopy As Local Probe of Agarose Gels Structure

Jérôme Labille, Nicolas Fatin-Rouge, Jacques Buffle.

Laboratory of Analytical and Biophysical Environmental Chemistry, University Sciences II of Geneva, 30 Quai E. Ansermet, CH-1211 Geneva 4.

Among the versatility of their applications, agarose gels are used as anti-fouling layer (~ 300 μm), deposited on electrochemical sensors working in environmental aquatic media, in order to prevent hydrodynamic variations and incoming of colloids and larger aggregates, while allowing quasi-free diffusion of small molecules. Agarose gel films are deposited upon cooling a hot aqueous polymer solution. A large rearrangement of agarose fibers occurs in a first time at the surface of the gel, characterized by a local over-concentration of polymer, due to dehydration. In a second time, introduction of the gel into an aqueous solution, induces a progressive hydration of the gel surface, tending to decrease polymer concentration in the interface.

A better knowledge of the respective gel/gas and gel/water interface structures is needed for a clear understanding and a better modeling of transport properties in this porous medium. Fluorescence Correlation Spectroscopy (FCS) was used in this aim, to measure the mobility of diffusing tracers in a micrometer-confocal volume inside the gel. The agarose fiber density distribution was probed orthogonally to the gel surface.

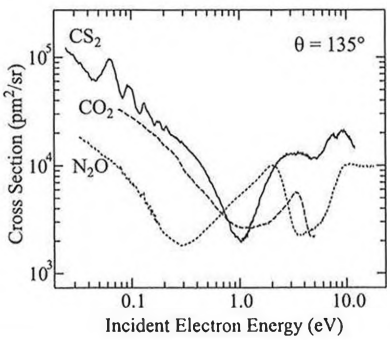
Physical Chemistry **308**

Measuring Data for Electron Driven Chemistry

Michael Allan

Department of Chemistry, University of Fribourg, chemin du Musée 9, CH-1700 Fribourg, Switzerland

Electron driven chemistry refers to chemical processes induced by impact of free electrons. It occurs in the upper atmosphere and in technological plasmas, widely used in the fabrication of integrated circuits and other industrial areas. The elementary processes are measured in a crossed molecular and electron beam apparatus and the results are expressed as cross sections.



The measuring technique has been substantially improved in Fribourg, mainly at very low energies, particularly relevant in the technological plasmas. The improved instrumentation permitted the discovery of sharp structures in the cross sections in CO_2, N_2O and CS_2, assigned as vibrational Feshbach resonances in the former two cases, and as high vibrational levels of the bound valence state of CS_2^- in the latter case.

Physical Chemistry **309**

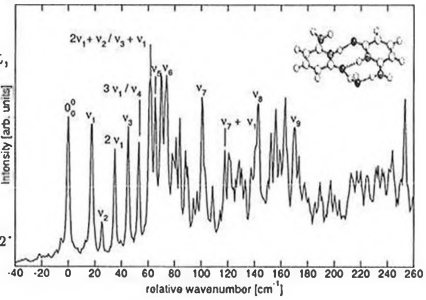
Microhydration of a Guanine dimer analogue

Roman Leist, Andreas Müller, and Samuel Leutwyler

Departement für Chemie und Biochemie, Universität Bern
Freiestrasse 3, CH-3012 Bern

The 2-amino-6-pyridone dimer, $(2A6P)_2$, provides a model for the guanine dimer.[1] Mass-selected $S_1 \leftarrow S_0$ vibronic spectra of the supersonically cooled H_2O solvated $(2A6P)_2$ dimer were measured by resonant two-photon ionization (R2PI) spectroscopy.

For $(2A6P)_2 \cdot H_2O$ all six intermolecular dimer vibrations (buckle, propeller twist, stagger, opening, shear, and stretch motions), as well as the low frequency H_2O out-of-plane wag, have been identified in the electronic excited state.



The R2PI spectra of $(2A6P)_2 \cdot (H_2O)_2$ show vibronic transitions, indicating C_i symmetry of this cluster.

Assignment of the vibronic bands in both spectra were based of excited state *ab initio* calculations, which are in good agreement with the experimental data.

[1] Nir E., Kleinermanns K., de Vries M.S., *Nature*, **2000**, *408 (6815)*, 949.

Physical Chemistry **310**

Surface Reactivity of Vibrationally Excited Molecules prepared by Stimulated Raman Pumping

R. D. Beck*, P. Maroni, D.C. Papageorgopoulos, T. Rizzo, T. T. Dang

Laboratoire de Chimie Physique Moleculecaire (LCPM)
Swiss Federal Institute of Technology, 1015 Lausanne, Switzerland

Recent progress in our laboratory has enabled state resolved measurements of gas-surface reactivity using pulsed laser preparation of specific rovibrational eigenstates [1]. In these experiments, we prepare CH_4 in the $2\nu_3$ state (antisymmetric C-H stretch overtone) via direct overtone excitation. However, infrared excitation is limited by the optical selection rules to vibrations with a nonzero dipole derivative. In order to extend our state resolved reactivity measurements to totally symmetric vibrational states, we intend to make use of stimulated Raman excitation. Here, two laser sources interact coherently with the molecule when their frequency difference matches the frequency of a Raman active mode. Due to the small Raman cross sections, high power pulsed laser beams are required for efficient Raman pumping. We use the second harmonic (532nm) of an injection seeded Nd:YAG laser as pump and generate the proper Stokes beam by stimulated Raman scattering in a specially designed Raman amplifier, seeded by a tunable dye laser. The system consists of a two meter long gas cell filled with up to 50 bar of the Raman active medium and includes internal gas circulation via a series of axial fans to avoid thermal lensing and optical breakdown. Currently, the system is used to prepare CH_4 in the symmetric stretch ν_1 vibration to measure its reactivity on Ni(100) and Ni(111) for comparison with recent measurements for $CH_4(\nu_3)$[2]. The question if ν_1 or ν_3 is more efficient in activating the dissocitative chemisorption of CH_4 on nickel has been addressed by recent calculations [3,4] and our measurement will provide stringent tests of these theoretical results.

[1] Schmid et al, J.Chem. Phys. 2002, **117**, 8603.
[2] Juurlink, L.B.F., et al., *Phys. Rev.Lett.* 1999, **83**, 86.
[3] Halonen, L., S. et al. *J. Chem. Phys.*, 2001, **115**, 5611.
[4] Milot, R., and A.P.J. Jansen, *Phys. Rev. B*, 2000, **61**, 5657.

Physical Chemistry **311**

2-Aminopyridine·2-Pyridone: N-H stretch vibrations of a Watson-Crick analogue of Adenine·Uracil

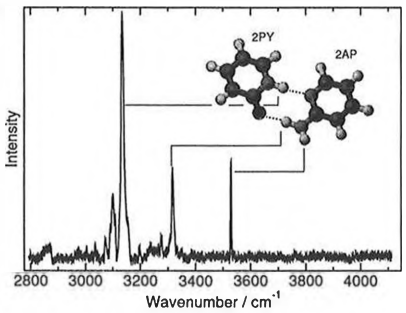
Andreas Müller, Jann A. Frey, and Samuel Leutwyler

Departement für Chemie und Biochemie, Universität Bern
Freiestrasse 3, CH-3012 Bern

The three N-H stretch vibrations of supersonically cooled 2-aminopyridine·2-pyridone (2AP·2PY) have been investigated by fluorescence-dip infrared (FDIR) laser spectroscopy.

2AP·2PY provides a hydrogen bonding topology analogous to the Watson-Crick structure of the adenine·uracil or adenine·thymine dimers.[1]

The two hydrogen bonded and the free N-H stretching vibrations are identified from FDIR spectra of 2AP·2PY (Figure) and of the corresponding singly and doubly deuterated dimers and by comparison to *ab-initio* calculations.



To discuss effects of hydrogen bonding on the N-H stretch vibrations involved in the intermolecular interaction, the FDIR spectra of the individual monomers (2PY and 2AP) have been recorded and are compared to the dimer spectra.

[1] A. Müller,F. Talbot, and S. Leutwyler, *JACS*, **2002**, *124(48)*, 14486-14494.

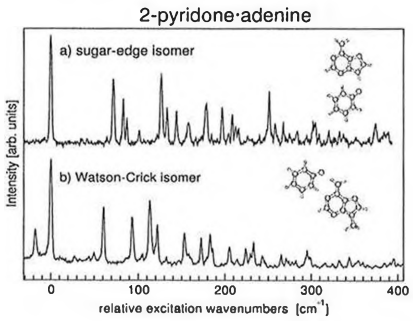
Physical Chemistry **312**

R2PI spectra of 2-pyridone·adenine Watson-Crick base pair

Jann A. Frey, Andreas Müller and Samuel Leutwyler

Departement für Chemie und Biochemie, Universität Bern,
Freiestrasse 3, 3012 Bern

2-pyridone (2PY) is a close hydrogen bonding analogue of uracil and thymine [1]. PW91/6-311++G(d,p) *ab initio* calculations show the 2PY·adenine (2PY·A) dimer bound through the sugar-edge to be the predominant isomer in the gas phase. Mass selected 2C-R2PI spectra (a) of this dimer were measured in a supersonic expansion.



The biologically more relevant Watson-Crick A·2PY dimer was synthesized by blocking the sugar edge with a methyl group. The 2C-R2PI spectra of this species (b) reveal different intermolecular vibrational frequencies in the S_1 state, such as opening, shearing and stretching motions. These are in good agreement with *ab initio* CIS calculations.

[1] A. Müller et al., *JACS*, **2002**, *124*, 14486.

313

EPR and DFT studies of the one electron reduction compounds of phosphinine derivatives

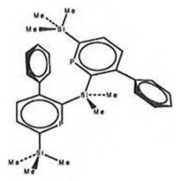
Laurent Cataldo[1], Sylvie Choua[1], Cosmina Dutan[1], Theo Berclaz[1], Pascal LeFloch[2], Michel Geoffroy[1]

[1]University of Geneva, 30 Quai Ernest Ansermet, 1211 Geneva, Swizerland
[2]Ecole Polytechnique, 91128 Palaiseau Cedex, France

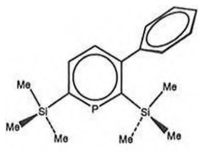
DFT calculations were performed for estimating hyperfine couplings and spin density distribution for both a reduced phosphinine ring and a two-phosphinines-containing-system (A) in the presence of a counter ion. The theoretical hyperfine tensors for the monophosphinine radical anion are in good agreement with the experimental values measured by EPR spectroscopy for $B^{\bullet-}$.

The chemical reduction at 200K of A on a K mirror leads to a EPR spectrum composed by 2 subspectra: the first one shows the same feature as the liquid solution spectrum of $B^{\bullet-}$. The second one is characterized by a coupling with 2 equivalent ^{31}P nuclei which suggests the formation of an intramolecular P-P bond. The experimental hyperfine values for the reduced bisphosphinine are rationalised by DFT calculation by assuming that two reduction products are formed for A. The first one is localized on a single phosphinine ring whereas the second species - delocalised on the two rings - corresponds to the first step in the formation of a P-P bond.

The ratio of the two reduced species is found to be dependent upon the reduction method.



A



B

Physical Chemistry 314

Electronic Solvation Dynamics in Supercritical Fluids

A. Cavina, P. Larregaray and M. Chergui

Institut de Physique de la Matière Condensée, Université de Lausanne, BSP, CH-1015 Lausanne, Switzerland

Over the past few years, renewed interest for supercritical fluids (SCFs) has appeared due to their remarkable properties and the many applications with benign fall outs for the environment (Green chemistry). However, the atomic level details of the solvation properties of SCFs are still not clearly understood. In particular, strong local density fluctuations near the critical point are expected to have a significant influence on the structure and dynamics of a solute in solutions.

In our laboratory, we have developed an original method that takes advantage of low-n Rydberg states of the NO molecule in order to investigate in real-time the ultrafast medium response in rare gas solids[1]. This approach is based on the fact that Rydberg states are extremely sensitive probes of the medium structure and dynamics because of their extended orbitals. Here, we present an extension of this approach to non polar SCFs. Results on the steady-state (absorption and fluorescence) spectroscopy of the lowest Rydberg states of NO in SCF Ar and preliminary femtosecond pump-probe measurements on the same system are presented and analysed by means of molecular dynamics simulations which provide insight into the details of the structural rearrangement dynamics.

[1]C. Jeannin, M. T. Portella-Oberli, S. Jimenez, F. Vigliotti, B. Lang and M. Chergui, Chem. Phys. Letters 316 (2000) 51-59

Physical Chemistry 315

Interactions between polyelectrolyte covered surfaces examined by direct force microsocopy

G. Papastavrou[+,•], L. Kirwan[+], C. Helm[•], M. Borkovec[+]

[+]Department of Inorganic, Analytical and Applied Chemistry, University of Geneva, Quai Ernest Ansermet, 30, 1211 Geneva 4 / Switzerland, * Applied Physics, University of Greifswald, 17487 Greifswald, Germany

The interaction forces between polyelectrolyte covered particles or the adhesion between colloidal particles and surfaces mediated by polyelectrolytes are of great interest due to the wide application of polyelectrolytes as dispersion stabilizers or surface modification agents.
Here poly(ethyleneimine) or poly(styrensulfonate) have been adsorbed on solid substrates and colloidal particles attached to AFM cantilevers allowing the direct measurement of interaction forces and adhesion. The long-range electrostatic forces have been shown to agree with DLVO-theory at different salt conditions. However in contrast to unmodified surfaces the adhesion behaviour can be not described in simple terms especially due to the occurrence of adhesion events on the single molecule level. First results indicate a strong dependence on salt concentration. Besides surface modification with polyelectrolytes also Au-coated AFM tips modified with different alkyl thiols can be employed to study the above effects. For instance the interaction forces between COOH-terminated AFM-tips and a PSS-coated surface show a strong dependence on pH-value.

Physical Chemistry 316

Ultrafast Intramolecular Dynamics after Overtone Excitation of CH_3I, C_2H_5I, CF_3CHFI, and C_7H_8 Molecules in the Gas Phase and in Solution

Vitaly Krylov, Max Nikitchenko, Martin Quack and Georg Seyfang

Lab. Phys. Chemie, ETH Zurich, Wolgang-Paulistrasse 10,8093 Zurich

The rapid redistribution of vibrational energy within a molecule is a central aspect of statistical rate theories, which assume that redistribution proceeds faster than reaction. Intramolecular energy redistribution defines the lifetime of vibrationally excited states and, thus, the times during which specific vibrational excitation can control the outcome of a chemical reaction [1]. To study intramolecular vibrational energy redistribution (IVR) two different approaches are possible and have been implemented successfully, resulting in a large number of insights into the dynamics of vibrationally excited molecules. IVR can be investigated directly by time resolved, and possibly state resolved pump-probe experiments [2,3], or can be deduced indirectly from high resolution IR-spectra [1,4]. It is of interest to apply both approaches to the same molecule.
We have applied sensitive, time delayed UV-absorption spectroscopy to measure IVR in the gas phase after overtone excitation of the CH-stretching vibration. Intramolecular relaxation times τ_1 between 3 - 7 ps have been found for CH_3I, C_2H_5I, CF_3CHFI, and C_7H_8. For CH_3I an additional short relaxation of 250 fs has been measured. In the liquid phase IVR is followed by fast collisional energy transfer to the solvent molecules. Assuming a two step kinetic mechanism two relaxation times τ_1 and τ_2 could be obtained from the fit to the experimental data. The relaxation time τ_2 obtained from the fit vary between 10 - 30 ps.

[1] M.Quack, *in 'Mode Selective Chemistry', J.Jortner, R.D.Levine, and B.Pullman (eds.), page 47-65, Kluwer Academic Publishers (1991), Chimia* **2003**, *57, 147*
[2] T.Elsaesser,W.Kaiser, *Ann.Rev.Phys.Chem.*, **1991**, *42*, 83.
[3] D.Bingemann,A.M.King,F.F.Crim, *J.Chem.Phys.*, **2000**, *113*, 5018.
[4] M.Quack, *Ann.Rev.Phys.Chem.*, **1990**, *41*, 839.

Physical Chemistry **317**

Ultrafast UV-visible and infrared study of the cyano complexes of myoglobin and hemoglobin I from Lucina Pectinata

J. Helbing ,J. Bredenbeck, P. Hamm
Physikalisch-Chemisches Institut, Universität Zürich, CH-8057 Zürich, Switzerland

L.Bonacina, F.Chaussard, A.Gonzalez-Gonzalez, F.van Mourik and M. Chergui
Institut de Physique de la Matière Condensée, Université de Lausanne, CH.1015 Lausanne, Switzerland

R. Pietri, C. Ramos-Alvarez, J. Lopez-Garriga
Chemistry Department, University of Puerto Rico, PO.Box 9019, Mayagüez, P.R. 00680, Puerto Rico

The monomeric hemoglobin I (HbI) found in the clam Lucina pectinata carries on its biological function in the ferric state, and shows an unusual distribution of aromatic residues surrounding the heme distal position. To explore the role of these residues in stabilizing ligands, and to investigate the dissociation and recombination mechanisms of a ligand-heme complex in the ferric state, femtosecond transient absorption measurements in the UV-visible region were performed on HbI-CN and on the cyanomet complex of myoglobin (MbCN) from horse skeletal muscle. MbCN was also studied by transient infrared spectroscopy, which allows to monitor the dynamics of the ligand directly.
While we observe very similar dynamics to that reported for ferrous Mb species, the ferric ground state heme and the use of the C-N stretching vibration as a local probe of electronic structure in our study, give important new insights into the ultrafast dynamics of heme proteins.
In particular, metal to ring electron transfer processes, which have been invoked in connection with ferrous hemes, but are very unlikely in the ferric complexes, do not seem to play an important role in the electronic relaxation of excited heme proteins. On the other hand, there are clear indications that electronic relaxation is not complete before the full recovery of MbCN with an approximately 4 ps time constant. This suggests that the state often referred to as HbI* in ferrous systems, is an electronically excited state, rather than a vibrationally hot ground state. In the light of these results, different relaxation channels will be presented and discussed.

Physical Chemistry **318**

Water vapor, temperature and wind patterns observations above the Aletsch Glacier (Switzerland)

I. Balin[1], C. Higgins[4], R. Nessler[1,5], I. Serikov[3], V. Simeonov[1], G. Larcheveque[1], S. Brobovnikov[3], M. Parlange[1,4], Y. Arshinov[3], B. Calpini[1,2] and H. van den Bergh[1]

[1] Swiss Federal Institute of Technology, Lausanne - CH
[2] SwissMeteo, Payerne - CH
[3] Institute of Atmospheric Optics, Russian Academy of Sciences, Tomsk
[4] Johns Hopkins University, Baltimore - US
[5] Paul Scherer Institute, Willigen - Switerland

The climate changes studies are continuously asking for more related atmospheric measurements. In this context new horizontal and vertical simultaneous profiles of atmospheric temperature and water vapor were performed in July 2002 and April 2003, at the Swiss Jungfraujoch High Alpine Observatory (3600 m) above the Aletsch glacier using a Raman lidar. Water vapor retrieval is based on the Raman vibrational shifts (N_2 at 387 nm and H_2O at 408nm) excited with 355nm while the temperature is obtained using the pure rotational Raman spectra around 532 nm excitation. Complementary measurements of wind patterns and temperature were systematically taken "in situ" on the glacier using sonics anemometers starting from April 2003. These results are presented and discussed here.

[1] G. Larchevêque, I. Balin, R. Nessler, P. Quaglia, V. Simeonov, H. van den Bergh, and B. Calpini, "Development of a multiwavelength aerosol and water vapor lidar at the Jungfraujoch Alpine Station (3580m ASL) in Switzerland", *Appl. Opt.*, **2002**, 41, pp.2781-2790

[2] I. Balin, G. Larchevêque, P. Quaglia, V. Simeonov, H. van den Bergh, and B. Calpini,: "Water vapor vertical profile by Raman lidar in the free troposphere from the Jungfraujoch Alpine Station", *Advances in Global Change Research*, , **2002** 10, Kluwer Academic Publishers,pp.123-138

Structure of zeolites under catalytic conditions **319**

Jeroen A. van Bokhoven

Inst.f.Chemie-/Bioingenieurwissenschaft. ETH Hönggerberg
HCI E 115, CH-8093 Zürich

Zeolites are important catalysts in industry and they are used for a wide variety of reactions, such as cracking and isomerization of alkanes, and for the production of fine-chemicals. Although these catalytic systems are extensively studied, very often structure – activity relations are lacking. Relevant techniques that determine the catalyst structure under catalytic conditions are unavailable. In many reactions, the aluminum atom is associated with catalytic activity, making an experimental tool that detects the aluminum coordination in a controlled atmosphere extremely valuable. Conventional methods often fail in providing such data.
This presentation describes the development of in-situ XAFS for low Z elements to study the Al K-edge in catalytic samples [1]. Progress in instrumentation and data-interpretation were made, enabling measurements in controlled gas-atmosphere at elevated temperature. A thorough theoretical interpretation of the XANES spectra using FEFF8 enables assignment of different aluminum coordinations in the samples. The measurements on zeolitic samples have shown that the aluminum coordination is a subtle function of the precise measurement conditions [2], which has consequences for interpretation of catalytic data. Moreover, measurements at extreme high temperature show the appearance of unique spectral features that can be attributed to a unique aluminum coordination previously not observed using ex-situ techniques.

[1] van der Eerden, A.M.J., van Bokhoven, J.A., Smith, A.D., Koningsberger, D.C. *Rev. Sci. Instrum.* **2000** *71*, 3260.
[2] van Bokhoven, J.A., van der Eerden, A.M.J., Koningsberger, D.C. *J. Am. Chem. Soc. Accepted.*

320

Photodissociation spectra of biological molecules in the gas phase

Anthi Kamariotou, Mercier Sébastien, Antoine Milon, Oleg Boiarkin, Rainer Beck,Thomas Rizzo
EPFL, Laboratoire de Chimie Physique Moléculaire
1015 Lausanne

We are currently developing a technique that combines electrospray ionization ion trap mass spectrometry and laser spectroscopy to measure electronic spectra of naturally occurring chromophores in molecules of biological interest.

