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CHIMIA

Fall Meeting 2001
2001 Herbstversammlung
Assemblée d'automne 2001

SCHWEIZERISCHE CHEMISCHE GESELLSCHAFT
SOCIETE SUISSE DE CHIMIE
SWISS CHEMICAL SOCIETY

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Analytical Chemistry	Analytische Chemie	www.swiss-chem-soc.ch/dac

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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 1 632 10 72
E-Mail: ganter@org.chem.ethz.ch

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Ms./Frau L. Etter
c/o Ciba Spezialitätenchemie AG, K-1354.3.06,
Postfach, CH-4002 Basel
Tel.: +41 61 696 66 26, Fax: +41 61 696 69 85
E-Mail: scg.etter@pharma.novartis.com
www.swiss-chem-soc.ch

Head Office of the Swiss Chemical Society
Geschäftsstelle der Schweizerischen Chemischen Gesellschaft
Dr. R. Darms
c/o Ciba Spezialitätenchemie AG, K-1354.3.07,
Postfach, CH–4002 Basel
Tel.: +41 61 696 67 96, Fax: +41 61 696 69 85
E-Mail: scg.darms@pharma.novartis.com

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
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CHIMIA-REPORT

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EDITORIAL

Invitation to Attend the Fall Meeting of the Swiss Chemical Society in Zürich, on Friday, October 12, 2001

On behalf of the Swiss Chemical Society (SCS) and the local Organizing Committee, it is an honor and our pleasure to invite you to attend the 2001 Fall Meeting of the SCS. Following the tradition of alternating universities to host this event, it is now Zürich's turn after Lausanne and we will do our best to offer you an interesting Fall Meeting in the comfortable facilities of the University Zürich–Irchel.

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. Again this year, there will be a jury in each session giving awards to the best poster presentations, as well as to the best oral contributions. This makes the Fall Meeting highly attractive. Substantial prizes encourage chemists to elaborate presentations of the best quality. As a consequence, participants to the Fall Meeting can take advantage of didactically well-prepared scientific contributions.

In the following pages of CHIMIA you will read more than 290 abstracts of scientific contributions of the Fall Meeting 2001. Please convince yourself of the diversity and outstanding creativity of chemists in Switzerland. The wealth and excellence of these contributions should lure you into participating in this meeting.

For the first time in the Fall Meeting's history an invitation to present a scientific contribution was made by asking the participants to send registration and abstract for CHIMIA not only as hard copies but also with files and electronic mail. Many contributions still came in printed form, but electronic ones are becoming more and more common. Abstracts and posters will be simply uploaded. This will be quick and comfortable for everybody. But the electronic technique cannot replace an oral presentation or a poster session with all their possible human contacts. These activities are more valuable than ever.

The Fall Meeting of the SCS is an excellent opportunity to get a living breath of chemistry. It allows different generations of scientists, experienced older and younger ones, to exchange ideas. And it stimulates elaboration of future projects and discussions around them. Swiss chemical research participates in the frontiers of science, sharing the borders with several other disciplines such as physics, biology, and materials science. This meeting represents the multifaceted aspects of chemistry, particularly those related to basic and applied research performed as well in academic institutions as in industry.

All elements and ingredients are prepared and ready. We therefore look forward to well-attended and lively sessions and to welcoming you in Zürich, and hope you will enjoy the 2001 Fall Meeting of the Swiss Chemical Society and participate to its success now and in the future.

PD Dr. Roland M. Wenger
Chairman
Division Chemical Research

Professor Heinz Berke
Chairman
Local organizing committee

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Fall Meeting 2001
Herbstversammlung 2001
Assemblée d'automne 2001

Friday, October 12, 2001
Freitag, 12. Oktober 2001
Vendredi, 12 octobre 2001

Zürich

Universität Zürich – Irchel
Winterthurerstrasse 190
8057 Zürich

CHIMIA 2001, 55, No. 7/8

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Tel.: +41 (0)1 635 46 80, Fax: +41 (0)1 635 68 02, E-Mail: scs@aci.unizh.ch

Informationen

Keine Anmeldung erforderlich, der Eintritt ist frei!

Studierende, die Mitglied der SCG sind, erhalten folgende Reisekosten zurückerstattet: Bahnbillett nach Zürich, 2. Kl. 1/2 Tax (Anreise aus dem Ausland: Rückerstattung der Reisekosten ab Schweizer Grenze). Das Bahnbillett ist dem Rückerstattungsantrag beizulegen. Der Rückerstattungsantrag ist unter Angabe der Arbeits- und Privatadresse, des Bank- oder PC-Kontos sowie – womöglich unter Beilage eines Einzahlungsscheines beim Sekretariat der SCG Frau *Lilly Etter*, c/o CIBA K-1354.3.06, CH–4002 Basel einzureichen.

Informations

L'inscription n'est pas nécessaire et l'entrée est gratuite!

Les étudiants membres de la SSC peuvent demander le remboursement des frais de voyage sur la base du billet de train Zürich et retour, 2e classe, 1/2 tarif (pour les membres qui viennent de l'étranger, seuls les frais de voyage sur territoire suisse sont remboursés). Le billet doit être joint à la demande de remboursement. Veuillez indiquer l'adresse du lieu de travail et privée, le compte bancaire ou postal et joindre, si possible, un bulletin de versement. La demande est à adresser au Secrétariat de la SSC, Mme *Lilly Etter*, c/o CIBA K-1354.3.06, CH-4002 Bâle.

Location

The Fall Meeting 2001 takes place on the campus of the Universität Zürich–Irchel, Winterthurerstrasse 190, CH–8057 Zürich.

Transportation

Albeit the university of Zürich–Irchel provides a parking on the campus, travel by train is recommended.
From the main station of Zürich, the Universität Zürich–Irchel is reached by tram no. 10 (tramstop Irchel, 15 min.) or by trams no 7 and no. 14 (tramstop Milchbuck, 10 min.). From both tramstops a walk of a few minutes takes you to the university buildings.

Morning			**Evening**		
Train from	Departure	Arrival Zürich	Departure Zürich	Arrival	Train to
Basel	08.20	09.20	18.02	18.52	Basel
Bern	08.17	09.26	18.04	19.13	Bern
Fribourg	07.51	09.26	18.04	19.34	Fribourg
Genève	06.30	09.26	18.07	21.16	Genève
Lausanne	07.06	09.26	18.07	20.33	Lausanne
Neuchâtel	07.08	08.53	18.07	20.51	Neuchâtel

Social

Stand-up Lunch: 12.15 – 13.30 — Sandwiches, coffee, and mineral water are served within the poster area (Lichthof) offered by the Swiss Chemical Society.

Coffee-breaks: 15.30 – 16.00, 17.00 – 17.15 — Coffee and mineral water will be served (Lichthof).

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Programme of the Fall Meeting 2001

10.00–10.40 Opening Ceremony
Room Werner

Presentation of the Werner Prize Laureate 2001
Lecture of the Werner Prize Laureate 2001
PD Dr. D. Luckhaus
Laboratorium für Physikalische Chemie,
ETH Zürich
'Spectroscopy and Quantum-Dynamics:
From Vibrations to Reactions'
Abstract 1

11.00–16.40 Analytical Chemistry

11.00–11.20 General Assembly of Members of DAC
Room Treadwell

11.20–12.20 Lectures: *Room Treadwell*
Abstracts 2–4

12.20–15.00 Poster Session: *Lichthof*
Abstracts 5–36
Stand-up lunch served within the poster area

15.00–16.40 Lectures: *Room Treadwell*
Abstracts 37–40

11.00–17.00 Medicinal Chemistry

11.00–11.20 General Assembly of Members of DMC
Room Reichstein

11.20–12.20 Lectures: *Room Reichstein*
Abstracts 41–43

12.00–13.00 Poster Session: *Lichthof*
Abstract 44
Stand-up lunch served within the poster area

14.00–17.00 Lectures: *Room Reichstein*
Abstracts 45–53

11.00–17.00 Chemical Research

13.45–14.00 General Assembly of Members of DCR
Room Karrer

11.00–17.00 Inorganic and Coordination Chemistry

11.00–12.15 Minisymposium In Memoriam Luigi Venanzi, 1st session
Room Werner
Abstracts 54–55

12.15–13.45 Stand-up lunch served within the poster area

14.00–15.15 Minisymposium In Memoriam Luigi Venanzi, 2nd session
Room Werner
Abstract 57

15.15–17.00 Poster Session: *Lichthof*
Abstracts 58–136

11.00–16.40 Organic Chemistry

11.00–13.45 Poster Session: *Lichthof*
Abstracts 137–214

12.15–13.30 Stand-up lunch served within the poster area

13.45–14.00 General Assembly of Members of DRC

14.00–16.40 Lectures: *Room Karrer*
Abstracts 215–222

14.00–16.40 Lectures: *Room Ruzicka*
Abstracts 223–230

14.00–16.40 Lectures: *Room Prelog*
Abstracts 231–238

11.00–17.00 Physical Chemistry

11.00–12.40 Lectures: *Room Clusius*
Abstracts 239–243

12.40–14.00 Poster Session: *Lichthof*
Abstracts 244–269
Stand-up lunch served within the poster area

14.00–15.40 Lectures: *Room Clusius*
Abstracts 270–274

15.40–17.00 Poster Session: *Lichthof*
Abstracts 244–269

11.00–16.40 Computational Chemistry

11.00–13.45 Poster Session: *Lichthof*
Abstracts 275–288
Stand-up lunch served within the poster area

14.00–16.40 Lectures: *Room Kohn*
Abstracts 289–296

17.00–17.15 Awards for the Best Oral and Poster Presentations
Lichthof

Analytical Chemistry
1 poster and 1 oral presentation
Jury: *J.-L. Veuthey, R. Zenobi*

Medicinal Chemistry
1 poster and 1 oral presentation
Jury: *R. Giger, W. Froestl*

Inorganic and Coordination Chemistry
2 posters
Jury: *A. Williams, T. Ward, P. Pregosin*

Organic Chemistry
3 posters and 3 oral presentations:
Jury: *H.-J. Borschberg, S. Pitsch, S. Bienz*

Physical Chemistry
1 poster and 1 oral presentation
Jury: *M. Quack, S. Seeger*

Computational Chemistry
1 poster and 1 oral presentation
Jury: *J. Weber*

DETAILED PROGRAMME

Analytical Chemistry

11.00–11.20 **General Assembly of Members**
Room Treadwell

Lectures: *Room Treadwell*
Abstracts 2–4, 37–40
Chairmen: *J.-L. Veuthey, R. Zenobi*

11.20–11.40 ***C. Yeretzian***[a], *M. Graus*[b], *A. Jordan*[b], *W. Lindinger*[b], *T. Märk*[b]
[a]Nestlé Research Center, P.O. Box 44, Lausanne; [b]Institut für Ionenphysik, Leopold-Franzens-Universität, Innsbruck, Austria
'In-Mouth Coffee Aroma: Breath-by-Breath Analysis of Nose-Space while Drinking Coffee'
Abstract 2

11.40–12.00 ***S. Chesnov,*** *L. Bigler, M. Hesse*
University of Zürich, Institute of Organic Chemistry
'Characterization of Polyamine Containing Compounds in Spider Venoms by On-Line Coupled Analytic Methods'
Abstract 3

12.00–12.20 ***C. Stella***[a], *S. Rudaz*[a], *P. Seuret*[b], *P. Lanteri*[c], *J.-Y. Gauvrit*[c], *P.-A. Carrupt*[d], *J.-L. Veuthey*[a]
[a]Laboratory of Pharmaceutical Analytical Chemistry-University of Geneva; [b]Laboratory of Pharmaceutical Organic Chemistry-University of Geneva; [c]Laboratory of Chemometrics-University of Lyon-ESPCE-Villeurbanne-France; [d]Institute of Therapeutic Chemistry-BEP, Lausanne
'Characterization of Reversed-phase Stationary Phases and Selection of Test Compounds by Chemometrics (QSAR and PCA)'
Abstract 4

12.20–13.45 Stand-up lunch served within the poster area; offered by DAC
Poster Session
Lichthof
Abstracts: 5–36

14.00–15.00 **Poster Session**
Lichthof
from 14.30 Coffee & snack served by the poster area; offered by DAC

15.00–15.40 **Plenary Lecture:** ***Prof. D.J. Harrison***
Department of Chemistry, University of Alberta, Edmonton, Canada
'Developing a Proteomics 'Lab on a Chip''
Abstract 37

15.40–16.00 ***P. Michel,*** *C. Vollet, F. Reymond, J. Rossier*
DiagnoSwiss SA, Route de l'Ile au bois, Montey
'Protein Affinity Microchip for Zeptomol Detection'
Abstract 38

16.00–16.20 ***J.M. Daniel,*** *S. Wendt, R. Zenobi*
Department of Chemistry, ETH Zürich
'Electrospray Time-of-Flight Mass Spectrometry: Investigation of Non-covalent Protein-Ligand Interactions'
Abstract 39

16.20–16.40 ***Z. Zencak,*** *S. Skopp, M. Oehme*
University of Basel, Organic Analytical Chemistry
'Ion Trap Positive Ion Chemical Ionization of Chlordane Compounds with Non Conventional Reagent Gases'
Abstract 40

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

Medicinal Chemistry

11.00–11.20 **General Assembly of Members**
Room Reichstein
- Review of the activities of 2001, Election of the Committee for the period 2002–04, Outlook on the activities 2002

Lectures: *Room Reichstein*
Abstracts: 41–43
Chairman: *R. Giger*

11.20–11.40 ***S. Hintermann,*** *S. Roggo, V. Rasetti, M. Tintelnot-Blomley, U. von Krosigk*
Nervous System, Novartis Pharma AG, Basel
'Synthesis of Broad Spectrum Caspase Inhibitors and their Biological Activities'
Abstract 41

11.40–12.00 ***P. Schnider,*** *M. Bös, T.M. Ballard, G. Galley, T. Godel, G.A. Higgins, T. Hoffmann, W. Hunkeler, S.M. Poli, A.J. Sleight, H. Stadler*
Pharma Research, F. Hoffmann-La Roche Ltd., Basel
'Design and Synthesis of Potent and Selective, Orally Active NK1 Receptor Antagonists'
Abstract 42

12.00–12.20 ***A. Horvath,*** *M.A. Grassberger, E. Haidl, G. Schulz, H. Sperner*
Novartis Research Institute, Vienna, Austria
'Novel Ascomycin Analogues Modified in the Binding Domain'
Abstract 43

12.00–13.00 **Poster Session**
Lichthof
Abstract: 44

***R. Demange**, P. Vogel*
Institute of Organic Chemistry, University of Lausanne
'Synthesis of C-linked Disaccharides, Mimetics of the Thomsen-Friedenreich (T) Epitope'
Abstract 44

Lectures: *Room Reichstein*
Abstracts: 45–50
Chairman: *W. Froestl*

14.00–14.20 ***J. Zimmermann**, E. Buchdunger, P. Manley*
Oncology, Novartis Pharma AG, Basel
'Case Study: Gleevec – A New Treatment Modality for CML'
Abstract 45

14.20–14.40 ***R. Jakob-Røtne**, A. Alanine, R. Norcross, T. Hoffmann, C. Hertel, B. Levet-Trafit, M.B. Pepys*
Pharma Research, F. Hoffmann-La Roche Ltd. Basel and Centre for Amyloidosis and Acute Phase Proteins, Department of Medicine, Royal Free and University College Medical School, London
'Inhibitors of SAP-Amyloid Binding'
Abstract 46

14.40–15.00 ***E. Altmann**, J. Renaud, J. Green*
Arthritis and Bone Metabolism, Novartis Pharma AG, Basel
'Na-Acyl-L-leucine-(2-phenylamino-ethyl)-amides – Novel and Highly Potent Inhibitors of Cathepsin K'
Abstract 47

15.00–15.20 ***E. Pinard**[a], A. Alanine[a], A. Bourson[b], B. Büttelmann[a], R. Gill[b], M.P. Heitz[a], G. Jaschke[a], V. Mutel[b], G. Trube[b] and R. Wyler[a]*
[a]Discovery Chemistry and [b]Preclinical CNS Research, Pharma Division, F. Hoffmann-La Roche Ltd., Basel
'4-Aminoquinolines as a Novel Class of NR1/2B Subtype Selective NMDA Receptor Antagonists'
Abstract 48

15.20–15.40 ***P. Furet**, P. Imbach, V. Guagnano, M. Lang, P. Fürst, D. France, M. Noorani, J. Rösel, D. Scholz, J. Zimmermann, C. Garcia-Echeverria*
Oncology, Novartis Pharma AG, Basel
'Structure-Based Optimization of a New Class of Proteasome Inhibitors'
Abstract 49

15.40–16.00 ***T.J. Woltering**[a], G. Adam[a], E. Goetschi[a], J. Wichmann[a], S. Gatti[b], J. Kew[b], F. Knoflach[b], V. Mutel[b]*
[a]PRBC-M and [b]PRBN-P, F. Hoffmann-La Roche, Basel
'Synthesis and Characterization of 8-ethynyl-1,3-dihydro benzo[b][1,4]diazepin-2-one Derivatives as Potent Non-competitive Metabotropic Glutamate Receptor 2/3 Antagonists'
Abstract 50

Lectures: *Room Reichstein*
Abstracts: 51–53
Chairman: *R. Giger*

16.00–16.20 ***Y.P. Auberson***
Nervous System, Novartis Pharma AG, 4002 Basel
'Competitive AMPA Antagonism: a Novel Mechanism for Antiepileptic Drugs?'
Abstract 51

16.20–16.40 ***G. Tuchscherer**[a], J. Fernandez-Carneado[a], P. Durieux[a], D. Grell[a], Y. Tatsu[a], B. Hengst[a], L. Patiny[a], C. Kardinal[b], S. Feller[b]*
[a]Institute of Organic Chemistry, BCH, University of Lausanne; [b]Laboratory of Molecular Oncology, MSZ-Institute for Medical Radiation and Cell Research, Würzburg
'Pseudo-Proline Libraries for Tuning Inhibitors of SH3 Domain-Mediated Protein-Protein Interactions'
Abstract 52

16.40–17.00 ***O. Zerbe**[a], R. Bader[a], M. Lerch[a], G. Folkers[a], A.G. Beck-Sickinger[b]*
[a]Institute of Pharmaceutical Sciences, ETH Zürich; [b]Institute of Biochemistry, University of Leipzig
'Structural Features for Receptor Subtype-Specificity of Neuropeptide Y (NPY) und Mutants studied by NMR'
Abstract 53

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

Chemical Research

13.45–14.00 **General Assembly of Members**
Room Karrer

Inorganic and Coordination Chemistry

Minisymposium: **In Memoriam Luigi Venanzi**
Room Werner
Chairman: *P. Pregosin*

11.00–11.30 ***T. Ward***
Institut de Chimie, Université de Neuchâtel
'If it is not Steric, it's Electronic'
Abstract 54

11.45–12.15 ***A. Togni***
Laboratorium für Anorganische Chemie, ETH Zürich
'Coordination Chemical Aspects of Asymmetric Catalysis'
Abstract 55

14.00–14.30 ***M.L.H. Green***
Inorganic Chemistry Laboratory, University of Oxford
'Reactions of Organometallic Compounds with Strong Lewis Acids'

14.45–15.15 ***G. van Koten***
Faculty of Chemistry, Utrecht University
'Sustainable Homogeneous Catalysts Based on Tridentate Ligands'
Abstract 57

15.15–17.00 **Poster Session**
Lichthof
Abstracts 58–136

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

Organic Chemistry

11.00–13.00 **Poster Session**
Lichthof
Abstracts 137–214

13.00–13.45 **Lunch**

Lectures: *Room Karrer*
Abstracts 215–222
Chairman: *H.-J. Borschberg (ETH Zürich)*

14.00–14.20 ***M. Rueping,*** *D. Seebach*
Laboratorium für Organische Chemie, ETH Zürich
'Homologs of Amino Acids: Synthesis and Structural Investigations of β-and γ-Peptides'
Abstract 215

14.20–14.40 ***B. Baumeister,*** *N. Sakai, S. Matile*
Département de Chimie Organique, Université de Genève
'Artificial Ion Channels Formed by Rigid-Rod β-Barrels'
Abstract 216

14.40–15.00 ***C. Pissot Soldermann,*** *R. Neier*
Institut de chimie, Université de Neuchâtel
'Recent Progress Towards a Practical Synthesis of Porphobilinogen'
Abstract 217

15.00–15.20 ***K. Abou-Hadeed,*** *H.-J. Hansen*
Organisch-chemisches Institut der Universität Zürich
'A New 'One-Pot' Synthesis of Resorcinols also Applicable to the Formation of the Aromatic Ring of Colchicinoids'
Abstract 218

15.20–15.40 ***G. Koch,*** *K.-H. Altmann, D. Fuentes, A. Jantsch, O. Loiseleur, A. Schmidt*
Novartis Pharma AG, Basel
'Investigation of Aldol Processes for the Total Synthesis of the Epothilones and Their Derivatives'
Abstract 219

15.40–16.00 ***E. Stulz,*** *Yiu-Fai Ng, A.D. Bond, J.K.M. Sanders*
University Chemical Laboratory, University of Cambridge
'Phosphine Substituted Porphyrins in Supramolecular Assemblies'
Abstract 220

16.00–16.20 ***J. Haas,*** *T. Wirth*
Department of Chemistry, Cardiff University
'Chiral I^+?'
Abstract 221

16.20–16.40 ***P. Panchaud,*** *C. Ollivier, P. Renaud*
Departement für Chemie und Biochemie, Universität Bern
'Pyrrolizidines and Indolizidines *via* a Radical Addition-Azidation Procedure'
Abstract 222

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

Lectures: *Room Ruzicka*
Abstracts 223–230
Chairman: *S. Pitsch*

14.00–14.20 ***M. Lochner,*** *L. Mu, M. Müller, W.-D. Woggon*
Institut für Organische Chemie der Universität Basel
'A Crown-Capped Iron Porphyrin as New Active Site Model of Cytochrome P450cam'
Abstract 223

14.20–14.40 ***P. Holzer,*** *W.-D. Woggon*
Institut für Organische Chemie der Universität Basel
'A New Receptor for the Binding of β,β-Carotene'
Abstract 224

14.40–15.00 ***S. Terenzi,*** *P. Strazewski*
Institut für Organische Chemie der Universität Basel
'Synthesis and Characterization of 3'-Peptidyl-RNAs'
Abstract 225

15.00–15.20 ***N. Quang Nguyen-Trung,*** *P. Strazewski*
Institut für Organische Chemie der Universität Basel
'From 3'-Aminoacyl Ribonucleosides to 3°-Aminoacyl RNA'
Abstract 226

15.20–15.40 *D. Summerer, C. Schneider,* ***A. Marx***
Kekulé-Institut für Organische Chemie und Biochemie, Universität Bonn
'DNA Replication Fidelity besides Nucleobase Recognition'
Abstract 227

15.40–16.00 ***S. Furegati,*** *A. Linden, P. Rüedi*
Organisch-chemisches Institut, Universität Zürich
'Acetylcholine-Mimetic Organophosphates as Inhibitors of Acetylcholinesterase'
Abstract 228

16.00–16.20 ***D. Wahler***[a], *F. Badalassi*[b], *P. Crotti*[b], *J.-L. Reymond*[a]
[a]Departement für Chemie und Biochemie, Universität Bern
[b]Dipartimento di Chimica Bioorganica e Biofarmacia, Università di Pisa
'A General Chromo/Fluorogenic Assay for Hydrolytic Enzymes'
Abstract 229

16.20–16.40 *M. Machuqueiro, T. Darbre*
Departement für Chemie und Biochemie, Universität Bern
'Models for Zn-dependent Methyltransferases'
Abstract 230

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

Lectures: *Room Prelog*
Abstracts 231–238
Chairman: *S. Bienz* (Universität Zürich)

14.00–14.20 ***F. Viton,*** *C.M. Saudan, V. Alezra, E.P. Kündig*
Département de Chimie Organique, Université de Genève
'Chiral Ru(II) and Fe(II) Lewis Acids:
New Developments and Mechanistic Insights'
Abstract 231

14.20–14.40 *A. Blanc, C. Helgen,* ***C.G. Bochet***
Département de Chimie Organique, Université de Genève
'Orthogonal Photolysis of Protecting Groups'
Abstract 232

14.40–15.00 ***V. Desvergnes-Breuil,*** *J.J. Jodry, J. Lacour*
Département de Chimie Organique, Université de Genève
'Asymmetric Aziridination of Prochiral Olefins and Predetermination of Configuration of $[Cu(LL')_2]^+$ Complexes by Chiral Phosphate Anions'
Abstract 233

15.00–15.20 ***R. Hartmann,*** *P. Chen*
Laboratorium für Organische Chemie, ETH Zürich
'Novel Bimetallic Mechanism for High-activity Asymmetric Hydrogenation of Ketones with Ruthenium Catalysts'
Abstract 234

15.20–15.40 ***K. Gademann,*** *E.N. Jacobsen*
Chemistry and Chemical Biology, Harvard University, Cambridge MA
'Highly Enantio- and Diastereoselective Hetero Diels-Alder Reactions with Inverse Electron Demand Catalyzed by Chromium (III) Schiff Base Complexes'
Abstract 235

15.40–16.00 ***S.P. Schmid,*** *A. Pfaltz*
Institut für Organische Chemie der Universität Basel
'Iridium Complexes of New, Chiral P,N Ligands for the Enantioselective Hydrogenation of Unfunctionalised Alkenes and Ketones'
Abstract 236

16.00–16.20 *S. Bachmann,* ***A. Mezzetti***
Department of Chemistry, ETH Hönggerberg, Zürich
'Electronic Effects in the Asymmetric Cyclopropanation of Olefins Catalyzed by $[RuCl(PNNP)]^+$'
Abstract 237

16.20–16.40 ***S. Amrein,*** *A. Studer*
Fachbereich Chemie der Philipps-Universität Marburg
'Silylated Cyclohexadienes as New Radical Reducing Agents'
Abstract 238

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

Physical Chemistry

Lectures: *Room Clusius*
Abstracts 239–243
Chairman: *J.R. Huber (Universität Zürich)*

11.00–11.20 ***V. Schwartz,*** *M. Sun, R. Prins*
Laboratory for Technical Chemistry, ETH Zürich
'EXAFS Study of the Structure of Sulfided W/Al_2O_3 and NiW/Al_2O_3'
Abstract 239

11.20–11.40 ***S. Pelet,*** *J.-E. Moser, M. Grätzel*
Laboratory for Photonics & Interfaces, EPF Lausanne
'Ultrafast Dynamics of Photo-induced Electron Injection From Eosin into a Wide Band Gap Semiconductor'
Abstract 240

11.40–12.00 ***O. Nicolet,*** *E. Vauthey*
Département de chimie physique, Université de Genève
'Ultrafast Charge Recombination Dynamics of Excited Donor–Acceptor Complexes'
Abstract 241

12.00–12.20 ***P. Faller***[a], *A. Boussac*[a], *R. J. Debus*[b], *K. Brettel*[a], *A.W. Rutherford*[a]
[a]Section de Bioénergétiques, DBCM, CEA Saclay, CNRS URA 2096, Gif-sur-Yvette, Cedex; [b]Department of Biochemistry, University of California
'Tyrosyl Radicals in Photosystem II: The Stable Tyrosyl D and the Catalytic Tyrosyl Z'
Abstract 242

12.20–12.40 ***L. Cataldo***[a], *S. Choua*[a], *T. Berclaz*[a], *M. Geoffroy*[a] *N. Mézailles*[b], *L. Ricard*[b], *F. Mathey*[b], *P. Le Floch*[b]
[a]Dept. of Physical Chemistry, University of Geneva [b]Laboratoire 'Hétéroéléments et Coordination', UMR CNRS 7653, Ecole Polytechnique, Palaiseau Cedex
'Formation of a Phosphorus-Phosphorus Bond by Successive One-Electron Reductions of a Two-Phosphinines-Containing Macrocycle: Crystal Structures and EPR'
Abstract 243

12.40–14.00 **Lunch/Posters**

Poster Session
Lichthof
Abstracts 244–269

Lectures: *Room Clusius*
Abstracts: 270–274
Chairman: *M. Quack (ETH Zürich)*

14.00–14.20 ***N. Solcà**, O. Dopfer*
Institut für Physikalische Chemie, Universität Basel
'Spectroscopy of Protonated Aromatic Molecules in the Gas Phase'
Abstract 270

14.20–14.40 ***M. Hippler, L. Oeltjen**, M. Quack*
Laboratorium für Physikalische Chemie, ETH Zürich
'High Resolution cw-Diode Laser Cavity Ring-Down Spectroscopy of the HF Dimer in a Pulsed Slit Jet Expansion: The N=2 Overtone Triad Near 1.3 μm'
Abstract 271

14.40–15.00 ***S. Albert**, V. Boudon, M. Quack*
Laboratorium für Physikalische Chemie, ETH Zürich
'The Infrared Spectrum of CDBrClF: A Rovibrational Analysis of the ν_5 Band'
Abstract 272

15.00–15.20 ***M. Gottselig**, R. Berger, M. Quack, M. Willeke*
Laboratorium für Physikalische Chemie, ETH Zürich
'Parity Violation Dominates the Dynamics of Chirality in Dichlorodisulfane'
Abstract 273

15.20–15 40 ***K. Pervushin***
Laboratorium für Physikalische Chemie, ETH Zürich
'Substrate Recognition by Chorismate Mutase Studied by TROSY NMR'
Abstract 274

15.40–17.00 **Poster Session**
Lichthof
Abstracts 244–269

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

Computational Chemistry

11.00–13.45 **Poster Session**
Lichthof
Abstracts: 275–288

Lectures: *Room Kohn*
Abstracts: 289–296
Chairman: *J. Weber*

14.00–14.20 ***T. Heine**, A.M. Köster, A. Vela*
Département de Chimie Physique, Université de Genève
'Slow Expensive DFT Calculations Made Fast and Cheap – Some Features of DeMon 2001'
Abstract 289

14.20–14.40 ***J. VandeVondele**, U. Röthlisberger*
Laboratory of Inorganic Chemistry, ETHZ
'A Novel Dynamical Scheme for the Exploration of Free Energy Surfaces: Observing the Formation of the Bromonium Ion in Solution'
Abstract 290

14.40–15.00 ***C. Corminboeuf**[a], T. Heine[a], E.P. Kündig[b], C.M. Saudan[b], J. Weber[a]*
Département de [a]Chimie Physique et de [b]Chimie Organique, Université de Genève
'Modelling the Inversion Barrier in the Lewis Acid [CpRu(BINOP-F)]$^+$ by Density Functional Theory'
Abstract 291

15.00–15.20 ***S.P. Agostinetti,** P. Carloni, U. Röthlisberger*
Laboratory of Inorganic Chemistry, ETHZ
'Flexibility and Function in HIV-1 PR: the Role of the Compensatory Mutations'
Abstract 292

15.20–15.40 ***M.C. Colombo,** A.Laio, U. Röthlisberger*
Laboratory of Inorganic Chemistry, ETHZ
'Study of $H_2PO_4^-$ Anion in Water Using Car-Parrinello Mixed Quantum Mechanics/Molecular Mechanics Simulation'
Abstract 293

15.40–16.00 ***A. Laio,** J. VandeVondele, U. Röthlisberger*
Laboratory of Inorganic Chemistry, ETHZ
'RESP Charges from Car-Parrinello Mixed Quantum Mechanics/Molecular Mechanics (QM/MM) Simulation'
Abstract 294

16.00–16.20 ***P. Maurer,** A. Magistrato, U. Röthlisberger*
Laboratory of Inorganic Chemistry, ETHZ
'First-Principle Simulation of C–S Bond Cleavage in Thioether Complexes of Technetium, Rhenium and Ruthenium'
Abstract 295

16.20–16.40 ***F. Mariotti,** A. Bencini, C. Daul*
Département de Chimie de l'Université de Fribourg
'*o*-Dioxolenes: a DFT Study'
Abstract 296

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

Additional rooms:

– for discussions

– for preparations (slide projector, beamer)

Last-minute posters:

Additional boards will be available.

1

Spectroscopy and Quantum-Dynamics: From Vibrations to Reactions

Dr. D. Luckhaus

Laboratorium für Physikalische Chemie, ETH-Zentrum, 8092 Zürich

Unravelling the mechanisms of energy transfer on a molecular level is one of the central problems of chemical reaction kinetics. Most intriguing from the chemists point of view is the connection between dynamical and structural properties. Although empirically well established this relationship leaves many open questions. Which are its microcopic foundations ? Are there transferable properties of functional groups and how do they determine the course of chemical reactions ?

Modern spectroscopy opens a unique approach to these problems. The key is provided by the interpretation of molecular spectra in terms of explicit quantum-mechanical models of the underlying molecular motion. Studies of OH- and NH_2 –groups in different environments demonstrate how experiment and theory combine to draw a detailled picture of the molecular quantum-dynamics. The hydrogen motion in a series of model systems elucidates important aspects of the N/O/H chemistry, with implications for radical and atmospheric chemistry. In perfect analogy to the separation of electronic and nuclear motion in the Born-Oppenheimer approximation characteristic motions of individual structural features are adiabatically separated from the overall system dynamics. This phenomenon of vibrational adiabaticity will play a central role in our understanding of the microscopic foundations of empirical structure-reactivity relationships.

2

In-Mouth Coffee Aroma: Breath-By-Breath Analysis of Nose-Space while Drinking Coffee

Chahan YERETZIAN[1]*, Martin GRAUS[2], Alfons JORDAN[2], Werner LINDINGER[2], Tilmann MÄRK[2]

[1]Nestlé Research Center, P.O. Box 44, CH-1000 Lausanne 26, Switzerland

[2]Institut für Ionenphysik, Leopold-Franzens-Universität, Technikerstr. 25, 6020 Innsbruck, Austria

One objective of instrumental (analytical) flavour science is to find quality markers for the cup of coffee, which correlate with the sensory assessment of expert coffee tasters. For this, volatile flavour compounds are usually either stripped by a flow of gas or extracted with solvents and analysed by gas chromatography. While this has been extremely valuable to our understanding of coffee aroma, one might wonder how well this reflects the coffee aroma profile as it is experienced during a real situation of coffee consumption. Coffee drinking conditions have additional factors such as mixing, mastication and salivation, heating and interactions with the mouth tissue. This can lead to alterations of the physical and chemical state of its constituents (e.g. melting, emulsification, adsorption) and modify the release of volatiles flavour compounds relative to headspace profiles.

Here, we will discuss a novel approach called "nose-space" analysis. It is a method to sample aroma compounds directly released from humans through the nose when consuming food [1,2]. The main benefit is the ability to investigate the aroma during the actual situation of consumption. It is applied to the breath-by-breath analysis of volatiles exhaled through the nose while drinking coffee.

* *Corresponding author: chahan.yeretzian@rdls.nestle.com*

1. Linforth R.S.T., Savary I.; Pattenden B.; Taylor A.J. *J. Sci. Food Agric., 65*, 241-247 **(1994)**
2. Taylor A.J.; Linforth R.S.T. In *Flavor Release*: Roberts D. and Taylor A., Eds.; American Chemical Society: Washington, D.C., pp. 8-21 **(2000)**

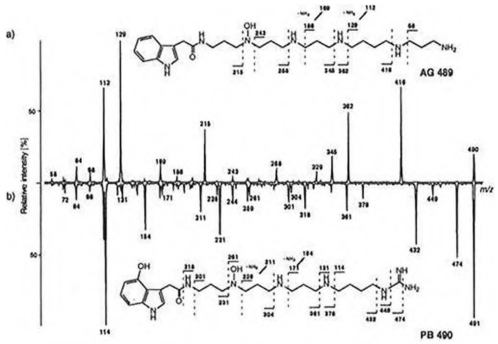
Analytical Chemistry

3

Characterization of Polyamine Containing Compounds in Spider Venoms by On-Line Coupled Analytic Methods

Sergiy Chesnov, Laurent Bigler, and Manfred Hesse*
University of Zurich, Institute of Organic Chemistry
8057 Zurich, Switzerland

The venoms of several spider species from the families Agelenidae, Amaurobiidae, Araneidae, and Ctenidae were analyzed by on-line coupled HPLC-UV(DAD)-APCI-MS and HPLC-UV(DAD)-APCI-MS/MS techniques [1,2]. The structures of different acylpolyamines even those present in low and very low concentrations were elucidated. The possible biological role of some low molecular weight compounds in the spider venoms will be discussed.



MS/MS analysis of the main acylpolyamines from the venoms of the spiders Agelenopsis aperta *(a) and* Paracoelotes birulai *(b)*

[1] S. Chesnov, L. Bigler, and M. Hesse, *Helv. Chim. Acta* **2000**, *83*, 3295.
[2] S. Chesnov, L. Bigler, and M. Hesse, *Helv. Chim. Acta* **2001** (in print)

Analytical chemistry

4

Characterization of reversed-phase stationary phases and selection of test compounds by chemometrics (QSAR and PCA)

UNIVERSITÉ DE GENÈVE

Stella C[1]., Rudaz S.[1], Seuret P.[2], Lanteri P.[3], Gauvrit J.-Y.[3], Carrupt, P.-A[4]. ,Veuthey J.-L.[1]

[1]Laboratory of Pharmaceutical Analytical Chemistry-University of Geneva, 1211 Geneva 4
[2]Laboratory of Pharmaceutical Organic Chemistry-University of Geneva, 1211 Geneva 4
3Laboratory of Chemometrics-University of Lyon-ESPCE-Villeurbanne-France
[4]Institute of Therapeutic Chemistry-BEP-1015 Lausanne

Reversed-phase liquid chromatography (RP-HPLC) has become a powerful and widely employed technique in the analysis of a great variety of substances, in particular basic compounds. These compounds are present in various areas such as environmental, agro-industrial and pharmaceutical industries. In pharmacy it is estimated that over 80% of drugs possess a basic function.
However, secondary interactions between the analyte and residual silanols with traditional silica packings produce peak tailing which affect resolution, sensitivity and reproducibility. Therefore, in order to overcome the problems encountered with this kind of compounds, a great number of "base deactivated" stationary phases have been developed. Thus, a fast procedure is needed to evaluate the appropriate columns.

In this work, a particular test for the characterization of RP-HPLC stationary phases for the analysis of basic compounds was developed. With this purpose, a set of test compounds was selected, combining basic products proposed by McCalley [1] with other compounds selected in our laboratory. From a data set of chromatographic parameters (k', As, N), obtained on different LC columns, Principal Component Analysis (PCA) was applied:

- to ensure that selected molecules present pertinent properties to characterize a stationary phase
- to evaluate differences and resemblance between columns;

Finally a Quantitative Structure-Activity Relationships (QSAR) approach was applied:

- in order to better understand relations between chromatographic and physical chemical properties of test compounds
- to modeling the chromatographic behavior.

[1] D.V. McCalley, R.B. Brereton, J. Chromatogr. A (1998) 407-420

Analytical Chemistry **5**

Enantiomeric Analysis of Five Monohydroxylated Metabolites of Methaqualone in Human Urine by Chiral Capillary Electrophoresis

F. Prost and W. Thormann

University of Bern, Department of Clinical Pharmacology
3010 Bern, Switzerland

Methaqualone (MQ, 2-methyl-3-o-tolylquinazolin-4(3H)-one) is a hypnotic and anticonvulsive drug in which the rotation about the nitrogen-to-aryl bond between the planar 2-methyl-quinazolin-4(3H)-one structure and the o-tolyl moiety is sterically hindered at body temperature. MQ and its five major monohydroxylated metabolites found in urine, 4'-hydroxymethaqualone (4'OH-MQ), 2'-hydroxymethaqualone (2'OH-MQ), 3'-hydroxymethaqualone (3'OH-MQ), 2-hydroxymethaqualone (2OH-MQ) and 6-hydroxymethaqualone (6OH-MQ), are thus chiral substances whose enantiomers are shown to be separable by chiral capillary electrophoresis at pH 2.1 in presence of 50 mM (2-hydroxypropyl)-β-cyclodextrin (OHP-β-CD). With OHP-β-CD, simultaneous analysis of the enantiomers of MQ and its five metabolites is hampered by the difficulty in separating MQ and 4'OH-MQ, the major urinary metabolite. A two-step solid phase extraction process is shown to permit discrimination between these two compounds. Analysis of extracts of enzymatically hydrolyzed urines that were collected overnight after administration of 250 mg of racemic MQ reveals the distribution of the enantiomers of the five hydroxymetabolites of MQ and, for the first time, insight into the stereoselectivity of the MQ metabolism. The major metabolite, 4'OH-MQ, is shown to be excreted almost exclusively as single enantiomer. The two urinary enantiomers of 6OH-MQ are present at about equal amounts, whereas unequal amounts are noted for the enantiomers of 3'OH-MQ, 2OH-MQ and 2'OH-MQ.

This work was supported by the Swiss National Science Foundation.

Analytical Chemistry **6**

Determination of Carbohydrate-Deficient Transferrin in Human Serum by Capillary Electrophoresis

C. Lanz[1], W. Thormann[1], M. Zuliani[2] and F. Tagliaro[2]

1) University of Bern, Department of Clinical Pharmacology, 3010 Bern, Switzerland
2) University of Verona, Institute of Forensic Medicine, Verona, Italy

Serum transferrin comprises several isoforms with variable residues of sialic acid and neutral sugars. Carbohydrate-deficient transferrin (CDT) encompasses isoforms that are deficient in sialic acid residues (asialo-, monosialo- and disialo-transferrin) and is a marker for chronic alcohol abuse. A method for CDT determination in human serum by capillary zone electrophoresis (CZE) has been developed. CZE is performed on a P/ACE 5500 or a P/ACE MDQ within an uncoated fused-silica capillary using a pH 8.3 borate buffer containing 2.25 mM diaminobutane for dynamic coating of the capillary wall. Serum samples are saturated with iron before analysis and peak identification is accomplished with immunosubtraction. The CZE method is robust and reproducible. Data are evaluated as area % of disialo-transferrin in relation to tetrasialo-transferrin, the normal value for disialo-transferrin determined in Verona with about 110 healthy subjects being ≤ 2.27 %. The data reveal a significant increase for disialo-transferrin (but not for trisialo-transferrin) in alcoholics compared to control subjects, including social drinkers.

This work was supported by the Liver Foundation, Bern, Switzerland.

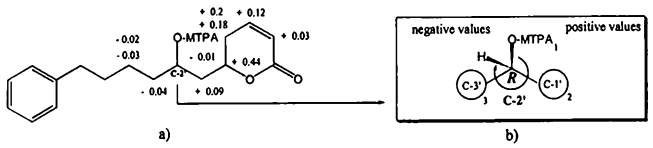
Analytical Chemistry **7**

Determination of the absolute configuration of two 6-alkylated α-pyrones by LC/NMR analysis of their Mosher esters

E. F. Queiroz, J.-L. Wolfender, G. Raoelison, C. Terreaux and K. Hostettmann

Institut de Pharmacognosie et Phytochimie, Université de Lausanne
1015, Lausanne, Switzerland.

Determination of the absolute configuration at the asymmetric centers of two α-pyrones isolated from *Ravensara crussifolia* (Lauraceae) was performed using Mosher's method [1]. Conventional analysis of the ester derivatives by ^{1}H NMR was replaced by LC/NMR [2] analysis of the crude reaction mixture. Similar chemical shift differences to those observed using conventional ^{1}H-NMR were recorded under stop-flow LC/NMR conditions. The main advantages of this new method are its rapidity and sensitivity. Typically only a few tenths of a microgram have to be injected on-column and no clean-up procedures are necessary. These aspects are very important in natural product chemistry since often the sample amounts are very limited.



[1]. Ohtani I, Kusumi T, Kashman Y, Kakisawa H. 1991. High-field FT NMR application of Mosher's method. The absolute configurations of marine terpenoids. *J. Am. Chem. Soc.* **113**: 4092-4096.

[2]. Wolfender JL, Ndjoko K, Hostettmann K. 1998. LC/NMR in natural product chemistry. *Curr. Org Chem.* **2**: 575-596.

Analytical Chemistry **8**

Qualitative and quantitative determination of yohimbine in commercial aphrodisiacs by LC/DAD/MS.

B. Zanolari, K. Ndjoko, J.-R. Joset, A. Marston and K. Hostettmann

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

Since its commercialization, Viagra® has been the focus of huge media attention and has created massive public interest in the availability of aphrodisiacs and remedies for erectile dysfunction. There has been a resurgence in sales of more easily-available herbal remedies. Many of these are based on yohimbe (*Pausinystalia yohimbe* [K. Schumann] PIERRE ex BEILLE (Rubiaceae)), a tree native to tropical West Africa which has long been considered as an aphrodisiac. The bark is used extensively by local populations as part of traditional health care systems and has been exported to Europe for both prescription and herbal markets.

It is of vital importance to evaluate the quality and safety of commercial preparations as several side effects of yohimbine (the main alkaloid) have been reported [1, 2]. A rapid and sensitive method based on HPLC/DAD/MS was developed and validated. LC/MS detection was selective enough for the detection of yohimbine in complex mixtures such as plants extracts. Multiple stage mass spectrometry (MS^n) experiments allowed the identification of the alkaloid. The separation was performed on a C_{18} reversed phase column (125 x 2 mm i.d.) with an acetonitrile-water (0.01 M triethylamine buffer) gradient. Quantification was made with two internal standards: codeine for the DAD detection and deuterated yohimbine for the MS detection. In total, 20 commercially available aphrodisiac preparations were analyzed.

[1] Teloken, C., et al. 1998. *Journal of Urology*. 159: 122-4.
[2] Sandler, B., Aronson, P.. 1993. *Urology*. 41: 434-5.

9

Use of experimental design to investigate CE-ESI-MS enantioseparation with the partial filling technique.

S. Rudaz[1], S. Cherkaoui[1], JY. Gauvrit[2], P. Lantéri[2], JL. Veuthey[1]
[1]Laboratory of Pharmaceutical Analytical Chemistry, University of Geneva
[2]Laboratory of Chemometric, University of Lyon

Capillary electrophoresis (CE) is known to be a powerful separation technique in the field of optical isomer separation. The CE enantioseparation requires the addition of a chiral selector in the buffer. Among the available selectors reported in the literature, cyclodextrins (CDs) are the most widely used. Neutral and charged CDs derivatives have been recently developed to enhance enantioselectivity.
In order to increase sensitivity, the coupling of chiral CE with electrospray ionisation mass spectrometry (CE-ESI-MS) is a promising combination. For successful coupling of CE with MS, the coaxial sheath-flow interface is the most popular and suitable configuration. For the latter, it is necessary to add a make-up flow and a nebulizing gas at the capillary outlet to attain the optimal conditions of electrospray ionization.
The main problem encountered when coupling CE with MS is the risk of the MS contamination by non volatile additives such as CDs. The partial filling technique is generally recommended to avoid the chiral selector appearing in the MS ion source. This technique involves filling a portion of the capillary with a separation buffer containing a suitable amount of chiral selector to achieve enantioseparation. In the case of basic compounds, negatively charged CDs were used and application of the electric field results in a counter current process in which the chiral selector and the drug enantiomers migrate in opposite directions.
Using methadone as a model compound, three relevant experimental factors were investigated for optimization of the partial filling technique in CE-ESI-MS configuration; 1. the chiral selector concentration , 2. the length of the filled portion and 3. the nebulisation pressure used to assist droplet formation. For this purpose, a chemometric approach was chosen and a face-centered central composite design was selected to determine the influence of the selected factors as well as their interactions. Experiments were conducted with various CDs (charged, partially charged and uncharged) to establish the counter-current contribution.

Analytical chemistry

11

Analyse de substances basiques par RP-HPLC à pH élevé

UNIVERSITÉ DE GENÈVE

Mottaz, M. Stella C., Rudaz S.,Veuthey J.-L.

Laboratory of Pharmaceutical Analytical Chemistry-University of Geneva, 1211 Geneva 4

En chromatographie en phase liquide à polarité de phase inversée (RP-HPLC), la phase stationnaire est généralement constituée de particules sphériques de gel de silice greffées avec différents groupements fonctionnels (principalement des chaînes hydro-carbonées). Selon la nature de la substance à analyser, différents types d'interactions entre les analytes et la phase stationnaire vont avoir lieu.

Le cas d'une substance basique est le plus complexe car à pH neutre des interactions du type liaisons hydrogène et échange d'ions entre les analytes et les silanols résiduels de la phase stationnaire vont apparaître. Une forte asymétrie du pic chromatographique va alors poser des problèmes au niveau de l'analyse quantitative, de la sensibilité, de la reproductibilité et de la résolution lors de la séparation de mélanges complexes.
Afin de minimiser ces interactions, il est nécessaire de travailler à des valeurs de pH soit plus basses (silanols non dissociés) soit plus élevées (molécules basiques sous forme moléculaire).

Dans ce travail, des analyses à pH élevé ont été effectuées sur le support chromatographique Zorbax Extend C18 avec une phase mobile contenant de l'ammoniaque. A pH élevé, il n'y a pas d'interactions secondaires du type échange d'ions entre la phase stationnaire et les substances basiques, pour autant que ces dernières se trouvent entièrement sous forme moléculaire (pKa inférieur de 2 unités à la valeur du pH).
Quinze analytes basiques possédant une large gamme de propriétés physico-chimiques (encombrements stériques différents, accessibilité aux silanols différente et couvrant une large gamme de pKa (de 5.2 à 10.0) ont été utilisés.
Les analyses ont également été effectuées à pH neutre et acide afin de pouvoir comparer les paramètres chromatographiques.

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Analytical chemistry

DIFFERENTES APPROCHES DE VALIDATION RAPIDE DE COMPOSES PHARMACEUTIQUES PAR ELECTROPHORESE CAPILLAIRE

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

Laboratoire de Chimie Analytique Pharmaceutique, 20 Bd d'Yvoy,
Université de Genève, CH-1211 Genève 4.

Pour quantifier des principes actifs contenus dans une formulation pharmaceutique, des méthodes analytiques performantes (exactes et précises) et rapides sont nécessaires. Pour ce faire, l'électrophorèse capillaire (CE) est une alternative intéressante à la chromatographie en phase liquide (LC). En effet, la CE permet de développer rapidement des méthodes analytiques économiques: capillaire peu coûteux, pas ou peu de consommation de solvant organique, faible volume d'échantillon, etc.
Contrairement à la LC, la CE ne permet pas d'injecter les échantillons dès la fin de l'analyse précédente, mais nécessite généralement un conditionnement du capillaire entre chaque injection, ce qui génère de plus longs temps d'analyse.
Différentes stratégies sont évaluées dans ce travail, afin de réduire le temps total entre deux injections sans pour autant entraver les performances de la méthode. L'utilisation d'un capillaire court (32,5 cm) est la technique la plus couramment employée pour diminuer les temps d'analyse et de conditionnement du capillaire. D'autres stratégies sont également envisagées, telles que l'injection du côté court du capillaire et les injections multiples d'échantillons. Dans le premier cas, la courte longueur effective du capillaire (8,5 cm) diminue le temps de séparation. Dans le second cas, un seul conditionnement du capillaire permet la séparation simultanée de plusieurs échantillons.
Afin d'estimer les performances analytiques de ces stratégies, deux anesthésiques locaux ont été sélectionnés, la prilocaïne (composé test) et la procaïne (standard interne). Les différentes approches sont discutées après validation selon les normes SFSTP [1]. Les temps d'analyse et les performances quantitatives des différentes méthodes sont comparées.

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Analytical chemistry

12

Use of restricted access materials for fast analysis of methadone in serum with liquid chromatography-mass spectrometry

UNIVERSITÉ DE GENÈVE

Souverain S., Ortelli D., Rudaz S., Veuthey J.L.
Laboratory of Pharmaceutical Analytical Chemistry
University of Geneva, 1211 Geneva 4

The use of restricted access materials (RAM), allowing direct injection of biological fluids in a chromatographic system, was evaluated for the direct analysis of methadone (MTD) in serum by liquid chromatography and mass spectrometry (LC/MS). Two methods were developed for the determination of methadone and its major metabolite (EDDP) in serum samples in the concentration range of 10 to 500 ng ml-1. The first method was performed in the single column approach using a Pinkerton GFF II (100 x 2.1 mm I.D.) analytical column. In this mode, the same column is used for the sample preparation and the analysis. The total analysis time was less than 15 min with a limit of quantification of 10 ng ml-1. At this level, repeatability values of 11.8% and 15.8% were obtained for MTD and EDDP, respectively. The second method used a column switching device. A RP-4 ADS (25 x 2 mm I.D.) precolumn was coupled to a LC column to achieve a total analysis time of less than 8 minutes. At the LOQ, repeatability values of 3.2% and 7.6% were obtained for MTD and EDDP respectively. Comparatively to classical liquid-liquid extraction, the use of RAM as stationary phases has proved to be very convenient. Both methods gave short analysis time with a minimum of sample handling and allowed quantitative determination of MTD and EDDP in serum.

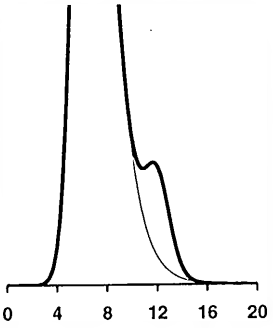
Analytical Chemistry Division **13**

A procedure for the quantification of rider peaks

Simon Jurt[a] , Martin Schär[a], Veronika R. Meyer[b]

[a]University of Applied Sciences, Department of Chemistry, Pestalozzistrasse 20, CH-3400 Burgdorf, Switzerland
[b]EMPA St. Gallen, Swiss Federal Laboratories for Materials Testing and Research, Lerchenfeldstrasse 5, CH-9014 St. Gallen, Switzerland

Rider peaks are small peaks which are not well resolved from a large and asymmetrical neighbour but sit on its trailing side. The usual case is a large, tailed peak which is eluted just in front of the small one although also the opposite situation can occur (a small peak in front of a large one with fronting). The common integration techniques (separating the peaks by vertical drop or by a tangent and determining area or height) give erroneous results. We propose a method for their quantification with low error. It is necessary to set up a "two-dimensional" calibration by varying both concentrations, i.e. of the large peak and of the rider. This leads to a series of linear equations which describe the rider size, as found by the integrator, as a function of the size of the large peak. The y axis intercepts i of these equations show a linear relationship with the concentration x of the rider analyte whereas the slopes s follow a quadratic relationship. These equations can be used to solve the equation $y = s(x)\cdot z + i(x)$ for x (y and z are the integrated peak sizes of rider and large peak, respectively). The procedure was tested with computer-generated peak pairs as well as with HPLC separations of 2,3-dimethylaniline (large tailing peak) and 2,3-dimethylphenol (symmetrical rider peak).



Analytical Chemistry **14**

Short Path Thermal Desorption - SPME-CT-GC-MS: Analysis of trace organic compounds present in hot volcanic gases with high sulfur, water and acid matrix.

F.M. Schwandner[1], A.P. Gize[2], K. Hall[3], T.M. Seward[1], V.J. Dietrich[1]

[1]ETH-Zentrum, Inst. of Mineralogy, 8092 Zürich, CH
[2]Univ. of Manchester, Dept. Earth Sci., Manchester, M13 9PL, UK
[3]Hall Analytical Ltd., Manchester, M23 9YJ, UK

The significance of organic emissions from quiescent volcanic degassing to stratospheric chemistry is that the negligible aqueous solubility of most emitted organic compounds does not lead to a quantitative tropospheric washout effect as postulated for explosive volcanic HCl and HF emissions.

All previous attempts (eg. [1]) have two major analytical problems in common: a) loss and modification of compounds through photolysis, catalysis, adsorption, oxidation, & reaction with not separated condensate during sampling; b) insufficient chromatographic separation due to the high sulfur, water and mineral acid content of the gas. Sampling and analysis of organic compounds in hot (up to 900°C) volcanic gases therefore has to be customized to the difficult matrix of volcanic discharges.

We successfully developed and applied *Short-Path Thermal Desorption-Solid Phase Microextraction-Cryotrapping-GC-MS* (SPTD-SPME-CF-GC-MS) as a reliable standard protocol, together with new sampling techniques. It meets the required analytical accuracy and precision for reproducible (externally standardized) quantitative sampling and analysis.

Among the over 100 detected and quantified compounds are several alkanes, alkenes, arenes, phenols, furans, PAH's and their halogenated, methylated and sulfonated derivatives, and various heterocyclic compounds. All reported compounds are found well above laboratory, ambient air, adsorbent and field blank values. For some analytes (e.g., CFC-11, CH_2Cl_2 , CH_3Br), concentrations are up to several orders of magnitude greater than even midlatitudional industrial urban air maxima.

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Analytical Chemistry **15**

Pressure pinched injection of sub nL volume

Xiaoxia Bai, Joel Rossier and Hubert H. Girault

Laboratoire d'Electrochimie
Ecole Polytechnique Fédérale de Lausanne
CH-1015 Lausanne, Suisse
email: hubert.girault@epfl.ch (H. H. Girault)

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Micro total analysis system (μTAS) is an instrumentation trend for analytical chemistry. Different functional parts were connected externally or directly fabricated onchip. The dominant method used for injection and separation on microchip[1] is electrophoretic mode mainly because the fluid is comparatively easy to manipulate with high potential. On the other hand, the electrokinetic mode will induce some unwanted effects, such as injection deviation among different charged species[2]. In the presented work, mechanic injection mode was investigated for microsystem, polymeric chip. The flow was controlled through a multiports valve.

Laser photoablation has been used for the fabrication of micro network[3] and the integrated carbon ink microelectrodes[4]as on-chip conductivity detector. Therefore the injector, separation part and detector are directly fabricated on-chip. A special injection system was introduced via a multiport valve for injecting volume as low as 1 nL by means of pressure pinched injection similarly to what has been presented with electrokinetical means[5].

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Analytical Chemistry **16**

Methanol Oxidation Studied by Pulse Thermal Analysis

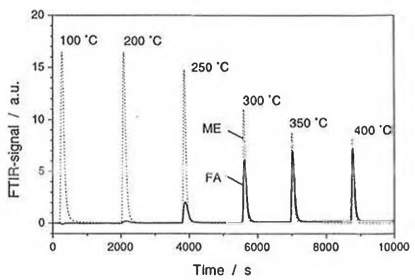
F. Eigenmann, M. Maciejewski and A. Baiker

Laboratory of Technical Chemistry, Swiss Federal Institute of Technology, ETH-Zentrum, CH-8092 Zürich, Switzerland

The potential of pulse thermal analysis (PulseTA®) [1] for investigating heterogeneous catalytic reactions in transient mode under atmospheric pressure was studied. PulseTA® is based on the injection of a given amount of the reactive gas or liquid into a carrier gas stream and monitoring changes in mass and gas composition by a coupled TA-FTIR system.

The application of PulseTA® in catalytic studies is demonstrated by comparing methanol oxidation over MoO_3 catalyst with corresponding steady state measurements. An important advantage of the PulseTA® technique is that only differential changes of the catalyst composition after each injected pulse can be investigated in relation to compostional changes of the gas phase.

The conversion and selectivity to the main product (formaldehyde) determined in steady state and pulse measurements were in good accordance.



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Analytical Chemistry **17**

HRGC-EI-MS methode for detection of microbial volatile organic compounds (MVOCs) in indoor air

S. Heekmann and M. Oehme

University of Basel, Organic Analytical Chemistry, Neuhausstr. 31, CH-4057 Basel

In the industrialised countries 80 - 90 % of the time is spent indoors [1]. The effect of indoor exposures is therefore very important for people's health and well-being.

Microscopic magnification of *Aspergillus sp*

Among other sources fungi such as *Aspergillus sp* (see picture) are made responsible for affecting the air quality and therefore the indoor climate negatively by emitting odours and substances which cause irritations. Especially microbial volatile organic compounds (MVOCs) such as verbenone, camphor, borneol, geosmin or 3-octanol are suspected to contribute to the sick building syndrome (SBS) [2]. Furthermore, fungi growth is sometimes difficult to detect, since spores are missing and their growing site is hidden. Emitted MVOCs facilitate detection.

Aim of this work is to develop a method for detecting mould growth in buildings by MVOC analysis. MVOCs might origine also from other sources such as building materials or paints. An enantiomer selective analysis by HRGC-EI-MS of those MVOCs being chiral allows to differentiate between biotic and non-biotic sources. For the long term sampling of ambient air diffusive/passive samplers were used and compounds were solvent desorbed by diethylether.

Methodological aspects and first applications will be presented.

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Analytical Chemistry **18**

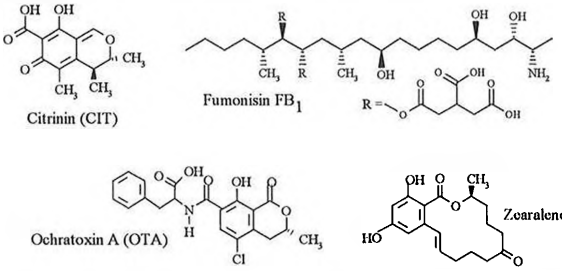
A screening trace method for mycotoxins in cereals by LC-MS/MS

D. Griesshaber and M. Oehme

University of Basel, Organic Analytical Chemistry, Neuhausstr. 31, CH-4057 Basel

Mycotoxins can be present in cereals due to fungal infection by different species such as *Fusarium*, *Aspergillus* or *Penicillium* during plant growth or storage. There is a need for a reliable screening technique allowing to detect simultaneously a large number of different mycotoxins. The aim of this work is to extend a validated LC-MS/MS for trichothecene analysis [1] (mycotoxins from *Fusarium* species) to a large variety of biotoxins being present in Central Europe.

Challenges are the wide polarity range of the toxins to be selected (see Figure for some structures) making sample clean-up difficult and to find a suitable ionisation technique for a simultaneous detection. Moreover, matrix residues should not influence ionisation. Sufficient selectivity is gained by MS^{2-3}. At present atmospheric pressure chemical ionisation in the positive ion mode looks most promising. Results from method optimisation will be presented.



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Analytical Chemistry **19**

Evaluation of Dedicated HPLC Pumps for Fast Splitless Gradient Runs in Capillary-LC/MS

Fabian Kuhn[1], Michael Oehme[1] and Michael Schleimer[2]

[1]Organic Analytical Chemistry, University of Basel, Neuhausstr. 31, CH-4057 Basel, Switzerland, [2]Analytical Technologies, Basilea Pharmaceutica Ltd, P.O. Box 3255, CH-4002 Basel, Switzerland

High performance liquid chromatography (HPLC) using packed columns with inner diameters in the µm (capillary-LC, 150-500 µm) or low mm range (micro-LC 0.5-1 mm) has outstanding advantages over larger diameters (1.5-4.6 mm) due to its better mass sensitivity and very low sample volume requirements. Furthermore, microcolumn-LC yields a better ionization efficiency of pneumatically assisted electrospray the most widely applied ionization method.

Up to now, the method of choice for the generation of small flow rates in the range of 0.5-50 µL/min was mobile phase flow-splitting. However, changes of the column's flow resistance also alter the split ratio resulting in not controllable variabilities of the flow rate during a sequence of analytical runs. Although microcolumn-HPLC has been in focus for a while, dedicated microflow pumps have become commercially available only recently. For this reason different pumping systems were tested for their ability to perform rapid gradient runs without flow-splitting.

Splitless gradient runs of 5-15 min were performed at flow rates between 1-10 µL/min. The precision of mobile phase delivery was controlled by discrete gradient steps. Relative to the expected step heights, the measured values varied between 69 % and 131 %. In addition, robustness of mobile phase delivery was studied by determining the variability of the retention times of several test compounds during a linear gradient analysis of protein-precipitated samples obtained from microsomal incubations. The found relative standard deviations of the retention times and peak areas were well below the limits acceptable for drug discovery analysis (± 10 %).

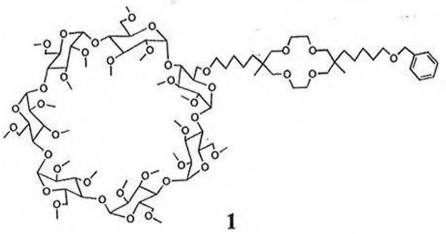
Analytical Chemistry **20**

Synthesis and Chromatographic Properties of a Permethylated β-Cyclodextrin Substituted Crown-Ether

M. Tharin[a], S.G. Claude[a], S. Cherkaoui[b] and R. Tabacchi[a]*

[a] University of Neuchâtel, Institute of Chemistry, Bellevaux 51, 2000 Neuchâtel, Switzerland
[b] University of Geneva, Laboratory of Pharmaceutical Analytical Chemistry, 20 Bd. D'Yvoy, 1211 Geneva 4, Switzerland

Since several years, we are interested in the development of new versatile phases for GC, HPLC or CE. Until now, no universal selector has been found which is able to separate simultaneously all compounds of interest, as well as their respective isomers. Thus, there is a great need for phases offering new and different selectivities. The propensity of Crown Ethers and Cyclodextrins to form inclusion complexes and to discriminate between isomers led us to imagine and synthesize the following compound.



1

Here we report the total synthesis of **1**, its incorporation as selector in chromatographic systems and the subsequent tests of its separation properties

1) as component of the stationary phase in GC
2) as an additive to the buffer solution in capillary electrophoresis.

Analytical chemistry **21**

Pushing the frontier into the deep blue: SNOM and Raman spectroscopy with UV light

M. De Serio, Ch. Fokas, V. Deckert, and R. Zenobi

Laboratorium für Organische Chemie, ETH Zürich
Universitätstr. 16, 8092 Zürich, Switzerland

Optical microscopy is developing into a powerful tool, which is being adopted by an increasing number of research fields. Its success stems from the potential of optically imaging samples with a lateral resolution well below 100 nm combined with a spectroscopic analysis of the sample [1].
In this work the capabilities of Scanning Near-Field Optical Microscopy (SNOM) using a laser light source in the ultraviolet region are investigated. Thereby special attention is focused on fluorescence and Raman as spectroscopic and analytical tools.
Fluorescence studies can be then made on a much wider range of materials including minerals and biological samples.
Also optical imaging using near-field Raman spectroscopy could be substantially improved. The limitation of Raman spectroscopy origins from the small scattering cross section and from the luminescence signal that can completely obscure the weak Raman bands of certain materials. With UV light the advantage of Resonant Raman Scattering (RRS) can be exploited [2] together with the increase of the signal intensity due to its dependence from the fourth power of excitation frequency. This tool will give us the necessary sensitivity to study processes occurring at the interface between two liquids.

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Analytical Chemistry **22**

Mass Spectrometry for Trace Analysis of Gas Standards

H.-P. Haerri, B. Niederhauser, J.-F. Perrochet, D. Zickert

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

The Section for Analytical Chemistry of METAS is mainly responsible for the traceability to the SI of gas standards used for official measurements of gases from combustion processes and of air pollutants in Switzerland. In order to assure the quality of gas measurements, the trace composition of gas standards, specially for immissions with low amount of substance fractions of analytes, needs to be known. In order to distinguish substances with isotopes of similar relative atomic weights, METAS has purchased an ion-molecule reaction (IMR) mass spectrometer (MS) **[1,2]** .

$$X + e \longrightarrow X^+ + 2\,e$$

$$X^+ + A \longrightarrow X + A^+$$

X: primary ionization gas (Kr, Xe)
A: analyte

Ionization scheme for IMR-MS (soft ionization)

The metrological requirements for the instrument, its main characteristics, the improvements, the application for the analysis of gas standards and results of various samples are reported.

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Analytical Chemistry **23**

Determination of Benzoylurea Insecticides in Vegetables and Fruit with LC/MS

Markus Zehringer[a], Marco Brumec[b], Kurt Vögtli[b], Daniel Gygax[b] and Hans-Ruedi Schmutz[b]
[a] State-Laboratory Basel-City, Kannenfeldstr. 2, Postfach, CH-4012 Basel
[b] University of Applied Sciences Basel (FHBB), Department of Chemistry, CH-4132 Muttenz

Diflubenzuron was introduced as the first benzolyurea in 1975 following several other insecticides of the same class in the eithies. The benzoylurea insecticides act as inhibitors of chitin production and are stomach and contact poisons for insects. They are used selectively against gypsy moth, forest tent caterpiller and as larvae control chemicals in mushrooms. These insecticides show low toxicity against birds, bees and aquatic organisms, low persistency in soil and rapid degradation in plants. Benzoylurea insecticides are thermolabile and therefore not directly accessible to analyse with gaschromatography. Analytical HPLC methods for food were developed using UV, diode array [1] and MS detection [2, 3].
A simplified, robust method with LC/MS was developed successfully. After a single extraction of the fruit or vegetable sample the determination of diflubenzuron, flucycloxuron, flufenoxuron, lufenuron, hexaflumuron and teflubenzuron was performed by an LC coupled with an ion trap mass spectrometer. The analytes were separated on a 2 mm Prodigy 3µ RP 18 column and analysed in full scan mode (m/z 100-500) after negative, atmospheric pressure chemical ionisation.
Recovery studies were carried out in apples, tomatoes and potatoes.

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Analytical Chemistry **24**

Characterisation of pectic substances from the cellulosic residue of apples

Rahel Oechslin, Alexandra L. Kocher, Marc V. Lutz, Renato Amadò

Institute of Food Science, Swiss Federal Institute of Technology Zurich, CH-8092 Zurich, Switzerland

The pectic substances from the cellulosic residue (CR) of two varieties of ripe apples was analysed. The ripe fruits of the two varieties show different textural characteristics. The project should elucidate the existence of pectic substances and provide information about the structural elements of a possible linkage.

The yield of the CR after alkaline extraction of the DR was similar for both varieties (50% of the dry matter of the DR). Substantial amounts of galacturonic acid residues were found: 10% of the dry matter in Golden Delicious and 7.5% in Glockenapfel.

The following approach on analysing the CR was chosen: degradation of the CR by a cellulase and further degradation by a pectin degrading enzyme. The degraded fractions were separated by ultrafiltration and analysed with HPSEC and methylation analysis. Degradation by cellulase followed by ultrafiltration (MWCO 10'000) led to an enrichment of pectic substances. The amount of galacturonic acid residues was increased to 13% of the dry matter for Golden Delicious and to 11% for Glockenapfel. The enzymatic treatment of the CR removed about 60% of the cellulose. Methylation analysis of the cellulase-degraded CR revealed the occurring pectic substances mainly to consist of hairy regions. Indication for this is the ratio galacturonic acid to rhamnose and structural elements side chains (linear galactan and arabinan). No major differences in the distribution of neutral sugars between the two varieties were found, but glucose could still be detected. The pectin of the CR of Golden Delicious had a calculated MW of approx. 400'000 compared to 230'000 of the Glockenapfel.