The molecular ions produced by electrospray ionization, are pre-trapped in a hexapole ion guide for tens of milliseconds, before the ions of interest are mass selected in a first quadrupole, and subsequently irradiated by a UV laser pulse in an octupole ion guide. We monitor the depletion of the parent ion due to photodissociation as a function of the wavelength of the UV laser.

This poster will present the depletion electronic spectra measured so far, for the protonated positively charged amino acid: Tryptophane and for Tryptophane containing oligopeptides that can still be dissociated by a UV laser pulse in the timescale of our experiment.

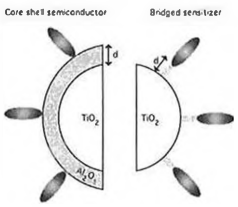
Physical Chemistry **321**

Distance Dependence of Dye Sensitizer to Semiconductor Photoinduced Electron Transfer Kinetics

Bernard Wenger*, Michael Graetzel, and Jacques-E. Moser

ICMB, Ecole Polytechnique Fédérale de Lausanne, CH-1015 Lausanne

In dye-sensitized solar cells, electron injection from a dye adsorbed onto a wide bandgap nanocrystalline semiconductor (e.g. TiO_2) is a crucial step. One of the key issues in the field is the mechanism of long-range electron transfer. Femtosecond transient absorption spectroscopy was used to study the distance dependence of the electron transfer from a ruthenium(II) complex to modified TiO_2 mesoporous thin films. The contribution of the electronic factor to charge transfer kinetics was highlighted by varying the transfer distance and the electronic properties of the sensitizer. Modulation of the electron transfer distance was achieved employing two different approaches:



TiO_2 mesoporous films were coated with Al_2O_3 layers using chemical vapour deposition. This technique allowed a controlled growth of insulating layers whose thickness was ranging from 0.6 to 6 nm. The damping factor coefficient for the injection reaction was estimated at $\beta = 0.1\ \AA^{-1}$. A series of $Ru^{II}(tpy)(NCS)_3$ complexes which terpyridyl ligands contain spacer groups was synthesized. For these dyes the damping factor is $0.25\ \AA^{-1}$. The rather weak dependence of ET rates upon the distance suggests electronic coupling is mediated by C-C bonds of spacer bridges and oxide insulating solid layers. These results justify the use of similar strategies for improving dye-sensitized solar cells and provide an insight on the tunnelling processes for electron transfer through the bandgap of an insulator material.

Computational Chemistry **322**

Basic Terms of Band Structures – Introduction by Means of an Interactive Mathcad Course

Marc Meyer, Stephan Glaus, and Gion Calzaferri
University of Bern, Freiestr. 3, 3012 Bern

The concept of energy bands with the related terms and ideas is often unfamiliar to chemistry students. We have therefore created a Mathcad course consisting of about 60 pages, which acts as an introduction to the theory of band structures. The course, which has been successfully used for several years, explains the concepts and application of energy bands, translational symmetry, crystal orbitals, Bloch functions, wave vectors, the Peierls distortion, density of states (DOS), crystal orbital overlap population (COOP) and Brillouin zones. [1]
We present an easily comprehensible flow from elementary quantum mechanics to research level topics such as the quantum-chemical description of three dimensional crystalline systems. At the end of the course, the student is capable and encouraged to use the research-level tight binding program package BICON-CEDiT, which includes oscillator strength calculations and many more options. [2]

[1] M. Meyer, S. Glaus, and G. Calzaferri *J. Chem. Edu.* **2003**, in press
[2] M. Brändle, R. Rytz, S. Glaus, M. Meyer, and G. Calzaferri *BICON-CEDiT*, Available at http://www.dcb.unibe.ch/groups/calzaferri

Computational Chemistry **323**

A DFT study of mixed valent hexacyano Mn(II/III) cluster

Cédrick RAUZY*, Mohammed SAHNOUN and Claude A. DAUL

Département de Chimie CH 1700-Fribourg, Switzerland

The study of cluster involving mixed valent compound species is not trivial. Indeed we face the challenging problem by studying the following Prussian blue like compound: $Mn_a^k[Mn_b(CN)_6]_l$ 6 H_2O which is designed to be magnetic and transparent. We propose to tackle the problem by first investigating a mononuclear complex $[Mn(CN)_6]^{z-}$ and then go further by studying the binuclear $[Mn_2(CN)_{11}]^{z-}$ cluster. We have first to face of:

- the oxidation state of the manganese (Mn^{II}, Mn^{III} and Mn^{IV}), the N-coordination or the C-coordination of the cyano bridging ligand,
- the low spin or high spin electronic configuration.

The results of the mononuclear complex bring clearly the proof that high spin configuration is more stable with N-coordination ligand and low spin is more stable with C-coordination ligand. That is we studied the dimer $[Mn_2(CN)_{11}]^{z-}$ for z equal to 5 or to 6: and this for several Mn-Mn oxidation states (II-IV, III-III, IV-II, III-II, II-III) as well as for low spin or high spin configuration in each cases. The results obtained so far confirms what chemical intuition suggest, namely a succession of Mn^{II} (HS link to nitrogen atom) and Mn^{III} (LS link to the carbon atom) for the most stable configuration. Using Amsterdam Density Functional program package performed the calculation. The geometry used was the experimental one.

Computational Chemistry **324**

A Hybrid Time-dependent Density Functional/ Molecular Mechanics investigation of Aminocoumarins in Solution.

M. Sulpizi[1], P.Carloni[2] and U. Röthlisberger[1]

[1]*Lab. of Comp. Chem. and Biochemistry, Federal Institute of Technology (EPFL) CH-1015 Lausanne, Switzerland.*
[2]*SISSA, International School for Advanced Studies, 34013 Trieste, Italy.*

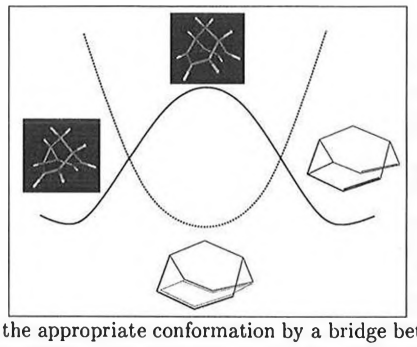
Here we present a hybrid quantum mechanical /molecular mechanics approach (QM/MM) [1] to describe the optical properties of the aminocoumarins. In the approach we use the solute (aminocoumarin) is treated at the first principle level with TDDFT [2], while the solvent is treated with a classical force field. We study the ground and first excited state properties of C151, C35 and C153, three aminocoumarins for which a homogeneous set of experimental data is available [3]. Our approach is able to quantify the effects of the chemical substituents, and to reproduce the spectral redshift due to the increased alkylation at the amino position. Solvation is described through a molecular approach, which permits to include in the calculations the effects due to the inhomogenities of the solvent. We can quantitatively reproduce the solvent spectral redshift for water and acetonitrile [4], two solvents which present a different behavior in terms of H-bond properties. Our approach is able to give quantitative information on the spectral shifts and opens the way to treatment of more complex systems, such as chromophore in a protein environment. Moreover, it can be a useful instrument for the rational design of new compounds with specific spectral properties.

[1] Laio, A.; *et al J.Phys.Chem.B* **2002**, *106*, 7300-7307
[2] M.E. Cassida, in Recent advances in density functional methods, (Vol. 1), Ed. D.P. Chong (World Scientific, Singapore, **1995**); Hutter J., (**2003**), J Chem. Phys. 118 (9): 3928-3934.
[3] Gustavsson, T *et al J.Phys.Chem.A* **1998**, *102*, 4229-4245.
[4] M. Sulpizi, P.Carloni and U. Rothlisberger, sunmitted to *PCCP*.

Computational Chemistry **325**

A C_{2v} symmetrical Barbaralane

Barbara Kirchner
Institute of Physical Chemistry, University of Zürich, 8057 Zürich



Barbaralane is one of the fluxional molecules that undergo a degenerate Cope rearrangement. It was proposed by W. von E. Doering that the activation barrier of the Cope rearrangment is lower in barbaralane than in 3,4-homotropilidene as barbaralane is already fixed in the appropriate conformation by a bridge between the two corner carbon atoms. The objective is to lower this barrier even further, i.e. to transform the double-minimum system into one with a single minimum by increasing the symmetry by changing from a C_s- to a more symmetric (C_{2v}) ground-state structure. We employed density functional theory (DFT) (with the functional BP86 and the hybrid functional B3LYP), second-order Møller–Plesset (MP2) perturbation theory, the coupled-cluster models CCSD and CCSD(T), and multi-configuration SCF calculations to gain a consistent picture independent of the method. A candidate for the first barbaralane derivative with "inverse" barrier according to the different methods [1] will be presented.

[1] M. Reiher, B. Kirchner Angew. Chem. 41 (2002), 3429–3433.

Computational Chemistry **326**

Theoretical and Experimental Study of the Racemisation of a [4]Heterohelicenium Cation

Delphine Bas[1], Christelle Hersc[2], Jérôme Lacour[2], Pierre-Yves Morgantini[1], Jacques Weber[1] and Tomasz Adam Wesolowski[1].

University of Geneva
Department of Physical Chemistry[1] and Organic Chemistry[2],
30 quai Ernest Ansermet, CH-1211 Geneva 4, Switzerland

The study of the racemisation process for the 1,13-dimethoxy-5,9-dipropyl quinacridium cation was carried out using density functional theory (DFT) calculations. This molecule, involved in the synthesis of novel triazaangulenium dyes of high chemical stability is a chiral [4]helicenium[1].
The racemization barrier of this quinacridinum cation was determined using the Gaussian98[2] package applying the BP86[3-5] exchange-correlation functional with the DZVP basis set.
By this method the minimum and saddle point structures of the compound were optimised and characterized by frequencies calculations. The determination of these stationary points provides us some highlight concerning the pathway for the interconversion of the two enantiomers (racemization). The racemization barrier was first estimated as the energy difference between the minimum and the transition state without the zero point correction. The theoretical value obtained from our calculations (36 kcal/mol) is in good agreement with the experimental barrier (40 kcal/mol).

[1] Laursen B. W.; Krebs F. C. *Angew. Chem. Int. Ed.* **2000**, *39*, 3432.
[2] Frisch M. J.,*et al.*,Gaussian 98 (Revision A.7),Gaussian, Inc., Pittsburgh PA,1998.
[3] Becke A. D. *Phys. Rev. A* **1988**, *38*, 3098.
[4] Perdew J. P. *Phys. Rev. B* **1986**, *33*, 8822.
[5] Bas D.; Morgantini P.-Y.; Weber J.; Wesolowski T. A. *Chimia* **2003**, *57*, 173.

Computational Chemistry **327**

Theoretical investigation of infrared spectra and pocket dynamics of photodissociated carbonmonoxy myoglobin

David R. Nutt, Markus Meuwly*

University of Basel, Klingelbergstr. 80, CH-4056 Basel, Switzerland

Experimentally, agreement seems to have been reached on the events following photodissociation of CO from Mb [1]. Strong evidence has been presented for the presence of a docking site within the protein, adjacent to the heme, which reversibly binds CO [2]. The spectroscopic signature of a CO molecule within the docking site is a splitting of 10 cm^{-1} in the infrared adsorption band of CO.

Although Molecular Dynamics (MD) simulations support the notion of a docking site [3], the experimentally observed splitting has not yet been reproduced. We will present results from MD simulations of photodissociated carbonmonoxy myoglobin which use a new fluctuating charge model for CO [4]. From these simulations, infrared spectra are calculated which are found to reproduce the experimentally observed splitting. In addition, the splitting can be directly attributed to the presence of two different (opposite) orientations of CO within the so-called docking site, as proposed experimentally. Rotational and translational energy barriers are also calculated and found to give good agreement with experiment. The temperature dependence of the infrared spectrum of photodissociated CO is also investigated.

[1] A. Ostermann, R. Waschipky, F.G. Parak, G.U. Nienhaus, *Nature*, **2000**, *404*, 205.
[2] M. Lim, T.A. Jackson, P.A. Anfinrud, *Nature Struct. Biol.*, **1997**, *4*, 209.
[3] J. Meller, R. Elber, *Biophys. J.*, **1998**, *74*, 789.
[4] D.R. Nutt, M. Meuwly, *Biophys. J.*, submitted.

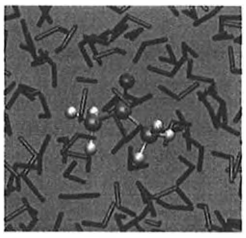
Computational Chemistry **328**

QM/MM Molecular Dynamics Study of the Absorption and Fluorescence Spectra of Acetone in Water

Ute F. Röhrig, Ursula Röthlisberger*

Laboratory of Computational Chemistry and Biochemistry, Swiss Federal Institute of Technology, 1015 Lausanne (Switzerland).

We present a hybrid Car-Parrinello quantum mechanical/molecular mechanical (QM/MM) approach that is capable of treating the dynamics of molecular systems in electronically excited states in complex environments [1]. The potential energy surface in the excited state is described either within the restricted open shell Kohn-Sham (ROKS) formalism [2] or within time-dependent density functional theory (TDDFT) [3]. As a test case, we apply this technique to the study of the solvent effects on the ground state and on the first excited singlet state of acetone in water.



The excited state energies calculated with ROKS are red shifted by a constant value compared to the TDDFT results, while the relative variations of the excitation and the fluorescence energy for different configurations are in very good agreement. Excited state dynamics carried out with ROKS yield the relaxation of the solute and the rearrangement of the solvent structure on a picosecond timescale. The experimentally observed blue shift of the excitation energy in going from gas phase to condensed phase is correctly reproduced, as well as the observed Stokes shift. This study opens the way for application of our methodology to more complex systems, e.g. photoactive proteins.

[1] A. Laio et al., *J. Chem. Phys.* **2002**, *116*, 6941.
[2] I. Frank et al., *J. Am. Chem. Soc.* **1998**, *108*, 4060.
[3] J. Hutter, *J. Chem. Phys.* **2003**, *118*, 3928.

Computational Chemistry **329**

Models for Time Dependent Density Functional Theory in Chemistry and Biochemistry

I. Tavernelli, U. Röthlisberger

Ecole Polytechnique Fédèrale de Lausanne, Laboratoire de Chimie et Biochimie computationelle, 1015 Lausanne, Switzerland

Our interest is focused on *ab initio* (first principle) molecular dynamics methods (MD) for the simulation of molecules both in the ground state (GS) and in the excited state (ES). Since the main goal of our research is the study of molecules in their biological environment, the implementation of these techniques in the hybrid QM/MM [1] (quantum mechanics / molecular mechanics) code constitutes an important progress. Conventional *ab initio* ground state MD is based on the 'on the fly' computation of energies and energy derivatives (forces). The most commonly used methods are the so-called Born-Oppenheimer (BO) and the Car-Parrinello dynamics [2] both implemented in the CPMD code. DFT methods for the calculation of excited state properties (energies and oscillator strengths) and excited state dynamics are also available. These are based either on the restricted open-shell Kohn-Sham method (ROKS) or on time-dependent linear response density functional theory (TDDFT)[3]. In this work we present an implementation of real time TDDFT in which the time dependent Schrdinger-like equation for the Kohn-Sham (KS) orbitals is used to propagate the states. The method is applied to the calculation of spectra for molecules and to the computation of ground/excited state *ab initio* MD within the (mean field) Ehrenfest approximation.

[1] A. Laio, J. VandeVondele and U. Röthlisberger, *J. Chem. Phys.*, **2002**, *116*, 6941.
[2] R. Car, M. Parrinello, *Phys. Rev. Lett.*, **1985**, *55*, 2471.
[3] J. Hutter, *J. Chem. Phys.*, **2003**, *118*, 3928.

Computational Chemistry **330**

Driving Chemical Reactions via Biases of Molecular Orbitals

Leonardo Guidoni and Ursula Röthlisberger

Laboratory of Computational Chemistry and Biochemistry, Swiss Federal Institute of Technology EPFL, CH-1015 Lausanne, Switzerland

Chemical reactions often have activation barriers too high to be observed on the typical picosecond timescale of first-principles dynamics simulations. To overcome these barriers, a bias potential can be applied, that drives the system toward the transition states [1,2]. Thermodynamic properties of the unbiased system, such as the height of the activation barrier, can thus be derived from the shorter biased dynamics runs. Density Functional Theory offers useful concepts, such as Kohn-Sham molecular orbitals, hardness, electronic and nuclear Fukui functions [3,4], that could be used for the construction of appropriate electronic bias potentials for accelerating rare reactive events.
In the present contribution, we developed a bias potential scheme, which depends only on the electronic states of the reactive system. Different reaction pathways and bias potentials for accelerating prototypical reactions are investigated.

[1] J. VandeVondele and U. Röthlisberger, *J.A.C.S., in press* **2002**.
[2] R. Vuilleumier and M. Sprik, *Chem. Phys. Lett.* 365, 305 **2002**.
[3] R.G. Pearson, *Chemical Hardness: Application from Molecules to Solids*, Wiley & Sons, New York **1997**.
[4] R. Vuilleumier and M. Sprik, *J. Chem. Phys.* 115, 3454 **2001**.

Computational Chemistry **331**

Ab Initio QM/MM Calculations of Dihydrofolate Reductase

O.A. von Lilienfeld-Toal*, Leonardo Guidoni*, Peter Cummins†, Jill E. Gready†, Ursula Röthlisberger*

* Ecole Polytechnique Fédèrale de Lausanne, Laboratoire de Chimie et Biochimie Computationelle, 1015 Lausanne, Switzerland
† Computational Proteomics and Therapy Design Group, John Curtin School of Medical Research, Australian National University, Canberra ACT 2601, Australia

Ab initio quantum mechanical and molecular mechanics (QM/MM) studies of dihydrofolate reductase (DHFR) have been carried out. We have used the recently developed hybrid method for plane wave based QM/MM Car-Parrinello calculations [1] in order to investigate the hydride-ion transfer step in the enzymic reduction of dihydrofolate (DHF). We compare our results to former computational investigations of DHFR using classical mechanics and semiempirical QM/MM studies [2]. Furthermore, we present first results for the use of systematically optimized linking dummy atoms which truncate the QM region [3]. The systematic optimization of the analytic pseudopotentials [4] for the dummy atoms is carried out within the framework of linear response implemented in CPMD [5, 6].

[1] A. Laio, J. VandeVondele and U. Röthlisberger, *J. Chem. Phys.*, **2002**, *116*, 6941.
[2] P.L. Cummins, S.P. Greatbanks, A.P. Rendell, J.E. Gready, *J. Phys. Chem. B*, **2002**, *106*, 9934.
[3] O.A. von Lilienfeld-Toal, D. Sebastiani, I. Tavernelli, U. Röthlisberger, to be submitted to *J. Chem. Phys.*.
[4] S. Goedecker, M. Teter, J. Hutter, *Phys. Rev. B*, **1996**, *54*, 1703.
[5] Car-Parrinello Molecular Dynamics code, `http://www.cpmd.org`, CPMD, Copyright IBM Corp 1990-2001, Copyright MPI für Festkörperforschung Stuttgart 1997-2001.
[6] A. Putrino, D. Sebastiani and M. Parrinello, *J. Chem. Phys.*, **2002**, *112*, 7102.

Computational Chemistry **332**

Theoretical Investigations on Azotobacter Vinelandii Ferredoxin I: Effects of Electron Transfer on Protein Dynamics

Markus Meuwly

Department of Chemistry, University of Basel, Klingelbergstrasse 80, CH-4056 Basel

Proteins containing iron-sulphur clusters play important roles in biological systems. One example includes aconitase where iron-sulphur centers are involved in cluster degradation, conversion, or redox processes.[1] The iron-sulphur clusters are important as structure-determining entities and because the clusters can accept, release, shift and store electrons. Recently, the coupled electron-proton transfer involving a [3Fe-4S] cluster in the Azotobacter vinelandii protein Ferredoxin I (FdI) has been investigated in some detail.[2] The protein contains two iron-sulphur clusters, one of which ([3Fe-4S]) is believed to play a central role in the electron-coupled proton transfer. The main conclusions from the experimental investigations concerned the role of the Asp15 residue.
We present results of structural, energetic and dynamical studies of FdI for the native and mutant forms.[3,4] In particular, the possibility of water-assisted electron coupled proton transfer is examined. Molecular dynamics simulations show that water molecules are dynamically stable near the [3Fe-4S] cluster for tens of ps. Calculations for the native protein and a mutant (D15E) in which the Asp15 is replaced by a Glu15 are compared. In the case of the D15E mutant water is less likely to escape from the region around the [3Fe-4S] cluster than for the native protein. This finding suggests an alternative mechanism for the electron coupled proton transfer and could explain, in part, the lower rate constant experimentally observed for the mutant.

[1] H. Beinert, M. C. Kennedy and C. D. Stout, *Chem. Rev.*, **1996**, *96*, 2335.
[2] K. Chen, J. Hirst, R. Camba, C. A. Bonagura, C. D. Stout, B. K. Burgess and F. A. Armstrong, *Nature*, **2000**, *405*, 814.
[3] M. Meuwly and M. Karplus, *Faraday Discuss.*, **2003**, *124*.
[4] M. Meuwly and M. Karplus, *Biophys. J.*, **2003**, *submitted*.

Computational Chemistry **333**

The effect of the choice of the basis set on the results of the minimization of the total energy bi-functional $E[\rho_1,\rho_2]$.

Marcin Dulak, Tomasz A. Wesolowski

Univ. of Geneva, 30 quai E.-Ansermet, CH-1211 Geneva 4, Switzerland

The minimization of the Hohenberg-Kohn energy functional ($\min_\rho E[\rho]$) can be formulated equivalently as the minimization of the bi-functional $E[\rho_1,\rho_2]$, ($\min_{\rho_1}\min_{\rho_2} E[\rho_1,\rho_2]$), where ρ_1,ρ_2 are electron densities of two interacting subsystems [1]. For a given $\rho_2(\mathbf{r})$, the minimum of $E[\rho_1,\rho_2]$ is obtained using the one-electron Kohn-Sham-like equations with the following embedding effective potential [3]:

$$V^{emb} = V^{emb(KSCED)}[\mathbf{r},\rho_1,\rho_2] = -\sum_{\alpha}^{N_2}\frac{Z_\alpha}{|\mathbf{r}-\mathbf{R}_\alpha|} + \int\frac{\rho_2(\mathbf{r}')}{|\mathbf{r}'-\mathbf{r}|}d\mathbf{r}' + \frac{\delta E_{xc}[\rho]}{\delta\rho_1}\Big|_{\rho=\rho_1+\rho_2} - \frac{\delta E_{xc}[\rho]}{\delta\rho}\Big|_{\rho=\rho_1} + \frac{\delta T_s^{nad}[\rho_1,\rho_2]}{\delta\rho_1},$$

where $T_s^{nad}[\rho_1,\rho_2] = T_s[\rho_1+\rho_2] - T_s[\rho_1] - T_s[\rho_2]$.
The minimization of $E[\rho_1,\rho_2]$ has been recently implemented into the computer program deMon [2]. Compared to our earlier implementation [4], in which only atomic orbitals of the s, p, and d type could be used, the deMon implementation uses also f and g functions. In this work, we analyze various properties of several weakly bound intermolecular complexes (interaction energy, energy components, orbital energies, and dipole moment), derived from the minimization of $E[\rho_1,\rho_2]$. The effect of the choice of the atomic basis sets is discussed in detail.

[1] P. Cortona, *Phys. Rev. B*, **1991**, *44*, 8454.
[2] A. Koester et al., Program deMon (version 0.1, March 2002), Copyright by National Research Council, Ottawa, Canada
[3] T.A. Wesolowski and A. Warshel, *J. Phys. Chem.*, **1993**, *97*, 8050.
[4] T.A. Wesolowski and J. Weber, *Chem. Phys. Lett.*, **1996**, *248*, 71.

Computational Chemistry **334**

Theoretical Study of Neutral and Cationic Clusters Involving Phenol

F. Tran, T. A. Wesołowski

Department of Physical Chemistry, University of Geneva, 1211 Geneva 4, Switzerland

Geometry and interaction energy of clusters $Ph^{(+)}$–L (L=Ar, N_2,...) involving neutral and cationic phenol were determined using the density functional theory formalism based on electron density partitioning KSCED [1][2], applying a GGA type of approximation for the exchange-correlation and nonadditive kinetic energy components of the total energy bifunctional [3]. For the neutral complexes, the interaction energies range from 1 kcal/mol for the Ph–Ar complex to about 10 kcal/mol for the Ph–NH_3 complex. For any ligand L the interaction energy is stronger for the cationic case than for the neutral one. Comparison is made with experimental values and the KSCED method is shown to give interaction energies in good agreement with the experimental ones.

[1] P. Cortona, *Phys. Rev. B* **1991**, *44*, 8454.
[2] T.A. Wesołowski, A. Warshel, *J. Phys. Chem.* **1993**, *97*, 8050.
[3] T.A. Wesołowski, *J. Chem. Phys.* **1997**, *106*, 8516.

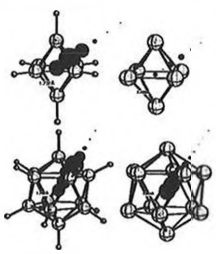
Computational Chemistry **335**

Do Antiaromatic Inorganic Clusters Exist ?

J. Bohmann[a], Z. Chen[b,c], C. Corminboeuf[d], T. Heine[c], B. King[b], P.v.R. Schleyer[b,c], J. Weber[d]

[a]Department of Chemistry, Texas Lutheran University, Seguin, Texas 78155 USA. [b]Department of Chemistry and Center for Computational Quantum Chemistry , University of Georgia, Athens, Georgia 30602 USA. [c]Institut für Organische Chemie, Universität Erlangen-Nürenberg, Henkestr. 42, Erlangen, D-91054, Germany, [d]Department of Physical Chemistry, University of Geneva, 30 quai Ernest-Ansermet, CH-1211, Genève 4, Switzerland, [e]Institut für Physikalische Chemie, Technische Universität Dresden, D-01062 Dresden, Germany

As shown by detailed nucleus-independent chemical shift (NICS) analyses of the contributions of each molecular orbital (MO-NICS)[1], the very recently reported gas-phase all-metal $Al_4Li_3^-$ anion[2] and its relatives are *aromatic* rather than antiaromatic. The paratropic four π electron contribution is overcome by the predominating effects of σ-aromaticity. However, true antiaromatic all-metal clusters do exist, as for example Zintl compounds such as Sn_6^{2-}. Zintl compounds include also high-symmetry borane and silicon clusters. Entirely unlike the aromatic closo $B_nH_n^{2-}$ borane dianions, the isoelectronic Si_6^{2-} and Si_{12}^{2-} are antiaromatic. Their O_h and I_h symmetries are responsible, as the other deltahedral silicon dianion clusters do not exhibit this behavior. These high symmetries prevent mixing among the degenerate lone pair and skeletal orbitals; this leads to the paratropic behavior shown.



[1] Heine, T.; Corminboeuf, C.; Schleyer, P. v. R.; Seifert, G.; Reviakine, R. Weber, J. *submitted*.
[2] Kuznetsov, A.R.; Birch, K. A.; Boldyrev, A.I.; Li, X.; Zhai, A.I., Wang, L. S. *Science* **2003**, *300*, 622.

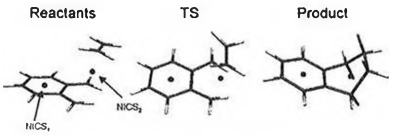
Computational Chemistry **336**

Change of aromaticity along a Diels-Alder reaction path

Clémence Corminboeuf[a], Thomas Heine[b], Jacques Weber[a]

[a]Department of Physical Chemistry, University of Geneva, Switzerland, clemence.corminboeuf@chiphy.unige.ch
[b]Institut für Physicalische Chemie, Technische Universität Dresden, D-01062 Dresden

The new MO-NICS analysis[1] provides detailed informations of single molecular orbitals contribution to aromaticity and complements nicely the other indices of aromaticity.



O-quinodimethanes are highly reactive in the presence of dienophile because a Diels-Alder cycloaddition reestablishes a benzoid ring which results in aromatic stabilization. The degree of aromaticity of this benzoid ring along the geometries of the Diels-Alder reaction path and the role of the π orbitals is studied by density-functional in terms of orbital shape, energies and magnetic aromaticity contributions[2]. ^{13}C NMR and MO-NICS calculations have shown that the aromatic character of the benzoid ring is increasing along the reaction path, especially between transition state and formation of the product, even though the number of π orbitals is dropping from five for the reactants to three for the product.

[1] Heine, T.; Corminboeuf, C.; Schleyer, P. v. R.; Seifert, G.; Reviakine, R. Weber, J. *submitted*.
[2] Corminboeuf, C.; Heine, T.; Weber, J. *Org. Lett.* . **2003**, *5*, 1127.

Computational Chemistry **337**

Density Functional Theory study for bonding of Carbon monoxide and Carbon dioxide to Alkali Metal cations in ZSM5 zeolite.

Delphine Bas[1], Jacques Weber[1] and Tomasz Wesolowski[1]

Department of Physical Chemistry[1]
University of Geneva, 30 quai Ernest Ansermet,1211 Geneva 4, Switzerland

The interaction between carbon monoxide and alkali cation in ZSM5 zeolite can provide useful indications for understanding intra-zeolite processes. The different modes of coordination of this probe molecule are characterized by the change in CO stretching frequency and intensity.[1] In a previous study[2], it has been shown that the interaction between the CO molecule and the alkali cation zeolite through the C-end gives rise to a blue shift of this frequency in good agreement with experimental data. The purpose of this work was to study the O-bonding coordination mode of the carbon monoxide in cation zeolite and to compare the calculated shifts obtained with the red shift experimentally observed.

In our calculations, the electron density of the cation-probe molecule complex (ρ_1) is derived from variational calculations in which the first-principles based orbital-free embedding potential is expressed as a load function depending on the electron density ρ_1 and the electron density ρ_2 of the cluster cut out the periodic zeolite's framework. The calculations were carried out for the three alkali cations (Li^+, Na^+, K^+) and the red shift characterizing the interaction through the O-end, observed experimentally was also reproduced by our calculations. The coadsorption[4] of carbon monoxide trough the O-end and the C-end, as well as the adsorption of the carbone dioxide[5] in ZSM5 zeolite, were also considered and the first results reveal a good agreement with the experimental observations.

[1] C.O. Areán, A.A. Tsyganenko, E.E. Platero, E. Garrone, A. Zecchina, *Angew. Chem. Int. Ed.*, **1998**, *37*,3161.
[2] T.A. Wesolowski, A. Goursot, J. Weber; *J. Chem. Phys.*, **2001**, *115*, 4791.
[3] T.A. Wesolowski, A. Warshel, *J. Phys. Chem.*, **1993**, *97*, 8050.
[4] C. Otero Arean, O.V. Manoloiva, M. Rodriguez Delgado, A.A. Tsyganenko and E. Garrone, *Phys. Chem. Chem. Phys.*, **2001**,*3*,4187.
[5] B. Bonelli, B. Civarelli, B. Fubini, P. Ugliengo, C. Otero Arean and E. Garrone, *J. Phys. Chem. B*, **2000**, *104*, 10978

Computational Chemistry **338**

Determination of Absolute Configuration using Vibrational Circular Dichroïsm DFT Calculations: A [4]Heterohelicenium Cation

Delphine Bas[1], Christelle Herse[2], Thomas Bürgi[3], Jérôme Lacour[2], Pierre-Yves Morgantini[1], Jacques Weber[1] and Tomasz Adam Wesolowski[1].

University of Geneva
Department of Physical Chemistry[1] and Organic Chemistry[2],
30 quai Ernest Ansermet, CH-1211 Geneva 4, Switzerland

Institute of Chemical and Bioengineering[3], ETH-Hönggerberg, HCI D-127, Wolfgang Pauli Strasse 10, CH-8093 Zürich, Switzerland

Density functional theory calculations (DFT) calculations were performed to determine the absolute configuration of the 1,13-dimethoxy-5,9-dipropyl quinacridium cation. This molecule, involved in the synthesis of novel triazaangulenium dyes of high chemical stability is a chiral [4]helicenium[1]. The theoretical study reported in this work was carried out to determine the absolute configuration of the separated enantiomer using vibrational circular dichroïsm spectroscopy.

This theoretical study was carried out using the Gaussian98[2] package applying the BP86[3-5] exchange-correlation functional with the 6-31G** basis set. Infrared and VCD spectra were calculated using the DFT/GIAO methodology and assigned. The comparison between the experimental results and the theoretical calculations reveals a good agreement[6] that allows us to attribute the absolute configuration for the carbenium ion.

[1] Laursen B. W.; Krebs F. C. *Angew. Chem. Int. Ed.* **2000**, *39*, 3432
[2] Frisch M. J.,*et al.*,Gaussian 98 (Revision A.7),Gaussian, Inc., Pittsburgh PA,1998
[3] Becke A. D. *Phys. Rev. A* **1988**, *38*, 3098
[4] Perdew J. P. *Phys. Rev. B* **1986**, *33*, 8822
[5] Bas D.; Morgantini P.-Y.; Weber J.; Wesolowski T. A. *Chimia* **2003**, *57*, 173
[6] Herse C.,*et al. Angew. Chem. Int. Ed., accepted for publication*

Computational Chemistry **339**

Neural Networks for Structure Elucidation of Oligosaccharides

Matthias Studer, Andreas Stoeckli, Beat Ernst*

Institute of Molecular Pharmacy, Pharmacenter of the University of Basel
Klingelbergstrasse 50, CH-4056 Basel, Switzerland

Artificial Neural Networks (ANNs) provide a potent classification tool for the extraction of the relevant information from the flood of data easily accessible. They allow the analysis of the fundamental cohesions, which are hardly never obvious.

The elucidation of chemical structures based on spectroscopic data is a promising application of ANNs. The challenge of establishing reliable correlations between different types of spectra (IR, MS, ^{1}H-NMR, ^{13}C-NMR, etc.) attracted the attention of numerous groups working on computerized structure elucidation processes [1].

The aim of the project is to develop an ANN for the analysis of oligosaccharides, containing glucose, galactose and mannose. In a first attempt an ANN is established with a commercial platform [2] and trained with ^{13}C-NMR data. This allows the identification of individual carbohydrate components of oligosaccharides and their linkage-pattern. In a second step, a user-friendly application, equipped with an overall graphical user interface is developed.

The rapid on-line control of the carbohydrate composition is a prerequisite for the production of therapeutic glycoproteins. With an ANN a contribution to low-cost and rapid analysis of the carbohydrate components of glycoproteins may be possible.

[1] J. Zupan, J. Gasteiger, *Neural Networks in Chemistry and Drug Design*, 2nd Ed. Weinheim, Wiley-VCH **1999**, 293-315;
B. Meyer et al., *Science* **1991**, *251*, 542-544.
[2] StatSoft, Inc. (**2003**). STATISTICA für Windows [Software-System für Datenanalyse] Version 6. www.statsoft.com

Computational Chemistry **340**

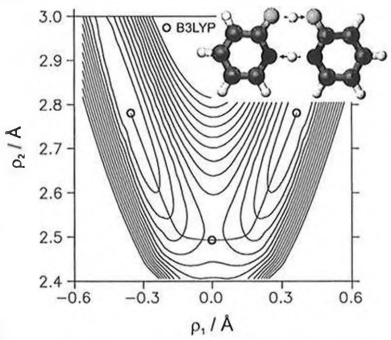
Dynamics and infrared spectra of DNA base-pair analogous

Andreas Müller,[1] Markus Meuwly,[2] and Samuel Leutwyler[1]

[1]Departement für Chemie und Biochemie, Universität Bern
Freiestrasse 3, CH-3012 Bern
[2]Department für Chemie, Universität Basel
Klingelbergstrasse 80, CH-4056 Basel

The dynamics and infrared (IR) spectrum of the double proton transfer (DPT) in the hydrogen bonded 2-pyridone·2-hydroxypyridine (2PY·2HP) dimer were studied using quantum chemical and classical molecular dynamics methods and compared to recent experimental work.[1]

DPT potential energy barriers are calculated by MP2 and density functional methods to be 8 - 8.5 kcal/mol. This barrier is of the order of the frequency of the coupled N-H/O-H stretching mode in the harmonic frequency analysis of the minimum energy structure.



Two-dimensional potential energy surfaces (PES) and the minimum-energy path (MEP) for the DPT reaction have been calculated (see Figure). Using activated dynamics, IR spectra for proton transferring and non transferring trajectories were calculated from classical molecular dynamics.

[1] M. Meuwly, A. Müller, and S. Leutwyler *PCCP*, **2003**, *in press.*

Computational Chemistry **341**

Experimental and theoretical study of $H3O^+$ trapped in DB18C6 crown ether.

M. Dulak, K. M. Fromm, E. Gueneau, T. A. Wesolowski

Univ. of Geneva, 30 quai E.-Ansermet, CH-1211 Geneva 4, Switzerland

The equilibrium structure and IR vibrational frequencies of H_3O^+ ion and the H_2O molecule trapped in the DB18C6 crown ether were derived using several variants of density functional theory. The approximate exchange-correlation functionals of the generalized gradient approximation type and hybrid functionals were considered. The results were used to assign some bands in the IR spectrum for the H_3O^+..DB18C6 crown ether complex. Based on the theoretical results, the effect of protonation of the H_2O molecule on the structure and IR frequencies and intensities of the complex was discussed in detail.

Computational Chemistry **342**

Electronic structure, chemical bonding, and optical properties of Tantalum Carbide

M. Sahnoun [1], C. Daul [1], M. Zbiri [1], C. Demangeat [2], J. C. Parlebas[2] and M. Driz [3]

[1] Département de Chimie, Université de Fribourg, Pérolles, CH-1700 Fribourg, Switzerland
[2] IPCMS-GEMM, UMR 7504 CNRS, 23, rue du Loess, F-67037 Strasbourg, Cedex, France
[3] Laboratoire de Sciences des Matériaux, Université Djillali Liabes - Sidi Bel Abbes, Algeria

Abstract:
The electronic-energy band structure, angular-momentum decomposed density of states (***DOS***) and charge-density contours of tantalum carbide **TaC** in the rock-salt structure are calculated by the first-principles full-potential linearized and augmented plane waves method with local-orbital approximation using density-functional theory (**DFT**) in its **GGA** approximation. The total ***DOS*** is compared to the experimental valence-band X-ray photoemission spectrum. From the ***DOS*** analysis, as well as charge-density studies, we conclude that the bonding between **Ta** and **C** is mainly covalent with secondary contributions of metallic bonding.
Using the projected ***DOS*** and band structure we have analyzed the interband contribution to the optical properties of **TaC**. The real and imaginary parts of the dielectric function and hence the optical constants (such as the reflectivity, refraction index, extinction coefficient, absorption coefficient, and the electron energy loss spectrum) are calculated. The calculated spectra are compared with the experimental results for **TaC** and are found to be in good agreement with the experimental data in the low-energy regions. The role of band-structure calculation as regards the optical properties of **TaC** is discussed.

Computational Chemistry **343**

FP-LAPW investigation of the 3d-electron states in $LaCoO_3$

M. Sahnoun [1], C. Daul [1], M. Zbiri [1], and M. Driz [2]

[1] Département de Chimie, Université de Fribourg, Pérolles, CH-1700 Fribourg, Switzerland
[2] Laboratoire de Sciences des Matériaux, Université Djillali Liabes - Sidi Bel Abbes, Algeria

Abstract:
The aim of this work is to show up the fundamentally different descriptions of $LaCoO_3$ appearing in the current literature by presenting 3 different electronic structures for the 3d electrons.
At low temperatures the low-spin state (***LS***) is realized for 6 d electrons (spins) that is characterized by S=0. The electrons (spins) are put subsequently one by one on the single-electron states formed for 1 d electron in the octahedral crystal: lower triplet t_{2g} and higher doublet e_g. With increasing temperatures the LS state transforms to the high-spin (***HS***) state with S=2. Korotin et al. [1] pointed out the existence of the intermediate spin (***IS***) state with S=1 at the middle temperature region.
The electronic-energy band structure, angular-momentum decomposed density of states (DOS) and charge-density contours of $LaCoO_3$ in the perovskite structure are calculated by the first-principles full-potential linearized and augmented plane waves method with local-orbital approximation using density-functional theory (**DFT**).

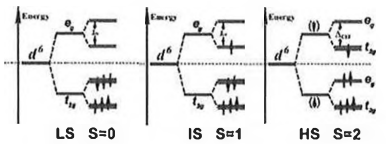


Figure : Single-electron discrete energy spectrum of the Co^{3+} ion in $LaCoO_3$

[1] Korotin et al. Phy. Rev. B 54, 5309 (**1996**)

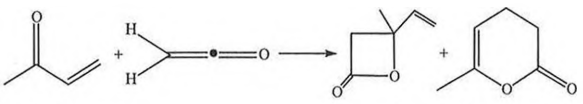
Computational Chemistry **344**

Lewis Acid catalysis and Periselectivity of Addition of Ketene to Methylvinylketone – Insights from Computational Study

V. Tamilmani[ab], V. Prabha[a] and P. Venuvanalingam[a], Claude A. Daul[b]

[a]Department of Chemistry, Bharathidasan University, India
[b]Department of Chemistry, University of Fribourg, Switzerland

Lewis acids are known to catalyze Diels Alder reactions and have profound influence on their regio and stereoselectivities. Methylvinylketone reacts with ketene to give exclusively [4+2] adduct in the absence of the catalyst. But the same



No catalyst (Δ)	0	100
$ZnCl_2$(20°c)	91	9

partners, in the presence of Lewis acid catalyst $ZnCl_2$, react to give [2+2] and [4+2] adducts in a 10:1 ratio This is an interesting case where a Lewis acid catalyst changes periselectivity of a reaction and here is a mechanistic cross over. The Lewis acid catalyst naturally binds with ketone lowers the LUMO and activates the reaction towards [2+2] path over the [4+2] path. A through computational study on the mechanism of the above catalyzed and unanalyzed reactions would throw more light on the factors that are responsible for switching such selectivities.

Computational Chemistry **345**

Variational and Diffusion Monte Carlo basics Applications to atoms and molecules

Mohamed Zbiri, Claude Daul, Mohammed Sahnoun

Department of Chemistry, University of Fribourg, Pérolles 1700-Fribourg Switzerland

We report some recent progress in the development of Quantum Monte Carlo methods including Variational (VMC) and Diffusion (DMC) Monte Carlo. The advantages, achievements and perspectives demonstrate that Quantum Monte Carlo is a very promising approach for calculating properties of many-body quantum systems.

	I. IP	$^5D \rightarrow {}^3F$	$^5D \rightarrow {}^5F$	EA
HF	6.35	7.94	2.06	-2.36
LSDA	7.93	3.04	0.1	...
VMC	7.61	4.73	0.84	-0.72
DMC	7.67	4.24	0.84	-0.03
Exp.	7.87	4.07	0.87	0.15

Table: VMC and DMC [1] first ionisation potential (I. IP), electron affinity (EA) and excitation energies (eV) of the Fe atom as compared with experiment and other calculations.