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Analytical Chemistry

New methods for the analysis of tannins, inhibitors of an enzyme produced by *Botrytis cinerea*

Camille Perret, Roger Pezet[1] and Raffaele Tabacchi[2]

[1] Station Fédérale de Recherches en production végétale de Changins, Route de Duillier, CH-1260 Nyon
[2]Institut de chimie, Université de Neuchâtel, Av. de Bellevaux 51, CH-2000 Neuchâtel

Grey mould, caused by *Botrytis cinerea* is one of the most important diseases of grapes. The fungus infects flowering clusters, although it does not develop in the berries until ripening. An unfavorable environment, caused by the presence of resveratrol and pterostilbene in the immature berries, probably maintains this quiescent stage. *B. cinerea* produces a hydroxystilbene-degrading enzyme identified as a laccase-like stilbene oxidase, which oxidizes both resveratrol and pterostilbene to form non-toxic compounds[1]. This enzyme is in turn, inhibited by the tannins contained in the grape berries.
Different methods of tannins fractionation and analysis have been developed in our laboratories to prove the inhibition of the enzyme by these compounds. Polymeric tannins have been fractionated according to their degree of polymerization using a divinylbenzene phase. Oligomeric tannins have been isolated with exclusion gels. Each fraction was characterized by mass spectrometry (LC/ESI-MS and MALDI-TOF) and tested with the stilbene oxidase in order to demonstrate the inhibition of the enzyme by the tannins.

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Analytical Chemistry 26

Analysis of Furan Fatty Acids in Dried Green Herbs using Ion Trap GC-MS/MS

Isabelle A. Sigrist, Giuseppe G.G. Manzardo and Renato Amadò

Institute of Food Science, Swiss Federal Institute of Technology, ETH-Zentrum, CH-8092 Zurich, Switzerland

Dimethyl furan fatty acids (diMeF) occur widely in different plants, vegetables oils, seafood and mammals. This class of lipid compounds is reported to have antioxidant properties and is also considered as precursor of flavour compounds. The objective of this study was the analysis of diMeF in different dried green herbs (basil, chervil, dill, leek, savory, tarragon). For this purpose a method using ion trap GC-MS/MS was developed. GC-MS/MS allows a direct identification of these minor components of the lipid fraction without a prior separation step like in multidimensional GC [1] or HPLC-GC [2]. The two most abundant diMeF found in the samples belong to the representatives with a pentyl side chain (Fig. 1). The amounts differed from a few ppm (savory, basil) to more than 100 ppm (tarragon).

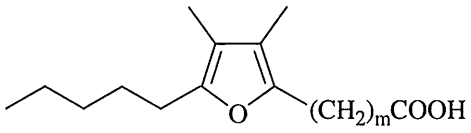

Fig. 1: Pentyl diMeF (m = 1-10)

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Analytical Chemistry 27

Gas phase potassium basicities of common MALDI matrices

J. Zhang, E. Dyachokva, R. Knochenmuss, and R. Zenobi*

Laboratory of Organic Chemistry, ETH Zentrum, CH-8092 Zürich, Switzerland

The gas-phase potassium ion basicities (GKB) of four common MALDI (matrix assisted laser desorption) matrices are measured using equilibrium method on a Fourier transform ion cyclotron resonance mass spectrometer (FT ICR MS). These values are important for clarifying MALDI mechanism [1].

Gas phase potassium basicity is defined as negative value of free energy of a potassium complex formation reaction: $M + K^+ \longrightarrow [M+K]^+$, GKB (M) = $-\Delta G$. By monitoring gas phase potassium transfer reaction between potassiated matrix molecule (M) and a reference base (R) with known gas phase potassium basicity (GKB(R)) the equilibrium constant K_{eq} can be measured, as shown in following reaction:

$$[M+K]^+ + R \underset{}{\overset{K_{eq}}{\rightleftharpoons}} M + [R+K]^+$$

The gas phase potassium basicity of a MALDI matrix can be calculated using the gas phase potassium basicity of reference base (GKB(R)) and the measured equilibrium constant of the gas phase potassium transfer reaction (1):

$$GKB(M) = GKB(R) - RT \cdot \ln(K_{eq}) \quad (1)$$

MALDI matrices investigated in this work are: 2,5-dihodroxy benzoic acid, trans-3,5-dimethoxycinnamic acid and 2,4,6-trihydroxyacetophenone.

[1] R. Knochenmuss, A. Stortelder, K. Breuker, R. Zenobi, J. Mass Spectrom. 35 (2000) 1237-1245.

Analytical Chemistry 28

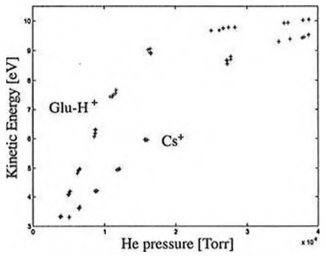
Resolution of Isobaric Ions in a Conventional ESI-Tandem-MS by Low-Pressure Ion-Mobility-Measurements

Rolf Dietiker, Christian Adlhart and Peter Chen*

Swiss Federal Institute of Technology, 8092 Zurich, Switzerland.

A deficiency of mass spectrometry is that ions are only separated by their mass over charge ratio (*m/z*) and therefore ions with the same *m/z* (isobaric or isomeric ions) remain unresolved.

In this project isobaric ions are resolved in a conventional Finnigan TSQ 700 electrospray-ionization-tandem-mass-spectrometer (ESI-Tandem-MS) in the collision cell by accurate measurement of retarding potentials at different pressure of He as collision gas. Cs^+ was distinguished from Glu-H^+ as well as were *o*-, *m*-, and *p*-$C_6H_4(COOMe)_2H^+$ extending the methodology introduced by Bowers *et al.* [1] by measuring kinetic energy of ions pathing a low pressure collision cell at different pressure of He.



Collisional cross sections can be obtained using a hard sphere elastic scattering model and the exponential dependence of translational energy of the ions after the collision cell on the number of collisions c. Comparing cross sections of different halogenated anilines with those measured in a high-resolution high-pressure collision cell [2] show excellent agreement.

[1] A. C. Gill, K. R. Jennings, T. Wyttenbach, M. T. Bowers, *Int. J. of Mass Spec.* **2000**, *195/196*, 685-697.
[2] G. R. Asbury, H. H. Hill Jr. *Anal. Chem.* **2000**, *72*, 580-584.

Analytical Chemistry **29**

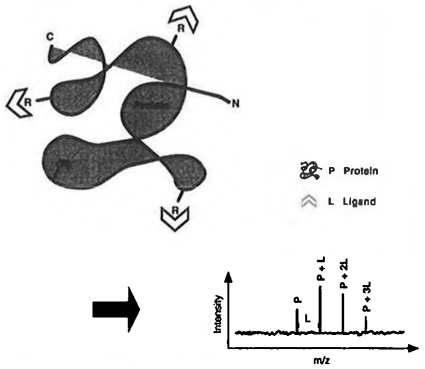
Noncovalent Complexes in MALDI MS: Selective Detection of Amino Acid Residues

Sebastian D. Friess and Renato Zenobi

Department of Chemistry, 8092 ETH Zurich

Mass spectrometry is a method that does not usually yield structural information (e.g. of biomolecules). However, noncovalent complexes that form between amino acid residues in peptides/proteins and specific ligands can be related to structural properties. Using matrix-assisted laser desorption/ ionization mass spectrometry, we are studying the interaction of Cibacron Blue F3G-A with Arg, Lys, His and the amino terminus [1] and thus we can determine the total number of exposed basic residues (see scheme).

We have further developed this methodology for the complexation of arginines only using naphthylsulfonates [2], and a new routine for the complexation of carboxylic residues is presented as well [3]. In this recent study, we employ different arginine functionalities to elucidate the role of the guanidinium-group(s) involved in complex formation.



References

[1] Salih B, Zenobi R, *Anal. Chem.* **1998**, 70, 1536-1543.
[2] Friess SD, Zenobi R, *J. Am. Soc. Mass Spectrom.* **2001**, 12, 810-818.
[3] Friess SD, Daniel JM, Hartmann R, Zenobi R., *Int. J. Mass Spectrom.* **2001**, *in preparation*

Chimie Analytique **30**

Détermination du soufre par ICP-OES. Intensité du signal suivant le composé soufré.

A. Fornage, R. Cicciarelli*

HEVS, filière chimie, CH-1950 Sion, Suisse

La mesure du soufre par ICP-OES peut être effectuée très facilement et des limites de détection de l'ordre du ng/ml sont facilement atteintes. Or l'intensité du signal mesuré dépend très fortement de la forme chimique sous laquelle le soufre est présent. Par rapport au soufre sous forme de sulfate, le signal obtenu, à concentration égale en soufre, peut être plus faible ou plus intense (jusqu'à un facteur 100) suivant la forme sous laquelle le soufre est présent. Si ceci est un inconvénient pour la quantification, peut, dans certains cas, représenter un avantage du fait que les limites de détection sont pour certaines espèces abaissées, cas do SO2. Pour la mesure des thiols, par exemple, cette méthode peut s'avérer très intéressante.

Analytical Chemistry **31**

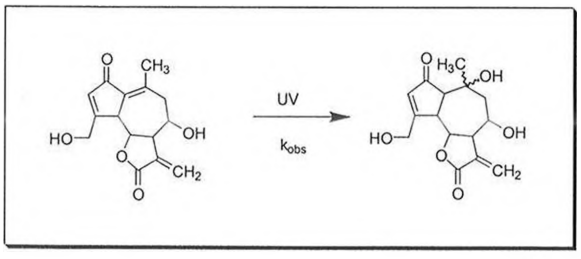
Degradation of Sesquiterpene Lactones in Chicory Extract: Kinetics and Identification of Degradation Products by HPLC-MS

J. Claude[a], S. Crelier,[b] M.-A. Juillerat[b], U. Frey[a]*

(a) University of Applied Science, HEVs, 1950 Sion, Switzerland
(b) Nestlé Research Center, 1000 Lausanne 26, Switzerland

Inulin, a valuable ingredient due to its bifidogenic, cholesterol-lowering, texturing or fat-replacing properties, is found in large amounts in chicory roots.[1] A major problem for an industrial process aiming at the production of food-grade inulin are the extremely bitter co-extracted sesquiterpene lactones. The major contributors to the overall bitterness are lactucine, lactucopicrin and 8-deoxylactucin, either in their free or glycosylated form. One possibility to decrease the bitterness is the photo-degradation of these compounds by UV treatment.

This study concentrates on the degradation of lactucin, formerly obtained by semi-preparative HPLC, in a model solution. The dependence of the degradation kinetics depending on the initial lactucin concentration and the temperature were investigated. The major degradation product was characterised by HPLC-MS and NMR.



[1] Gibson, G.R.; Willis, C.L., Van Loo J. *Int. Sugar JNL*, 1994, *96*.

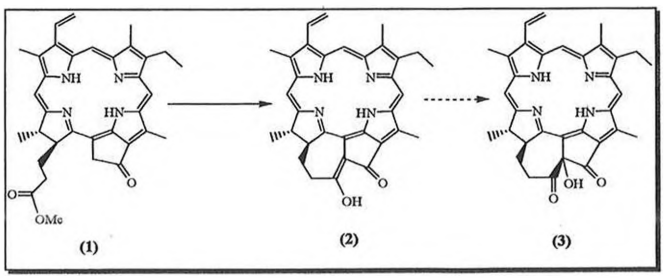
Analytical Chemistry **32**

Identification of Chlorophyllone *a*, by on-line RP-HPLC/APCI-MS

Nebahat Aydin and Fazil O. Gülaçar

Laboratory of Mass Spectrometry, Department of Physical Chemsitry, University of Geneva, 1211 Geneva , Switzerland

A class of natural anti-oxidants, chlorophyll *a* related chlorins have been synthesized and characterized by on-line RP-HPLC/APCI-MS in positive and negative ionization mode. The unstable 13^2,17^3-cyclopheophorbide *a* enol (CPP516, **2**) obtained from the Claisen-type intramolecular condensation of pyropheophorbide *a* methyl ester (ppme, **1**) is mainly converted into α and β-chlorophyllone when applied to normal phase silica gel column chromatography or dissolved in organic solvents under oxic conditions [1]. However, recently only the α epimer of chlorophyllone was observed in surface sediment extract of Lake Voua la Motte, indicating that the sedimentary formation of chlorophyllone *a* is a enzymatic process [2].



[1] Goericke, R., Strom, S.L., Bell, M.A., *LIMNOL OCEANOGR*, 2000, 45, 200-211.
[2] Chillier, X.Fr.D., Gülaçar, F.O., Buchs, A., *Chemosphere*, 1993, 27, 2103-2110.

Analytical Chemistry **33**

Trace Analysis of PAHs with L2MS – Quantification on the picogram level

M. Kalberer, B. Morrical and R. Zenobi

ETH Zürich, Laboratory of Organic Chemistry
8092 Zürich, Switzerland

Many polycyclic aromatic hydrocarbons (PAH) found in ambient aerosols have carcinogenic and mutagenic properties. Two Step Laser Mass Spectrometry (L2MS) was shown in the past to be a very sensitive method for analyzing PAHs on aerosols [1]. However, up to now this method was mostly qualitative and only relative abundances of different PAHs could be obtained. We present here a method of quantification for PAHs on aerosols with L2MS. The quantitative results are compared with conventional GC-MS.
A model aerosol consisting of a $(NH_4)_2SO_4$ core and an outer layer of different PAHs was generated in the laboratory and collected on a Teflon coated quartz fibre filter. After collection a solution containing 50ng of an internal standard was deposited by electrospray onto the sample. The filter was rotated during the electrospray process to assure an even coating of the internal standard. The filter was then introduced without further preparation into the L2MS. The whole sample preparation and measurement time was about 15min. Detection limits for different PAHs is in the low pg range for the whole filter. The small amount of internal standard added did not affect the measurement of the covered aerosol with the L2MS. The same PAH coated $(NH_4)_2SO_4$-aerosols were also measured with GC-MS. Sample preparation for the GC-MS included sonication of the filter in hexane and evaporation of the solvent to a volume of about 100µl. The sensitivity of L2MS is 10^3–10^4 times higher than for GC-MS.

[1] Haefliger O. P., T. D. Bucheli, R. Zenobi, *Environ. Sci. Technol.*, 34, 2184-2189, 2000.

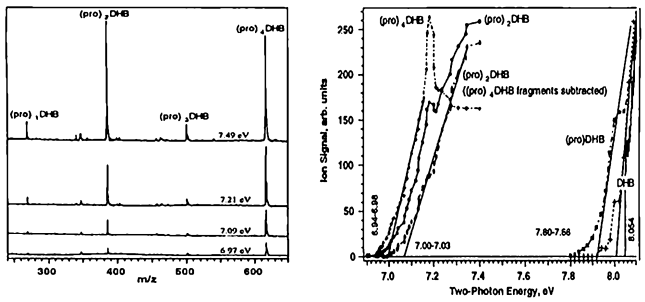
Analytical Chemistry **34**

Two-photon ionization thresholds of analyte-matrix clusters: A possible ionization pathway in MALDI?

Patrick D. Setz, Richard Knochenmuss and Renato Zenobi

Department of Chemistry, 8092 ETH Zurich, Switzerland

In spite of its analytical importance, the ionization mechanisms in MALDI are poorly understood. Two-photon ionization is a possibility, to evaluate it, ionization potentials (IP) must be known.Here we report on $(pro)_n$DHB clusters (pro = proline, DHB = 2,5-dihydroxybenzoic acid) as a model system. By scanning the ionization laser wavelength while monitoring the cluster ion signal intensities in the mass spectra the photoionization efficiency curves were obtained (see scheme).



The IPs drop as the cluster size increases from n=1 to 2 to 4. The IP found for the $(pro)_4$DHB cluster was 6.94-6.98 eV, well below the 2-photon energy of the usual UV laser employed for MALDI: 337 nm (nitrogen laser, 7.36 eV). It is thought that this effect is due to analyte-matrix interactions (e.g. hydrogen bonds) that destabilize the neutral HOMO.

Analytical Chemistry **35**

New Applications of Open cell design for Internal Source MALDI FTICR-MS

Vladimir Frankevich, Juan Zhang, and Renato Zenobi
Department of Chemistry, Swiss Federal Institute of Technology (ETH), Universitätstrasse 16, CH-8092 Zürich, Switzerland.

A new FTICR cell design is described that improves the performance of internal source MALDI applications. The design employs a capacitively coupled open FTICR cell and a ring electrode placed between the ion source and the ICR cell. The flexibility of our open cell design allows the use of several different trapping schemes for ion detection, which include dynamic ion trapping in an open cylindrical cell. With the ionization of large molecules by MALDI the produced ions have high kinetic energies. This requires a deceleration of the ions in the axial direction of the ICR cell because large kinetic energy complicates both ion trapping and ion detection. A new method of ion deceleration in the first trapping cylinder of the FTICR open cell is proposed and experimentally evaluated. In this work we also present the design of an FTICR open cell developed for the direct detection of laser induced fluorescence.

MALDI experiments were performed on a FTMS equipped with a 4,7 T magnet and an internal MALDI source. The additional ring electrode placed between the ion source (MALDI target) and the ICR cell serves as an axial focusing lens. Ion trapping is achieved by applying RF or DC potentials to the trap cylinders.

Reduction of the drift time dependence for trapping MALDI ions, RF ion selection and accumulation, both positive and negative ion trapping, and improved trapping of MALDI ions desorbed at an angle to the surface normal are shown. The single laser shot MALDI/FTICR mass spectrum of bovine serum albumine (BSA, m/z=66.430 Da) was detected after the ion deceleration in the first trapping cylinder.

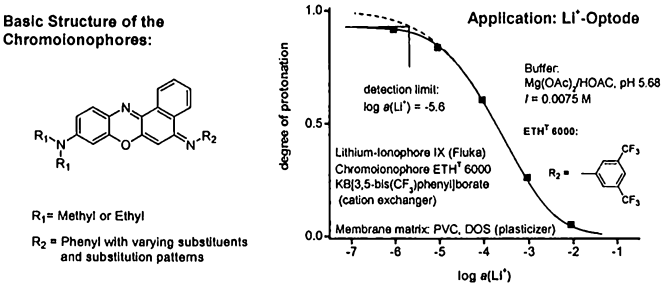
Analytical Chemistry **36**

Neutral Chromoionophores Covering a wide pK_a Range for the Application in Cation Selective Liquid Membrane Optodes

Michael Linnhoff, Luzi Jenny and Ursula E. Spichiger

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

Besides neutral ionophores with high selectivity for a specific analyte cation, neutral H^+-selective indicator dyes, *i.e.* chromoionophores, are incorporated into ion selective liquid membrane optodes to transduce the analyte ion activity into an optical signal. The measuring range of such optical chemical sensors can be specifically adjusted both by the pH of the buffered aqueous sample or the pK_a of the chromoionophore which has to be known for the respective polymer membrane matrix.
We have synthesized and characterized novel nile blue derivatives as chromoionophores with pK_a between 4.6 and 8.8 in PVC membranes, plasticized with bis-2-ethylhexylsebacate (DOS). In combination with the chromoionophores of pK_a values above 9 that have been characterized by Bakker *et al.* some years ago [1], it is now possible to optimize the response range of optodes for a given sample pH, which is desired when activities of different ions shall be determined simultaneously by an optode array.



[1] E. Bakker *et al.*, Anal. Chim. Acta 278 211-225 (1993).

Analytical Chemistry **37**

Developing a Proteomics "Lab on a Chip"

D. Jed Harrison

Dept of Chemistry, University of Alberta
Edmonton AB, T6G 2G 2 Canada

Microfluidic devices have been proposed as the basis of "lab on a chip" or micro-total analysis systems. A key, already demonstrated promise of microfluidic technology has been the ability to integrate chemical and biochemical reactions, along with separations, to provide a range of sample processing steps on a chip. However, the ultimate goals for automation of sample preparation require increasingly complex sample processing procedures be integrated within the microchip format. This challenge is only beginning to be met, and will require further invention of microfluidic elements. This presentation will focus on advances in protein sample preparation for electrospray mass spectroscopy (ESMS), and on methods to multiplex affinity assay techniques within microchips. Our ESMS chip integrates protein digestion, preconcentration, electrophoretic separation and ESMS. The work illustrates the competing fluid management issues and solvent compatibility problems which integration creates, and demonstrates functional solutions. The affinity assay device study demonstrates the challenges associated with multiplexing microfluidic devices to increase the sample throughput, illustrating the difficulties and the payoff of such an approach. These studies demonstrate forward progress towards sophisticated sample processing on-chip, aimed towards a true "Lab on a chip" product.

Chimie Analytique. **38**

Protein affinity microchip for zeptomol detection

Ph. Michel, C. Vollet, F. Reymond and J. Rossier.
DiagnoSwiss SA, Route de l'Ile au bois , CH-1870 Monthey , Switzerland.
Tel : + 41 24 471 49 00. Fax : + 41 24 471 49 01.
E-mail : info@diagnoswiss.com.

The development of low cost and disposable polymer microchips with integrated microelectrodes for affinity-based medical tests is discussed. Mass production is performed by means of plasma etching, a method developed for the fabrication of Printed Circuit Board [1]. Microchannels with integrated electrodes can be fabricated with different surface properties [2]. The microchips can be advantageously adapted for the development of Immunoassays (ELISA). Antibodies are attached to the chip surface and immunosorbent assays are performed with short incubation time due to the short diffusion distance between the bulk solution and the surface. The use of electrochemical detection is advantageous because it is proportional to the concentration of redox molecules present in the channel even in small volumes (<100 nL). Furthermore, this approach aims at reducing the cost of analyses by the reduction of the sample and reagent consumption. The performances of the chips will be illustrated by presenting a highly sensitive immunoassay for the measurement of alkaline phosphatase (Reactions I and II) with a detection limit of 3×10^{-21} mol.

Alkaline phosphatase

$$\text{4-aminophenyl phosphate} + H_2O \rightarrow \text{4-aminophenol} + H_3PO_4 \quad \text{(I)}$$

$$\text{4-aminophenol} \rightarrow \text{quinonimide} + 2e^- + 2H^+ \quad \text{(II)}$$

[1] www.dyconex.com [2] Rossier et al. Langmuir 1998

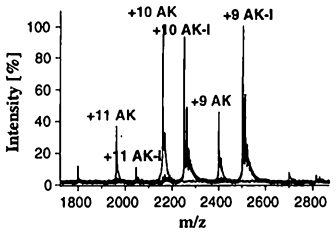
Analytical Chemistry **39**

Electrospray Time-of-Flight Mass Spectrometry: Investigation of non-covalent Protein-Ligand Interactions

Jürg M. Daniel, Silke Wendt, and Renato Zenobi

Department of Chemistry, 8092-ETH Zürich

Since electrospray mass spectrometry is a soft ionization method, it has been used to study noncovalent interactions of proteins and their binding partners, either other proteins or their substrates and inhibitors [1]. However, in mass spectrometry, molecules are in the gas phase during analysis. To investigate if and to what extend the situation in solution is reflected by the situation in the gas phase, our goal is the determination of the binding constant of a known system. Thus, we will be able to compare the binding constant determined by MS with the binding constant in solution. For this purpose we chose adenylate kinase (AK) as a model system since the binding constant of its inhibitor Di-adenosin-pentaphosphate (I) is described in the literature [2]. First results show that we can indeed detect the non-covalent complex between adenylate kinase and its inhibitor I on our instrument (see figure).



[1] J.A. Loo, *Mass Spectrometry Reviews* (1997), **16**, 1-23.
[2] M. Hamada, S.A. Kuby, *Arch Biochem Biophys* (1978), **190(2)**, 772-792.

Analytical Chemistry **40**

Ion Trap Positive Ion Chemical Ionization of Chlordane Compounds with Non Conventional Reagent Gases.

Z. Zencak, S. Skopp and M. Oehme

University of Basel, Organic Analytical Chemistry, Neuhausstr. 31, CH-4057 Basel

Positive ion chemical ionization (PICI) mass spectrometry often allows to increase selectivity and/or sensitivity for selected compound classes by using reagent gases with different proton affinities and ion-molecule formation properties. In addition, it offers the possibility to differentiate between isomers [1]. The ion trap mass spectrometer enables the trapping of ions over relatively long periods (ms) increasing the number of collisions between analyte molecules and reagent gas ions tremendously. This allows to obtain PICI conditions with only ppm concentrations of reagent gas so that reagents with a rather low vapor pressure can be applied [2,3].

The ionization of some compounds of the technical pesticide chlordane (heptachlor, cis/trans-chlordane and cis/trans-nonachlor) by PICI in an ion trap was studied using acetonitrile, acrylonitrile and dichloromethane as non conventional reagent gases. These reagent gases initiated specific fragmentation reactions (e.g. a retro-Diels-Alder and a cyclic fragmentation) and resulted in different response factors. All reagent gases enabled detection limits in the low pg range for heptachlor, whereas the detection limits of cis- and trans-chlordane and cis- and trans-nonachlor were in the middle pg range. Additionally, acetonitrile and dichloromethane PICI allowed to differentiate between the cis- and trans- stereoisomers of chlordane and nonachlor by their mass spectra.

[1] N. J. Oldham, et al.; *Rapid Commun. Mass Spectrom.*, **1999**, 13, 331.
[2] R. E. March; *Rapid. Comm. Mass Spectrom.* **1998**, 12, 1543.
[3] J. F. J. Todd, et al.; *Int. J. Mass Spectrom. Ion Process.*, **1990**, 99, 139.

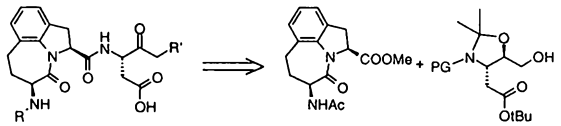
Medicinal Chemistry **41**

Synthesis of broad spectrum caspase inhibitors and their biological activities.

S. Hintermann, S. Roggo, V. Rasetti, M. Tintelnot-Blomley, U. von Krosigk

Pharmaceutical Research, Nervous System, Novartis Pharma AG, CH-4002 Basel

The caspases (Cysteinyl ASPartic ProteASES) were shown to be the key mediators in apoptosis. So far, 14 caspases of human origin have been identified, which can be grouped into 3 major classes: Mediators of inflammation (e.g. Csp-1), activators of Apoptosis (e.g. Csp-8) and effectors of Apoptosis (e.g. Csp-3). [1]



On the way to broad caspase-inhibitors for the indication stroke, we started off with short peptide sequences derived from natural substrates. Using the tools of molecular modelling with known X-ray structures of different caspases and combinatorial chemistry, we optimised the inhibitors by incorporation of natural and unnatural amino acids, as well as peptide mimetics. A set of irreversible inhibitors proved to be the compounds of choice, since they are brain penetrable broad caspase inhibitors and are potent *in vitro* and *in vivo*.

The synthesis of inhibitor as well as the scale-up and the optimisation of the synthesis of the two corresponding building blocks will be outlined. In addition to synthetic details, an overview about the biological activities and the pharmacokinetic properties of this very promising class of inhibitors will be given.

[1] Thornberry, NA. Chem. Biol. 1998, 5(5), R97-R103.

Medicinal Chemistry **42**

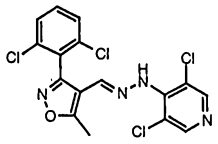
Design and Synthesis of Potent and Selective, Orally Active NK1 Receptor Antagonists

P. Schnider, M. Bös, T. M. Ballard, G. Galley, T. Godel, G. A. Higgins, T. Hoffmann, W. Hunkeler, S. M. Poli, A. J. Sleight and H. Stadler

Pharma Research, F. Hoffmann-La Roche Ltd., CH-4070 Basel, Switzerland

Neurokinin (NK) receptors belong to the family of G-protein coupled receptors and can be divided into three subtypes: NK1, NK2 and NK3. The endogenous ligand for NK1 receptors is the neuropeptide substance P, one of the five mammalian tachykinins. Following the discovery of the first non-peptide NK1 receptor antagonist CP-96,345, a remarkable number of small molecule NK1 receptor antagonists were identified by many pharmaceutical companies in the last decade. Moreover, recent clinical trials have demonstrated an important therapeutic application for NK1 receptor antagonists in the control of chemotherapy induced emesis and in the treatment of mood disorders such as anxiety and depression.

Following random screening of our corporate library Ro-16-2515/000 (**1**) was discovered which showed moderate affinity for the NK1 receptor. In this presentation we will describe the design, synthesis, structure activity relationship and biological evaluation of a variety of derivatives emerging from this hit structure which led to the rapid identification of potent and selective, orally active NK1 receptor antagonists.



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Medicinal Chemistry **43**

Novel Ascomycin Analogues Modified in the Binding Domain

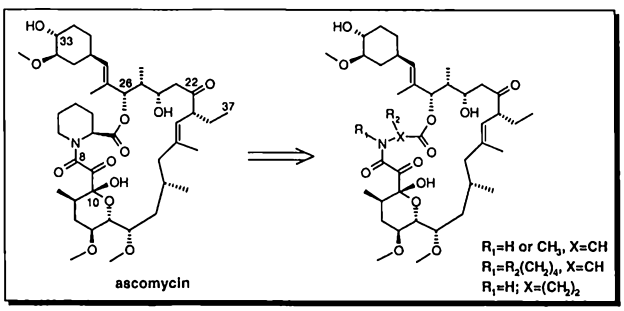
A. Horvath, M.A. Grassberger, E. Haidl, G. Schulz, H. Sperner

Novartis Research Institute 1235 Vienna, Austria, Brunnerstrasse 59

Ascomycin derivatives represent a novel class of anti-inflammatory macrolactams. Two semisynthetic methods were developed to prepare a series of novel ascomycin analogues in which the *L*-pipecolinic acid moiety is replaced by α or β amino acids.

The syntheses started with the degradation of selectively protected ascomycin to produce C_{10}–C_{37} partial structures. The key steps in the reconstruction of the macrolactam were the acylation of these intermediates with an appropriate amino acid equivalent, introduction of the C_8,C_9 unit and macrolactonization. The tricarbonyl sequence of ascomycin was restored by regioselective dihydroxylation and Swern oxidation. Removal of the protecting groups and reoxidation afforded the desired target compounds.

The two novel semisynthetic routes will be presented and their application will be discussed.



Therapeutic Chemistry **44**

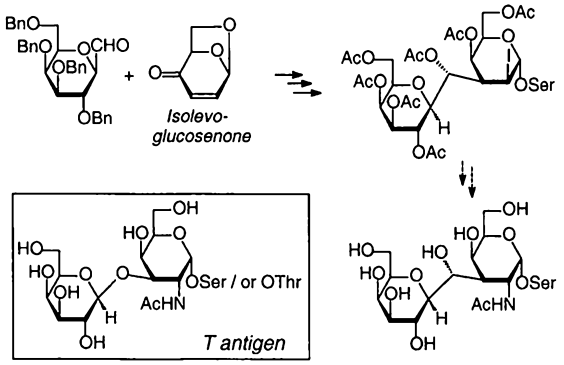
Synthesis of *C*-linked Disaccharides, Mimetics of the Thomsen-Friedenreich (T) Epitope

Raynald Demange and Pierre Vogel

Institute of Organic Chemistry, University of Lausanne, BCH, CH-1015 Lausanne-Dorigny, Switzerland

Among the tumor associated carbohydrate antigens, the Thomsen-Friedenreich antigen (T antigen) is found in carcimona-associated mucins. The T antigens have been prepared and their immunogenicity in conjugate vaccines has been confirmed [1].

We report here our efforts toward the synthesis of a C-glycoside analogs of epitope T using our recently developed methodology for the synthesis of C(1→3) linked disaccharides [2].



[1] G. D. MacLean, M. A. Reddish, M. B. Bowen-Yacyshyn, S. Poppema, B. M. Longenecker; *Cancer Invest.* **1994**, *12*, 46-56.

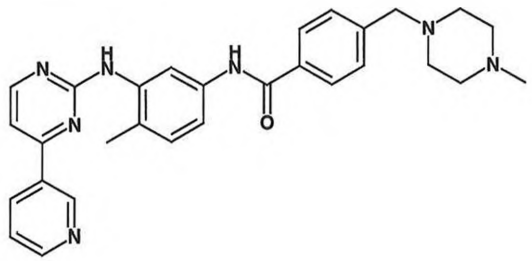
[2] Y.-H. Zhu, R. Demange, P. Vogel; *Tetrahedron: Asymmetry* **2000**, *11*, 263-282; Y.-H. Zhu, P. Vogel; *Synlett* **2001**, 79-81.

Medicinal Chemistry **45**

Case Study: Gleevec – A new Treatment Modality for CML

J. Zimmermann, E. Buchdunger, P. Manley
Pharma Research, Novartis, CH-4002 Basel

Gleevec is a protein-tyrosine kinase inhibitor which potently inhibits the Abl tyrosine kinase *in vitro* and *in vivo*. The compound specifically inhibits proliferation of *v-abl* and *bcr-abl* expressing cells, suggesting that it is not a general antimitotic agent. In addition, Gleevec is a potent inhibitor of the platelet-derived growth factor receptor kinase (PDGF-R) and of the receptor kinase for stem cell factor (SCF), c-Kit, and inhibits PDGF- and SCF-mediated biochemical events. In contrast, it does not affect signal transduction mediated by other stimuli including epidermal growth factor (EGF), insulin and phorbol esters. Pharmacokinetic studies in various animal species demonstrate that pharmacologically relevant concentrations are achieved in the plasma following oral administration of the drug. STI571 shows anti-tumor activity as a single agent in animal models at well tolerated doses. On May 10, 2001, the U.S. Food and Drug administration announced the fast track approval of Gleevec™ (imatinib mesylate), our treatment for patients with chronic myeloid leukemia (CML) in blast crisis, accelerated phase or chronic phase after failure of interferon-alpha therapy. The FDA approval came in just over 10 weeks after Novartis filed its New Drug Application, and just two months after the FDA notified us that it had granted Gleevec a priority review.



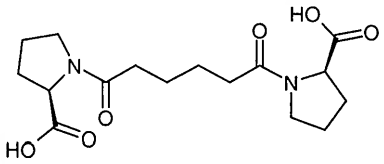
Medicinal Chemistry **46**

Inhibitors of SAP-Amyloid Binding

R. Jakob-Røtne, A. Alanine, R. Norcross, T. Hoffmann, C. Hertel, B. Levet-Trafit, M.B. Pepys.

Pharma Research, Medicinal Chemistry, F. Hoffmann-La Roche Ltd, CH-4070 Basel; Centre for Amyloidosis & Acute Phase Proteins, Department of Medicine, Royal Free and University College Medical School, London

Serum amyloid P component (SAP) is a glycoprotein that binds in a calcium-dependent manner to the amyloid fibrils in all types of amyloidosis. It is extremely proteinase resistant and it is catabolized *in vivo* only by hepatocytes. The coating of amyloid fibrils by SAP protects the fibrils from degradation *in vitro* and may do so *in vivo*, contributing to the pathogenesis of amyloidosis. Furthermore SAP knockout mice are relatively resistant to experimental induction of amyloidosis. Inhibition of the binding of SAP to the amyloid fibrils may therefore be a new approach to therapy of systemic and cerebral amyloidosis.
A high throughput screening was performed to identify inhibitors of SAP-amyloid binding. Hit compounds were optimized in a chemistry programme with regard to *in vitro* and *in vivo* potency and metabolic stability. (R)-1-[6-[(R)-2-carboxy-pyrrolidin-1-yl]-6-oxo-hexanoyl]-pyrrolidine-2-carboxylic acid (Ro 63-8695) was selected for clinical testing.



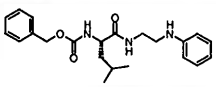
Ro-63-8695

Medicinal Chemistry **47**

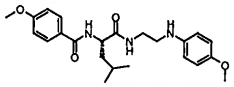
Nα-Acyl-L-leucine-(2-phenylamino-ethyl)-amides- Novel and highly potent Inhibitors of Cathepsin K

Eva Altmann*, Johanne Renaud, Jonathan Green
Novartis Pharma Research, Arthrithis and Bone Metabolism, 4002 Basel

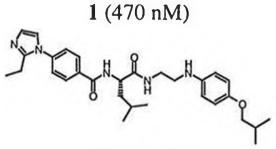
Healthy bone tissue is maintained by a delicate balance between bone formation and bone degradation. This remodelling process is effected by two higly specialized cell types, namely the bone forming osteoblasts and the bone resorbing osteoclasts. Cathepsin K, a member of the papain-cysteine protease family, has been shown to be highly and almost exclusively expressed in osteoclasts. Cathepsin K exhibits potent collagenolytic activity against type-I collagen and is further involved in the degradation of other components of the extracellular bone matrix. Thus, selective inhibition of cathepsin K may provide an effective treatment for diseases characterized by excessive loss such as osteoporosis.
We have discovered a new class of cathepsin K inhibitors and report on one of our optimization strategies for our lead compound **1** (Fig. 1), involving the investigation of different acyl moieties as well as the effect of substituents on the anilino phenyl ring. This strategy led to the identification of highly potent and remarkably selective cathepsin K inhibitors (Fig. 1).
Figure 1: Inhibition of rabbit cathepsin K (IC_{50}'s)



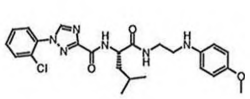
1 (470 nM)



2 (14 nM)



3 (< 3 nM)



4 (< 3 nM)

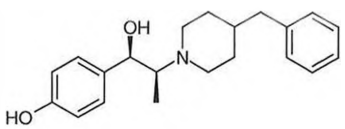
Medicinal Chemistry **48**

4-aminoquinolines as a novel class of NR1/2B subtype selective NMDA receptor antagonists

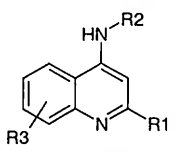
E. Pinard[a], A. Alanine[a], A. Bourson[b], B. Büttelmann[a], R.Gill[b], M. P. Heitz[a], G. Jaeschke[a], V. Mutel[b], G. Trube[b] and R. Wyler[a]

Pharma Division, [a]Discovery Chemistry and [b]Preclinical CNS research, F. Hoffmann-La Roche Ltd., CH-4070 Basel, Switzerland

During the last decade, a number of ifenprodil like NR1/2B subtype selective NMDA receptor antagonists have been described. Interestingly, these compounds showed robust neuroprotective effect in animal models of cerebral ischaemia without inducing the adverse cardiovascular and CNS side effects associated with many non selective NMDA antagonists.
Screening of the Roche compound collection led to the identification of 4-aminoquinolines **1** as structurally novel NR1/2B subtype selective NMDA receptor antagonists. The structure activity relationship which was developed in this series resulted in the discovery of highly potent and in vivo active blockers.



Ifenprodil



1

Medicinal Chemistry **49**

Structure-Based Optimization of a New Class of Proteasome Inhibitors

Pascal Furet, Patricia Imbach, Vito Guagnano, Marc Lang, Peter Fürst, Dennis France, Maria Noorani, Johannes Rösel, Dieter Scholz, Johann Zimmermann, Carlos Garcia-Echeverria

Novartis Pharma Inc., Oncology Research Department, CH-4002 Basel, Switzerland

Due to its key role in the degradation of regulatory proteins involved in cell cycle progression and cell proliferation, the ubiquitin-proteasome pathway has emerged as an important target in oncology drug research. In particular, inhibition of the proteolytic activity of the 20S proteasome, the final enzymatic reaction in the pathway, is a possible strategy in the search for new antitumor agents. Following this direction, we have engaged in a programme aiming at the identification of inhibitors of the chymoptrypsin-like activity of the proteasome on the basis that blocking this specific activity is sufficient to induce apoptosis in cancer cells.
In the course of the programme, we identified 2-aminobenzylstatine derivatives as a novel class of non-covalent inhibitors of the proteasome. We will describe the optimization of this new class of inhibitors by structure-based design, using a model of the human proteasome constructed by homology to the X-ray crystal structure of the yeast proteasome.

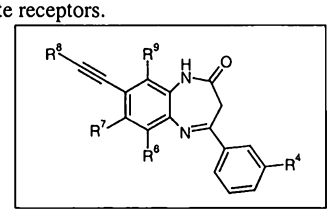
Medicinal Chemistry **50**

Synthesis and Characterization of 8-Ethynyl-1,3-dihydro-benzo[b][1,4]diazepin-2-one Derivatives as potent non-competitive metabotropic Glutamate Receptor 2/3 Antagonists

T.J. Woltering,[1] G. Adam,[1] E. Goetschi,[1] J. Wichmann,[1] S. Gatti,[2] J. Kew,[2] F. Knoflach[2] and V. Mutel[2]

[1]*PRBC-M and* [2]*PRBN-P, F. Hoffmann-La Roche, Grenzacherstrasse CH-4070 Basel, Switzerland*

We have synthesized and characterized the properties of a series of 8-ethynyl-1,3-dihydro-benzo[b][1,4]diazepin-2-one derivatives which are potent and selective non-competitive mGlu2/3 receptor antagonists. These derivatives partially inhibited the binding of ^{3}H-LY-354740 to the mGlu2 receptor with IC_{50} values in the low nM range. The antagonist properties could also be demonstrated ex vivo, measuring the ability of these compounds to reverse LY-354740 mediated inhibition of the medial perforant path field excitatory postsynaptic potential. The selectivity of this new class of non-competitive mGlu2/3 receptor antagonists was demonstrated versus mGlu1, mGlu4 mGlu5 and mGlu8 receptors and ionotropic glutamate receptors.



These compounds represent useful pharmacological tools for the study of the role of group II mGlu receptors in disorders such as psychosis and Alzheimer's disease. The synthesis and the SAR of this new class of non-competitive mGlu2/3 receptor antagonists will be discussed in detail.

Medicinal Chemistry **51**

Competitive AMPA antagonism: a novel mechanism for antiepileptic drugs?

Yves P. Auberson

Novartis Pharma AG, Nervous System Department 4002 Basel, Switzerland

Epilepsy is one of the most common neurological disorders, with a prevalence in excess of 0.5% of the world population. Despite a variety of antiepileptic drugs (AEDs) available, there is still a high medical need for improved treatments of epilepsy. About 40% of patients see their seizures inadequately controlled, and many of those who become free of seizures suffer from adverse effects, the most frequent patient complaints being cognitive impairment and decrease in overall energy level.
Glutamate is the main excitatory neurotransmitter in the human brain, and acts at two families of ionotropic and metabotropic receptors. There are three subtypes of ionotropic glutamate receptors, which are pharmacologically classified as NMDA and non-NMDA (AMPA and kainate) receptors. It has been shown that competitive NMDA receptor antagonists have potent anticonvulsant effects in a variety of animal models. In clinical trials however, they lack anticonvulsant action and elicited unacceptable neurotoxic side effects. AMPA/kainate receptors antagonists also possess a broad spectrum of anticonvulsant activity in preclinical models of epilepsy, and although no clinical data on their antiepileptic potential is available, there is some evidence that they may be better tolerated in humans. As it is now well established that the activation of AMPA receptors is involved in the initiation and propagation of seizures, AMPA receptors antagonism may represent a promising mechanism for AED action.

Medicinal Chemistry **52**

Pseudo-Proline Libraries for Tuning Inhibitors of SH3 Domain-Mediated Protein-Protein Interactions

Gabriele Tuchscherer[a]*, Jimena Fernandez-Carneado[a], Patricia Durieux[a], Daniel Grell[a], Yoshiro Tatsu[a], Beatrice Hengst[a], Luc Patiny[a], Christian Kardinal[b], Stephan Feller[b]
[a]Institute of Organic Chemistry, BCH, University of Lausanne, CH-1015 Lausanne, Switzerland; [b]Laboratory of Molecular Oncology, MSZ-Institute for Medical Radiation and Cell Research, D-97078 Würzburg, Germany

Specific protein-protein interactions are essential facets in cellular communication often regulated by binding to proline (Pro)-rich peptides. Pro-rich ligands of the consensus sequence Pro-Xaa-Xaa-Pro adopt a left-handed PPII conformation and bind to a highly conserved patch of aromatic amino acids of e.g. Src homology 3 (SH3) domains. In the search of novel inhibitors, recently introduced pseudo-prolines (ΨPro)[1] were used to study ligand-receptor interactions of Pro-rich peptides. Binding affinities in the order typically found for SH3-mediated interactions and, most notably, enhanced binding specificity as well as inhibition of Grb2 SH3 (N)-SoS complex formation illustrate that ΨPro exert a dual functionality, i.e. i) enhancing the relevant PPII conformation and ii) increasing and optimizing van der Waals contacts and hydrogen bonding to the receptor molecule[2]. To further optimize ligand-receptor interactions, *2-C* substituted ΨPro libraries applying post-insertion strategies have been generated allowing for rapid screening of ligands that optimally complement the SH3 topography. Condensation of Cys with Boc-protected glycinale results in an NH_2-group at *2-C* of ΨPro for the covalent ligation of a broad palette of various substituents either on solid phase or in solution. First results on the biostructural characterization and inhibitory activity of the ΨPro libraries will be presented.

[1] Wöhr, T., Wahl, F., Nefzi, A., Rohwedder, B., Sato, T., Sun, X., Mutter, M., *J. Am. Chem. Soc. 118*, 9218 (1996), and references therein.
[2] Tuchscherer, G., Grell, D., Tatsu, Y., Durieux, P., Fernandez-Carneado, J., Hengst, B., Kardinal, C., Feller, S., *Angew. Chem. Int. Ed.* 2001, in press.

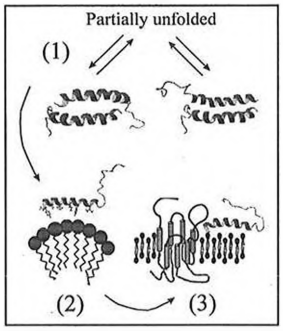
CHIMIA 2001, 55, No. 7/8

Medicinal Chemistry **53**

Structural Features for Receptor Subtype-Specificity of Neuropeptide Y (NPY) and Mutants studied by NMR

R. Bader[1], M. Lerch[1], G. Folkers[1], A.G. Beck-Sickinger[2], O. Zerbe[1]
[1]Institute of Pharmaceutical Sciences, ETH Zürich, CH-8057 Zürich
[2]Institute of Biochemistry, University of Leipzig, D-4103 Leipzig

Different receptor-subtypes may be involved in the regulation of rather diverse biological function. In the case of the neurohormone Y (NPY) five different subtypes have been discovered up to now. Their functions include cardiovascular regulation, the control of food intake and memory retention.



For binding of NPY to its receptor we propose a three step model that includes membrane association as a important step preceding receptor recognition (see Fig. on the left side). We have previously structurally and dynamically characterized NPY bound to a model membrane[1-2] and determined the binding topology.
Recently, we developed a key motif to derive agonists that selectively bind to the Y_5-receptor-subtype of NPY[3]. We subsequently determined the structure and dynamics of one such mutant both in solution and when bound to the membrane and identified residues from the membrane-hormone interface. The data indicated that the part of the molecule containing the message is differently oriented with respect to the membrane. Hence, residues forming receptor contacts are placed in a different location with respect to the membrane-water interface. From these data we have now developed a structural model for the initial event during receptor recognition thereby possibly explaining receptor-subtype specificity. Presently we are working on chimera of NPY and pancreatic polypeptide (PP) that display interesting subtype-specificity profiles.

[1] Bader, R., Bettio, A., Beck-Sickinger, A.G. , Zerbe, O. (2001), *J. Mol. Biol.*, **305**, 307-329.
[2] Bader, R., Lerch, M., Folkers, G., Zerbe, O. (2000) *Chimia*, **54**, 627-632.
[3] Cabrele, C., Langer, M., Bader, R., Wieland, H. A., Doods, H. N., Zerbe, O. & Beck-Sickinger, A. G. (2000) *J. Biol. Chem.*, **275**, 36043-36048.

54

If It Is Not Steric It Is Electronic

Thomas R. Ward
Insititut de Chimie, Université de Neuchâtel, Avenue de Bellevaux 51, CP 2
CH-2007 Neuchâtel

The rationalization of molecular recognition events, be it in catalysis or supramolecular chemistry, is by and large based on steric arguments. In recent years however, considerable progress has been made in enantioselective catalysis by introduction of electronic asymmetry in the first coordination sphere of a metal catalyst. Such systems rely both on steric and electronic discrimination to achieve high levels of enantioselection. This talk will present our efforts directed towards the design of enantioselective catalysts and cation receptors based on electronic- rather than steric discrimination. In this context, our reasoning relies on qualitative molecular orbital and hard-soft acid-base arguments rather than molecular modelling.

Inorganic Chemistry **55**

Coordination-chemical aspects of asymmetric catalysis

A. Togni

Department of Chemistry, ETH Hönggerberg, CH-8093 Zürich

Recent examples of enantioselective reactions catalyzed by transition metal complexes shall illustrate the importance of coordination-chemical considerations, when studying mechanistic aspects. Thus, knowing geometry and configuration of the metal complexes involved in the catalytic cycle helps defining the origin of enantioselectivity, and is therefore important when trying to improve the catalyst's properties. Experimental investigations and computational studies concerning the Pd-catalyzed hydrosilylation of olefins and the Ti-catalyzed fluorination of 1,3-dicarbonyl compounds will be presented.

Inorganic Chemistry **57**

Sustainable Homogeneous Catalysts Based on Tridentate Ligands

G. van Koten

Department of Homogeneous Catalysis and Metal-Mediated Synthesis
Debye Institute - Utrecht University
Padualaan 8 - 3584 CH Utrecht - The Netherlands

The reactivity of Pt(NCN)X (NCN = $C_6H_4(CH_2NMe_2)2$-2,6-anion) has been studied in nitration and sulphonation reactions to arrive selectively at the para-NO_2 and SO_3 substituted Pt(NCN)X derivatives, respectively. The self-assembly of water-soluble anionic para-SO_3-NCN-metal complexes with core-shell dendrimers having a rigid cationic core are reported and the use of these nanosize aggregates in catalysis and the construction of rigid core molecules of 2-3 nm with catalytically active NCN-metal complexes at their periphery. They show perfect retention in a membrane reactor and therefore are suitable homogeneous catalysts for use in continuous flow reactors.

CHIMIA 2001, 55, No. 7/8

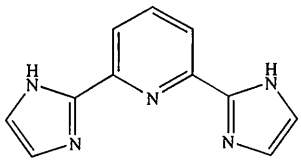
Inorganic chemistry **58**

Stabilisation of high oxidation states of 3d metals by deprotonation of a coordinated imidazole

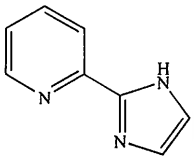
G.Stupka and A.F. Williams

University of Geneva, Sciences II, Department of Inorganic Chemistry
Quai E. Ansermet 30, CH-1211 Geneva 4
e-mail : Gilles.Stupka@chiam.unige.ch

Access to higher oxidation states by deprotonation of the imidazole moiety of ligand 1 for several divalent metal ions in ML_2 complexes has been well established. To stabilise manganese in its +3/+4 oxidation states should be interesting for biological oxygen chemistry (photosystem II for example). In this way we have prepared dinuclear manganese III/IV with ligand 2 and tried to deprotonate the coordinated imidazole. Similar complexes with ligand 1 are in preparation.



L 1



L 2

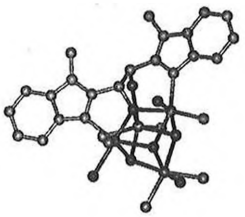
Inorganic Chemistry **59**

1,2-bis(1-methyl-benzimidazolyl)ethanediol as a bridging ligand

K. Isele and A.F. Williams

University of Geneva, Sciences II, Department of Inorganic Chemistry
Quai E. Ansermet 30, CH-1211 Geneva 4
e-mail : Katharina.Isele@chiam.uni-ge.ch

We have previously shown that 1,2-bis(1-methyl-benzimidazolyl)ethanediol acts as a facially coordinating tridentate ligand. We now show that at low ligand:metal ratios the ligand can form polynuclear complexes with the deprotonated alcohol function bridging two or more metal ions.
Co(II) forms a cuboidal tetranuclear complex $[Co_4(ligand(-H))_4]^{4+}$ characterized by X-ray crystallography. The core is formed by a tetrahedron of cobalt atoms with a bridging deprotonated alcohol centering each face of the tetrahedron. The octahedral coordination sphere of each cobalt is completed by two benzimidazoles and an alcohol. The magnetic susceptibility of the complex is reported.
With copper(II) an entirely different tetranuclear complex $[Cu_4(ligand)_3Cl_2]^{2+}$ is formed in which the ligand shows two different bridging modes which will be discussed in detail.



Part of the tetranuclear complex $[Co_4(ligand(-H))_4]^{4+}$

Inorganic & Coordination Chemistry **60**

Magnetic Exchange in Molecular Grids

D. Cati[a], J. Ribas[b], H. Stoeckli-Evans[a*]

[a]University of Neuchâtel, Institute of Chemistry, CH-2007 Neuchâtel, Switzerland; [b]Univesity of Barcelona, Institute of Inorganic Chemistry, 08028 Barcelona, Spain.

Metal-ion directed self-assembly currently provides a very efficient method of access to coordination arrays of predetermined nuclearity and spatial composition. The rigidity of the ligand plays an important role for the design of the expected structure and its properties.

Here we present a new conformationally rigid, Ni^{II} based 4+ cationic molecular [2x2]G grid, $[NiLCl]_4$ (**1**), and the first Cu^{II} based 4+ cationic molecular [2x2]G grid, $[CuL(ClO_4)]_4$ (**2**), where $\mathbf{H_2L}$ is Pyrazine-2,3-dicarboxylic acid bis-[(pyridin-2-ylmethyl)-amide].

The crystal structures and magnetic properties of these complexes will be discussed.

Inorganic Chemistry **61**

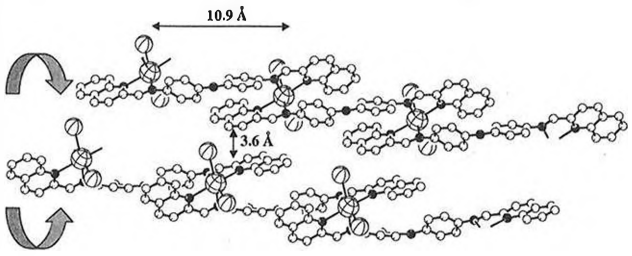
Synthesis and characterization of complexes of some Shiff base ligands with d^{10} metal ions

A. Tesouro Vallina and H. Stoeckli-Evans*

University of Neuchâtel, Institute of Chemistry
Avenue de Bellevaux, 51, 2007 Neuchâtel, Switzerland

The design of new nitrogen-donor multidentate ligands and the study of their metallosupramolecular chemistry are of interest not only from the point of view of their potential applications but also from a strictly structural point of view. Depending on the ligand structural features such as the flexibility and the length and nature of the spacer group between the coordinating moieties, different 3D motifs can be generated.

We will present the synthesis and the crystal structures of some Zn(II), Hg(II) and Cd(II) complexes containing different Shiff base bis-bidentate ligands. These complexes present different motifs going from dimers to step-like or single-helical polymers.



Polymeric structure of the complex $[Cd(L7)I_2]_n$

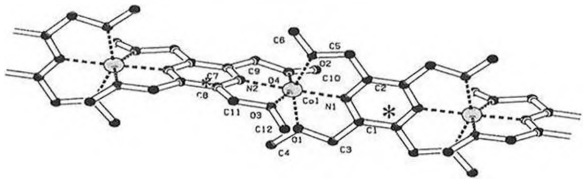
Inorganic Chemistry **62**

Coordination Chemistry of new Ether Ligands derivatives of Pyrazine

Gilles Gasser, Ana Tesouro Vallina, Helen Stoeckli-Evans*

University of Neuchâtel, Institute of Physical Chemistry
2007 Neuchâtel, Switzerland

New ether ligands derivatives of tetrakis(bromomethyl)-2,3,5,6 pyrazine have been synthesised and a study of their coordination chemistry with transition metal salts has been carried out. These ligands show a very high capacity to form coordination complexes with a large variety of first row and d^{10} transition metals. For example, crystals of complexes with the ligand tetrakis(methylether)-2,3,5,6-methylpyrazine (**L1**) have been obtained with copper(II), zinc (II), cobalt(II), cadmium(II), mercury(II) and nickel(II) salts. X-ray analysis has shown that different structural types can be obtained, for example, polymers, columnanes, and mononuclear and binuclear complexes. The magnetic properties of a polymer containing Cu(II) have been examined. Attempts have also been made to couple magnetic and optical properties by a careful choice of ligand substituents.



Polymeric Structure obtained with **L1** in presence of $Co(BF_4)_2$

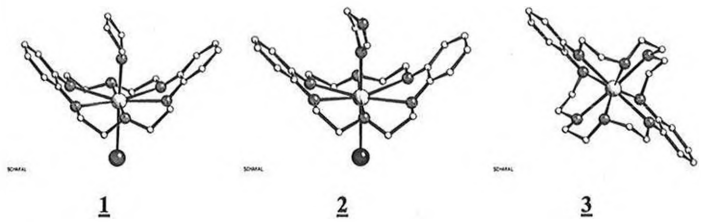
Inorganic chemistry **63**

Synthesis and characterization of novel crown ethers complexes

E. Gueneau and K. M. Fromm

University of Geneva, Sciences II, Department of Inorganic Chemistry
Quai E. Ansermet 30, CH-1211 Geneva 4
e-mail : Estelle.Gueneau@chiam.unige.ch

Reaction between NaI and dibenzo-18-crown-6 in polar solvents leads to the formation of new crown ether complexes. The crystal structures of [Na⊂(DB18C6)I(thf)] **1** and [Na⊂(DB18C6)I(1,3-dioxolane)] **2** are presented, both forming molecular units with asymmetric coordination of the metal ion. Compound **2** also shows the physical property of optical birefringence.
The symmetric complex [Na⊂(DB24C8)]I **3** was obtained with the larger dibenzo-24-crown-8 that wraps around the cation, thereby excluding the complexation of further ligands.[1]



1 **2** **3**

[1] K. M. Fromm, E. D. Gueneau, J. P. Rivera, G. Bernardinelli, H. Goesmann, *in preparation.*

Inorganic chemistry **64**

Clusters of Alkali and Alkaline Earth Metals : further synthesis and characterization.

E. Gueneau and K. M. Fromm

University of Geneva, Sciences II, Department of Inorganic Chemistry
Quai E. Ansermet 30, CH-1211 Geneva 4
e-mail : Estelle.Gueneau@chiam.unige.ch

In our attempts to make alkaline earth metal cluster compounds analogous to transition metal clusters, we now report on a general reaction scheme involving reaction of $[M(thf)_5I_2]$ (M = Sr, Ba) with $LiOBu^t$ in THF, in the presence of hydroxide, to yield volatile mixed alkali and alkaline earth metal clusters.
Herein the crystal structures of $[IM(OBu^t)_4\{Li(thf)\}_4(OH)]$ (M = Ba : (**1**) [1]; Sr : (**2**) [2]) are presented, and the chemical nature of the bonding in such compounds is approached through theoretical calculations using the *elf* program. [3]

$$[MI_2(thf)_5] + 4\,[LiOBu^t] + LiOH$$

THF ⇓ 1 : M = Ba, 2 : M = Sr

$$[IM(OBu^t)_4\{Li(thf)\}_4(OH)] + LiI$$

Preliminary tests have been carried out on these mixed metal clusters as potential precursors for oxide materials such as high Tc superconductors.

[1] K.M. Fromm, E.D. Gueneau, H. Goesmann, *Chem. Commun.*, **2000**, 2187
[2] K. M. Fromm, E. D. Gueneau, G. Bernardinelli, H. Goesmann, J. Weber, M.-J. Mayor-López, P. Boulet, T. Tybell, J.-Y. Genoud, H. Chermette, *in preparation.*
[3] A. D. Becke, K. E. Edgecombe, *J. Chem. Phys.*, **1990**, *92*, 5397.

Inorganic Chemistry **65**

A supramolecular approach derived from inorganic H-bonded polymers of alkaline earth metal halides: toward structure prediction

Gérald Bernardinelli[a], Katharina M. Fromm*[b], Helmut Goesmann[c]

[a]Laboratoire de Cristallographie, Université de Genève, CH-1211 Genève 4
[b]Département de Chimie Minérale, Analytique et Appliquée, Université de Genève, Sciences II, 30 Quai E.-Ansermet, CH-1211 Genève 4
[c]Institut für Anorganische Chemie, Universität Karlsruhe, Engesserstr., D-76128 Karlsruhe, Germany

One of the great challenges of today's chemistry is the implementation of supramolecular devices in molecular based materials in order to generate spatially confined and macroscopically ordered compounds, in other words the structure prediction.

Within the non-covalent binding modes used in supramolecular chemistry, metal ion complexation and hydrogen bonding are here combined in order to construct inorganic polymers with varying dimensionality. The influences of the type of ligand, crystal packing and stoichiometry have been studied [1].

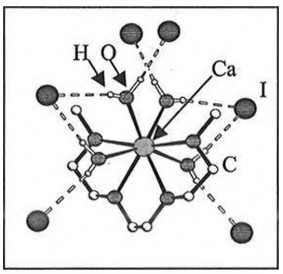


Figure 1

The rules derived from four different dimensional Ca- and Ba-compounds will allow structure predictions in this context. (Fig. 1) [2, 3].

The poster will present these structures, illustrating the rules.

[1] K. M. Fromm, G. Bernardinelli, H. Goesmann, M.-J. Mayor-Lopez, J. Weber, *Z. Anorg. Allg. Chem.* **2000**, *7*, 1685-1691
[2] K. M. Fromm, G. Bernardinelli, H. Goesmann, *Polyhedron*, **2000**, *19*, 1783-1789
[3] K. M. Fromm, *Chem. Eur. J.*, **2001**, in the press

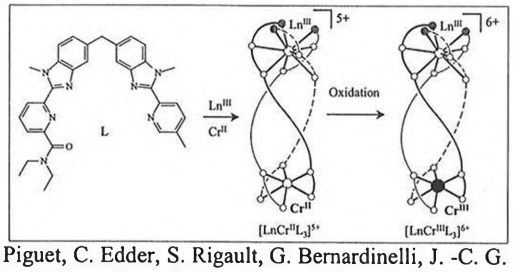
Inorganic and coordination chemistry **66**

Use of inert Cr^{III} for the design of organized bimetallic 3d-4f architectures: synthesis and photophysical properties.

Martine Cantuel,[a] Claude Piguet,[a]* Daniel Imbert,[b] Jean-Claude G. Bünzli[b] and Gérald Bernardinelli[a].

[a] Department of Inorganic Chemistry, University of Geneva, CH-1211 Geneva 4
[b] Institute of Inorganic Chemistry, University of Lausanne, CH-1205 Lausanne

The segmental ligand L is used to specifically coordinate lanthanide (Ln^{III}) and 3d block (M^{II}) ions. Triple helices $[LnML_3]^{5+}$ (M=Zn, Fe, Co), obtained when reacting together L, Ln^{III} and M^{II} in a 3:1:1 ratio, present tunable physical and magnetic properties [1]. As described for Co^{III} [2], the incorporation of inert Cr^{III} into the helical edifice requires the previous formation of $[LnCrL_3]^{5+}$ by strict self-assembly followed by subsequent oxidation with air to yield the inert complexes $[LnCrL_3]^{6+}$, whose structural and physical properties are presented in this contribution. Particular attention will be focused on luminescence properties of complexes with Ln=Eu, Tb, involving intermetallic Ln-Cr communications.



[1] C. Piguet, C. Edder, S. Rigault, G. Bernardinelli, J. -C. G. Bünzli, G. Hopfgartner, *J. Chem. Soc., Dalton Trans.*, **2000**, 3999.
[2] S. Rigault, C. Piguet, G. Bernardinelli, G. Hopfgartner, *J. Chem. Soc., Dalton Trans.*, **2000**, 4587.

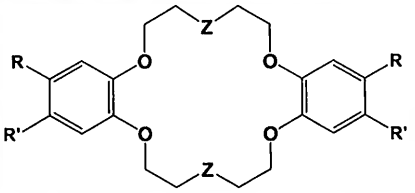
Inorganic & Coordination Chemistry **67**

Towards Mesogenic Crown Ether Complexes with Lanthanides

Olimpia Mamula[1], Stéphane Suárez[1], Claude Piguet[2] and Jean-ClaudeG. Bünzli[1]*

[1]Institute of Inorganic and Analytical Chemistry, University of Lausanne, 1015 Lausanne, Switzerland
[2]Department of Inorganic, Analytical and Applied Chemistry, Sciences II, University of Geneva, 1211 Geneva 4, Switzerland

In the field of supramolecular functional materials, the synthesis of metallomesogens containing rare-earth elements is beginning to attract interest in view of the interesting luminescent and magnetic properties of these metal ions [**1, 2**].



L1a,b : R' = H ; R= -OCO-C_6H_4-$C_{12}H_{25}$
L2a,b: R = R' = -OCO- C_6H_4-$C_{12}H_{25}$
Z = O (a) or N (b)

We present here the synthesis and characterisation of new ligands based on dibenzo-18-crown-6 and diazadibenzo-18-crown-6 ether cores substituted by two (**L1**) or four (**L2**) mesogenic arms. Complexation studies with Ln(III) cations as well as the properties of the new compounds will be discussed.

[1] K. Binnemans *et al.*, *J. Am. Chem. Soc.*, **2000**, *122*, 4335.
[2] H. Nozary, C. Piguet, J.-P. Rivera, P. Tissot, G. Bernardinelli, N. Vulliermet, J. Weber, J.-C. G. Bünzli, *Inorg. Chem.*, **2000**, *39*, 5286.

Inorganic & Coordination Chemistry **68**

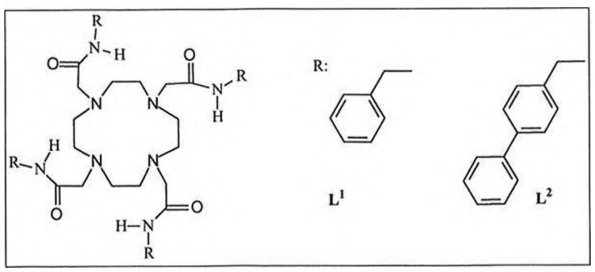
Highly Luminescent Lanthanide Chelates based on the Cyclen Framework using Phenacyl Moieties

G. Zucchi, A.-C. Ferrand, R. Scopelliti, and J.-C. G. Bünzli*

University of Lausanne, Institute of Inorganic and Analytical Chemistry, 1015 Lausanne, Switzerland

Two new ligands, $\mathbf{L^1}$ and $\mathbf{L^2}$, derived from cyclen (1,4,7,10-tetraazacyclododecane) and containing two different phenacyl moieties have been recently synthesized [**1**]. We present here the structural and spectroscopic properties of the 1:1 complexes of these ligands with lanthanide ions.

X-ray diffraction shows that $[Tb(\mathbf{L^1})(H_2O)]^{3+}$ has a $\Delta(\lambda\lambda\lambda\lambda)$ conformation and the water molecule in the inner coordination sphere is located on the C_4 axis. Quantitative measurements allowed us to determine the quantum yields of the metal-centred luminescence of the Sm(III), Eu(III), Tb(III) and Dy(III) complexes in water, which have interest in the development of multiplex fluoroimmunoassays. Relatively large values have been found for $[Tb(\mathbf{L^1})(H_2O)]^{3+}$ and $[Eu(\mathbf{L^2})(H_2O)]^{3+}$, 23 % and 25 % respectively.



[1] G. Zucchi, PhD dissertation, University of Lausanne, 2000.

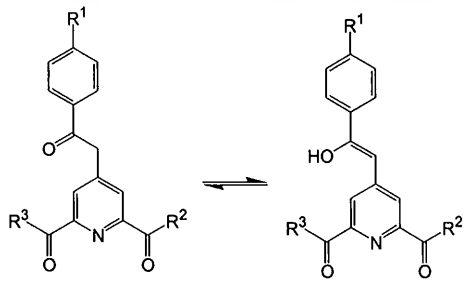
Inorganic & Coordination Chemistry **69**

Self-assembled triple-stranded lanthanide monometallic helicates from 4-substituted dipicolinic acid derivatives

Anne-Sophie Chauvin, Sandrine Gras and Jean-Claude G. Bünzli*

University of Lausanne, CH-1015 Lausanne, Switzerland

The wrapping of meridionally tri-coordinated ligand strands around lanthanide (Ln^{III}) ions, in particular dipicolinic acid derivatives [**1**], produces well-protected coordination sites with interesting structural and electronic characteristics. We are currently substituting the 4-position of dipicolinic acid by chromophoric groups favoring light harvesting and energy transfer to the metal ion. The syntheses of these new ligands will be presented as well as the properties of their complexes with lanthanide ions $[LnL_3]^{3+}$ (Ln= La, Lu, Eu, Tb).



R^1 = H, Ph
R^2, R^3 = OMe, OH, NEt_2

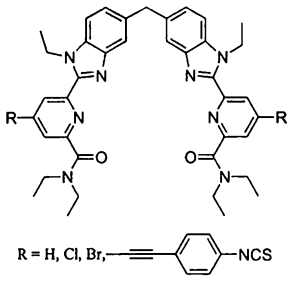
[1] Renaud, F.; Piguet, C.; Bernardinelli, G.; Bünzli, J. -C. G.; Hopfgartner, G. *Chem. Eur. J.*, **1997**, *3*, 1646-1659.

Inorganic & Coordination Chemistry **70**

Self-assembled triple-stranded lanthanide dimetallic helicates with a ditopic ligand derived from bis(benzimidazole)pyridine

Raphaël Tripier,[a] Marcel Hollenstein,[a] Mourad Elhabiri,[a] Anne-Sophie Chauvin,[a] Claude Piguet[b] and Jean-Claude G. Bünzli[a]*

[a] University of Lausanne, CH-1015 Lausanne, Switzerland
[b] University of Geneva, CH-1211 Geneva 4, Switzerland



In the course of our work on the development of supramolecular functional architectures containing lanthanide ions, we have shown that co-ordination of the Ln^{III} ions can be controlled by semirigid aromatic tridentate ligands such as 2,6-bis(benzimidazole)pyridines **[1][2]**; the connection of two such units by a methylene bridge leads to ditopic ligands forming stable dimetallic helicates $[Ln_2(L)_3]^{6+}$ in acetonitrile **[3]**. The ligand strands are wrapped about 9-coordinate Ln^{III} ions with tricapped trigonal prismatic geometry. The pyridine 4-position is amenable to substitution by various functional groups, *e.g.* isothiocyanatophenylethynyl moieties, which are known to easily couple with antibodies. Here we present the influence of these relatively bulky groups on the self-assembly of the dimetallic helicates and on their photophysical properties.

[1] C. Piguet and J.-C. G. Bünzli, *Chem. Soc. Rev.*, **1999**, *28*, 347.
[2] S. Petoud, J.-C. G. Bünzli, F. Renaud, C. Piguet, K.J. Schenk and G. Hopfgartner, *Inorg. Chem.*, **1997**, *36*, 5750
[3] C. Platas, M. Elhabiri, M. Hollenstein, J.-C. G. Bünzli and C. Piguet, *J. Chem. Soc., Dalton Trans.*, **2000**, 2031 and references therein

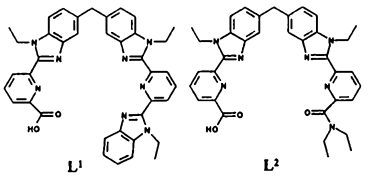
Inorganic and Coordination Chemistry **71**

HETERODIMETALLIC LANTHANIDE-CONTAINING HELICATES

N. André,[a] M. Elhabiri,[b] G. Hopfgartner,[c] C. Piguet,[d] and J.-C. G. Bünzli[a]

[a] *Institute of Inorganic and Analytical Chemistry, University of Lausanne, BCH 1403, CH-1015 Lausanne, Switzerland*
[b] *Laboratoire de Physico-Chimie Bioinorganique, UMR 7509, Institut de Chimie, 1 rue Blaise Pascal, 67000 Strasbourg, France*
[c] *F. Hoffman-La Roche Ltd, PRNS, Bld 68/142, CH-4070 Basel, Switzerland*
[d] *Dept. of Inorganic, Analytical and Applied Chemistry, University of Geneva, CH-1211 Geneva-4, Switzerland*

In contrast to homodimetallic complexes, heterodimetallic lanthanide-containing helicates cannot be easily obtained because of the similar chemical properties of the various Ln^{3+} ions. Previously, only one X-ray structure of a heterodimetallic complex synthesised through stepwise introduction of each individual Ln^{3+} cation has been reported [1]. Heterodimetallic species may provide two luminescent probes in one molecule and therefore present interest for multiplex fluoroimmunoassays. Furthermore, they are potential precursors for doped materials incorporating metal ions at a fixed distance.



In a self-assembly process, the two coordination sites of the novel ligands $L^{1,2}$ recognise two different Ln^{3+} ions to form $[LnLn'(L^{1,2}\text{-}H)_3]^{3+}$ helicates. Electrospray-MS shows the formation of $[LnLn'(L^{1,2}\text{-}H)_3]^{3+}$ up to 80 % and provides a rare example of a ligand differentiating between two lanthanide cations.

[1] J. P. Costes, F. Dahan, A. Dupuis, S. Lagrave, J. P. Laurent. *Inorg. Chem.* **1998**, *37*, 153.

Inorganic Chemistry **72**

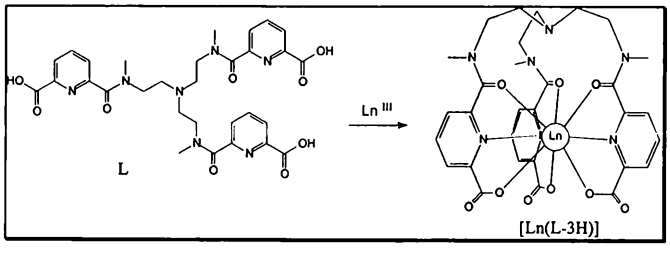
Synthesis and Properties of New Nine-Coordinate Lanthanide Podates

Jean-Michel Senegas, Claude Piguet*

University of Geneva, Department of Inorganic Chemistry, 30 quai E. Ansermet, CH-1211 Geneva 4

Podates in which three polydentate coordinating arms are attached to a central linking unit are common ligands for conferring high stability on metal complexes.

A new podand ligand was prepared by the connection of tris(2-(N-methyl)aminoethyl)amine tripod to three tridentate pyridine-2,6-dicarboxylate binding units to give the podand (L) that exists as a statistical mixture of four conformers in solution. This ligand differs from a previous analog by the presence of the three terminal carboxylate groups instead of carboxamide units [1] which increase thermodynamic stability. In aqueous solution, the protonated apical nitrogen atom of the tripod (pKa = 6.18) adopts a conformation compatible with the formation of intramolecular bi and trifurcated hydrogen bonds with the oxygen atoms of the carboxamide groups. Reactions of **L** with $Ln(ClO_4)_3$ provide nine-coordinate podates [Ln(L-3H)]. The complexes are characterized by NMR spectroscopy and X-Ray crystallography. Much attention will be paid to the photophysical properties of the Europium and Terbium complexes.



[1] F. Renaud, C. Piguet, G. Bernardinelli, J-C. Bünzli, G. Hopfgartner, *J. Am. Chem. Soc.* 1999, *121*, 9326-9342

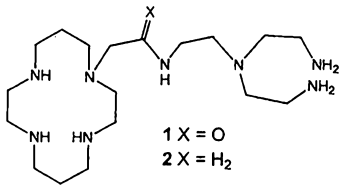
Inorganic Chemistry **73**

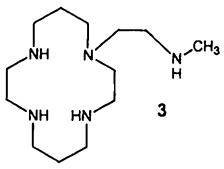
Heteroditopic ligands with a macrocyclic unit

A. Schlageter, D. Saladin, L. Siegfried, Th.A. Kaden

Institute for Inorganic Chemistry, Spitalstr. 51, 4056 Basel, Switzerland

We have synthesized the two new ditopic ligands **1** and **2**, which combine a macrocyclic unit with an open chain chelator, and studied their complexation potential with Cu^{2+} and Ni^{2+}.





Both **1** and **2** react with one equivalent metal ion to give 1:1 species in which the metal ion is bound by the macrocycle. Depending on the pH the open chain ligand is more or less strongly protonated so that a series of species MLH_n (n = 3 – 0) is found. Interesting is that in the case of **2** the deprotonation of $CuLH_3$ to $CuLH_2$ is accompanied with a shift of the absorption maximum from 531 nm to 574 nm indicating that the coordination sphere of the Cu^{2+} changes. A study of the model compound **3** shows the same effect so that we propose that in this step the side chain amino group becomes deprotonated and axially binds to the Cu^{2+}.

Addition of a second equivalent of metal ion gives the M_2L complexes, which have been characterized by their UV-VIS spectral properties. In the case of M = Cu^{2+} an additional hydroxo species M_2LH_{-1} is observed.

A few experiments with two different metal ions have also been run. It is possible to prepare two isomeric species CuNiL, in which depending on the sequence of metal ion addition the Cu^{2+} and the Ni^{2+} ions bind either to the macrocycle or to the open chain ligand.

Inorganic and Coordination Chemistry **74**

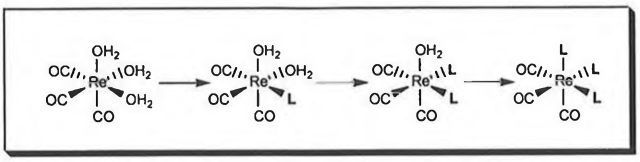
Investigation of the Ligand Substitution Mechanism on *fac*-$[(OC)_3Re(OH_2)_3]^+$

P. Grundler,[a] S. Cayemittes-Shematsi,[a] R. Alberto,[b] R. Hedinger,[c] K. Hegestschweiler,[c] A.E. Merbach[a]*

[a]University of Lausanne, Institute of Inorganic and Analytical Chemistry
1015 Lausanne, Switzerland
[b]University of Zürich, Institute of Inorganic Chemistry
8057 Zürich, Switzerland
[c]University of Saarland, Inorganic Chemistry
66041 Saarbrücken, Germany

To determine the mechanism for the ligand substitution on *fac*-$[(OC)_3Re(OH_2)_3]^+$ in aqueous solution, the water exchange rate and the complex formation rates have to be compared.

For this purpose the water exchange rate has been measured by ^{17}O NMR using the fast injection technique [1] as a function of pH and temperature. On the other hand the complex formation with several ligands bearing N or S as donating atom (thiocyanate, thioureas, thioethers, nitriles, heterocycles, etc.) was investigated by multinuclear NMR and UV-Vis spectroscopy.



[1] P. Bernhard, L. Helm, A. Ludi, A.E. Merbach *J. Am. Chem. Soc.* **1985**, *107*, 312.

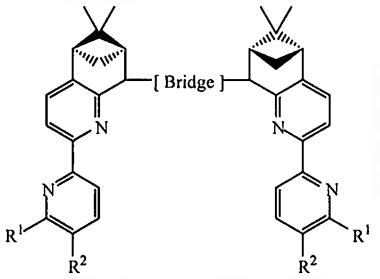
Inorganic and Coordination Chemistry **75**

New CHIRAGEN-Ligands for the Self-Assembly of Helical Structures and as Precursors for Macrocycles

Mathias Düggeli, Christophe Bonte and Alex von Zelewsky

Department of Chemistry, University of Fribourg, Pérolles, 1700 Fribourg,
E-mail: Mathias.Dueggeli@unifr.ch

Self-assembly of helicates with labile metal centres has been recently a subject of great interest in the field of supramolecular chemistry. 5,6-CHIRAGEN[*p*-xyl] **L1b** spontaneously forms a sixfold, circular helicate with Ag^I and Cu^I. [1]



L1: $R^1 = R^2 = H$
L2: $R^1 = p$-MeO-Ph, $R^2 = H$
L3: $R^1 = H$, $R^2 = p$-MeO-Ph
Bridge: **a** = 0, **b** = *p-xyl*, **c** = *m-xyl*

New 5,6-CHIRAGEN-ligands such as **L2a-c**, **L3a-b** have been synthesised and structurally characterised. We are investigating the formation of coordination compounds by self-assembly with several labile metal ions.

Thanks to the Methoxy-groups of these ligands they can be used as precursor for the formation of macrocyles, especially 5,6-CHIRAGEN[0]{5'-*p*-MeO-Ph} **L3a.**

[1] O. Mamula, A. von Zelewsky, *Angew. Chem. Int. Ed.*, **1998**, 37, 3, 290.

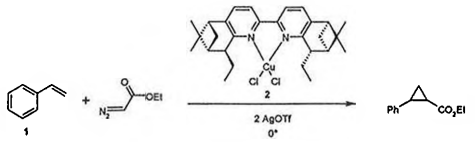
This work is supported by the Swiss National Science Foundation.

Inorganic and Coordination Chemistry **76**

Asymmetric Copper-Catalyzed Cyclopropanations Using Chiral Bipyridine-Complexes

Didier Lötscher and Alex von Zelewsky
University of Fribourg, Departement of Chemistry, Pérolles 1700 Fribourg.
e-mail: Didier.Loetscher@unifr.ch

Recently we published successful enantioselective copper-catalyzed cyclopropanations of styrene using chiral bipyridne ligands.[1] In our investigations the cyclopropanation of styrene **1** with ethyldiazoacetate in the presence of 1 mol% of the copper complex **2** at 0°C gave the corresponding *cis*-cyclopropanecarboxylate in 90% *ee* , and the *trans*-isomer in 87% *ee*. The diastereoselectivity was found to be 22:78 in favour of the *trans*-cyclopropanecarboxylate. We are investigating now the effect of the diazoester using *t*-butyldiazoacetate and (+)-, respectively, (-)-menthyldiazoacetate.



This work is supported by the Swiss National Science Foundation.

[1] D. Lötscher, S. Rupprecht, H. Stoeckli-Evans, A. von Zelewsky, *Tetrahedron: Asymmetry*, **2000**, *11*, 4341

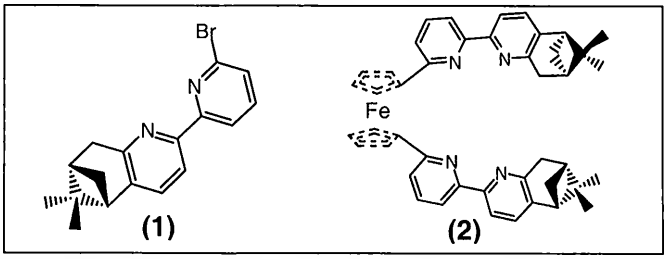
Inorganic Chemistry **77**

NEW CHIRAL BUILDING BLOCKS CONTAINING FERROCENE AND THEIR REACTIONS IN SELF-ASSEMBLY

Boris Quinodoz and Alexander von Zelewsky

University of Fribourg, Department of Chemistry
1700 Fribourg, Switzerland. e-mail : Boris.Quinodoz@unifr.ch

During the past few years, chiral ligands used as building blocks have been synthesised in order to predetermine the configuration at the metal center. Recently a new compound (**1**), was synthesised as a new variety of the CHIRAGEN ligand family. [1] One example is (**2**) containing a ferrocene moiety as bridge, thereby increasing the flexibility of the ligand due to the potential rotation of the ferrocene.



This new ligand could lead to intersting phenomena in supramolecular structure due to its redox active site.

This work is supported by the Swiss National Science Foundation.

[1] A. von Zelewsky, *Coord. Chem. Rev.*, **1999**, 190-192, 811-825.

CHIMIA 2001, 55, No. 7/8

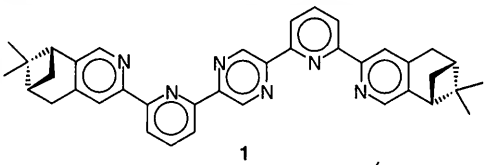
Inorganic and Co-ordination chemistry **78**

Oligopyridyl-pyrazine-type Ligands for the Fabrication of Chiral Molecular Squares

Thomas Bark, Alex von Zelewsky.

University of Fribourg, Dep. of Chemistry,
1700 Fribourg, Switzerland. thomas.bark@unifr.ch

The syntheses of an achiral and three chiral 2,5-Bis-bipyridinyl-pyrazines (**1** as an example) are presented. These ligands yield chiral, tetrameric complexes with first row transition metals. The introduction of chiral terpene moieties allows stereoselective synthesis of the corresponding complexes.[1]
We also synthesised a family of chiral derivatives of the known ligand 2,5-Di-pyridyl-pyrazine. (e.g. **2**) Co-ordination properties of these ligands have been investigated with Cu^+ and Ag^+.



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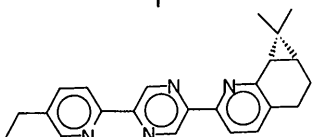


2

This work is supported by the *Swiss National Science Foundation.*

[1]- T. Bark, M. Düggeli, H. Stoeckli-Evans, A. von Zelewsky, *Angew. Chem.* **2001**, accepted.

Inorganic and Coordination Chemistry **79**

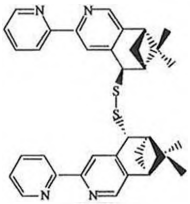
Chiral Ligands Containing Sulfur: Synthesis and Characterisation

Simona Ciobanu and Alex von Zelewsky

University of Fribourg, Department of Chemistry, Pérolles, CH - 1700 Fribourg (E-mail : Simona.Ciobanu@unifr.ch)

The synthesis of metal complexes with predeterminated chirality at metal centers has been the subject of widespread interest in coordination chemistry over recent years.[1]
Generally, pyridine and bipyridine-pinene ligands can be used to synthesize coordination compounds in which the stereochemistry at the metal center is predetermined by the configuration of the ligands. We are investigating the chiral pinene bipyridine derivatives such as 5,6-pinenebipy (L1) and 4,5-pinenebipy(L2) containing sulfur and their metal complexes.
The sulfuration reaction that leads to disulfur bridged ligands is not completely stereoselective. [2]

L(1)



L(2)

[1] U. Knof, A. von Zelewsky, *Angew. Chem.*, **1999**, 111, 312;
[2] G. Chelluci, D. Berta, D. Fabri, G.A. Pinna, A. Saba, F. Ulgheri, *Tetrahedron: Assymetry*, **1998**, 9, 1933.

This work is supported by the Swiss National Science Foundation.

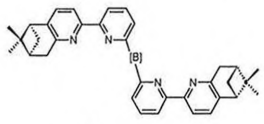
Inorganic and Coordination Chemistry **80**

Towards a Predetermined Chiral Molecular Knot

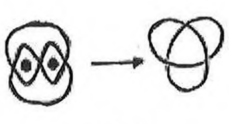
Laure-Emmanuelle Perret-Aebi and Alexander von Zelewsky

University of Fribourg, Department of Chemistry
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).
Our project is to construct a predetermined chiral molecular trefoil knot around two copper(I) centers used as a template. For this purpose we prepared a new series of chiral ligands as precursor (**1**).



(1)



Trefoil knot

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.

Inorganic Chemistry & Coordination Chemistry **81**

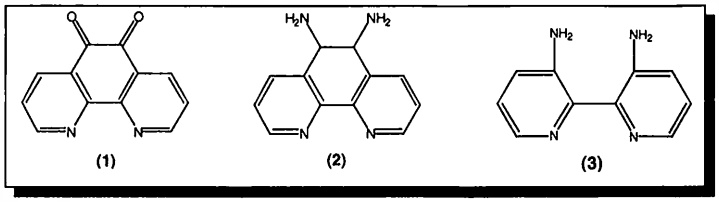
An Exploration into the Use of Bidentate Ligands as Useful Building Blocks for the Self-Assembly of Novel Molecule-Based Materials.

M. Cristina Senna[a], Melanie Pilkington[a], Silvio Decurtins[a] and John D. Wallis[b]

[a]Departement für Chemie und Biochemie, Universität Bern, Freiestrasse 3, 3012 Bern, Switzerland; e-mail: senna@iac.unibe.ch; [b]Chemistry and Physics Department, Nottingham Trent University, Clifton Lane, Nottingham, NG11 8NS, England.

Using molecular building blocks to self-assemble lattices supporting long-range magnetic order is currently an active area of research at the frontier of solid-state chemistry. Consequently, it is the realm of supramolecular chemistry that synthetic chemists are turning to in order to develop techniques for the controlled synthesis of novel structurally well-defined solids with interesting chemical and physical properties.

In this respect, we are currently investigating the versatility of bidentate building blocks for applications in the field of molecule-based materials. The chemical reactivity and co-ordination properties of three organic building blocks, namely 1,10-phenanthroline-5,6-dione **1**, 5,6-diamino-1,10-phenanthroline **2** and 2,2'-bipyridine-3,3'-diamine **3** will be presented.



(1) (2) (3)

Inorganic Chemistry **82**

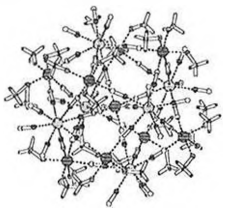
High-Spin Molecules : Solid State and Solution Magnetic Properties of two New Cyano Bridged $Ni_9^{II}Mo_6^{V}$ and $Ni_9^{II}W_6^{V}$ Clusters with an S = 12 Ground State.

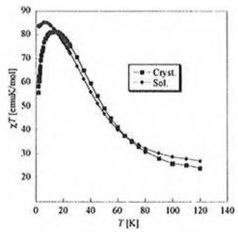
Federica Bonadio[a], Mathias Gross[a], Helen Stoeckli-Evans[b] and Silvio Decurtins[a]

[a]Departement für Chemie und Biochemie, Universität Bern, Freiestrasse 3, 3012 Bern, Switzerland; e-mail: federica.bonadio@iac.unibe.ch; [b]Institut de Chimie, Université de Neuchâtel, Avenue Bellevaux 51, 2000 Neuchâtel, Switzerland

The synthesis and investigation of magnetic properties of novel molecular clusters containing paramagnetic transition metal ions is currently attracting a great deal of interest [1].

Here we report the structural and magnetic properties of two novel molecular clusters of stoichiometry $[Ni^{II}\{Ni^{II}(MeOH)_3\}_8(\mu\text{-}CN)_{30}\{M^{V}(CN)_3\}_6]\cdot xMeOH\cdot xH_2O$, where M^{V} is Mo^{V}, or W^{V}. Magnetic measurements were made on the crystals in frozen ether (Cryst.) and in methanol solution (Sol.). The solid state and the dissolved compound show a ferromagnetic intracluster exchange interaction, by lowering of the temperature, for a ground state spin S=12. In solution we are able to isolate the single cluster without any intercluster exchange interaction which is present in the solid state.





[1] J. Larionova, M. Gross, M. Pilkington, H. Andreas, H. Stoeckli-Evans, H. U. Güdel, and S. Decurtins, *Angew. Chem, Int. Ed,* **2000**, 39, 1605-1609

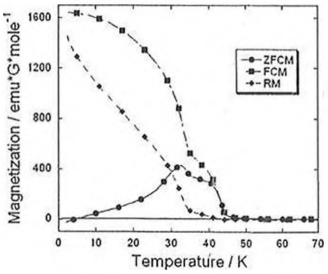
Inorganic Chemistry **83**

Mössbauer studies on ferromagnetic $[Nb\{(\mu\text{-}CN)_4Fe(H_2O)_2\}_2]$ x 4 H_2O

Patrick Franz[a], Jürgen Ensling[b], Philipp Gütlich[b] and Silvio Decurtins[a]

[a]Universität Bern, Departement für Chemie und Biochemie, Freiestrasse 3, 3012 Bern, Switzerland; [b]Institut für Anorganische Chemie und Analytische Chemie, Johannes Gutenberg-Universität, Staudingerweg 9, 55099 Mainz, Germany

The title compound of stoichiometry $[Nb\{(\mu\text{-}CN)_4Fe(H_2O)_2\}_2]$ x 4 H_2O has been shown by single crystal X-ray diffraction to crystallize in a 3-dimensional network, where the two paramagnetic metal ions are connected via cyanide linkages. In the magnetic point of view, the interactions between the paramagnetic $[Nb(CN)_8]^{4-}$ (d^1) ions with the paramagnetic high-spin ions Fe(II) (d^6) give rise to 3-dimensional magnetic ordering below ca. 41 K as shown by the zero field cooled (ZFCM), field cooled (FCM) and remnant (RM) magnetization (Figure 1). During the course of these measurements we observed unusual steps around 35 K in the susceptibility curves and this behavior was investigated further by Mössbauer spectroscopy.



The temperature dependent Mössbauer measurements confirm the occurrence of long-range magnetic order below ca. 41 K. Above this temperature, the observation of one distinct quadrupole-split Mössbauer absorption for paramagnetic iron(II) shows the existence of only one crystallographic Fe(II) site (impurities are less than 3 %). The spectra below the critical temperature however, exhibit two magnetic hyperfine patterns for iron(II) with a different line width and different temperature dependence of the area fractions. This behavior strongly suggests that the above compound possesses a more complex magnetic structure in this temperature range.

Coordination Chemistry **84**

Bridged Asymmetrical Quater- and Quinquepyridine Type Ligands and Their Complexes with Co(II), Ni(II) and Cu(II/I)

Inger Annette Hougen[1], Edwin C. Constable[2], Cathrine E. Housecroft[2] and Louise Ann Whall[1]

1) Universität Basel, Institut für Anorganische Chemie, Spitalstrasse 51, 4056 Basel, Switzerland
2) The University of Birmingham, School of Chemistry, Edgbaston, Birmingham B15 2TT, UK

New asymmetric quaterpyridine and quinquepyridine type ligands are being synthesized for the study or self-assembly processes with metal cations, such as Co(II), Ni(II) and Cu(II/I). Double stranded dinuclear helicates have been prepared and EPR spectroscopy has been used to investigate metal-metal interactions within the complexes.

Related complexes in which the ligands consist of quaterpyridine and quinquepyridine moieties connected by hexaethyleneglycol linkers have also been prepared and studied, again with an emphasis on metal-metal interactions.

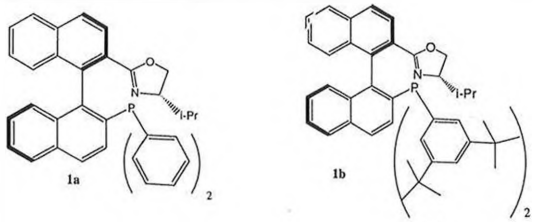
Inorganic Chemistry & Coordination Chemistry **85**

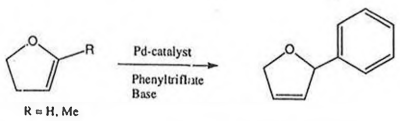
3,5-Dialkyl Meta Effect on Enantioselectivity: Binaphtyl-Phosphino-Oxazoline-Ligands and Complexes with Palladium

Pascal Dotta, Alberto Albinati and Paul S. Pregosin

Laboratory of Inorganic chemistry, ETH Zentrum , CH-8092 Zürich, Switzerland

Using 3,5-dialkyl substituents on the aryl groups of ligand **1b** (relative to **1a**) affords significantly improved ee's, in the Heck reaction of 2,3-dihydrofurans with Phenyltriflate in toluene.





ligand	dihydrofuran	conditions	yield	ee
1a	2,3-dihydrofuran	3 days/ 40°C	52%	80%
1b	2,3-dihydrofuran	7 days/ 40°C	26%	90%
1a	2-methyl-2,3-dihydrofuran	6 days/ 70°C	18%	81%
1b	2-methyl-2,3-dihydrofuran	12 days/ 70°C	41%	97%

Intermediates, e.g. $PdBr(p\text{-}CNC_6H_4)$(**1b**) will be presented.

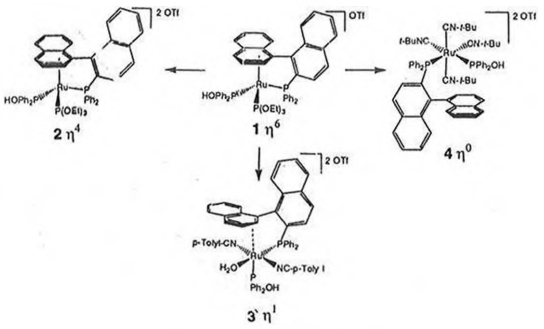
Inorganic Chemistry & Coordination Chemistry **86**

Tuning Hapticity from 6 to 0 in Arene-Ruthenium(II)-Complexes

Tilmann J. Geldbach, Daniela Drago and Paul S. Pregosin

Laboratory of Inorganic Chemistry, ETH-Zentrum, CH-8092 Zurich, Switzerland

Presently, there is a significant interest in Ruthenium-Arene complexes as catalysts for various transformations such as the Diels-Alder reaction or Hydrogenation.
We have recently reported the synthesis of **1**[1] which arises via P-C-bond cleavage from the well known Ru(bisphosphine)(bisacetate) complex. **1** with a variety of ligands demonstrates the ability of the arene to change its coordination mode towards the metal depending on the electronic and steric properties of the ligand. Thus allowing the metal to react with either phosphines, nitriles or isonitriles, the hapticity changes from 6 in **1** to pseudo 4 (**2**) to 1 (**3**) to 0 (**4**).



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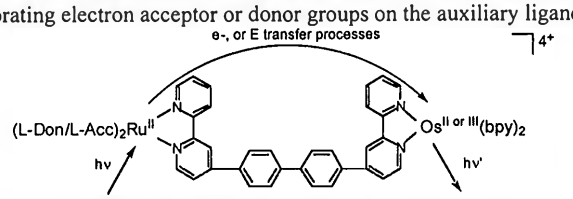
Inorganic Chemistry **87**

Study of Energy or Electron Transfer Processes in Bridged Dinuclear Metal Complexes

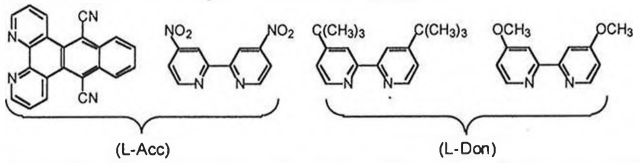
Peter Belser and Nunzio Salluce

Department of Inorganic Chemistry, University of Fribourg
CH-1700 Fribourg, E-mail: nunzio.salluce@unifr.ch

Photoactive molecular wires incorporating polypyridine metal complexes has been synthesised. Such complexes show interesting photoinduced energy and electron transfer processes. These kinds of systems can be able to perform functions such as charge separation and conversion of light into chemical energy[1].
To study the directional energy and electron transfer processes we have modified the Ru(II) sensitizer unit in the dinuclear metal complexes by incorporating electron acceptor or donor groups on the auxiliary ligands.



We have used the following kinds of auxiliary ligands:



The rate of the above mentioned processes (energy or electron transfer) depends upon the nature of the donor (L-Don) or acceptor (L-Acc) ligands used.

[1] F. Barigelletti, L. Flamigni, *Chem. Soc. Rev.* **2000**, 29, 1-12.

Inorganic Chemistry **88**

A NEW CHIROPTICAL MOLECULAR SWITCH

P. Belser and M. Querol
Dept. Of Chemistry University of Fribourg
CH 1700 Fribourg. E-mail: manelquerol@hotmail.com

It is well known that helically shaped overcrowded alkenes can function as chiroptical molecular switches. The switching process is based on a photoinduced cis/trans isomerization of the central double bond (fig 1) [1]. This process can be used for optical data storage and as a phototrigger in LCD technology [1].

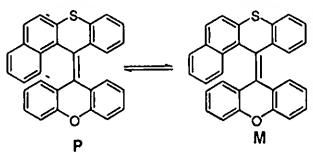


Figure 1

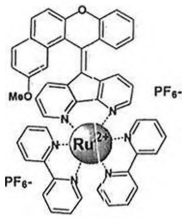


Figure 2

The main drawback of these kind of systems is that, due to mechanistic considerations associated to the singlet-singlet double bond excitations, very low *ee* can be achieved and therefore the output detection becomes difficult. One way to overtake this problem is the use of triplet-triplet sensitizers. This contribution will present the synthesis of the first helically shaped overcrowded alkene suitable to hold in a built-in fashion an internal triplet-triplet energy transfer sensitizer (fig 2) to perform the sensitized double bond isomerization, as well as the preliminary photochemical studies.

References:

[1] B. L. Feringa, R. A. van Delden, N. Koumura, E. M. Geertsema. Chem. Rev. **2000**, *100*, 1789-1816

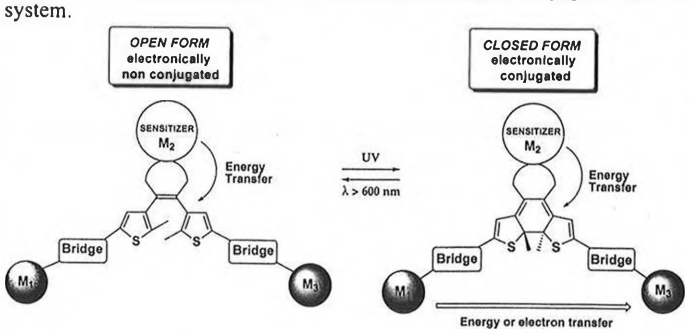
Inorganic Chemistry **89**

Developing new opto-electronic devices

Vincent Adamo and Peter Belser

Department of Chemistry, University of Fribourg,
CH-1700 Fribourg, E-mail: vincent.adamo@unifr.ch

The study of new materials with polyfunctionnal features has become very important during the last years, due to their potential applications in the field of memory storage. Specific molecules that have switching properties can be used for these purposes. In fact, the dithienylethene unit developed by Irie and Lehn [1] can undergo an electrocyclic isomerization by light irradiation, transforming the unit into an electronically conjuged, wire-like system.



In this work, we will present the preparation of the central switching unit between M_1/M_3. In order to stimulate the switching unit by an energy transfer, we are in progress to attach a metal complex as sensitizer to shift the UV irradiation into the visible region. Photophysical properties of the developed system will be discussed.

[1] a) A. Fernandez-Acebes, J.- M. Lehn, *Chem. Eur. J.* **1999**, *5*, 3285;
b) T. Yamada, M. Irie, *J. Am. Chem. Soc.* **2000**, *122*, 1589.

CHIMIA 2001, 55, No. 7/8

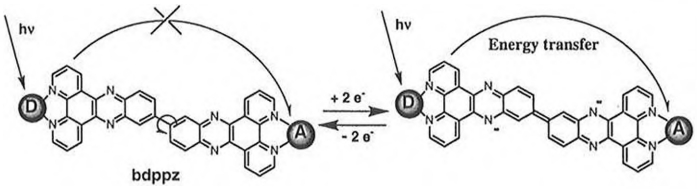
Inorganic Chemistry **90**

A Molecular Switch for Photoinduced Electron/Energy Transfer

Peter Belser, Mara Staffilani*, Frantisek Hartl*, Luisa De Cola*

Department of Inorganic Chemistry, University of Fribourg
CH-1700 Fribourg, E-mail: Peter.Belser@unifr.ch
*University of Amsterdam, Nieuwe Achtergracht 166, NL-1018 WV Amsterdam, The Netherlands

The development of new photoinduced switching molecules is a challange in the area of molecular electronics. Our investigation in this area targets the redox-switching of fluorescence in dimetallic donor-acceptor systems through ligand centred redoxcouples. Therefore, we have developed a novel bis(dipyridophenazine), bdppz, bridging ligand.



We have prepared the homo- and heteronuclear metal complexes having Ruthenium(II) and Osmium(II) as metal centres. By stepwise two-electron reduction, the bdppz is converted from the twisted to the planar conformation. When the bdppz bridges a donor (e.g. $Ru^{II}(bpy)_2$) and an acceptor (e.g. $Os^{II}(bpy)_2$) moieties, the central C-C bond of the reduced ligand open the bridging ligand for the transfer of electronic energy from the photoexcited donor towards the acceptor site.

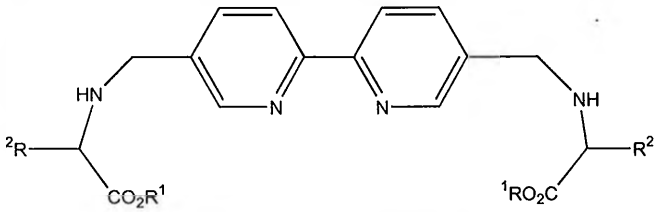
Inorganic Chemistry **91**

The Stereoselective Synthesis of Complexes of Substituted 2,2'-Bipyridine

S.G. Telfer, A. F. Williams and G. Bernardinelli

Department of Inorganic Chemistry, University of Geneva,
Quai E. Ansermet 30, CH-1211 Geneva 4
e-mail : shane.telfer@chiam.unige.ch

We have shown that the L-valine substituted ligand **1** forms Δ-[ML_3] complexes diastereospecifically. The amino acid arms were also shown to encapsulate a chloride ion in the solid state.
We now present the results of further investigations on this family of ligands. The influence of the anion, pH, solvent, and the nature of the amino acid arm have has been studied with respect to the observed diastereoselectivity. The possibility of such complexes functioning as anion receptors in solution has also been investigated. Finally, the ligands have been used to construct stereospecific polynuclear helicates.



1 $R^1 = H$, $R^2 = CH(CH_3)_2$
2 $R^1 = CH_3$, $R^2 = CH(CH_3)_2$
3 $R^1 = H$, $R^2 = CH_3$

Inorganic Chemistry **92**

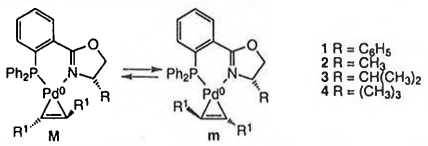
[(η^2-Alkene)palladium(0)(phosphinooxazoline)] Complexes.

Silvia Schaffner[a], Markus Neuburger[a], Margareta Zehnder*[a], Martin Jufer[b], Dietmar A. Plattner*[b]

[a] Institut für Anorganische Chemie der Universität Basel, CH-4056 Basel
[b] Laboratorium für Organische Chemie, ETH Zentrum, CH-8092 Zürich

Chiral bidentate phosphinooxazoline ligands have been successfully applied in asymmetric Pd-catalyzed reactions [1]. (Phosphinooxazoline)-palladium(0) complexes are of great interest as they are involved in many of these reactions.

For a better understanding of these important intermediates, we synthesized several [Pd^0(alkene)(phosphinooxazoline)] complexes variing with respect to the oxazoline and the olefin ligands.



1 R = C_6H_5
2 R = CH_3
3 R = $CH(CH_3)_2$
4 R = $(CH_3)_3$

X-ray diffraction data reveal that the molecular structure is dependent on the bulk of the oxazoline substituent. In derivatives **1** and **4** (R^1 = CN) the oxazoline and the adjacent olefin substituent are on opposite sides of the coordination plane (diastereomer **M**). The methyl derivative **2** adopts configuration m in the solid state.

NMR studies assess that in complexes **1** and **4** (R^1 = CN, R^1 = COOMe) with oxazoline substituents reaching into the olefin area the pseudo-*anti* arrangement is favored. Complexes with less bulky auxiliaries (**2** and **3**) do not demonstrate any diastereoselectivity.

DFT/B3LYP calculations confirm the structural features found in the solid-state structures.

[1] G. Helmchen, A. Pfaltz, *Acc. Chem. Res.* **2000**, *33*, 336 and references therein.

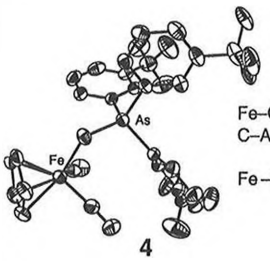
Inorganic Chemistry **93**

Synthesis, Structure, and Reactivity Towards Olefins of New Iron Arsoniummethylide Complexes

P. Egli and A. Togni

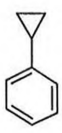
Department of Chemistry, ETH Hönggerberg, CH-8093 Zürich

The complexes [$CpFe(CO)_2(CH_2AsR_3)$]BF_4 (with R = Ph (**1**), 4-F-Ph (**2**), 4-Cl-Ph (**3**), 3-CF_3-Ph (**4**) and 4-CF_3-Ph (**5**)) have been prepared. The X-ray crystal structure of **2**, **3** and **4** is reported. Derivatives **4** and **5**, bearing electron-withdrawing trifluoromethyl groups efficiently react with styrene affording cyclopropylbenzene (**6**) in 84% and 83% yield, respectively. However, in experiments aiming at finding a catalytic reaction utilizing in situ generated arsoniummethylides and [$CpFe(CO)_2(THF)$]BF_4 as catalyst, no cyclopropanes were formed. Two new chiral ferrocenylarsines and their corresponding arsoniummethyl derivatives have also been prepared and characterized. The reaction of the resulting $CpFe(CO)_2$ complexes with 1-cyclohex-1-enyl-4-methoxy-benzene yielded racemic 1-(4-methoxyphenyl)bicyclo[4.1.0]heptane (**7**).



4

Fe–C 2.057(5) Å
C–As 1.892(5) Å
Fe–C–As 120.9(2) °



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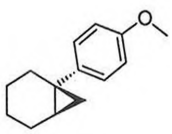


7

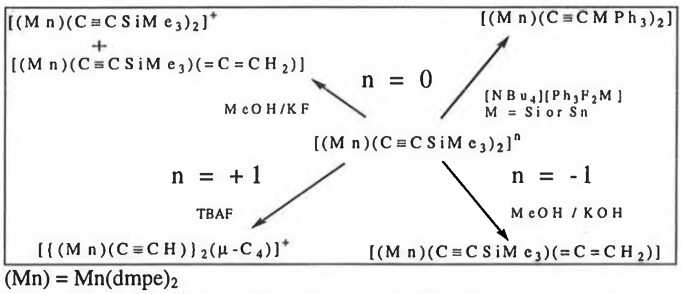
Inorganic Chemistry **94**

Synthesis of Redox-active Rigid-rod Complexes Using $[Mn(dmpe)_2(C{\equiv}CSiMe_3)_2]^n$ (n = -1, 0, +1) Species as Starting Materials.

F. J. Fernández, M. Alfonso, H. W. Schmalle, O. Blacque and H. Berke*

University of Zürich, Institute of Inorganic Chemistry
8057 Zürich, Switzerland

This work has explored the deprotection chemistry of acetylide groups in $[Mn(dmpe)_2(C{\equiv}CSiMe_3)_2]^n$ (n = -1, 0, +1) complexes and revealed that the Me_3Si units are strongly bound to the alkynyl ligands in Mn^{II} species but are easily removable in the case of Mn^{I} or Mn^{III} compounds. A important finding is that using one equivalent of TBAF the Mn^{III} species $[Mn(dmpe)_2(C{\equiv}CSiR_3)_2]^+$ are transformed into the $[Mn(dmpe)_2(C{\equiv}CH)_2]^+$ compound, which is stable in solution at –20°C. At 10°C it transforms into the dinuclear mix-valent complex $[\{Mn(dmpe)_2(C{\equiv}CH)\}_2(\mu\text{-}C_4)]^+$.



(Mn) = $Mn(dmpe)_2$

[1] a) F. J. Fernández, M. Alfonso, H. W. Schmalle and H. Berke, *Organometallics*, **2001** in press. b) F. J. Fernández, O. Blacque, M. Alfonso and H. Berke, *Chem. Commun.* **2001** in press.

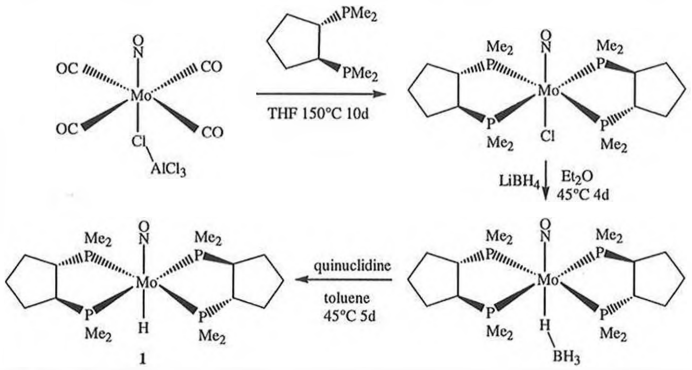
Inorganic Chemistry **95**

Synthesis and Reactivity of a New Chiral Molybdenum Hydride Complex

Y. Zhao, H. W. Schmalle and H. Berke

University of Zürich, Institute of Inorganic Chemistry
8057 Zürich, Switzerland

In search for new activated transition metal hydrides[1], the synthesis of the C-chiral bisphosphane ligand nitrosyl molybdenum hydride complex, $Mo(NO)[(1S,2S)\text{-}C_5H_8(PMe_2)_2]H$ (1), is reported. The hydride complex has been fully characterized by NMR spectroscopy. Fruthermore investigations of the reactivity of the Mo-H bond toward chiral alcohols are presented.



[1] H. Jacobsen, H. Berke, *Recent Advances on Hydride Chemistry*, Elsevier, 2001. im press

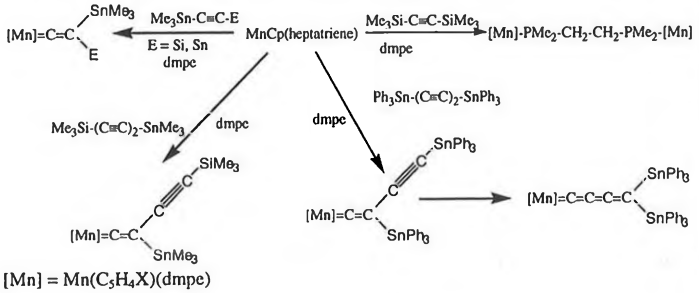
Inorganic Chemistry **96**

Synthesis of New Manganese C_2 and C_4 cumulenic Species Using $Mn(C_5H_4X)$(heptatriene) (X = H, Me) as Starting Material

V. Koushik, F.J. Fernández, T. Fox, M. Alfonso, H.W. Schmalle, and H. Berke*

University of Zürich, Institute of Inorganic Chemistry
8057 Zürich, Switzerland

The reaction of $Mn(C_5H_4X)$(heptatriene) (X = H, Me)[1] with $R^1\text{-}C_2\text{-}R^2$ ($R^1 = SnR_3$; $R^2 = SiMe_3$, SnR_3, Ph, H, $-C{\equiv}CSiMe_3$, $-C{\equiv}CSnR_3$) in the presence of dmpe yield the corresponding manganese vinylidene complexes $[Mn](=C=CR^1R^2)$. In the case of $R^2 = -C{\equiv}CSnPh_3$ a further photolytic activation of the $C_{sp2}\text{-}SnPh_3$ bond leads to the C_4 cumulenic species $[Mn]\{=C=C=C=C(SnPh_3)_2\}$. The reaction of the $(Mn)\{=(C=C)_n(SnR_3)_2\}$ (n = 1 and 2) compounds with TBAF (5% H_2O) yield the corresponding deprotected cumulenic species $(Mn)\{=(C=C)_nH_2\}$.



[Mn] = $Mn(C_5H_4X)$(dmpe)

[1] P.L. Pauson, J.A. Segal, *J. Chem. Soc., Dalton Trans.* **1975**, 2387

Inorganic Chemistry **97**

Approaching a Catalytic Ketene Synthesis: Tuning the Catalyst.

P. Jaunky, M. Huttenloch, H. Berke*
University of Zürich, Institute of Inorganic Chemistry, 8057 Zürich, Switzerland.

A catalytic metal-mediated build up of ketene moieties is currently under investigation. It is expected to follow the equation :

$R_1R_2CHX + CO + Base \rightarrow [BaseH]X + R_1R_2C{=}C{=}O$.

The process involves a metal carbonyl complex catalyst and is based on initial oxidative addition of an alkyl halide followed by a CO insertion step. Subsequent deprotonation of the acyl complex readily affords the ketene complex. Ultimately, the ketene ligand is displaced by CO, regenerating the starting carbonyl complex, thus closing the catalytic cycle. Attempts to generate ketenes using $Fe(CO)_3(PMe_3)_2$[1] or $Fe(CO)_3(PEt_3)_2$[2] as the catalyst have failed although every single step of the cycle has been successfully tested. The oxidative addition step appeared to be too slow as only alkylated bases were recovered.

Currently, novel dicarbonyl complexes of iron and ruthenium are under investigation. Multidentate phosphine ligands are being used to enhance the reactivity of the metal complexes towards oxidative addition.

[1] M. Huttenloch, unpublished results.
[2] Kandler H., Bidell W., Jänicke M., Knickmeier M., Veghini D., Berke H *Organometallics*, **1998**, 17, 960-971

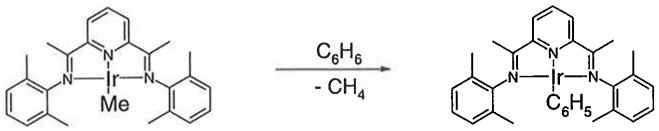
Inorganic Chemistry **98**

Rh(I) and Ir(I) complexes with sterically demanding diimine pyridine ligands

Stefan Nückel and Peter Burger*

University of Zürich, Institute of Inorganic Chemistry
8057 Zürich, Switzerland

Presently, there is a rapid development of the coordination chemistry of the diimine pyridine ligand (see reaction scheme) [1, 2, 3]. To achieve our longstanding goal to access late transition metal oxo complexes, we prepared Rh(I) and Ir(I) precursor complexes with Cl, OTf, OMe, OPh, Ph and Me substituents [4]. The chemistry of these novel complexes will be presented; the facile thermal C-H activation process of the iridium methyl complex shown below is of particular interest. Details of the mechanism elucidated by DFT calculations and kinetics will be reported.



[1] Haarman, H. F.; Ernsting, A. L.; Spek, A. L.; Elsevier, C. J.; van Leeuwen, P. W. N. M.; Vrieze, K. *Organometallics* **1997**, *16*, 887.
[2] Small, B. L.; Brookhart, M.; Bennett, A. M. A. *J. Am. Chem. Soc.* **1998**, *120*, 4049.
[3] Britovsek, G. J. P.; Gibson, V. C.; Kimberley, B. S.; Maddox, P. J.; McTavish, S. J.; Solan, G. A.; White, A. J. P.; Williams, D. J. *Chem. Comm.* **1998**, 849.
[4] Nückel, S; Burger, P. *Organometallics* (accepted)

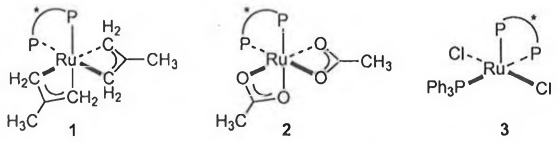
Inorganic and Coordination Chemistry **99**

Ru-catalyzed Hydrogenation with P-Stereogenic Ligands

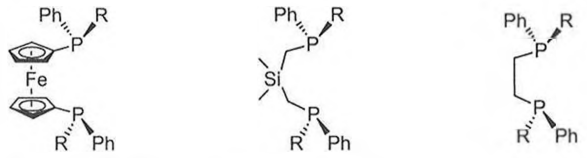
F. Santoro, [a] F. Maienza,[a] F. Spindler,[b] B. Pugin,[b] and A. Mezzetti [a,*]

[a] Department of Chemistry, ETH Hönggerberg, CH-8093 Zürich
[b] Solvias AG, CH-4002 Basel

We are investigating the ruthenium complexes **1**, **2**, and **3** as catalysts for the asymmetric hydrogenation of C=C and C=O double bonds.



Complexes **1-3** contain the P-stereogenic diphosphines **4-9**, which are prepared in high enantiomeric purity as reported previously [1,2].



R = 1-Np (**4**), *o*-An (**5**) R = 1-Np (**6**), *o*-An (**7**) R = 1-Np (**8**), *tert*-Bu (**9**)

The best results are observed with complex $[RuCl_2(PPh_3)(4)]$ (**3**) in the hydrogenation of methyl acetamidocinnamate (42% ee) and of ethyl 3-oxo-butanoate (52% ee). Further results and details will be reported.

[1] R. Stoop, A. Mezzetti, F. Spindler, *Organometallics*, **1998**, *17*, 668.
[2] F. Maienza, M. Wörle, P. Steffanut, A. Mezzetti, F. Spindler, *Organometallics* **1999**, *18*, 1048.

Inorganic Chemistry **100**

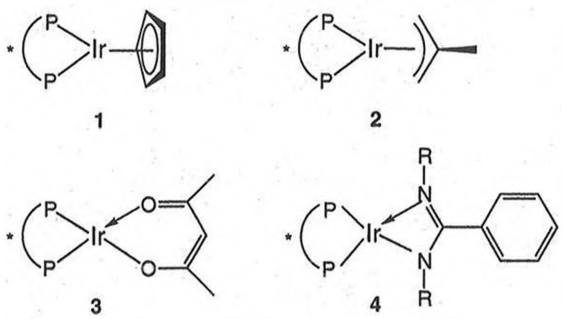
Chiral Ir(I) Complexes and their reactivity in catalytic C-N and C-C bond formation

R. Aufdenblatten and A. Togni

Department of Chemistry, ETH Hönggerberg, CH-8093 Zürich

Complexes of the type [IrCp(PP)], **1** (PP=chiral diphosphine) have been found to be active catalysts for the asymmetric hydroarylation of norbornene with benzamide [1].

We present now the synthesis and characterization of the new derivatives **2-4** and report about their catalytic activity in the hydroamination reaction.



[1] Aufdenblatten, R.; Diezi, S.; Togni, A. *Monatshefte für Chemie* **2000**, *131*, 1345.

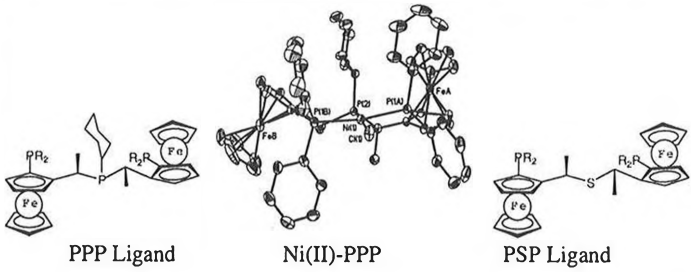
Inorganic Chemistry **101**

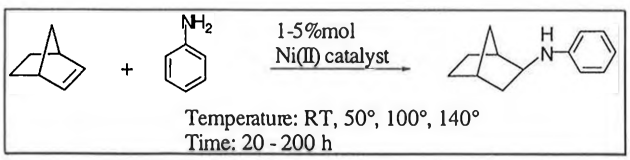
New Catalyst for Olefin Hydroamination: Synthesis and Reactivity of Ni(II)-PPP and Ni(II)-PSP Complexes

Luca Fadini, Diego Broggini and Antonio Togni

Department of Chemistry, ETH Hönggerberg, CH-8093 Zürich

Ni(II) complexes of the type $[Ni(PPP)L]X_n$ and $[Ni(PSP)L]X_n$ and (L=Cl or solvent; X=PF_6 or BF_4; n=1 or 2) containing tridentate ferrocenyl ligands [1], have been prepared and characterized. These derivatives are catalysts for the addition of aniline to norbornene, a model hydroamination reaction [2]. These complexes display a promising catalytic activity (at 1-5 %mol catalyst) with TON between 2 and 15. An important side reaction observed under various conditions is the corresponding olefin hydroarylation [3].





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[2] Senn H.M., Blöchl P.E., Togni A., *J. Am. Chem. Soc.* **2000**, *122*, 4098.
[3] Aufdenblatten R., Diezi S., Togni A., *Monatsh Chem.* **2000**, *131*, 1345.

Inorganic Chemistry **102**

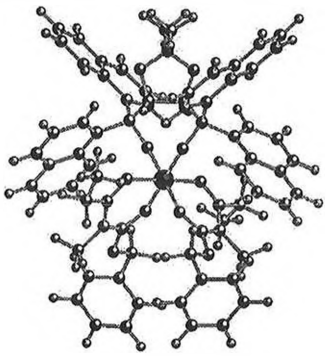
Ti(TADDOLato) Complexes Relevant to Catalytic Enantioselective Fluorination

M. Perseghini, I. Devillers, L. Hintermann, M. Sanna and A. Togni

Department of Chemistry, ETH Hönggerberg, CH-8093 Zürich

The first example of a catalytic and enantioselective fluorination was recently reported from our laboratory [1].

In view of elucidating coordination-chemical aspects related to this reaction, several Ti(TADDOLato) complexes, such as **1**, have been prepared and structurally characterized.



1

The bis(enolato) derivative **1** reacts with F-TEDA affording two equivalents of fluorinated product with the same enantioselectivity as for the catalytic reaction.

[1] Hintermann, L.; Togni, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 4359.

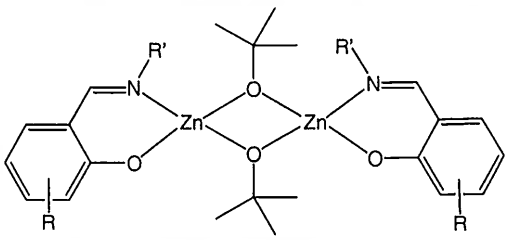
Inorganic & Coordination Chemistry **103**

Zinc Complexes of the Type (Salicylaldiminato)Zn(O^{t}Bu) as Catalyst for Ring-Opening Copolymerisation of Cyclohexenoxide and CO_2

E. Schön, D. Plattner, P. Chen*

Swiss Federal Institute of Technology, 8092 Zürich, Switzerland

The synthesis of zinc complexes of the general formula (salicylaldiminato)Zn(O^{t}Bu) starting from Zinc bis[bis(trimethylsilyl)amide], readily available salicylaldimines and t-butanol is reported. The – to the best of our knowledge – novel structure of these complexes was confirmed by X-ray, elemental analysis and NMR-spectroscopy.



R = 3-Me, 3-^{i}Pr, 3-Ph, 5-Me, 3,5-dinitro
R' = ^{i}Pr, 2,6-diisopropylphenyl

These dimeric zinc complexes showed varying activity towards the cyclohexenoxide/CO_2 copolymerisation. The most promising results showed the catalyst with R = 3-Me and R' = ^{i}Pr. This catalyst gave comparable activity and selectivity to previously reported zinc phenoxide complexes [1] under significantly milder conditions (80 °C, 14 bar).

[1] Darensbourg, D.J. et al. *J. Am. Chem. Soc.* **1999**, *121*, 107.

Chimie minérale et de coordination **104**

Kinetics and Equilibria of Complex Formation between Ruthenium(II) and Catalytically Important Water Soluble Phosphine Ligands in Aqueous Solutions

G. Laurenczy,[1] J. Kovács[1,2], A. Cs. Bényei[2], L. Nádasdi[1,2], F. Joó[2]

[1]*Institut de Chimie Minérale et Analytique, Université de Lausanne, 1015 Lausanne*
[2]*Institute of Physical Chemistry Kossuth University, H-4010 Debrecen, Hungary*

The reactions between the hexaaqua ruthenium(II) and the catalytically important water soluble phosphine ligands PTA, *m*TPPTS, *m*TPPMS, *p*TPPMS and the bidentate DPPETS (PTA=1,3,5-triaza-7-phosphaadamantane; *m*TPPTS= tris(*meta*-sulphophenyl)phosphine; *m*TPPMS= (*meta*-sulphophenyl)diphenyl-phosphine; *p*TPPMS= (*para*-sulphophenyl) diphenyl-phosphine; DPPETS= 1,2 (*meta*-sulphophenyl)phenyl-phosphino ethane) were studied in aqueous solutions.

Ligand excess leads to the *bis* complex formation in case of the sulphonated mono-phosphine ligands, while the smaller PTA (cone angle 102°) and the bidentate DPPETS can replace up to four water molecules in the first coordination sphere of the Ru(II). Multinuclear NMR was used to follow the complex formation kinetics and to characterise the complexes in solution.

The crystal structure of the diprotonated bis $[(HPTA)_2Ru(H_2O)_4]tos_4 \cdot 2H_2O$ has been determined, showing the two N protonated PTA ligands in trans position.

[1] G. Laurenczy, F. Joó, L. Nádasdi, *Inorg. Chem.*, **2000**, *39*, 5083
[2] F. Joó, G. Laurenczy, L. Nádasdi, J. Elek, *Chem. Comm.*, **1999**, 971.

The L'Office Fédéral de l'Education et de la Science, Suisse (OFES C98.0011) and the Fonds National Suisse (2100-061653.00/1) are thanked for financial support. This research is part of the collaboration within the COST Action D10/0001 Working Group.

Inorganic Chemistry **105**

Reduction of carbon dioxide in a biphasic aqueous/ionic liquid system

C.A. Ohlin, G. Laurenczy*

Institute of Inorganic and Analytical Chemistry, University of Lausanne, 1015 Lausanne, Switzerland

The reduction of CO_2/carbonate salts by H_2 is a reaction of high potential importance (see equation), providing a possible alternative source of hydrocarbons.

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

Work has been carried out by Noyori *et al.* and Baiker *et al.* in sc-CO_2 in the presence of amines [1], as well as in water [2]. The latter system suffers from difficult catalyst recovery and product/reactant separation while the first one yields formamides as products. The potential for neutral room temperature ionic liquids, RTILs, as media for immobilising catalysts in pseudo-homogeneous reactions has recently received much attention, as has the behaviour of CO_2/RTIL systems [3]. Reduction of CO_2 in a sc-CO_2/RTIL system in the presence of amines has been reported but the product proved to be highly soluble in the ionic liquid [4]. We have in our laboratory successfully carried out the reduction of CO_2/carbonates by H_2 in a biphasic system comprising an aqueous and an ionic liquid phase, the latter serving to immobilise the catalyst.

[1] (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
[2] Joo, F.; Laurenczy, G.; Nádasdi, L.; Elek, J. *Chem. Commun.* **1999**, 971-972
[3] (a) Blanchard, L.A.; Hancut, D.; Beckman, E.J.; Brennecke, J.F. *Nature* **1999**, *399*, 28-29 (b) Kazarian, S.G.; Briscoe, B.J.; Welton, T. *Chem. Commun.* **2000**, 2047-2048
[4] Liu, F.; Abrams, M.B.; Baker, R.T.; Tumas, W. *Chem. Commun.* **2001**, 433-434

The Fonds National Suisse (2100-061653.00/1) is thanked for financial support.

Inorganic & Coordination Chemistry **106**

Chemical Principles of the Sulfidation of Tungsten Oxides

André van der Vlies, Roel Prins and Thomas Weber

Laboratory for Technical Chemistry, Swiss Federal Institute of Technology (ETH), CH-8092 Zürich

As processes for the catalytic removal of sulfur (HDS) and nitrogen (HDN) from crude oil fractions become more important due to environmental legislation, a better understanding of these catalysts is necessary. W-based catalysts have excellent hydrogenation properties, making them particularly favorable in the HDN reaction. In contrast to molybdenum, much less is known about elementary reaction steps during the sulfidation of oxidic W-based hydrotreating catalyst precursors. In order to find a mechanistic description of the sulfidation reaction, we have combined findings from molecular and solid-state inorganic chemistry with spectroscopic results:

1. Inorganic compounds like $(NH_4)_2WS_4$ and $(NH_4)_2WO_2S_2$ represent well-documented reference cases for possible tungsten and sulfur environments that may be encountered in the catalysts. The decomposition reactions of these mononuclear complexes mimic, at least to some extent, steps in the sulfidation of oxidic catalysts.
2. The crystalline tungsten oxides WO_3 and $WO_3 \cdot H_2O$ are highly suited to mimic the sulfidation reaction of the amorphous oxidic phase of a real catalyst.
3. Oxidic and sulfidic W/Al_2O_3 phases constitute realistic models for industrial hydrotreating catalysts

The first step in the sulfidation reaction of WO_3 is a partial reduction of the W centers to form $H_{0.23}WO_3$. At higher temperatures more W centers undergo reduction leading to a shear oxide intermediate phase of the stoichiometry $W_{20}O_{58}$. It reacts by further sulfur uptake, and subsequent W-S redox processes to the final product WS_2. We propose a similar reaction pathway for the sulfidation of our WO_3/Al_2O_3 catalyst models.

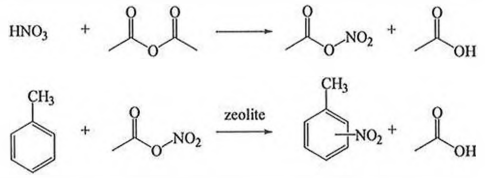
Inorganic Chemistry **107**

Nitration of Toluene over Zeolite Beta: Study of the Properties Influencing the *para*-Selectivity

Samantha Bernasconi, Mohamed Haouas, Gerhard Pirngruber, Roel Prins

Laboratory of Technical Chemistry, Swiss Federal Institute of Technology (ETH), CH-8092 Zurich, Switzerland

The liquid phase nitration of toluene with acetyl nitrate is an excellent method to study the enhanced *para*-selectivity of beta zeolite [1].



^{15}N MAS NMR study showed that acetyl nitrate is the major species present in the solid-liquid reaction mixture and is considered to be the actual reactive nitrating agent [2]. Since beta is typically microcrystalline, the dependence of its selectivity on the size of the crystals was studied. The results showed that *para*-nitration did not occur selectively using macrocrystalline beta zeolite (H-MCBeta), while dealumination of this zeolite led to a shift of the product composition in favor of *para*-substituted isomer. ^{27}Al MAS-NMR of the samples showed a decrease of both the octahedral and tetrahedral aluminium after the modifications. IR measurements confirmed these results indicating a decrease of the peak corresponding to the Brønsted acid sites. In light of these results, we formulated the hypothesis, that beta zeolites are just the reaction vessels for the nitration reactions. At present we ascribe the effects of selectivity to an adsorption induced steric blockage of the *ortho*-position.

[1] K.Smith, A.Musson, G.A. DeBoos, *J. Org. Chem.* **1998**, *63*, 8448
[2] M. Haouas, A.Kogelbauer, R.Prins, *Cat. Lett.* **2000**, *70*, 61

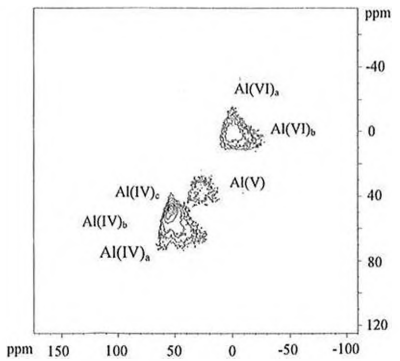
Inorganic Chemistry **108**

Post-synthesis modifications of zeolites studied by ^{27}Al MQ MAS NMR

A. Omegna, M. Haouas, G. Pirngruber, A. Kogelbauer and R. Prins

Laboratory of Technical Chemistry, ETH, CH-8092 Zurich, Switzerland

Acid-base properties of zeolites depend closely on the framework aluminium content. The Si/Al ratio can be adjusted either during crystallization or via post-synthetic modifications. The incorporation of aluminium into the framework of zeolites by reaction with aluminium compounds was described [1]. However, the precise nature of aluminium species created during post-synthesis treatments is not clear. The present work is a study of post-synthesis modifications of zeolites by a detailed investigation of the aluminium coordination by means of ^{27}Al MQ MAS NMR spectroscopy. This technique allows the detection of pure isotropic spectra, which enables an unambiguous assignment of the aluminium coordination.



^{27}Al MQ MAS NMR spectrum of zeolite beta aluminated with $Al(OPr)_3$.

[1] K. Yamagishi, S. Namba, T. Yashima, J. Catal. 121, 1990, 47

Inorganic Chemistry and Coordination Chemistry **109**

Synthesis, Characterization and Hydrotreating Activity of Supported Metal Phosphide Catalysts

V. Zuzaniuk, C. Stinner, R. Prins

Laboratorium für Technische Chemie, Eidgenössische Technische Hochschule Zürich, Universitätsstrasse 6, CH-8092 Zürich

Transition metal carbides and nitrides are well-known catalysts in the field of hydrotreating, i.e. hydrodesulfurization (HDS) and hydrodenitrogenation (HDN), and have been widely studied [1,2]. On the contrary, transition metal phosphides are novel materials in this field and more work has to be carried out in order to characterize this type of materials and to test them in HDS/HDN reactions. Recently, a variety of transition metal phosphides, i.e. MoP, Ni_2P, Co_2P, WP, NiMoP and CoMoP, have been prepared by reducing their respective metal oxide/phosphate precursors with H_2 at elevated temperatures [1,2] according to the following reaction:

$$z\,MO_x \,.\, y\,P_2O_5 + (5y+zx)\,H_2 \rightarrow M_zP_{2y} + (5y+zx)\,H_2O$$

In order to increase the active surface area and improve their thermal stability, transition metal phosphides supported on metal oxides (MO), namely SiO_2 and γ-Al_2O_3, were prepared. Co_2P/MO, Ni_2P/MO, MoP/MO, CoMoP/MO and NiMoP/MO were characterized by TPR, XRD and ^{31}P NMR. Their activity was also tested in the HDN of o-methylaniline. The information obtained from the characterization techniques on the structure of the materials was then correlated to the results of the catalytic tests and the different catalysts were compared.

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[3] Stinner, C., Prins, R., and Weber, T., *J. Catal.* **191**, 438 (2000).
[4] Stinner, C., Prins, R., and Weber, T., to be published.

CHIMIA 2001, 55, No. 7/8

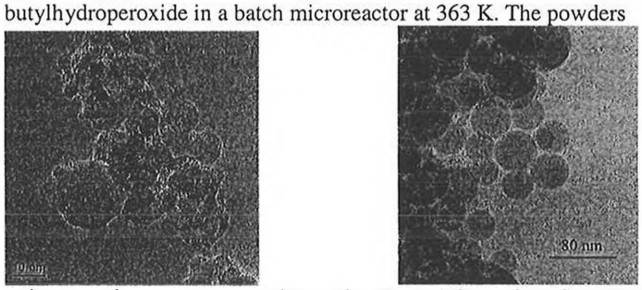
Inorganic Chemistry **110**

Titania/Silica Nanoparticles for the Epoxidation of Olefins

Wendelin J. Stark [1,2], Sotiris E. Pratsinis [1] and Alfons Baiker [2]

[1] Institut für Verfahrenstechnik, ETH Zentrum, CH-8092 Zürich
[2] Laboratorium für Technische Chemie, ETH Zentrum, CH-8092 Zürich

Titania/Silica is a widely used mixed oxide catalyst for the epoxidation of olefins [1]. Up to now, most catalyst preparations were done at low temperatures by a wet chemical process. Here we report on structural and catalytic properties of titania/silica nanoparticles prepared in a methane-oxygen diffusion flame [2]. Catalytic performance was tested for the demanding epoxidation of an allylalcohol, 2-cyclohexenol, using *tert.*-butylhydroperoxide in a batch microreactor at 363 K. The powders



Influence of preparation conditions for titania/silica: short flame (left) and long flame (right) resulting in larger, spherical particles.

showed improved efficiency with respect to peroxide and olefin consumption compared to corresponding aerogels. Powders were characterized using TEM, LA-ICP-MS, DRIFTS and UV-VIS.

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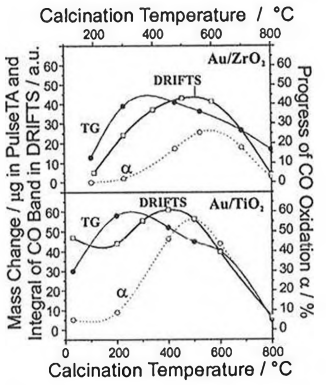
Inorganic Chemistry **111**

Gold Model Catalysts for CO Oxidation: A Study by Thermal Analysis, Infrared Spectroscopy, Electron Microscopy and X-ray Diffraction

J.-D. Grunwaldt, M. Maciejewski, P. Fabrizioli and A. Baiker
Laboratorium für Technische Chemie, ETH Zentrum, CH-8092 Zürich

Catalytically active gold catalysts can be prepared by different methods, i.e. deposition-precipitation, coprecipitation, chemical vapour deposition, and adsorption of gold complexes [1]. In order to prepare gold model catalysts on different metal oxide supports, the use of "size-controlled" gold colloids is a useful alternative [2].

Here we report on the comparison of catalytic properties of Au/TiO_2 and Au/ZrO_2, prepared in such way, in order to gain more insight into the role of particle size, adsorption properties and carbonaceous impurities. Maximal activity was obtained for the catalysts calcined at 500 °C (Au/TiO_2) and 560 °C (Au/ZrO_2), respectively (cf. Figure) with higher activity on Au/TiO_2. In both cases metallic gold particles of 2 – 3 nm size were present. Sintering of gold was observed above 600 °C, where also the catalytic activity decreased. Adsorption of CO, O_2 and CO_2 have been investigated by pulse thermal analysis (PulseTA). Additionally, infrared spectroscopy studies (DRIFTS) were applied to gain further information on the CO adsorption and the nature of the gold sites. CO adsorption does not seem to play the crucial role for the activity.