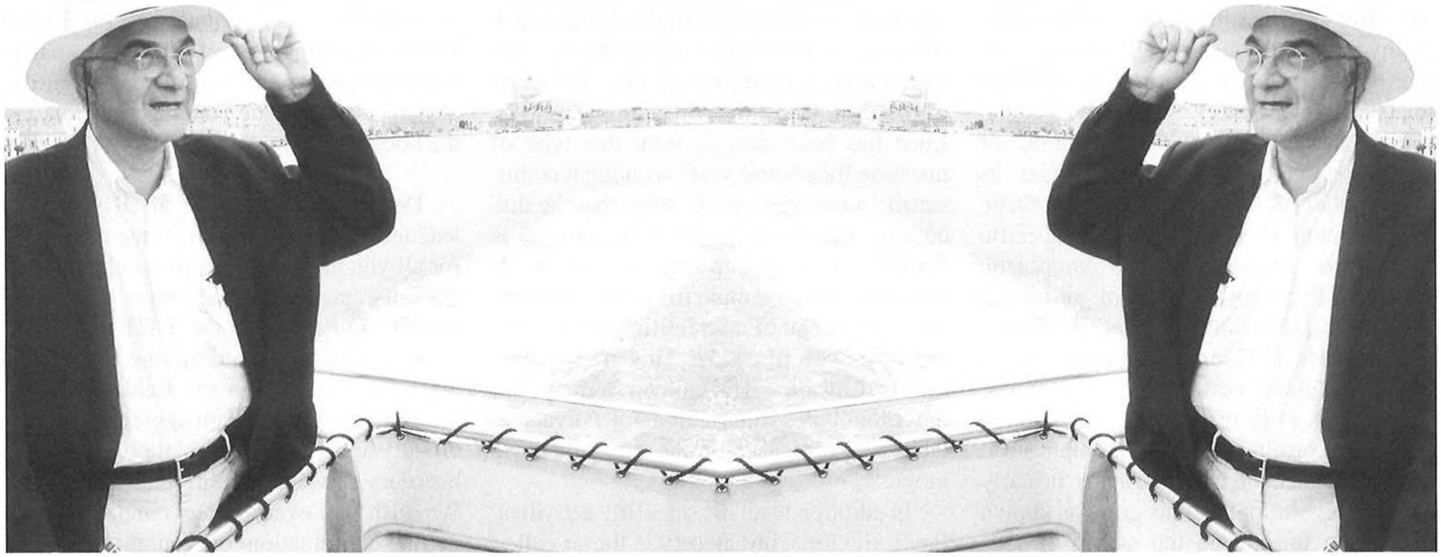
[1] P. A. Christiansen, J. Chem. Phys. 95, 361 (1991)
[2] J. C. Philips, Phys. Rev. B 47, 14132 (1993)
[3] W. M .C. Foulkes and all Review of Modern Physics, Vol. 73, No. 1, January 2001

Author Index

Chimia 57 (2003) 471–474

ISSN 0009-4293

Pier Luigi Luisi Retires from the ETH



After more than 30 years as teacher and research scientist at the ETH in Zürich, Prof. Pier Luigi Luisi retires this year from the ETH to continue his scientific activity in the Biology Department of the Università degli Studi Roma Tre in Rome. Born on May 23, 1938, in Piombino, in the Tuscany (Italy), Luisi grew up mainly on the Island of Elba, studied in Pisa, and graduated 1963 from the Scuola Normale Superiore di Pisa with a degree in chemistry (1964) on the conformation of optically active isotactic macromolecules. This work was partially carried out at the University of St. Petersburg (Russia) in the group of Prof. Mikhail V. Volkenstein. After undertaking research at the Institute of Organic Chemistry in the Scuola Normale Superiore di Pisa until 1967, as an assistant in the group of Prof. Piero Pino – who later became a full professor at the ETH (1968–1988) – Luisi then spent almost three years as a postdoctoral fellow, first in the group of Prof. S. Claesson at the University of Uppsala (Sweden), then in the Macromolecular Center in Strasbourg (France) and in the group of Prof. Sidney A. Bernhard at the Institute of Molecular Biology at the University of Oregon in Eugene, Oregon (USA). In 1970, Luisi moved to the ETH, first as senior assistant in the group of Prof. Pino and later as assistant professor ('Privatdozent', 1973–1979) and Extraordinarius ('ausserordentlicher Professor', 1980–1984), before he became Ordinarius ('ordentlicher Professor') for Macromolecular Chemistry in 1984 (until 2003).

Originally belonging to the Technical Chemistry Laboratory of the Chemistry Department of the ETH, Pino (Polymer Chemistry) and Luisi (Biopolymers) founded in 1982 together with Prof. Joachim Meissner (full professor in Polymer Physics between 1974 and 1996) the Institute of Polymers (IfP) [1]. Later on – under the guidance of Prof. Ulrich W. Suter (Polymer Chemistry, since 1988 as full professor), Prof. Hans-Christian Öttinger (Polymer Physics, since 1996 as full professor), Prof. Paul Smith (Polymer Technology, since 1995) and Prof. Pier Luigi Luisi (Supramolecular Chemistry), the IfP became part of the Department of Materials ('Departement Werkstoffe', founded in 1989, and which has recently been enlarged and renamed 'Departement Materialwissenschaft').

Luisi was warmly accepted in this Department, but had to combine this given definition of a 'materials man' with his great interests in biochemical, biological, and also philosophical questions. For several years, he was therefore embedded in a somehow mixed situation: his group belonged to the Department of Materials, while he himself remained an associated member of the Department of Materials with a chair of Macromolecular Chemistry in the Department of Chemistry. He was also the Head of the Department of Chemistry between 1996 and 1998. After this period, his chair was absorbed by the Department of Materials.

The research activities of Pier Luigi Luisi during his career at the ETH are remarkable, also in the sense that he was never tired to start something new. He never ceased to learn from the new and fast and fascinating developments at the interface between chemistry and the biological sciences. Due to these broad and variable interests, Luisi was always, and still is, someone who does not hesitate to ask simple, critical questions – about seemingly established facts – questions that others were and are often afraid to ask: 'Why are enzymes macromolecules?' [2]. For many PhD students and postdocs, Luisi opened a wide door to a world that is not as narrow minded as it appears in many research teams. His

interdisciplinary, critical approach and way of thinking was (and is) often remarkable.

Starting with the investigation of the conformation of synthetic optically active macromolecules [3], his research interests involved the following, partially overlapping, topics, listed more or less in chronological order: mechanistic studies of dehydrogenases [4]; conformational properties of aromatic amino acid-containing oligopeptides [5]; spectroscopic properties of polypeptides and proteins [6]; the use of proteases for catalyzing the synthesis of peptides [7]; the isolation and characterization of plant proteases and protease inhibitors [8]; the solubilization of enzymes in inverted (reverse) micelles (Luisi was one of the pioneers to open the field of micellar enzymology) [9]; organogels and cubic phases [10]; self-organization of aggregates [11]; gels and liposomes as drug delivery systems [12]; synthetic minimal cells [13]; biogenesis of specific biopolymer sequences [14]; autopoietic systems [15]; reproduction of surfactant aggregates [16]; functionalized liposomes and micelles [17]; micromanipulation of cell-sized (giant) vesicles [18]; emergence in chemistry [19]; origin of life [20]. In the field of the origin of life he has emphasized the importance of compartments in early prebiotic evolution; and his group is known for having introduced the notion of self-reproducing micelles and vesicles.

During the last ten years, Pier Luigi Luisi has initiated and partially chaired three COST chemistry actions for 'Molecular Recognition Chemistry' (action D7, 1992–1997), 'Supramolecular Chemistry' (action D11, 1998–2003), and 'Prebiotic Chemistry and Early Evolution' (action D27, 2001–2007), [21].

The two main research projects that Luisi has followed during the last couple of years at the ETH are briefly mentioned here, as these projects are the ones he will 'export' to Rome. These projects have the working titles 'Minimal Cell' and 'Never Born Proteins'. Luisi is interested in the construction of a 'minimal cell'. Using liposomes (vesicles) as models for the cell compartment, and utilizing the know-how of his group to introduce biological macromolecules and other biochemicals into the liposomes, Luisi asks the question: 'What is the minimal and sufficient number of genes/enzymes to introduce into a liposome, so that this becomes viable minimal cellular life?'

The newest project of Luisi has to do with the 'never born proteins', a subject at the border between chemistry and molecular biology, starting from the realization that the number of proteins we have on Earth is a tiny fraction of the theoretically possible number (Luisi says that the ratio of existing proteins to possible proteins corresponds to the ratio of the size of the universe to the size of an atom!). Based on totally random DNA sequences that are not present in any data bank, novel proteins are synthesized by the so-called phage display technique and studied for their structural and biochemical properties. With this project, Luisi plunges – as he says – into 'the universe of the never born proteins'.

Dealing with research on questions on the origin of life, one is confronted with a multi-disciplinary problem, and one is even inevitably confronted with the difficult task of trying to formulate a definition of a living system, a definition of life, that Luisi draws from his studies on autopoiesis [22]. Luisi has been dealing with this type of question for several years with great enthusiasm and energy and the wish that the discussion and thoughts about life's origin is spread to the broader public. For this, he also initiated for example the production and wrote the script of a scientific movie about the origin of life [23]. This movie won the 2001 award – The Golden Serpent – in the Filmóbidos International Festivals at Óbidos (Portugal), for the best scientific movie.

In addition to all his scientific activities, Pier Luigi Luisi initiated 1985 the so-called 'Cortona week', an unique one-week gathering in Cortona (Tuscany, Italy), for the benefit of ETH PhD students and young researchers [24]. The 'Cortona idea' came from the recognition that the academic training is capable of 'producing' excellent specialists in one single discipline, but society's problems cannot be solved by one discipline alone, they need the combination and integration of many disciplines – and university students often miss completely this kind of integration. In Cortona, science students meet with famous scientists and philosophers from other universities, but also with artists, economists, poets, psychologists, religious leaders. In addition to traditional lecture presentations, followed by extended discussions, there are practical workshops in the arts – that should remind one of the importance of music, painting, body awareness, and spirituality [24].

Among the other activities in the integration between science and humanities, the successful interdisciplinary series of lectures organized in the winter term 2000/01 is mentioned: 'From the Origin of the Universe to the Evolution of the Consciousness' ('Vom Ursprung des Universums zur Evolution des Geistes') [25].

Along the many diverse activities during the last thirty years at the ETH, Luisi certainly met many different people from different disciplines and cultures. Among those who had a significant influence on his life, he likes to remember his mentor Prof. Piero Pino (1921–1989), who always believed in Luisi's ideas and supported him in difficult moments; and particularly important was the friendship with the late Francisco J. Varela (1946–2001). Together with Varela, Luisi has been participating in the Mind and Life meetings, hosted every two years by His Holiness the 14th Dalai Lama, where scientists of the West meet with Buddhist Tibetan scholars.

Finally, it is worth noting that Pier Luigi Luisi has also written several Italian books, including some for children, partly with the aim of spreading basic scientific principles among the young generation, *i.e.* the booklet 'Remedius l'Alchimista' [26].

Dear Luigi, on behalf of all your colleagues and friends at ETH, we thank you for all you have done for the students, PhD students, postdocs, and other coworkers during your years at the ETH in Zürich. Your scientific contributions and your teaching were within the field of macromolecules and surfactant aggregates with a broadly appreciated elimination of existing boarders between the different disciplines. We wish you every success and happiness in the continuation of your activities in Rome.

Peter Walde
Department of Materials,
ETH Zürich, Universitätstrasse 6,
CH-8092 Zürich.

Received: June 28, 2003

[1] P.L. Luisi, 'The Institute of Polymers at the Swiss Federal Institute of Technology in Zürich', *Polymer News* **1985,** *10*, 312.
[2] a) P.L. Luisi, 'Why are Enzymes Macromolecules?', *Naturwissenschaften* **1979,** *66*, 498; b) P.L. Luisi, 'Warum sind Enzyme Makromoleküle?', *Chimia* **1983,** *37*, 73.
[3] a) P.L. Luisi, E. Chiellini, P.F. Franchini, M. Orienti, 'Stereoregularity and Dipole Moments of Optically Active Poly-Alkyl-Vinyl-Ethers', *Macromolecul. Chem.* **1968,** *112*, 197; b) P.L. Luisi, P. Pino, 'Conformational Properties of Optically Active Poly-α-olefins in Solution', *J. Phys. Chem.* **1968,** *72*, 2400; c) P.L. Luisi, 'Calculation of the Conformational Properties of Isotactic Poly(α-olefins) in Solution', *Polymer* **1972,** *13*, 232; d) P.L. Luisi, 'Conformational Properties of Optically Active Stereoregular Polymers', *Internat. J. Polym. Mater.* **1975,** *4*, 33.
[4] a) P.L. Luisi, R. Favilla, 'Mechanistic Studies on Horse Liver Alcohol Dehydrogenase. Influence of Different Premixings

on the Transient Kinetics of Aldehyde Reductions', *Biochemistry* **1972,** *11*, 2303; b) P.L. Luisi, A. Baici, A. Olomucki, M.-O. Doublet, 'Temperature-Determined Enzymatic Functions in Octopine Dehydrogenase', *Eur. J. Biochem.* **1975,** *50*, 511; c) A. Baici, P.L. Luisi, 'Further Investigations of the Transient Kinetics of Alcohol Oxidation Catalysed by Horse Liver Alcohol Dehydrogenase', *J. Mol. Biol.* **1977,** *114*, 267.

[5] a) R. Guarnaccia, G.P. Lorenzi, V. Rizzo, P.L. Luisi, 'Co-Oligopeptides of Aromatic Amino Acids and Glycine with a Variable Distance Between Aromatic Residues. I. Synthesis of Co-Oligopeptides of Tryptophan and Glycine', *Biopolymers* **1975,** *14*, 2329; b) V. Rizzo, P.L. Luisi, 'Co-Oligopeptides of Aromatic Amino Acids and Glycine with a Variable Distance Between Aromatic Residues. V. pH-Dependent Conformational Changes In Peptides Containing Two Adjacent Tryptophyl Residues as Evidenced By Circular Dichroism Studies', *Biopolymers* **1977,** *16*, 437; c) V. Rizzo, P.L. Luisi, B. Straub, R. Guarnaccia, 'Co-Oligopeptides of Aromatic Amino-Acids and Glycine with a Variable Distance Between Aromatic Residues. VI. Circular Dichroism Studies of Co-Oligopeptides of L-Phenylalanine, L-Tryptophan, and Glycine', *Biopolymers* **1977,** *16*, 449; d) P.P. Wiget, P.L. Luisi, 'Co-Oligopeptides Containing Aromatic Residues Spaced by Glycyl Residues. IX. Fluorescence Properties of Tryptophan-Containing Peptides', *Biopolymers* **1978,** *17*, 167; e) P. Skrabal, V. Rizzo, A. Baici, F. Bangerter, P.L. Luisi, 'Co-Oligopeptides Containing Aromatic Residues Spaced by Glycyl Residues. X. Proton Magnetic Resonance Study of Co-Oligopeptides of Tryptophan and Glycine', *Biopolymers* **1979,** *18*, 995; f) A. Baici, V. Rizzo, P. Skrabal, P.L. Luisi, 'Co-Oligopeptides Containing Two Aromatic Residues Spaced by Glycyl Residues. 11. A Conformational Study of Tryptophan- and Glycine-Containing Oligopeptides Based on the Temperature Dependence of ^{1}H-NMR Spectra', *J. Am. Chem. Soc.* **1979,** *101*, 5270; g) H. Jäckle, P.L. Luisi, 'Conformational Study of Histidine- and Tryptophan-Containing Peptides in Solution Based upon the Combination of Nuclear Magnetic Resonance, Circular Dichroism, and Fluorescence Measurements', *J. Phys. Chem.* **1984,** *88*, 1767.

[6] a) P.L. Luisi, A. Olomucki, A. Baici, D. Karlovic, 'Fluorescence Properties of Octopine Dehydrogenase', *Biochemistry* **1973,** *12*, 4100; b) A.A. Aboderin, E. Boedefeld, P.L. Luisi, 'Alkaline Conformational Transition of Chicken Egg White Lysozyme', *Biochim. Biophys. Acta* **1973,** *328*, 31; c) R. Joppich-Kuhn, P.L. Luisi, 'Circular Dichroic Properties and Conformation of Thionicotinamide Dinucleotides Bound to Horse-Liver Alcohol Dehydrogenase', *Eur. J. Biochem.* **1978,** *83*, 593; d) H. Reutimann, B, Straub, P.L. Luisi, A. Holmgren, 'A Conformational Study of Thioredoxin and Its Tryptic Fragments', *J. Biol. Chem.* **1981,** *256*, 6796; e) P. Walde, H. Jäckle, P.L. Luisi, C.J. Dempsey, B.E.C. Banks, 'Spectroscopic Investigations of Peptide 401 from Bee Venom', *Biopolymers* **1981,** *20*, 373; f) M. Ehrat, P.L. Luisi, 'Synthesis and Spectroscopic Characterization of Insulin Derivatives Containing One or Two Poly(ethylen oxide) Chains at Specific Positions', *Biopolymers* **1983,** *22*, 569.

[7] a) R. Saltman, D. Vlach, P.L. Luisi, 'Co-oligopeptides of Aromatic Amino Acids and Glycine with Variable Distance Between the Aromatic Residues. VII. Enzymatic Synthesis of N-Protected Peptide Amides', *Biopolymers* **1977,** *16*, 631; b) A. Pellegrini, P.L. Luisi, 'Pepsin-Catalyzed Peptide Synthesis', *Biopolymers* **1978,** *17*, 2573; c) G. Anderson, P.L. Luisi, 'Papain-induced Oligomerization of α-Amino Acid Esters', *Helv. Chim. Acta* **1979,** *62*, 740; d) R. Jost, E. Brambilla, J.C. Monti, P.L. Luisi, 'Papain Catalyzed Oligomerization of α-Amino Acids. Synthesis and Characterization of Water-Insoluble Oligomers of L-Methionine', *Helv. Chim. Acta* **1980,** *63*, 375.

[8] a) P. Walde, P.L. Luisi, S. Palmieri, 'Proteolytic Activity in Sunflower Seeds *(Helianthus annuus* L.)', *J. Agr. Food Chem.* **1984,** *32*, 322; b) E. Menegatti, S. Palmieri, P. Walde, P.L. Luisi, 'Isolation and Characterization of a Trypsin-Inhibitor From White Mustard *(Sinapis-alba* L.)', *J. Agr. Food Chem.* **1985,** *33*, 784.

[9] a) P.L. Luisi, F. Henninger, M. Joppich, A. Dossena, G. Casnati, 'Solubilization and Spectroscopic Properties of α-Chymotrypsin in Cyclohexane', *Biochem. Biophys. Res. Commun.* **1977,** *74*, 1384; b) P.L. Luisi, F.J. Bonner, A. Pellegrini, P. Wiget, R. Wolf, 'Micellar Solubilization of Proteins in Aprotic Solvents and their Spectroscopic Characterization', *Helv. Chim. Acta* **1979,** *62*, 740; c) R. Wolf, P.L. Luisi, 'Micellar Solubilization of Enzymes in Hydrocarbon Solvents, Enzymatic Activity and Spectroscopic Properties of Ribonuclease in n-Octane', *Biochem. Biophys. Res. Commun.* **1979,** *89*, 209; d) P. Meier, P.L. Luisi, 'Micellar Solubilization of Biopolymers in Hydrocarbon Solvents. II. The Case of Horse Liver Alcohol Dehydrogenase', *J. Solid Phase Biochem.* **1980,** *5*, 269; e) C. Grandi, R.E. Smith, P.L. Luisi, 'Micellar Solubilization of Biopolymers in Organic Solvents. Activity and Conformation of Lysozyme in Isooctane Reverse Micelles', *J. Biol. Chem.* **1981,** *256*, 837; f) S. Barbaric, P.L. Luisi, 'Micellar Solubilization of Biopolymers in Organic Solvents 5. Activity And Conformation of α-Chymotrypsin In Isooctane-AOT Reverse Micelles', *J. Am. Chem. Soc.* **1981,** *103*, 4239; g) P. Lüthi, P.L. Luisi, 'Enzymatic Synthesis of Hydrocarbon-Soluble Peptides with Reverse Micelles', *J. Am. Chem. Soc.* **1984,** *106*, 7285; h) P.L. Luisi, 'Enzyme als Gastmoleküle in inversen Mizellen', *Angew. Chem.* **1985,** *97*, 449; 'Enzymes Hosted in Reverse Micelles in Hydrocarbon Solution', *Angew. Chem. Int. Ed.* **1985,** *24*, 439; i) M.E. Leser, G. Wei, P.L. Luisi, M. Maestro, 'Application of Reverse Micelles for the Extraction of Proteins', *Biochem. Biophys. Res. Commun.* **1986,** *135*, 629; j) B. Steinmann, H. Jäckle, P.L. Luisi, 'A Comparative Study of Lysozyme Conformation in Various Reverse Micellar Systems', *Biopolymers* **1986,** *25*, 1133; k) P.L. Luisi, M. Giomini, M.P. Pileni, B.H. Robinson, 'Reverse Micelles as Hosts for Proteins and Small Molecules', *Biochim. Biophys. Acta* **1988,** 947, 209; l) P. Walde, Q. Peng, N.W. Fadnavis, E. Battistel, P.L. Luisi, 'Structure and Activity of Trypsin in Reverse Micelles', *Eur. J. Biochem.* **1988,** *173*, 401; m) M. Caselli, P.L. Luisi, M. Maestro, R. Roselli, 'Thermodynamics of the Uptake of Proteins by Reverse Micelles: A First Approximation Model', *J. Phys. Chem.* **1988,** *92*, 3899; n) M.E. Leser, P.L. Luisi, S. Palmieri, 'The Use of Reverse Micelles for the Simultaneous Extraction of Oil and Proteins from Vegetable Meal', *Biotechnol. Bioeng.* **1989,** *34*, 1140; o) Q. Peng, P.L. Luisi, 'The Behavior of Proteases in Lecithin Reverse Micelles', *Eur. J. Biochem.* **1990,** *188*, 471; p) P. Walde, A.M. Giuliani, C.A. Boicelli, P.L. Luisi, 'Phospholipid-Based Reverse Micelles', *Chem. Phys. Lipids* **1990,** *53*, 265; q) M.E. Leser, P.L. Luisi, 'Application of Reverse Micelles for the Extraction of Amino Acids and Proteins', *Chimia* **1990,** *44*, 270; r) G. Marcozzi, N. Correa, M. Caselli, P.L. Luisi, 'Protein Extraction by Reverse Micelles: A Study of the factors Affecting the Forward and Backward Transfer of α-Chymotrypsin and Its Activity', *Biotechnol. Bioeng.* **1991,** *38*, 1239; s) M.E. Leser, K. Mrkoci, P.L. Luisi, 'Reverse Micelles in Protein Separation: the Use of Silica for the Back-Transfer Process', *Biotechnol. Bioeng.* **1993,** *41*, 489.

[10] a) R. Scartazzini, P.L. Luisi, 'Organogels from Lecithin', *J. Phys. Chem.* **1988,** *92*, 829; b) P.L. Luisi, R. Scartazzini, G. Haering, P. Schurtenberger, 'Organogels from Water-in-Oil Microemulsions', *Colloid Polym. Sci.* **1990,** *268*, 356; c) M. Portmann, E.M. Landau, P.L. Luisi, 'Spectroscopic and Rheological Studies of Enzymes in Rigid Lipidic Matrices: The Case of α-Chymotrypsin in a Lysolecithin/Water Cubic Phase', *J. Phys. Chem.* **1991,** *95*, 8437; d) C. Colombo, C. Nastruzzi, P.L. Luisi, R.M. Thomas, 'Chiroptical Properties of Lecithin Reverse Micelles and Organogels', *Chirality* **1991,** *3*, 495; e) E.M. Landau, P.L. Luisi, 'Lipidic Cubic Phases as Transparent, Rigid Matrices for the Direct Spectroscopic Study of Immobilized Membrane Proteins', *J. Am. Chem. Soc.* **1993,** *115*, 2102.

[11] P.L. Luisi, 'Are Micelles and Vesicles Chemical Equilibrium Systems?', *J. Chem. Educ.* **2001,** *78*, 380.

[12] a) C. Nastruzzi, R. Gambari, E. Menegatti, P. Walde, P.L. Luisi, 'Tumor Cell Growth Inhibition by Liposome-Encapsulated Aromatic Polyamidines', *J. Pharm. Sci.* **1990,** *79*, 672; b) H. Williman, P.

Walde, P.L. Luisi, A. Gazzaniga, F. Stroppolo, 'Lecithin Organogel as Matrix for Transdermal Transport of Drugs', *J. Pharm. Sci.* **1992,** *81*, 871.

[13] a) T. Oberholzer, R. Wick, P.L. Luisi, C. K. Biebricher, 'Enzymatic RNA replication in Self-Reproducing Vesicles: An Approach to a Minimal Cell', *Biochem. Biophys. Res. Commun.* **1995,** *207*, 250; b) J.W. Szostak, D.P. Bartel, P.L. Luisi, 'Synthesizing Life', *Nature* **2001,** *409*, 387; c) P.L. Luisi, T. Oberholzer, A. Lazcano, 'The Notion of a DNA Minimal Cell: A General Discourse and Some Guidelines for an Experimental Approach', *Helv. Chim. Acta* **2002,** *85*, 1759.

[14] R.M. Thomas, J.W. Vrijbloed, P.L. Luisi, 'Towards Random Polypeptide Synthesis', *Chimia* **2001,** *55*, 114.

[15] a) P.L. Luisi, F.J. Varela, 'Self-Replicating Micelles. - A Chemical Version of Minimal Autopoietic Systems', *Origins Life Evol. Biosphere* **1990,** *19*, 633; b) P.A. Bachmann, P. Walde, P.L. Luisi, J. Lang, 'Self-Replicating Reverse Micelles and Chemical Autopoiesis', *J. Am. Chem. Soc.* **1990,** *112*, 8200; c) P.L. Luisi, 'Autopoiesis: A Review and a Reappraisal', *Naturwissenschaften* **2003,** *90*, 49.

[16] a) P.A. Bachmann, P.L. Luisi, J. Lang, 'Self-Replication of Reverse Micelles', *Chimia* **1991,** *45*, 266; b) P.A. Bachmann, P. Walde, P.L. Luisi, J. Lang, ,Self-Replicating Micelles: Aqueous Micelles and Enzymatically Driven Reactions in Reverse Micelles', *J. Am. Chem. Soc.* **1991,** *113*, 8204; c) P.A. Bachmann, P.L. Luisi, J. Lang, 'Autocatalytic Self-Replicating Micelles as Models for Prebiotic Structures', *Nature* **1992,** *357*, 57; d) P. Walde, R. Wick, M. Fresta, A. Mangone, P.L. Luisi, 'Autopoietic Self-Reproduction of Fatty Acid Vesicles', *J. Am. Chem. Soc.* **1994,** *116*, 11649; e) K. Morigaki, S. Dallavalle, P. Walde, S. Colonna, P.L. Luisi, 'Autopoietic Self-Reproduction of Chiral Fatty Acid Vesicles', *J. Am. Chem. Soc.* **1997,** *119*, 292; f) H.H. Zepik, E. Blöchliger, P.L. Luisi, 'A Chemical Model of Homeostasis', *Angew. Chem. Int. Ed.* **2001,** *40*, 199.

[17] a) S. Bonaccio, P. Walde, P.L. Luisi, 'Liposomes Containing Purine and Pyrimidine Bases: Stable Unilamellar Liposomes from Phosphatidyl Nucleosides', *J. Phys. Chem.* **1994,** *98*, 6661; b) A. Veronese, P.L. Luisi, 'An Autocatalytic Reaction Leading to Spontaneously Assembled Phosphatidyl Nucleoside Giant Vesicles', *J. Am. Chem. Soc.* **1998,** *120*, 2662; c) C. Heiz, U. Rädler, P.L. Luisi, 'Spectroscopy and Recognition Chemistry of Micelles from Monoalkyl Phosphoryl Nucleosides', *J. Phys. Chem. B* **1998,** *102*, 8686.

[18] a) R. Wick, M. Angelova, P. Walde, P.L. Luisi, 'Microinjection into Giant Vesicles and Light Microscopy Investigation of Enzyme-Mediated Vesicle Transformations', *Chem. Biol.* **1996,** *3*, 105; b) P. Bucher, A. Fischer, P.L. Luisi, T. Oberholzer, P. Walde, 'Giant Vesicles as Biochemical Compartments: The Use of Microinjection Techniques', *Langmuir* **1998,** *14*, 2712.

[19] P.L. Luisi, 'Emergence in Chemistry: Chemistry as the Embodiment of Emergence', *Found. Chem.* **2002,** *4*, 183.

[20] a) P. Walde, A. Goto, P.-A. Monnard, M. Wessicken, P.L. Luisi, 'Oparin's Reactions Revisited: Enzymatic Synthesis of Poly(adenylic acid) in Micelles and Self-Reproducing Vesicles', *J. Am. Chem. Soc.* **1994,** *116*, 7541; b) P.L. Luisi, 'Self-Reproduction of Micelles and Vesicles for the Mechanisms of Life from the Perspective of Compartemented Chemistry', *Adv. Chem Phys.* **1996,** *92*, 425; c) P.L. Luisi, P. Walde, T. Oberholzer, 'Lipid Vesicles as Possible Intermediates in the Origin of Life', *Curr. Opin. Colloid Interf. Sci.* **1999,** *4*, 33; d) M. Blocher, D. Liu, P. Walde, P.L. Luisi, 'Liposome-Assisted Selective Polycondensation of α-Amino Acids and Peptides', *Macromolecules* **1999,** *32*, 7332; e) M. Blocher, D. Liu, P.L. Luisi, 'Liposome-Assisted Selective Polycondensation of α-Amino Acids and Peptides: The Case of Charged Liposomes', *Macromolecules* **2000,** *33*, 5787; f) T. Hitz, P.L. Luisi, 'Enhancement of Homochirality in Oligopeptides by Quartz', *Helv. Chim. Acta* **2002,** *85*, 3975.

[21] European co-operation programs in the field of scientific and technical research, *http://cost.cordis.lu/*

[22] P.L. Luisi, 'About Various Definitions of Life', *Origins Life Evol. Biosphere* **1998,** *28*, 613.

[23] 'The Origin of Life: What Science Has to Say', running time: 43', CNR Italy and VISMEDIA ETH Zürich, **1999.** Film directed by L. Morettini with scientific advice from P.L. Luisi.

[24] a) *http://www.cortona.ch;* b) P.L. Luisi (Ed.), 'Treffpunkt Zukunft. Die Ganzheit des Lebens erfassen: Aspekte aus Naturwissenschaft, Philosophie, Medizin und Psychologie', Verlag Bonn Aktuell GmbH, Stuttgart, **1991;** c) P.L. Luisi (Ed.), 'Im Einvernehmen mit der Natur: Die Zukunft von Ökologie, Wirtschaft, Gesellschaft', Verlag Bonn Aktuell GmbH, Stuttgart, **1991.**

[25] P. Walde, P.L. Luisi (Eds.), 'Vom Ursprung des Universums zur Evolution des Geistes', vdf, Hochschul-Verl. an der ETH, **2002.** Proceedings of a series of lectures within the frame of the so-called 'Interdisziplinäre Veranstaltungsreihe' of the University Zürich and ETH Zürich.

[26] a) P.L. Luisi, 'Remedius l'alchimista', Giunti Gruppo Editoriale, Firenze, **1996;** b) P.L. Luisi, 'L'ombra dei fichidindia: storie elbane quasi tutte vere', ETS Editrice Pisa, **1987;** c) P.L. Luisi, 'Oltre i regni di Uthanak', Giunti Gruppo Editorale, Firenze, **1994;** d) P.L. Luisi, 'Selenio e i pirati etruschi', Nuove Edizioni Romane, Roma, **1994;** d) P.L. Luisi, 'Matrimonio a mezzanotte', 'Il Libraio' Editore, Portoferraio, **1995;** e) P.L. Luisi, 'Suo padre era un albatros', Adriano Salani Editore, Firenze, **1990;** f) P.L. Luisi, 'I lampi tranquilli della mente', Gianni Iuculano Editore, Pavia, **2000.**

CHIMIA 2003, 57, No. 7/8

FH – HES

Fachhochschulen – Hautes Ecoles Spécialisées

Chimia 57 (2003) 475–476

ISSN 0009–4293

Neues modulares Konzept für den Studiengang Chemie und Biologische Chemie der Zürcher Hochschule Winterthur

Eduard Gamp*

New Modular Curriculum for Chemistry and Biological Chemistry Diploma Programs at the Zurich University of Applied Sciences Winterthur

Abstract: Starting with the fall semester 2003, the Zurich University of Applied Science Winterthur (ZHW) will switch to fully modularized curricula in all its diploma programs, including chemistry and biological chemistry. For students this will mean that they will be graded by ECTS-Credit Points (ECTS = European Credit and Transfer System) and that they can collect some of the credits in other European universities and colleges. Individualized curricula become possible with the option to acquire credit points in the fifteen diploma programs of ZHW, ranging from business administration to computer science or mechatronics.

Keywords: Diploma Program in Chemistry and Biological Chemistry · ECTS-Credits · Zurich University of Applied Sciences Winterthur

Mit Beginn des Wintersemesters 2003/2004 wird der Studiengang Chemie und Biologische Chemie einen weiteren grossen Schritt in Richtung eines im Sinne der Bologna-Deklaration europatauglichen Studiums machen, indem das gesamte Lehrangebot – wie übrigens auch in allen andern Studiengängen der ZHW – modularisiert wird. Dies bringt für die neuen Studierenden unter anderem die folgenden Neuerungen mit sich:

- Alle Fächer werden als klar abgegrenzte Module definiert, welche semesterweise mit individuellen Prüfungen abgeschlossen werden.
- Jedem Modul ist eine bestimmte Anzahl Kreditpunkte zugeordnet (sog. ECTS-Credits; ECTS = European Credit and Transfer System), die erteilt werden, wenn das Modul erfolgreich abgeschlossen worden ist.
- Studierende können ein oder mehrere Semester an einer anderen Hochschule im In- oder Ausland absolvieren und sich die dort erbrachten Studienleistungen mittels ECTS-Punkten anrechnen lassen.
- *Ca.* 80% der Kreditpunkte sind im Rahmen von studiengangspezifischen Modulen zu erzielen, der Rest kann auch in einem der andern zwölf Studiengänge der ZHW gesammelt werden. Dies bietet dank der Grösse und Interdisziplinarität der ZHW viel Raum für eine Verbreiterung der Ausbildung je nach Neigungen der Studierenden, z.B. in den Bereichen Management und Ökonomie, Verfahrenstechnik oder Informatik.
- Das FH-Diplom wird erteilt, wenn mindestens 180 Kreditpunkte akquiriert und die Diplomarbeit mit Erfolg abgeschlossen worden sind.
- Die Zahl der Kontaktlektionen wurde um *ca.* 10% auf 30 pro Woche gesenkt, um das für die Entwicklung der Selbständigkeit besonders wichtige Selbststudium zu fördern.

*Korrespondenz: Prof. Dr. E. Gamp
Leiter Studiengang Chemie
Zürcher Hochschule Winterthur
Technikumstrasse 9
CH-8401 Winterthur
Tel.: +41 52 267 7345
Fax: +41 52 268 7345
E-Mail: eduard.gamp@zhwin.ch

Struktur des Studiums

Die in der Fig. schematisch dargestellte Struktur basiert auf den Zielen und Inhalten des bestehenden Fachhochschul-Studienganges der ZHW mit seinen beiden Studienrichtungen Biologische Chemie, bzw. Chemie (in der Fig. symbolisiert durch die grüne, bzw. blaue Umrandung):

• Im ersten Jahr, der sog. Assessmentstufe, werden Unterschiede in den mathematischen und naturwissenschaftlichen Vorkenntnissen ausgeglichen und eine solide Basis für das nachfolgende Fachstudium gelegt. Die Fähigkeit zum selbständigen Arbeiten wird durch ein begleitetes Selbststudium gefördert.

- In der auf das 2. Semester folgenden Assessmentprüfung belegen die Studierenden, dass sie sich das theoretische und methodische Rüstzeug für ein modularisiertes und flexibles Fachstudium angeeignet haben. Bei bestandener Assessmentprüfung werden pauschal 60 ECTS-Punkte vergeben.
- Im Fachstudium sind *ca.* 60% der Module (Englisch, Ökologie, Informatik, Ingenieurfächer sowie die Grundlagen der chemischen und biologischen Fachausbildung) für beide Studienrichtungen obligatorisch, um die an der ZHW gepflegte Breite der naturwissenschaftlichen Ausbildung zu gewährleisten (vgl. Tab.).
- Die restlichen ECTS-Kreditpunkte sind in für die gewählte Studienrichtung spezifischen Modulen zu erzielen. Sie erlauben den Studierenden eine beschränkte Spezialisierung dank der Vertiefung entweder in den klassischen chemischen Disziplinen oder in biologischen Fächern.
- Die Spezialisierung wird praxisorientiert abgerundet mit dem Vertiefungspraktikum im letzten Semester, wo die Studierenden an Entwicklungsprojekten in einem der F&E-Teams der ZHW mitarbeiten. Während dieser Zeit und vor allem in der danach folgenden Diplomarbeit eröffnet die ZHW als grösste Mehrsparten-Fachhochschule der Schweiz den Studierenden vielfältige Möglichkeiten interdisziplinärer Zusammenarbeit mit KommilitonInnen und Dozierenden anderer Studiengänge, z.B. der Informationstechnologie, der Verfahrenstechnik, der Datenanalyse oder der Mechatronik.
- Zusätzlich zu den total gesammelten 180 ECTS-Punkten ist zuletzt noch eine mindestens zwölf Wochen dauernde Diplomarbeit zu absolvieren, bevor das FH-Diplom als Chemikerin oder Chemiker mit Studienrichtung Chemie oder Biologische Chemie vergeben wird.

Weitere Informationen unter:
www.zhwin.ch

Eingegangen am 2. Juli, 2003

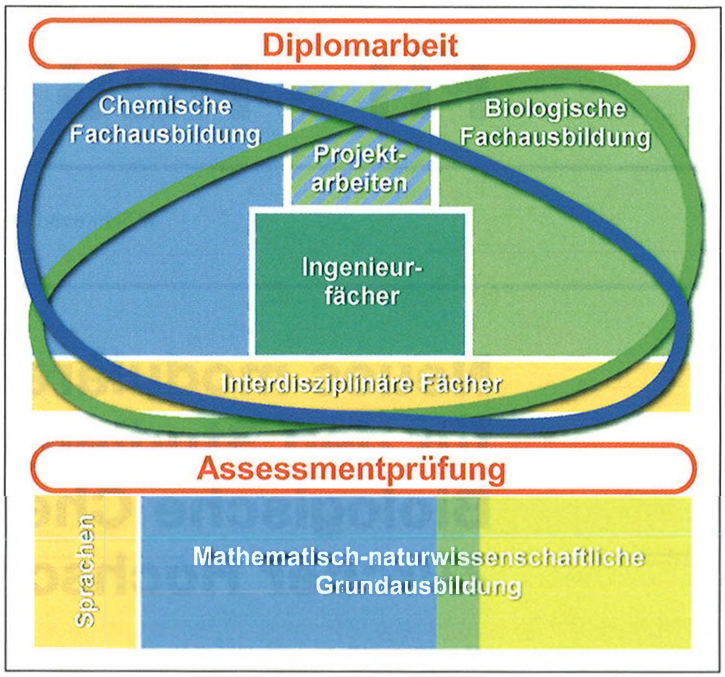


Fig Struktur des modularisierten Studiums

Tab. Modulgruppen und ECTS-Kreditpunkte

A. Assessmentjahr (1. und 2. Semester; 60 ECTS)	
Mathematisch-naturwissenschaftliche Grundausbildung (obligatorisch) • Mathematik • Physik • Allgemeine Chemie • Analytische Chemie 1 • Organische Chemie 1 • Biologie • Informatik • Konvergenzpraktikum • Analytisches Grundpraktikum	**Sprachen und Kommunikation (obligatorisch)** • Sprachl. Kommunikation 1: Schreiben • Sprachl. Kommunikation 2: Lesen und Verstehen • Englisch

B. Fachstudium (3. bis 6. Semester; 120 ECTS)	
Ingenieurfächer (obligatorisch; 17 ECTS) • Prozesstechnik • Verfahrens- und Umwelttechnik 1 • Mess-, Steuerungs- und Regeltechnik • Automation und Simulation • Verfahrenstechnisches Praktikum	**Interdisziplinäre Module (obligatorisch; 16 ECTS)** • Sprachl. Kommunikation 3: Rethorik • Englisch • Literaturrecherchen uned Datenbanken • Risiko- und Qualitätsmanagement • Oekologie • Interdisziplinäre Wahlmodule
Chemische und biologische Grundausbildung (obligatorisch; 38 ECTS)	
• Analytische Chemie 2 • Organische Chemie 2 • Physikalische Chemie 1 • Biochemie 1 & 2 • Bioanalytik	• Mikro- & Zellbiologie 1 • Praktikum physikalisch-chem. Messtechnik • Analytisches Praktikum • Organisches Praktikum
Fachausbildung Studienrichtung Chemie (37 ECTS) • Analytische Chemie 3 • Anorganische Chemie • Industrielle Chemie • Verfahrens- und Umwelttechnik • Pysikalische Chemie 2 • Organische Chemie 3 • Industriell-chemisches Praktikum • Organisches Praktikum 2	**Fachausbildung Studienrichtung Biologische Chemie (37 ECTS)** • Mikro- & Zellbiologie 2 • Biochemie 3 • Molekulargenetik • Bioingenieurtechnik • Mikro- & zellbiologisches Praktikum • Biochemisches Praktikum • Bioingenieurtechnisches Praktikum
Vertiefungspraktikum (12 ECTS) Projektarbeiten in einem der folgenden Fachgebiete:	
• Analytische Chemie • Industrielle Chemie • Organische Chemie • Physikalisch-chemische Messtechnik	• Verfahrens- und Umwelttechnik • Biochemie • Mikro- und Zellbiologie • Bioingenieurtechnik

C. Diplomarbeit (12 Wochen; 20 ECTS)

SCHWEIZERISCHE CHEMISCHE GESELLSCHAFT
SOCIETE SUISSE DE CHIMIE
SWISS CHEMICAL SOCIETY
www.swiss-chem-soc.ch

DIC Division Industrielle Chemie

Bericht zur Mitgliederversammlung 2003 mit Firmenbesuch vom 15.05.2003 bei der Firma Rohner in Pratteln

Visp, 02.07.2003

Liebe Mitglieder der Division Industrielle Chemie

Zur Jahresversammlung 2003 der Division Industrielle Chemie trafen sich 51 Mitglieder und Gäste/Referenten bei der Firma Rohner in Pratteln. Nach dem Empfang mit Kaffee und Gipfeli wurden wir durch die Herren Fricker, Habegger, Schwarz und Bürli herzlich begrüsst. Herr Fricker gab uns einen kurzen Überblick auf den Standort Pratteln und die Tätigkeitsfelder der Firma Rohner.

Vorgängig der Mitgliederversammlung konnten wir erneut den Teilnehmern drei Fachvorträge präsentieren. Zwei davon setzten sich mit den Möglichkeiten des Einsatzes von Mikroreaktoren in der chemischen Produktion auseinander:

Herr Dr. Michael Hohmann, CPC-Cellular Process Chemistry Systems GmbH aus Frankfurt am Main gab mit seinem Referat zum Thema **"Kontinuierliche chemische Synthese in Mikroreaktoren vom Labor bis zur Produktion"** einen generellen Überblick auf die Möglichkeiten im Einsatz von Mikrostrukturen in der chemischen Industrie.

Herr Dr. Arnold Gloor, Roche Vitamins AG, Kaiseraugst konnte mit seinem Beitrag **"Evaluation von mikrostrukturierten Apparaten für den Einsatz in der Prozesstechnik"** anhand der Resultate einer konkreten Entwicklungsarbeit, die Möglichkeiten von Mikroreaktoren aufzeigen.

Der **Sandmeyer-Preis 2003** wurde durch Frau Dr. Claudia von Scala-Reichenbach de Sousa, Sulzer Chemtech AG, Winterthur, vorgestellt. Frau von Scala präsentierte den Vortrag als Mitglied der Arbeitsgruppe von Peter Moritz, Sulzer Chemtech. Das Thema beinhaltete den Werdegang eines **"Verfahrens zur Kontinuierlichen Herstellung von kosmetischen Fettsäure-Isopropylester mit Reaktivdestillation".** Die Arbeitsgruppe hat in sehr kurzer Zeit ein Verfahren zur kontinuierlichen Herstellung von kosmetischen Fettsäure-Isopropyl-Estern zur kommerziellen Reife gebracht. Die elegante Kombination von chemischer Reaktionsführung und Verfahrenstechnik führte zu einem sehr leistungsfähigen und kosteneffizienten Produktionsprozess.