CO oxidation activity and the amount of adsorbed CO on Au/ZrO_2 and Au/TiO_2 as function of the calcination temperature

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Inorganic Chemistry **112**

Ir Black in the Selective Catalytic Reduction of NO_x Using Hydrocarbons

M. Maciejewski, C. Wögerbauer, A. Baiker
Laboratory of Technical Chemistry, Swiss Federal Institute of Technology, ETH-Zentrum, CH-8092 Zurich, Switzerland

Ir black exhibits surprisingly high activity at high space velocities for the selective catalytic reduction of NO_x by propene. The conversion of NO to N_2 under lean conditions as well as oxidizability and reducibility of the Ir-IrO_2 system were found to strongly depend on the Ir crystallite size [1]. With increasing crystallite size selectivity to N_2 is greatly enhanced mainly by the suppression of a reaction pathway leading to NO_2.

The interplay between NO and O_2 in their ability to adsorb on and oxidize Ir are the key factors in the selective reduction of NO over Ir. It is shown that NO chemisorbs on Ir at room temperature and that with increasing temperature the process of Ir oxidation by NO begins to be competitive to NO adsorption. The adsorption experiments carried out under atmospheric pressure by the PulseTA technique [2] revealed that the amount of active adsorption centres for NO is distinctly smaller than for oxygen. The relative surface concentration of NO increases, whereas the oxygen surface concentration decreases. The decrease in oxygen concentration has two important consequences: it reduces the chance for NO to be oxidized to NO_2 and it reduces the degree of unselective hydrocarbon consumption.

The influence of the reducing agent on the reduction behaviour was studied and evidence was found that carbonaceous deposits from hydrocarbon fragmentation over Ir could contribute to an adsorbate-assisted mechanism of NO reduction.

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Inorganic Chemistry **113**

Synthesis and Characterization of a New Synthon for Macromolecular MRI Contrast Agents

S. Laus, É. Tóth, R. Ruloff and A. E. Merbach*

University of Lausanne, Institute of Inorganic and Analytical Chemistry
1015 Lausanne, Switzerland

Gd(III) chelates are widely used as contrast agents in medical Magnetic Resonance Imaging (MRI). The key features to attain high relaxivity, thus high efficiency for these agents are fast water exchange and slow rotation of the chelate (Fig.1) [1]. Whereas slow rotation can be relatively easily achieved by using macromolecules, the fine-tuning of water exchange rate is a more difficult task. Here we report the synthesis and characterization of a new Gd-chelate which has optimal water exchange rate, thus can be used as a synthon to construct highly efficient macromolecular MRI contrast agents. Moreover, this chelate has sufficiently high thermodynamic stability in order to be used as a safe drug.

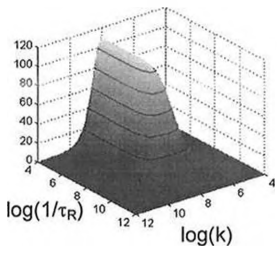


Fig. 1. Proton relaxivity (efficiency) of Gd(III) based MRI contrast agents as a function of the rotational correlation time (τ_R) and water exchange rate (k). B=0.5 T.

[1] The Chemistry of Contrast Agents in Medical Magnetic Resonance Imaging, eds. É. Tóth, A. E. Merbach, Wiley, 2001.

114

Synthesis of Derivatized Cyclopentadienyl-tricarbonyl Complexes of ^{99m}Tc in Water with an *in situ* CO Source.

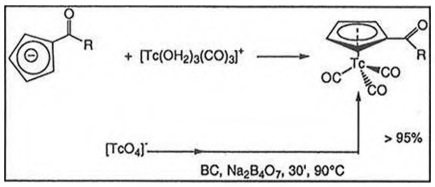
Roger Alberto,[1] Joachim Wald[1], Kirstin Ortner,[1] Lukas Candreia[1]

[1]Institute of Inorganic Chemistry, University of Zürich, CH-8057 Zürich

Derivatized cyclopentadienyl complexes of "$[M(CO)_3]$" are interesting for the labelling of various receptor-targeting biomolecules [1]. Despite many attempts of synthesizing $[(R\text{-}Cp)Tc(CO)_3]$ **1** in water there was no reasonable route to this type of compound so far.

We found that introduction of the acetyl group in the Cp-ring (acetyl-Cp) resulted in a reasonably low pK_a value of 8.3. Reaction with $[^{99}Tc(OH_2)_3(CO)_3]^+$ in water gives **1** in 20-40% yield, however with ^{99m}Tc the yield is almost quantitative. In order to have a real one step synthesis of **1** as required for routine application, we used an additional compound which releases CO in water when heated to about 70°C „Borano-carbonate", $[H_3BCO_2]^{2-}$ (BC) can act as a versatile in situ CO source for the purpose of preparing Tc-CO complexes [2].

Indeed, when $[^{99}TcO_4]^-$ was heated in the presence of RCp and BC compounds $[(R\text{-}Cp)^{99m}Tc(CO)_3]$ formed quantitativly after 30' at 90°C. This surprisingly convenient reaction gives for the first time access to half sandwich complexes on a routine base and, thus, to $[CpTc(CO)_3]$ labelled biomolecules.



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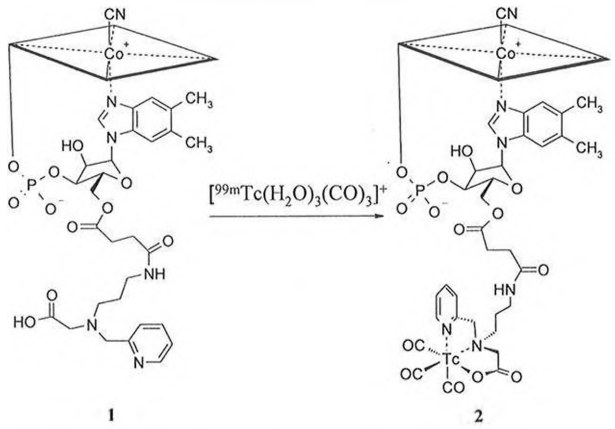
Inorganic Chemistry **115**

^{99m}Tc-labeled Vitamin B12 derivatives

Susanne Kunze, Stefan Mundwiler and Roger Alberto

University of Zurich, Institute of Inorganic Chemistry
8057 Zurich, Switzerland

The uptake of Vitamin B12 (cobalamin) and cobinamide in tumor cells is very efficient. This makes cobalamin derivatives promising compounds for tumor targeting.
We describe the attachment of the tridentate ligand PAMA (picolylamin monoacetic acid) to the 5'-OH group of the ribose unit via a succinate linker to give compound (**1**). This compound can be labeled with $[^{99m}Tc(H_2O)_3(CO)_3]^+$ to yield complex (**2**) with high specific activity [1].
In a similar way, the secondary alcohol group of cobinamide was treated to give the analogous cobinamide-compound of (**2**).



1 2

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Inorganic Chemistry **116**

Kinetic and Mechanistic Studies of the Reactions of Ferryl Myoglobin and Ferryl Hemoglobin with Nitrogen Monoxide and Nitrite

Franz-Josef K. Rehmann, Susanna Herold

Laboratorium für Anorganische Chemie, ETH-Zentrum
8092 Zürich, Switzerland

Ferryl, oxoiron(IV)myoglobin ($MbFe^{IV}$=O) and its protein radical ($^{\bullet}MbFe^{IV}$=O), formed *in vivo* by reaction of myoglobin and hydrogen peroxide, have been proposed to be involved in tissue injury resulting from reperfusion and reoxygenation of ischemic myocardium. It has been reported that nitrogen monoxide ($NO^{\bullet}$) reduces ferryl myoglobin to its iron(III) form $MbFe^{III}$ and that it may therefore exhibit a strong antioxidant effect against oxidative damage produced by $MbFe^{IV}$=O and thus, indirectly, by hydrogen peroxide. In contrast, nitrite dramatically enhances the H_2O_2-mediated toxicity. To evaluate the relevance of these reactions *in vivo*, we have carried out detailed kinetic and mechanistic studies.

We have determined that the reaction between $MbFe^{IV}$=O and $NO^{\bullet}$ is very fast (1.7×10^7 M^{-1} s^{-1} at pH 7.0 and 20 °C) and proceeds *via* an intermediate nitrito-iron(III)-myoglobin complex ($MbFe^{III}ONO$) which decays to $MbFe^{III}$ and nitrite (Eq. 1). Comparable results were obtained when the reaction was carried out with ferryl hemoglobin ($HbFe^{IV}$=O) (3.3×10^7 M^{-1} s^{-1} at pH 7.0 and 20 °C).
Nitrite can also reduce $MbFe^{IV}$=O to $MbFe^{III}$ but at a significantly lower rate (64.7 M^{-1} s^{-1} at pH 6.7 and 20 °C). Product analysis shows that half an equivalent of nitrite and nitrate are formed, respectively. This result suggests that the reaction is likely to proceed *via* the formation of nitrogen dioxide (Eq. 2), which might be responsible of the observed toxicity. Indeed, it was shown that the reaction of nitrite with $^{\bullet}MbFe^{IV}$=O leads to the nitration of both, protein bound and added free tyrosine.

$$MbFe^{IV}{=}O + NO^{\bullet} \longrightarrow MbFe^{III}\text{-}ONO \xrightarrow{H_2O} MbFe^{III}\text{-}OH_2 + NO_2^- \quad (1)$$

$$MbFe^{IV}{=}O + NO_2^- \longrightarrow MbFe^{III} + NO_2^{\bullet} \longrightarrow 0.5\ NO_2^- + 0.5\ NO_3^- \quad (2)$$

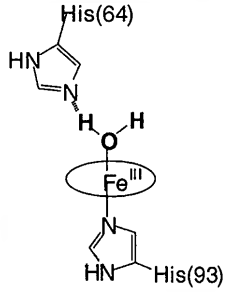
Inorganic Chemistry **117**

Peroxynitrite Isomerization Catalyzed by His64 Myoglobin Mutants

Susanna Herold

ETH Zurich, Institute of Inorganic Chemistry
8092 Zurich, Switzerland

The iron(III)-form of myoglobin (metMb) is the only heme-containing protein studied up to now in which the heme-center does not appear to react with peroxynitrite. In the present work we show that the reactivity of metMb towards peroxynitrite is regulated by the presence of the distal histidine (His64), which partly blocks the active site and stabilizes, *via* a strong hydrogen bond, the water ligand coordinated to the iron. We report here that the distal histidine myoglobin mutants H64A and H64D are efficient catalysts for the decomposition of peroxynitrous acid (k_{cat} = $(4.5 \pm 0.1) \times 10^6$ M^{-1} s^{-1} for H64D and $(6.0 \pm 0.1) \times 10^6$ M^{-1} s^{-1} for H64A, at pH 7.4 and 20 °C). In contrast, H64L only slightly accelerates its decomposition rate (k_{cat} = $(6.7 \pm 0.2) \times 10^4$ M^{-1} s^{-1}) whereas in the presence of wild-type metMb the lifetime of peroxynitrite is almost unchanged (k_{cat} = $(1.4 \pm 0.1) \times 10^4$ M^{-1} s^{-1}). Preliminary results show that H64A is an efficient scavenger also in the presence of 1.2 mM CO_2 (k_{cat} = $(9.6 \pm 0.2) \times 10^6$ M^{-1} s^{-1} at pH 7.3 and 20 °C).



Ion chromatographic analysis of the nitrogen-containing products shows that in the presence of 0.01 eq. of H64A nitrate is formed quantitatively. HPLC-analysis reveals that 0.05 eq. H64A prevents almost completely nitration of added free tyrosine and tryptophan by peroxynitrite both in the presence and in the absence of 1.2 mM CO_2.

Aknowledgment. I thank Prof. Y. Watanabe and Dr. T. Matsui for providing the myoglobin mutants.

Inorganic Chemistry **118**

Peroxynitrite-mediated Nitration of Tyrosine Residues in Myoglobin

Martin Mehl, Michael Exner and Susanna Herold

ETH Zurich, Institute of Inorganic Chemistry
8092 Zurich, Switzerland

Peroxynitrite ($ONOO^-$), a strong oxidizing and nitrating agent generated *in vivo* from the diffusion controlled reaction between $NO^{\bullet}$ and $O_2^{\bullet-}$), reacts with hemoproteins to generate high valent iron forms and/or nitrated tyrosyl residues. We have recently shown that the reactions of peroxynitrite with oxyhemoglobin ($HbFeO_2$) and oxymyoglobin ($MbFeO_2$) proceed in two steps with the formation of the ferryl species $HbFe^{IV}$=O and $MbFe^{IV}$=O:

$$MbFeO_2 + HOONO \longrightarrow MbFe^{IV}{=}O$$

$$MbFe^{IV}{=}O + HOONO \longrightarrow MbFe^{III}$$

We have investigated peroxynitrite-treated oxymyoglobin, metmyoglobin (metMb) and apomyoglobin (apoMb) by HPLC-analysis after complete hydrolysis as well as after enzymatic digestions. Additionally, nitrotyrosine was detected with nitrotyrosine antibodies and peptide fragments were analyzed by MALDI-TOF mass spectroscopy. Our results show that peroxynitrite is able to nitrate tyrosine residues of oxymyoglobin in a concentration dependent way, but in very low yields. When added in equimolar amounts, peroxynitrite nitrates less then 1% of the available tyrosine residues of MbO_2.

Larger nitrotyrosine amounts are detected when peroxynitrite is allowed to react with metMb but the most efficient nitration occurs in the reaction with apoMb. Incubation of apoMb with small amounts of peroxynitrite results in the nitration of tyrosine residue 146 and tryptophan residues. A larger excess of peroxynitrite nitrates also tyrosine residue 103.

Furthermore, we show that $MbFeO_2$ protects free tyrosine from peroxynitrite—mediated nitration. About 1/10 of equivalents of $MbFeO_2$ (relative to the free tyrosine) are required to inhibit tyrosine nitration (IC_{50}). We conclude that because of its low yield the nitration is not likely to be relevant *in vivo* but that hemoglobin as well as myoglobin may protect against peroxynitrite-mediated nitrations.

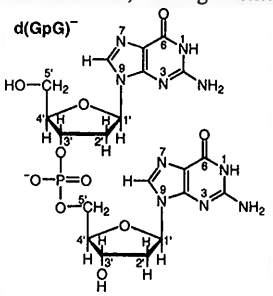
Inorganic and Coordination Chemistry **119**

Acid-Base and Metal Ion-Binding Properties of 2'-Deoxyguanylyl(3'→5')-2'-Deoxyguanosine [d(GpG)$^-$]

Carla P. Da Costa and Helmut Sigel*

Institute of Inorganic Chemistry, University of Basel, Spitalstrasse 51,
CH-4056 Basel, Switzerland

The antitumor drug Cisplatin, *cis*-$(NH_3)_2PtCl_2$, exerts its biological action by binding to DNA; this adduct formation causes bending of the DNA double strand, leading eventually to the death of cancerous cells [1]. It is nowadays commonly accepted that *cis*-$(NH_3)_2Pt^{2+}$ binds preferentially to N7 sites of adjacent guanine residues in the same strand, i.e. to -d(GpG)- units [1]. This raised our interest on GG dinucleotides and therefore, we started a series of studies which include d(GpG)$^-$ (see Figure). By potentiometric pH titrations in aqueous solution (25 °C; I = 0.09-0.12 M, $NaNO_3$) we determined the acidity constants for the deprotonation of the (N1)H sites of the two guanine moieties: $pK^H_{d(GpG)}$ = 9.37 ± 0.03 and $pK^H_{[d(GpG)-H]}$ = 10.39 ± 0.07. The stability constants of the 1:1 complexes formed between $[d(GpG)-H]^{2-}$ and Mg^{2+}, Ni^{2+} or Cd^{2+} are given in the Table. These preliminary results, if compared with those obtained previously for 2'-deoxyguanosine (dGuo), i.e. pK^H_{dGuo} = 9.24 ± 0.03 and $\log K^{Ni}_{Ni(dGuo-H)}$ = 3.20 ± 0.18 [2], indicate that metal ion binding occurs predominantly at one of the guanine residues with little contribution from other sites because the effect expected for the negative charge at the phosphate-diester bridge amounts to about 0.40 ± 0.15 log unit [3].



M^{2+}	$\log K^M_{M[d(GpG)-H]}$
Mg^{2+}	1.35 ± 0.15
Ni^{2+}	3.79 ± 0.15
Cd^{2+}	3.50 ± 0.10

Supported by the Swiss National Science Foundation and via COST D20 by the Swiss Federal Office for Education & Science.

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Inorganic and Coordination Chemistry **120**

Stability of Metal Ion Complexes Formed with Phosphonatomethylcholine (PMCh$^-$)

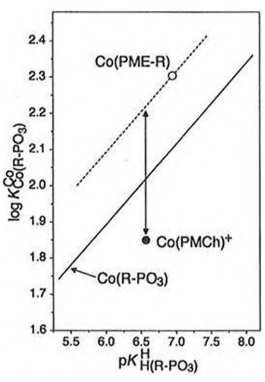
Alfonso Fernández-Botello,[a,b] Raquel B. Gómez-Coca,[a] Antonín Holý,[c] Virtudes Moreno,[b] and Helmut Sigel[a,*]

[a]Inst. of Inorg. Chemistry, University, Spitalstr. 51, CH-4056 Basel, Switzerland; [b]Inorg. Chem. Dept., University, E-08028 Barcelona, Spain; [c]Inst. of Org. Chem. and Biochem., Acad. of Sciences, CZ-16610 Prague, Czech Republic

Alkylphosphocholines have useful therapeutic effects [1] and in this context we are studying the metal ion (M^{2+}) binding properties of the phosphocholine analogue PMCh$^-$

	$(CH_3)_3\overset{+}{N}$-CH_2CH_2-O-$P(O)_2^-$-alkyl
PMCh$^-$	: $(CH_3)_3\overset{+}{N}$-CH_2CH_2-O-CH_2-PO_3^{2-}
PME-R^{2-}:	R-CH_2CH_2-O-CH_2-PO_3^{2-}

in aqueous solution (pot. pH titrations; 25°C; I = 0.1 M, $NaNO_3$). It is our aim to reveal the influence of the positively charged $(CH_3)_3N^+$ residue on the coordinating properties of the phosphonate group. For the evaluation of the measured stability constants we use the previously determined log $K^M_{M(R\text{-}PO_3)}$ *versus* $pK^H_{H(R\text{-}PO_3)}$ straight-line plots from our phosph(on)ate (R-PO_3^{2-}) studies [2,3] as well as the stabilities of the M(PME-R) species involving chelate formation with the ether O atom [4]; PME-R^{2-} is a derivative of (phosphonomethoxy)-ethane with a 'non-affecting' residue R (see Structure). Our preliminary results for the M(PMCh)$^+$ complexes of Co^{2+} (Fig.), Ni^{2+} and Zn^{2+} indicate that the stability inhibition amounts to about 0.4 log unit.



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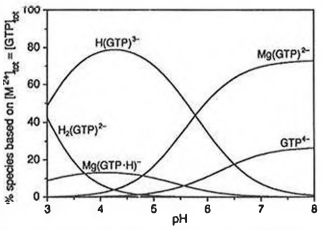
Inorganic and Coordination Chemistry **121**

Metal Ion-Binding Properties of Guanosine 5'-Triphosphate (GTP^{4-}) and Inosine 5'-Triphosphate (ITP^{4-}) in Aqueous Solution

Emanuela M. Bianchi and Helmut Sigel*

Institute of Inorganic Chemistry, University of Basel,
Spitalstrasse 51, CH-4056 Basel, Switzerland

Nucleoside 5'-triphosphates are enzymic substrates usually as complexes of divalent metal ions (M^{2+}). Via potentiometric pH titrations (25 °C; I = 0.1 M, $NaNO_3$ or $NaClO_4$) we measured the stability constants of several M(NTP·H)$^-$, and M(NTP)$^{2-}$ species, where NTP^{4-} = GTP^{4-} or ITP^{4-} [1]. In the monoprotonated M(NTP·H)$^-$ species H^+ is at the γ-phosphate group as is M^{2+}, which however may in addition interact with N7 of the purine residue [1]. More important, all M(NTP)$^{2-}$ complexes, which are relevant for the physiological pH range (Figure), show an increased stability (log Δ), compared to that expected for a sole triphosphate coordination; this is attributed to macrochelate formation of the phosphate-bound M^{2+} with N7 of the purine nucleobase. The macrochelated isomer is always more important for the M(GTP)$^{2-}$ species compared to the M(ITP)$^{2-}$ ones [1] (Table), which agrees with the higher basicity of N7 in GTP^{4-} (pK_a ≃ 2.9) compared to ITP^{4-} (pK_a ≃ 1.9) [2]. The pK_a of $H(NTP)^{3-}$, which quantifies the release of the H^+ from the γ-phosphate group, is always close to 6.50 [2].



NTP^{4-}	M^{2+}	$\log K^M_{M(NTP)}$	log Δ	% $M(NTP)^{2-}_{cl}$
GTP^{4-}	Mg^{2+}	4.31 ± 0.04	0.10 ± 0.06	21 ± 11
	Cu^{2+}	7.38 ± 0.08	1.52 ± 0.08	97 ± 1
	Cd^{2+}	5.82 ± 0.05	0.75 ± 0.06	82 ± 2
ITP^{4-}	Mg^{2+}	4.29 ± 0.04	0.08 ± 0.06	17 ± 11
	Cu^{2+}	6.71 ± 0.10	0.85 ± 0.10	86 ± 3
	Cd^{2+}	5.62 ± 0.05	0.55 ± 0.06	72 ± 4

Supported by the Swiss National Science Foundation.

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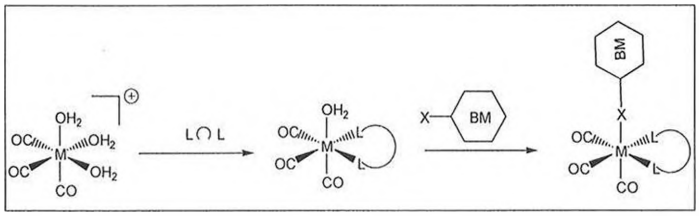
Inorganic Chemistry **122**

Labeling of bioactive molecules with $[^{99m}Tc(CO)_3]^+$ by using the [1+2] or [2+1] mixed ligand concept

M. Kündig, K. Ortner and R. Alberto

University of Zürich, Institute of Inorganic Chemistry
8057 Zürich, Switzerland

The synthesis and reactivity of complexes of the type $[M(CO)_3(L\cap L)X]$ (M = ^{99m}Tc, Re; L∩L = bidentate ligand, X = monodentate ligand) is presented. In these complexes a biomolecule (represented by e.g. a dipeptide) is either linked to the bidentate ligand L∩L ([1+2]) or to the monodentate ligand X ([2+1], see figure). The unlinked ligands may then serve to finetune the physicochemical properties of the complexes. The two different approaches will be presented together with the kinetic and thermodynamic behaviour of the complexes.



Inorganic Chemistry **123**

A DNA-Intercalating Complex of a Pyrene Derivative with the $^{188}Re(CO)_3$-Moiety as a Potentially Improved Radiotherapeutic Drug

P. Haefliger, K. Ortner, R. Alberto

University of Zürich, Institute of Inorganic Chemistry,
8057 Zürich, Switzerland

N-(2-Amino-ethyl)-N'-pyren-1-ylmethyl-ethane-1,2-diamine (P_1) reacts in water within 30 minutes at 90°C with the $[^{188}Re(CO)_3(H_2O)_3]^+$ precursor to form the complex $[^{188}Re(CO)_3(P_1)]^+$ (**1**) in quantitative yield. A crystal structure of this complex with $^{185/187}$Re is shown in Figure 1.

When brought into the nucleus of cancer cells by an adequate carrier (e.g. peptide), the ^{188}Re complex **1** should intercalate into DNA through its intercalating moiety, and ultimately induce, through its highly energetic β-particles, DNA strand breaks that should be lethal to the cancerous cell.

The intercalation affinity of complex **1** with calf-thymus DNA has been evaluated with spectroscopic methods. We further intend to derivatise the triamine ligand with a cancer-targeting biomolecule in order to perform toxicological tests on cells.

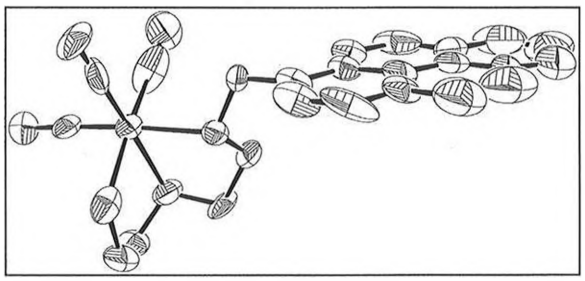


Figure 1: ORTEP plot of the cationic complex **1**.

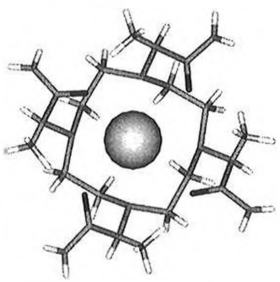
Inorganic and Coordination Chemistry **124**

What can we learn from slow water exchanging [Ln(DOTA-tetraamide)$(H_2O)]^{3+}$ complexes?

Frank A. Dunand and André E. Merbach

Université de Lausanne, Institut de Chimie Minérale et Analytique, BCH, CH-1015 Lausanne, Switzerland

Intensive research is still running to understand the physico-chemical properties of Gd(III) based MRI contrast agents. Their Eu(III) derivatives are often used because structural NMR can be performed. Since a slow water exchange has allowed the observation of the bound water signals by ^{1}H NMR on the $[Eu(DOTAM)(H_2O)]^{3+}$ complex,[1] we have focused our attention in understanding the solution dynamics of these compounds. This complexes exist in solution in two isomeric forms named **M** and **m**, which can exchange through arm rotation or ring inversion. NMR experiments at variable temperature and pressure were used to elucidate the mechanism of the water exchange as well as its role in the isomerization processes.[2] The influence of the ligand substitution on the solution structure and dynamics was also investigated. Other features should be pointed out from complexes with other lanthanides.



[1] S. Aime, A. Barge, M. Botta, A. S. De Sousa, and D. Parker, *Ang. Chem., Int. Ed. Engl.*, **1998,** *37,* 2673-2675.

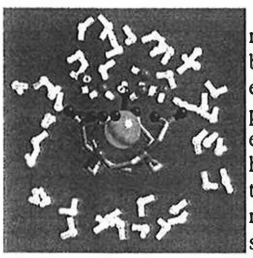
[2] F. A. Dunand, S. Aime, and A. E. Merbach, *J. Am. Chem. Soc.*, **2000,** *122,* 1506-1512.

Inorganic & Coordination Chemistry **125**

Combined Analysis of NMR and EPR Relaxation Data of Gd(III) Complexes in Aqueous Solution

A. Borel, F. Yerly, L. Helm and A.E. Merbach*

Institut de Chimie Minérale et Analytique,
Université de Lausanne, BCH, 1015 Lausanne,
Switzerland



Gd^{3+} complexes are used as magnetic resonance imaging (MRI) contrast agents because of the magnetic relaxation rate enhancement they induce on neighboring water protons, the so-called *relaxivity*. Multiple experiments (^{17}O–NMR, ^{1}H–NMR and EPR) have been performed in the past to understand the microscopic parameters that control relaxivity. Their simultaneous analysis[1] has shown that the generally accepted theory of the electron spin relaxation of S = 7/2 ions such as Gd^{3+} (i.e. the modulation of a transient zero–field splitting) is unsatisfactory.

Recently, an improved theory, including both a static and a transient ZFS, has been developed and tested on experimental EPR data[2]. The model has also been extended beyond the electronic Redfield limit[3]. We present here the first simultaneous fitting of ^{17}O–NMR, ^{1}H–NMR and EPR using a rigorous approach of the electron spin relaxation. The consequences on future experiments are also discussed.

[1] D. H. Powell, O. M. Ni Dhubhghaill, D. Pubanz, L. Helm, Ya. S. Lebedev, W. Schlaepfer, and A. E. Merbach, *J. Am. Chem. Soc.* 1996, *118,* 9333.

[2] S. Rast, E. Belorizky, P.H. Fries,, *J. Chem. Phys.* 2000, *113,* 8724; S. Rast, A. Borel, L. Helm, E. Belorizky, P.H. Fries, and A.E. Merbach, *J. Am. Chem. Soc.* 2001, *123,* 2637.

[3] S. Rast, P.H. Fries, E. Belorizky, A. Borel, L. Helm and A.E. Merbach, submitted

Inorganic & Coordination Chemistry **126**

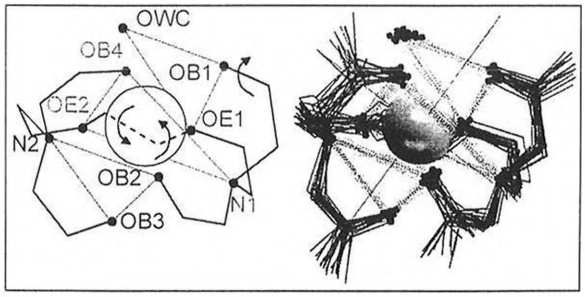
Molecular dynamics simulation of $[Gd(EGTA)(H_2O)]^-$ in aqueous solution

F. Yerly, L.Helm and A.E. Merbach

Université of Lausanne, Institut de chimie minérale & analytique
1015 Lausanne, Switzerland

To increase the inner sphere relaxivity of Gd^{3+} complexes used as MRI contrast agents, one has to increase the water exchange rate, and decrease rotational motions. $[Gd(EGTA)(H_2O)]^-$ is known to have a higher water exchange rate than similar polyaminocarboxylate complexes.[1] Simulations of the aqueous solution were performed and analysed in order to understand the relationship between the internal motions of the complex and the water exchange.

Calculated rotational correlation times, Connolly volumes of the hydrated and non hydrated simulated structures of the complex and symmetry characterization of the coordination polyhedron are presented.



[1] S. Aime, A. Barge, A. Borel, M. Botta, S. Chemerisov, A. E. Merbach, U. Müller, D. Pubanz, *Inorg. Chem.* **1997**, *36*, 5104-5112.

Inorganic & Coordination Chemistry **127**

Eu^{II} and Gd^{III} Chelates: Similarities and Differences with Regard to Magnetic Resonance Imaging

L. Burai, E. Tóth and A. E. Merbach

University of Lausanne, Institute of Inorganic and Analytical Chemistry
1015 Lausanne, Switzerland

The recent interest in the aqueous solution chemistry of Eu^{II} chelates has been prompted by two main aspects [1]. First, Eu^{II} is isoelectronic with Gd^{III}, therefore studying relaxation phenomena on the Eu^{II} analogues can give further insight into the mechanisms that govern relaxation on Gd^{III} complexes as well and thus help the development of novel MRI contrast agents. On the other hand, one can take advantage of the redox abilities of Eu^{II} complexes and design Eu^{II}/Eu^{III} based responsive MRI contrast agents which are sensitive to the redox state of the biological environment. We will present recent results related to these aspects.

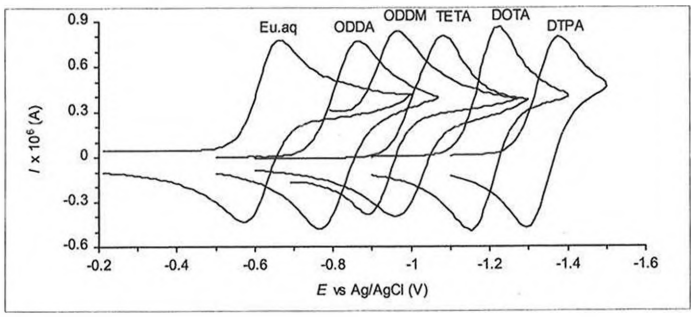


Fig.1. The redox potential of Eu^{II}/Eu^{III} changes substantially as a function of the ligand

[1] Tóth E., Burai L. and Merbach A.E., Coord. Chem. Reviews, (2001) in press.

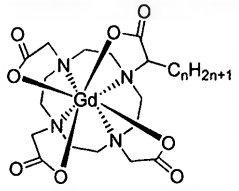
Inorganic & Coordination Chemistry **128**

Potential Micellar Contrast Agents for MRI: A ^{17}O NMR and ^1H NMRD Investigation

Gaëlle Nicolle,[1] Éva Tóth,[1] Klaus-Peter Eisenwiener,[2] Helmut Mäcke[2] and André E. Merbach[1]

[1] *Institut de Chimie Minérale et Analytique, Université de Lausanne BCH-Dorigny, CH-1015 Lausanne, Switzerland*
[2] *Institute of Nuclear Medecine, Division of Radiological Chemistry, University Hospital Basel, CH-4031 Basel, Switzerland*

In the last decade, different macromolecular assemblies (dendrimers, surfactants, complexes bound to protein) have been tested in Medical Magnetic Resonance Imaging, to image the blood pool thanks to their sufficient retention in the intravascular space and their longer rotational correlation time. Micellization of monomer Gd(III) complexes could fulfill those requirements [1] and could also be useful to image the liver.



A series of four micellar Gd(III) complexes, with different length of side-chain has been investigated by NMR: to determine i) their critical micellization concentration (CMC) [2] ii) the dynamic relaxation features affecting the relaxivity of the monomer and of the aggregated form.

[1] in *The Chemistry of Contrast Agents in Medical Magnetic Resonance Imaging, (*Eds.: A. E. Merbach, E. Tóth), John Wiley & Sons LTD, **2001**, pp. 78.
[2] C. Glogard et al., *J. Chem.Soc., Perkin Trans. 2*, **2000**, 1047.

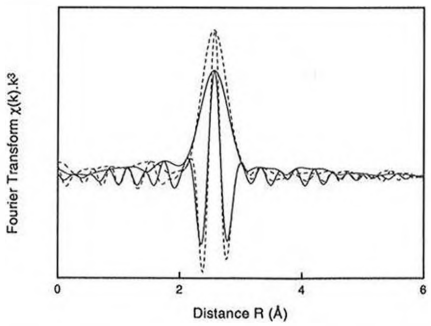
Inorganic and Coordination Chemistry **129**

Structural Investigation of the Aqueous Eu^{2+} Ion : Comparison with Sr^{2+} using the XAFS Technique

Gilles Moreau,[a] Lothar Helm,[a] Juris Purans[b] and André E. Merbach[a*]

[a] Institute of Inorganic and Analytical Chemistry, University of Lausanne
[b] Institute of Solid State Physics, University of Riga, Latvia

Structural parameters of the Sr^{2+} and, for the first time, of the Eu^{2+} ions in aqueous solution were determined using the X-ray Absorption Fine Structure (XAFS) method.



Comparison between Fourier transforms of the experimental XAFS $\chi(k)\,k^3$ spectra of 0.14 M Sr^{2+} (- - -) and 0.15 M Eu^{2+} (—) solutions.

The use of an improved theoretical approach led to a first shell coordination number of 7.9(3) for the Sr^{2+} and a Sr-O distance of 2.599(3) Å. The same approach was applied to the analysis of the Eu^{2+} XAFS spectra in aqueous solution and resulted in a first coordination shell of Eu^{2+} formed by 7.0(5) water molecules and an Eu-O distance of 2.583(5) Å. An equilibrium between coordination numbers 7 and 8 cannot be excluded for the Eu^{2+} ion in aqueous solution.

CHIMIA 2001, 55, No. 7/8

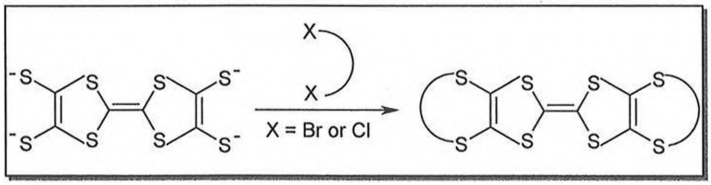
Inorganic Chemistry & Coordination Chemistry **130**

New Efficient Synthesis of Functionalized BEDT-TTF Derivatives

Shi-Xia Liu[a], Stefan Dolder[a], Melanie Pilkington[a], Silvio Decurtins[a] and John D. Wallis[b]

[a]Departement für Chemie und Biochemie, Universität Bern, Freiestrasse 3, 3012 Bern, Switzerland; e-mail: liu@iac.unibe.ch; [b]Chemistry and Physics Department, Nottingham Trent University, Clifton Lane, Nottingham, NG11 8NS, England.

Since 1985, the syntheses of new functionalised TTF derivatives have paved the way for the use of the TTF system as a building block within the wider context of supramolecular and materials chemistry [1]. As a consequence, considerable attention has been paid to molecular systems containing a redox-active functionality, as well as a host unit capable of cation binding. The aim of our current research is to design and synthesize suitably functionalized BEDT-TTF derivatives in attempt to prepare novel organic conducting materials featuring TTF moieties within metal binding ligand systems. It is expected that these materials could exhibit altered electrochemical properties in the presence of appropriate metal cations. Here, various synthetic approaches to BEDT-TTF derivatives with different functional groups (*e.g* see equation below) are described.



[1] T. Jøgensen, T.K. Hansen and J. Becher, *Chem. Soc. Rev.*, 1994, **23**, 41.

Inorganic Chemistry **131**

A Highly Flexible Vanadate Layer as the Common Structural Characteristic of Nanotubes and Related Crystalline Phases

F. Krumeich, M. Wörle, F. Bieri, and R. Nesper

Laboratory of Inorganic Chemistry, ETH Zürich
8092 Zürich, Switzerland

The structural characterization of vanadium oxide nanotubes (VO_x-NTs) by TEM has revealed that the tube walls consist of bent VO_x layers between which amine or diamine molecules are embedded [1]. Furthermore, a new type of VO_x-NTs with alternating short and long inter-distances has been obtained recently. Remarkably, the diffraction patterns of all these tubular phases are similar: some reflections correspond to the inter-layer distance while others indicate a square lattice with a ≈ 0.61 nm inside the VO_x layers, leading to a cell with tetragonal metric. Since it is appropriate to discuss a tube wall structure in respect of related three-dimensional structures, a first model for the VO_x-NT structure has been derived in relation to the structure of BaV_7O_{16} [2]. More information is now available from new vanadates that have been prepared on a route similar to that leading to VO_x-NTs. The similar lattice parameters of these new phases and of the VO_x-NTs point to a close structural relationship.

[1] F. Krumeich, H.-J. Muhr, M. Niederberger, F. Bieri, B. Schnyder, R. Nesper, *J. Am. Chem. Soc.* **121** (1999) 8324.
[2] X. Wang, L. Liu, R. Bontchev, and A. J. Jacobson, *Chem. Commun.* 1009 (1998).

Inorganic Chemistry **132**

Carbon coated nano-materials.

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

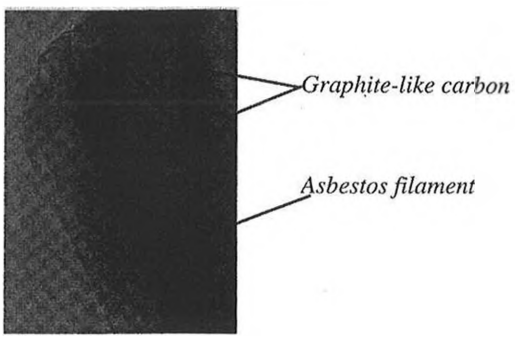
Laboratory of Inorganic Chemistry, ETH-Zürich, 8092 Zürich

Graphite oxide is a well known chemical compound. It has very good absorption properties and converts at 200°C back to a graphite-like material. Another remarkable property is stability of its colloids in strong base solutions.

We carried out a number of experiments with an aqueous graphite oxide colloid and porous nanomaterials (including asbestos, vanadium oxide nanotubes, iron oxide sticks and others). Decompositions of graphite oxide intercalated with various alkylammoniums were also performed.

The products were characterized with a X-ray powder diffraction and transmission electron microscopy (TEM). The graphite reflection (002) was present on all powder diffraction diagrams. The final powders contain thin carbon shawls arranged around different structures. For example asbestos microfibrous are perfectly packed in such shawl (see Image below).

We followed the decomposition of graphite oxide by means of high temperature X-ray measurements as well. The obtained data show the transformations of the graphite layer structure.



Inorganic Chemistry **133**

NEW RARE EARTH SILICIDES AND STRUCTURAL RELATIONS IN THE TERNARY SYSTEM Yb/Mg/Si

C. Kubata and R. Nesper

Laboratory of Inorganic Chemistry, ETH Zürich, Switzerland

Systematic thermochemical investigations of the ternary system Yb/Mg/Si yielded the new compounds $Yb_{2+x}Mg_{1-x}Si_2$ and $Yb_7Mg_2Si_8$. $Yb_7Mg_2Si_8$ crystallizes in the orthorhombic space group *Pnma* (a=6.980(1) Å, b=14.401(1) Å, c=7.536(1) Å) and $Yb_{2+x}Mg_{1-x}Si_2$ tetragonal in *P4/mbm* (a=7.0567(11) Å, c=4.1343(6) Å). Together with YbMgSi [1] they form an interrelated structural set. It is part of the larger RE/Sr/Si set (RE= La, Y), which forms a strongly structurally coupled family [2]. The structure of $Yb_7Mg_2Si_8$ contains two sets of $[Si_2^{6-}]$-dumb-bell blocks with different cation coordinations. If only one of the two sets is removed, the structure of $Yb_{2+x}Mg_{1-x}Si_2$ evolves (Fig. 1). The structure of YbMgSi can directly be derived from $Yb_{2+x}Mg_{1-x}Si_2$ by cutting the Si-Si bonds. Consequently, YbMgSi contains only isolated Si^{4-}- anions. YbMgSi crystallizes in the TiNiSi-type, which is related as well to the $PbCl_2$-structure.

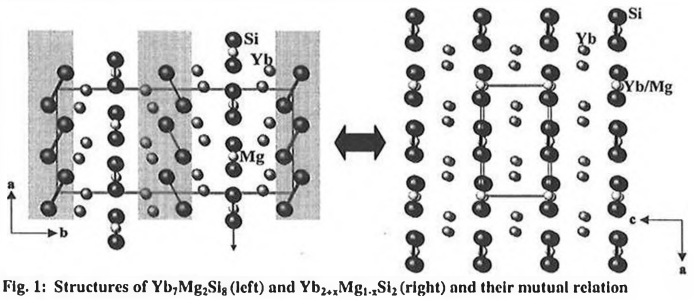


Fig. 1: Structures of $Yb_7Mg_2Si_8$ (left) and $Yb_{2+x}Mg_{1-x}Si_2$ (right) and their mutual relation

[1] Merlo F. et al., J. Alloys Compd. 1993, 196, 145
[2] Kubata C., Leoni S., Nesper R., 9th International Conference On Inorganic Ring Systems 2000, Saarbrücken, Germany

Inorganic Chemistry **134**

Synthesis and Structure of a new Calciumnitridosilicate

F. Ottinger and R. Nesper

Laboratory of Inorganic Chemistry, ETH Zürich, Switzerland

Containing corner-sharing as well as edge-sharing SiN_4-tetrahedra as the main building blocks, very complex Si-N-networks are possible in ternary nitridosilicates. Therefore the structures of nitridosilicates are a significant extension to the structures found in the family of oxosilicates.

So far, $Ca_2Si_5N_8$ was the only Calcium nitridosilicate that has been characterized by X-ray single-crystal diffraction [2]. Crystals of transparent, pale yellow $Ca_{28}Si_{16}N_{40}$ were obtained by reaction of $CaSi_2$ and Ca_3N_2 at temperatures of 1400 °C in sealed Niobium ampoules. We received metallic Calcium as a by-product, as it is not possible to synthesize $Ca_{28}Si_{16}N_{40}$ stoichiometrically from only $CaSi_2$ and Ca_3N_2. Moreover, Calcium is acting as a flux and enables the formation of large single crystals.

$Ca_{28}Si_{16}N_{40}$ crystallizes in the monoclinic space group P $2_1/c$ (No. 14) with a = 5.913(3) Å, b = 20.336(1) Å, c = 9.518(6) Å and β = 105.62(1)°, Z = 1, R(Fo) = 0.0263, wR_2(I) = 0.0501.

In $Ca_{28}Si_{16}N_{40}$ puckered layers of SiN_4-tetrahedra consist of one zwölfer and two fünfer rings. The two fünfer rings are connected via the only two edge-sharing SiN_4-tetrahedra. This edge-sharing leads to a very short Si-Si distance of only 2.360(1) Å. The shortest Si-Si distance in ternary nitridosilicates so far has been 2.556 Å in $Ba_5Si_2N_6$ [3]. We made an ELF calculation to verify if there are any electrons localized between these Silicon atoms but found no evidence for a Si-Si bond. All Si-N distances are within the usual ranges for nitrido-silicates, Si-N[1] between 1.740(1)-1.761(1) Å and Si-N[2] between 1.689(1) - 1.827(1) Å. With its very low Si/N ratio of only 0.4 $Ca_{28}Si_{16}N_{40}$ has one of the lowest degrees of condensation compared to other ternary nitridosilicates.

[1] H. Huppertz, W. Schnick, *Chem. Eur.* J. **1997**, *3*, 679
[2] T. Schlieper, W. Schnick, *Z. anorg. allg. Chem.* **1995**, *621*, 1037
[3] H. Yamane, F. J. DiSalvo, *J. Alloys. Comp.* **1996**, *240*, 33

Inorganic Chemistry **135**

High Pressure Experiments with MgB_2C_2

Michael Wörle[1], Urs Fischbach[1] Reinhard Nesper[1], Jürgen Evers[2], Roland Stalder[3], Peter Ulmer[3]

[1]Laboratorium für Anorganische Chemie, ETH Zürich, Switzerland; [2]Institut für Anorganische Chemie, Ludwig-Maximilians-Universität München, Germany; [3]Institut für Mineralogie und Petrographie, ETH Zürich, Switzerland

The orthorhombic structure of MgB_2C_2 contains slightly puckered graphite related layers $_\infty^2[BC]^-$, with an alternating intra- and inter-layer boron-carbon distribution [1]. This compound is structurally related to the AlB_2 structure type which gained a lot of interest since it was discovered recently, that one of its representants, MgB_2, becomes superconducting at 39 K [2].

In contrast to AlB_2, only half of the metal atom positions are occupied in MgB_2C_2. Therefore a pressure induced puckering of the layers might lead here to a formation of intra-layer B-C bonds, resulting in a three dimensional boron-carbon framework [3]. Experiments at a pressure of 80 kbar and 1100 °C lead to microcrystalline samples of a new high pressure phase of MgB_2C_2. An ab-initio structure determination on powder data and subsequent rietveld refinements could be performed. A basic feature of the new high pressure modification is a rearrangement of the Mg atoms, which now form linear chains instead the four membered clusters present in the ambient pressure form.

[1] M. Wörle, R. Nesper, J. Alloys Comp., **216** (1994) 75.
[2] J. Nagamatsu, N. Nakagawa, T. Muranaka, Y. Zenitani, J. Akimitsu, Nature **410** (2001) 63
[3] R. Nesper, K. Vogel, P. E. Blöchl, Angew. Chem. Int. Edit **32** (1993) 701

Inorganic Chemistry **136**

New synthesis of carbon filaments.

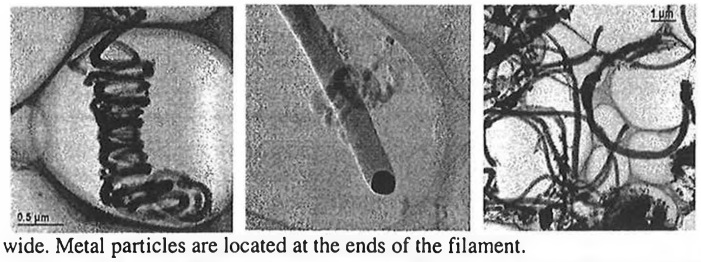
A.Ivantchenko, R.Nesper, F.Krumeich, C.Frei

Laboratory of Inorganic Chemistry, ETH-Zuerich, 8092 Zuerich

The carbon filament is the oldest-known nanostructure of graphite-like carbon. The standard industrial synthesis method for their growth is high temperature decomposition of hydrocarbons on transition metal catalysts.

In this work, we present an alternative synthesis of such carbon structures in which a special catalyst preparation is not required. In our experiments acetylene was passed throw the molten salt in a gas-liquid reactor. The growth of carbon filaments occurs at temperatures of about 550°C.

The final products were studied by X-ray powder diffraction, TEM, EDX, ESI and EELS. Filaments are primarily helical, 1- 20 µm long and 0.1- 0.5 µm



wide. Metal particles are located at the ends of the filament.

The variation of solution, temperature, crucible types, and reaction geometry seems to have a strong influence on the carbon yield and its micro- and nanostructure, respectively.

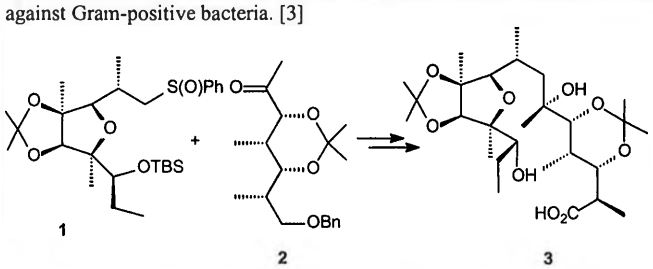
Organic Chemistry **137**

Total Synthesis of an analogue of Sporeamicin A

Sandrine Gerber Lemaire-Audoire, Simon Ainge, Cécile Glanzmann and Pierre Vogel

Section de Chimie de l'université de Lausanne, BCH, 1015 Lausanne-Dorigny

The urgent need for new antibiotics [1] has stimulated the search for new microorganism metabolites and chemically modified known antibiotics. Sporeamicin A was isolated from *Saccharopolyspora* sp. and characterized by Morishita and coll. in 1992. [2] This compound revealed a strong activity against Gram-positive bacteria. [3]



We report here the total asymmetric synthesis of an analogue of the aglycon part of Sporeamicin A which was obtained from the macrolactonization of intermediate **3**. This seco-acid resulted form the diastereoselective condensation of methyl ketone **2** with the anion derived from sulfoxide **1**. The polysubstituted furane ring was prepared by the stereoselective functionalization of 7-oxabicyclo[2.2.1]hept-5-en-2-one derivatives.

[1] "Antibiotic Resistance : Origins, Evolutions, Selection and Spread", Chadwick, D.J.; Goode, J. Eds; Ciba Foundation Symposium 207, John Wiley: Chichester, **1997**.
[2] Morishita, A.; Yaniguma, S. *J. Antibiotics* **1992**, *45*, 607-612.
[3] Morishita, A.; Mutoh, N.; Ishizawa, K.; Suzuki, T.; Yokoiyama, S.; Yaniguma, S. *J. Antibiotics* **1992**, *45*, 613-617.

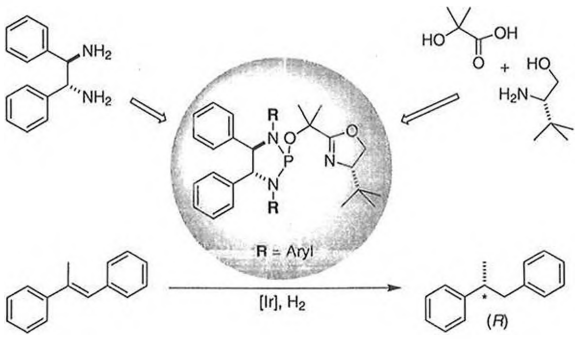
Organic Chemistry **138**

CHIRAL BIS(*N*-ARYLAMINO)-PHOSPHINE-OXAZOLINES AS LIGANDS IN ASYMMETRIC CATALYSIS

Marc Schönleber and Andreas Pfaltz*

Institute of Organic Chemistry, University of Basel, St. Johanns-Ring 19, CH-4056 Basel, Switzerland, email Marc.Schoenleber@stud.unibas.ch

A series of *P,N*-ligands containing a chiral oxazoline ring and a chiral bis(*N*-arylamino)-phosphine group derived from 1,2-diphenylethylenediamin[1] has been prepared.
The synthesis of these new ligands is straightforward:



These compounds proved to be efficient ligands for enantiocontrol of iridium-catalyzed hydrogenations of functionalised and unfuncionalised olefins and of palladium-catalyzed allylic alkylations.

[1] R. Hilgraf, A. Pfaltz *Synlett*, **1999**, 1814.

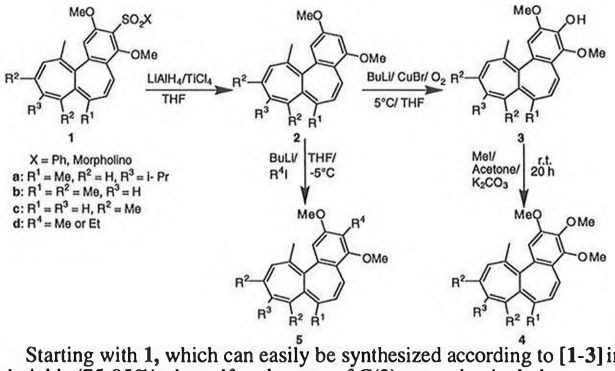
Organic Chemistry **139**

Studies for a Variable Synthesis of Colchicinoids: Substitution Reactions at Ring A of Protocolchicinoids

S. El rayes, K. Abou-Hadeed and H.-J. Hansen*

University of Zurich, Institut of Organic Chemistry
8057 Zurich, Switzerland

Although colchicine could be a medicament against many diseases, such as cancer, mediterranean fever, leukemia, schistosomiasis....etc., its cytotoxicity hinders its application. So, one aim of our group is the synthesis of new colchicinoids and the study of their biological activity.



Starting with **1**, which can easily be synthesized according to **[1-3]** in good yields (75-85%), the sulfonyl group of C(3) can reductively be removed to get **2** in 74-90% yields. Hydroxylation of **2** according to **[4]** gives **3** in good yields (70-85%). Methylation of **3** yields **4** in over than 95%. Finally, the alkylation of **2** leads to the new class of protocolchicinoids **5** (R^4 = Me 65-81% and R^4 = Et 50-70%).

[1] K. Abou-Hadeed and H.-J. Hansen, *Helv. Chim. Acta* **1997**, *80*, 2535.
[2] M. Lutz, A. Linden, K. Abou-Hadeed and H.-J. Hansen, *Helv. Chim. Acta* **1999**, *82*, 372.
[3] M. Mayer, K. Abou-Hadeed and H.-J. Hansen, *Helv. Chim. Acta* **2000**, *83*, 2383.
[4] G. J. Lambert, R. P. Duffley, H. C. Dalzell and R. K. Razdan, *J. Org. Chem.* **1982**, *47*, 3350.

Organic Chemistry **140**

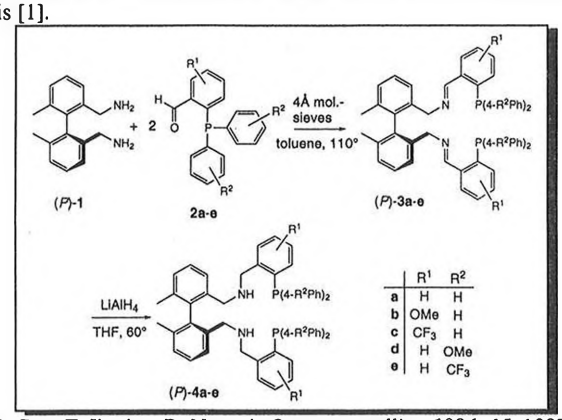
Synthesis of New Axially Chiral N_2^P_2-Ligands for Asymmetric Transition-Metal Catalysis

M. Furegati, A.J. Rippert*

University of Zurich, Institute of Organic Chemistry
8057 Zurich, Switzerland

The synthesis of differently substituted, axially chiral, tetradentate diimine-diphosphane ligands **3a-e** and their reduction using $LiAlH_4$ to the corresponding diamine-diphosphane ligands **4a-e** is reported (see equation below). The challenge was to synthesize 2-(diphenylphosphino)-4-trifluoromethylbenzaldehyde (**2c**) carrying an electronwithdrawing substituent in the benzaldehyde part. This benzaldehyde **2c** could be condensed in the usual manner with either (*P*)- or (*M*)-6,6'-dimethyl-1,1'-biphenyl-2,2'-dimethylamine (**1**).

The X-ray crystal structure of a corresponding Ruthenium(II)(**4a**)-complex will be discussed, such complexes can be used in asymmetric catalysis [1].



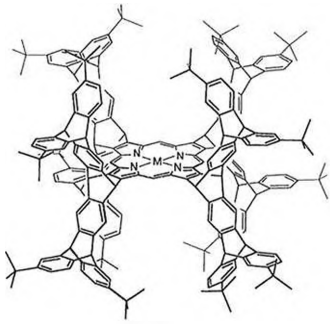
[1] J.-X. Gao, T. Ikariya, R. Noyori, *Organometallics*, **1996**, *15*, 1087.

Organic Chemistry **141**

D_4-symmetric Calixporphyrins

Sigrid Ostermann, Johann Schlögl, Bernhard Kräutler*
Institute of Organic Chemistry, University of Innsbruck,
Innrain 52a, A-6020 Innsbruck, Austria

We report here a synthetic route to D_4-symmetric Zn- and Co(II)-calixporphyrins. The relevant stereochemistry was introduced in a highly diastereoselective Diels-Alder-reaction of 2,6-di-*tert*-butylanthracene with fumaric acid di-(-)menthyl ester, catalyzed by aluminium chloride.[1] The porphyrin framework was built up as described.[2] Applying Horeau's principle, the chiral calixporphyrin was calculated to be present in an enantiomeric excess of at least 2.5×10^{18}:1.



M = Zn
M = Co(II)

The NMR-spectral properties of the two calixporphyrins were compared and characteristic differences in chemical shifts due to the presence/absence of a paramagnetic Co(II)-center were found.
Calixporphyrins may act as rigid hosts for organic guest molecules [2] and chiral biconcave porphyrins are useful as chiral shift reagents [3].

[1] R. Schwenninger, Y. Ramondenc, K. Wurst, J. Schlögl, B. Kräutler, *Chem. Eur. J.* **2000**, *6*, 1214.
[2] J. Schlögl, B. Kräutler, *Synlett* **1999**, *S1*, 969.
[3] R. Schwenninger, J. Schlögl, J. Maynollo, K. Gruber, P. Ochsenbein, H.-B. Bürgi, R. Konrat, B. Kräutler, *Chem. Eur. J.* **2001**, in press.

This work was supported by the Austrian National Bank (project P-7889).

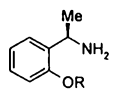
Organic chemistry **142**

Asymmetric Syntheses and Applications of New Chiral 2-(1-Amino-Ethyl)-Phenols

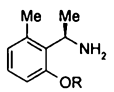
Candice Botuha, E. Peter Kündig, Lionel Saudan, Sylvie Thibault.

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

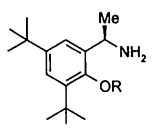
The development of new routes of access to enantiomerically pure 1,3-aminoalcohols constitutes an active area of investigation in organic chemistry owing to their potential as chiral building blocks and as chiral ligands for asymmetric synthesis.[1]



(R)-1a R=Me
(R)-1b R=H



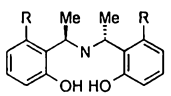
(R)-2a R=Me
(R)-2b R=H



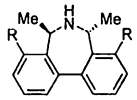
(R)-3a R=Me
(R)-3b R=H

Here we describe the asymmetric synthesis of enantioenriched 2-(1-amino-ethyl)-phenols **1**, **2** and **3**, obtained in high enantiomeric purity by three complementary approaches.

The chiral building blocks **1a** and **2a** have been successfully applied in the diastereoselective synthesis of new chiral C_2-symmetric tridentate ligands **4**, **5** and dibenzo [c,e] azepine **6**.[2] The latter has found application in enantioselective lithiation reactions.[3]



4: R = H, 5: R = Me



6: R = H

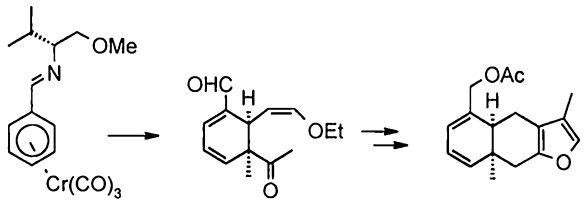
[1] G. Bernardinelli, D. Fernandez, R. Gosmini, P. Meier, A. Ripa, P. Schüpfer, B. Treptow and E. P. Kündig, *Chirality* **2000**, *12*, 529.
[2] L. A. Saudan, G. Bernardinelli, E. P. Kündig *Synlett.* **2000**, 483.
[3] S. Pache, C. Botuha, R. Franz, E. P. Kündig, J.Einhorn, *Helv. Chim. Acta*, **2000**, *83*, 2436.

Organic Chemistry **143**

Asymmetric Synthesis of (+)-15-Acetoxytubipofuran

R. Cannas, E. P. Kündig* M. S. Laxmisha, R. Liu and S. Tchertchian
Department of Organic Chemistry, University of Geneva, CH-1211 Geneva 4

The natural product 15-acetoxytubipofuran (**3**) belonging to the cis-eudesmane group of sesquiterpenes [1] possesses a cis-decalin moiety and a cyclohexadiene ring. Our analysis of this fused ring system suggested that it should be accessible by an asymmetric dearomatisation of the benzaldehyde derived chromium carbonyl complex **1**.[2] In this communication we report on the successful achievement of this strategy.



1 **2** **3**

Key features of the synthesis are

- A chiral auxiliary directed regioselective and diastereoselective nucleophilic addition followed by an acylation-alkylation sequence to get to the keto-aldehyde **2** in a one-pot sequence from **1**.
- The transformation of the key intermediate **2** to the natural product **4** employing as key step either a Pd catalysed allylic substitution reaction or a [3,3] sigmatropic rearrangement.

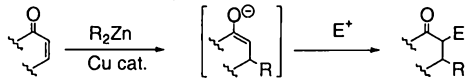
[1]. K. Iguchi, K. Mori, M. Suzuki, H. Takahashi and Y. Yamada, *Chem.Lett.*, **1986**, 1789.
[2] A. R. Pape, K. P. Kaliappan, E. P. Kündig, *Chem. Rev.* **2000**, *100*, 2917.

Organic Chemistry **144**

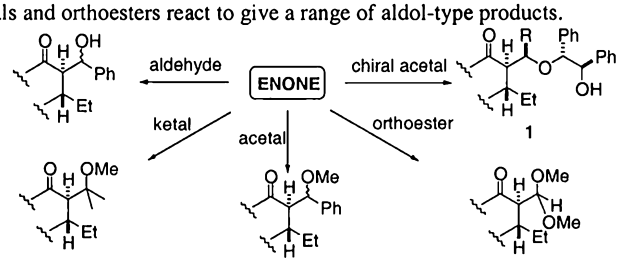
Tandem Asymmetric Michael Addition-Aldol Reactions

Dr. Oliver Knopff Dr. G. Trevitt Prof. A. Alexakis
Université de Genève, Departement de Chimie, CH-1211

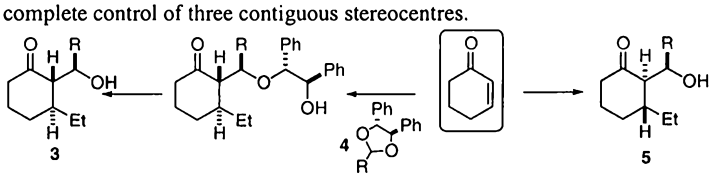
Recent work has focused on studying the chemical behavior of the zinc enolate intermediate formed in the course of the copper catalysed addition of organozincs to Michael acceptors.



The reaction of diethylzinc with a range of enones and electrophiles has been studied. Initial investigations have shown that aldehydes, acetals, ketals and orthoesters react to give a range of aldol-type products.



Recent results using chiral acetals (**4**) have shown that *syn* and *anti* aldols can be formed as a single diastereomer. Using a chiral ligand in the first step, **3** and **5** were formed from **2** following removal of the auxiliary, with complete control of three contiguous stereocentres.



The use of alternative electrophiles is currently under investigation.

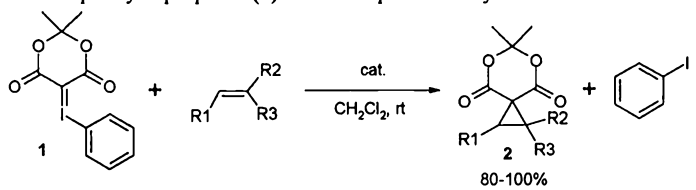
Organic chemistry **145**

Olefin cyclopropanation with phenyliodonium ylides

P. Müller, Y. Allenbach and E. Robert

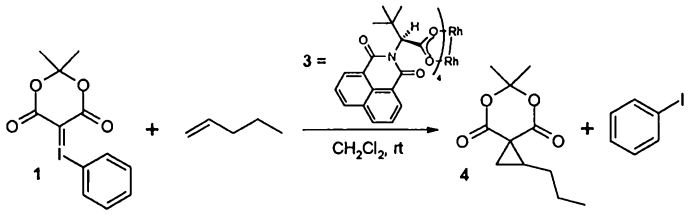
Département de Chimie Organique, Université de Genève,
30, Quai Ernest-Ansermet, CH-1211 Genève 4, Switzerland.

The transition metal-catalyzed cyclopropanation of olefins with phenyliodonium ylides derived from cyclic 1,3-dicarbonyl compounds such as **(1)** has been investigated with the objective of developing an alternative to the reaction involving diazo compounds, which are toxic and potentially explosive. Ylides such as **(1)** are easy to synthesize and purify and are considerably more stable than those derived from acyclic precursors. The transition metal-catalyzed cyclopropanation with **(1)** is stereospecific, and affords spirocyclopropanes **(2)** in almost quantitative yield:



80-100%

An asymmetric version of the reaction is under development. Thus, the cyclopropanation of pent-1-ene with the rhodium carboxylate **(3)** afforded the spirocyclopropane **(4)** in 97% yield with 59% ee:

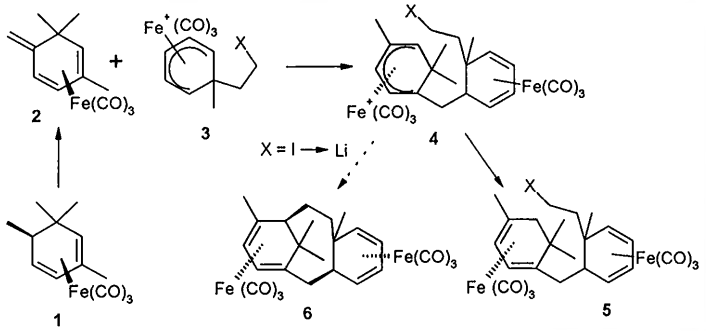


Organic Chemistry **146**

ORGANOMETALLIC APPROCH TO TAXANE SKELETON INVOLVING IRON CABONYL COMPLEX

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.
Oxidation of an optically active cyclohexadiene complex, accessible from (-)-β-pinene in high yield in two steps [1], under Perrier conditions leads to the planar chiral triene complexe **2**.
This complex couples with the achiral electrophilic cationic complex **3**, which in turn is synthetized straightforward in 3 steps from the Birch reduction product of dihydrobenzofuran.
The newly obtained intermediate **4** is either quenched with $NaBH_4$ to yield the binuclear complex **5**, or cyclized to **6** by internal alkylation after halogen metal exchange completing thereby the taxane skeleton.



[1] T.A. Jenny, L. Ma, *Tetrahedron Lett.*, **1991**, 32, 6101

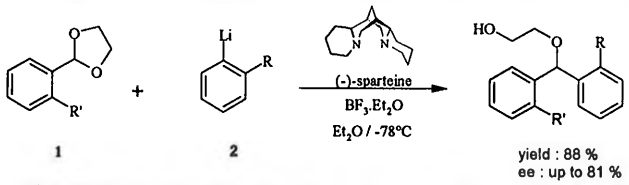
Organic chemistry **147**

Nucleophilic desymmetrisation of *meso* acetals by organometallic reagents

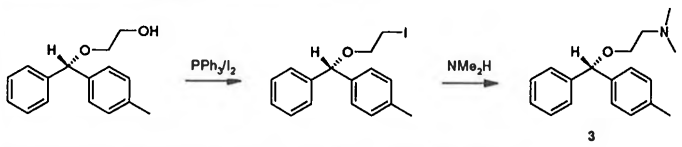
P. Müller, A. Ferrand and P. Nury

Département de Chimie Organique, Université de Genève,
30, Quai Ernest-Ansermet, CH-1211 Genève 4, Switzerland.

Acetals are widely used as protecting groups of carbonyl compounds against organometallic nucleophiles such as organolithium, Grignard or organocopper reagents. Although an enantioseclive ring opening of *meso*-1,3-dioxolanes using a chiral Lewis acid has been reported [1], no efficient combination of an organometallic reagent with a chiral ligand has been developed. We recently reported an enantioselective ring-opening of *meso* 2-substituted-1,3-dioxolanes (**1**) by aryllithium reagents **2** mediated by (-)-sparteine in presence of BF_3 [2].



The reaction was also applied to the asymetric synthesis of the antihistaminic drug (S)-neobenodine **3** [3].



[1] M.Kinugasa, T.Harada, A. Oku, *J. Org. Chem.* **1996**, *61*, 6772-6773.
[2] P. Müller, P. Nury, *Org. Lett.* **2000**, *2*(18), 2845-2847.
[3] P. Müller, P. Nury, G. Bernardinelli *Eur. J. Chem.*, submitted for publication.

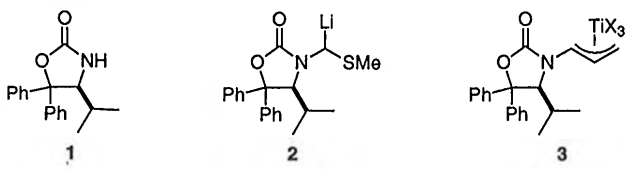
Organic Chemistry **148**

New Applications of 4-Isopropyl-5,5-diphenyloxazolidinone in Asymmetric Synthesis

Christoph Gaul and Dieter Seebach*

Laboratorium für Organische Chemie
der Eidgenössischen Technischen Hochschule Zürich,
ETH Hönggerberg, 8093 Zürich, Switzerland

New N-alkyl derivatives of 4-isopropyl-5,5-diphenyloxazolidinone **1** are prepared and their applicability as chiral reagents which are synthetically equivalent to formyl anions and homoenolates is demonstrated [1]. Thus, lithium reagent **2** can be used for the enantioselective nucleophilic formylation of aldehydes, ketones, imines and enones. Furthermore, promising results obtained with allyltitanium compound **3** for the enantioselective preparation of 4-hydroxy carbonyl derivatives ("homoaldols") are presented.