Anschliessend an den fachlichen Teil wurde durch den Präsidenten der DIC H.R. Dettwiler die **Mitgliederversammlung** mit folgender Traktandenliste eröffnet und abgewickelt:

- Rückblick auf das Geschäftsjahr 2002
- Jahresrechnung 2002
- Budget des Geschäftsjahres 2003
- Revisorenbericht, Entlastung des Vorstandes
- Reglementsänderung bez. Finanzkompetenz des Vorstandes
- Wahlen, Bestätigung Vorstand der DIC
- Resultate der Umfrage vom Februar 2003
- Bemerkungen zum Tätigkeitsfeld der Schweizerischen Chemischen Gesellschaft
- Zukünftige Veranstaltungen
- Varia, Verdankungen, Schluss der Versammlung

Der Jahresbericht 2002 der Division wurde im Rahmen des Rechenschaftsberichtes der SCG in der CHIMIA **2003,** *57*, 82 veröffentlicht. Speziell erwähnt seien an dieser Stelle:

– Die Mitgliederversammlung 2002 der DIC vom 4.5.2001 bei den Firmen CIMO und Orgamol in Monthey und Evionnaz.

– Die Messen 'r+d in life sciences' und 'REACH for Process Solutions' in Basel vom 15. bis 18. Oktober 2002. Anlässlich dieser Messen wurde durch die DIC ein Seminar zum Thema "Simulation Tools and Their Application in Chemical Manufacturing" (siehe auch Beiträge in CHIMIA **2003,** *57*(1-2), 45) organisiert.

Die Nutzung des **Skill Inventory** durch die Mitglieder ist immer noch zaghaft.Wir möchten allen wärmstens empfehlen ihr Profil im Skill Inventory zu hinterlegen. Das Skill Inventory ist über die WEB-Page der Sektion zugänglich *(www.swiss-chem-soc.ch/DIC/home.html).*

Für die Verleihung des **Sandmeyer Preis** sind Vorschläge aus dem Bereich angewandter industrieller Arbeiten aus der Entwicklung oder chemischen Produktion sehr erwünscht. Die Anträge sind einzureichen an: Swiss Chemical Society (SCS), Bärenplatz 2, CH-3011 Bern.

Der Vorstand unter Federführung von Walter Jucker ist an der Vorbereitung eines **CHIMIA-Schwerpunkthefts** zum Thema **"Chemiewehren der Schweiz".** Das Heft wird 2004 publiziert werden.

Der **Kassenbericht 2002** wurde in ausführlicher und kompetenter Weise vom Kassier Dr. Kurt Käser erläutert. Der Revisor, Dr. P. Pfister, bestätigte die korrekte Rechnungsführung. Die Versammlung konnte damit dem Kassier einstimmig Entlastung erteilen und die Arbeit mit Applaus verdanken. Unser Vermögen von rund Fr. 100'000.- gibt uns wesentlichen Spielraum zur Organisation qualitativ guter Veranstaltungen. Das Budget 2003 konnte ebenfalls auf das Wohlwollen der Versammlung zählen. Auf die spezielle Präsentation der Zahlen wird an dieser Stelle verzichtet.

Der gesamte **Vorstand** und der neue **Rechnungsrevisor** wurden in einem kurzen Wahlakt mit Akklamation **in ihren Ämtern bestätigt.**

Eine **formale Anpassung im Reglement der DIC** betreffend Artikel 5.5, der die Finanzkompetenzen von Vorstand und Quästor regelt, wurde ebenfalls durch die Versammlung einstimmig genehmigt. Das Reglement der DIC ist auf der Homepage einsehbar.

Der Vorstand hat in einer **Umfrage vom Februar 03** versucht, eine Rückmeldung der Mitglieder bezüglich Nutzen und Bekanntheitsgrad der Homepage der DIC zu erhalten. Die Resultate liegen vor, die Auswertung durch den Vorstand und entsprechende Beschlüsse stehen noch aus.

Der Präsident orientiert kurz über die **Tätigkeitsfelder der Schweizerischen Chemischen Gesellschaft (SCG),** an denen auch die DIC über die Mitarbeit im Vorstand der SCG beteiligt ist. Entsprechende Informationen können über die Homepage der SCG und dort speziell über das Departement Strategie und Aussenbeziehungen eingesehen werden.

Als weiterer wichtiger Anlass im laufenden Geschäftsjahr sei auf das **6. Freiburger Symposium 2003 vom 25./26. September 2003** hingewiesen. Der Themenbereich **"Sichere Prozessführung in der Chemischen Industrie"** bietet Gewähr für eine fachlich aktuelle Weiterbildungsmög-

lichkeit und soll dem beruflichen Erfahrungsaustausch in einem für die chemische Produktion zentralen Bereich breiten Raum bieten. Wir bitten die Mitglieder von diesem Angebot gebrauch zu machen und auch weitere Berufskollegen auf die Veranstaltung hinzuweisen.

Im Anschluss an die Mitgliederversammlung offerierte uns Rohner das Mittagessen wobei auch der firmenübergreifenden Fachdiskussion Raum geboten werden konnte.

Der Betriebsrundgang am Nachmittag erfolgte unter kundiger Führung durch Betriebskader und gab uns einen eingehenden Einblick in die neuerstellten cGMP-Produktionsanlagen im Bau 40. Für die in der Entwicklung u. Produktion tätigen Chemiker u. Chemieingenieure sind diese Einblicke in andere Betriebe und die damit verbundenen Diskussionen wichtig. Die Möglichkeit zum Erfahrungsaustausch bringt doch immer wieder Erkenntnisse und Erfahrungen, die für das Gesamtwohl der produzierenden chemischen Industrie in der Schweiz wichtig sind.

Wir verdanken der Firma Rohner diesen sehr informativen und lehrreichen Einblick in ihr Fachgebiet und die erwiesene Gastfreundschaft recht herzlich und hoffen, uns im nächsten Jahr in einer ähnlich angenehmen Umgebung wieder treffen zu können.

Der Präsident DIC,
H. R. Dettwiler

The 2003 Chemistry Olympiad

The 35th International Chemistry Olympiad took place in Athens, July 4–14, 2003, with 232 candidates coming from 59 countries from all continents except Africa, which was represented solely by Egypt. Two countries sent observers: Peru and Tajikistan. As a matter of interest the candidates must be younger than 20 and not yet at University.

The Olympic competition is divided over two days, one for the theoretical tasks, and one for the practical tasks. Both competitions last five hours. After correction and arbitration the best competitors are awarded gold, silver, and bronze medals.

The four delegates from Switzerland were:
– Jeremy Deuel, 9000 St Gallen, from Kantonsschule Burggraben,
– Arnaud Haemmerlé, 1227 Carouge-Genève, from Collège de Staël,
– Jonas Häner, 3043 Uettlingen, from Kantonsschule Neufeld/Bern,
– Sebastien Heer, 9472 Grabs, from Kantonsschule Sargans.

The accompanying Swiss mentors were Maurice Cosandey (1162 St-Prex) and Thomas Bark (1700 Fribourg).

None of our students won a medal, but three of them (J.D., A.H., J.H.) obtained a Honorable Mention for having carried out perfectly one of the two practical tasks, with the corresponding calculations. The three best students of the competition were from Belarus, India, and China.

It should be highlighted that the Olympic level is much higher than our high school qualification. In all countries except Switzerland the competitors are specially trained by the Ministry of Education in camps sometimes spread out over several weeks. In our country, this cannot be done for lack of a common system of education and for lack of money. In Austria for example, Olympic training in regular classes is paid to the teachers as supplementary hours. As long as the training in Switzerland is based on a voluntary basis, we cannot train our students as it is done abroad. Our students are selected after two preparatory weekends and a training week around Easter time. We just hope to find somewhere a real gem. And we found some in the past, since Switzerland has obtained 17 medals since 1990, namely 2 gold, 5 silver, and 10 bronze.

The theoretical problems presented solved in Athens will not be reported here, because they were all multiple choice. The practical tasks were a dipeptide synthesis and a surprising titration of ascorbic acid with iodate ions which produces partly ICl and partly iodide ions.

Apart from the competition itself the participants had the opportunity of taking part in plenty of cultural activities, like visits to Delphi, Mykenes, Epidavros, Korinthos, and to an aluminum factory, despite the tropical temperature (sometimes 39 °C).

The next Olympiads will be in Kiel (D) 2004, Taiwan 2005, Korea 2006, Lithuania 2007, and Hungary 2008. Switzerland will take part of course, but the present mentors are getting old. We would be pleased to hear from some interested and enthusiastic professors, research fellows or teachers who would like participate to the Olympic adventure and maybe take up the torch. Do not hesitate to get in touch with the author.

Maurice Cosandey
Ch. Etourneaux 1
CH-1162 St-Prex
E-Mail: maurice.cosandey@bluewin.ch

New Members

Abraham, Anuji, 8093 Zürich
Alanine, Alexander, Dr., 4070 Basel
Angelov, Todor, 3007 Bern
Bagabas, Abdulaziz, Stillwater, OK, USA
Baillod, Pascal, 1015 Lausanne
Balin,Ioan, 1015 Lausanne
Barrelet, Timothée, 3012 Bern
Barron, Denis, Prof. Dr., 1010 Lausanne
Bättig, Pio, 6024 Hildisrieden
Benito, Samantha M., 4014 Hofstetten
Benny, Paul, 8057 Zürich
Bieri, Stefan, 1211 Genève
Bigler, Peter, Prof. Dr., 3012 Bern
Binggeli, Martin, Dr., 3415 Hasle-Rüegsau
Boato, Francesca, 8057 Zürich
Boccini, Francesca, 8093 Zürich
Bonacina, Luigi, 1015 Lausanne
Brasey, Thomas, 1015 Lausanne
Bucher, Denis, 1015 Lausanne
Bunten, Kevin, Dr., 8057 Zürich
Burai, Laszlo, 1015 Lausanne
Burri, Estelle, 1015 Lausanne
Cakara, Dusko, 1211 Genève
Callegari, Andrea, Dr., 1015 Lausanne
Caravati, Matteo, 8093 Zürich
Chappellet, Sabrina, Dr., 1211 Genève
Christen, Daniel, Prof. Dr., 3400 Burgdorf
Ciobanu-Salluce, Simona, Dr., 1700 Fribourg
Cuendet, Michel, 1015 Lausanne
Daher, Sawsan, 1211 Genève
Dang, Tung, 1015 Lausanne
Darmency, Vincent, Dr., 1015 Lausanne
Datta Chaudhuri, Piyali, 1211 Genève
De Agostini, Antonio, Dr., 8603 Schwerzenbach
Denes, Fabrice, Dr., 3012 Bern
Diezi, Simon, 8093 Zürich
Dumas, Jean-François, 2000 Neuchâtel
Fasan, Rudi, 8052 Zürich
Fatin-Rouge, Nicolas, Pontarlier, France
Fenaille, François, 1000 Lausanne
Frey, Jann, 3012 Bern
Furet, Pascal, Dr., 4002 Basel
Gapian Bianké, Jean-Paul, 3012 Bern
Gaschen, Annina, 3012 Bern
Gauthier, Sébastien, 1015 Lausanne
Ghanem, Ashraf, 1211 Genève
Gillet, Ludovic, 8008 Zürich
Goddard, Jean-Philippe, Dr., 3012 Bern
Gossens, Christian, 1015 Lausanne
Grote, Zacharias, 1015 Lausanne
Guidoni, Leonardo, Dr., 1015 Lausanne
Hannemann, Stefan, 8093 Zürich
Heck, Markus, 8057 Zürich
Helm, Lothar, Dr., 1015 Lausanne
Hermatschweiler, René, 8093 Zürich
Houriet, Raymond, Dr., 1015 Lausanne
Huber, Dominique, 8093 Zürich
Humbert, Patrice, Dr., 1006 Lausanne
Jakab Toth, Eva, Dr., 1015 Lausanne
Jazzar, Rodolphe, Dr., 1211 Genève
Jean-Denis, Bernard, 2000 Neuchâtel
Jimenez, Rodrigo, 1022 Chavannes
Joshi, R.V., Dr., Mumbai, India
Kavran Belin, Gamze, 1211 Genève
Keresszegi, Csilla, 8093 Zürich
Kirchner, Barbara, Dr., 8098 Zürich
Kola, Heliana, 1227 Genève
Küpfer, Pascal, 3012 Bern
Kurz, Christophe, 8093 Zürich
Labille, Jérôme, Dr., 1211 Genève
Lacrampe, Fabienne, 1211 Genève
Lammers, Sven, 4056 Basel
Larregaray, Pascal, Dr., 1015 Lausanne
Lehaire, Marie-Line, 1015 Lausanne
Leiggener, Claudia, 3012 Bern
Leist, Roman, 3012 Bern
Lomberget, Thierry, Dr., 1211 Genève
Mader, Heinz, 3095 Spiegel
Mahmood, Azad, 4056 Basel
Maris, Mihaela, 8093 Zürich
Maroni, Plinio, 1015 Lausanne
Marti, Sébastien, 4056 Basel
Meilert, Kai, Dr., 1015 Lausanne
Merkofer, Martin, 8093 Zürich
Mosimann, Markus, 3012 Bern
Müller, Christian, Weil am Rhein, Germany
Nagel, Matthias, Dr., 8600 Dübendorf
Narancic, Sanja, 8093 Zürich
Noël, Stéphane, 1211 Genève
Nutt, David, 4056 Basel
Orain, David, Dr., 4002 Basel
Pages, Stéphane, Gaillard, France
Papastavrou, Georg, Dr., 1211 Genève
Papina, Alina, 8093 Zürich
Pericet Camara, Ramon, 1211 Genève
Peters, Jens-Uwe, Dr., 4070 Basel
Piacentini, Marco, 8093 Zürich
Piccardi, Riccardo, 3012 Bern
Pirngruber, Gerhard, Dr., 8093 Zürich
Polianski, Mikhail, 1015 Lausanne
Quebatte, Laurent, 1015 Lausanne
Ramin, Michael, 8093 Zürich
Rauzy, Cedrick,Dr., 1746 Prez-vers-Noreaz
Reddy, Dubbaka s., 1015 Lausanne
Reinhard, Christine, 3012 Bern
Renaudet, Olivier, Dr., 3012 Bern
Riegert, David, 1211 Genève
Ritchie, Tim, Dr., London, UK
Rizvi, Syed, Atlanta, GA, USA
Röck, Gabriele, 8052 Zürich
Roehrig, Ute F., 1015 Lausanne
Rohr, Markus, 8093 Zürich
Roussel, Christophe, Dr., Pontarlier, France
Rucareanu, Simona M., Dr., 1700 Fribourg
Ruloff, Robert, Dr., 1022 Chavannes-près-Renens
Sahnoun, Mohammed, 1700 Fribourg
Salluce, Nunzio A., 1700 Fribourg
Salom-Roig, Xavier, 3012 Bern
Sambourova, Vera, 8093 Zürich
Schappler, Julie, 1211 Genève
Schär, Pascal, 3012 Bern
Schärer, Claude, 4460 Gelterkinden
Scherer, Lukas, 4056 Basel
Schiller, Alexander, 1015 Lausanne
Seeberger, Peter H., Prof. Dr., 8093 Zürich
Siegenthaler, Hans, Prof. Dr., 3600 Thun
Sonderegger, Otmar, 8093 Zürich
Sour, Angelique, 1015 Lausanne
Stoeckli, Andreas, 4056 Basel
Strobel, Reto, 8092 Zürich
Studer, Matthias D., 4056 Basel
Sulpizi, Marialore, Dr., 1015 Lausanne
Tafelmeyer, Petra, 1015 Lausanne
Tanyanyiwa, Jatisai, 4056 Basel

Tavernelli, Ivano, Dr., 1015 Lausanne
Tercier-Waeber, Marie-Louise, 1211 Genève
Tiouabi, Mustapha, 2000 Neuchâtel
Tona, Rolf, 3018 Bern
Tonti, Dino, Dr., 1015 Lausanne
Ugurtas, Bernadette, 1015 Lausanne
Urakawa, Atsushi, 8093 Zürich
Urwyler, Bernhard, Dr., 4133 Pratteln
Valet, Martial, 1211 Genève
van Bokhoven, Jeroen A., Dr., 8045 Zürich
van Staveren, Dave, Dr., 8053 Zürich
Verdan, Simon, 1211 Genève
Verdes, Dorinel, 8057 Zürich
Vitali, Francesca, 8050 Zürich
von Lilienfeld-Toal, Anatole, 1015 Lausanne
Wanner, Hans, Dr., 5306 Tegerfelden
Wenger, Bernard, 1015 Lausanne
Wirz, Ronny, 8093 Zürich
Wortmann, Arno, 8093 Zürich
Yongzheng, Yang, 3012 Bern
Zabala Ruiz, Arantzazu, 3012 Bern
Zivanov, Svetlana, 1700 Fribourg
Zobi, Fabio, 8057 Zürich
Zoete, Vincent, 4056 Basel

INFORMATION

Congresses – Conferences – Workshops

SensLab2 Conference: Sensors from Research to Market

17–18 June 2004, Technopark Zurich, Switzerland

Celebrating the Decennial of CCS (The Centre for Chemical Sensors and Chemical Information Technology) founded by Prof. Ursula E. Spichiger-Keller.

For more information please contact: CCS, ETH Zurich-Technopark, Technoparkstr. 1, CH-8005 Zurich, Switzerland.
E-mail: info@chemsens.pharma.ethz.ch
Webpage: http://www.chemsens.ethz.ch

News

The IUPAC Prize for Young Chemists 2004 – Invitation for Submission

IUPAC Prize for Young Chemists has been established to encourage outstanding young research scientists at the beginning of their careers. The prize will be given for the most outstanding PhD thesis in the general area of the chemical sciences, as described in a 1000-word essay. IUPAC awards up to four prizes annually, each prize consisting of USD 1000 cash and subsidized travel expenses to the next IUPAC Congress. Prizes are presented biennially at the IUPAC Congress.

Entrants must have received their PhD (or equivalent) degree, or completed all PhD requirements, including successful defense of the doctoral thesis, during the 2003 calendar year.

The research described in the entrant's thesis must be in the field of the chemical sciences, defined as 'chemistry and those disciplines and technologies that make significant use of chemistry', and the work must have been performed while the entrant was a graduate student.

The deadline is February 1, 2004 for entrants who receive their PhDs (or equivalent) degrees during the calendar year 2003.
<http://www.iupac.org/news/prize.html>

2nd BioValley Life Sciences Week: October 13–17, 2003, at Basel

After the great success of the first BioValley Life Sciences week held in October 2002 in Basel, a new week will be organized in October 2003 and will take place in Basel, Colmar/Strasbourg, Freiburg, and Lörrach.

The week, organized by BioValley Basel AG, offers a platform for experts and executives in the BioValley region. Strategies, results and consequences in the life sciences will be presented and discussed in a generous scope with extensive audience appeal.

The trinational program on Monday is followed by the University Day where frontiers in biomedical research and new technologies are the focus.

On Wednesday, BioValley Connect, a partnering and finance conference allows biotech companies to meet with representatives of big pharmaceutical and financial institutions. Selected start-ups as well as small and mid-sized pharmaceutical companies will give presentations about their products and services. In the BioValley Exhibition Village the companies also have the possibility to present themselves.

On Thursday there is the annual forum 'Technik & Gesellschaft', dealing with management concepts of responsibility and sustainability in biosciences. The afternoon forum concentrates on personalized medicine and its horizons, followed by an evening event of the 'Handelskammer beider Basel' with the topic 'Limits of Biopatents'.

On Friday the college day is organized together with the Gymnasium of Liestal, in order to introduce the topic of biotechnology to the young generation.

Information:
BioValleyBasel AG,
Blumenrain 23,
CH-4051 Basel
Tel.: +41 61 269 88 38;
Fax: +41 61 269 88 34;
E-mail: info@biovalleybasel.com

39th Symposium on Theoretical Chemistry

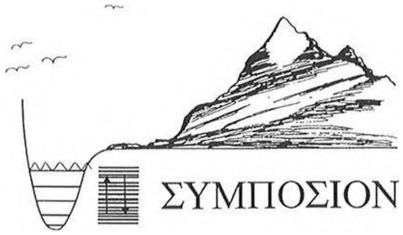
MOLECULAR SPECTROSCOPY AND DYNAMICS

28 September to 2 October 2003

Gwatt, Lake Thun, Switzerland

Organized by:

Hans-Peter Lüthi, Martin Quack (ETH Zürich), and Jürgen Stohner (ZHW Winterthur)



Under the Auspices
of the Division Chemical Research of the Swiss Chemical Society
and the
Arbeitsgemeinschaft Theoretische Chemie (DBG, DPG, GDCh)

Contact: webpage *http://www.stc03.ethz.ch:8086*

The conference aims at describing the current status and most recent advances of Theoretical Chemistry in relation to all aspects of Molecular Spectroscopy and Molecular Dynamics. Molecular Spectroscopy has always had a special relation to Theoretical Chemistry and a particular goal of this meeting is to bring together also theoreticians and interested experimentalists in this general field.
Exciting new developments in experiments on high-resolution molecular spectra and their analysis as well as new theoretical developments in the calculations of such spectra and the related time-independent and time-dependent quantum dynamics of molecules have led to new answers but also to new questions in the fields of molecular kinetics, molecular reaction dynamics, molecular chaos, and statistical mechanics as well as fundamental symmetries in molecular processes. Particular stress will be placed on fundamental aspects and new directions. The meeting allows for invited lectures and contributed lectures and poster sessions. All sessions will be plenary.

Location and Travel
The location is in Gwatt in a conference center directly located on the shore of Lake Thun surrounded by the Bernese alps of Switzerland. Gwatt is a small village adjacent to the town of Thun. It can be easily reached by car (freeway exit Thun Süd) or by frequent high speed trains via Bern/Thun or by air via Zürich and Geneva airports (connected by train to Thun or by a 1-2 hour car ride from the airport to Gwatt).

Registration and Deadlines
Registration, all meals including the conference dinner and other events, as well as lodging for four days are provided (arrival Sunday afternoon 28 September 2003, departure Thursday 2 October 2003 afternoon) at several flat rates depending on accommodation (ranging from simple 'student' to 'comfortable'), some accommodation is available as well in nearby hotels.