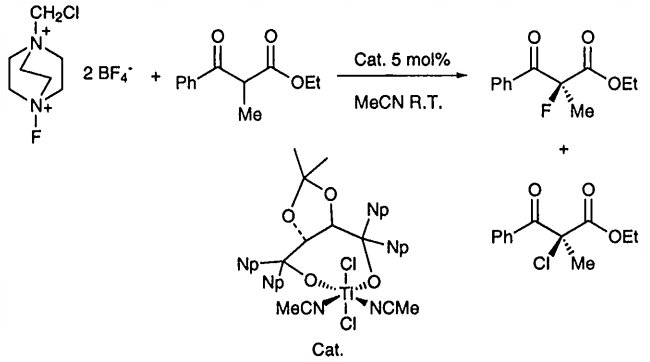
[1] a) C . Gaul, D. Seebach *Org. Lett.* **2000**, *2*, 1501. b) C. Gaul, K. Schärer, D. Seebach *J. Org. Chem.* **2001**, in print.

Organic Chemistry **149**

Towards Understanding Catalytic Enantioselective Fluorination

I. Devillers, L. Hintermann, M. Perseghini, M. Sanna and A. Togni
Department of Chemistry, ETH Hönggerberg, CH-8093 Zürich

We have recently reported the first catalytic enantioselective fluorination reaction [1], an important breakthrough in the field of organofluorine chemistry [2].



With the aim of improving and understanding this novel catalytic reaction, we have addressed selected mechanistic aspects.
We report here about kinetic investigations and spectroscopic measurements clarifying the nature of the intermediate reactive species, a neutral TiCl(enolato) species, giving a clue as to the origin of enantioselectivity. The mechanism of formation of the chlorinated by-product, observed for certain substrates, is also discussed.

[1] Hintermann, L.; Togni, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 23, 4359-4362.
[2] Muñiz, K. *Angew. Chem. Int. Ed.* **2001**, *40*, 9, 1653-1656.
[3] Hintermann, L.; Togni, A. *Helv. Chim. Acta* **2000**, *83*, 2425-2435.

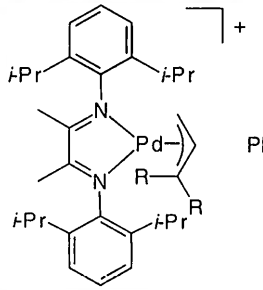
Organic Chemistry **150**

Kinetic investigations on the Pd – catalysed insertion polymerisation using an ESI-Mass Spectrometer

Gerd Gerdes, Peter Chen*

Swiss Federal Institute of Technology, 8092 Zürich, Switzerland

Determination of polymerisation kinetics remains a challenging subject if individual rate constants instead of mean values are needed. The kinetics of the polymerisation of norbonene by Brookhart – type Allyl – Pd complexes (**1a-c**) [1] have been investigated by means of ESI-Mass Spectrometry.



PF_6^-

1a, R = H
1b, R = Me
1c, R = Ph

From mass spectra of samples taken directly from the reaction mixture we were able to reveal the relative rate constants for each single reaction step. Given are the ratio of initiation rate to propagation rate k_i/k_p, the chain transfer rate k_{CT} as well as the specific propagation rates k_1, k_2, k_3 and k_4. Furthermore we showed that the reaction is stopped through backbiting by the allylic double bond after the third insertion step.

1a-c were structurally characterised by NMR – spectroscopy and X – Ray crystallography. They become active catalysts through rearrangement of the allylic ligand from π - to σ - coordination. This dynamic behaviour was shown by Saturation Transfer NMR experiments.

[1] L. K. Johnson, C. M. Killian, M. Brookhart, *J. Am. Chem. Soc.* **1995**, *117*, 6414.

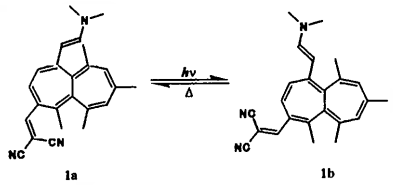
Organic Chemistry **151**

Chromogenic π-Systems: Merocyanine Dyes based on Heptalenes as Molecular Switches

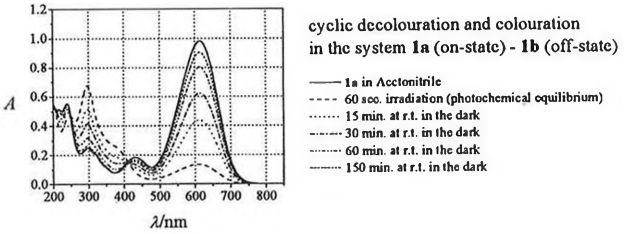
T. Landmesser and H.-J. Hansen*

University of Zurich, Institute of Organic Chemistry
8057 Zurich, Switzerland

Heptalenes substituted by auxochromic groups such as **1a** show strong colour-changing effects when the cyclic double-bonds are shifted either thermally or by irradiation. This process is reversible, giving these dyes a potential as molecular switches for technical applications like chemical data storage. The shown switching principle differs from other known chromogenic systems since only the distribution of π-bonds is altered while leaving the σ-system intact.



1a **1b**



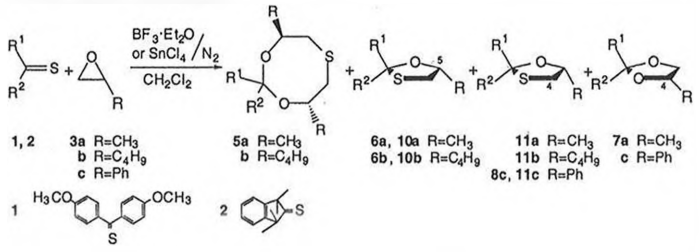
Organic Chemistry **152**

Lewis Acid Catalyzed Regioselective Reactions of Thioketones with Asymmetrically Substituted Oxiranes

C. C. Fu, A. Linden and H. Heimgartner*

Institute of Organic Chemistry, University of Zürich
Winterthurerstrasse 190, CH–8057 Zürich

The reactions of thiocarbonyl compounds with 2,3-disubstituted oxiranes in the presence of a *Lewis* acid have been investigated recently [1, 2]. The $BF_3{\cdot}Et_2O$- or $SnCl_4$-catalyzed reactions of *4,4'-dimethoxythiobenzophenone* (**1**) with 2-substituted oxiranes **3a-c** yielded regioselectively the 1,3-oxathiolanes **6a-b**, **8c**, the 1,3-dioxolanes **7a**, **7c** and the unexpected 1:2-adducts **5a-b**. In the reaction of *1,1,3,3-tetramethylindane-2-thione* (**2**) and **3a-c** with $BF_3{\cdot}Et_2O$ as a catalyst, mixtures of 1:1-adducts, i.e., 1,3-oxathiolanes **10a-b** and **11a-c** were formed. The structures of **5a**, **8c**, **10a**, **11a** and **11c** were confirmed by X-ray crystallography. The influence of alkyl- and aryl-substituents upon the regioselectivity of the ring-opening of the complexed oxirane by the nucleophilic attack (S_N2) of the thiocarbonyl S-atom will be discussed.



[1] M. Blagoev, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **1999**, *82*, 2316-2335.
[2] M. Blagoev, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2000**, *83*, 3163-3178.

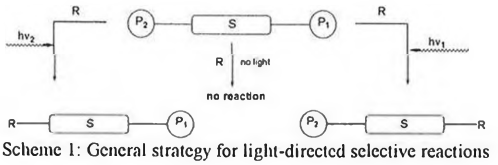
Organic Chemistry **153**

Selective activation of functional groups using monochromatic light

Céline Helgen, Aurélien Blanc and Christian G. Bochet*

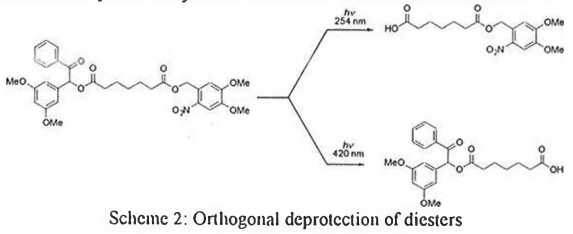
Université de Genève, Département de chimie organique,
Quai Ernest-Ansermet 30, CH-1211 Genève 4

A major challenge in organic synthesis is the selective reaction of a functional group in the presence of others. This can be achieved by using an appropriate reagent, tuned to react exclusively at the desired center. An alternate approach would be to use a single reagent, and to transmit from the *outside* the information to where it should react. This work describes the use of light as a controlling element; indeed, in addition to the intensity, the change of the wavelength gives an additional handle to direct the chemoselectivity (Scheme 1)



Scheme 1: General strategy for light-directed selective reactions

This concept could be applied to the orthogonal photochemical deprotection of polyfunctional molecules by using monochromatic light (*e.g.* Scheme 2), or to the thermodynamically unfavorable transformation amide → ester.



Scheme 2: Orthogonal deprotection of diesters

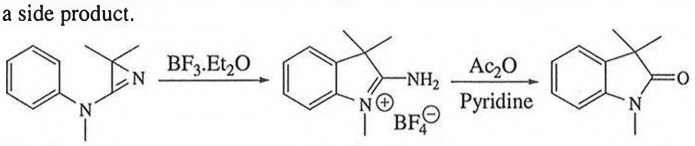
Organic Chemistry **154**

A New Synthetic Approach to 1,3,3-Trimethyloxindol from the Corresponding 3-Amino-2*H*-azirine.

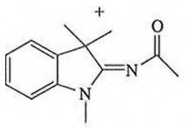
M. K. G. Mekhael, R. Smith, S. Bienz, A. Linden and H. Heimgartner

Organisch-chemisches Institut, Universität Zürich
Winterthurerstrasse 190, CH – 8057 Zürich

Natural products containing oxindol as a main structural unit are considered to show biological activity.Therefore, several attempts were made to synthesize oxindol ring structure using either chemical or photochemical reactions. The prepared oxindol is further used in the total synthesis of some important biologically active alkaloids such as Physostigmine and Physovenine [1].
A novel synthetic approach via a cyclization reaction is achieved by the treatment of 2,2-dimethyl-3-(*N*-methyl-*N*-phenylamino)-2*H*-azirine with borontrifluoride etherate to give the corresponding 2–amino-3*H*-indolium borontetrafluoride which further reacts with acetic anhydride in the presence of pyridine to yield the corresponding oxindol and its *N*–acetylated imine as a side product.



The *N*–acetylated imine is believed to be the reaction intermediate [2], and the mechanism of the reaction is rationalized via the formation of this interesting side product which could be further hydrolysed to oxindol.



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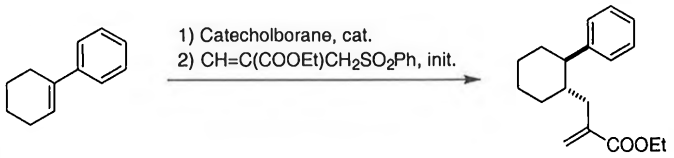
Organic Chemistry **155**

Radical Allylation and Vinylation of Organoboranes

Arnaud-Pierre Schaffner and Philippe Renaud

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

Hydroboration represents an unique and highly versatile tool for functionalization of alkenes. The use of organoboranes as radical precursors has been reported in the early seventies by Brown [1] and efficient conjugate additions to enones [2] and other radical traps [3] have been recently reported.
We describe here an efficient method for the vinylation and the allylation of B-alkylcatecholboranes using vinyl and allyl sulfones as radical trap.



[1] H. C. Brown, G., M. M. Midland, *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 692.
[2] C. Ollivier, P. Renaud *Chem. Eur. J.* **1999**, *5*, 1468.
[3] C. Ollivier, P. Renaud, *Angew. Chem. Int. Ed. Engl.* **2000**, *39*, 925.

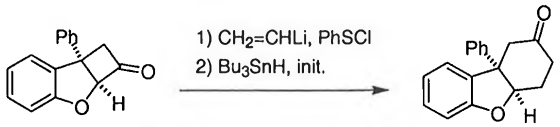
Organic Chemistry **156**

A Novel Approach for Ring Expansion of Cyclobutanones

Rachel Chuard and Philippe Renaud

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

We report an efficient way of generating alkoxyl radicals from allylic sulfoxides using the Mislow-Braverman-Evans rearrangement. A two steps procedure for one or two carbon ring expansion of cyclobutanones has been developed. The key element of this procedure is the well known beta-fragmentation of alkoxyl radicals.



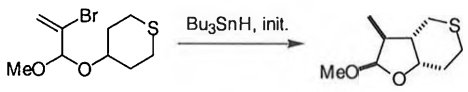
Organic Chemistry **157**

Preparation of Polysubstituted Tetrahydrofurans via 1,5-Hydrogen Abstraction

Florent Beaufils, Laurence Feray and Philippe Renaud

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

Isolated cases of diastereoselective 1,5-hydrogen atom transfers have been reported [1] but the stereoselectivity of these processes has never been investigated in a systematic way [2].
We present here a systematic investigation of diastereoselective 1,5-hydrogen atom transfers starting from bromovinyl acetals. This strategy allows the preparation of polysubstituted tetrahydrofurans derivatives.



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[2] For an exception, see: C.Imboden, F. Villar, P.Renaud, *Organic Letters* **1999**, *1*, 873.

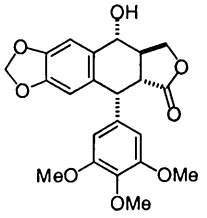
Organic Chemistry **158**

Synthesis of Dehydrodeoxypodophyllotoxin and Podophyllotoxin via a Radical Cascade Reaction

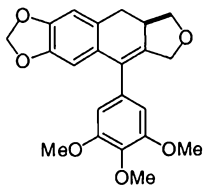
Tanja Kovac, Félix Villar and Philippe Renaud

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

Podophyllotoxin is a plant natural product that binds to tubulin and exhibits potent antimitotic activity. Etoposide, its glucosylated C(4) epimer acts by promoting topoisomerase II-mediated DNA strand scission and is widely used for the treatment of small cell lung cancer. A flexible synthetic approach should help identifying members with high antitumor activity and low toxicity [1]. We present here a new approach for the synthesis of podophyllotoxin and analogues. The key step is a tin free radical cascade reaction (5-*exo*-cyclization followed by radical arylation).



Podophyllotoxin



Dehydrodeoxypodophyllotoxin

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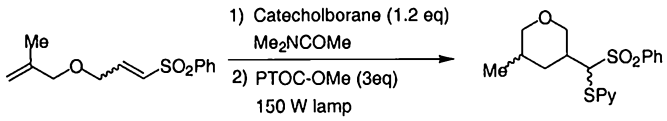
Organic Chemistry **159**

Radical Cyclizations of Organoboranes

Barbara Becattini, Cyril Ollivier and Philippe Renaud

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

Recently, we have shown that *B*-alkylcatecholboranes are excellent radical precursors for conjugate addition [1]. We present here the first examples of cyclizations involving the regioselective hydroboration of a polyene followed by an intramolecular radical conjugate addition.



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Organic Chemistry **160**

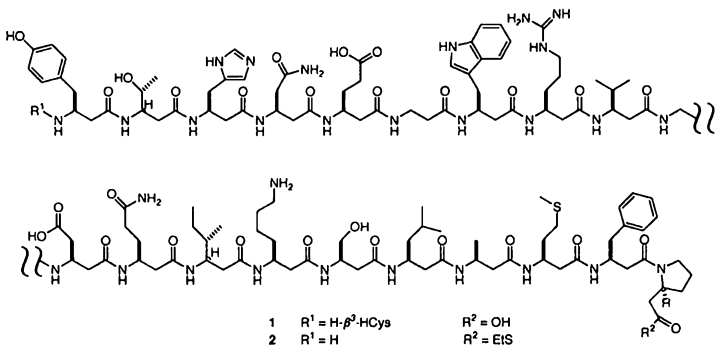
Synthesis of Large β-Peptides and Experiments to Cross the Border to β-Proteins

T. Kimmerlin, A. Sewing, D. Seebach*, and D. Hilvert

Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule, CH-8092 Zürich, Switzerland

The chemoselective ligation methods, which have made a considerable progress in recent years, offer a new route for the synthesis of larger peptides and proteins [1]. In the course of our investigation on β-peptides, we applied, for the first time, the native thiol ligation methodology to prepare larger β-peptides.

The requirements for the thiol ligation are an *N*-terminal Cys and a *C*-terminal thiolester fragment. Here, we report the synthesis of β^3-peptide **1** consisting of the 20 homologated proteinogenic α-amino acid residues with an *N*-terminal β-HCys using the recently improved Fmoc strategy on a solid support [2] and the preparation of β^3-peptide **2** containing a *C*-terminal thiolester by the Fmoc compatible solid-phase synthesis of peptide thiolesters [3]. Furthermore, experiments to carry out the thiol ligation of fragments **1** and **2**, and the ligation of β-peptides with α-peptides are presented.



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Organic Chemistry **161**

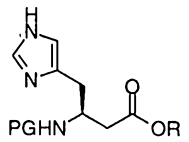
Synthesis of β^3-Histidine and Its Incorporation into β-Peptides for Metal Complexation

Gérald Lelais and Dieter Seebach*

Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule Zürich, ETH Hönggerberg, 8093 Zürich, Switzerland

β-Amino acids, although less abundant in nature than α-amino acids, have become increasingly important during the last decade. It has been shown that short-chain oligomers built only from β-amino acids (β-peptides) form stable secondary structures [1] and due to their biological stability [2] are candidates for medicinal applications.

Histidine is one of the most important amino acids in nature and is involved in many biocatalytic reactions (i.e. serin protease and zinc finger). Herein we report the synthesis of the β^3-analogue of histidine and its incorporation into β-peptides for studying metal complexations.



R = Me, H
PG = Boc, Fmoc

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[2] a) T. Hintermann, D. Seebach, *Chimia* **1997**, *51*, 244.
b) D. Seebach, S. Abele, J. V. Schreiber, B. Martinoni, A. K. Nussbaum, H. Schild, H. Schulz, H. Hennecke, R. Woessner, F. Bitsch, *Chimia* **1998**, *52*, 734.

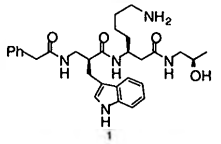
Organic Chemistry **162**

Synthesis of a β-Dipeptide Somatostatin Mimetic

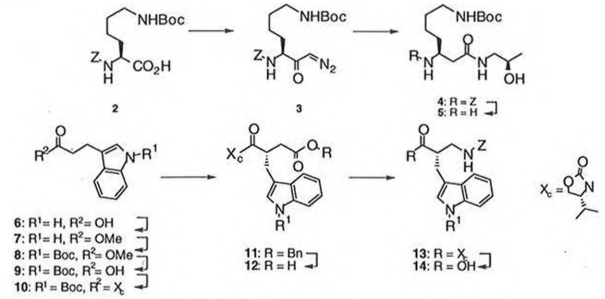
P. Micuch and D. Seebach*

Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule, CH-8092 Zürich, Switzerland

The tetradecapeptide Somatostatin was first isolated in 1972 [1]. The type II' β-turn around the aminoacids Phe^7-Trp^8-Lys^9-Thr^{10} was proposed as a recognition motif for the protein receptors [2].
In order to find non-α-peptidic mimetics of Somatostatin we intend to prepare β-peptide **1** with a proposed β^2-HTrp-β^3-HLys 10-membered H-bonded turn which is comparable to a β-turn in α-peptides. β-Peptides containing β^2-HLys-β^3-HTrp were synthesised previously and have been shown to exhibit high affinity for a Somatostatin receptor [3].



The β^3-HLys building block **5** was prepared by Wolf rearrangement of diazoketone **3** in the presence of the corresponding aminoalcohol. The β^2-HTrp building block **14** was prepared enantioselectively according to the following scheme.



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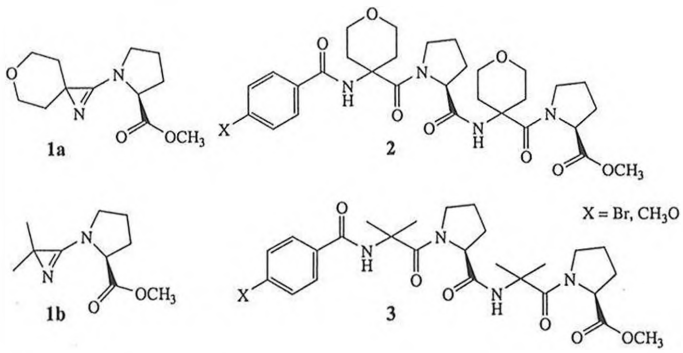
Organic Chemistry **163**

Structural Studies on Highly Strained Peptides

Sv. Stoykova, A. Linden, H. Heimgartner*

University of Zurich, Winterthurerstr. 190, CH-8057 Zurich

3-Amino-2*H*-azirines are suitable synthons for the preparation of peptides containing α,α-disubsituted α-amino acids [1]. Previous work proved that aminoazirines **1a** and **1b** can conveniently be synthesized and used for the incorporation of heterocyclic α-amino acid and Aib-Pro dipeptide units, respectively [2] [3].



These aminoazirines were successfully used as building blocks in order to synthesize model peptides. Highly strained peptides of type **2** and **3** were obtained in good yields. Our present efforts are concentrated on the establishment of their structure in the crystal state and in solution.

[1] H. Heimgartner, *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 238.
[2] G. Suter, Sv. A. Stoykova, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2000**, *83*, 2961.
[3] R. Luykx, C. B. Bucher, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **1996**, *79*, 527.

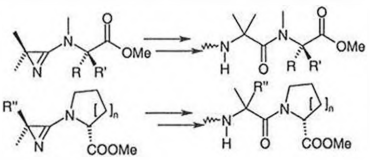
Organic Chemistry **164**

Scope and Limitation of 2*H*-Azirine-3-amines as Dipeptide Synthons

Roland André Breitenmoser and Heinz Heimgartner

Organisch-chemisches Institut, Universität Zürich Winterthurerstrasse 190, CH-8057 Zürich

We have shown that 2*H*-azirine-3-amines can be used as synthons for α,α-disubstituted glycines in peptide synthesis. In the last few years, the first three representatives of a novel type of 2*H*-azirine-3-amines have been prepared and found to be suitable as dipeptide synthons for the sequences Aib-Pro [1], heterocyclic amino acid-Pro [2], and Aib-Hyp [3].
In this presentation, we describe the further applicability of 2*H*-azirine-3-amines as dipeptide synthons showing how far this principle can be generalized and which limitations apply.
We have revealed that the corresponding 2*H*-azirine-3-amines can be used conveniently as dipeptide synthons for the sequences Aib-(Me)Ala, Aib-(Me)Val, Aib-Homoproline and Iva-Pro in the 'azirine/oxazolone method'. The coupling with amino or peptide acids proceeds in good yields. A limitation appears in the synthesis of the necessary starting materials, which failed in some cases.



[1] R. Luykx, C. B. Bucher, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **1996**, *79*, 527.
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[3] R. A. Breitenmoser, T. R. Hirt, R. T. N. Luykx, H. Heimgartner, *Helv. Chim. Acta* **2001**, *84*, 972.
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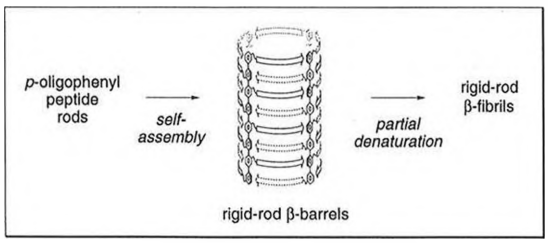
Organic Chemistry **165**

Hierarchical Self-Organization of Rigid-Rod Molecules: From Tertiary β-Barrel to Quarternary β-Fibril Structures

G. Das[a], L. Ouali[b], B. Baumeister[a], K. J. Wilkinson[b], and S. Matile[a]*

University of Geneva, Department of Organic Chemistry[a] and Analytical and Biophysical Environmental Chemistry (CABE)[b], 1211 Geneva, Switzerland

Quite recently, some of us have discovered that difficulties to synthesize β-sheet tertiary structures can be bypassed using *p*-oligophenyl rods instead of β-sheets as β-barrel "staves" [1,2]. Here we report that this powerful preorganization strategy can be expanded from tertiary β-barrel structures to quarternary β-fibril structures [3]. Controlled transformation of "rigid-rod" β-barrels into "rigid-rod" β-fibrils and their self-organization into higher-order supramolecular architectonics is characterized by circular dichroism, fluorescence spectroscopy, and atomic force microscopy.



[1] B. Baumeister, G. Das, N. Sakai, S. Matile, *Chimia* **2001**, *55*, 302.
[2] S. Matile, *Chem. Soc. Rev.* **2001**, *30*, 158.
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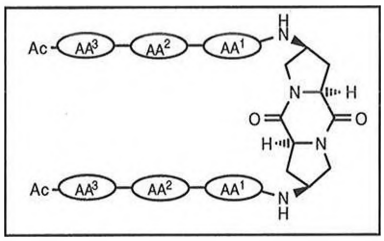
Organic Chemistry **166**

Proline-Diketopiperazine: A Template for a Parallel β-Sheet?

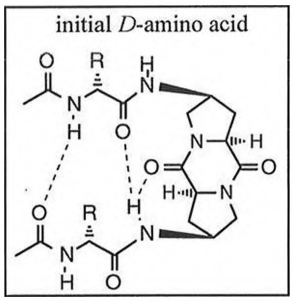
Matthias Nold and Helma Wennemers*

Institute of Organic Chemistry, University of Basel
St. Johanns Ring 19, CH-4056 Basel

In the course of our research towards novel synthetic receptors binding peptides with high affinity and selectivity[1] we examined the binding properties of several "diketopiperazine receptors". Combinatorial screenings



revealed that only receptors with L-amino acids in position AA^1 bind peptides with high specificity while initial D-amino acids prevent binding.



Conformational searches utilizing MacroModel suggest that the diketopiperazine with initial L-amino acids does not adopt a defined secondary structure. In contrast, initial D-amino acids lead to the formation of a parallel β-sheet thereby preventing intermolecular interactions.

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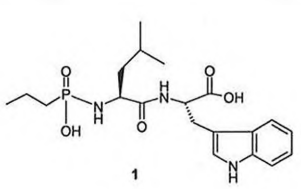
Organic Chemistry **167**

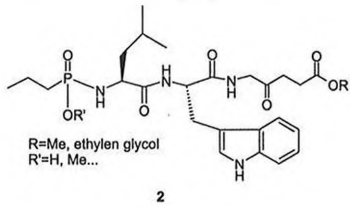
Phosphono-peptides Containing Derivatives of 5-Aminolevulinic Acid as Inhibitors of Endothelin Converting Enzyme to Control Human Cancer Progression.

Laurent Ingrassia, Yann Berger, Reinhard Neier* and Lucienne Juillerat-Jeanneret*

Université de Neuchâtel, Institut de Chimie, Bellevaux 51, Case postale 2, 2007 Neuchâtel

Endothelin is a potent vasoconstrictor peptide. The conversion of a precursor form to endothelin by endothelin converting enzyme (ECE) is essential for expression of full biological activity of the mature peptide. The control of intracellular as well as extracellular production of active endothelin from inactive precursor by ECE seems also to be necessary in the control of tumor cell survival. The phosphono-peptide **1** is known to inhibit this enzyme extracellularly. No inhibition of intracellular production has been shown and therefore no study has determined their efficiency in the context of cancer cells. Consequently, for this novel approach, it's necessary to improve cell penetration of compound **1**. In photodynamic therapy of cancer (PDT), esters of 5-aminolevulinic acid (ALA), a precursor of the photosensitizer protoporphyrin IX (Pp IX), display improved cell penetration to the cytoplasmic compartment. Therefore, we decided to modify free carboxylate of the compound **1** in order to obtain phosphono-peptide derivatives of ALA **2**. After preparation of this type of compounds, we'll estimate the intracellular inhibition of ECE and so we'll evaluate if this approach is an efficient way to control human cancer progression.





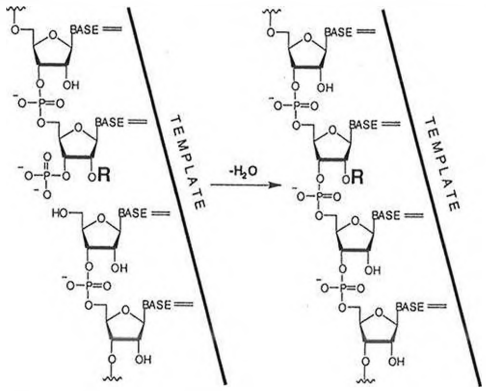
Organic Chemistry **168**

Template Directed Chemical Ligation of Oligoribonucleotides

Alfred Stutz and Stefan Pitsch*

Laboratorium für Organische Chemie, ETH Zentrum
Universitätstr. 16, CH-8092 Zürich

A general method for the preparative chemical ligation of RNA was developed. The regioselective formation of natural 3'→5' linkages was achieved by blocking the 2'-OH-group at the ligation-site by a photolabile protecting group, which at the end can be removed under mild conditions. The effect of different templates (2'-OMe-RNA, DNA, RNA), reaction conditions and the sequence dependance on the ligation-efficiency was investigated.



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[2] S. Pitsch, P.A. Weiss, X. Wu, D. Ackermann, T. Honegger, *Helv. Chim. Acta* **1999**, *82*, 1753.

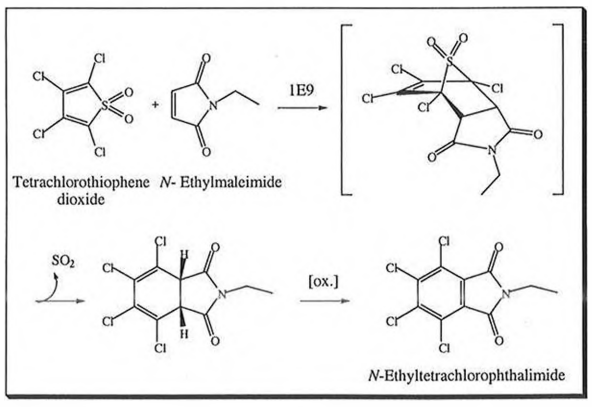
Organic Chemistry **169**

Catalysis of a Diels-Alder reaction by chimeric Fab fragments of antibody 1E9

A. Piatesi and D. Hilvert*

Laboratorium für Organische Chemie, Swiss Federal Institute of Technology Zürich *(ETH)*, 8092 Zürich, Switzerland

Monoclonal antibody 1E9, which catalyzes the [4+2]-cycloaddition between tetrachlorothiophene dioxide and *N*-ethylmaleimide[1], has been reengineered for expression as a chimeric Fab fragment in *E. coli*. Stabilizing mutations in the variable regions of the antibody have been introduced using the *Canonical Sequence Approximation*[2] approach, which improve the yield of an otherwise poorly expressed protein. Importantly, these mutations do not alter the catalytic efficiency of the antibody. The modified antibody is being further mutagenized to determine the origins of its selectivity and catalytic efficiency.



[1] Xu, J. A. *et al.* (1999) *Science*, **286**, 2345-2348.
[2] Steipe, B. *et al.* (1994) *J. Mol. Biol.*, **240**, 188-192

Organic chemistry **170**

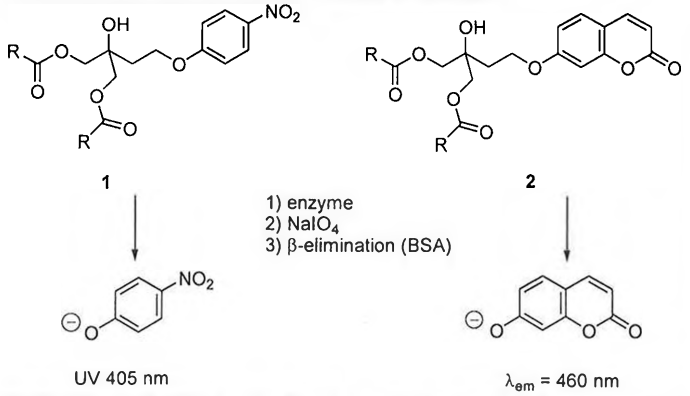
Fluoro/Chromogenic Glycerol Derivatives for Screening Lipases

E. González García and J.-L. Reymond.*

Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, 3012 Bern

A new versatile fluorogenic assay for hydrolytic enzymes has recently been reported by our group [1]. This versatile assay is based on the release of chromophores/fluorophores from substrates of type: amides, phosphates, epoxides or esters, after enzymatic hydrolysis followed by oxidation ($NaIO_4$) and β-elimination (BSA, pH>7).

We present here the application of this cascade reactions pathway for compounds **1** and **2** (R = alkyl chains), which carry a branched glycerol skeleton. These substrates are structurally closely related to glycerides, the natural lipase substrates. The synthesis evaluation of these substrates with various enzymes will be presented. Results on related substrates targeted to phosphatases and phospholipases will also be discussed.



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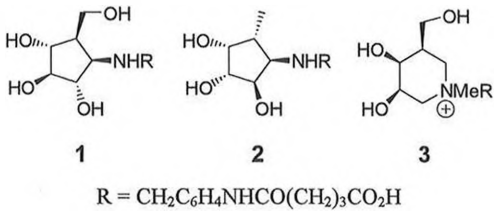
Organic Chemistry **171**

Investigation of glycosidase inhibitors as haptens for raising catalytic antibodies

Lucas Gartenmann and Jean-Louis Reymond*
Universität Bern, Dept. für Chemie & Biochemie, Freiestr. 3, 3012 Bern

Haptens **1**, **2** and **3** are derived from competitive inhibitors of β-glucosidase, α-L-fucosidase and αβ-galactosidase respectively [1]. Immunisation with haptens **1**, **2** and **3** might lead to antibodies with selective β-glucosidase, α-L-fucosidase and α- or β-galactosidase activity.



We will report the synthesis of hapten protein conjugates, their use for immunisation and the implementation of a high-throughput purification / fluorescence assay to identify monoclonal antibodies with glycosidase activity.

[1] a) Boss, O.; Leroy, E.; Blaser, A.; Reymond, J.-L. *Org. Lett.* **2000**, 2 151 b) Blaser, A.; Reymond, J.-L. *Helv. Chim. Acta*, **1999**, *82*, 760 c) Hansen, S. U.; Bols, M. *J. Chem. Soc., Perkin Trans. 1*, **2000**, 911

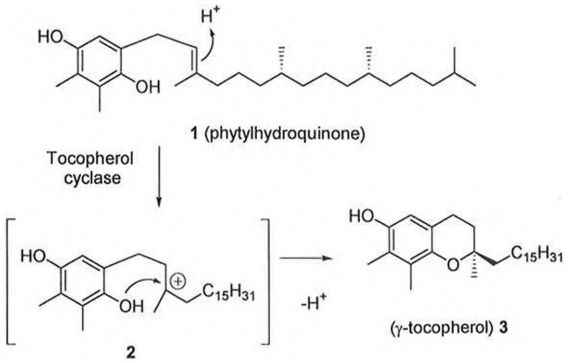
Organic Chemistry **172**

Towards Tocopherol Cyclase Catalytic Antibodies

R. Manetsch [a], M. T. Reymond [b], W.-D. Woggon* [a] and J.-L. Reymond*[b]

[a] University of Basel, Institute of Organic Chemistry, St. Johanns-Ring,19, CH-4056 Basel, [b] Departement für Chemie und Biochemie, Universität Bern, Freiestrasse 3, CH-3012 Bern

The tocopherol cyclase from cyanobacterium *Anabaena variabilis* Kützing catalyzes the formation of γ-tocopherol **3** from the phytylhydroquinone **1**, a key step in the biosynthesis of vitamin E [1]. The reaction involves double bond protonation to form the carboncationic intermediate **2**, followed by intramolecular cyclization. We report here the activity of monoclonal catalytic antibody 16E7, which has been obtained against a transition state analog of the reaction, and catalyzes a similar acid promoted process involving enolethers [2] related to phytylhydroquinone (**1**).



[1] A. Stocker, T. Netscher, W.-D. Woggon, *Helv. Chim. Acta*, **1994**, *77*, 1721.
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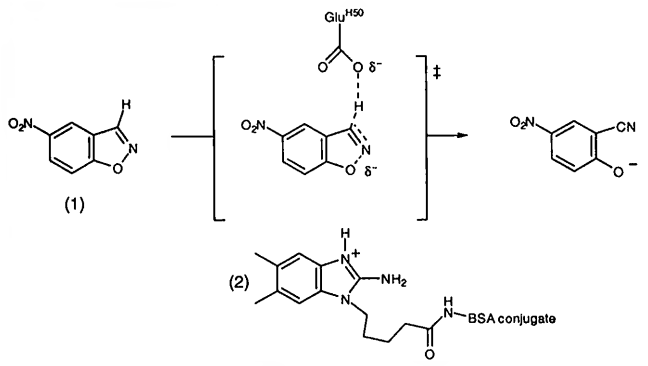
Organic Chemistry **173**

Identification of the catalytically active base in antibody 34E4

F.P. Seebeck, K. Hotta, D. Hilvert*
Laboratorium für Organische Chemie, Swiss Federal Institute of Technology *(ETH)*, 8092 Zürich, Switzerland

The catalytic antibody 34E4 catalyzes the *Kemp elimination* (1) which serves as model reaction for proton abstractions [1]. 34E4 was raised against a benzimidazole derivative (2) to yield a highly active catalyst that accelerates the reaction by a 10^8 fold [2]. Chemical modification, pH behavior and computer modeling suggest that a glutamic acid in the heavy chain, Glu^{50H}, acts as general base to abstract the proton from the substrate. In the present study, its role in catalysis was confirmed by mutagenesis. Detailed kinetic analysis of these and other mutants shed light on the origin of catalytic efficiency in this system.



[1] Casey, M.L. et al. J.org. Chem. **1973**, 38, 2295-2301.
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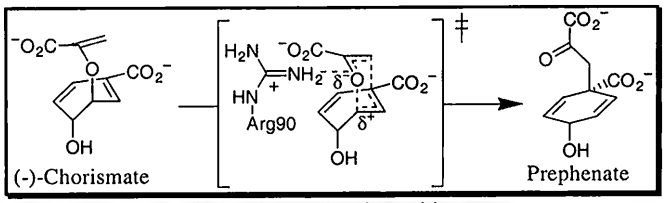
Organic Chemistry **174**

Substitution of Arg-90 in the active site of *Bacillus subtilis* Chorismate Mutase with non-proteinogenic aminoacids

A. Kienhöfer and D. Hilvert*
ETH-Zürich, Universitätstr. 16, 8092 Zürich

Chorismate mutase (CM) catalyzes the Claisen-rearrangement of (-)-chorismate to prephenate, the first committed step in the biosynthesis of Phe and Tyr. Mutagenesis, enzymological and crystallographic studies[1] have shown that Arg-90 is very important for the 10^6-fold rate acceleration provided by the enzyme, probably by stabilizing the developing negative charge at the ether oxygen in the transition state. To determine whether the ability of Arg to form hydrogen bonds or its positive charge is essential for catalysis, we have replaced it with non-proteinogenic analogs by chemical semisynthesis. For this, the enzyme is split in two parts at Cys-88. The C-terminal 40 amino acids were synthesized by SPPS. The N-terminal 87 residues were biosynthesized in *Escherichia coli* as an intein fusion [2]. After capturing the intein splicing intermediate with a thiol, this fragment was obtained as a thioester. The two fragments were then coupled by native chemical ligation[3].
The wild-type enzyme could be obtained in a fully active form, whereas mutants that do not have a positive charge at position 90 show a dramatic loss in activity which supports the role of electrostatics in catalysis.



Reaction catalyzed by CM with postulated transition state

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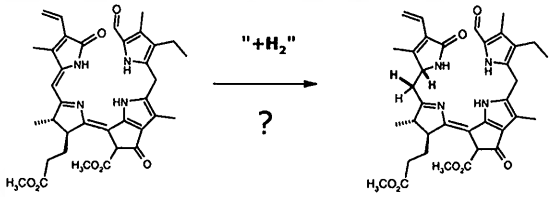
[2] Noren, C. J. *et al.* (2000) *Angew. Chem. Int. Ed.*, **39**, 450-466
[3] Daweson, P. E. *et al.* (2000) *Annu. Rev. Biochem.*, **69**, 923-960

Organic Chemistry **175**

Synthetic Access to Fluorescing Chlorophyll Catabolites

M. Oberhuber, W. Mühlecker, J. Berghold, B. Kräutler*
Institute of Organic Chemistry, Leopold-Franzens University of Innsbruck, Innrain 52a, A-6020 Innsbruck

The final products of chlorophyll breakdown in higher plants appear to be colourless tetrapyrroles, the so-called non-fluorescing chlorophyll catabolites (NCCs) [1]. The formation of NCCs from chlorophyll a requires multiple steps and involves at least 4 enzymes. Ring opened intermediates could not be trapped except for trace amounts of fluorescing compounds, presumably direct precursors of NCCs, which were detected during high rates of chlorophyll turnover.
Extracts with the enzymatic activity of pheophorbide a oxygenase (PaO)/red chlorophyll catabolite reductase (RCCR) were shown to convert pheophorbide a to a primary fluorescing chlorophyll catabolite (pFCC) [2]. Neither structure nor biochemistry of these enzymes are known.
Here we present a chemical reduction of Me-RCC to Me-FCC, which might serve as a model reaction for the corresponding biochemical transformation.



This work was supported by the *Austrian National Science Foundation* (FWF, project P-13503).

[1] Kräutler, B., Matile, Ph., *Acc. Chem. Res.* **1999**, *32*, 35-43.
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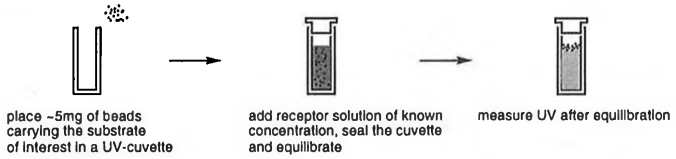
Organic Chemistry **176**

Influence of the Solid Support on the Determination of Binding Affinities in on-bead Binding Assays

Matteo Conza and Helma Wennemers*

Institute of Organic Chemistry, University of Basel
St. Johanns Ring 19, CH-4056 Basel

Combinatorial on-bead assays have become a powerful tool for the development of novel receptors with highly selective binding properties.[1,2] As a result, the determination of binding energies on the solid support has established itself as a useful means for obtaining a relative measure of the binding affinities to solid-supported substrates: An accurately measured amount of the solid-phase bound substrate is placed in a UV-cuvette, the solution of the coloured receptor is added and the mixture is allowed to equilibrate.



So far the influence of the nature and the loading of the solid support on the binding affinity has not been examined. We have addressed this question by measuring the binding affinities of a dye-marked diketopiperazine receptor[2] towards its peptidic substrate which was immobilized on various kinds of resins, e.g. polystyrene, Tentagel, PEGA.

[1] for reviews see: W.C. Still, *Acc. Chem. Res.* **1996**, *29*, 155; M.W. Peczuh, A.D. Hamilton, *Chem. Rev.* **2000**, *100*, 2479.
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Organic Chemistry **177**

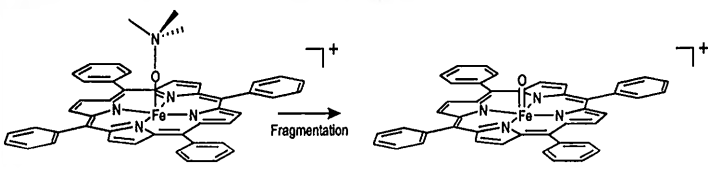
Oxygen Transfer from Oxoiron(IV) Tetraphenylporphyrin^{+} to Olefins. An Electrospray Tandem Mass Spectrometric Study.

M. Jufer, D. A. Plattner

Laboratorium für Organische Chemie
ETH Zürich, Universitätstrasse 16, CH-8092 Zürich

Cytochrome P450's, a ubiquitous class of heme proteins with over 350 members, catalyze a variety of reactions, such as aliphatic and aromatic hydroxylations, epoxidations and heteroatom oxidation by transfer of a single oxygen atom to the substrat. The catalytically active species of the transformation is believed to be an oxyferryl (Fe=O) complex of the heme unit, the so-called compound I.

We present results upon the intrinsic reactivity of the oxyferryl complex of tetraphenylporphyrin. The Oxoiron(IV)porphryin radical cation $C_{44}H_{28}N_4FeO^+$ was generated by fragmentation of a precursor in the tube lens region of an electrospray tandem mass spectrometer. Reaction of the selected oxyferryl species in the collision cell of the instrument with different olefins und saturated hydrocarbons yielded insight into the intrinsic reactivity of the compound I analogue.



Whereas oxygen transfer to activated olefins as dihydrofuran was observed, unactivated olefins as 1-buten or saturated hydrocarbons as hexane did not display any apparent reactivity toward the oxyferryl cation.

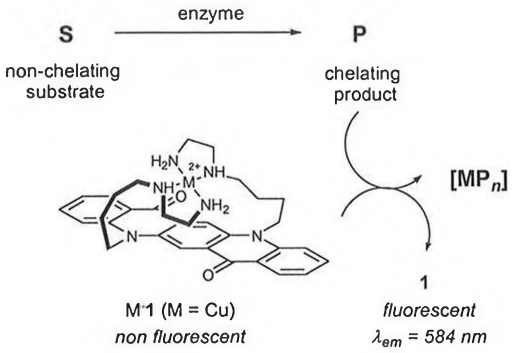
Organic chemistry **178**

An Enzyme Assay Using pM

G. Klein and J.-L. Reymond.*

Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, 3012 Bern

We have recently reported a new concept for assaying enzyme activities by fluorescence, which is based on recording modulation in pM (pM = -log[M], M = free metal ions) upon reaction progress [1]. The principle was initially demonstrated on amidases using the orange fluorescent quinacridone ligand **1** [2] and Cu^{2+} as reporter metal ion. We report developements of the assay, which now operates with completely water soluble fluorescent ligands and encompasses further reaction types.



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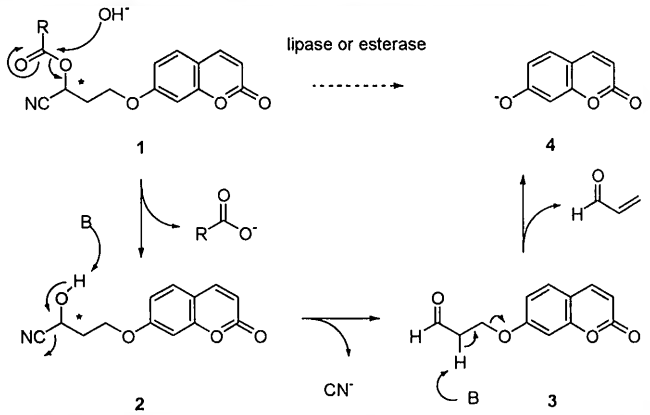
Organic Chemistry **179**

Cyanohydrins Used in Fluorogenic Assay of Lipases and Esterases

N. Bensel, E. Leroy and J.-L. Reymond*

Universität Bern, Dept für Chemie & Biochemie, 3012 Bern, Switzerland.

Kinetic resolution of chiral racemic esters using lipases and esterases is the most commonly used biotransformation in organic synthesis. Herein we report a simple fluorogenic assay for high-throughput screening of enantioselective esterases and lipases. Thus, chiral cyanohydrin esters (**1**) are hydrolyzed to cyanohydrin **2**, which then releases the fluorescent product umbelliferone (**4**) *via* aldehyde **3** upon the catalytic action of bovine serum albumin (BSA). By contrast to previous assays from our laboratory [1], no auxiliary oxidant is needed for this fluorogenic process.



[1] a) G. Klein and J.-L. Reymond, *Helvetica Chimica Acta* **1999**, *82*, 400; b) F. Badalassi, D. Wahler, G. Klein, P. Crotti and J.-L. Reymond, *Angew. Chem.* **2000**, *112*, 4233.

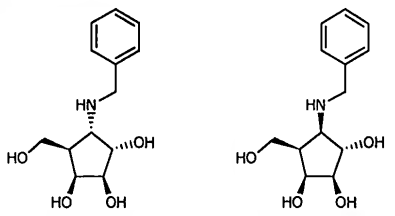
Organic Chemistry **180**

Synthesis and Glycosidase Inhibition Properties of α- and β-D-*galacto*-aminocyclopentitols

E. Leroy and J.-L. Reymond*

Universität Bern, Dept für Chemie & Biochemie, 3012 Bern, Switzerland.

We have recently shown that aminocyclopentitol analogs of protonated glycosides are potent inhibitors of the corresponding glycosidases [1]. In particular the anomeric selectivity of the inhibitors correlates well with the relative configuration of the amino-substituent . We now report the first comparative study of the inhibitory effect of an α/β pair of aminocyclopentitols on the corresponding α– and β–glycosidases, this at the example of galactosidases.



The synthesis of compounds **1** and **2**, and their inhibition test results will be described. The relationship between the inhibitor structure and the inhibition on different enzymes will be discussed.

[1] a) E. Leroy, J.-L. Reymond, *Org. Lett.* **1999**, *1*, 775; b) A. Blaser, J.-L. Reymond, *Org. Lett.* **2000**, *2*, 1733; c) O. Boss, E. Leroy, A. Blaser, J.-L. Reymond, *Org. Lett.* **2000**, *2*, 151.

Organic Chemistry **181**

Methylation of nucleobases in RNA oligonucleotides mediates duplex-hairpin conversion

Claudia Höbartner[1], Werner Pils[2], Karl Grubmayr[2], Marc-Olivier Ebert[3] and Bernhard Jaun[3], Ronald Micura[1]*

[1]Leopold Franzens Universität, Institut für Organische Chemie, 6020 Innsbruck, [2]Johannes Kepler Universität, Institut für Chemie, Altenbergerstrasse 69, 4040 Linz, [3]ETHZ, LOC, 8092 Zürich

We have systematically investigated the duplex into hairpin conversion of oligoribonucleotides under the aspect of nucleobase methylation. The first part of our study refers to the palindromic sequence of rCGCGAAUUCGCGA which forms a stable Watson-Crick base paired duplex under various buffer conditions. It is shown that this sequence type is forced to adapt a hairpin conformation if one of the central six nucleotides is replaced by the corresponding methylated nucleotide, such as 1-methyl guanosine (m^1G), N^2,N^2-dimethyl guanosine ($m^2{}_2G$), N^6,N^6-dimethyl adenosine ($m^6{}_2A$), or 3-methyl uridine (m^3U). On the other hand, the duplex structure is retained or even stabilized by replacement of a central nucleotide with N^2-methyl guanosine (m^2G) or N^4-methyl cytosine (m^4C). A borderline case is represented by N^6-methyl adenosine (m^6A). Although generally a duplex-preserving modification, our data indicate that m^6A in specific strand positions and at low strand concentrations is able to effectuate the duplex-hairpin conversion.

duplex —methylation→ **hairpin**

Moreover, our studies comprise the ssu ribosomal helix 45 sequence motif, $rGACCm^2GGm^6{}_2Am^6{}_2AGGUC$. In analogy, it is demonstrated that the tandem $m^6{}_2A$ nucleobases of this oligoribonucleotide are responsible to prevent duplex formation with complementary strands. Therefore, it can be concluded that nucleobase methylations at the Watson Crick base pairing site provide the potential not only to modulate but to substantially affect RNA structure by formation of different secondary structure motifs.

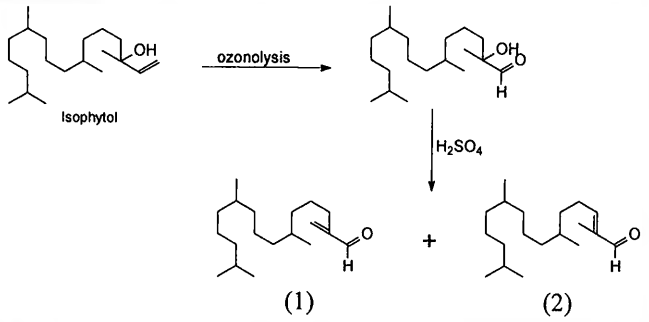
Organic Chemistry **182**

A naturally occurring acyclic norditerpene aldehyde from *Teucrium abutiloïdes*

R.Harb, S.M. Farahi, B. Muckensturm, J.P. Reduron

Université de Haute Alsace, Ecole Nationale Supérieure de Chimie de Mulhouse, 3, rue A. Werner, F-68093 Mulhouse CEDEX, France.

T.abutiloïdes : this plant is originating from Madeira. GC-MS analyses of the crude extract of "aerial parts", showed that the sesquiterpene hydrocarbons formed the main fraction, amounting 45% of the total volatils components (calculated as peak areas of the gas chromatogram). Two diterpenoïds : phytol and isophytol represented also an important fraction (12 %). The identity of the compounds was assigned by comparison of their retention indices and mass spectra with corresponding data of reference compounds. Two derivatives of isophytol were isolated and identified by spectroscopic analysis:
(1): 6,10,14-trimethyl-2-methylenpentadecanal
(2): 2,6,10,14-tetramethylpentadecan-2-al.
This last one, is isolated for the first time as a natural product. Its synthesis is given below.



R.Harb, S.M. Farahi, B. Muckensturm, J.P. Reduron, *Phytochem.*, awaiting publication.

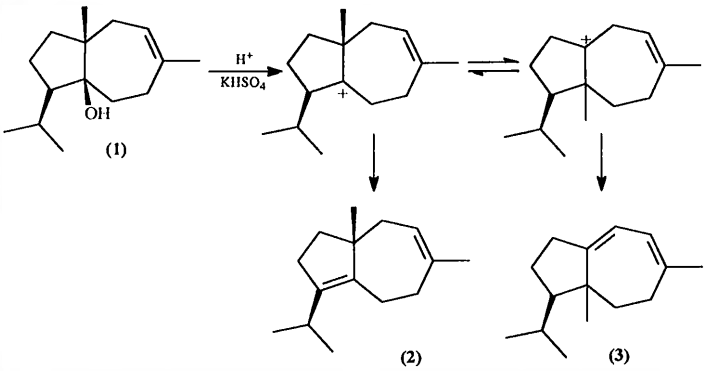
Organic Chemistry **183**

A new natural daucane derivative from *Azorella trifucarta*

E.Mayte, S.M. Farahi, R.Harb, B. Muckensturm, JP. Reduron

Université de Haute Alsace, Ecole Nationale Supérieure de Chimie de Mulhouse, 3, rue Alfred Werner, F-68093 Mulhouse France.

The daucane class of sesquiterpenes is a relatively small group of compounds which seemed to be restricted to membres to the plant family Umbelliferea. A new daucane derivative was isolated from the roots of *Azorella trifucarta* which we called Azorellene (3). The structure was identified by spectroscopic analysis and confirmed by dehydratation of carotol (1) giving two sesquiterpenes : daucene (2) and azorellene.



E.Mayte, S.M. Farahi, R.Harb, B. Muckensturm, JP. Reduron, *Phytochem.*, awaiting publication

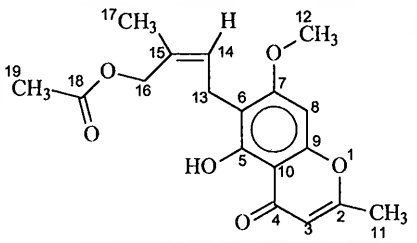
Organic Chemistry **184**

A new natural chromone from *Seseli Galloprovinciale*

M. Kodeih, R. Harb, S.M. Farahi, B. Muckensturm, J.P. Reduron

Université de Haute Alsace, Ecole Nationale Supérieure de Chimie de Mulhouse, 3, rue A. Werner, F-68093 Mulhouse cedex, France.

A new prenylchromone was isolated from the leaves of *Seseli galloprovinciale*, a species never described. Its structure was established by MS and (^{1}H, ^{13}C, DEPT-135, HMBC, HMQC and NOE) NMR (table 1.) spectral analysis. Its stucture is given below.



16-acetoxy-7-methoxy-peucenin

N°C	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
^{13}C	166 (S)	108 (d)	182 (S)	158 (S)	111 (S)	162 (S)	89 (d)	156 (S)	105 (S)	20 (q)	55 (q)	21 (t)	127 (d)	129 (S)	63 (t)	21 (q)	171 (S)	21 (q)
^{1}H	12.7 S1H		6.02 S1H				6.34 S1H			2.33 S3H	3.86 S3H	3.38 d2H	5.49 t1H		4.81 S2H	1.71 S3H		2.08 S3H

Table 1. ^{1}H, ^{13}C NMR spectral data

Analytical Chemistry **185**

Chemical Constituents and Insecticidal Activity of Sri Lankan Essential Oil of *Callistemon citrinus*

S. Mohottalage[1], R.Tabacchi[1] and P. Guerin[2]

[1] University of Neuchâtel, Institute of Chemistry, 2000, Neuchâtel, Switzerland
[2] University of Neuchâtel, Institute of Zoology, 2000, Neuchâtel, Switzerland

The Sri Lankan essential oil of *Callistemon citrinus* (syn. *C. lanceolatus,* Myrtaceae) leaves was extracted and tested insecticidal activity against adults of *Musca domestica* (house fly) and we found that this oil is insecticidal. This oil showed almost equal activity as Ceylon citronella oil (*Cymbopogon nardus*) which is reported to be known as insecticide [1]. The LC_{50} values of *Callistemon citrinus* are 21.2 & 20.4 mg/dm^3 and for Ceylon citronella are 25.6 & 24.6 mg/dm^3 for 24 and 48 hr exposure periods respectively.

Published data revealed that the leaf oil obtained from fifteen year old Pakistani *Callistemon citrinus* plant contained 1,8 cineole as a major component followed by α-terpineol and δ-cadinene where as flower oil contained α–pinene as a major followed by 1,8-cineole and δ-cadinene [2]. We report here on GC and GC/MS studies of a *Callistemon citrinus* leaf oil from Sri Lanka where 1,8-cineole (53.8%) as a major followed by α–pinene (26.4%) and *p*-cymene (2.4%). One β-diketone, 3,3,5,5,8,8-hexamethyl-7-oxabicyclo [4.3.0]-non-1(6)-ene-2,4-dione and two β–triketones, flavesone and leptuspermone were also found among the minor constituents. These three compounds believed to be first report to this plant.

[1]. S. R. Krishnarajah, V. K. Ganesalingam and U. M. Senanayake, *Trop. Sci.* **25**, 249-252 (1985).

[2]. Riaz, M and Chaudhary, M. *J. Ess. Oil Res.*, **2**, 327-328 (1990).

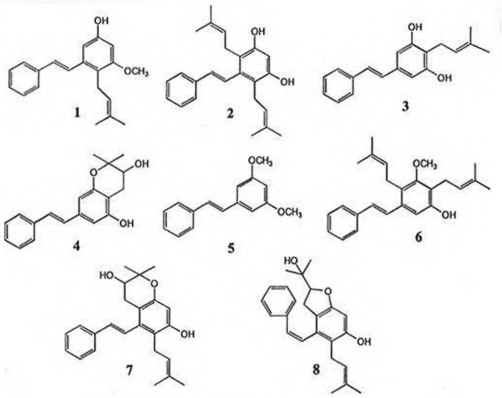
Organic Chemistry **186**

New antifungal and larvicidal prenylated stilbenes from *Lonchocarpus chiricanus*

Jean-Robert Ioset,[a] Andrew Marston,[a] Mahabir P. Gupta,[b] and Kurt Hostettmann [a]

[a] Institut de Pharmacognosie et Phytochimie, Université de Lausanne, BEP, 1015 Lausanne, Switzerland
[b] Center for Pharmacognostic Research on Panamanian Flora (CIFLORPAN), Apartado 10767, College of Pharmacy, University of Panama, Panama, Republic of Panama

Besides the known longistylines C (**1**), D (**2**) and 3,5-dimethoxystilbene (**3**) [1], five new prenylated stilbenes, named chiricanines A-E (**4-8**), have been isolated from the root bark of *Lonchocarpus chiricanus,* an endemic Panamanian tree belonging to the Leguminosae family. Chemical structures were resolved on the basis of spectrometric methods including 1H, 13C and 2D NMR experiments and mass spectrometry. Compound **5** demonstrated antifungal effects against *Cladosporium cucumerinum* while **1, 2, 3** and **5** showed toxic properties against larvae of the yellow fever-transmitting mosquito *Aedes aegypti*. Compound **3** was found to be as potent as rotenone in larvicidal dilution tests.



[1] Delle Monache F, Marini-Bettolo GB, Marletti F, De Mello JF, De Lima OG. 1977. Isolation and structures of longistylines A, B, C and D, new prenylated stilbenes from *Lonchocarpus violaceus*. *J. Nat. Prod.*, *40* : 201-208

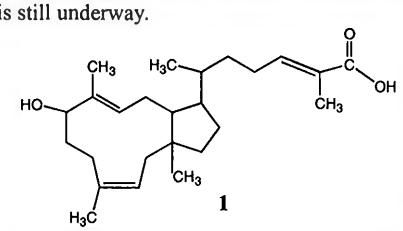
Organic Chemistry **187**

A new sesterterpenoic acid from *Henriettella fascicularis*

A.I. Calderón[a], C. Terreaux[a], K. Schenk[b], M.P. Gupta[c] and K. Hostettmann[a]

[a] Institut de Pharmacognosie et Phytochimie, Université de Lausanne, BEP, CH-1015 Lausanne, Switzerland
[b] Institut de Cristallographie, Université de Lausanne, BSP, CH-1015 Lausanne, Switzerland
[c] Center for Pharmacognostic Research on Panamanian Flora (CIFLORPAN), College of Pharmacy, University of Panama, Panama, Republic of Panama

Henriettella fascicularis (Sw.) C. Wright (Melastomataceae) is a plant growing in the rainforest of Panama. During our ongoing research on this plant, a novel sesterterpenoid (**1**) has been isolated from the dichloromethane extract of the branches. The sesterterpenes are very rare compounds in higher plants [1]. Structures of the side chain and certain fragments of (**1**) were determined by means of spectroscopic methods, including 2D-NMR correlation experiments such as HSQC, HSQC-TOCSY, HMBC and NOESY. In order to confirm the atomic arrangement and to assess the structure of the macrolide ring, single crystals were grown from ethanol/H_2O and an X-ray crystal structure analysis was performed. The relative configuration could be drawn from the data originated by the X-ray crystallographic examination. The absolute stereochemistry of the five chiral carbons is still underway.



1

[1] Hanson, J., H., Natural Products Reports, **1992**, 484.

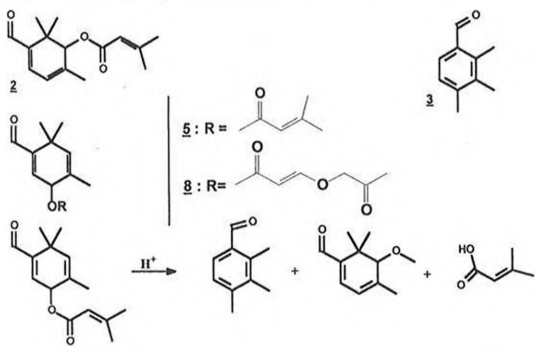
Organic Chemistry **188**

A new natural product from *Selinum broteri*

S.M. Farahi, B. Muckensturm, R. Harb, J.P. Reduron

Université de Haute Alsace, Ecole Nationale Supérieure de Chimie de Mulhouse, 3, rue Alfred Werner, F-68093 Mulhouse, France.

A new natural product, isoferulyl senecioate was isolated from the crude etheral extract of the leaves of *Selinum broteri* by directing the fractionation with the Brine Shrimp Lethality test (B.S.T.), and elucidated by differents spectroscopics analysis.
The TLC chromatogram of the crude etheral extract showed several UV spots and some minor constituents with pink fluorescence at 254nm. The extract was prefractionated with silica gel CC to obtain four fractions A-D. Craig distribution of fraction D and absequent semipreparative HPLC afforded four compounds, ferulyl senecioate 5, isoferulyl senecioate 2, an ester terpene 8, and 2,3,4-trimethylbenzaldehyde 3 as an artifact.



R : Angelate, Senecioate, Tiglate

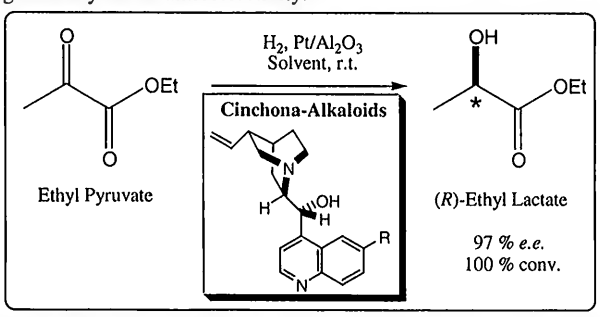
S.M. Farahi, B. Muckensturm, R. Harb, J.P. Reduron, *Phytochem.*, awaiting publication.

Organic Chemistry **189**

New Modifiers for the Heterogeneous Enantioselective Hydrogenation of α-Ketoesters

Ch. Exner [#], A. Pfaltz [#*], St. Burkhardt [§], M. Studer [§],
[#] Department of Chemistry, University of Basel, St. Johanns-Ring 19, CH-4056 Basel
[§] Solvias AG, Klybeckstrasse 191, CH-4002 Basel

Modification of the metal surface by chiral additives is an attractive concept in heterogeneous catalysis. Within this area, the *Orito* system[1] is one of the most frequently studied reactions because of its high activity and enantioselectivity.[2]



However, the scope of this reaction is quite narrow and only α-ketoesters and a few related substrate-types show high selectivity. Here we present results obtained with new modifiers derived from the original alkaloids or synthetic amino-aryl compounds.

[1] Orito Y., Imai S., Niva S., *J. Chem. Soc. Jpn.* **1979**, 1118.
[2] a) Pfaltz A., Heinz Th., *Topics Catal.* **1997**, *3*, 887.
b) Schürch M., Heinz Th., Aeschimann R., Mallat T., Pfaltz A., Baiker A., *J. Catal.* **1998**, *173*, 187. c) Blaser H.-U., Jalett H.P., Lottenbach W., Studer M., *J. Am. Chem. Soc.* **2000**, *122*, 12675.

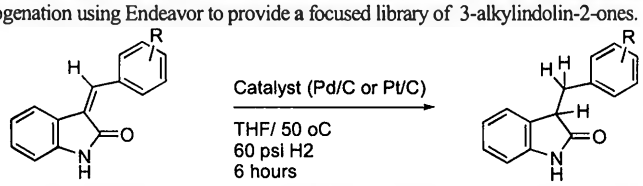
Organic Chemistry **190**

The Power of a Parallel Approach for Homo-/Heterogeneous Catalytic Hydrogenations

A. Abou-Hamdan[1], J.W. Labadie[2], Y. Yun[2], G. Hsiao[2], T. Long[2], F. Gebrehiwet[2] and P. Wright[2]
[1]Argonaut Technologies, St. Jakob-Strasse 148, CH- 4132 Muttenz 2
[2]Argonaut Technologies, 887 Industrial Road, San Carlos, CA 94070

Catalytic hydrogenation is a widely practiced transformation in organic synthesis and is one of the most efficient methods of introducing chiral centers into organic molecules. Many hydrogenations require the use of elevated pressures for the desired conversion and selectivity. Methods development and optimization of hydrogenations at elevated pressure are often hampered by the low throughput and poor monitoring capability of existing pressure reactors. This presentation will describe a new parallel pressure reactor system, Endeavor™, and key issues regarding its application to catalytic hydrogenation.
An important aspect in performing optimization studies on catalytic hydrogenation is to characterize the reactor configuration for gas-liquid mass transfer of hydrogen to the reaction solvent. The parallel configuration and pressure monitoring capability of Endeavor allows for rapid determination of effective mixing and fill parameters for a given reaction.

In addition to optimization, the Endeavor was applied to the synthesis of an analog series of 3-alkylindolin-2-ones. The key precursor was synthesized in parallel using a Quest 205. Eight analogs of this intermediate are subjected to catalytic hydrogenation using Endeavor to provide a focused library of 3-alkylindolin-2-ones.



The use of standard pressure vessels limits the parameter space which can be explored due to time constraints. Endeavor is a powerful tool for systematic optimization of the normal spectrum of parameters, including temperature, pressure, solvent, and ligand structure.

Organic Chemistry **191**

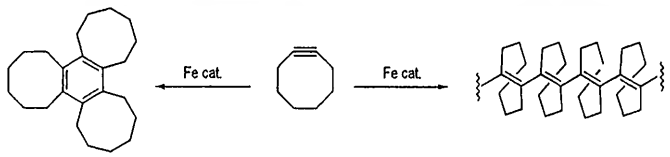
[2+2+2] CYCLOTRIMERIZATIONS AND HYDROGENATIONS MEDIATED BY AN IRON CATALYST

Manuel Raemy and Titus A. Jenny*

Chemistry Department, University of Fribourg
CH-1700 Fribourg, Switzerland

We will present a new iron catalyst, which is generated *in situ* by reacting $FeCl_2$ with hydride donors in toluene solution. This catalyst catalyzes the intermolecular cyclotrimerization of both terminal alkynes and sterically crowded internal alkynes to the corresponding substituted benzenes at room temperature.

Depending on the reaction conditions polymerization instead of cyclotrimerization is observed. This property is especially pronounced for reactive alkynes such as cyclooctyne.



The same iron catalyst hydrogenates various olefins under mild conditions (1-3 bar H_2, r.t.). In contrast to other known homogeneous iron hydrogenation catalysts[1] which act only for specific substrates, this new catalyst, although sensitive to certain functional groups, shows general applicability.

[1] a) Bianchini, C.; Meli, A.; Peruzzini, M.; Frediani, P.; Bohanna, C.; Esteruelas, M. A.; Oro, L. A. *Organometallics* **1992**, *11*, 138. b) Radhi, M. A.; Markó, L. *J. Organomet. Chem.* **1984**, *262*, 359.

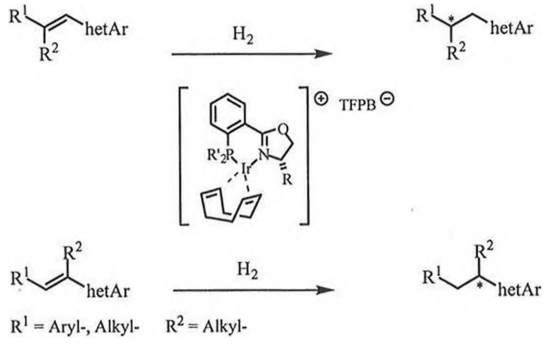
Organic Chemistry **192**

α,β-Unsaturated Heteroaromatic Systems in the Ir-Catalysed Asymmetric Hydrogenation

B. Wüstenberg and A. Pfaltz*

University of Basel, Institute of Organic Chemistry
4056 Basel, Switzerland

We have previously reported that Ir-complexes of P,N-ligands are efficient catalysts for the asymmetric hydrogenation of unfunctionalised carbon-carbon double bonds.[1] We are now investigating this reaction with a range of different substrates.
Trisubstituted alkenes containing heteroaromatic substituents on the double bond were synthesised in a stereoselective way. These prochiral α,β-unsaturated heteroaromatic compounds have been applied in the Ir-catalysed asymmetric hydrogenation, leading to chiral products with the stereogenic center either in α- or in β-position to the heterocycle with high conversion and enantiomeric excess up to 97%.