Preliminary List of Speakers
Lorenz Cederbaum (Heidelberg), **Claude Daul** (Fribourg), **Gernot Frenking** (Marburg), **Jürgen Gauss** (Mainz), **Martina Havenith** (Bochum), **Bernd Hess** (Erlangen), **Kimihiko Hirao** (Tokyo), **Martin Jungen** (Basel), **Wim Klopper** (Karlsruhe), **Sam Leutwyler** (Bern), **Marius Lewerenz** (Paris), **John P. Maier** (Basel), **Roberto Marquardt** (Paris), **Fréderic Merkt** (Zürich), **William H. Miller** (Berkeley), **Jeppe Olsen** (Aarhus), **Michele Parrinello** (Manno), **Tom Rizzo** (Lausanne), **Joachim Sauer** (Berlin), **Martin Suhm** (Göttingen), **Walter Thiel** (Mühlheim), **Jürgen Troe** (Göttingen), **Hans-Joachim Werner** (Stuttgart), **Regina de Vivie-Riedle** (München), **Tomasz Wesolowski** (Genève)

Lectures

Institut de Chimie, Université de Neuchâtel

Mercredi	Cours ERASMUS
24 september 2003	Prof. *David Fenton*
10h30	University of Sheffield, UK
Petit Auditoire	Le titre sera annoncé plus tard

Département de Chimie Organique, Université de Genève

Sciences II, Auditoire A-100, 16h30
30, quai Ernest Ansermet, Genève

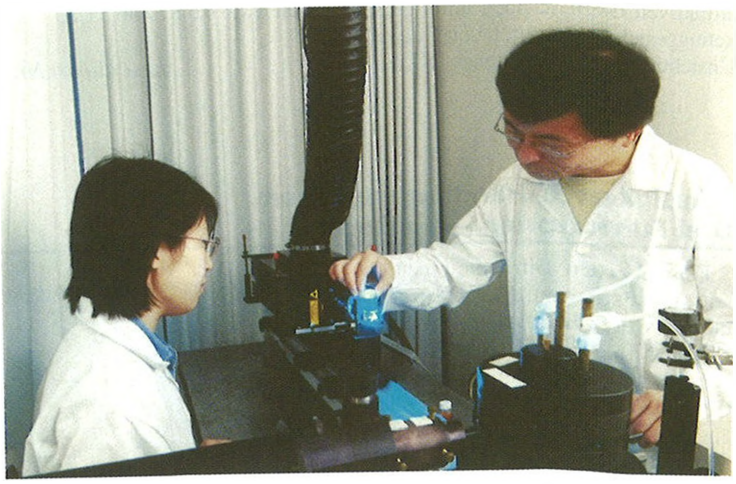
Vendredi 5 septembre	Prof. *Koichi Mikami* Tokyo Institute of Technology, Japan 'Tropos or Atropos? That is the Question!'
Lundi 15 septembre	Prof. *Max Malacria* Université Pierre et Marie Curie, Laboratoire de chimie, (Paris VI), France 'Reactions de polycyclisations en cascade'
Jeudi 25 septembre	Prof. *Jonathan Clayden* University of Manchester, Department of Chemistry, Manchester, UK 'Stereoselectivitity and Synthesis with Rotationally Restricted Amides'

CHIMIA-REPORT

Bitte an die Inserenten

Richten Sie Ihre Beiträge für die Rubrik CHIMIA-REPORT nicht an die Redaktion, sondern ausschliesslich an: Kretz AG, Postfach, CH-8706 Feldmeilen Besten Dank!

New instruments further polymer research at Nanyang



Research characterizing polymer-surfactant systems at Nanyang Technological University in Singapore has been given a boost recently in the form of several new pieces of equipment from Brookhaven Instruments. Michael KC Tam, Professor at the School of Mechanical and Production Engineering, explained: "Our research focuses on the microscopic and macroscopic properties of selfassembly systems, such as block copolymers, associative polymers and surfactants, which have potential applications in enhanced dnug release, gene therapy and environmentally friendly coating systems."

"Part of our work involves synthesizing polymers using atom transfer radical polymerization (ATRP) and examining their physical characteristics using static and dynamic light scattering, for which we have used a Brookhaven Bl-200SM goniometer with 9000AT autocorrelator for many years. With the recent purchase of our new instruments, including a ZetaPlus Analyzer and a Bl-MwA Molecular Weight Analyzer, we can perform much more detailed molecular analyses on these complex systems. The instruments are very easy to use and we can now do so much more than before."

Professor Tam concluded: "I have always been pleased with Brookhaven's technical support. Bruce Weiner, the MD of Brookhaven, is well versed in optical theory and has taught us how to get the most from the instruments."

For more information about Brookhaven products, please contact:

- Dr. Bruce Weiner
  Brookhaven Instruments Corporation,
  750 Blue Point Road,
  Holtsville, NY 11742 U.S.A.
  Telephone: +1(631) 758-3200
  Fax: +1(631) 758-3255
  e-mail: info@bic.com
  www.bic.com

- Dr. Peter McFadyen
  Brookhaven Instruments Limited,
  Chapel House, Stock Wood,
  Redditch, Worcestershire,
  B96 6ST, UK.
  Telephone: + 44 (0) 1386 792727
  Fax: + 44 (0) 1386 792720
  e-mail: info@brookhaven.co.uk
  www.brookhaven.co.uk

Leserdienst Nr. 2

Rotronic auf der Ineltec 2003 (Halle 1.1 Stand D21)

Die Messebesucher der diesjährigen Ineltec erhalten einen Einblick in das umfassende Sortiment der Firma Rotronic AG. Gesamtlösungen für die Industrie von der Rotronic AG sind keine Papiertiger. Vom 19"-Schrank über den IPC-Rechner, die USV-Anlage, Stromversorgungen bis hin zu den Messgeräten erhält der Kunde alles aus einem Haus.

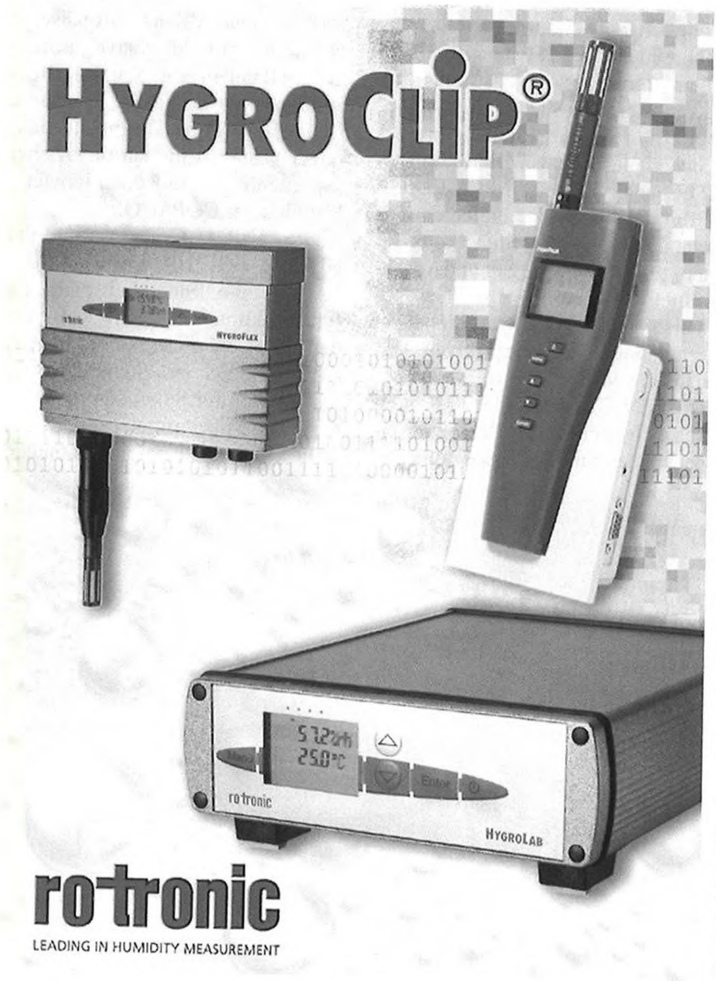
Feuchte- und Temperaturmessung

Rotronic zeigt die gesamte Palette der in der Schweiz entwickelten und produzierten Messgeräte für Feuchte und Temperatur.

Neu stellt Rotronic Messumformer in eleganter Raumausführung vor, die aktuellste digitale Technologie mit messtechnischer Raffinesse vereinigen.

Im Rahmen der Ineltec wird ein Referenz-Set für die Feuchtemessung zu einem Messe-Vorzugspreis angeboten. Das Handmessgerät HygroPalm mit dem Referenzfühler HygroClip S in einem robusten Messkoffer sind ein Muss für jeden Feuchtemessprofi.

Die neuesten Sensorentwicklungen der Hygromer-Serie, wie z.B. beheizbare Feuchtesensoren und Feuchtesensoren zum Einsatz bis zu 200 °C, runden den Messeauftritt ab.



Elektronische Geräte

Das umfassende Gerätesortiment der neuesten Generation besticht durch seine kundenorientierten Funktionen. Namhafte Hersteller wie Finest, Escort, TTI, KIKUSUI oder Elektro-Automatik (EA) präsentieren ihr Sortiment vom Low-Cost Handmultimeter bis hin zu Mess- und Netzgeräten der höchsten Präzisionsklasse.

Der Labormöbelhersteller Hera zeigt seinen neusten Fertigungsarbeitstisch mit den entsprechenden Messgeräten. Als 3-Phasen Partner von Powerware und High Power Partner von APC verfügt die Rotronic AG über grosse Erfahrung im USV Bereich. An der Messe sehen Sie das ganze Spektrum.

Elektronik Packaging Lösungen

Neben den bekannten 19" Standardschränken hat die Rotronic ihr Produktsortiment weiter ausgebaut. Edelstahl- und Elektroschränke sind in fast jeder Dimension erhältlich.

Gehäuse für 19"-Anwendungen sowie Speziallösungen nach Kundenwunsch werden präsentiert. Das vielseitige Angebot der Hersteller apra und Schroff erlaubt Rotronic, praktisch jeden Kundenwunsch zu erfüllen.

Industrie-PC und Systeme

Die Firma Rotronic AG präsentiert dieses Jahr neue, kompakte, stabile und innovative Industriecomputersysteme. Mit den Marken Roline und Axiomtek folgt Rotronic den neusten Markttrends.

- Rotronic AG
  Postfach 451
  CH-8303 Bassersdorf
  Telefon: 01-838 11 11
  Telefax: 01-836 44 24
  E-Mail: info@rotronic.ch
  www.rotronic.com

Leserdienst Nr. 3

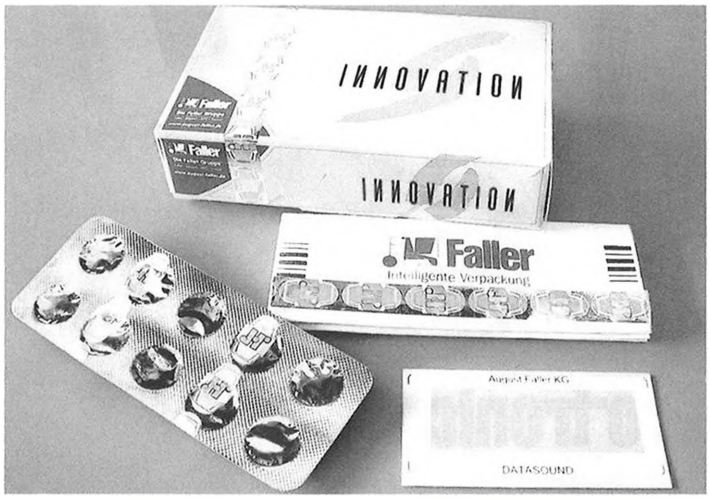
MEDICA PROTEC: Durchgängiges Sicherheitssystem für Primär- und Sekundärverpackungen

Nicht zu knacken

Die Faller Gruppe (Waldkirch, Lörrach und Schopfheim), einer der führenden Spezialisten für Arzneimittelverpackungen, stellt seine Kompetenz in Sachen Anti-Counterfeiting mit der Realisierung des Sicherheitssystems MEDICA PROTEC unter Beweis. Mit MEDICA PROTEC bietet die Faller Gruppe ein durchgängiges Sicherheitssystem für Primär- und Sekundärpackmittel der Pharma- und Gesundheitsbranche. Systempartner bei der Entwicklung der innovativen Verpackungslösung war die HUECK FOLIEN GmbH & Co. KG (Weiden), Hersteller von flexiblen Verpackungen und Folienspezialitäten.

Die Faller Gruppe ist Gründungsmitglied der COPAPHARM EUROPE, einer Allianz europäischer Hersteller für Pharmaverpackungen, und neben Karl Knauer (Biberach/Baden), der Rob. Leunis & Chapman Gruppe (Berlin und Hannover) und Limmatdruck/Zeiler (Spreitenbach und Köniz/Schweiz) Mitglied der COPACO.

Die Faller Gruppe und die HUECK FOLIEN GmbH & Co. KG, die u.a. Sicherheitselemente für Banknoten herstellt (z.B. für den Euro), entwickelten mit MEDICA PROTEC ein Sicherheitssystem sowohl für Sekundär- als auch für Primärpackmittel, das Massstäbe setzt: Übereinstimmende Sicherheitsmerkmale werden sowohl für den Blisterstreifen als auch für Faltschachtel, Packungsbeilage und Haftetikett verwendet. Praktisch: Der Kunde muss für die Anbringung der verschiedenen Sicherheitsmerkmale keine Veränderungen an der Verpackungslinie durchführen.



Mit der eingesetzten Technik entsteht banknotenähnliche Sicherheit für alle Elemente der Packung. Als Trägermaterial dienen bei MEDICA PROTEC Hologrammstreifen mit sichtbaren und geheimen Merkmalen. Diese schwer fälschbaren Hightech-Sicherheitsstreifen übernehmen zudem die Aufgabe eines Gütesiegels und sind wegen ihrer attraktiven Optik auch unter Marketinggesichtspunkten von Nutzen. Unsichtbare enthaltene Sicherheitsfeatures, die nur mittels eines speziell dafür abgestimmten Equipments ausgelesen werden können, komplettieren den Schutz. Die Kombination aus beidem macht die Verpackung zum Produkttresor!

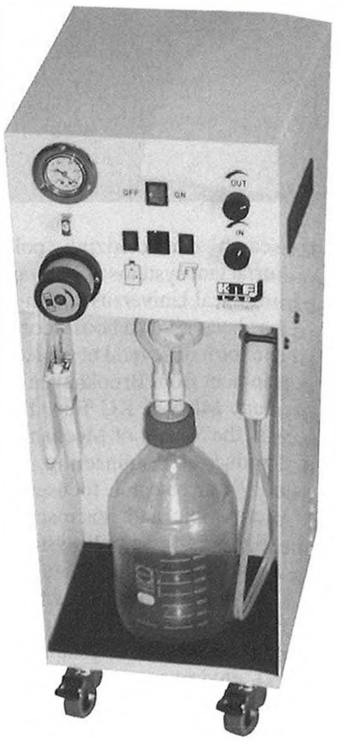
Die Tatsache, dass Faller zur Realisierung dieser Packaging-Lösung eine gezielte Projektpartnerschaft suchte, unterstreicht den Anspruch, den Kunden aus dem Pharma- und Gesundheitsbereich Full-Service-Dienstleistungen rund um die Verpackung anzubieten.

- August Faller KG
  Freiburger Strasse 25
  D-79183 Waldkirch
  Telefon: 076 81 / 40 50
  Telefax: 076 81 / 40 51 10

Leserdienst Nr. 4

Flüssigkeits-Handling im Labor: Drei Funktionen – ein Gerät

Flüssigkeiten filtrieren, pipettieren und absaugen: Viele Prozesse im Labor erfordern diese Schritte. Bisher benötigte man dazu drei verschiedene Vakuumquellen und Geräte: Eine Vakuumpumpe oder einen anderen Vakuum-Anschluss für die Filtration, ein Pipettiergerät und eine Absaugeinrichtung mit Auffangbehälter. Der neue KNFLab@-Tower vereint dagegen alle drei Funktionen – in einer platzsparenden und bedienerfreundlichen Einheit.



Um zu filtrieren, schliesst man ein Vakuum-Filtrationsgerät – über einen Schlauch mit Schnelikupplung – an den Tower an. Dieser liefert das notwendige Vakuum, das durch eine chemiefeste Membranpumpe erzeugt wird. Für das Pipettieren ist ein Pipettiergerät mit Sterilfilter an der zentralen Vakuumeinheit des Towers angeschlossen. Dank dieser Anordnung benötigt das Pipettiergerät keine eigene Pumpe und Batterien – mit dem Vorteil eines sehr geringen Gewichts. Zum Absaugen stehen verschiedene Absauggeräte als Zubehör zur Wahl. Aufgenommen wird die abzusaugende Flüssigkeit von einer autoklavierbaren 2-Liter-Flasche, die kontaminationssicher verschlossen ist. Ein Vakuummeter zeigt den Druck in der Vakuumflasche an. Sowohl die Förderleistung beim Absaugen und Filtrieren als auch die Ansaug- und Abgabegeschwindigkeit beim Pipettieren lassen sich regulieren.

Der mit feststellbaren Rollen ausgerüstete Tower passt unter den Labortisch und nimmt in der Breite lediglich etwa 25 Zentimeter in Anspruch. Er eignet sich für Rechts- wie Linkshänder gleichermassen und zeichnet sich durch einen äusserst geringen Schallpegel aus.

- KNF Neuberger AG
  Stockenstrasse 6
  CH-8362 Balterswil
  Tel. 071 971 14 85
  Fax 071 971 13 60
  knf@knf
  www.knf.ch

Leserdienst Nr. 5

VEGAPULS 60 – Das kleinste Füllstand-Radar der Welt

Mit den Radarsensoren der Serie VEGAPULS 60 geht die bewährte Mikrowellen-Puls-Technologie bei VEGA in die dritte Generation. Die Erfahrungen aus mehr als zwölf Jahren Radar-Füllstandmesstechnik und weltweit über 60.000 erfolgreichen Installationen bildeten die Grundlage bei der Entwicklung der neuen Zweileiter-Radarsensoren. Das Ergebnis ist die Serie VEGAPULS 60 – die weltweit kleinsten Radarsensoren zur Füllstandmessung.

Die einzelnen Geräte der Serie VEGAPULS 60 unterscheiden sich durch die Art der Mikrowelleneinkopplung. Robuste Hornantennen aus Edelstahl bis hin zu gekapselten Antennensystemen für den Pharma- und Lebensmittelbebreich ermöglichen die berührungslose Füllstandmessung mit Radar in nahezu allen Bereichen der Industrie.

Als Mitglied der plics®-Serie minimiert das VEGAPULS die Kosten über den gesamten Lebenszyklus des Gerätes. Das beginnt bereits bei der einfachen Auswahl des passenden Gerätes. Vier Gehäuse, drei Elektroniken und unzählige Prozessanschlüsse erlauben die optimale Anpassung an jede Anwendung. Und das mit allen gängigen Zulassungen.

Die einfach verständliche Bedienung mit dem Anzeige- und Bedienmodul PLICSCOM oder über den PC mit PACTware nach dem DTM/FDT-Konzept spart ebenfalls viel Zeit bei der Inbetriebnahme.

plics®-Radarsensoren von VEGA – Technik neuster Stand.

• VEGA Messtechnik AG
Barzloostrasse 2
CH-8330 Pfäffikon
Tel: +41 (1) 950 57 00
Fax: +41 (1) 950 57 13
E-Mail: info@ch.vega.com
www.vega.ch

Leserdienst Nr. 6

Ist Ihre Luft sauber oder rein?

Es ist unser Job, Ihre Sicherheit für die Zukunft zu gewährleisten. Nutzen Sie unser Know-how als Experten der Reinraumtechnik!

Indem Sie Service und Qualifizierungen von Reinraumanlagen erfahrenen Profis überlassen, können Sie sich das Leben leicht machen. Die SKAN AG ist seit 35 Jahren Hersteller und Marktleader in diesem Bereich. Von Anfang an hat sich das Schweizer Unternehmen mit heute über hundert Mitarbeitern durch einen sehr persönlichen Kundendienst ausgezeichnet.

Nehmen Sie also einen solchen Kundendienst für Reinraumtechnik in Anspruch, wo Sie können. Sie brauchen sich z. B. nicht selbst um vorbeugende Anlagenkontrollen bemühen. Dabei geht es als erstes um Sie, das heisst um den Nachweis, dass Personal ausreichend geschützt ist. Ebenso müssen vielleicht Ihre empfindlichen Produkte oder die Arbeitsumgebung geschützt werden. Daher wird die volle Funktionstüchtigkeit von LaminarFlow-Anlagen, z. B. von mikrobiologischen Sicherheitswerkbänken genau überwacht. Es werden in Labor- und Produktionsisolatoren, Powderhandling-Anlagen und Zytostatika-Werkbänken auch sensible oder reaktive Substanzen verarbeitet. Daher müssen sie regelmässig kontrolliert werden. Die wichtigste Frage lautet: Filtern die Luftfilter solcher Anlagen noch ausreichend oder nicht? Genaue Filterprüfungen (in situ-Lecktest) mit vertrauenswürdigen Messergebnissen geben die Antwort. Zum typischen Kundendienst gehören auch Montage- und Demontagearbeiten, kurzfristige Reparaturen, Dekontaminationen und komplette Umzugsarbeiten. Gegebenenfalls führen Servicetechniker für Sie die fachgerechte Entsorgung reinraumtechnischer Anlagen durch, falls sie z. B. heutigen hohen Qualitätsansprüchen nicht mehr entsprechen. Sichere Fachkunde und langjährige Praxiserfahrung können Sie jedenfalls auf allen genannten Einsatzgebieten erwarten.

Für Kontrollen, Prüfungen und Qualifizierungen reinraumtechnischer Anlagen reicht eine umfassende Kenntnis der international gültigen Reinraumnormen nicht aus. Hier muss besondere bei den Messungen und ihrer Dokumentation aufgewendet werden. Behördliche Inspektoren werden selbst keine Gegenmessungen durchführen, sie beurteilen besonders nach Eindruck und Aussagekraft der vorgelegten Dokumente. Beim dokumentierten Nachweis gilt im Hinblick auf Inspektion und Audit, dass er vollständig und durchgängig erstellt sein muss – natürlich in der jeweiligen Sprache des Kunden. Nebenbei zählt noch das Minimierungsgebot: Soviel Dokumente wie nötig, so wenig wie möglich. Die Dokumentationen werden dann durch ein unabhängiges Qualitätssicherungswesen mit Quality Compliance Officer begutachtet. Für die SKAN AG ist das eine zusätzliche kritische Selbstverpflichtung innerhalb der Zertifizierung nach EN ISO 9001. So profitieren Kunden von vielen Erfahrungen mit GMP- und GAMP-lastigen Projekten. Ein jahrzehntelanges intensives Engagement in der internationalen Pharmazie und Forschung gewährleistet Verfahren nach dem Stand der Technik. Die ausführenden Qualifizierungstechniker müssen sowohl in der Theorie professionell geschult sein, als auch in der Praxis Messgeräte und deren Besonderheiten sehr gut beherrschen. Alle eingesetzten Messinstrumente sind

dauernd auf dem neuesten Stand zu halten. Sie sind also optimal gewartet und regelmässig kalibriert. Das ist kein geringer Aufwand.

Ob Kundendienst, Prüfungen nach Standardverfahren oder eine Qualifizierung nach IQ/OQ – welche reinraum- und raumlufttechnischen Aufgaben Sie vergeben wollen, wir sind Ihr Partner. Unsere Techniker beraten Sie unverbindlich zu den aktuellsten Anforderungen.

- SKAN AG
  Postfach
  CH-4009 Basel
  Telefon ++41 (0)61 485 45 55
  Telefax ++41 (0)61 485 44 45
  www.skan.ch

Leserdienst Nr. 7

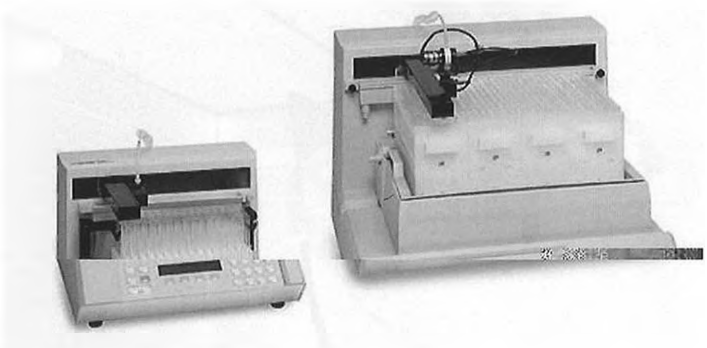
Gilson FC 204 und FC 203B – Fraktionensammler für Mikroplatten

Gilson ist weltweit bekannt als Hersteller von Präzisionsinstrumenten, wie Mikropipetten, Probenvorbereitungs- und HPLC-Systeme. Hinzu kommt ein profundes Wissen auf dem Gebiete der präparativen HPLC, das sich in der kontinuierlichen Verbesserung und Ausweitung des Gilson Sortiments wiederspiegelt. In diesem Zusammenhang dürfen der robuste Gilson Fraktionensammler FC 204 und der kompaktere FC 203B als Beispiel erwähnt werden. Zur klassischen Anwendung im ml-Bereich kommt jetzt auch die Sammlung von ul-Mengen hinzu. Dafür braucht es eine spezielle Mikro-Dispensiernadel, ein 3-Wegventil und ein Mikroplatten-Rack. So kann der FC 204 in vier 96-er Mikroplatten (shallow- oder deep-well) und der FC 203B in eine Platte sammeln. Es stehen vier Sammelmethoden zur Auswahl und die benötigten Parameter werden einfach über das eingebaute Keypad eingegeben. Auch manuelle Änderungen nach dem Programmstart sind jederzeit möglich. Die Fraktionensammler sind sowohl für den Stand-alone-Betrieb als auch für die Anbindung an die gängigsten HPLC-, MPLC- und Flash-Systeme konzipiert. Benutzt man sie als Teil einer automatischen, präparativen HPLC-Anlage, wird vorzugsweise im Peak-Modus gearbeitet, d.h. es wird nach UV oder nach einem anderen Analog-Signal gesammelt. Gestartet oder gestoppt werden die Geräte über Kontakte und ein eingebauter "Event Marker" erlaubt die Aufzeichnung des Fraktionenwechsels. Bei einfacheren HPLC-Anlagen, ohne PC-Software oder Detektor, steht der Zeitmodus (Eingabe der Zeitdauer pro Sammelgefäss) zur Verfügung. Natürlich lassen sich die Sammler auch manuell bedienen (Manual Modus), wobei das Schalten auf die nächste Position individuell bestimmt wird. Diese Flexibilität und die ausgesprochene, lange Lebensdauer machen die Gilson Fraktionensammler weltweit zu beliebten Laborgefährten in Chemie-, wie auch in Biochemie- und Molekularbiologie-Laboratorien.

Mehr Infos zu allen Fraktionensammler und HPLC-Modulen von Gilson erhalten sie bei:

- Gilson (Schweiz) AG,
  Untere Bahnhofstrasse 14
  CH-8932 Mettmenstetten,
  Tel. 01/768 56 00
  eMail: info-ch@gilson.com

Leserdienst Nr. 8



Die Verfügung zur Gesamtsanierung der Sondermülldeponie Kölliken wird rechtskräftig

Gestützt auf die Altlastenverordnung des Bundes hat das Baudepartement des Kantons Aargau die Sanierungsverfügung für die Durchführung der Gesamtsanierung der Sondermülldeponie Kölliken (SMDK) durch das sanierungspflichtige Konsortium SMDK erlassen. Damit wird das vorliegende Sanierungsprojekt rechtlich verbindlich. Am 21. Oktober 2003 findet zum Thema "Sicherung und Gesamtsanierung – Aufgaben und Lösungen" in Kölliken wiederum eine Fachtagung statt.

Ab 2005 soll die rund sieben Jahre dauernde Sanierung beginnen. Dabei werden der gesamte Deponiekörper und allfällige Verunreinigungen bis 5 m Tiefe unter der Deponiesohle entfernt und umweltgerecht entsorgt. Bei diesen Arbeiten werden die Beeinträchtigungen der Umgebung durch Geruch, Lärm oder Verkehr mit sehr aufwändigen technischen Massnahmen so gering wie möglich gehalten.

Bevor die Sanierung beginnen kann, müssen die sichernden Grundwasserschutzmassnahmen abgeschlossen und weitere Bewilligungsverfahren durchlaufen werden. Neben der Baubewilligung durch die Standortgemeinde Kölliken erfordert die verkehrstechnische Erschliessung zusätzliche Bewilligungsverfahren. Das Sanierungsprojekt sieht einen Gleisanschluss für die vorgesehenen Abfalltransporte per Bahn und eine neue Linienführung der Kantonsstrasse vor.

Im Februar 2003 hat das Konsortium SMDK bei den kantonalen Behörden ein entsprechendes Sanierungsprojekt eingereicht, das anschliessend von den verschiedenen kantonalen Fachstellen unter der Mitwirkung der Standortgemeinde Kölliken und dem Bundesamt für Umwelt, Wald und Landschaft (BUWAL) gründlich geprüft worden ist.

Die Arbeiten werden unter strengsten Auflagen zum Schutze der Bevölkerung und der Umwelt durchgeführt. Der gesamte Rückbau der Deponie sowie die Verpackung der Abfälle zum Abtransport finden in festen, teilweise mit dem Arbeitsfortschritt umsetzbaren Hallen unter Unterdruck statt. Die Abluft der Hallen wird mehrstufig gereinigt. Diese und zahlreiche weitere Umweltschutzmassnahmen sind durch die Sanierungsverfügung bindend festgelegt.

Mit der Realisierung des rund 400 Millionen Franken teuren Projektes wird mit sehr hoher Wahrscheinlichkeit erreicht, dass nach dem Jahr 2015 keine weiteren Sanierungsmassnahmen mehr nötig sein werden.

Das aus dem Sanierungsprojekt entwickelte Bauprojekt soll bereits Ende September 2003 bei der Gemeinde eingereicht werden. Die Erschliessungsplanung und das Strassenbauprojekt werden mit dem Baubewilligungsverfahren koordiniert. Spätestens Ende Mai 2004 sollen die nötigen Bewilligungen vorliegen, sodass mit den Sanierungsarbeiten termingerecht anfangs 2005 begonnen werden kann.

Am 21. Oktober führt die SMDK unter dem Titel "Sicherung und Gesamtsanierung – Aufgaben und Lösungen" auch dieses Jahr eine Fachtagung durch. Dabei kann die Abschirmung Süd besichtigt werden. Sie besteht aus einem 600 m langen Werkstollen in 20 Metern Tiefe, sowie den 130 Drainagebrunnen, die mit 80 cm Durchmesser im Abstand von 4 Metern über diesem Werkstollen gebohrt worden sind. Diese liefern seit März 2003 teils kontaminiertes, teils sauberes Wasser aus dem Umfeld der Deponie.

Eingebettet in neun Fachreferate und eine Besichtigung der Abschirmung Süd werden auch zwei Filme gezeigt. Der erste hat den Bau der Abschirmung Süd zum Thema, der zweite basiert auf den digitalen Daten der Planer und vermittelt einen Eindruck darüber, wie die Gesamtsanierung der Sondermülldeponie Kölliken in den nächsten Jahren strukturell vorbereitet und danach vonstatten gehen wird. Das detaillierte Programm und die Anmeldung befindet sich zum downloaden auf dem Internet unter www.smdk.ch unter der Rubrik "Aktuell"

- smdk Sondermülldeponie
  Safenwilerstrasse 27
  CH-5742 Kölliken
  Tel. 062 / 737 80 10
  Fax 062 / 737 80 20
  info@smdk.ch
  www.smdk.ch

Leserdienst Nr. 9

TORUSMILL® SK Innovative Tauchmühle – made in Germany

Die bekannte TORUSMILL®-Produktreihe ist nun von der Firma VMA-GETZMANN GMBH um die neue Serie "SK" erweitert worden.

Während die patentierte TORUSMILL® TM die bekannten Verfahren der Vordispergierung mit der Dissolverscheibe und das Feinstmahlen mit dem Mahlkorb mit einer Maschine realisiert, wurde die neue SK-Produktreihe als reine Tauchmühle konzipiert. Das Mahlsystem der TORUSMILL® SK ist baugleich mit dem der TORUSMILL® TM.

Zum Dispergieren wird der mit Mahlperlen gefüllte Mahlkorb der TORUSMILL® SK einfach in den Behälter, in dem sich das vordispergierte Mahlgut befindet, eingetaucht. Die Mahlperlen werden dann durch das Mahlwerkzeug in Bewegung gebracht und das Mahlgut im Mahlkorb dispergiert. Das patentierte Pumprad sorgt durch seine turbinenartige Wirkung im Einsaugbereich des Mahlkorbes für

- hohe Durchsatzraten auch bei hochviskosen Produkten
- hervorragende Mahlergebnisse in sehr kurzer Zeit, sowie für ein
- enges Teilchengrössenspektrum.

Der Anwender kann mit der TORUSMILL® SK leicht seine eigenen Behälter verwenden und optional sind auch spezielle Deckel für den geschlossenen Betrieb, kundenspezifische Abstreifsysteme und SPS-Prozesssteuerungen zur Realisierung von automatisierten Produktionsbetrieb lieferbar.

Mit der TORUSMILL® SK ist somit eine besonders wirtschaftliche Tauchmühle verfügbar, die für mobile Basisbehälter der Grössen 100, 250, 500 und 1000 l Inhalt lieferbar ist. Die TORUSMILL® SK ist aber auch als Anlage mit bis zu drei jeweils 3000 l grossen, in einer Arbeitsplattform fest eingelassenen Behältern lieferbar. Für Laborversuche stehen Geräte für Produktmengen von 250 ml bis 10 l zur Verfügung.

Fordern Sie bitte für weitere Informationen über die neue TORUSMILL® SK den brandneuen Katalog 2003 bei der VMA-GETZMANN an.

- VMA-GETZMANN GmbH
  Verfahrenstechnik
  Euelerhammerstrasse 13
  D-51580 Reichshof
  Telefon 0 22 96 / 8 03-0
  Telefax 0 22 96 / 8 03 33
  www.vma-getzmann.de

Leserdienst Nr. 10

Neuer Ausbau Glycart AG, Schlieren

Standort:	Schlieren
Bauherrschaft:	Glycart biotechnology AG
Bezug:	Februar 2003
Laborsystem:	Serie RL1 und RL2
Anzahl Labors:	3
Anzahl Abzüge:	2
Labornutzfläche:	ca. 300 m²

Im Jahr 2000 in Zürich als spin-off-Firma der ETH gegründet, konnte die Glycart biotechnology AG schon in kürzester Zeit grosse Erfolge im Gebiet der Glykosylierungstechnik verbuchen.

Durch ihr Engagement in der Krebsforschung erhielt sie unter anderem den W.A. de Vigier-Preis; den höchsten Innovationsaward der Schweiz. Auch internationale namhafte Auszeichnungen blieben nicht fern.

So wurde Glycart aufgrund ihrer bahnbrechenden Technologie im November 2001 von Wallstreet Journal Europe mit dem "Inaugural Technology Innovation Award" geehrt und wurde mit den Titeln "Gold Winner Overall Technology 2001" und "Winner Category Medical/Biotechnology 2001" ausgezeichnet.

Die Glycart biotechnology AG realisierte einen Ausbau an der Wagistrasse 18 in Schlieren/ZH; die Räumlichkeiten (1000 m²) konnte Glycart im Februar dieses Jahres beziehen. Die Rotkreuzer Renggli AG richtete hier drei grosse Labors mit zwei Renggli-Kapellen ein.

- Renggli AG
  Industrie-Ost
  CH-6343 Rotkreuz
  Tel. +41 (0)41 798 14 14
  Fax +41 (0)41 798 14 20
  sales.ch@renggli.com
  www.renggli.com

Leserdienst Nr. 11

Die Unterbauelemente und Tischplatten sind beim Laborsystem RL 1 zu einer Einheit zusammengebaut.

Leserdienst 'CHIMIA-REPORT'

CHIMIA-Leserdienst Heft 7-8/2003

Chimia-Report (Talon 3 Monate gültig)
Ich bitte um Unterlagen zu den angekreuzten Kennziffern:

1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
11	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**
21	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**

Name

Firma

Strasse

PLZ/Ort

Datum

Unterschrift

Die Beiträge der Rubrik «CHIMIA-REPORT» sind mit einer Kennziffer markiert.
Wenn Sie zu einem oder mehreren der auf diese Weise gekennzeichneten Informationsangebote zusätzliche Auskünfte erhalten möchten, empfiehlt sich als einfachster und billigster Weg:

1. Entsprechende Nummer(n) auf dem nebenstehenden Leserdienst-Talon anzeichnen;
2. Absender angeben;
3. Talon an untenstehende Adresse faxen oder einsenden.

Ihre Anfragen werden sofort an die einzelnen Firmen weitergeleitet, die Ihnen die gewünschten Unterlagen gerne zur Verfügung stellen werden. Wir freuen uns, wenn Sie unseren Leserdienst benutzen!

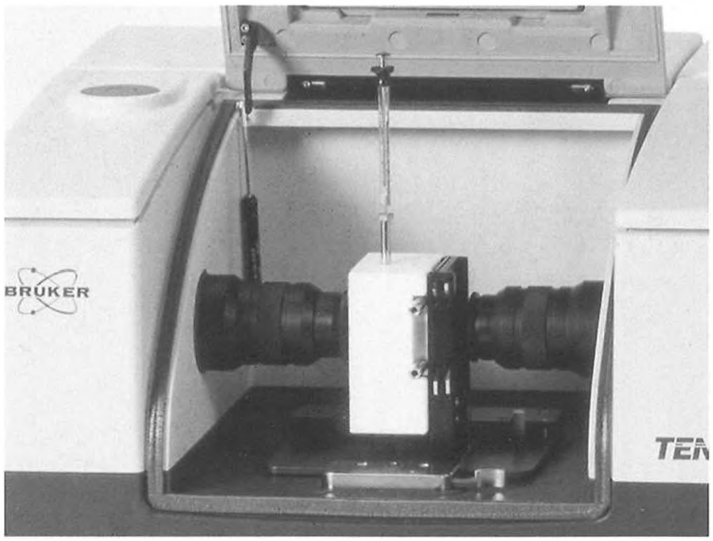
KRETZ AG
CHIMIA-Leserdienst
Postfach
CH–8706 Feldmeilen
Telefon 01 · 925 50 60, Telefax 01 · 925 50 77

Conformational analysis of proteins by FTIR spectroscopy

Bruker Optics now offers a new dedicated FT-IR system for protein secondary structure analysis. The CONFOCHECK system introduces a new analysis concept to researchers in Proteomics based on FT-IR spectroscopy, which is capable of providing information of secondary structure on almost every protein in almost any sampling environment. Aqueous protein solutions are analyzed in a special cell which can be loaded in a flow through manner. Using a very sensitive detector, typical acquisition time is less than a minute. Multivariate calibration is used for secondary structure determination accomplished by using an internal protein spectra library. Beside the determination of α-helix and β-sheet elements this method is very suitable to reveal conformational changes in proteins. Structural changes due to protein ligand binding or changes in the chemical or the physical environment are detected with high sensitivity. The integrated temperature control allows to study temperature induced unfolding/refolding processes. For the study of membrane proteins a dedicated ATR cell is available.

- BRUKER Optics GmbH
  Indutriestrasse 26
  CH-8117 Fällanden
  Tel: +41 1 825 91 11
  Fax: +41 1 825 96 38
  Email: optics@bruker.ch
  URL: *www.brukeroptics.com*

Leserdienst Nr. 12



NuGenesis Technologies und Metrohm geben Partnerschaft bei NuGenesis SDMS bekannt

Die NuGenesis Technologies Corporation, führend auf dem Gebiet der Verwaltung wissenschaftlicher Daten, und Metrohm, führend im Marktsegment Ionenanalyse, gaben heute ihre Partnerschaft bekannt. Die TiNet-Solftware und das Titrando-Titrationsssystem, die IC Net-Ionenchromatographie-Software und die VA Computrace-Elektroanalysesysteme von Metrohm werden in NuGenesis SDMS integriert.

"Der zunehmende Bedarf nach einer langfristigen Datenarchivierung und Datenverwaltung erfordert eine enge Zusammenarbeit zwischen Instrumentenherstellern und Software-Unternehmen", ist sich Markus Steinke, Marketing Manager Titration bei Metrohm Ltd., sicher. "Durch diese Partnerschaft geniessen unsere Kunden den Vorteil, dass Metrodata-Software und Instrulinente nahtlos in NuGenesis SDMS integriert sind."

"Die Partnerschaft zwischen NuGenesis und Metrohm macht in der pharmazeutischen Industrie ein umfassendes und kompatibles Datenmanagement-System für diese wichtigen Ionenanalyse-Anwendungen möglich" so Steinke weiter.

NuGenesis SDMS ist eine anwendungsunabhängige, Web-basierte Plattform, die durch ihre beispiellose Technologie alle Analyserohdaten und Berichtsdaten von vorhandenen Instrumenten und anderen Softwareanwendungen erfasst und sicher speichert. Über durchdachte Vorlagen extrahiert NuGenesis SDMS bei der Erfassung der Daten die darin enthaltenen Inhalte und erstellt einen Datenbankkatalog, damit die Daten bei Bedarf wieder abgerufen werden können – sicher, schnell und problemlos. NuGenesis Technologies bietet Endbenutzern, Datensystemanbietern und Instrumentenherstellern einen verbesserten Support, damit sich der Inhalt der elektronischen Datensätze schnell und einfach erfassen lässt.

Info zu NuGenesis Technologies

Die NuGenesis Technologies Corporation wurde 1996 gegründet und hat ihren Firmensitz in Westborough, Massachusetts/USA. Geschäftsstellen in den USA und Europa sowie Vertriebskanäle in Irland, Puerto Rico, Japan und Korea stellen die weltweite Erreichbarkeit sicher. Die Produkte und Dienstleistungen des Unternehmens schaffen die Basis für die Sicherung wissenschaftlicher Daten und für die unternehmensweite Integration des Informationsflusses. NuGenesis Technologies spielt bei der Verwaltung wissenschaftlicher Daten von A bis Z eine wichtige Rolle und schafft hochqualifizierten Forschern mehr Freiraum für die eigentliche Analyse, Interpretation und Entscheidungsfindung.

NuGenesis® Scientiflc Data Management System (SDMS) erhöht in nicht unerheblichem Mass den Wert der Informationen und ermöglicht messbare Produktivitätszuwächse. Mit weltweit mehreren tausend Anwendern in mehreren hundert Labors ist NuGenesis SDMS im Bereich der Verwaltung wissenschaftlicher Daten marktführend. NuGenesis SDMS bietet eine Komplettlösung für das IT-Management, d.h. für die Verwaltung im Labor- und Geschäftsbereich, auch unter behördlichen Aspekten und Auflagen. NuGenesis SDMS lässt sich in die bestehende IT-Infrastruktur integrieren und ermöglicht es dem Kunden, seine Geschäftsziele zu erreichen und gleichzeitig die gesetzlichen Auflagen zu erfüllen.

- In Europa:
  Annelies Landsman
  NuGenesis Technologies B.V.
  Pompmolenlaan 13
  NL-3447 GK Woerden
  Tel. +31 348 490 072
  news@nugenesis.com
  www.nugenesis.com

Leserdienst Nr. 13

10 Jahre IC-Suppressor Garantie

wenn es nur für alles eine solche Garantie gäbe

Der neue Standard in der Ionenchromatographie – simple Bedienung, einfach zu betreiben – niedrige Unterhaltskosten

Komplettes IC-Programm, Verbrauchsmaterial, Dienstleistungen, Software und Zubehör. Hochwertige Labor- und Online-Geräte mit überlegener Innovation, die man auch bezahlen kann, Zuverlässigkeit, überragende Metrohm-Qualität unterstützt durch sprichwörtlich guten Service.

Metrohm
Ionenanalytik

Metrohm AG
CH-9101 Herisau/Schweiz
Tel. +41 71 353 85 85
Fax +41 71 353 89 01
www.metrohm.ch
info@metrohm.ch