[1] A. Lightfoot, P. Schnider, A. Pfaltz, *Angew. Chem. Int. Ed.* **1998**, *37*, 2897.

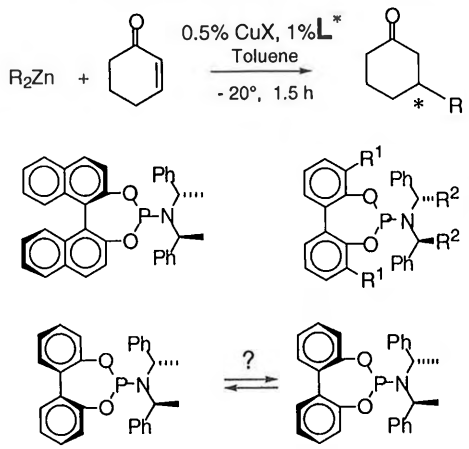
Organic Chemistry **193**

Biphenol Phosphoramidite Ligands for the Cu Catalysed Asymmetric Conjugate Addition

A. Alexakis*, S. Rosset, J. Alaman and S. March

University of Geneva, Department of Organic Chemistry
1211 Geneva, Switzerland

The copper catalysed enantioselective conjugate addition of dialkyl zinc reagent occurs in the presence of 0.5-2% of chiral phosphorus ligand. Many ligands are based on the chirality of binaphthol. We shall present the results with atropoisomerically flexible biphenols, which allow up to 98% enantioselectivity in the conjugate addition to several Michael acceptors.

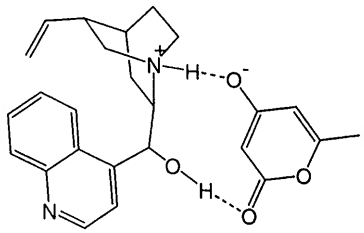


Pd-catalysed Enantioselective Hydrogenation of a Hydroxymethylpyrone: A Mechanistic Study 194

*W.-R. Huck, T. Bürgi, T. Mallat and A. Baiker**
Laboratory of Technical Chemistry, Swiss Federal Institute of Technology ETH-Zentrum, CH- 8092 Zürich, Switzerland

The Pd-cinchonidine (CD) is an efficient catalyst system for the enantioselective hydrogenation of C=C bonds affording up to 53 and 72% ee in the hydrogenation of aliphatic and aromatic , -unsaturated acids, respectively [1, 2]. Recently we have found, that the reduction of the pseudo-aromatic **1** to the corresponding 5,6-dihydropyrone afforded 85% ee with chirally modified Pd [3].

Here we report a mechanistic study of the nature of reactant - modifier interaction to rationalize the sense of enantio-differentiation. We propose a model involving two H-bonding interactions between CD and **1**, as shown on the left in a top view. NMR-experiments proved that **1** (pK_a of 4.7) protonates the quinuclidine N atom of CD. There is a second H-bond between the carbonyl O atom of **1** and the OH group of CD. This type of interaction has been confirmed by catalytic and spectroscopic measurements, and quantum chemical calculations, involving several derivatives of CD and **1**.



CD 1

[1] Borszeky, K., Mallat, T. and Baiker, A., *Tetrahedron: Asym.* **10**, 4781 (1999).
[2] Nitta, Y. and Kobiro, K., *Chem. Lett.* (1996) 897.
[3] Huck, W.-R., Mallat, T., Baiker, A., *J. Catal.* **193**, 1 (2000).

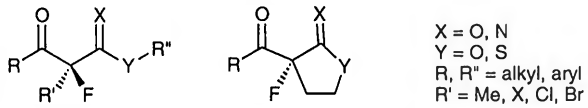
Organic Chemistry 195

Further Development of Catalytic Enantioselective Fluorination

M. Sanna, I. Devillers, L. Hintermann, M. Perseghini and A. Togni
Department of Chemistry, ETH Hönggerberg, CH-8093 Zürich

The first catalytic and enantioselective C-H bond-forming reaction uses Ti(TADDOLato) complexes as effective catalysts and β-keto esters as enolizable substrates [1].

Electronic and steric modifications of the β-keto ester were performed and the catalytic system has been successfully transferred to other classes of substrates, such as, e.g., keto-lactones, β-keto amides, and 1,3 diketones. Those substrates smoothly react with F-TEDA. However, the enantioselectivity of those reactions is in general lower than with β-keto esters.



[1] Hintermann, L.; Togni, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 4359.

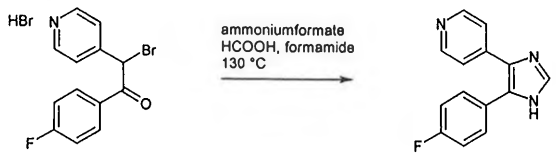
Organic Chemistry 196

Laboratory Automation in Process R&D; Investigation of the Bredereck Reaction for the Preparation of Disubstituted Imidazoles

G. Koch and W. Prikoszovich

Novartis Pharma AG, CHAD, Process R&D
4002 Basel, Switzerland

The condensation/cyclization of α-haloketones with excess of formamide at high temperatures is known as the Bredereck reaction [1]. Using automated parallel solution phase synthesis equipment excellent reaction conditions for the synthesis of bisarylimidazoles [2,3] were found. Screening of reagents and reaction parameters resulted in process conditions which lead to high yield and high purity products. The process was successfully transferred into the production scale. Optimization and investigation of alternative building blocks will also be discussed.



[1] Bredereck, H.; *et al. Angew. Chemie* **1959**, *71*, 753.
[2] Revesz, L. *et al. Bioorg. Med. Chem. Lett.* **2000**, *10*(11), 1261.
[3] Revesz, L. *PCT Int. Appl.* **1999**, WO 9901449 A1.

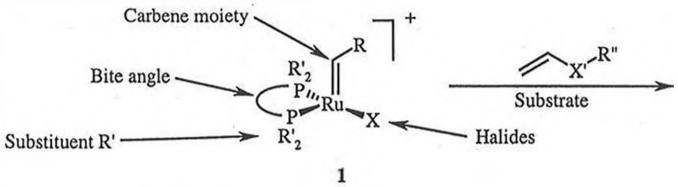
Organic Chemistry 197

Catalyst Screening by Electrospray Ionization Tandem Mass Spectrometry: Hofmann Carbenes for Olefin Metathesis

Christian Adlhart[a], Martin A. O. Volland[b], Peter Chen[a] and Peter Hofmann[b]

[a]Swiss Federal Institute of Technology, 8092 Zürich, Switzerland.
[b]University of Heidelberg, 69120 Heidelberg, Germany.

A new screening methodology combining *in situ* synthesis of complexes with an assay by electrospray ionization tandem mass spectrometry (ESI-MS) was introduced, in order to investigate the highly active Hofmann ruthenium carbene catalysts $[R_2P(CH_2)_nPR_2\text{-}\kappa^2P)XRu{=}CHR']_2(OTf)_2$ [1] in ring opening olefin metathesis (ROMP) . The parameter space, defined by systematic variation of four structural features of the catalyst **1**, the halogen ligand, the diphosphine bite angle, the steric bulk of the phosphine, and the carbene ligand, plus variation of the metathesis substrate, was mapped out. Chloride as anionic ligand X, a small chelating angle (n = 1), and reduced steric demand of the substituents R' (Cy *versus* ^{t}Bu) lead to the most reactive complex in acyclic olefin metathesis, whereas variation of the carbene moiety CHR has only little influence.



1

The overall rate depends on the π-complex preequilibrium and metallacyclobutane formation, which was found to be the rate-determining step. In ROMP reactions backbiting has a profound influence on the overall rate. Moreover, we were able to establish that the reactivity trends determined in the gas phase parallel solution phase reactivity.

[1] Hansen, S. M.; Volland, M. A. O.; Rominger, F.; Eisenträger, F.; Hofmann, P. *Angew. Chem. Int. Ed.* **1999**, *38*, 1273.

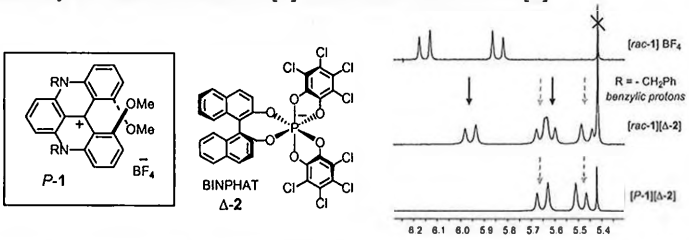
Organic Chemistry **198**

One-Step Synthesis, Resolution and Configurational Stability of Novel [4]-Helicenium Cationic Dyes

Christelle Herse, Bo Laursen, Jérôme Lacour *

Department of Organic Chemistry, Université de Genève, Switzerland

Stabilized carbenium ions such as triarylmethyl, xanthyl and acridinium cations are organic compounds of scientific and commercial importance. Recently, Laursen and Krebs reported a simple one-step synthesis of novel cationic dyes, e.g. $DMQA^+$ **1**, of unusually high chemical stability.[1] We now present preliminary results on the resolution and configurational stability of these new cationic [4]-helicenium derivatives. [2]



Simple treatment of [*rac*-**1**][BF_4] (R = *n*-Pr, Bn) with [Me_2NH_2][Λ-BINPHAT (**2**)] salts affords diastereomeric [*rac*-**1**][Λ-**2**] ion pairs which are easily monitored by ^{1}H NMR as anion **2** behaves as a NMR chiral shift agent. [*P*-**1**][Λ-**2**] and [*M*-**1**][Λ-**2**] salts are then separated by precipitation. Hydride reduction affords enantioenriched neutral triarylmethane derivatives free of the chiral auxiliary. Reoxidation affords enantioenriched [*P*-**1**] or [*M*-**1**][X] salts (X = I or PF_6). Initial studies indicate a high configurational stability for cations **1** as racemization is observed only at or above 170 °C.

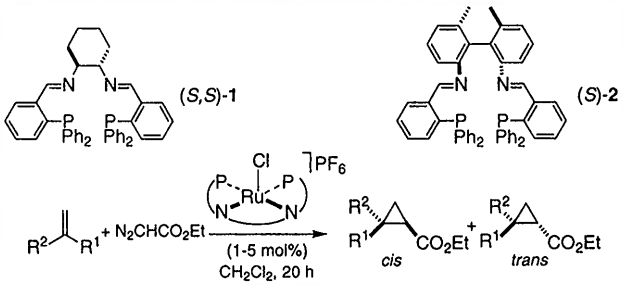
[1] Laursen, B. W.; Krebs, F. C. *Angew. Chem. Int. Ed.* **2000**, *39*, 3432. [2] Katz, T. J. *Angew. Chem. Int. Ed.* 2000, *39*, 1921 and references therein. [3] Lacour, J.; Londez, A.; Goujon-Ginglinger, C.; Buss, V.; Bernardinelli, G. *Org. Lett.* **2000**, *2*, 4185.

Inorganic and Coordination Chemistry **199**

Asymmetric Cyclopropanation of Olefins Catalyzed by [RuCl(PNNP)]$^+$

Stephan Bachmann and Antonio Mezzetti*
Department of Chemistry, ETH Hönggerberg, CH-8093 Zürich

We have reported that five-coordinate $[RuCl(1)]^+$ is a highly cis- and enantioselective catalyst for the cyclopropanation of styrene with diazoesters (ee>90%) [1]. Herein we describe the reaction with other olefins:



run	cat.	mol%	R^1	R^2	yield (%)	cis:trans	ee cis (%)	ee trans (%)
1	**1**	5	Ph	Me	82	86 : 14	49	7
2	**2**	1	Ph	Me	89	49 : 51	75	27
3	**1**	5	C_6H_{13}	H	20	60 : 40	64	18
4	**2**	1	C_6H_{13}	H	65	24 : 76	85	57

With 1-Me-styrene and 1-octene, ligand **1** gives the highest cis selectivity, but **2** yields the cis isomer with the higher enantioselectivity. 2-Methylstyrene, a 1,2-disubstituted olefin, is nearly unreactive. We also investigated the substrate-based electronic effects in the cyclopropanation of *para*-substituted styrenes, showing that yield, enantio-, and diastereoselectivity increase with increasing electron density at the olefin.

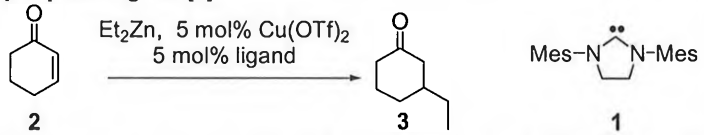
[1] S. Bachmann, M. Furler, A. Mezzetti, *Organometallics*, **2001**, *20*, 2102.

Organic Chemistry **200**

Copper catalysed 1,4-conjugate additions using diaminocarbenes

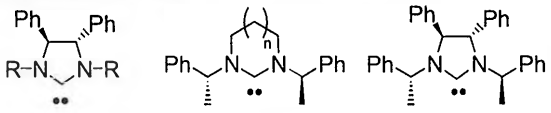
Prof. A. Alexakis Dr F. Guillen Dr C.L. Winn
Université de Genève, Departement de Chimie, Quai Ernest-Ansermet 30, CH-1211, Genève

The copper catalysed addition of organozincs to a range of Michael acceptors using electron rich phosphorus based ligands has been the subject of much investigation.[1] Recently, it has been shown that it is also possible to use the stabilised carbene ligand (**1**) due to its electronic similarity to the phosphorus ligands.[2]



2 **3** **1**

The reaction is carried out using the corresponding imidazolinium salt which is deprotonated *in situ* to give the desired carbene. Initial investigations have shown that it is possible to achieve enantiomerically enriched products (**3**) when chiral diaminocarbene complexes are employed such as those shown below.



The scope of this reaction, its optimisation and extension to include the use of other electrophiles is curently under investigation.

[1a] Alexakis, A.; Frutos, J.C.; Mangeney, P., *Tetrahedron Asymmetry*, **1993**, *4*, 2427-2430. [1b] Krause, N.; Hoffmann-Roder, A., *Synthesis*, **2001**, 121-196.
[2] Fraser, P.K.; Woodward, S., *Tetrahedron Lett.*, **2001**, *42*, 2747-2749.

Organic Chemistry **201**

HDN network of 2-methyl-piperidine on $NiMo/Al_2O_3$catalyst

M. Egorova, Y. Zhao, P. Kukula, R. Prins
Laboratory for Technical Chemistry
Swiss Federal Institute of Technology (ETH), 8092 Zuerich, Switzerland

Hydrodenitrogenation (HDN) ranks among the main hydroprocessing reaction. Pyridine (Py) is one of the simplest heterocyclic N-molecules which are known to be the most difficult to convert to hydrocarbons. Although a lot is known and has been published about the mechanism and kinetics of Py HDN [1], the side reaction of condensation and formation of such a product as N-pentylpiperidine hinder the quantitative analysis [2]. However, the presence of one methyl group in the molecule at the position next to nitrogen can fully prevent the formation of unwanted products.

The reaction network of 2-methyl-piperidine has been studied in order to clarify the mechanism of HDN of 2-methyl-pyridine on $NiMo/Al_2O_3$ catalyst. The overall scheme of the reaction is shown in Figure1. The cleavage of 2-methyl-piperidine ring mostly takes place between the nitrogen atom and the methylene group and not between the nitrogen atom and the carbon substituted with methyl group.

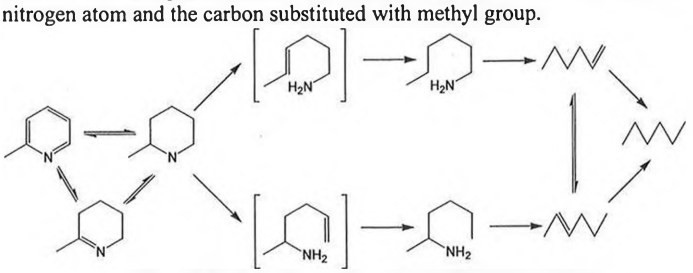


Figure1. Hydrodenitrogenation network of 2-methyl-pyridine.

[1] H.G. McIlvried, Ind. Eng. Chem. Process Des. Dev., 10, 125, (1971)
[2] M.J. Gigis, B.C. Gates, Ind. Eng. Chem. Res., 30, 2021, (1991).

CHIMIA 2001, 55, No. 7/8

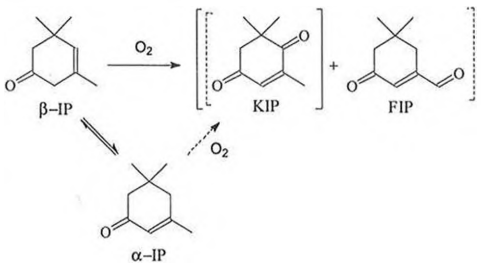
Organic Chemistry **202**

Isophorone Oxidation to Ketoisophorone

E.F. Murphy and A. Baiker

Laboratory of Technical Chemistry,
Swiss Federal Institute of Technology,
ETH-Zentrum, CH-8092 Zürich, Switzerland

Selective aerobic allylic oxidation of cyclic olefins, such as isophorone, is a chemically demanding reaction [1]. Industrial interest in the conversion of α-isophorone (α-IP) to ketoisophorone (KIP) stems from its ready availability and the utility of ketoisophorone as an intermediate for the preparation of various flavoring and fragrance fine chemicals. Our investigations have provided improved homogeneous catalysts, new supported catalysts via heterogenization of homogeneous precursors, and an evaluation of the gas phase for oxidation of isophorone. NMR H/D-exchange experiments and quantum calculations are used to rationalize the different behaviors of the isophorone isomers in solution.



[1] E.F. Murphy, T. Mallat, A. Baiker, *Catal. Today* **57** (2000) 115.

Organic Chemistry **203**

Waterproof Polyacrylonitrile Textiles by application of a Low-Pressure Plasma Process

[a]F. Hochart, [b]J. Grützmacher-Levalois*, [a]R. De Jaeger

[a]Laboratoire de Spectrochimie Infrarouge et Raman, USTL, F-59655 Villeneuve d'Ascq.
[b]Laboratorium für Anorganische Chemie, ETH-Z, Universitätstr. 6, CH-8092 Zürich.

Fluorine derivatives - monomers, oligomers or polymers – are widely used for the coating of substrates such as textiles, papers, leather, wood, etc. in order to obtain oil- and water-repellent surfaces. For this purpose, fluoroalkyl compounds and particularly the perfluoalkyl(meth)acrylates, as their homo and copolymers, are actually the most effective.

Several wet treatments have been previously made, but the increase interest in industrial applications prompted the search for more profitable and environmentally clean processes, such as low-pressure plasma techniques. Moreover, the effect of the plasma treatment has the advantage to be mostly limited to the surface thickness of the material.

The application of a low-pressure plasma process to waterproof polyacrylonitrile textiles is presented. In a first step, the kinetic of homopolymerisation of AC8 [$C_8F_{17}(CH_2)OC(O)CH=CH_2$] was studied. The grafting and the polymerisation were evidenced by IR(ATR) and MEB spectroscopies and the impermeability of the textiles by Schmerber tests.

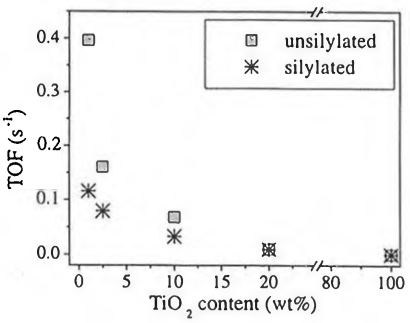
These tests allowed us to appreciate also the effect of a superficial reorientation of the fluorinated chains and also the role played by addition of a small amount of cross-linking agent on the surface properties.

Organic Chemistry **204**

Nature of Active Sites in Sol-Gel TiO_2-SiO_2 Epoxidation Catalysts

Carsten Beck, Tamas Mallat, Thomas Bürgi and Alfons Baiker

Laboratorium für Technische Chemie, ETH-Zentrum
CH-8092 Zürich.



A series of titania-silica aerogels with 0 - 100 wt% TiO_2 content were synthesized and characterized by N_2-physisorption, DRIFT, UV-Vis, XPS and ^{29}Si CP/MAS NMR analysis. It is shown that kinetic analysis of the epoxidation of 2-cyclohexene-1-ol (**1**) with TBHP is an informative test reaction providing insight into the nature of active sites. The surface area, pore volume, hydrophobicity and the relative abundance of Ti-O-Si linkages in the aerogels decreased with increasing Ti/Si ratio. Parallel to these changes, also the initial rate of epoxide formation per Ti site (TOF, see Figure) and the epoxide selectivity decreased but the productivity of the catalysts went through a maximum at 10 wt% TiO_2. We propose that due to kinetic effects in the sol-gel synthesis the whole range of active Ti sites may be present in the mixed oxides, spanning from tetrahedral Ti isolated by four SiO- groups to octahedral Ti surrounded by six TiO-groups in titania nanodomains. Ether formation from **1** was catalyzed by Brønsted sites present only on high titania-containing aerogels. Oligomerization was a major side reaction on all catalysts including Ti-free silica. Si-free titania was the most active in allylic oxidation of **1** to cyclohexenone. Silylation, or amine (Me_2BuN) addition to the reaction mixture, eliminated ether formation and suppressed oligomerization.

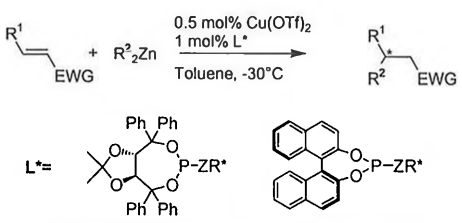
Organic Chemistry **205**

Improved Diversity of Michael Acceptors in Asymmetric Conjugate Addition reactions

Alexandre Alexakis and Cyril Benhaim

Université de Genève, Département de chimie organique,
Quai Ernest-Ansermet 30, CH-1211 Genève 4

The copper catalysed 1,4 conjugate addition of diorganozinc reagents to α,β insaturated systems is a good way to introduce new carbon carbon bond.[1]



We have synthesised a large variety of chiral ligands containing a TADDOL or binaphthol moiety, and tested them in the 1,4 conjugate addition of organozincs to different kinds of enones.[2] More recently they have been tested with success onto nitro olefins.[3] We now report the first copper catalysed asymmetric conjugate addition of organozincs onto alkyl and arylidene malonates with good yield and selectivities.[4]

[1] Alexakis, A.; Frutos, J.; Mangeney, P. *Tetrahedron: Asymmetry* **1993**, *4*, 2427; Alexakis, A.; Vastra, J.; Mangeney, P. *Tetrahedron: Asymmetry* **1997**, *38*, 7745-7748.
[2] Alexakis, A.; Vastra, J.; Burton, J.; Benhaim, C.; Mangeney, P. *Tetrahedron Lett.* **1998**, *39*, 7869; A. Alexakis, C. Benhaim, X. Fournioux, A. Van den Heuvel, J.M. Levêque, S. March, S. Rosset, *Synlett* **1999**, 1911.
[3] A. Alexakis, C. Benhaim; *Org. Lett.*, **2000**, 2579-2581.
[4] A. Alexakis, C. Benhaim; *Tetrahedron: Asymmetry* **2001**, In Press.

Organic Chemistry **206**

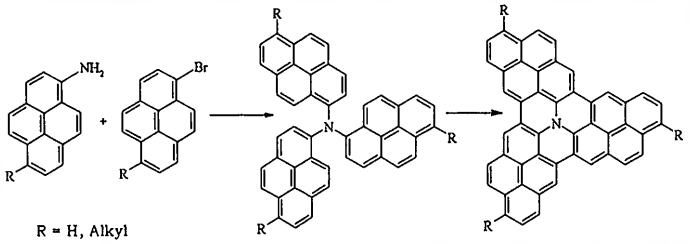
Synthesis and Investigation of New Triaryl Amine Compounds

B. Alameddine, and T.A. Jenny

University of Fribourg, Institute of Organic Chemistry
1700 Fribourg, Switzerland

Self assembled organic molecules have gained a lot of interest in the last two decades [1] among others in the field of electronic emission and luminescence phenomena. Our study focuses on the synthesis and the characterization of an extended nitrogen containing aromatic systems able to arrange themselves in highly conducting stacks. Alkyl chains act as solubilizing substituents, the central nitrogen atom is expected to enhance the charge carrier properties.

Suitably substituted pyrene derivatives are coupled under palladium catalysis according to a standard protocol [2]. The oxidative coupling is achieved by Fe(III) in nitromethane.



[1] A.M. Van de Craats, J.M. Warman, K. Müllen, Y. Geerts, J.D., Brand, *Adv. Mater.* 1998,10,*36*
[2] T. Yamamoto, M. Nishiyama, Y. Koie, *Tetr. Lett.*, 1998,39,*2367*

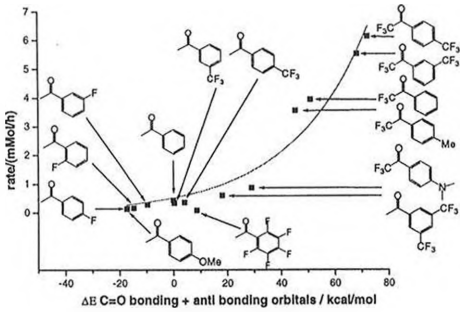
Organic Chemistry **207**

Origin of Rate Acceleration in Enantioselective Hydrogenation of α-functionalised Ketones over Cinchona Alkaloid Modified Platinum.

A. Vargas, T. Bürgi and A. Baiker*

Swiss Federal Institute of Technology, Laboratory of Technical Chemistry
8049 Zurich, Switzerland

A striking correlation between the reactivity of the carbonyl group towards hydrogenation and the stability of the carbonyl π orbitals of substituted acetophenones leads to an explanation of the often observed rate acceleration in the enantio-selective hydrogenation of ketones over cinchona alkaloid modified platinum. The proposed hydrogen bond interaction between the alkaloid and the ketone [**1**] lowers the carbonyl orbitals energy promoting their interaction with the surface hydrogen orbitals. This leads to a lowering of the transition state energy for the enantioselective with respect to the racemic pathway and thus to the observed rate acceleration.



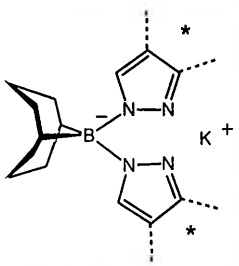
[**1**] O. Schwalm, B. Minder, J. Weber and A. Baiker, *Catal. Lett.*, 1994, **23**, 271 .

Organic and Inorganic Chemistry **208**

Synthesis and Catalytic Asymmetric Applications of Chiral Pyrazolylborate Anions

Virginie Hebbe and Jérome Lacour*

Department of Organic Chemistry, Université de Genève, 1211 Genève 4



Pyrazolylborate anions, first introduced by Trofimenko in 1967, have been widely used in coordination chemistry.[1] Recently, novel bis(pyrazolyl)borate anions containing a 9-borabicyclo[3.3.1] (9-BBN) fragment have been synthesized and studied by Trofimenko and Venanzi.[2] However, only little work has been devoted to these derivatives in enantiopure form. We therefore envisioned preparing chiral bis(pyrazolyl)borate anions made of chiral 1-pyrazolyl ligands –derived from camphor, β-pinene or menthone– and 9-BBN, and study their behavior as chiral ligands or auxiliaries.

We now report the synthesis and the characterization of these derivatives as their Rh and Ir complexes and their first applications in enantioselective hydrogenation reactions. Further use of these borate anions in enantioselective aziridination reaction will also be presented.

[1] a) S. Trofimenko, *J. Am. Chem. Soc.* **1967**, *86*, 6288; b) S. Trofimenko, *Chem. Rev.* **1993**, *93*, 943.
[2] a) S. Trofimenko, J. Calabrese, J. Thompson, *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 205; b) M. Bortolin, U. Buchner, H. Rüegger, L. Venanzi *Organometallics* **1992**, *11*, 2514.

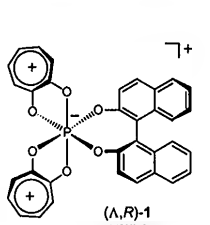
Organic Chemistry **209**

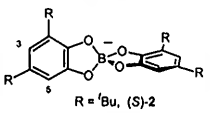
One-Step Asymmetric Synthesis and Applications of a New C_2-Symmetric Hexacoordinated Phosphorus Cation

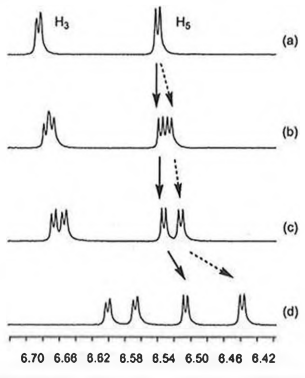
Laurent Vial and Jérôme Lacour*

Department of Organic Chemistry, Université de Genève, Switzerland

Chiral cations are the subject of attention due to the potential of these molecules to serve as asymmetric phase transfer catalysts.[1] In this context, we are looking into the use of hexacoordinated phosphates as structural scaffolds for these derivatives.[2] Herein, we report on the asymmetric synthesis of a new chiral phosphate cation (**1**, BINTROP) prepared in one-step from tropolone, BINOL and PCl_5 (d.e. > 96%) and on its NMR chiral shift properties.[3]







^{1}H RMN (400 MHz, $CDCl_3$) : (a) *rac*-**2**; (b) *rac*-**2** + 0.07 [Λ-1]Cl; (c) *rac*-**2** + 0.14 [Λ-1]Cl; (d) *rac*-**2** + 0.58 [Λ-1]Cl.

[1] (a).Nelson, A. *Angew. Chem. Int Ed.* **1999**, *38*, 1583; (b). Ooi, T; Takeuchi, M.; Kameda, M.; Maruoka, K. *J. Am. Chem. Soc.* **2000**, *122*, 5228; [2] (a). Sheldrick, W.S.; Schmidpeter, A.; von Griege, T. *Z. Naturforsch. B., Teil B*, **1978**, *33*, 583; (b). Muetterties, E.L.; Wright, C.M. *J. Am. Chem. Soc.* **1964**, *86*, 5132; [3] Vial, L.; Lacour, J. *Submitted*.

CHIMIA 2001, 55, No. 7/8

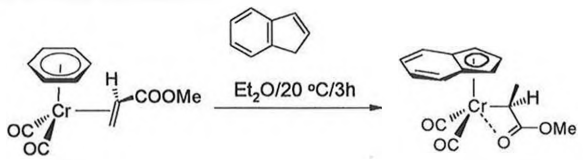
Organic chemistry **210**

Labilizing a Robust Arene-Metal Bond: Mechanistic and Catalytic Studies

Mikhail Kondratenko, E. Peter Kündig, Gérald Bernardinelli, Fabrice Robvieux, Patrick Romanens

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

Complexation of an arene to the electrophilic $Cr(CO)_3$ moiety dramatically changes the reactivity of the arene and this has led to many applications in synthesis[1]. With the target of a catalytic electrophilic activation of arenes we have investigated derivatives that allow arene exchange under mild conditions and found that the acrylate ligand in **1** drastically lowers the barrier for arene exchange.[2] In this communication we present new chemistry of this system. For example, complex **1** reacts at 20 °C with indene to undergo arene exchange, haptotropic rearrangement and H-migration to the acrylate to form the new Cr-enolate **2**.



1 **2** (80%)

In a further development of the use of the labile complex **1**, we have now found that **1** is an efficient catalyst for cycloaddition reactions under mild conditions.

[1] Pape, A. R.; Kaliappan, K. P.; Kündig, E. P. *Chem. Rev.* **2000**, *100*, 2917.

[2] Kondratenko, M.; Romanens, P.; Kündig, E. P. *Ang. Chem. Int. Ed. Engl.*, **1998**, *37*, 3146.

Organic Chemistry **211**

Synthesis of New *P^N*-Ligands with Configurationally Unstable Axial Chirality

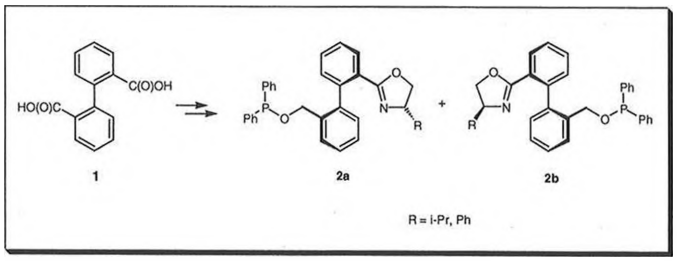
M. Kalbermatter and A.J. Rippert*

University of Zurich, Institute of Organic Chemistry
8057 Zurich, Switzerland

Starting from diphenic acid (**1**) the new axially chiral *P^N*-Ligands **2** have been synthesized efficiently (see equation below). Key step is the reduction of an ester group in the presence of a dihydrooxazole ring.

The resulting diastereoisomers **2a** and **2b** are interconvertable at rt but on the NMR time-scale the two different isomers can be observed clearly. Upon complexation to a metal ion the axial chirality is fixed and therefore two diastereomeric complexes can be formed to influence the selectivity of asymmetric transition-metal catalysed reactions.

Synthesis, spectroscopic data and first results in asymmetric catalysis will be presented and compared with corresponding ligands bearing the same functional groups but containing a fixed axial chirality.



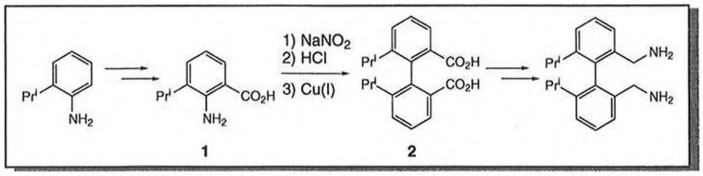
Organic Chemistry **212**

A Biphenyl Carrying Sterically Demanding *Ortho*-Substituents

F. Keller, A. Linden, A.J. Rippert*

University of Zurich, Institute of Organic Chemistry
8057 Zurich, Switzerland

The synthesis of 6,6'-diisopropyl-1,1'-biphenyl-2,2'dicarboxylic acid (**2**) is shown below.



The starting compound is 2-isopropylaniline, which can be transformed *via* the isopropyl substituted isatin to the 3-isopropylanthranilic acid (**1**) [1]. Coupling of the corresponding diazonium salt, derived from **1**, was performed in the usual manner [2]. We could isolate **2** in up to 50% yield. An X-ray crystal structure analysis of **2** showed a significant increase of the torsion angle between the aromatic planes compared with the dimethyl analogue [3] (85°—> 95°).

Transformation of the acid groups and optical resolution is described.

[1] C.A. Demerson, L.G. Humber, A.H. Philipp, *J. Med. Chem.* **1976**, *19*, 391.

[2] F. Keller, A.J. Rippert, *Helv Chim. Acta*, **1999**, *82*, 125.

[3] R.E. Gerkin, *Acta Cryst. C*, **1998**, *C54*, 1369.

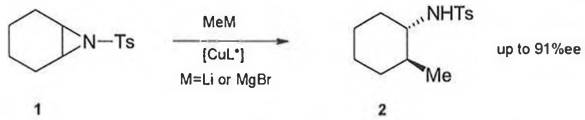
Organic chemistry **213**

Desymmetrisation of *meso*-aziridines

P. Müller, P. Nury and D. Ricgert

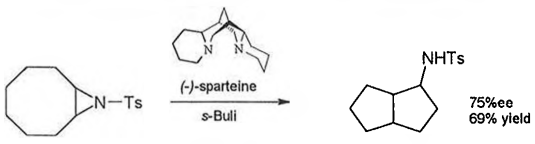
Département de Chimie Organique, Université de Genève,
30, Quai Ernest-Ansermet, CH-1211 Genève 4, Switzerland.

Enantioselective ring-opening of *meso*-epoxides is a well established process allowing access to enantiopure 2-substitued alcohols. In contrast, the corresponding desymmetrisation of aziridines is much less known. Herein we report two different approaches for desymmetrisation of *N*-sulfonated aziridines : the cyclohexene *N-p*-toluenesulfonylimine **1** *(scheme 1)* undergoes ring-opening to **2** upon treatment with Grignard or organolithium reagents such as MeLi in the presence of a chiral Cu-catalyst with up to 91% enantiomeric excess.[1]



scheme 1

Desymmetrisation of *meso*-aziridines may also be realized *via* enantioselective α-deprotonation *(scheme 2)* with *s*-BuLi in conjunction with a chiral ligand such as *(-)*-sparteine. The intermediate carbanion suffers α-elimination to afford a carbene wich reacts further by hydrogen migration to afford an allylic sulfonamide, or by insertion into an appropriately situated CH bond.[2]



scheme 2

[1] P. Müller, P. Nury, *Org. Letters* **1999**, 1 (3), 439-441.

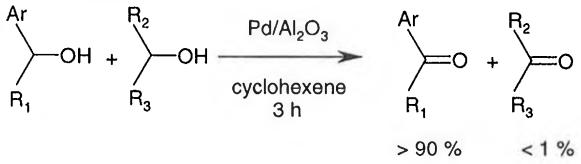
[2] P. Müller, P. Nury, *Helv. Chim. Acta*, **2001**, *84*, 662-677.

Organic Chemistry **214**

Selective Transfer Dehydrogenation of Aromatic Alcohols on Supported Palladium

Cs. Keresszegi, T. Mallat and A. Baiker
Laboratory of Technical Chemistry, ETH Zentrum, CH–8092 Zurich

Oxidation of alcohols to carbonyl compounds is a fundamental reaction in synthetic chemistry. From an environmental point of view, a highly attractive method is the oxidative dehydrogenation over heterogeneous noble metal catalysts in aqueous medium, using molecular oxygen as oxidant.[1] Replacing molecular oxygen by an unsaturated organic compound (e.g. ethylene) offers the possibility of the selective oxidation of water-insoluble alcohols.[2] In our study liquid olefins were chosen as hydrogen acceptors in the transfer dehydrogenation of various alcohols over heterogeneous palladium catalysts. Pd/Al_2O_3 together with cyclohexene in refluxing cyclohexane is the most active and selective system, affording the simple and convenient laboratory synthesis of aromatic ketones. Hydrogenolysis type side reactions can be suppressed by minute amounts of a tertiary amine (selective poisoning of Pd). Aliphatic and cycloaliphatic alcohols are barely reactive under these conditions. This behaviour offers the possibility of the selective transformation of aromatic alcohols even in the presence of an aliphatic OH group, as shown in the model reaction below.



[1] T. Mallat and A. Baiker, *Catal. Today*, **19** (1994) 247.
[2] M. Hayashi, K. Yamada and S. Nakayama, *J. Chem. Soc. Perkin Trans.* **1** (2000) 1501.

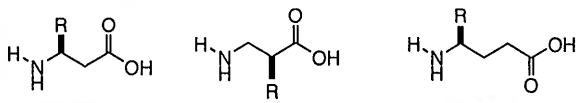
Organic Chemistry **215**

Homologs of Amino Acids Synthesis and Structural Investigations of β- and γ-Peptides

M. Rueping and D. Seebach*

Laboratorium für Organische Chemie
der Eidgenössischen Technischen Hochschule Zürich
Universitätstrasse 16, CH-8092 Zürich, Switzerland

The design, synthesis and structural characterization of molecules forming specific and predictable secondary structures offer new possibilities in the field of molecular recognition, catalysis and protein folding [1]. Therefore unnatural oligomers consisting of β- (**1**,**2**) and of γ-amino acids (**3**) have attracted great attention: these compounds adopt stable secondary structures in solution and in the solid state, fold by a non-cooperative mechanism, are stable to peptidases, mimic α-peptides and show affinity for protein receptors.



Structures such as helices, sheets and turns have been discovered [2]. The influences of side chain and backbone modification on different hydrogen-bonding patterns leading to 3_{14}- or 12/10-helices are discussed. Detailed 2D-NMR spectroscopic studies were undertaken to obtain high-resolution data of the conformations in solution.

[1] E.A. Baron, R.N. Zuckermann, *Curr. Opin. Chem. Biol.*, **1999**, *3*, 714
[2] D. Seebach, J.L. Matthews, *Chem. Commun.*, **1997**, 2015

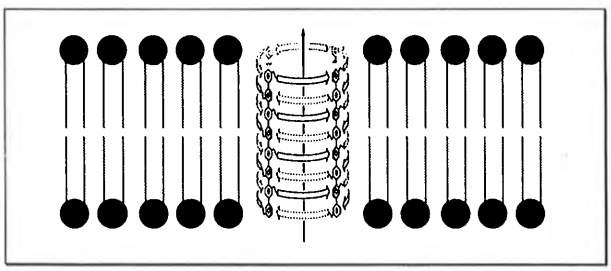
Organic Chemistry **216**

Artificial Ion Channels Formed by Rigid-Rod β-Barrels

B. Baumeister, N. Sakai, and S. Matile*

University of Geneva, Department of Organic Chemistry
1211 Geneva, Switzerland

Design, synthesis and characterization of artificial ion channels formed by rigid-rod β-barrels are reported (*see schematic figure below*) [1-3]. Emphasis is on introduction and expansion of rationally designed functional plasticity. Examples include ion channels with pH-gating, ion channel hosts for membrane-spanning "mini"-B-DNAs, and catalytic ion channels with hydrolytic activity for a broad variety of mono- and oligomeric substrates.



[1] B. Baumeister, N. Sakai, S. Matile, *Angew. Chem., Int. Ed.* **2000**, *39*, 1955.
[2] N. Sakai, B. Baumeister, S. Matile, *ChemBioChem* **2000**, *1*, 123.
[3] B. Baumeister, G. Das, N. Sakai, S. Matile, *Chimia* **2001**, *55*, 302.

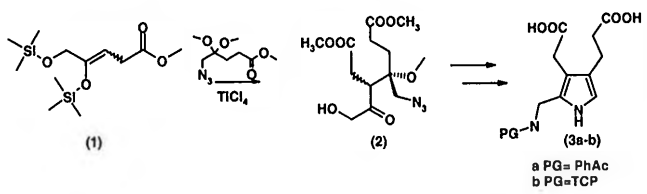
Organic chemistry **217**

Recent progress towards a practical synthesis of porphobilinogen

Carole Pissot Soldermann, Reinhard Neier*
Université de Neuchâtel, Institut de chimie, Av. Bellevaux 51,
2007 Neuchâtel, Switzerland

A biomimetic synthesis of Porphobilinogen (PBG), the pyrrolic precursor of the tetrapyrrolic skeleton of all 'pigments of life' was developed in our group based on the enzyme mechanism postulated by Shemin in 1968 [1]. A protected form of PBG could be synthesized [2]. However, the deprotection proved to be the major obstacle in our synthetic strategy.

An efficient and convergent preparation of a stable PBG precursor in a "ready to use" form has been achieved using a Mukaiyama crossed aldol reaction affording the key intermediate (**2**). Moreover, the deprotection step via an enzymatic way (**3a**) or via mild condition (**3b**) suffice to provide readily free PBG.



[1] D.L. Nandi, D. Shemin, J. Biol. Chem., **1968**, 243, 1236
[2] A. R. Chaperon, T. M. Engeloch, R. Neier, Angew. Chem. Int. Ed. , **1998**, 37, 338

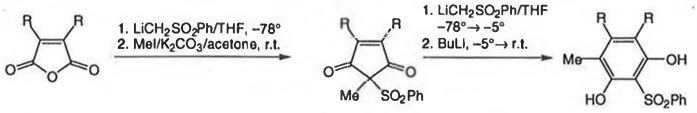
Organic Chemistry **218**

A New "One-Pot" Synthesis of Resorcinols also Applicable to the Formation of the Aromatic Ring of Colchicinoids

K. Abou-Hadeed, H.-J. Hansen*

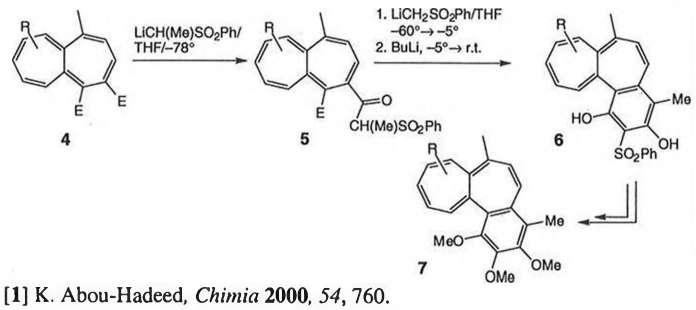
Organisch-chemisches Institut der Universität
CH-8057 Zürich, Winterthurerstrasse 190

Maleic anhydride derivatives **1** can easily be transformed into substituted resorcinols **3** as shown below [1].



1 **2** **3**

The described reaction sequence is also applicable to heptalene-4,5-dicarboxylates **4**, which are transformed with α -lithioethyl phenyl sulfone into **5**. Further transformation of **5** as indicated gives directly the phenylsulfonyl substituted 4-methyl-benzo[*a*]heptalene-1,3-diols **6**. Finally, after reductive removal of $PhSO_2$ group, the 1,3-dimethoxy-benzo[*a*]heptalene can be oxidized with BuLi/CuBr/O_2 in THF to yield, after methylation, the 4-methyl-1,2,3-trimethoxy-benzo[*a*]heptalenes **7**.



4 **5** **6** **7**

[1] K. Abou-Hadeed, *Chimia* **2000**, *54*, 760.

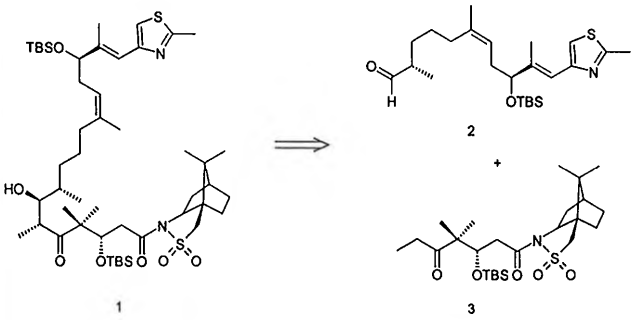
Organic Chemistry **219**

Investigation of Aldol Processes for the Total Synthesis of the Epothilones and Their Derivatives

G. Koch, K.-H. Altmann, D. Fuentes, A. Jantsch, O. Loiseleur and A. Schmidt

Novartis Pharma AG, 4002 Basel, Switzerland

The stereoselective aldol reaction is a powerful methodology for the construction of complex natural products. We discuss herein the elaboration of a process which relies on intrinsic stereocontrol for the connection of the fragments **2** and **3** to the Epothilone precursor **1**.



1 **2** **3**

The application of this process to a new efficient synthetic approach towards the Epothilones and their derivatives will also be presented.

Organic Chemistry **220**

Phosphine substituted Porphyrins in Supramolecular Assemblies

Eugen Stulz, Yiu-Fai Ng, Andrew D. Bond and Jeremy K.M. Sanders*

University Chemical Laboratory, University of Cambridge
Cambridge CB2 1EW, UK.

We have recently synthesised non-covalently assembled heterometallic porphyrin oligomers, driven by the synergistic coordination of orthogonally substituted porphyrins, employing Zn(II)-nitrogen, Sn(IV)-oxygen and Ru(II)-nitrogen affinity [1]. Additionally, we have begun to explore Ru(II)-phosphorous coordination to obtain new building blocks for supramolecular arrays [2]. Here we describe the synthesis and characterisation of mono- and bis-phosphino substituted porphyrins and their coordination behaviour to metallo porphyrins containing soft metals such as Ru(II) and Rh(III). The coordination arrays were characterised by NMR spectroscopy, MALDI-TOF mass spectrometry and X-ray crystallography.

Fig 1: X-ray structure of a Ru(II) porphyrin, complexed by two diphenyl phosphine substituted Ni(II) porphyrins.

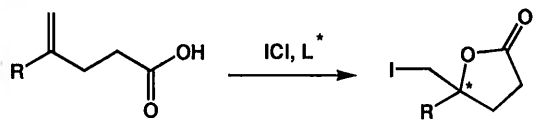
[1] H.J. Kim, N. Bampos and J.K.M. Sanders, *J. Am. Chem. Soc.* **1999**, *121(35)*, 8120.
[2] S. L. Darling, E. Stulz, N. Feeder, N. Bampos, J.K.M. Sanders, *New J. Chem.* **2000**, 261.

Organic Chemistry **221**

Chiral I^+?

J. Haas, T. Wirth*
Department of Chemistry, Cardiff University, P.O. Box 912, Cardiff CF10 3TB, United Kingdom (wirth@cf.ac.uk)

Iodocyclisations (like **1** -> **2**) have been well-known for a long time and the conditions often applied are still similar to the original ones, using iodine and a base in an aqueous solvent.[1] Other conditions and sources of I^+ have also been successfully investigated leading to very mild reactions.[2] These reactions are versatile in heterocyclic synthesis, allowing key intermediates in the syntheses of complex target molecules to be prepared easily.



1 **2**

While *substrate-controlled* lactonisations with the chiral moiety covalently attached to the molecule often result in good stereoselectivities,[3] *reagent-controlled* versions applying a chiral ligand are hitherto unknown. We found that enantiopure primary amines are efficient ligands for the reaction shown above. Results towards the development of stereoselective halocyclisations will be presented.

[1] M. J. Bougault, *Ann. Chim. Phys.* **1908**, *14*, 145.
[2] J. H. Schauble, J. W. Magee, R. D. Evans, *Synthesis* **1988**, 863–868.
[3] S. Najdi, D. Reichlin, M. J. Kurth, *J. Org. Chem.* **1990**, *55*, 6241–6244.

Organic Chemistry **222**

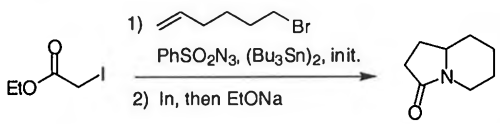
Pyrrolizidines and Indolizidines via a Radical Addition-Azidation Procedure

Philippe Panchaud, Cyril Ollivier and Philippe Renaud

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

We have recently reported that simple radical azidations [1] as well as intramolecular tandem addition-azidation processes [2] are very efficiently performed with sulfonyl azides.

We report here that radicals generated from halides or dithiocarbonates can be used for intermolecular radical addition to alkenes followed by azidation of the resulting radical. Applications to the synthesis of alkaloids such as pyrrolizidines and indolizidines will be presented.



[1] C. Ollivier and P. Renaud, *J. Am. Chem. Soc.* **2000**, 122, 6496.
[2] C. Ollivier and P. Renaud, *J. Am. Chem. Soc.* **2001**, 123, 4717.

Organic Chemistry **223**

A Crown-Capped Iron Porphyrin as New Active Site Model of Cytochrome P450cam

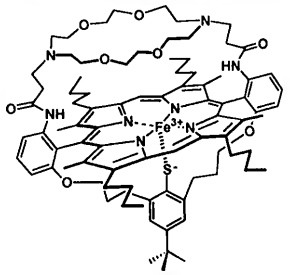
M. Lochner, L. Mu, M. Müller and W.-D. Woggon*

University of Basel, Institute of Organic Chemistry,
St. Johanns-Ring 19, 4056 Basel, Switzerland

The cytochrome P450 family of enzymes is involved in a variety of important biological oxidation reactions.

The crystal structure of the resting state of P450cam [1] revealed a water cluster in the substrate binding pocket whereas one of the water molecules is coordinating to iron as sixth ligand. Surprisingly, this complex is mainly in a low spin state.

We report the synthesis of crown-capped iron porphyrin **1** as novel resting state analogue for P450cam. To investigate whether charges at the protein surface of the substrate binding domain can influence changing of spin states we studied the binding of different ligands and cations to **1** and characterised the spin states of the corresponding complexes by EPR.



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[1] T. L. Poulos *et al.*, *Biochemistry* **1986**, *25*, 5314.

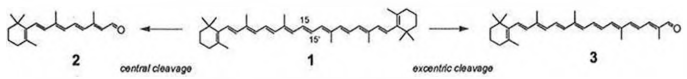
Organic Chemistry **224**

A New Receptor for the Binding of β,β-Carotene

Philipp Holzer, Wolf-D. Woggon*

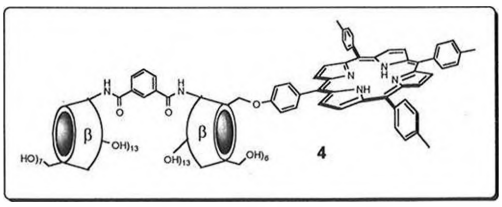
University of Basel, Institute of Organic Chemistry,
St. Johanns-Ring 19, CH – 4056 Basel

The enzymes carotene oxygenases which cleave β,β-carotene (**1**) to provide retinal (**2**) as a precursor for vitamin A are of significance to animal and human nutrition. To date, two modes of cleavage of **1** have been proposed: *i)* the central cleavage of **1** which gives retinal directly, and *ii)* the more recently discovered excentric cleavage which yields first apo-carotenals, such as **3**, which may be degraded to **2** by *β*-oxidation (Scheme 1).



Scheme 1: Metabolism of β,β-carotene

We have recently shown that the central cleavage of **1** can be accomplished using a Ru-porphyrin bis-cyclodextrin catalyst [1][2]. We report here the synthesis of **4**, a new receptor of **1** to furnish a supramolecular system for excentric cleavage.



[1] R.R. French, J. Wirz, W.-D. Woggon, *Helv. Chim. Acta*, **1998**, 1521
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Organic Chemistry **225**

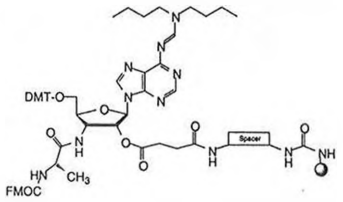
Synthesis and Characterization of 3'-Peptidyl-RNAs

Silvia Terenzi and Peter Strazewski

University of Basel, Institute of Organic Chemistry
4056 Basel, Switzerland

Peptide-oligonucleotide conjugates gained importance in the past years as potential antisense therapeutic agents to inhibit gene expression. The peptidyl moiety can enhance the cellular uptake of oligonucleotides and improve their resistance to nucleases. Conjugates are useful tools not only in molecular biology but they can also be used for structural studies. The goal of our research is to use peptide-RNA conjugates mimicking tRNAs as model molecules to investigate the mechanisms involved in protein biosynthesis.

We report here the synthesis and the characterization of a 3'-peptidyl-RNA consisting of a 22-mer hairpin mimicking the acceptor stem of *E.coli* $tRNA^{Ala}$ linked to an oligoalanine peptide. A new strategy was developed for the synthesis. A fully protected adenosine analog was used as building block after immobilization on solid support.



Different spacers were used to attach the molecule on solid support to study their influence on the quality of the synthesis. CD spectroscopy was used to study the secondary structure of our constructs.

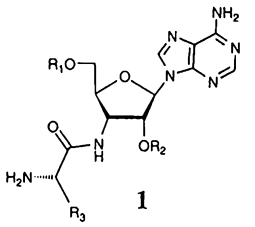
Organic Chemistry **226**

FROM 3'-AMINOACYL RIBONUCLEOSIDES TO 3'-AMINOACYL RNA.

Nhat Quang Nguyen-Trung & Peter Strazewski
Institute of Organic Chemistry, University of Basel,
St. Johanns-Ring 19, CH-4056 BASEL.

Now that the crystal structure of a 50S ribosomal subunit cocrystallized with puromycin analogs is available at 3.3 Å resolution [1], a more reliable knowledge of the ribosomal peptidyl transfer reaction seems within close reach. Studies on the intrinsic conformations of the peptide-accepting 3'-terminus of aminoacyl-tRNA using spectroscopic and computational techniques allows for a better understanding.

We have synthesized puromycin analogs, 3'-aminoacyl-ribonucleosides **1**, have tested their *in vitro* peptide release activity on *E. coli* ribosomes and have studied their conformations by ^{1}H-NMR spectroscopy. We report here the synthesis of oligo 3'-aminoacyl ribonucleotide oligomers **2** of some analogs, obtained by solid-support synthesis, and we analyze the influence on conformation and bioactivity of structures more close to the natural aminoacyl tRNA.



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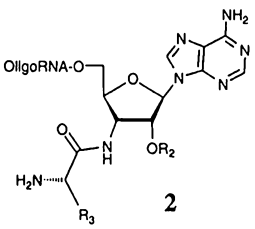


2

[1] Poul Nissen, Jeffrey Hansen, Nenad Ban, Peter B. Moore, Thomas A. Steitz, *Science* **2000**, 289, 920-930.

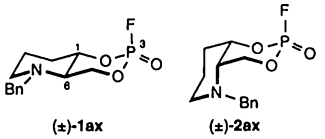
Organische Chemie **228**

Acetylcholine-Mimetic Organophosphates as Inhibitors of Acetylcholinesterase

Stefan Furegati, Anthony Linden, Peter Rüedi*

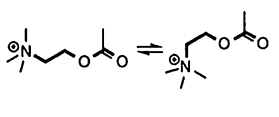
Organisch chemisches Institut, Universität Zürich
Winterthurerstrasse 190, CH-8057 Zürich

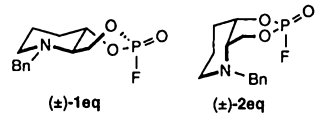
Continuing our studies concerning the irreversible inhibition of acetylcholinesterase (AChE) by organophosphates we have prepared the 7-aza-7-benzyl-3-fluoro-2,4-dioxa-3λ^5-phosphabicyclo[4.4.0]decan-3-ones (±)-**1** and (±)-**2** and the corresponding 7-azonia triflates (±)-**3ax** and (±)-**4ax**. The compounds represent another type of conformatively restricted acetylcholine-mimetics of our aza-oxaphosphadecaline series.



(±)-**1ax**

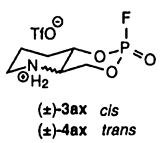
(±)-**2ax**





(±)-**1eq**

(±)-**2eq**



(±)-**3ax** *cis*
(±)-**4ax** *trans*

The *N*-benzylated organophosphates were synthesized from the *cis*- and *trans*-1-benzyl-3-hydroxy-2-(hydroxymethyl)piperidines with $POFCl_2$. The benzyl protecting group of the F-axially substituted congeners were removed by hydrogenolysis to yield (±)-**3ax** and (±)-**4ax**.

The X-ray structures of (±)-**1ax**, (±)-**1eq**, (±)-**2ax** and (±)-**2eq** show the influence of the anomeric effect on the conformations: the F-equatorially substituted epimers crystallized in the unusual chair-twistboat ((±)-**1eq**) and the chair-envelope form ((±)-**2eq**), respectively.

The kinetic survey showed that five of the six acetylcholine-mimetics are irreversible inhibitors of AChE. The resulting tetrahedral phosphate is regarded as a stable transition state analogue of AChE and its natural substrate acetylcholine.

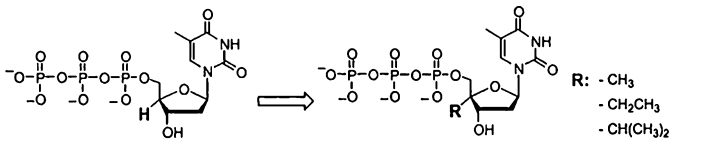
Organic Chemistry **227**

DNA Replication Fidelity besides Nucleobase Recognition

Daniel Summerer, Christian Schneider, and Andreas Marx

Kekulé-Institut für Organische Chemie und Biochemie, Universität Bonn, Gerhard-Domagk-Str. 1, D-53121 Bonn, Germany, a.marx@uni-bonn.de

Among numerous proteins involved in the entire DNA replication machinery DNA polymerases are the central enzymes and contribute to overall selectivity to a great extend [1]. Little is known about sugar recognition processes in DNA replication and their contributions to selectivity. To monitor steric constraints in DNA polymerases within the nucleotide binding pocket acting on the sugar moiety of an incoming nucleoside triphosphate we introduced alkyl side chains as probes [2].



We will report the synthesis of the alkylated triphosphates **T*TP** as well as their action on several DNA polymerases in canonical and non-canonical nucleobase pair formation.

[1] Recent reviews: a) Kunkel, T. A. & Bebenek, K. (2000) *Annu. Rev. Biochem.* **69**, 497–529; b) Kool, E. T., Morales, J. C. & Guckian, K. M. (2000) *Angew. Chem. Int. Ed.* **39**, 991–1009.

[2] Summerer, D. & Marx, A. manuscript submitted.

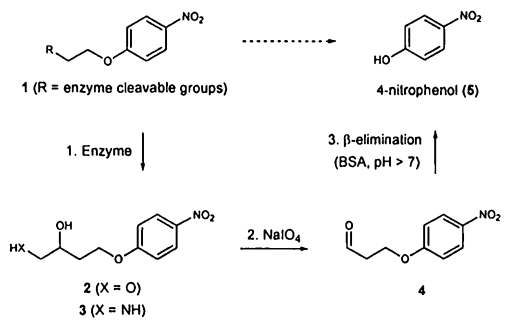
Organic Chemistry **229**

A General Chromo/Fluorogenic Assay for Hydrolytic Enzymes

D. Wahler[1], F. Badalassi[2], P. Crotti[2] and J.-L. Reymond[1,*]

[1]Universität Bern, Dept für Chemie & Biochemie, 3012 Bern, Switzerland
[2]Università di Pisa, Dipartimento di Chimica Bioorganica e Biofarmacia, 56126 Pisa, Italy

Compounds of type **1** have been used as chromogenic or fluorogenic reporters for biocatalysts screening [1,2]. In our method, the carbonyl intermediate **4** is obtained by sodium periodate-catalyzed oxidation of diol **2** or 1,2-amino-alcohol **3** (see figure), affording extended functionalization possibilities concerning the enzyme labile groups. Now more than one hundred derivatives with different side chains and functionalities have been synthesized, giving the possibility of screening for a broad variety of hydrolytic enzymes. We report on results observed in stability, selectivity and sensitivity.



[1] F. Badalassi, D. Wahler, G. Klein, P. Crotti, J.-L. Reymond, *Angew. Chem. Intl. Ed.* **2000**, *39*, 4067-4070.
[2] D. Wahler, J.-L. Reymond, *Curr. Opin. Chem. Biol.* **2001**, *5*, 152-158.

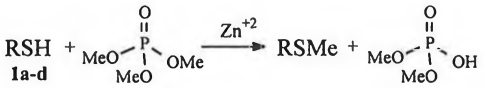
Organic Chemistry **230**

Models for Zn - dependent methyltransferases

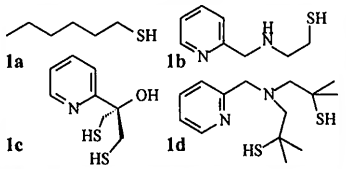
Miguel Machuqueiro and Tamis Darbre*

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

The methylation of thiols 1a-d by trimethyl phosphate (TMP) was investigated as a model for the Zn-dependent enzymatic systems such as the DNA repair protein Ada from E. coli, the cobalamin dependent and independent methionine synthases and others [1].



We observed that only the thiol group in N-(2-Mercaptoethyl)-picoline (1b) is methylated with TMP in the presence of Zn^{+2} under reflux in methanol. The reaction does not occur at RT or in the absence of Zn^{+2}. The preformed complex with two molecules of 1b chelated to the Zn^{+2} can be methylated at room temperature. Stable zinc bound thiolates are probably formed with the chelating thiols 1b-d; the measured rate constants are smaller than the one reported for dissociated thiolates [2]. In order to improve the model, the dinucleotide dTp(OMe)dT was also used as methylating agent.



[1] Matthews, R.G. and Goulding, C.W., Curr. Opin. Chem. Biol., 1, 332 (1997).
[2] Wilker, J.J., Lippard, S.J., Inorg. Chem., 36, 969-978 (1997).

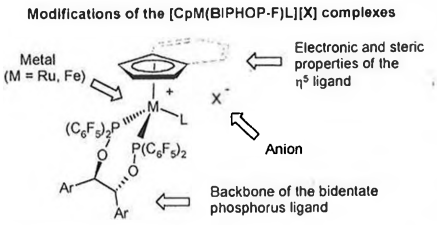
Organic Chemistry **231**

Chiral Ru(II) and Fe(II) Lewis Acids: New Developments and Mechanistic Insights

Florian Viton, Christophe M. Saudan, Valérie Alezra, E. Peter Kündig*

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

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] This contribution focuses on mechanistic insights and kinetic studies involving complexes of this family of Lewis acids. [2] We also report on the development of a new generation of Ru catalysts incorporating an indenyl ligand. These catalysts show very remarkable improvement of the *exo*/*endo* selectivity for the Diels-Alder reaction.



As a further demonstration of the value of this class of compounds, we will present ongoing work in the field of asymmetric catalytic 1,3-dipolar cycloaddition reactions of nitrones.

[1] E. P. Kündig, C. M. Saudan, F. Viton, *Adv. Synth. Catal.* **2001**, *343*, 51-56 and references cited.
[2] In collaboration with A. Merbach (Lausanne) and J. Weber (Geneva).

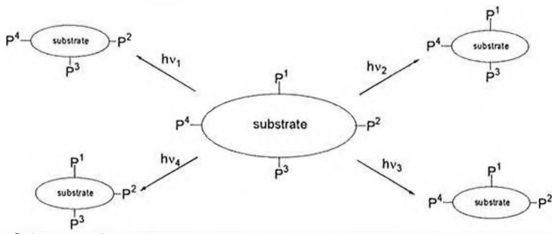
Organic Chemistry **232**

Orthogonal photolysis of protecting groups

Aurélien Blanc, Céline Helgen and Christian G. Bochet*

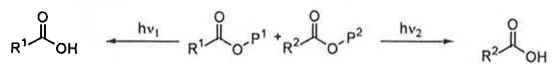
Université de Genève, Département de chimie organique, Quai Ernest-Ansermet 30, CH-1211 Genève 4

A critical goal in the chemistry of protecting groups is the orthogonality, that is, the possibility of selectively removing one group in the presence of others in any chronological sequence. Photolabile protecting groups form an attractive subclass of these groups, since their cleavage does not require any chemical reagent - just light. Chemical orthogonality is a common feature among the classical protecting groups, but chromatic orthogonality has so for never been observed [1] (Scheme 1).



Scheme 1: Chromatic orthogonality of photosensitive protecting groups

We will present our first results in the wavelength-controlled orthogonal deprotection of amines, alcohols and carboxylic acids (Scheme 2).



Scheme 2: Wavelength-selective deprotection of functional groups

[1] C.G. Bochet, *Angew. Chem. Int. Ed. Engl.* **2001**, *40*, 2071-2073.

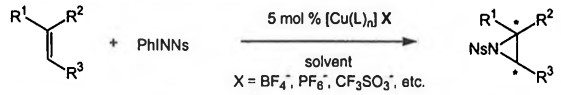
Organic and Inorganic Chemistry **233**

Asymmetric Aziridination of Prochiral Olefins and Predetermination of Configuration of $[Cu(LL')_2]^+$ Complexes by Chiral Phosphate Anions.

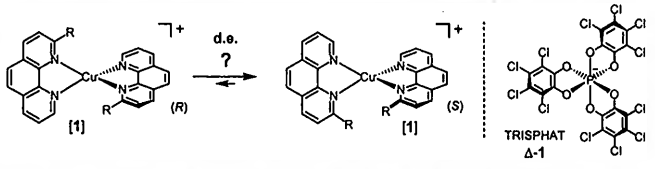
Valérie Desvergnes-Breuil, Jonathan J. Jodry, Jérôme Lacour*

Department of Organic Chemistry, Université de Genève, Switzerland

Enantioselective aziridination of prostereogenic olefins constitutes an appealing strategy for the synthesis of useful enantioenriched intermediates or products. In most studies, the influence on the selectivity of the anion associated with the metallic cations behaving as catalysts was overlooked. Recently, the stereochemical influence of a chiral borate anion on the reaction (ee_{max} 10%) was reported demonstrating the potential of chiral anions to behave as asymmetric inducers. [1]



In this context, we have been interested in studying the asymmetric discriminations occurring between chiral anions, e.g. TRISPHAT **1** [2], and chiral bis(diimine) Cu(I) complexes –these derivatives being potential pre-catalysts for enantioselective aziridination reactions. Preliminary results on the use of hexacoordinated phosphate anions as asymmetric inducers of onto chiral $[Cu(diimine)_2]^+$ complexes and as chiral promoters in asymmetric aziridination reactions are here reported.



[1] Llewellyn, D.B.; Andamson, D.; Arndtsen, B. A. *Org. Lett.* **2000**, *2*, 4165.and references therein. [2] Lacour, J.; Goujon-Ginglinger, C.; Torche-Haldimann, S. *Angew. Chem. Int. Ed.* **2000**, *39*, 3695 and references therein.

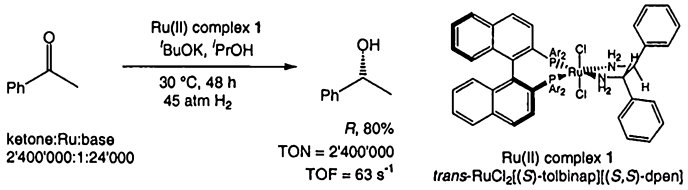
Organic Chemistry **234**

Novel Bimetallic Mechanism for High-activity Asymmetric Hydrogenation of Ketones with Ruthenium Catalysts

R. Hartmann and P. Chen*

Laboratorium für Organische Chemie,
Eidgenössische Technische Hochschule Zürich, Switzerland

Noyori's $RuCl_2$(diphosphine)(diamine) **1** catalysts are among the most exciting catalyst in the ruthenium-catalyzed asymentric hydrogenation of ketones [1]. Catalysts related to **1** show a high chemo- and enantioselectivity with substrate/catalyst (S/C) up to 2'400'000!



We report evidence for novel bimetallic mechanism for the asymmetric hydrogenation of ketones by **1** and seek to answer three important questions:

- What is the mechanistic basis for the high enantio- and chemoselectivity in reductions catalysed by **1**?
- Why does **1** reduce ketones with H_2 when related Ru(II) complexes invariably perform transfer hydrogenation with *iso*-propanol as the hydride source?
- How does **1** achieve S/C of greater than 100'000 when related Ru(II) complexes operate with S/C between 100 and 5000?

The mechanism is validated by salt effects on turn over frequencies (TOF) [2].

[1] R. Noyori, T. Ohkuma, *Angew. Chem. Int. Ed.* **2001**, *40*, 40-73. *Angew. Chem.* **2001**, *113*, 40-75.
[2] R. Hartmann, P. Chen, *Angew. Chem. Int. Ed.*, submitted.

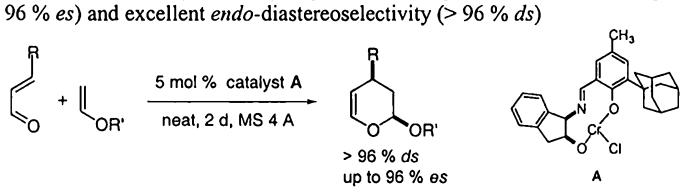
Organic Chemistry **235**

Highly Enantio- and Diastereoselective Hetero *Diels-Alder* Reactions with Inverse Electron Demand Catalyzed by Chromium(III) Schiff Base Complexes

Karl Gademann and Eric N. Jacobsen*

Chemistry and Chemical Biology, Harvard Univ., Cambridge MA, 02138

Previous examples of the catalytic, asymmetric hetero *Diels-Alder* reaction with inverse electron demand (HDAIED) have focused on the use of *activated* oxabutadienes with electron-withdrawing groups such as phosphonates, esters and sulfones [1].
We report in this communication the discovery and optimization of the HDAIED of simple *unactivated* aldehydes (R = Alkyl, Aryl) with vinyl ethers catalyzed by the tridentate Chromium(III) Schiff base complex **A** [2]. This novel method yields dihydropyrans with high enantioselectivity (up to 96 % *es*) and excellent *endo*-diastereoselectivity (> 96 % *ds*)



The scope and limitations of this new method, useful synthetic transformations of the products as well as potential applications to the synthesis of natural products will be discussed.

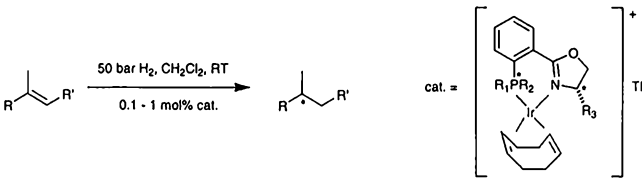
[1] a.) E. Wada, H. Yasuoka, S. Kanemasa, *Chem. Lett.* **1994**, 1637; b.) D. A. Evans, J. S. Johnson, *J. Am. Chem. Soc.* **1998**, *120*, 4895; c.) J. Thorhauge, M. Johannsen and K. A. Jorgensen, *Angew. Chem.* **1998**, *110*, 2543; d) D. A. Evans, E. J. Olhava, J. S. Johnson and J. M. Janey, *Angew. Chem. Int. Ed.* **1998**, *37*, 3372.
[2] A. G. Dossetter, T. F. Jamison, E. N. Jacobsen. *Angew. Chem. Int. Ed.* **1999**, *38*, 2398.

Organic Chemistry **236**

Iridium complexes of new, chiral P,N ligands for the enantioselective hydrogenation of unfunctionalised alkenes and ketones

Sebastian P. Smidt and Andreas Pfaltz*
University of Basel, Institute of Organic Chemistry, St. Johanns-Ring 19, CH-4055 Basel, Phone +41-61-267 1108, Fax +41-61-267 1103
e-Mail: Andreas.Pfaltz@unibas.ch

Chiral analogues of the Crabtree catalyst[1] were developed in recent years in our group.[2] The iridium complexes of these PHOX ligands show the best results so far in activity and enantioselectivities of up to 99% for a whole range of alkene substrates.



New derivatives of these ligands with the additional feature of a stereogenic phosphorus atom have now been synthesised by a new and efficient methodology. The results of the corresponding iridium complexes in the catalytic asymmetric hydrogenation of alkenes, ketones, and imines will be discussed, especially the effect of the second stereogenic centre. These complexes gave especially good results for the asymmetric transfer hydrogenation of ketones.

In addition, the synthesis of a completely new phosphinite/nitrogen ligand family derived from a *N*-heteroaromatic backbone and its use in iridium catalysed asymmetric hydrogenation reactions will be presented.

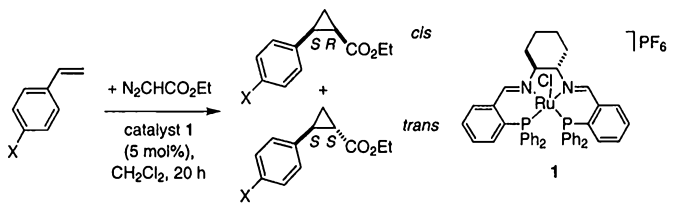
[1] R. Crabtree, *Acc. Chem. Res.* **1979**, *12*, 331-338.
[2] (a) A. Lightfoot, P. Schnider, A. Pfaltz, *Angew. Chem. Int. Ed.* **1998**, *37*, 2897-2899; (b) D. G. Blackmond, A. Lightfoot, A. Pfaltz, T. Rosner, P. Schnider, N. Zimmermann, *Chirality* **2000**, *12*, 442-449.

Organic Chemistry **237**

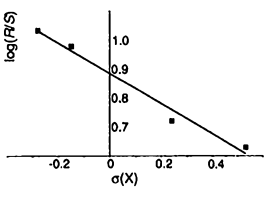
Electronic Effects in the Asymmetric Cyclopropanation of Olefins Catalyzed by $[RuCl(PNNP)]^+$

Stephan Bachmann and Antonio Mezzetti*
Department of Chemistry, ETH Hönggerberg, CH-8093 Zürich

The five-coordinate $[RuCl(PNNP)]^+$ (**1**) is a highly diastereo- and enantioselective catalyst for the cyclopropanation of styrene with diazo-esters, with up to >99% ee and 95% selectivity for the cis isomer [1]. We describe herein the substrate-based electronic effects in the cyclopropanation of *para*-substituted styrenes:



X	yield (%)	cis:trans	ee (%) cis	ee (%) trans
OMe	48	89 : 11	83	nd
Bu	86	87 : 13	81	nd
Cl	29	75 : 25	68	nd
CF_3	7	62 : 38	62	38



The above data show that yield, enantio-, and diastereoselectivity increase with increasing electron density at the olefin. The trend fits a linear free energy relationship with $\rho = -0.523$ ($R^2 = 0.981$). This opens the way to the electronic tuning of the PNNP ligand, as will be reported.

[1] S. Bachmann, M. Furler, A. Mezzetti, *Organometallics*, **2001**, *20*, 2102.

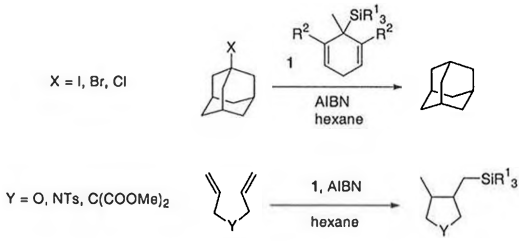
CHIMIA 2001, 55, No. 7/8

Organic Chemistry **238**

Silylated Cyclohexadienes as New Radical Reducing Agents

S. Amrein, A. Studer*
Fachbereich Chemie der Philipps-Universität Marburg
Hans-Meerwein-Straße, D–35032 Marburg

Recently, we introduced easily available silylated cyclohexadienes of type **1** as new radical reducing agents [1]. Using these *tin hydride substitutes*, radicals can be generated from conventional precursors, such as halides, phenylselenides and thionocarbonates, as shown for the dehalogenation of adamantylhalides. In the lecture, the scope and limitations of these reagents will be discussed. Furthermore, we present *metal-free* hydrosilylation/cyclization reactions of various dienes using these new reagents [2].



[1] A. Studer, S. Amrein, *Angew. Chem.* **2000**, *112*, 3196.
[2] S. Amrein, A. Timmermann, A. Studer, submitted for publication.

Physical Chemistry **239**

EXAFS Study of the Structure of Sulfided W/Al_2O_3 and NiW/Al_2O_3

Viviane Schwartz, Mingyong Sun, and Roel Prins

Laboratory for Technical Chemistry, ETH Zürich, 8092 Zürich, Switzerland

Hydrotreating is used to substantially reduce the content of sulfur, nitrogen, oxygen, and aromatics of petroleum feedstocks and it is one of the most important steps in refining [1]. Among the most common catalysts in hydrotreating are the tungsten-based materials. Of prime importance for the catalytic activity is the state of sulfidation of a hydrotreating catalyst. In this work, we applied extended X-ray absorption fine structure (EXAFS) spectroscopy to investigate the progress of sulfidation of alumina-supported tungsten-based catalysts. The catalysts were prepared from an oxidic precursor, WO_3, and from a sulfidic precursor, ammonium tetrathiotungstate (ATT), on unpromoted alumina and fluorided alumina. The influence of the nickel promoter on the sulfidation process was also investigated. The EXAFS spectra were acquired at the Swiss Norwegian Beam Line (SNBL), at the European Synchrotron Radiation Facility (ESRF), Grenoble, France. The catalysts were pressed in self-supported wafers, sulfided in the chemistry laboratory and mounted in a sealed EXAFS cell. Different sulfidation temperatures were used for this analysis. W L-edge and Ni K-edge EXAFS spectra were recorded in transmission mode at liquid nitrogen temperature. The program XDAP – version 2.3.3 was used to analyze and fit the data as described in the literature [2]. EXAFS showed that fluorination of alumina aids the sulfidation of tungsten and nickel and induces the formation of larger WS_2 particles. Ni K-edge spectra show that the nickel in the Ni-ATT catalyst is fully sulfided while the nickel in the Ni-WO3 catalyst is only partially sulfided at 400°C.

[1] H. Topsøe, B.S. Clausen, F.E. Massoth, Hydrotreating Catalysts, Science and Technology, Springer, New York, 1991.
[2] M. Vaarkamp, J.C. Linders, D.C. Koningsberger, Phys. Rev. B 209 (1-4), 159 (1995).

Physical Chemistry **240**

Ultrafast dynamics of Photo-induced Electron Injection From Eosin into a Wide Band Gap Semiconductor

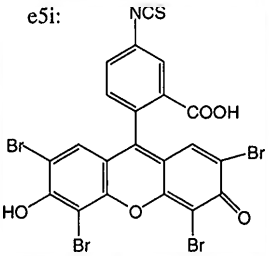
Serge Pelet, Jacques-E. Moser & Michael Grätzel

Laboratory for Photonics & Interfaces, Institute of Physical Chemistry, Swiss Federal Institute of Technology Lausanne, CH-1015 Lausanne

Early ns and ps studies showed that electron injection for Eosin-sensitized colloidal TiO_2 occurs with a time constant of 400 ps and a quantum yield of 0.38. ET appeared to only take place from the singlet excited state of the dye and to be limited by intersystem crossing [1]. Though, very recent studies employing fs time-resolution and a similar molecule (Fluorescein-27) on titania questioned these results, as time constants ranging from <100 fs to ~ 8 ps were obtained [2].

Time resolved stimulated emission and transient absorption from eosin-5-isothiocyanate (e5i) in solution were carried out. SE from the relaxed electronic excited state decays with 400 ps half-life time in accordance with the disappearance of the transient absorption of the singlet state. Tentative measurement of the electron injection kinetics has been undertaken by following the transient absorption of the cation and the disappearance of the SE of e5i adsorbed on colloidal TiO_2. Dye adsorbed on ZrO_2, a semiconductor where charge injection is thermodynamically unfeasible, was used as reference. It allowed us to discriminate between the different processes happening in the excited state and ascertain the real electron transfer lifetime, which was found to be on the order of ten ps.

e5i:



1. Moser, J.; Grätzel, M.; Sharma, D. K.; Serpone, N. Helv. Chim. Acta, 68 (1985) 1686; Moser, J.; Grätzel, M. J. Am. Chem. Soc., 106 (1984) 6557.
2. Benkö, G.; Hilgendorf, M.; Yartsev, A. P.; Sundström, V. J. Phys. Chem. B 105 (2001) 967.

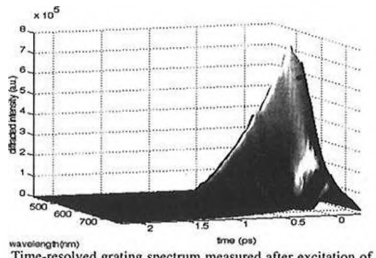
241

Ultrafast charge recombination dynamics of excited donor-acceptor complexes

Olivier Nicolet and Eric Vauthey

Département de chimie physique, Université de Genève, Sciences II, 30 Quai Ansermet, CH- 1211 Genève 4

The rate constant of charge recombination in excited donor-acceptor (EDA) complexes has been reported to increase exponentially with decreasing free energy, even at low exergonicity, in contradiction with the predictions of the Marcus theory.[1,2] Moreover, measurements by Mataga and co-workers have shown that the CR dynamics of EDA complexes composed of pyromellitic dianhydride (PMDA) as electron acceptor and methylbenzene derivatives does not exhibit any solvent dependence.[3] We will report on an investigation of the CR dynamics of EDA complexes composed of PDMA and methoxybenzene derivatives as electron donors, using both the multiplex transient grating technique[4] and the transient absorption spectroscopy.



Time-resolved grating spectrum measured after excitation of the complex PMDA/1,4-dimethoxybenzene in acetone.

We will show that free energy and solvent dependence of CR dynamics depart substantially from those reported so far.
The major reason for this difference is that CR occurs in the same timescale as vibrational relaxation and solvation. In this case the conventional electron transfer theories can no long be applied to analyse these ultra fast possesses.

(1) Hubig, S. M.; Bockman, T. M.; Kochi, J. K. *J. Am. Chem.* **1996**, *118*, 3842.
(2) Mataga, N.; Miyasaka, H. *Adv. Chem. Phys.* **1999**, *107*, 431.
(3) Asahi, T.; Ohkohchi, M.; Mataga, N. *J. Phys. Chem.* **1993**, *97*, 13152.
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Chemical Research **242**

Tyrosyl Radicals in Photosystem II: The Stable Tyrosyl D and the Catalytic Tyrosyl Z

P. Faller[a], A. Boussac[a], R.J. Debus[b], K. Brettel[a] and A.W. Rutherford[a]

[a]Section de Bioénergétiques, DBCM, CEA Saclay, CNRS URA 2096, 91191 Gif-sur-Yvette, Cedex France; [b]Department of Biochemistry, University of California at Riverside, Riverside, California 92521, USA

Tyrosyl radicals play key roles in the mechanisms of a wide range of enzymes. Understanding these roles and how proteins are able to control these reactive species in order to carry out quite specific chemical reactions has been an important aim of researchers in this area. One of the earliest demonstrations of redox active tyrosines was in photosystem II (PSII), the water oxidizing enzyme. This enzyme is of special interest since it contains two tyrosyl radical, TyrZ$^{\bullet}$ and TyrD$^{\bullet}$, which are located in a two-fold rotationally symmetrical position. This two tyrosyl radicals of PSII have only small apparent differences in their structural environments and yet they exhibit extremely different kinetics and play completely different functional roles in the enzyme. Thus they constitute an ideal system for understanding how the protein environment controls the reactivity of these reactive species.

Using EPR and time-resolved absorption spectroscopy we show that the oxidation of TyrD to TyrD$^{\bullet}$ occurs with a half time of 190 ns at pH 8.5 in the majority of the centers. This rate is around 10^5 times faster than was previously thought. At lower pH values this rapid donation from TyrD does not occur. The comparison of these results with the known parameters from TyrZ leads to new insights. This includes also information how the protein environments are able to impose different properties on the two tyrosyl radicals.

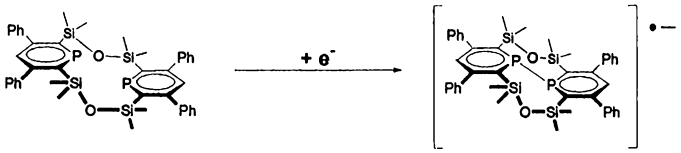
Physical Chemistry **243**

Formation of a Phosphorus-Phosphorus Bond by Successive One-Electron Reductions of a Two-Phosphinines-Containing Macrocycle : Crystal structures and EPR

L.Cataldo*, S. Choua*, T. Berclaz* and M. Geoffroy*
N. Mézailles**, L. Ricard**, F. Mathey** and P. Le Floch**

*University of Geneva, Dept. of Physical Chemistry
1211 Geneva, Switzerland
** Laboratoire "Hétéroéléments et Coordination", UMR CNRS 7653, Ecole Polytechnique, 91128 Palaiseau Cedex, France.

Chemical and electrochemical reductions of macrocycle **[1]** leads to the formation of a radical anion **[1]**$^{\bullet-}$ whose structure has been studied by EPR in liquid and frozen solutions.



[1] **[1]**$^{\bullet-}$

The resulting experimental ^{31}P hyperfine tensors show that the unpaired electron is localized in a P-P orbital. These results are consistent with the formation of a one electron P-P bond (and agree with DFT investigations). A subsequent reduction of this radical anion gives rise to the dianion **[1]**$^{2-}$ which could be crystallized by using , in the presence of cryptand, Na naphtalenide as a reductant agent.

Physical Chemistry **244**

Control of Combustion Conditions: Soot Generator for liquid Fuels. Reactions of Hexane Soot with NO_2

M. Sagrario Salgado and Michel J. Rossi

Laboratoire de Pollution Atmosphérique, Département de Génie Rural, EPFL, CH-1015 Lausanne

Micro particles emitted from combustion processes in high concentration affect the air quality. Due to their adverse health effect much effort has been done to measure and characterize these particles. Generally, the characteristics of soot particles emitted from fossil fuel combustion depend of the combustion conditions. Hence, the difficulty to stabilize the formation of soot particles in flames. In this sense, The CAST (Combustion Aerosol Standard) generator developed by Dr. Lianpeng Jing, at the Swiss Federal Institute of Metrology allow the generation of suspended particles in a wide size and concentration range with high reproducibility using gas fuels.

In this work, we have used the CAST burner, and adjusted it for use with liquid fuel. The fuel used is hexane, heated at adequate temperature in order to produce sufficient vapour pressure. The vapour is transported in a nitrogen stream into the burner across a fixed port. Changing the temperature and the air flow introduced into the burner, we modify the ratio fuel/air resulting in a controlled combustion of hexane. We have prepared in this way samples under two different conditions, and have studied their reactivity with NO_2 in a Knudsen Cell, thereby obtaining reproducibly results.

We have probed the chemical properties of hexane soot using its heterogeneous interaction with NO_2 in the following reactions:

$$NO_2 + \text{soot} \rightarrow HONO + \text{Products}$$
$$NO_2 + \text{soot} \rightarrow NO + \text{Products}$$

We will report on the kinetics of NO_2 uptake on different types of soot generated in the CAST as well as the product yields.

Physical Chemistry **245**

Heterogeneous Reactions of HCl and HNO_3 on Calcium Carbonate Surfaces

Christian Santschi and Michel J. Rossi

Laboratoire de Pollution Atmosphérique, Département de Génie Rural, EPFL, CH-1015 Lausanne

Mineral dust is the most abundant aerosol in the troposphere. The amount of mineral dust injected into the atmosphere has been estimated between 200 to 5000Mt/yr, representing about 50% of the total production of tropospheric aerosols by natural and anthropogenic sources together. The heterogeneous reactions on the surfaces of aerosol particles may affect the radiative budget and alter the content of atmospheric gas species.
Predicting the effect of changing anthropogenic emissions on atmospheric composition and climate will require an understanding of physiochemical processes on atmospheric dust/particles.

In order to study the heterogeneous reaction kinetics of HCl and HNO_3 on $CaCO_3$ surfaces experiment in a low pressure Knudsen Cell reactor have been performed on different types of surfaces like $CaCO_3$ powder and polished and milled marble. The gas-phase species have been monitored by a quadrupole mass-spectrometry.

The expected reaction mechanism is:

$$CaCO_3+2HCl \rightarrow CaCl_2+CO_2+H_2O \quad \text{for HCl and}$$
$$CaCO_3+2HNO_3 \rightarrow Ca(NO_3)_2+CO_2+H_2O \quad \text{for } HNO_3$$

In the case of HCl no uptake has been observed on a polished marble surface. In contrast, on an initial uptake on the order of $\gamma_{ini} = 0.1$ has been measured $CaCO_3$ powder. The mass balances show a deficiency of H_2O and CO_2. The appearance of CO_2 in the gas-phase is slightly delayed depending on the amount of surface adsorbed water, which indicates adsorbtion of CO_2 on the surface. In the case of HNO_3 interacting on marble surfaces no CO_2 has been measured in the gas-phase. The initial uptake coefficient has been measured on the order of $\gamma_{ini} = 0.1$ and a dependence of the HNO_3 concentration has been observed.

Physical Chemistry **246**

FTIR Absorption Spectroscopic Study of the HCl/Ice Interface : Characterization of the Condensed Phase under Atmospheric Conditions.

C. Delval, B. Flückiger, M.J. Rossi

Laboratoire de Pollution Atmosphérique, Département de Génie Rural
EPFL, 1015 LAUSANNE

Heterogeneous reactions occuring on PSC's (Polar Stratospheric Clouds) are known to play an important role in polar ozone depletion [1], by favouring the conversion of chlorine reservoirs HCl and $ClONO_2$ to photolycally active chlorine following the reaction:

$$ClONO_2(g)+HCl(ads)\rightarrow Cl_2(g)+HNO_3.$$

In continuation with recent studies led in our laboratory to characterize the HCl/Ice interface by investigating the gas phase [2], we have developed a low pressure chamber (10^{-4}–1torr) based on FTIR absorption in order to extract information on the interface.
Moreover, this cell can be used both under static conditions as well as a stirred flow reactor so that it allows studies in the temperature range relevant to atmospheric conditions (100-250K).
The deposition of HCl on an ice substrate at temperature as high as 240K has resulted in FTIR spectra wich depend on a specific deposition protocol, such as temperature of the deposition, warming of the HCl-doped ice film from 90K to 250K, and others. Kinetic measurements at conditions close to those found in a Knudsen flow reactor confirm both adsorption and evaporation rates of pure ice films in the temperature range 200 to 250K.
In addition both these rates are lowered by a factor of 5 in the presence of HCl adsorbed on the ice surface.

[1] Molina, M.J. *Atmos. Environ.*, 25A, 2535-2537, 1991.
[2] Flückiger, B *et al. J. Phys. Chem. A,* 104 (50), 11739-11750, 2000

Physical Chemistry **247**

Can Soot Particles Emitted from Aircraft Engines act as Nucleation Centers for Contrails and Cirrus Cloud Formation?

Carine Alcala-Jornod and Michel J. Rossi

Laboratoire de Pollution de l'Air (LPA), Département Génie Rural
Ecole Polytechnique Fédérale de Lausanne (EPFL), CH-1015 Lausanne

Soot is emitted by combustion processes and its presence in the atmosphere is principally due to internal combustion engines, especially Diesel motor vehicles. In the upper troposphere, soot emitted by airplanes is suspected to act as condensation nuclei for water vapor and lead to the formation of contrails or induced cirrus clouds. The increase in cloud cover is the subject of major interest in regards to climate change. Moreover, the presence of a given number of particles controls the size and the number of droplets constituting a cloud and may therefore change its albedo, which has a direct impact on the greenhouse effect.
In this work we have obtained the kinetic parameters of adsorbed H_2O in relation to the interaction of H_2O with two kinds of soot samples in terms of the surface residence time τ_s of adsorbed H_2O and the uptake rate expressed as uptake coefficient (γ_0). Soot have been samples produced by burning decane in a controlled air/fuel condition. Two types of soot have been prepared, the first with a high air/fuel ratio (black soot) and the second one with a low air/fuel ratio (grey soot). The experiment consists of injecting a known quantity of molecules into a tube coated with soot produced in the laboratory from a diffusion flame and recording the arrival time of the signal using mass spectrometry. A simulation model using Monte Carlo trajectories has been developed and is used to predict the experimental arrival time spectrum of the surviving molecules taking into account surface saturation.
H_2O interacting with both kind of soot has an uptake coefficient $\gamma_0 \leq 0.002$. However, at room temperature the residence time is between a fraction of milliseconds for grey soot and 15 ms in average for black soot. On the other hand, at low temperature of -80°C, the residence time is spread out over 150 milliseconds in average for grey soot, whereas for black soot, the residence time is already about 400 ms in average at –30°C showing a stronger interaction with H_2O.

Physical Chemistry **248**

New Insights into the Thermal Degradation Kinetics of Aqueous Aspartic Acid by High Temperature UV-Visible Spectrophotometry

J.S. Cox, T.M. Seward

ETH-Zentrum, Institute of Mineralogy and Petrography
8092 Zürich, Switzerland

Our research is currently focused on the experimental determination of the stabilities of selected amino acids under hydrothermal conditions. Kinetic data will be presented for the thermal degradation of aspartic acid and its principle degradation products up to 150 °C and 20 bar in degassed, unbuffered aqueous solutions.

Previous studies on the kinetics of decomposition of aspartic acid (eg. [1,2]) have been performed with varying experimental setups and under a variety of conditions, making it difficult to compare or evaluate literature data.

This study takes advantage of UV-vis spectrophotometry to observe the reactions of aspartic acid and its principle degradation products **in situ** under the chosen experimental conditions. For this purpose, a special spectrophotometric cell was constructed and connected to a flow through system such that the only wetted surfaces are gold, inert polymers, and glasses.

Our results indicate that the kinetics of the thermal degradation of aspartic acid under the above conditions are more complex than previously understood. The system as a whole and the proposed kinetic reaction scheme will be discussed.

[1] Bada, J. L. and S. L. Miller (1970). "The kinetics and mechanism of the reversible nonenzymatic deamination of aspartic acid." J. Am. Chem. Soc. 92(9): 2774-2782.

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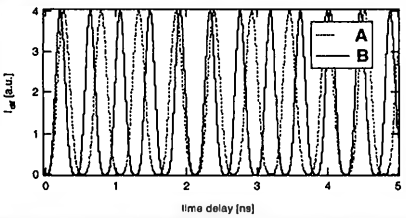
Physical Chemistry **249**

TRANSIENT EVANESCENT GRATING INVESTIGATIONS OF THE SPEED OF SOUND AT LIQUID-LIQUID INTERFACES

Pierre Brodard and Eric Vauthey

Department of Physical Chemistry of the University of Geneva
30, Quai Ernest Ansermet, CH-1211 GENEVA 4, Switzerland

Liquid-liquid interfaces play an important role in chemistry and biology. However, the exact chemical composition at the interface is still not known. Since the speed of sound is a property which strongly depends on the medium in which it propagates, we have devised an experiment in order to measure it: the transient density phase grating method (TDPG)[1]. The modulation of population induced by the two crossed pump pulses results in a heat releasing process taking place from the excited state. This leads to a spatial distribution of temperature, which because of thermal expansion is accompanied by a spatial modulation of the density. As a result, acoustic waves are generated and propagate in the sample. By probing with a delayed third pulse, we can determine the acoustic frequency ω_{ac} of this sound wave. Finally, this frequency is related to the speed of sound v_{sound} by the fringe spacing Λ of the grating. By using this technique in a evanescent mode [2], we can selectively determine the speed of sound at the interface.



Simulated signals from a TDPG experiment for A ethanol and B water (same conditions)

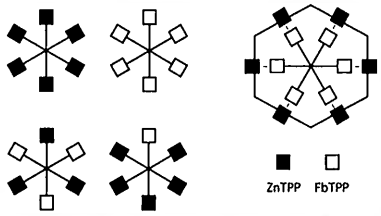
[1] P. Brodard and E. Vauthey, *Chem. Phys. Lett, 309,* **1999**, 198.
[2] P. Brodard and E. Vauthey, *Chimia, 54,* **2000**, 459.

Physical Chemistry **250**

Investigation of Ultrafast Excitation Energy Transfer Processes in Multiporphyrin Arrays

by Ana Morandeira and Eric Vauthey
Department of Physical Chemistry, University of Geneva, Switzerland
Nicolas Hoyler, Anne Schuwey, Olivier Mongin and Albert Gossauer
Institut für Organische Chemie der Universität Freiburg, Switzerland

The dynamics of intramolecular electronic energy transfer (EET) within multiporphyrin arrays has been investigated using several ultrafast techniques: fluorescence up-conversion and multiplex transient grating. These arrays contain Zn-tetraphenylporphine (ZnTPP) and free base tetraphenylporphine (FbTPP) moieties arranged as follows:



Three types of EET take place: energy hopping between ZnTPP moieties, energy hopping between FbTPP moieties and irreversible EET from ZnTPP to FbTPP, which acts as an energy trapping

These arrays can be considered as synthetic analogues of light harvesting antenna systems which transfer the absorbed energy to the reaction center of photosynthesis in higher plants and photosynthetic bacteria.

The dynamics of the individual energy transfer steps as well as the overall energy trapping efficiency of these arrays will be discussed in detail.

Physical Chemistry **251**

Gamma-Butyrolactone as an additive for electrolyte solutions in lithium–ion batteries

D. Goers, M. Lanz and P. Novak

Paul Scherrer Institute, Electrochemistry Section, CH-5232 Villigen PSI

The performance of lithium-ion batteries strongly depends on the formation of an electronically isolating film on the surface of the electrodes during the first charge step. The so called solid electrolyte interphase (SEI) protects the electrolyte from further decomposition. During the formation of the SEI gases like hydrogen, ethylene, propylene and carbon dioxide could be detected by differential electrochemical mass spectrometry [1].

The addition of gamma-butyrolactone (GBL) to electrolytes containing ethylene carbonate (EC), dimethylene carbonate (DMC) and propylene carbonate (PC) with 1M $LiBF_4$ showed a significant reduction of gas evolution [2]. Cells with EC-based electrolytes complete their gas evolution during the initial charge, whereas cells with PC-based electrolytes evolve propylene during the charge step of the second cycle. Therefore, we assume that the SEI of the PC-based electrolytes of this study insufficiently protects the electrolyte solution from further decomposition.

We acknowledge the support of Prof. A. Wokaun and Dr. O. Haas.

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Physical Chemistry **252**

Continuous Oxidation of Alcohols to Carbonyl Compounds in Supercritical Carbon Dioxide

G. Jenzer, M. S. Schneider, R. Wandeler, T. Mallat and A. Baiker

Laboratorium für Technische Chemie, ETH Zentrum, CH-8092 Zürich

The platinum metal catalyzed oxidation of alcohols to carbonyl compounds is an attractive, environmentally friendly process [1]. The method is widely used for the oxidation of di- and polyols in aqueous medium with molecular oxygen as oxidant. Partial oxidation of water-insoluble reactants can be performed in organic solvents, but safety problems can hinder the practical application. A feasible solution is the use of supercritical (sc) CO_2 as solvent, not only because it allows to control the reaction rate and selectivity by pressure variation, but also because it is inflammable and non-toxic.

After a preliminary paper on a batch reactor study [2], here we report the oxidation of some primary and secondary alcohols to the corresponding aldehydes and ketones over Pd- and Pt-based catalysts in a high pressure, continuous flow fixed bed reactor. Up to 95 % yields to carbonyl compounds have been achieved by varying pressure, temperature, feed composition, and contact time. No catalyst deactivation was observed even after several hundreds hours time-on-stream.

To get a better understanding of the reaction performance, the phase behavior of the mixture under reaction conditions was investigated in a computer controlled high-pressure view cell. At temperatures above 40 °C one liquid phase was in equilibrium with a gaseous ("sc") CO_2-rich phase. A swelling of the octanol-rich liquid phase with CO_2 could be observed. This swelling is expected to increase the concentrations of CO_2 and O_2 in that phase and improve the transport properties with respect to chemical reactions.

[1] T. Mallat and A. Baiker, Catal. Today, 19 (1994) 247.
[2] G. Jenzer, D. Sueur, T. Mallat and A. Baiker, Chem. Commun. (2000) 2247.

Physical Chemistry **253**

Continuous Semihydrogenation of Phenylacetylene over Amorphous $Pd_{81}Si_{19}$ in "Supercritical" Carbon Dioxide: Relation between Catalytic Performance and Phase Behavior

R. Tschan, M. S. Schneider, R. Wandeler, M. M. Schubert, and A. Baiker

Laboratorium für Technische Chemie, ETH Zentrum, CH-8092 Zürich

Catalytic performance of an amorphous $Pd_{81}Si_{19}$ alloy catalyst for the continuous semihydrogenation of phenylacetylene (PA) to styrene (ST) at high pressures, employing "supercritical" CO_2 as a solvent, has been studied. The reaction is applied for the removal of detrimental impurities prior to styrene polymerization [1]. Without further optimization or addition of modifiers, high conversion and selectivities up to 96% were obtained for the hydrogenation of pure PA. Phase behavior studies revealed that a single-phase system was an ideal reaction medium for such hydrogenation reactions (Fig. 1). Consideration of the phase behavior is shown to be indispensable for the optimization of such high-pressure reactions, since, e.g., the lower hydrogen concentration possible for the single-phase system will be far from ideal for hydrogenations in a multi-phase system. A binary fluid phase diagram is found to serve as a good model for the multi-component behavior [2]. It is generally demonstrated that a detailed consideration of phase behaviour of a reaction system is important in the development of a rational process design of "sc" high-pressure reactions.

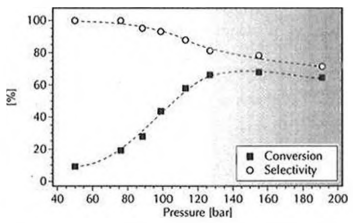

Fig. 1: Conversion and selectivity as a function of pressure. Single phase area is shaded. Conditions: 55°C, CO_2:(PA:ST):H_2 = 400:(1:9):10

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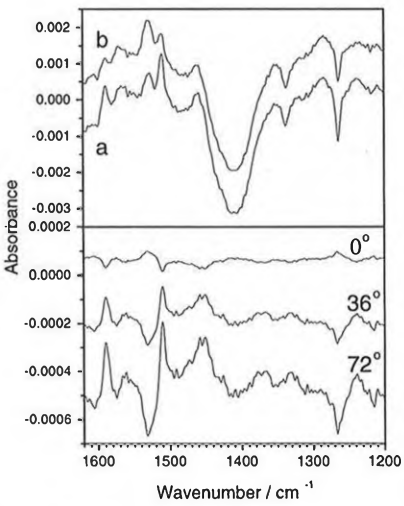
Physical Chemistry **254**

In Situ ATR-IR Spectroscopy using Phase Sensitive Detection: Application to Chiral Catalytic Solid-Liquid Interfaces

Thomas Bürgi, Davide Ferri and Alfons Baiker*
Laboratorium für Technische Chemie, ETH-Zentrum, CH-8092 Zürich

Catalytic solid-liquid interfaces are not much studied *in situ* by vibrational spectroscopy despite their importance. One reason for this is the experimental challenge to discriminate the weak signals associated with the interface from the solution signals. Furthermore, catalytic solid-liquid interfaces usually exhibit a high degree of complexity due to the many species present. We use attenuated total reflection (ATR) in combination with modulation techniques, i.e. the periodic variation of a reaction parameter such as concentration, for the study of catalytic solid-liquid interfaces. Phase sensitive detection of the modulated signal and subsequent demodulation helps to disentangle crowded spectra. The Figure shows spectra of cinchonidine (CD), the most powerful modifier in the heterogeneous enantioselective hydrogenation of activated carbonyl compounds [1], adsorbed on a Pt/Al_2O_3 model catalyst in contact with H_2-saturated CH_2Cl_2. The top spectra were recorded (a) after flowing a solution of CD (0.001M) and (b) 80 seconds after subsequently flowing neat solvent over the sample. The bottom spectra are obtained by demodulating (at three phase angles) the spectra recorded at different times during desorption, thus highlighting dynamic changes of this process.



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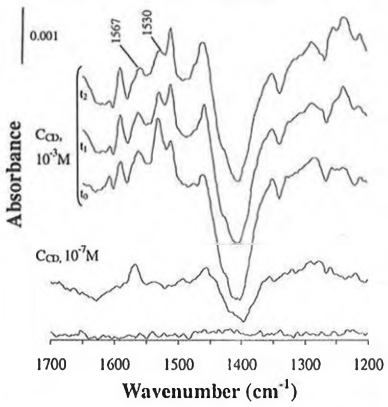
Physical Chemistry **255**

The surface chemistry of cinchonidine on Pt/Al_2O_3. An *in situ* ATR-IR study

D. Ferri, T. Bürgi and A. Baiker
Laboratorium für Technische Chemie, ETH-Zentrum, CH-8092 Zürich

Present mechanistic models for the enantioselective hydrogenation of alkyl pyruvates on Pt/Al_2O_3 assume a specific adsorption mode of the modifier, cinchonidine (CD), on the Pt surface. Since no spectroscopic information was available up to now describing the adsorption under real reaction conditions we close this gap using attenuated total reflection IR spectroscopy (ATR-IRS) using a flow-through cell [1]. Coverage-dependent adsorption has been found for CD on a Pt/Al_2O_3 model catalyst. ATR spectra of CD on Pt/Al_2O_3 adsorbed from an H_2-saturated solution at 283K showed signals corresponding to several CD species. The signal at 1567 cm^{-1} observed at the initial stages of adsorption and at low concentration is assigned to species having the quinoline ring nearly parallel to the surface. The new signal at 1530 cm^{-1} is assigned to species formed by α-H abstraction in analogy to pyridine adsorbed on Pt. At high coverage this species is eventually hydrogenated and a loosely bound species dominates the spectrum, which very much resembles the solution spectrum of CD. This last species is adsorbed *via* the quinoline-N and is removed by neat solvent flow.



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Physical Chemistry **256**

Indium Tin Oxide for OLED Application: Bulk and Surface Properties

F. Atamny, U. Betz, J. Marthy and E. Winkler
Unaxis Balzers AG, P.O. Box1000, FL-9496 Balzers, Liechtenstein
e-mail: fachri.atamny@unaxis.com

There has been enormous interest in organic light-emitting devices (OLEDs) primarily due to their application in flat panel displays. The typical OLED consists of multilayer sandwich of planar glass substrate, a layer of transparent-conductive-oxide, one or more organic layers, and a reflecting cathode.

Sn-doped In_2O_3 (Indium-Tin-Oxide: ITO) films have been considered as the most suitable candidate which can be used as anode/cathode for organic light-emitting devices. This is due to their excellent transparency (> 90% in the visible region), low resistivity, and relatively high work function (ca 5 eV). However, several „practical" obstacles still limits its application in flat panel display fabrication.

In this study, we focussed on structural, electronic, and optical properties of ITO thin films. Furthermore, we studied the influence of film process conditions on film uniformity deposited on large-scale ($1m^2$) glass substrate.

Fig. 1: SEM picture of 100 nm thin ITO.

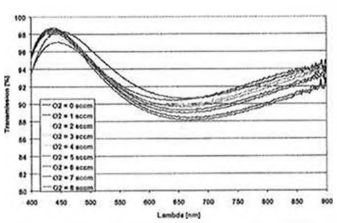


Fig. 2: Tranmittance of 100 nm thin ITO as a function of O2 content.

Physical Chemistry **257**

Hydrodenitrogenation of Methylcyclohexylamine over Fluorinated NiMoS Catalysts Supported on Alumina and Silica-Alumina

Lianglong Qu and Roel Prins

Laboratory for Technical Chemistry, Federal Institute of Technology (ETH), 8092 Zurich, Switzerland

The hydrodenitrogenation of methylcyclohexylamine has been studied at 310 to 350°C and 5.0 MPa in a continuous micro-flow reactor over sulfided and fluorinated sulfided NiMo catalysts supported on alumina and silica-alumina.

Different sites exist for the hydrodenitrogenation and hydrogenation reactions. The hydrodenitrogenation reaction proceeds via two pathways: the elimination of NH_3 to methylcyclohexene followed by olefin saturation to methylcyclohexane as well as direct C-N bond breaking to methylcyclohexane. The silica-alumina-supported catalysts exhibit higher hydrodenitrogenation activities than their alumina-supported counterparts, with a strong increase for the elimination step. *In-situ* fluorination promotes mainly the hydrodenitrogenation activity by enhancing the elimination step, while less effect is observed for the direct hydrogenolysis path.

Kinetic parameters were obtained for the hydrodenitrogenation reaction by fitting the results with Langmuir-Hinshelwood equations. The reaction rate constants increase substantially for the elimination step and slightly for the direct hydrogenation path after fluorination of all the catalysts, while the adsorption constants decrease. This indicates that not only the number of active sites for hydrodenitrogenation is increased but also the intrinsic activity of the active sites is modified.

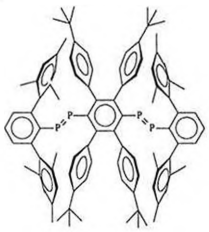
Physical Chemistry **258**

EPR investigations of new sterically protected bis-diphosphene and bis- diphosphaalkene radical anions

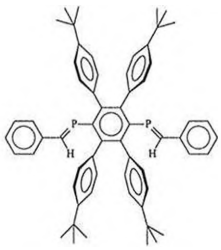
S. Choua[a], C. Dutan[a], T. Berclaz[a], M. Geoffroy[a], S. Shah[b], J.D. Protasiewicz[b]

[a]University of Geneva, Dept. of Physical Chemistry
1211 Geneva, Switzerland
[b]Case Western Reserve University, Cleveland, Ohio 44106-7708

The reduction products of a bis-diphosphene (DmpP=P-Ar_4C_6 –P=PDmp) (**1**) and two bis-diphosphaalkenes ((PhC(H)=P-Ar_4C_6-P=C(H)Ph (**2**) and DmpP=C(H)-C_6H_4-C(H)=PDmp (Dmp = 2,6-$Mes_2C_6H_3$)) were studied by EPR at various temperatures. These spectra, obtained after electrochemical or chemical reductions (K and Na mirror, Na naphtalenide), indicate a large spin delocalisation of the unpaired electron on both P=P (or P=C) moieties of the radical anion. This symmetric spin delocalisation leads to hyperfine couplings which are compared to those obtained by DFT calculations.



(1)



(2)

Physical Chemistry **259**

Vibrational Spectroscopy and *ab initio* Calculations for the CH-Chromophore Fermi Resonance in Formamide

Michael Hippler, Martin Quack, and Martin Willeke

Laboratorium für Physikalische Chemie, ETH Zürich, CH-8093 Zürich

Formamide ($HCONH_2$) is a prototype molecule to study the interplay of different high-frequency infrared chromophores (the CH- and NH_2-chromophores), which are expected to dominate the intramolecular vibrational redistribution dynamics in the sub-ps time domain. However, due to its very low vapour pressure and weak overtone absorptions, no overtone spectra of the high-frequency chromophores have been reported and analysed yet. Employing a high-resolution Fourier-transform spectrometer equipped with a long-path absorption cell (l= 40 m) which has been heated up to 340 K to increase the vapour pressure of formamide, we recorded the infrared absorption spectrum of formamide from 1200 cm^{-1} to 11000 cm^{-1} [1]. For the CH-chromophore, we identified and analysed a distinct anharmonic Fermi resonance between the CH-stretching and the in-plane CH-bending mode with a typical vibrational energy redistribution time of about 100 fs [1]. The analysis is corroborated by two-dimensional variational calculations on *ab initio* potential and electric dipole moment surfaces [1], and it is also in agreement with a high-resolution rovibrational analysis of the CH-stretching fundamental region near 2800 cm^{-1} [2].

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[2] Hans Hollenstein, Martin Quack, and Martin Willeke, to be published.

Physical Chemistry **260**

High-Resolution Analyses of the CH-Bending Fundamental and of the Fermi Resonance Band System in the CH-Stretching Region of Formamide ($HCONH_2$)

Hans Hollenstein, Martin Quack and Martin Willeke
Laboratorium für Physikalische Chemie,
ETH Zürich
CH-8093, Zürich, Switzerland

We have measured high-resolution FTIR spectra (0.004 cm^{-1} apodized instrumental band width) of formamide on our BOMEN DA002 spectrometer in the range 1000-1700 cm^{-1} (CH bending mode (ν_6)) and 2600-3000 cm^{-1} (Fermi resonance band doublet: $2\nu_6$, ν_3 (CH-stretching mode)) [1]. We employed a heatable long path White cell purchased from Portmann Instruments AG (Switzerland) to overcome the problems due to the low vapour pressure of formamide at room temperature. The rovibrational structures were analyzed by means of a Watson Hamiltonian in the A reduction including up to quartic terms. We obtained the band centers $\tilde{\nu}_i$ and the sets of rotational constants, and for the CH-bending mode additionally the quartic centrifugal distortion constants. From intensity ratios of corresponding rovibrational lines in $2\nu_6$ and ν_3 we derived a value for the effective cubic Fermi coupling constant k_{366}. Furthermore, from the band center of ν_6 and the deperturbed band center of $2\nu_6$ we estimated the anharmonic constant x_{66}.

Our effective cubic Fermi coupling constant k_{366} compares very well with the corresponding constant recently calculated *ab initio* employing a two-dimensional (q_3, q_6) potential energy and electronic dipole moment hypersurfaces and is also in excellent agreement with k_{366} resulting from an analysis of the CH overtone spectrum [2].

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[2] M. Hippler, M. Quack, and M. Willeke, to be published.

Physical Chemistry **261**

A high resolution infrared study of CDBrClF: Analysis of the ground state and the ν_4 state

Sieghard Albert and Martin Quack

Laboratorium fur Physikalische Chemie, ETH Zuerich
(Zentrum), CH-8092 Zurich, Switzerland

The rovibrational spectrum of the chiral molecule CDBrClF **[1,2]** recorded at room temperature with a Fourier transform infrared spectrometer (resolution 0.0024 cm^{-1}) has been analysed in the CF-stretch band region on the basis of an effective Hamiltonian. The assignment of the ν_4 rovibrational lines or the two major isotopomers $CD^{79}Br^{35}ClF$ and $CD^{81}Br^{35}ClF$ has been carried out with an interactive Loomis-Wood program. Around 800 lines up to J=80 have been assigned for each isotopomer. A combined analysis of the ν_4 and ν_5 fundamental bands **[3]** provides accurate rotational and quartic centrifugal distortion constants for the vibrational ground state of $CD^{79}Br^{35}ClF$ and $CD^{81}Br^{35}ClF$. The analysis of the ν_4 band determined the spectroscopic constants of the excited state for $CD^{79}Br^{35}ClF$ [ν_0(4)=1082.8118] and $CD^{81}Br^{35}ClF$ [ν_0(4)=1082.7966].

[1] A. Bauder, A. Beil, D. Luckhaus, F. Mueller and M. Quack, *J. Chem. Phys.*, **106**, 7558-7570 (1997)
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CHIMIA 2001, 55, No. 7/8

Physical Chemistry **262**

Parity Violation Induced Ro-vibrational Frequency Shifts and Thermodynamic Properties of Enantiomers

Martin Quack and Jürgen Stohner
ETH Zürich (Zentrum), Lab. for Physical Chemistry
CH 8092 Zürich

If one assumes left-handed/right-handed symmetry in free space, the heat of formation and the entropy of enantiomers must exactly be equal. Furthermore, the equilibrium constant for racemization is exactly equal to 1 at all temperatures [1,2] . The violation of this symmetry ("parity") introduces an energy difference between enantiomers and we discuss its implication on rovibrational frequency shifts [3,4] between enantiomers and on the equilibrium constant for racemization [5] .
High quality ab initio calculations (RPA, random phase approximation and CASSCF, complete-active-space self-consistent field) are performed to determine the small energy difference between R- and S-enantiomers of bromochlorofluoromethane (CHBrClF, CDBrClF) and fluorooxirane (H_3C_2OF) introduced by the parity violating weak interaction. Together with vibrational and rotational frequency shifts caused by parity violation, this is used to determine statistical thermodynamic quantities from the corresponding partition functions. Temperature dependent equilibrium constants for stereomutation are calculated and discussed in relation to biochemical homochirality [5] .

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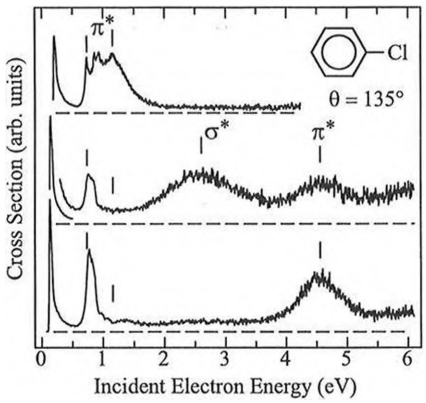
Physical Chemistry **263**

σ* and π* States of the Chlorobenzene Negative Ion Determined by the Electron Energy Loss Spectroscopy

T. Skalický, Ch. Chollet, N. Pasquier and M. Allan

University of Fribourg, Department of Chemistry
1700 Fribourg, Switzerland

The assignment of the σ* and π* states of the negative ions of halogenated aromatic hydrocarbons is important for understanding the dissociative reactions of these compounds induced by the attachment of an electron. We arrived at an unambiguous assignment of these states in chlorobenzene (which has recently been questioned [1]) using the selectivity of vibrational excitation by impact of slow electrons.



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Physical Chemistry **264**

Methanol Reforming Over A $Cu/ZnO/Al_2O_3$ Catalyst: A Study By Post-Reaction XPS and TPD

F. Raimondi, K. Geissler, J. Wambach, and A. Wokaun

Paul Scherrer Institut, General Energy Research
5232 Villigen PSI

The state of an industrial $Cu/ZnO/Al_2O_3$ catalyst after exposure to methanol reforming conditions was studied as a function of the temperature and of the O_2 to CH_3OH ratio in the feed. The effect of the presence of H_2O was also considered. X-ray photoelectron spectroscopy (XPS) showed a strong dependence of the Cu oxidation state on the reaction temperature and on the composition of the feed. Temperature-programmed desorption (TPD) experiments indicated that the nature and amount of adsorbed species changed markedly depending on the reaction conditions.

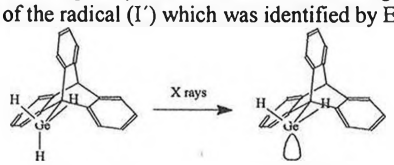
Physical Chemistry **265**

Intramolecular motion in triptycylgermane : a single crystal EPR study at variable temperature

C. Dutan, M. Brynda, T. Berclaz and M. Geoffroy

University of Geneva, Dept. of Physical Chemistry
1211 Geneva, Switzerland

Radiolysis of single crystals of the new air-stable germane[1] (I), led to the formation of the radical (I') which was identified by EPR.



I I'

The g tensor and the ^{71}Ge and ^{1}H hyperfine tensors were determined at 300K and 77K. It was shown that three conformations were blocked at 77K. A temperature dependence of the spectra was recorded for a chosen orientation of the crystal. The resulting spectra were analysed with a simulation program which used the density matrix formalism. They correspond to the eclipsed conformations of the GeH_2 group. The barrier of the rotation around the C-Ge bond, estimated from this temperature dependence of the spectra, is in good accordance with the values obtained from DFT calculations.

[1] M. Brynda, M. Geoffroy and G. Bernardinelli, Chem. Commun., 1999, 961-962

Physical Chemistry **266**

Influence of PMAA-graft-PEO copolymers on the formation of thin ZnO films from aqueous solutions

R. Hoffmann, T. Fuchs, T.P. Niesen, J. Bill, F. Aldinger

Max-Planck-Institut für Metallforschung/
Institut für Nichtmetallische Anorganische Materialien
Heisenbergstr. 5, 70569 Stuttgart, Germany

The formation of thin films at low temperatures from aqueous solutions has obvious advantages to vapour deposition techniques in high vacuum or sol-gel routes. It offers an easy to use and low cost alternative. Further the addition of water-soluble additives might enhance the deposition of the films or allow new surface morphologies. [1]
It has been shown, that self-assembled monolayers (SAMs) are useful substrates for the effective deposition of metal oxide films as ZrO_2, TiO_2, V_2O_5, SnO_2 and Fe_2O_3. [1,2]
We report here the deposition of homogeneous and adherent ZnO films on Si wafers by the hydrolysis of zinc salts. The addition of the polymers is necessary to supress the formation of undesired, larger zincite crystals, which otherwise form inevitably.
Using copolymers as polymethacrylic acid grafted with polyethylenoxide side chains we obtained homogeneous films of nanosized particles on Si wafers with SAMs, but also on unmodified wafers. According to EDX and XPS a part of the polymer remains attached to the precipitated particles, but can be removed by pyrolysis below 573K. Films obtained before and after annealing at 723K in air were characterized by AFM und SEM.

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Physical chemistry **267**

Static and dynamic adsorption of vapour mixtures by activated carbons

R. Sobota, D. Hugi-Cleary, F. Stoeckli

University of Neuchâtel, Institute of Chemistry
2007 Neuchâtel, Switzerland

Physical adsorption of vapours by activated carbons plays an important role in filtration technology. Under dynamic conditions, the removal of a single vapour from air can be described in a straightforward manner, but in the case of mixtures, predictions are more difficult. This can be achieved with the help of two distinct approaches developed in our laboratory. The first is based on the Myers-Prausnitz-Dubinin theory (MPD), which describes the adsorption equilibrium of vapour mixtures corresponding to miscible liquids (for example two organic compounds). The second approach, valid for the adsorption of vapours corresponding to immiscible liquids (for example an organic vapour and water), is based on the model of independent co-adsorption, using the Dubinin equation. It is shown that in the case of slow flow rates, one obtains a good agreement with the predictions of binary adsorption under static conditions.

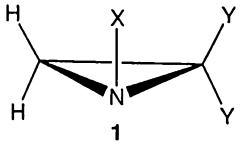
Physical Chemistry **268**

Parity Violation and Tunneling Dynamics in Asymmetrically Substituted Aziridines

Martin Quack and Achim Sieben
Laboratorium für Physikalische Chemie, ETH Zürich, CH-8093 Zürich

Due to the parity violating electroweak interaction, enantiomers of a chiral molecule have slightly different energies. We have studied these parity violating energy differences ΔE_{PV} for asymmetrically substituted aziridines **1** (fig. 1) employing the recently developed MC-LR approach [**1**]. We also estimated tunneling splittings $\Delta E_{\pm}$ for the stereomutation between these enantiomers using a simple Wentzel-Kramers-Brillouin method [**2**]. It turned out that for aziridines **1** tunneling splitting is extremly small ($\Delta E_{\pm} << 10^{-20}$ cm^{-1} in all cases shown). Domination of ΔE_{PV} over $\Delta E_{\pm}$, however, means that parity violation and not tunneling dominates stereomutation dynamics. This result is of fundamental importance for spectroscopic approaches towards parity violation in molecules [**3-6**].

Figure 1:



1

X=Cl Y=F $\Delta E_{PV} \approx 10^{-13}$ cm^{-1} (hc)
X=F Y=F $\Delta E_{PV} \approx 10^{-14}$ cm^{-1} (hc)
X=F Y=Cl $\Delta E_{PV} \approx 10^{-13}$ cm^{-1} (hc)
X=Cl Y=Cl $\Delta E_{PV} \approx 10^{-12}$ cm^{-1} (hc)

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Physical Chemistry: **269**

Nonlinear intensity dependence in the infrared multiphoton excitation and dissociation of methanol preexcited to different energies

Oleg V. Boyarkin, Tom R. Rizzo, David S. Rueda
Laboratoire de Chimie Physique Moléculaire
EPFL Ecublens, 1015 Lausanne

Martin Quack and Georg Seyfang
Laboratorium für Physikalische Chemie
ETH Zürich, 8092 Zürich

The question of nonlinear intensity dependence in the infrared multiphoton excitation of polyatomic molecules has been a long standing problem in IR-laser chemistry [1-3]. The recently introduced spectroscopic technique of IRLAPS [4] has been suggested to be in part aided by selectivity due to nonlinear intensity dependence [5]. We report here quantitative dissociation yields for the reaction CH_3OH (v_{OH}) $\xrightarrow{nh\nu}$ CH_3 + OH for the infrared multiphoton excitation of methanol preexcited to various levels of the OH stretching vibration (v_{OH} = 0, 1, 3, 5) by detecting OH using laser induced fluorescence. It is demonstrated, that for low levels of preexcitation (v_{OH} = 0, 1, 3) there is a substantial nonlinear intensity dependence, as a higher yield is found for self mode-locked CO_2 laser pulses (with higher peak intensity) as compared to single mode pulses of the same laser fluence, but lower peak intensity. In contrast at high levels of preexcitation (v_{OH} = 5) this nonlinear intensity dependence is absent. Quantitative model calculations are carried out using a case B/case C master equation approach which takes nonlinear intensity dependence into account. The calculations are consistent with the experimental results and confirm the prediction that an important part of the selectivity of the CO_2 laser excitation step in IR-LAPS (Infrared laser assisted photofragment spectroscopy) of CH_3OH is due to this nonlinear intensity dependence.

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CHIMIA 2001, 55, No. 7/8

Physical Chemistry **270**

Spectroscopy of Protonated Aromatic Molecules in the Gas Phase

Nicola Solcà and Otto Dopfer

Institut für Physikalische Chemie, University of Basel,
Klingelbergstrasse 80, CH-4056 Basel, Switzerland

Protonated aromatic molecules AH^+ are important species in (bio)chemistry. For example, arenium ions appear as reaction intermediates in electrophilic aromatic substitution reactions (σ-complex) and their stability often determine the kinetic and thermodynamic properties of the reaction [1]. No gas-phase spectroscopic information is available for these species, because of difficulties in the production of large number densities.

In this contribution, we present the first spectroscopic information on the gas-phase protonation of benzene, phenol and para-fluorophenol. For this purpose, infrared photodissociation (IRPD) spectra of protonated benzene (BzH^+), phenol (PhH^+) and para-fluorophenol ($pFPhH^+$) complexed with neutral ligands L (L=Ne, Ar, N_2) are analyzed in the region of the X–H stretch fundamentals (X=C, O). The ligand L is considered as a "messenger", which only slightly perturbs the stability of the bare monomer. The effects of complexation identify the protonation site (e.g., carbonium vs oxonium) and provide also information on the intermolecular potential and microsolvation of the bare ion [2].

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Physical Chemistry **271**

High-Resolution cw-Diode Laser Cavity Ring-Down Spectroscopy of the HF Dimer in a Pulsed Slit Jet Expansion: The N=2 Overtone Triad Near 1.3 μm

Michael Hippler, Lars Oeltjen, and Martin Quack

Laboratorium für Physikalische Chemie, ETH Zürich, CH-8093 Zürich

The analysis of $(HF)_2$ overtone spectra allows the study of intramolecular dynamic processes, *e.g.* predissociation, tunnelling and vibrational redistribution processes in highly vibrationally excited states [1]. Experimental overtone spectra are also required to test and to refine high-level *ab initio* calculations employing potential hypersurfaces in full dimensionality. Unfortunately, overtone transitions in HF dimer are very weak and HF dimer spectra are heavily congested by hot-band transitions and prevailing HF momomer absorptions under normal conditions.

Recently, we introduced cw-diode laser cavity ring-down spectroscopy of polyatomic molecules in pulsed supersonic slit jet expansions [2,3]. In the present study, we apply this new technique to observe all components of the N=2 triad of the first HF stretching overtone region near 1.3 μm [4]. With very low vibrational and rotational temperatures ($T_{rot} \approx 25$ K), hot-band congestion is virtually eliminated, and the reduced Doppler widths in the slit jet expansion allows the precise determination of predissociation line widths. We present spectral assignments and an analysis of tunnelling splittings, and we compare the results with our recent *ab initio* calculations [5].

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Physical Chemistry **272**

The infrared spectrum of CDBrClF: A rovibrational analysis of the ν_5 band

Sieghard Albert, Vincent Boudon[a] and Martin Quack

Laboratorium fur Physikalische Chemie, ETH Zuerich
(Zentrum), CH-8092 Zurich, Switzerland,

There exist only three chiral molecules to this date for which a rovibrational analysis of a high resolution infrared spectrum of one or several vibrational transitions has been achieved (CHBrClF [1], flouro oxirane, and deutero ethylene episulfoxide). We have undertaken a study of CDBrClF in order to complement this very short list of analyses in our group.

The rovibrational spectrum of the chiral molecule CDBrClF [2] within the ν_4 (CCl- stretch) region has been analysed on the basis of an effective Hamiltonian. The spectra have been recorded at room temperature with a Fourier transform infrared (FTIR) spectrometer (resolution 0.0024 cm^{-1}) and a supersonic jet diode laser spectrometer (resolution 0.001 cm^{-1}). The assignment of the ν_5 rovibrational lines of the two major isotopomers $CD^{79}Br^{35}ClF$ and $CD^{81}Br^{35}ClF$ has been carried out with an interactive Loomis-Wood program. Around 350 lines up to J=80 have been assigned for each isotopomer. Accurate rotational and quartic centrifugal distortion constants for the ν_5 vibrational state of $CD^{79}Br^{35}ClF$ and $CD^{81}Br^{35}ClF$ have been determined on the basis of the analysis of the ν_4 band [3] of CDBrClF.

Our results are discussed in relation to fundamental questions of the high resolution spectroscopy of chiral molecules and parity violation [4].

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[a]present address: Laboratoire de Physique de l'Universite de Bourgone, 21078 Dijon Cedex, France

Physical Chemistry **273**

Parity Violation Dominates the Dynamics of Chirality in Dichlorodisulfane

Robert Berger, Michael Gottselig, Martin Quack and Martin Willeke
Laboratorium für Physikalische Chemie, ETH Zürich
CH-8092, Zürich, Switzerland

Do molecules exist whose structure and dynamics are dominated by the parity-violating electroweak interaction? This interesting situation is to be expected for chiral molecules, if the minute parity-violating energy difference ΔE_{pv} between the two enantiomers that is caused by the electroweak force is substantially larger than the tunneling splitting $\Delta E_{\pm}$ in the lowest vibrational states [1,2]. For typical, stable chiral molecules this should be the rule, since our new approach to the calculation of electroweak parity violation yields values that are orders of magnitude larger than previously anticipated [3,4]. However, so far there was not any known example of a molecule for which explicit calculations of the parity-violating potentials and the tunneling splittings have proven this case. Dichlorodisulfane (ClSSCl) is the first system for which it is shown with explicit calculations of ΔE_{pv} and $\Delta E_{\pm}$ that parity violation dominates the structure and dynamics of this chiral compound. Parity-violating potentials were calculated with our recently introduced MC-LR approach [4] in the RP approximation. We developed a new method that allowed calculation of the extremely small torsional tunneling splitting in the lowest vibrational states. ΔE_{pv} is about $10^{-12}cm^{-1}$, while $\Delta E_{\pm}$ is many orders of magnitude smaller. Our results are encouraging for experimental efforts to directly measure the parity-violating energy difference [1,2].

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Substrate recognition by Chorismate Mutase studied by TROSY NMR

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Konstantin Pervushin

Laboratorium für Physikalische Chemie
Eidgenössische Technische Hochschule
8092 Zürich, Switzerland

B. subtilis Chorismate Mutase (EC 5.4.99.5) is an water soluble trimeric enzyme located at the branch point of the shikimate pathway which is responsible for biosynthesis of aromatic amino acids. BsCM catalyzes the unimolecular rearrangement of chorismate to prephenate. Although BsCM has been studied extensively for over two decades, only little of the mechanistic details of the enzyme-catalyzed rearrangement nor the origins of its 2x10e6-fold rate acceleration over the uncatalyzed reaction are known despite the availability of the 3D X-ray structures of BsCM alone and it's complexes with a transition state analog and prephenate. BsCM is a homotrimeric pseudo β-barrel surrounded by α-helices. Three solvent-accessible active sites are located at the subunit interfaces. BsCM uses an extensive array of interactions to bind and orient the flexible substrate for reaction. However, the role of the crystallographically ill-defined C-terminal tail close to the entrance of the substrate binding pocket is unclear although the removal or alteration of it resulted in two orders of magnitude reduction of binding affinity of substrate and transition state compounds to BsCM. We show that amino acids from the flexible C-terminal tail of BsCM could cap the active site and even provide additional contacts to the substrate in the transition state. Additional information is needed to clarify the nature of its contribution to catalysis, where NMR methods can provide detailed structural dynamical insight. Although BsCM trimer is not of an exclusively large size by TROSY standards, the temperature at which the NMR studies should be conducted might be as low as a few degrees Celsius, which is necessary to maintain the dynamical equilibrium between free and bound ligands in the slow-exchange regime. At this temperature the apparent correlation time of the overall protein tumbling can be comparable to that of proteins with molecular weight around 100000 Dalton, which makes the use of TROSY indispensable.

Computational Chemistry

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Theoretical Study of the Physisorption of H_2 on Graphite Surface Using the Density Functional Theory Formalism Based on Electron Density Partitioning

F. Tran, T. A. Wesolowski, and J. Weber

Department of Physical Chemistry, University of Geneva, CH-1211 Geneva 4, Switzerland

The solid particles, present in the interstellar medium (ISM) in the form of silicates, crystallines, or amorphous carbon, ices, etc., provide various types of surfaces acting as support and/or catalysts for the synthesis of a number of molecules which, otherwise, would not be formed in two-body reactions. The production of molecular hydrogen H_2 in ISM is one such typical example, and, a type of surface which could serve as catalysts for the production of H_2 is graphite surface. In this work the density functional approach based on the partition into subsystems [1-2] was applied to study the physisorption of H_2 on graphite surface which was represented by polycyclic aromatic hydrocarbons (PAH) of growing size (C_6H_6, $C_{10}H_8$, $C_{14}H_{10}$, $C_{16}H_{10}$, $C_{20}H_{12}$, $C_{24}H_{12}$, $C_{32}H_{14}$). The most stable position of H_2 is situated above the center of a ring with a converged (with the size of the PAH) interaction energy of about 1.25 – 1.30 kcal/mol, which compares very well with the experimental value of 1.2 kcal/mol.

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Computational Chemistry

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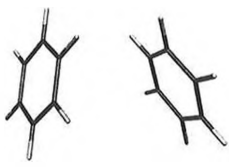
Theoretical Study of the Benzene Dimer Using the Density Functional Theory Formalism Based on Electron Density Partitioning

F. Tran, T. A. Wesołowski, and J. Weber

Department of Physical Chemistry, University of Geneva, CH-1211 Geneva 4, Switzerland

The density functional approach based on the partition into subsystems [1-2] was applied to study the benzene dimer $(C_6H_6)_2$. For several structures, the calculated interaction energy and intermolecular distance were compared with the previous theoretical results. A good agreement with high level *ab initio* correlated methods was found. For instance, the interaction energies obtained in this work and the CCSD(T) method agree within 0.1 – 0.6 kcal/mol depending on the structure of the dimer. The structure with the largest interaction energy is T-shaped, in agreement with CCSD(T) results. The T-shaped structure of benzene dimer was suggested by several experimental measurements. The calculated interaction energy of 2.09 kcal/mol agrees also well with experimental estimates based on the dissociation energy which ranges from 1.6 ± 0.2 to 2.4 ± 0.4 kcal/mol and the estimated zero point vibration energy of 0.3 – 0.5 kcal/mol.



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Chimie computationnelle

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Experimental and Calculated (DF theory) Absorption Spectrum of $[Ru(H_2O)_5L]^{+2}$ Complexes.

E. Sidorenkova[1], N. Aebischer[2], A.E. Merbach[2] and J. Weber[1]

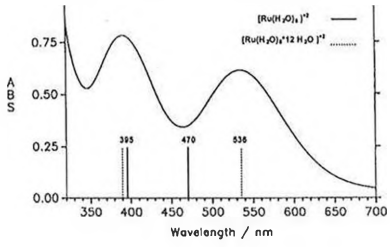
[1] Département de Chimie Physique, Université de Genève, CH-1211 Genève 4
[2] Institut de Chimie Minérale et Analytique, Université de Lausanne, CH-1015 Lausanne

The electronic spectra of $[Ru(H_2O)_5L]^{+2}$ complexes, L = H_2O, C_2H_4, CO, N_2, were calculated in present study.

The method for the calculation of the energies of proper spin and spatial symmetry adapted configuration state functions is based on the calculation of the energies of single determinantal wavefunctions. It is necessary to solve the Kohn-Sham equation for the symmetrically averaged density of the configurations (*average-of configuration* - AOC), corresponding respectively to the ground state and to each excited state in separate SCF calculations. This AOC calculation generates the orbitals, which will be used in all the Slater determinants. Those Slater determinants were calculated using DFT method.

The density functional theory (DFT) calculations have been performed the Amsterdam Density Functional (*ADF*) package of Baerends *et al.*

The electronic spectra (both vertical excitation energies and intensities) were calculated for $[Ru(H_2O)_5L]^{+2}$ complexes at LDA and GGA levels. The results show a good agreement with the experimental data.

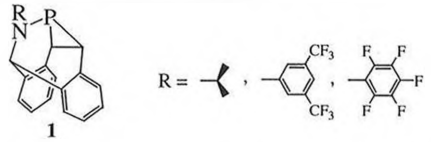


Computational Chemistry **278**

Reversible Metal Insertion into Phosphorus-Carbon Three-Membered Rings

G. Frison and H. Grützmacher*
Laboratory of Inorganic Chemistry, ETH-Zentrum, Universitätsstr 6, CH-8092 Zürich, Switzerland. E-mail: frison@inorg.chem.ethz.ch

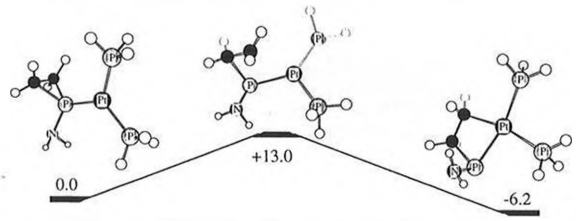
The synthesis of the novel polycyclic phosphiranes (**1**) has been recently reported in our group [1].



1

These new phosphorus-carbon cycles have electronic properties, which could make them interesting ligands in transition metal catalysed reactions. This has conducted to the observation of the first reversible insertion and deinsertion of a metal center into a three-membered heterocycle [2].

In order to determine factors which govern the phosphirane complex/metalla-phosphetane transformation, we have carried out DFT calculations on various Pt(0) complexes. The influence of the ligand on the potential energy surface will be discussed.



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Computational Chemistry **279**

Study of Photophysical and photochemical properties of the CpNiNO complexe. A Density Functional Theory Investigation.

Pascal Boulet[1,2], Henry Chermette[2] and Jacques Weber[1]
[1] Université de Genève, département de Chimie Physique, 30 quai E-Ansermet, CH-1211 Genève 4, Suisse.
[3] Université Claude Bernard Lyon 1, Laboratoire de Chimie-Physique Théorique, 41 bd du 11 novembre 1918, 69622 Villeurbanne Cedex, France et Institut de Recherches sur la Catalyse, CNRS, 2 av. Albert Einstein, 69626 Villeurbanne Cedex, France.

The photophysical properties of the cyclopentadienylnitrosylnickel complex ($Ni(C_5H_5)NO$) has been experimentally studied [1]. For a long time, it has been shown that the process of excitation leads to only one long-living metastable state (MS_{II}), with a distorted structure, namely a bended NiNO group of atoms. Recently, the second metastable state (MS_I), which corresponds to the $Ni(C_5H_5)ON$ species, with an inverted NO group of atoms has been identified [2].
We present in this poster a complete DFT investigation of the Potential Energy Curve (PEC) of the CpNiNO ground state complexe. Excited states of the ground- and metastable-states have been calculated using the Time-Dependent Density Functional Theory. From these results, the photochemistry of CpNiNO is presented.

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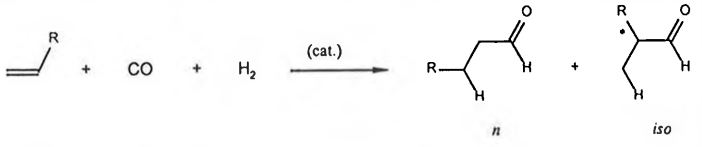
Computational Chemistry **280**

Dynamical vs. Static DFT Approaches to Activity in Rhodium-Catalyzed Hydroformylation

D. Gleich and J. Hutter

University of Zurich, Institute of Organic Chemistry, Winterthurerstrasse 190, CH-8057 Zurich, Switzerland

Hydroformylation is one of the largest scale processes of industrial homogeneous catalysis (see equation below) and therefore especially attractive for theoretical investigations [1]. Static DFT calculations with rhodium-phosphine systems of different electronic and steric properties (substrate = ethylene) are linked to those of Car-Parrinello MD simulations. Thereby, a deeper insight into the experimentally observed activity differences can be gained.



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Organic Chemistry **281**

Ab initio molecular dynamics simulations of excited-state proton transfer in chrysazin

Michael Odelius and Jürg Hutter

Organisch Chemisches Institut, Universität Zürich, Winterthurerstrasse 190, CH-8057 Zürich, Schweiz.

Ab initio molecular dynamics simulations were performed to study excited state proton transfer (ESPT) in chrysazin, $C_{14}O_4H_8$. The molecule was simulated in the ground state, using density functional theory, and in the first excited singlet state (S_1), using a restricted open-shell Kohn-Sham method [1]. To simulate chrysazine in a non-polar solvent such as cyclo-hexane [2], the simulation was performed of a molecule in gas phase, but the methodological framework allows for inclusion of an explicit solvent with both mixed quantum mechanics / molecular mechanics (QM/MM) and *ab initio* methods.

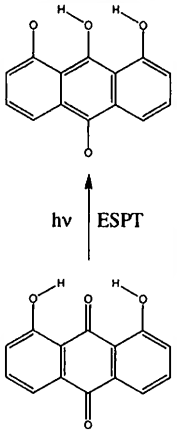

Figure 1: The excited state proton transfer (ESPT) in chrysazin (1,8-dihydroxyanthraquinone) is due to intra-molecular charge transfer. induced by transitions with $[n \rightarrow \pi^*]$ or $[\pi \rightarrow \pi^*]$ character.

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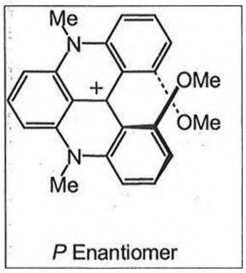
Computational Chemistry **282**

Density Functional Calculations of the Vibrational Circular Dichroïsm Spectra of a Helical Organic Cation

Delphine Bas[1], Christelle Herse[2], Jérôme Lacour[2], Jacques Weber[1] and Tomasz Wesolowski[1]

Departments of [1]Physical Chemistry and [2]Organic Chemistry, University of 1211 Geneva 4, Switzerland, Delphine.Bas@chiphy.unige.ch

Density functional theory (DFT) calculations were performed to study the structure and vibrational circular dichroïsm (VCD) [1] spectrum of 5H-Quino[2,3,4-kl]acridinium, 1, 13-dimethoxy-5,9-dimethyl- cation. This molecule -involved in the synthesis of novel triazaangulenium dyes of high chemical stability- is a chiral [4]-helicenium [2].



P Enantiomer

VCD measurements for this molecule are planned [3].The theoretical study reported in this work was carried out to enable the determination of the absolute configuration based on measured spectra.

A detailed analysis of the applicability of DFT calculations to this purpose was made. It involved the study of the effect of different basis sets and various exchange-correlation functionals on the results. Comparisons between the calculated geometry and the X-ray diffraction data were made. The calculations were performed using the Gaussian 98 suite of programs [4] for the *P*-enantiomer.

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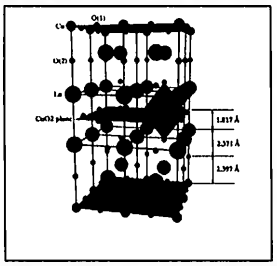
Computational Chemistry **283**

NMR chemical shielding tensors in high temperature cuprate superconductors

Samuel Renold[1], Pascal Boulet[2], Thomas Heine[2], Peter F. Meier[1], and Jacques. Weber[2]

[1] Physics Institute, University of Zürich, CH-8057 Zürich
[2] Department de chimie physique, Université de Genève, 1211 Genève
email: sam@physik.unizh.ch

Some theoretical approaches to explain the microscopic origin of high temperature superconductivity assume that antiferromagnetic correlations play a crucial role. A large amount of NMR Knight shift data has been accumulated mainly for copper and oxygen nuclei in the CuO_2 planes, which are the basic structural elements in the cuprate superconductors. Experimental information about static and dynamic spin susceptibilities is available by NMR measurements. To determine this quantity it is essential to know the chemical shifts. Experimentally, these are extracted from the Knight shifts at very low temperature, where, however, field inhomogeneities due to the vortex lattice impede precise measurements. Theoretically, the chemical shifts have, so far only been estimated by very crude models. Improved theoretical values would strongly help to understand both static and dynamic spin susceptibilities. Both, the ADF 2000 and Gaussian 98 packages provide tools for NMR calculations of open-shell systems. On this poster, we discuss preliminary results for NMR shielding tensors for copper and oxygen nuclei in CuO_2 layered materials.



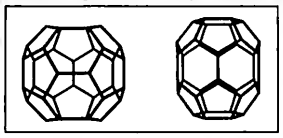
Computational Chemistry **284**

Structure and ^{13}C NMR spectra of $C_{36}H_x$ molecules

Clémence Corminboeuf[1], Patrick W. Fowler[2], and Thomas Heine[1]

[1] Department de chimie physique, Université de Genève, 1211 Genève
[2] School of Chemistry, University of Exeter, Stocker Road, Exeter, EX4 4QD, UK.

The possibility of stable fullerene forms of carbon with fewer than 60 atoms per molecular unit has been the subject of some debate since the initial experiments by Piskoti et al. [1] on a C_{36} solid. Recently, Koshio et al. synthesised $C_{36}H_4$, $C_{36}H_6$, $C_{36}H_4O$ and $C_{36}H_6O$ molecules. Experimental work on the ^{13}C NMR characterisation of these moieties is in progress [2]. Here, we present the complete scan over all topologically possible $C_{36}H_x$, x=2,4,6, structures based on the two C_{36} cage candidates with fewest pentagon adjacencies. These ~ 300000 molecules were optimised in geometry at the DFTB level. 21 isomers are possible candidates for the experimentally synthesised cages by means of energy [3]. Gradient-corrected DFT calculations of the ^{13}C NMR chemical shift at the IGLO-II/A2*/PBE level were performed for the 21 low-energy isomers and the idealised spectra are presented. They should assist with the ultimate identification of the $C_{36}H_x$ structure by ^{13}C NMR experiment.



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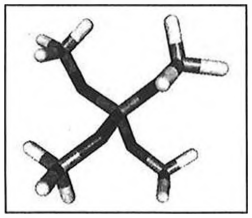
Computational Chemistry **285**

^{29}Si NMR calculations for silanes and their derivatives

Clémence Corminboeuf, Thomas Heine and Jacques Weber

Department of Physical Chemistry, University of Geneva, CH-1211 Geneva 4, Switzerland, Thomas.heine@chiphy.unige.ch

^{29}Si NMR calculations for silanes and their derivatives (methyl-, hydroxy-, methoxy-, methylmethoxysilanes and disiloxane) are performed using DFT molecular orbitals (obtained from the AllChem computer code[1]) and the IGLO[2] technique (as implemented in the MASTER package[3]). The quality of the basis set and auxiliary functions, which are used to represent the charge density, are tested both for geometries and chemical shift calculations. The LDA/DZVP/A2* level is found to give good results for all the classes of compounds studied here.



Chemical shift calculations are performed by using LDA and GGA (PW91, PBE) with the IGLOIII basis set and A2* auxiliaries. The results are compared with experiment and benchmarked against GIAO[4]-DFT and ab initio calculations (LDA, PW91, HF, MP2).

[1] Köster, A.M.; Heine, T.; Vela, A.; *AllChem* **2001**, Cinvestav-IPN, Mexico.
[2] Kutzelnigg, W. *Isr. J. Chem.* **1980**, 19, 193. Schindler, M.; Kutzelnigg, W. *J. Chem. Phys.* **1982**, 76, 1919.
[3] Malkin, V.G.; Malkina, O. L.; Salahub, D.R. *Chem. Phys. Lett.* **1993**, 204, 80 and 87. Malkin, V.G.; Malkina, O.L.; Casida, M. E.; Salahub, D.R. *J. Am. Chem. Soc.* **1994**, 116, 5898.
[4] Ditchfield, R. *Mol. Phys.* **1974**, 27, 789.

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Computational Chemistry **286**

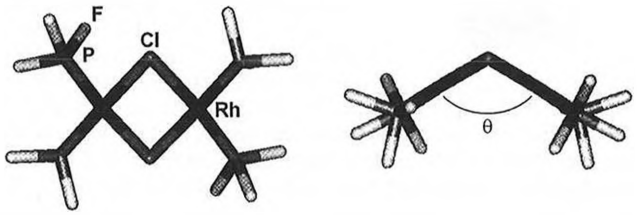
A density functional study of fluorophosphine complexes of rhodium precursors for chemical vapor deposition (CVD)

Seuret P.[1], Hoffmann P.[2], Wesolowski T.[1] and Weber J.[1]

[1] Department of Physical Chemistry, University of Geneva, 1211 Geneva 4, Switzerland
[2] Institute of Applied Optics, DMT, Ecole Polytechnique Fédérale de Lausanne, 1015 Lausanne-EPFL, Switzerland

Chemical vapor deposition (CVD) is a major technique for thin film manufacturing and local deposition of pure metal. It is based on controlled decomposition of volatile precursors transported in the gas phase to the substrate, resulting in a film deposit thereon. Decomposition of $[RhCl(PF_3)_2]_2$ with a focused electron beam was shown [1] to result in nanocomposits of metallic Rh clusters in an insulating matrix.

Several properties of gas phase $[RhCl(PF_3)_2]_2$ have been studied using density functional theory (DFT), such as geometry, IR frequencies, inversion barrier associated with angle θ (cf. scheme) and Rh-PF_3 dissociation energy.



For comparison, the corresponding properties of the homologous molecules $[RhBr(PF_3)_2]_2$ and $[RhI(PF_3)_2]_2$ were also determined.

[1] Ohta, T. and Hoffmann P., personal communication

Computational Chemistry **287**

DFT Study of the Ni(acac)$_2$py : conformational analysis

DAUL C., RAUZY C. and SCHLÄPFER C.W., Département de Chimie CH 1700-Fribourg, Switzerland

$Ni(tmhd)_2py_2$ can be obtained by the addition of two pyridines to $Ni(tmhd)_2$ molecule. This reaction proceeds in two steps

$$Ni(tmhd)_2 + py \rightleftharpoons Ni(tmhd)_2py$$
$$Ni(tmhd)_2py + py \rightleftharpoons Ni(tmhd)_2py_2$$

The final product has been analysed by X-ray diffraction and its structure is published. However, the intermediate: $Ni(tmhd)_2py$ can not be isolated and studied by the X-ray diffraction. The information contained in the NMR spectrum cannot be exploited. Some DFT calculations have already been carried out to better understand the reaction path. In this way, we can calculate the energies for different possible structures of the molecule and determine the most stable conformation. However, the energy differences are too small to determine unambiguously the most stable conformation. In the present communication we use the MM in QMM method to determine the correct structure of the $Ni(tmhd)_2py$ molecule. The result of this study will be presented.

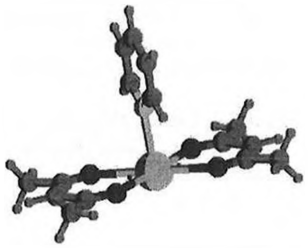


Fig. Structure of $Ni(tmhd)_2py$

Inorganic Chemistry **288**

Theoretical Study of the NLO properties of organic compounds

Valery Weber, Ilaria Ciofini, Claude A. Daul
Department of Chemistry, University of Fribourg, Switzerland

DFT and semi-empirical methods have been applied in order to study and understand organic and organometallic dipole structures. In particular we focused our study on helical organic structure such as heterohelicenes.
The ground state properties of M-(-)-tetrathia[7]heterohelicene (Fig. 1) have been studied using DFT and its UV-Vis spectra were fully characterized by the means of both TD-DFT and semi-empirical approaches. The results of the calculations are in good agreement with the available experimental data [1]. The NLO properties (static and dynamic polarizabilities as well as the hyperpolarizability) were also computed.

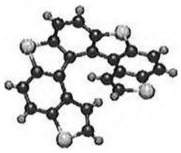


Fig. 1

This system has recently been functionalized with donor and acceptor group in order to enhance the NLO properties [2].
A first screening of the effect of the donor and acceptor groups on the NLO properties was performed mainly by the use of semi-empirical approaches.
Finally, the contribution of both electric and magnetic dipoles to NLO properties in case of chiral systems is under analysis and possible routes to compute the magneto-optical susceptibilities are currently studied.

[1] Groen *et al.* J. Am. Chem. Soc. **93**, 2968 (1971)
[2] S. Maiorana, A. Papagni, private communication

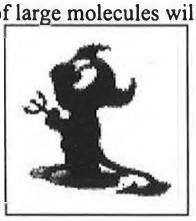
Computational Chemistry **289**

Slow expensive DFT calculations made fast and cheap - some features of deMon 2001

Thomas Heine[1], Andreas M. Köster[2] and Alberto Vela[2]

[1] Department de chimie physique, Université de Genève, 1211 Genève
[2] Department of chemistry, Cinvestav-IPN Mexico City, Mexico.

The new deMon 2001 DFT program package will be released in summer 2001. Two of its new techniques, which allow performing DFT calculations of large molecules will be presented in this talk:



- Transferable and parameter-free Density-Functional based Tight-Binding starting density for faster convergence to the correct state.
- Efficient use of Hermite Gaussian auxiliary functions for the computation of the Hartree and exchange-correlation integrals.

Some examples which illustrate the power of this code will be given in this talk. They include ^{13}C NMR calculations of endohedral fullerenes containing transition metal compounds $Sc_3N@C_{68}$ and $Sc_3N@C_{80}$ on the IGLO-II/A2*/PBE level, geometry optimisations of a set of alkanes ($C_{48}H_{98}$, $C_{60}H_{122}$, $C_{72}H_{144}$ and $C_{84}H_{170}$), and the accuracy of the SiOSi angle and the ^{29}Si chemical shift in disiloxane derivates $X_3SiOSiX_3$, X=Me, F, Cl, H. Special emphasis is given on the computational ressources needed for each type of calculation.

Computational Chemistry **290**

A novel dynamical scheme for the exploration of free energy surfaces; observing the formation of the bromonium ion in solution

Joost VandeVondele and Ursula Rothlisberger
ETH, Laboratory of Inorganic Chemistry, 8092 Zurich, Switzerland

One goal of molecular dynamics simulations is to provide a direct atomistic picture of chemical reactions and conformational changes. However, the timescale that is typical for these events (ms-days) can rarely be achieved with direct simulation (ps-ns). We present a novel molecular dynamics technique (CAFES) that performs a highly efficient free energy sampling. A combined dynamical scheme is employed in which a reactive subsystem performs an enhanced sampling of its free energy surface, whereas the environment, which is rigorously taken into account, follows adiabatically.

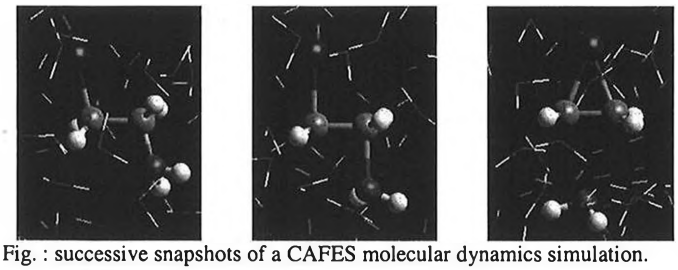


Fig. : successive snapshots of a CAFES molecular dynamics simulation.

In a first study we compute the free energy surface of a dipeptide in solution to verify our approach. These results indicate that new conformations can be found efficiently and accurately, even though naturally the interconversion would occur on millisecond timescales. Furthermore, a CAFES simulation within a QMMM (MM/CPMD) framework of a protonated 2-bromoethanol in explicit solvent enables us to observe the spontaneous formation of the bromonium ion , as shown in the figure.

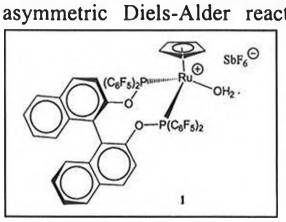
Computational Chemistry **291**

Modelling the Inversion-Barrier in the Lewis Acid [CpRu(BINOP-F)]$^+$ by Density Functional Theory

Clémence Corminboeuf[1], Thomas Heine[1], E. Peter Kündig[2], Christophe M. Saudan[2], and Jacques Weber[1]

Departments of [1]Physical Chemistry and [2]Organic Chemistry, University of Geneva, Switzerland, clemence.corminboeuf@chiphy.unige.ch

The 16-electron half-sandwich complexes of the type $CpM(L_2)^+$ (M = Fe, Ru, L = chiral bidentate phosphinite ligands) are efficient catalysts for the asymmetric Diels-Alder reaction between enals and dienes [1]. This contribution centers on the complex [CpRu(BINOP-F)(H_2O)] (**1**). It has been observed that the diastereotopic P atoms give rise to two doublets in the low temperature ^{31}P NMR spectrum but collapse to a singulet at 50 °C.[2] A possible mechanism is water dissociation, followed by a pendulum movement of the bidentate ligand and recoordination of the water molecule. The inversion of the pyramidal geometry through a planar intermediate or transition state renders the two P atoms equivalent. Complementary to kinetic studies of these processes [3], our approach involves modelling the potential energy surface of this movement in order to obtain an energy for the barrier of inversion. The calculations are performed at the DZVP/A2/PBE level of density functional theory using the AllChem computer code [4]



1

[1] E.P. Kündig, C.M. Saudan, F. Viton, *Adv. Synth. Catal.* **2001**, *343*, 51-56 and ref. cit.
[2] C.M. Saudan, Ph.D. thesis No. 3244, University of Geneva, 2001.
[3] V. Alezra, U. Frey, E. P. Kündig, A. Merbach, C.M. Saudan, F.Viton, article in preparation.
[4] A.M. Köster, T. Heine, A. Vela, *AllChem* **2001**, Cinvestav-IPN, Mexico

Computational Chemistry **292**

Flexibility and function in HIV-1 PR: the role of compensatory mutations.

Stefano Piana Agostinetti , Paolo Carloni, Ursula Roethlisberger

ETH Zurich, Inorganic Chemistry, Universitatstrasse 6, 8092 Zurich, Switzerland

HIV-1 PR is the major targets for anti AIDS drug therapies. One of the obstacles in current anti AIDS therapies is the emergence of drug resistance; drug-resistant HIV-1 PR mutants no longer bind the drug while retaining an appreciable catalytic activity. Several point mutations have been observed, often in combination. In these multiple variants, one mutation disrupts favorable enzyme-drug interactions, leading to loss of drug-binding, which is however accompanied by a loss of catalytic activity. The others are "compensatory" mutations in the sense that they are able to restore the enzymatic activity. Intriguingly, the "compensatory" mutations may occur in regions far from the active site and they do not lead to significant structural rearrangements.

Here we investigated the dynamics of the HIV-1 PR/substrate complex in the wild type and I46M/L63P mutated enzyme. By comparison of the two studies, we show that compensatory mutations are able to enhance the catalytic activity of HIV-1 PR by modulating the conformational flexibility of enzyme regions that are located far from the point mutation itself. Furthermore we show that different effects are observed when different steps of the catalytic cycle are considered. These findings allow to rationalize all the kinetic and structural data currently available for these mutants.

Computational Chemistry **293**

Study of $H_2PO_4^-$ anion in water using Car-Parrinello mixed Quantum Mechanics/Molecular Mechanics simulation (QM/MM)

M. C. Colombo, A. Laio and U. Röthlisberger

Institute of Inorganic Chemistry, ETH
8092, Zurich

Recently a QM/MM method [1] has been developed that allows to perform Car-Parrinello [2] molecular dynamics of a quantum solute embedded in a solvent described with a standard classical force field. Particular to our approach [1] is that the QM/MM interaction is described with an empirical pseudopotential in order to correctly reproduce the properties of a quantum water molecule solvated in classical water.

The correct description of phosphate anions is crucial for the study of DNA. Therefore, we investigate the accuracy of our QM/MM method applied to the prototypical anion $H_2PO_4^-$. We focus on the solvation properties of the QM/MM system and compare to both a full QM and MM description.

[1] A. Laio, J. VandeVondele, and U. Rothlisberger (submitted).
[2] R. Car and M. Parrinello, Phys. Rev. Lett. **55**, 2471 (1985).

Computational Chemistry **294**

RESP charges from Car-Parrinello mixed Quantum Mechanics/ Molecular Mechanics (QM/MM) simulations.

Alessandro Laio, Joost VandeVondele and Ursula Rothlisberger

Institute of Inorganic Chemistry, ETH
8092 Zurich

We present a method to obtain electrostatic potential derived (RESP) [1] atomic charges fitting their value to the potential and the forces on the MM atoms in a finite temperature Car-Parrinello[2] mixed Quantum Mechanics/ Molecular Mechanics (QM/MM) simulation [3].

We will show that charges fitted on a *single* molecular dynamics (MD) frame and restraining their magnitude to the Hirshfeld[4] value are in general consistent with "chemical intuition". In a finite temperature MD run, the charges display significant fluctuations that can be attributed to the polarizability of the atom. The change in the RESP values due to a chemical reaction can be clearly distinguished from these thermal fluctuations. Therefore, the RESP charges can be used as reliable and computationally cheap indicators of the chemical state of the system in a QM/MM simulation.

[1] U. C. Singh, P.A. Kollman, *J. Comp. Chem*, **5**, 129 (1984)
[2] R. Car, M. Parrinello, *Phys. Rev. Lett.*, **55**, 2471 (1985)
[3] A. Laio, J. VandeVondele and U. Rothlisberger, submitted
[4] F. L. Hirschfeld, *Theo. Chim. Acta*, **44**, 129 (1977)

Computational Chemistry **295**

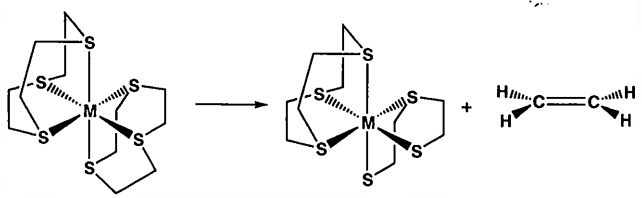
First-Principles Simulation of C-S Bond Cleavage in Thioether Complexes of Technetium, Rhenium and Ruthenium

Patrick Maurer, Alessandra Magistrato and Ursula Röthlisberger

Laboratory of Inorganic Chemistry, ETH Zentrum,
8092 Zurich, Switzerland

Among thioether compounds $[M(9S3)_2]^{n+}$, where M are metals from groups 7-12 of first, second and third row transition elements, 9S3 is 1,4,7-trithiacyclononane and n=1-3, $[Tc(9S3)_2]^{2+}$ and $[Re(9S3)_2]^{2+}$ clearly differ from their later transition metal congeners [1]. They do not only present the longest C-S bond lengths among these compounds, but they also differ in reactivity. In the presence of mild reducing agents such as ascorbic acid, in aqueous solution and at room temperature, they undergo instantaneous C-S bond cleavage to yield ethene and $[M(9S3)L]^+$, $(L=S(CH_2)_2S(CH_2)_2S)$.

Using static DFT calculations as well as *ab initio* molecular dynamics, we have performed a detailed characterization of the thioether complexes of the d^5 and d^6 ions of technetium, rhenium and ruthenium and provide an explanation for the observed reactivity.



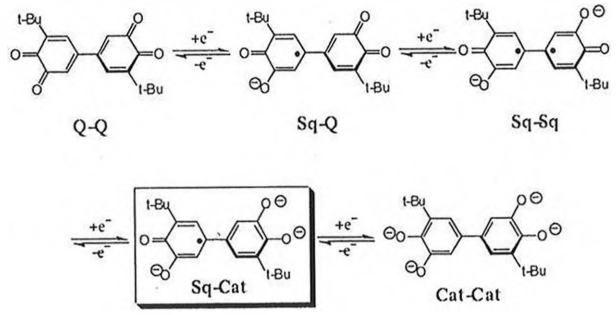
[1] Mullen, G.E.D.; Went, M.J.; Wocadlo, S.; Powell A.K.; Blower, P.J.; *Angew. Chem.* Int. Ed. Engl. **1997**, 36, 1205

Computational Chemistry **296**

o–dioxolenes: a DFT Study

F.Mariotti[1], A.Bencini[2], C.A.Daul[1]
[1)]University of Fribourg, Switzerland, [2)]University of Florence, Italy

Paramagnetic bridging ligands are of considerable interest for the design of materials showing peculiar physical properties. Their utilization for the synthesis of molecular wires, optical switches, and ferro– or ferri–magnetic chains has been proposed from several research groups[1].
Molecules containing linked o–dioxolenes may be of considerable interest in this framework because of their redox activity[2]. The bis–o–quinone (Q–Q) is part of a five–membered redox chain (Q–Q, Q–Sq, Sq–Sq, Sq–Cat, Cat–Cat) in which all the members are able to act as bis–bidentate ligands.



We propose a DFT characterization of geometrical parameters and magnetic properties which are the main characteristic of these systems. Coupling with vibrational states is as well considered and the potential energy surface is explored for e better understanding and in order to propose some hints for the synthesis of new materials.

1) Kahn, O. In Modular Chemistry; Michl, J., Ed.; Kluwer: Dordrecht, 1997. Gatteschi, D. AdV. Mater. 1994, 6, 35.
2) A.Bencini et al. Inorg. Chem. 2001, 40, 1582–1590.

Computational Chemistry **297**

A DFT Study of the excited states of chromium (III) hexachloride and chromium (III) hexacarbonyle ions : dependence of the system of coordinates

DAUL Claude and RAUZY Cedrick, Département de Chimie, CH 1700-Fribourg, Switzerland

The excited states of both complexes: chromium (III) hexachloride $[Cr(Cl)_6]^{3-}$ and chromium (III) hexacarbonyle $[Cr(CO)_6]^{3+}$, has been investigated using density functional theory. We have optimised the geometry for both complexes in octahedral symmetry. The influence of the multiplets energies as a function of the system of coordinates, i.e. a trigonal versus a tetragonal frame is considered. DOCLO K. and al [1] has showed, using ligand field theory, that the first order multiplet energies can be different for both cases. In this communication, we present a method of calculation, which is invariant upon the choice of system coordinates. Our method does incorporate second order corrections. This study allows us to discuss the influence of the reference axis upon the calculation of multiplet energies with ADF.

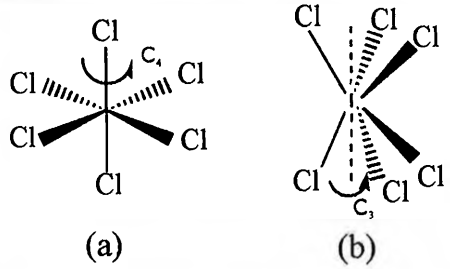


Fig. $[CrCl_6]^{3-}$ with (a) trigonal and (b) tetragonal axis

[1] : DOCLO K., DE CORTE D., DAUL C. and GÜDEL H., Inorg. Chem., **1998**, 37, 3842-3847.

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CONFERENCE REPORTS

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36th ESF/EUCHEM Conference on Stereochemistry

Bürgenstock, April 28–May 4, 2001

Per I. Arvidsson* and Jens Frackenpohl

Keywords: Bürgenstock · EUCHEM · Interdisciplinary–Chemistry & Biology · Organic chemistry · Stereochemistry

For more than 35 years, the ESF/EUCHEM conference on stereochemistry has followed a number of rules that help to preserve its mystery. As an example hereof, the program is kept secret until the registration, and none of the information presented is to be used elsewhere without the approval of the presenter. Another rule states that the conference should take place in a relaxed atmosphere at a suitable location. In this regard, nothing could be more suitable than the Bürgenstock! Located in the very heart of Switzerland, this mountain outside Lucerne hosts a series of luxury hotels with a truly spectacular view over the wonderful Vierwaldstätter See and the nearby Alps.

Given the reputation of the meeting and the terrific scenery, it was no surprise that this year's president, ***Andrea Vasella*** (ETH Zürich, Switzerland), and the local organizing committee composed of *Hans-Beat Bürgi* (University of Bern), *François Diederich* (ETH Zürich), *E. Peter Kündig* (University of Geneva), and *Klaus Müller* (Hoffmann-La Roche, Basel), had been able to attract several of the most prominent scientists from Europe and overseas. In total, 135 academic and industrial scientists, from 21 different countries around the world, gathered on the mountain for a five-day tribute to science. Although the title of the conference implies a stereochemical focus, this was by no means the only topic discussed! The organizers made clear that stereochemistry is indeed a central part of all undertakings in chemistry and biology, and had accordingly put together a highly interdisciplinary program spanning from organic synthesis to medicinal glycobiology. To honor this year's 'guest of honor' ***Duilio Arigoni*** (ETH Zürich, Switzerland), some emphasis was put on biosynthetic pathways.

Apart from many distinguished professors, and researchers from major European pharmaceutical companies, the audience consisted of several young scientists who had been given the opportunity to attend the meeting thanks to generous financial support from the *European Science Foundation* (ESF) and the *Swiss National Science Foundation* (SNSF). Several editors from the major European chemical journals also attended the meeting. This gave editors and authors an opportunity to exchange views and suggest improvements in the publication process.

The high level of the scientific program rapidly became obvious to all participants when *Jean-François Normant*

Happy faces of Duilio Arigoni (Guest of Honor) and Andrea Vasella (President).

Elias J. Corey

*Correspondence: Dr. P.I. Arvidsson
Laboratorium für Organische Chemie
ETH Zentrum
Universitätstrasse 16
CH–8092 Zürich
Tel: +41 1 632 47 81
Fax: +41 1 632 11 44
E-Mail: arvidsson@org.chem.ethz.ch

introduced ***Elias J. Corey*** (Harvard University, USA) as the first speaker. As *the* 'grand old man' of organic synthesis, Corey began by commenting on the current state of organic chemistry and the future of the discipline. He pleased the many organic chemists in the audience by testifying that organic chemistry is 'the language of life itself,' and that 'organic chemists are the artists of life'. Thus, the vitality of the field, and its central role in future exploration of chemistry and at the interfaces to biology and materials science, were then undeniably ascertained! In his lecture 'Catalytic Enantioselective Synthesis. Methods, Pathways and Applications', Corey moved on to give us a historical tour of his continuing developments of enantioselective Diels-Alder reactions. Exemplified by applications in total synthesis, he guided us through a 50-year odyssey; going from simple resolution, *via* auxiliary-based, and finally to catalytic enantioselective Diels-Alder reactions. Through mechanistic studies, utilizing low temperature NMR spectroscopic investigations on the reacting complexes in solution, he could rationalize the outcome of the reactions and continue to improve their performance. New and more effective syntheses of old target molecules could thus be realized, as well as a novel synthesis of Eunicenone A_1 [1].

Relaxed but intensive discussions during Sunday's poster session.

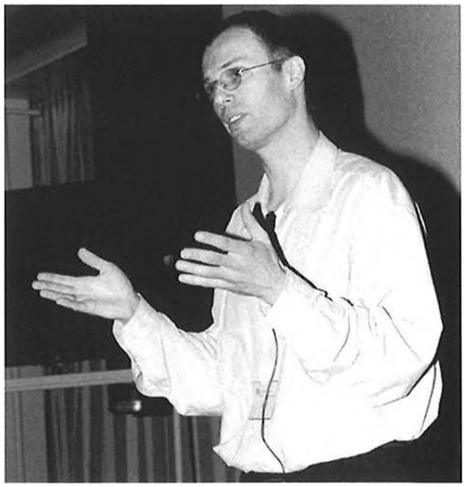
The second lecture entitled 'Catalytic and Stoichiometric Carbon-Carbon Coupling at Zirconium Complexes' was presented by ***Gerhard Erker*** (Universität Münster, Germany). Erker introduced us to the field of polymer chemistry and explained how different catalysts are able to influence the polymerization of propene to produce either atactic, syndiotactic, or isotactic polymers. His own work mainly deals with the development of new types of 'constrained geometry' Ziegler-Natta catalysts. Specifically, he exploits ligands having carbon atoms in the bridge between the cyclopentadienyl ligand and the nitrogen ligand, as compared to the silicon bridge usually present in these systems. Again, NMR spectroscopy was successfully used for mechanistic investigations of organometallic reactions; in this case, insight into the kinetics of competing processes was gained, and thus helped to impose stereocontrol on the polymerization process [2].

After a superb lunch, and some hours of recreation and informal discussions, the first poster session followed. Five of the 25 posters were selected for short oral presentations: *Valentine Ananikov* (Zelinsky Institute of Organic Chemistry, Russia, 'Stereo- and Regioselective Alkynes Conversion to Substituted Dienes: Pt(IV)-Catalyzed Triple Bond Activation and C–C Coupling Reactions'), *Shankar Balasubramanian* (University of Cambridge, UK, 'Inhibition of Human Telomerase Activity by an Engineered Protein that Binds Telomeric G-Quadruplex DNA'), *Masakazu Ohkita* (Hokkaido University, Japan, 'Syntheses of Acetylenic Oligophenylene Macrocycles Based on a Novel Dewar Benzene Building Block Approach'), *Martin D. Smith* (University of Cambridge, UK, 'An Approach to the Total Synthesis of Antascomicin B'), and *Jef Vekemans* (Eindhoven University of Technology, The Netherlands, 'Supramolecular Architectures in Protic Media: Transfer and Amplification of Chirality').

In the same vein as the lectures earlier in the day, the evening lecture also went in the direction of synthetic organic chemistry. Moderator *G. Michael Blackburn* introduced ***Tohru Fukuyama*** (University of Tokyo, Japan), who presented

Gerhard Erker

Tohru Fukuyama



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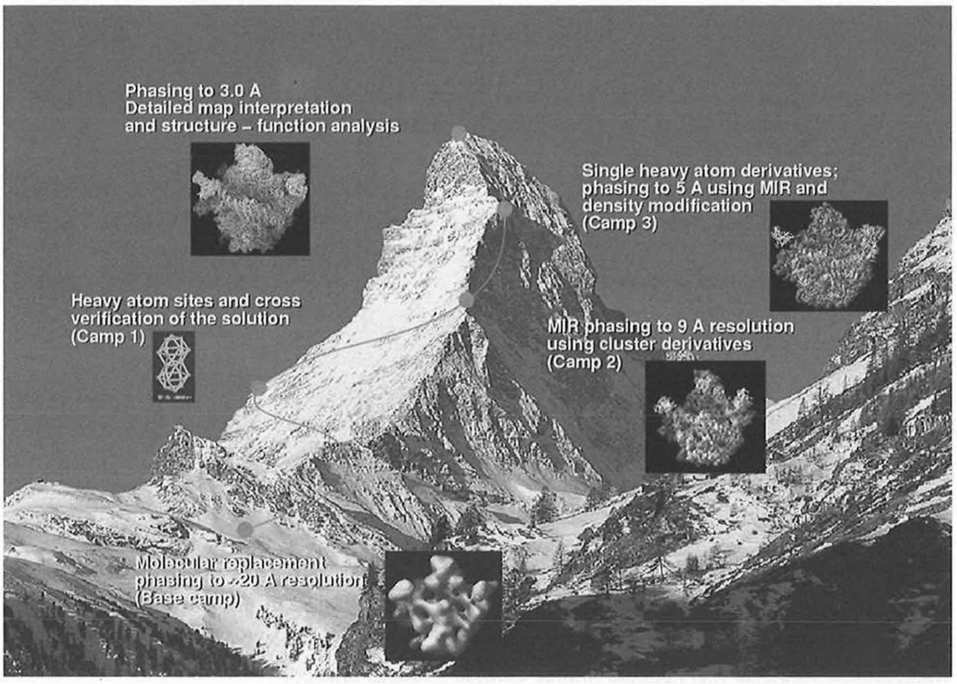
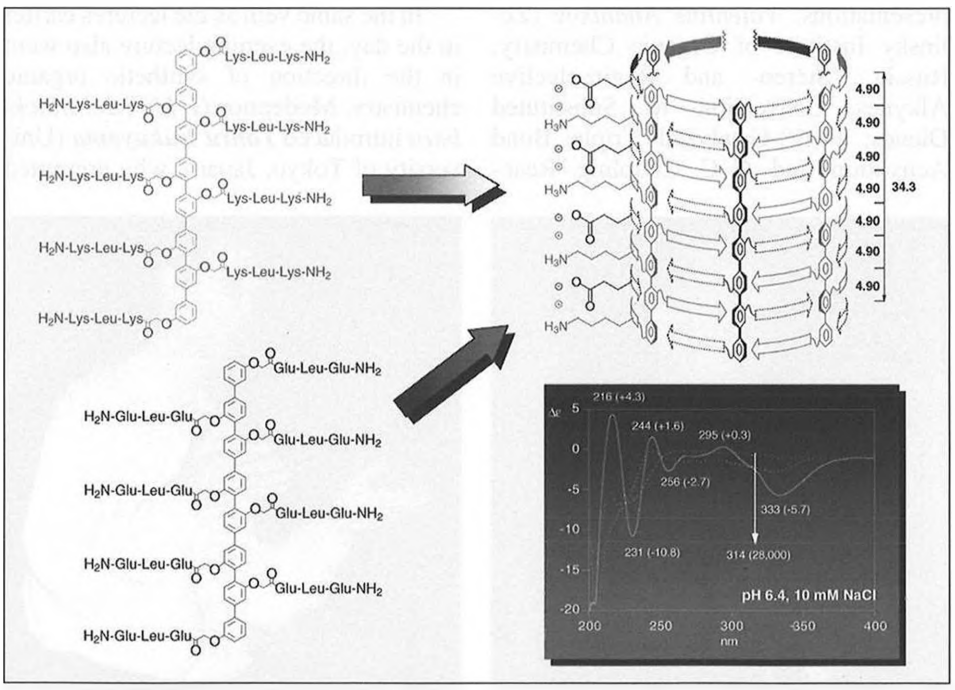


Fig. 1. A demanding climb towards the peak, solving the X-ray-structure of the large ribosomal subunit at 3.0 Å resolution

the lecture 'Synthetic Studies on Indole Alkaloids'. Fukuyama first showed how the indole skeleton could be assembled through a powerful one-pot radical cyclization of α-stannoimidoyl radicals, generated from O-isocyanostyrene derivatives. This procedure is also well suited for generating diversity, since a variety of groups can be introduced in the 2 and 3 positions of the indole ring. Fukuyama then exemplified his expertise in the area of indole chemistry through the successful synthesis of a large variety of indole containing natural products, including the very demanding (+)-inblastine [3].

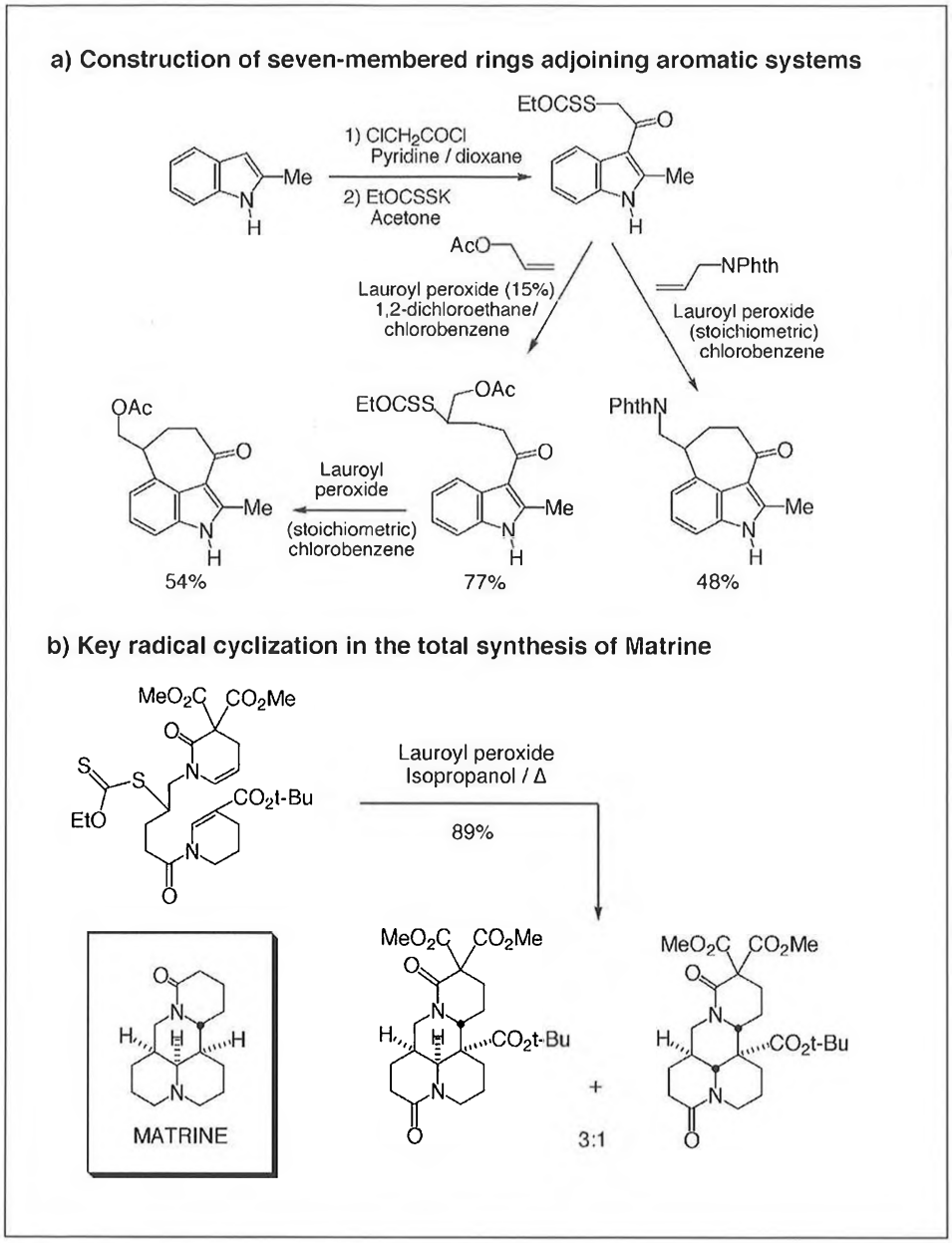
After a minor alteration of the program, Monday morning became devoted to more biological issues. ***Nenad Ban*** (ETH Hönggerberg, Zürich, Switzerland), introduced by *Jay Siegel*, gave a colorful presentation on his work towards the 'Structure and Function of the Large Ribosomal Subunit'. He carefully escorted us through the long and challenging climb that started with a low-resolution electron microscopy map and ended up in an impressive X-ray structure of the whole large ribosomal subunit at 3.0 Å resolution (Fig. 1). Indeed, Ban was right when he proclaimed, 'reaching the top of the mountain will allow you to have a good view'. The view in this case was not only beautifully colored pictures, but also a detailed blueprint that rationalizes how the 'protein synthesis machine' of the cell functions in atomic detail [4]. Knowing that many antibiotics act by blocking the tunnel through which the newly synthesized proteins emerge, and that drug-resistance can be caused by mutations in the proteins surrounding the exit of the tunnel, it may be anticipated that this structural information will aid rational design of new antibiotic agents. It was also interesting to note how this excellent mix of chemistry, biology, and crystallography crossed all borders between disciplines and sparked a lively and fertile discussion among the participants.



Scheme 1. Formation of rigid-rod molecules (monitored by CD spectroscopy)

'Bioorganic Chemistry of Rigid-Rod Molecules' was the topic when ***Stefan Matile*** (University of Geneva, Switzerland) presented the second lecture of the day. Reminiscing about his past artistic training, Matile showed how toroidal rigid rod molecules, composed of a polyphenyl backbone with attached peptide strands, could be architecturally self-assembled, through β-sheet formation of the peptide stands, to form large super barrels (Scheme 1). Fascinatingly, these supra-molecular complexes form stable channels when put into a membrane. Binding of DNA could be achieved by decorating the inside of the barrel with lysine residues, while incorporation of histidine residues turned the barrel into a catalytic ion-channel. The histidine-containing barrel was also shown to hydrolyze an entrapped ester derivative, with the same efficiency as the best *de novo* designed catalysts or catalytic antibodies. Appealing applications, such as non-ribosomal peptide synthesis and polyketide synthesis, by simple passage of reactants through a suitable barrel could be envisioned [5].

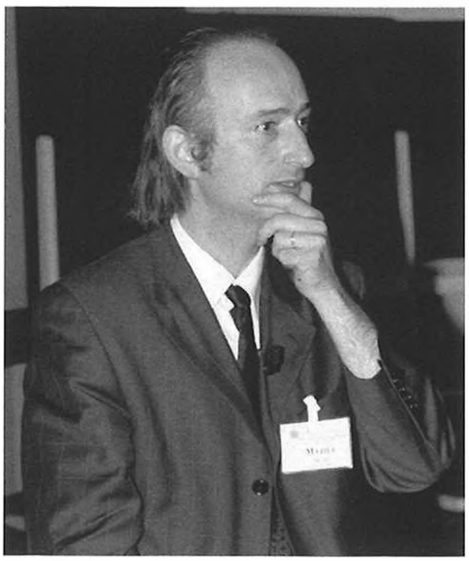
In the evening, radical chemistry was the issue when *Armido Studer* introduced ***Samir Z. Zard*** (Ecole Polytechnique Palaiseau, France). In his lecture 'Explorations in Radical Chemistry: Some New Reactions for Organic Synthesis', Zard taught us how to keep radicals 'calm' and give them time to react in the desired way. Instead of using tin-based chemistry, Zard employed xanthates and related dithiocarbonyl derivatives as radical precursors, and triggered the radical formation by addition of a catalytic amount of



Scheme 2. Xanthate-mediated synthesis of medium-sized rings and of alkaloids

lauroyl peroxide. This methodology could be efficiently employed for construction of medium-sized rings, and opened alternative pathways to indoles and other heterocyclic systems (Scheme 2). Applications in total synthesis were also realized as witnessed by the successful synthesis of Erythratidinone, Alloyohimbane, and Matrine. The mildness of the radical processes also makes them suitable for selective removal of hydroxyl groups in complex carbohydrate derivatives [6].

Biosynthetic pathways were the combining theme in the two lectures of the third day. *David Gani* first introduced ***Rowena G. Matthews*** (University of Michigan, USA), who talked about 'Cobalamin-Dependent Methyl Transfers'. Cobalamin cofactors are known to play critical roles in several types of biological reactions. Best understood is the involvement of adenosylcobalamin in radical generation; however, cobalamin and its close relatives, the corrinoids, also serve as cofactors for biological methyl transfer reactions. Matthews outlined her studies on the mechanism of the cobalamine dependent enzyme methionine synthase, responsible for the cellular synthesis of methionine from homo-cysteine. Since the rate-limiting step of this modular enzyme involves a series of conformational interconversions (Fig. 2), Matthews divided the enzyme into two parts. This retro-engineering approach allowed her to study the underlying chemistry of the four modules independently. Thus, it was suggested that the reaction between cobalamin and the methyl donor CH_3-H_4folate follows an S_N2 mechanism, while the reaction of methylcobala-



Stefan Matile

Samir Z. Zard

Rowena G. Matthews

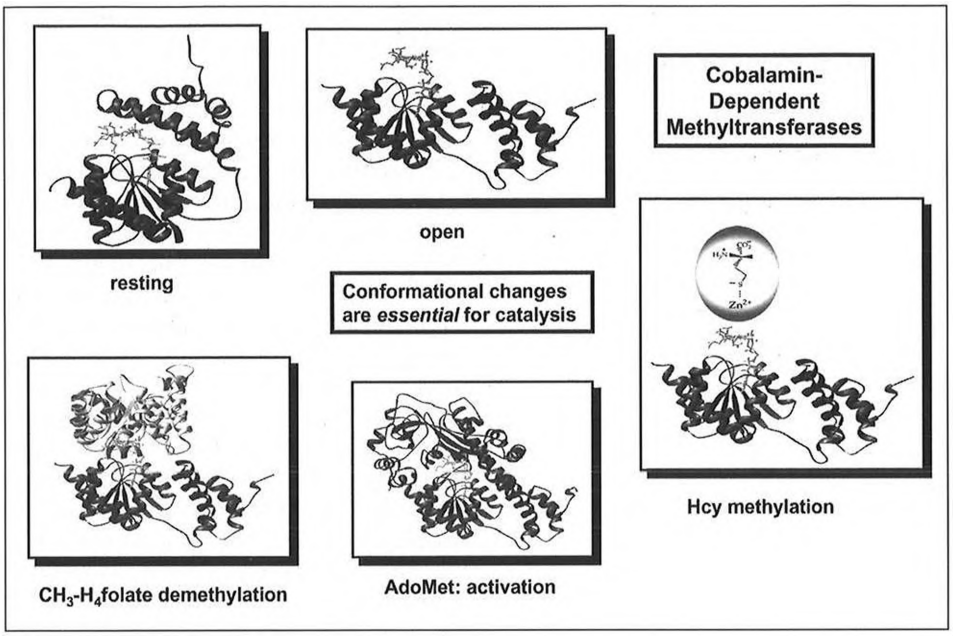


Fig. 2. Cobalamin-dependent methyltransferases: their conformational changes and mode of action

min with the homcysteine might employ an SET mechanism [7]. Given that no mechanism can ever be proven, these statements set off a lively discussion between the participants after the lecture.

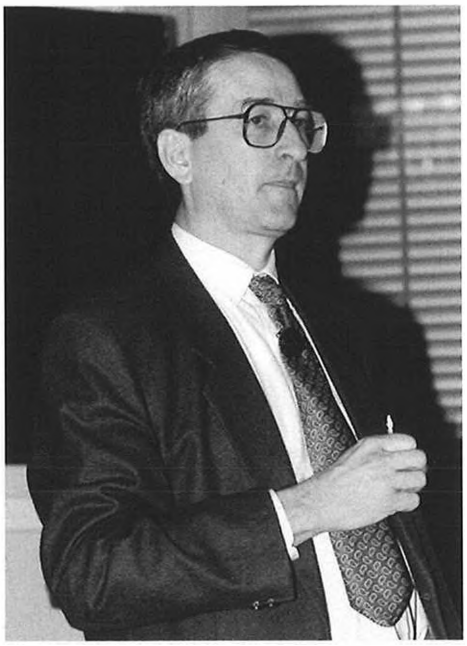
Enzyme mechanisms were also the topic of the lecture 'Structure and Mechanisms Involved in the Enzymatic Synthesis and Degradation of Polysaccharides' by ***Gideon Davies*** (University of York, UK). In his case, most emphasis was put on structural information gained through X-ray crystallographic analysis of carbohydrate synthesizing and degrading enzymes, in the absence and presence of their inhibitors. Initially, Davies addressed structure and mechanism of glycoside hydrolases, *i.e.* enzymes that hydrolyze the glycosidic bond in di-, oligo- and polysaccharides. These enzymes are important for food storage and utilization, as well as for cell–cell recognition and viral invasion. Furthermore, many of these enzymes find widespread industrial applications and the development of enzyme inhibitors, as therapeutic agents has recently attracted much attention with the anti-influenza drug *Ralenza* as a prime example. After concluding that much physical organic chemistry is still needed before we can properly understand the action of polysaccharide lyase enzymes, he went on to discuss Nature's way of synthesizing polysaccharides. Glycoside linkage formation is the most abundant enzyme-catalyzed reaction on earth, and Davies could show that the process proceeds with either retention or inversion at the C(α) of the glycosyl donor, depending on the donor and the class of enzyme involved [8]. Finally, Davies himself triggered the discussion by stating that the 'real mechanism of hen egg-white lysozyme involves a simple double displacement, and there are no exceptions!'.

On Tuesday evening, it was time for the traditional conference dinner at the Bürgenstock club. The delightful dinner was followed by lovely chamber music from the *Aura String Quartet* (Basel), who performed pieces from J.S. Bach, F. Mendelssohn, and G. Verdi, especially selected by president Vasella. When the last tunes from the string instruments (one of them actually a genuine Stradivarius) had faded out in the warm late-spring night, a relaxed reception conveyed the participants to new late-night discussions.

Introduced by *Beat H. Meier*, the lecturers of Wednesday morning gave the participants an overview of recent developments in analytical methods. ***Renato Zenobi*** (ETH Zürich, Switzerland), presenting 'New Applications for Soft Ionization Mass Spectrometry', showed how electrospray ionization (ESI) and matrix-assisted laser desorption ionization (MALDI) can be used to study non-covalent interactions. These modern ionization methods have opened new and unex-

Gideon Davies

Renato Zenobi

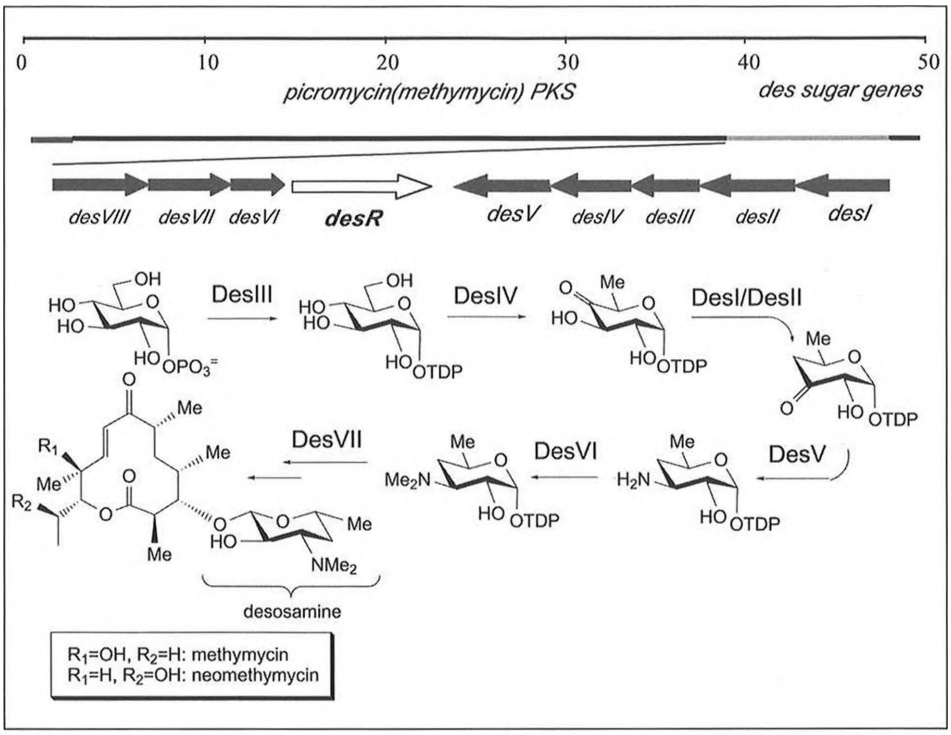


Steve W. Homans

pected applications for mass spectrometry. Apart from determining the stoichiometry of non-covalent complexes, insight into the nature of these interactions can be gained. Furthermore, it is often possible to determine the dissociation constant from mass spectrometry, something that is of great interest for the pharmaceutical industry when it comes to screening enzyme-inhibitor complexes. Zenobi also demonstrated how MALDI mass spectrometry might be used to gain structural information about proteins. Through proper selection of matrix anions, the number and nature (*i.e.* Lys or Arg) of exposed positively charged sidechains in a native protein could be determined [9]!

Recent developments in NMR spectroscopy were the topics of ***Steve W. Homans'*** (University of Leeds, UK) talk 'Structure, Dynamics and Interactions of Macromolecules in the Weakly Aligned State'. He described novel methods for rapid structure determination of proteins, with the ultimate goal of completely automating the process. Employing proteins with only the backbone atoms labeled allowed Homans to derive coupling constants more effectively than in the normal case, *i.e.* utilizing fully labeled proteins. Further studies of the protein in a weakly aligned state, such as in a phospholipid bilayer, provided the residual dipolar coupling. The two sets of complementary dipolar coupling constants could then be combined to determine the secondary structure of the protein through dihedral angle mapping of the backbone torsion angles. Finally, the tertiary structure was resolved by packing the secondary structural elements and taking restrictions from long-range NOEs into account. Later, Homans showed how NMR spectroscopy could be used in rational drug design and in structure–activity relationship studies. 'Intelligent ligand screening', and determination of the conformation of a ligand when bound to a protein, could be realized by studies of ^{13}C-labeled ligands in the presence of an aligned unlabeled protein [10].

After lunch, the second poster session began. Again, five out of the 23 posters were selected for short oral presentations: *Françoise Hénin* (Université de Reims-Champagne Ardenne, France, 'Gradual Generation of Linear Enolic Species in Neutral Medium and their Catalytic Asymmetric Protonation'), *Ivan Huc* (CNRS, IECB–Polytechnique, France, 'Interconversion of Single and Double Helices Formed from Synthetic Molecular Strands'), *Rodolfo Marquez* (Oxford University, UK, 'Studies towards the Synthesis of Fumagillin and Related Analogues'), *Nathalie Solladié* (CNRS, Laboratoire d'Electrochimie & Chimie Physique, France, 'Synthesis and Preliminary Physico-Chemical Studies of a Tetranucleotidic Pentaporphyrin'), and *Motokazu Uemura* (Osaka Prefecture University, Japan, 'Asymmetric Reactions Utilizing Planar Chiral (Arene) Chromium Complexes: Axially Chiral Biaryl Synthesis').



Scheme 3. Biosynthetic pathway for TDP-D-desosamine

In contrast to many other conferences, both poster sessions were highly popular events. The eminent, and limited number of, participants were certainly a good reason, also for professors, to stand proud in front of the posters and present recent findings, as one surely received valuable comments and suggestions from colleagues with vastly different backgrounds.

The evening lecture, 'Learning Nature's Strategy for Making Unusual Sugars' by ***Hung-wen Liu*** (University of Texas, USA), resumed the bio-synthetic focus of the previous day. Under the chairmanship of *Bernhard Kräutler*, Liu reasoned that novel glycoconjugates could be a good source for new drug candidates. Considering that about seventy percent of all pharmaceutical compounds

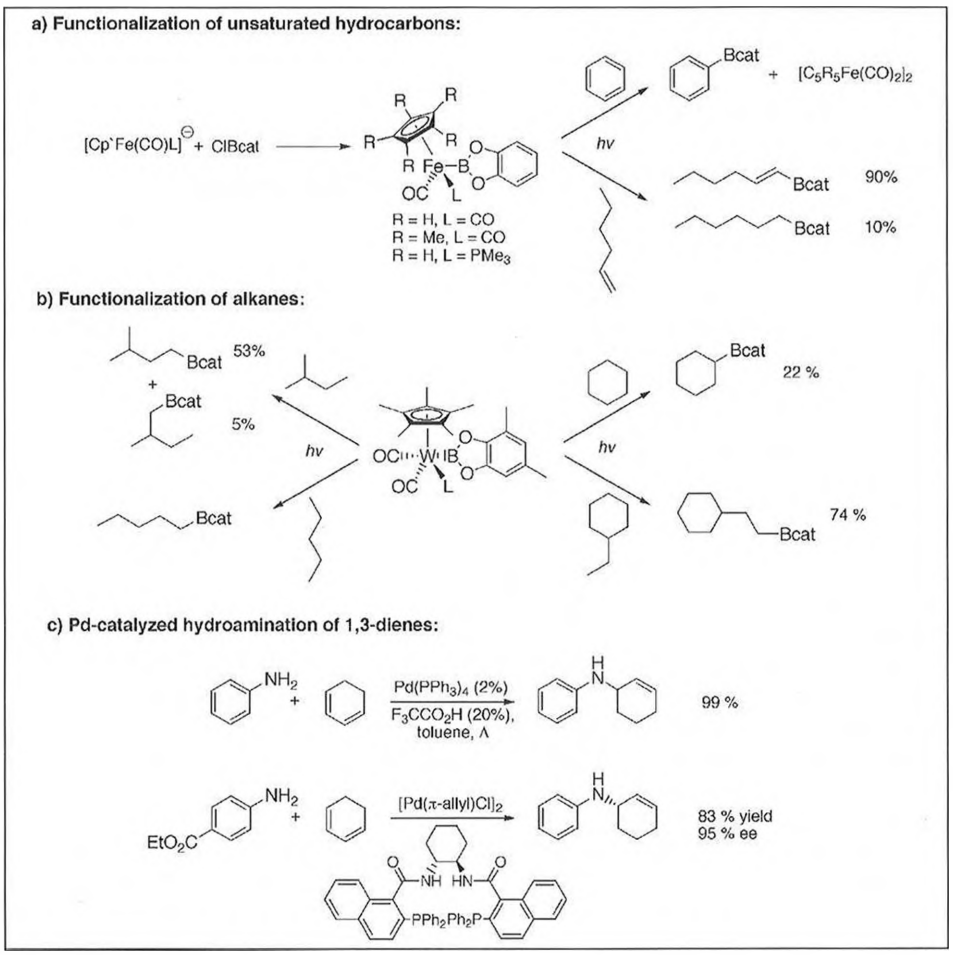
Hung-wen Liu

John F. Hartwig

come from natural sources, and that many of these contain a carbohydrate part (which is often essential for activity), he might very well be right. Liu then went on to highlight some of his many studies on the biosynthesis of unusual sugars and the mechanisms by which the involved enzymes work (Scheme 3). He explained how this information could be used to design inhibitors of the enzymes, and how the biosynthetic machinery could be genetically manipulated to develop new glycoconjugates with potential clinical applications [11].

The final day started with two lectures devoted to organometallic chemistry. First, *Peter Chen* introduced ***John F. Hartwig*** (Yale University, USA) presenting a lecture entitled 'Transition Metal-Catalyzed Saturated Carbon-Heteroatom Bond Formation'. Hartwig, like many of the other lecturers, demonstrated the power of detailed mechanistic investigations as foundations for further developments. Here, the knowledge gained was used to design new transition metal catalysts for functionalization of hydrocarbons. Through newly developed iron or tungsten boryl complexes, it was possible to introduce a catecholboryl unit on unsaturated hydrocarbons and on alkanes (Scheme 4). Amines, alcohols, and cross-coupling precursors could thus be prepared from simple starting materials. Further, Hartwig illustrated highly stereoselective hydroaminations of 1,3-dienes catalyzed by palladium complexes [12].

Highly stereoselective catalysts were also described by ***Gregory C. Fu*** (Massachusetts Institute of Technology, USA) in his lecture 'Asymmetric Catalysis with 'Planar-Chiral' Heterocycles'. His focus was on chiral nucleophilic catalysts based on heterocycles. Planar chirality was introduced in a heterocycle, like pyridine, by introducing a substituent in the 2-position and a π-complexed transition metal on the ring. Suitable selection of the metal complex allowed a tunable (in terms of steric and electronic properties) and stable catalyst, with minimal conformational flexibility, to be designed. Fu illustrated the utility of these catalysts in a variety of catalytic enantioselective reactions, including addition of alcohols to ketenes, rearrangement of O-acylated enolates, kinetic resolution of alcohols and amines, as wells as desymmetrization of epoxides (Scheme 5). Although moderate enantioselectivities were obtained initially, mechanistic investigations and ligand tuning often lead to excellent ee's after optimization. Fu also incorporated the element of planar chirality



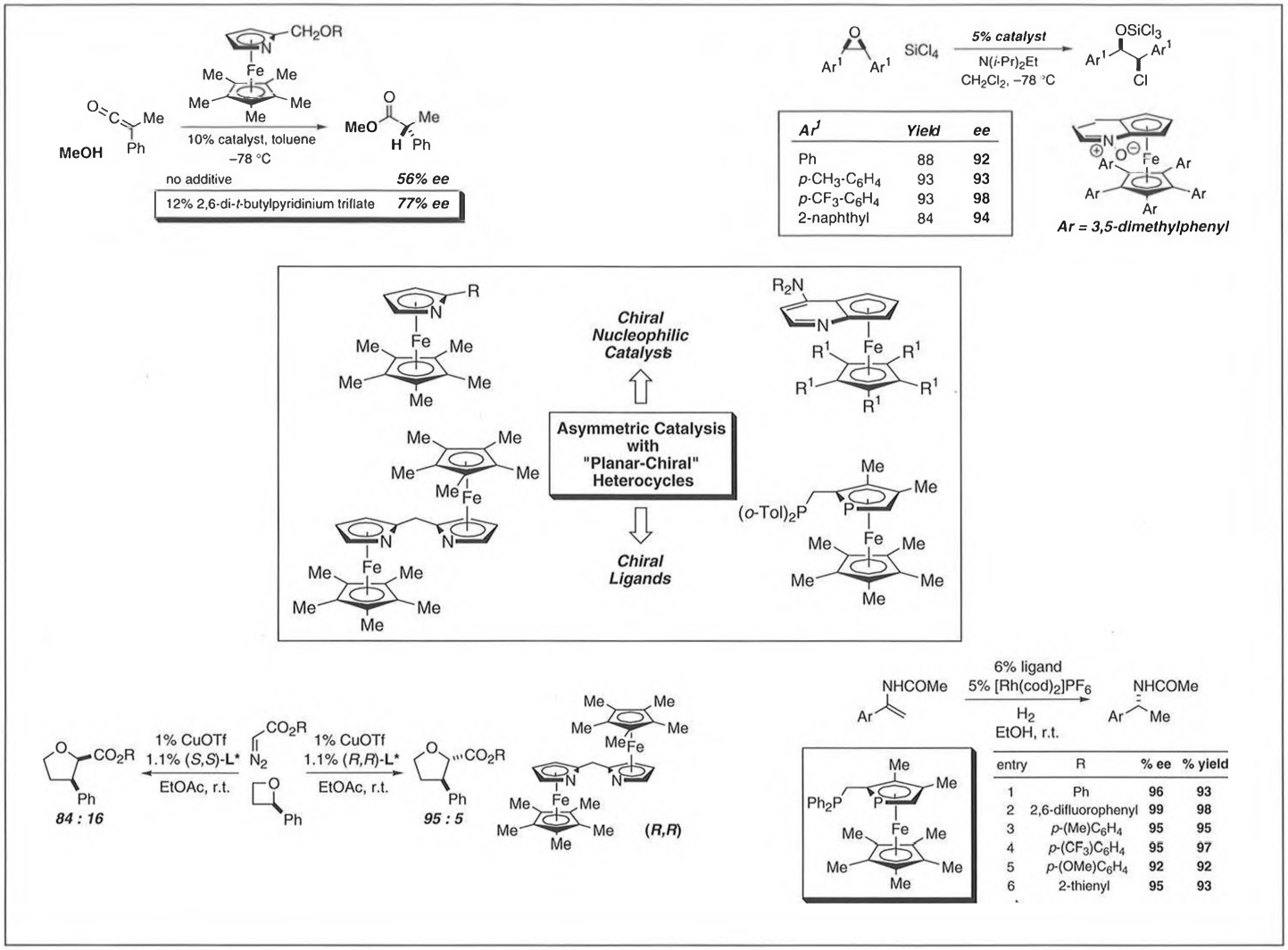
Scheme 4. Functionalization of saturated and unsaturated hydrocarbons with iron and tungsten boryl complexes, and Pd-catalyzed hydroamination

in innovative chiral ligands for transition metals, once more with excellent results [13].

Lia Addadi introduced the last lecturer of the conference. ***Gerald W. Hart*** (John Hopkins University, USA) returned to the topic of biological carbohydrate chemistry when he talked about 'Dynamic O-Glycosylation of Nuclear & Cytoskeletal Proteins: A New Paradigm for Regulation and Signal Transduction'. Hart recently discovered a new form of protein glycosylation – O-GlcNAc modi-

Gregory C. Fu

Gerald W. Hart



Ar¹	Yield	ee
Ph	88	92
p-CH3-C6H4	93	93
p-CF3-C6H4	93	98
2-naphthyl	84	94

entry	R	% ee	% yield
1	Ph	96	93
2	2,6-difluorophenyl	99	98
3	p-(Me)C6H4	95	95
4	p-(CF3)C6H4	95	97
5	p-(OMe)C6H4	92	92
6	2-thienyl	95	93

Scheme 5. 'Planar-chiral' heterocycles as chiral nucleophilic catalysts and chiral ligands

fication. This ubiquitous and dynamic post-translational modification is found in all eukaryotes, and affects a myriad of nuclear and cytoplasmic proteins. Interestingly, the same proteins that undergo phosporylation also experience O-GlcNAc modification; furthermore, the two processes appear to be synchronized, suggesting a regulative role also for O-GlcNAc. Indeed, a number of biologically relevant processes have already been shown to involve O-GlcNAc modification, *e.g.* activation of genes connected to diabetes, regulation of proteasome mediated protein degradation, and regulation of protein-DNA binding. Furthermore, O-GlcNAc binding sites have been found on many proteins with known and unknown function [14]. The research in Hart's laboratory now focuses on the biosynthesis, removal, attachment sites, and functions of this exciting post-translational modification.

The meeting was concluded by Bürgenstock veteran ***Jay Siegel*** (University of California San Diego, USA), who picked up the old Bürgenstock tradition of presenting a lecture at the blackboard using only a piece of chalk. Through a series of formulas and word-puzzles, he managed to summarize the five days of lectures and intense discussions in a highly amusing way! On behalf of the organizers, *Klaus Müller* thanked this year's president and introduced next year's president ***Lia Addadi*** (Weizmann Institute of Science, Israel) and vice-president ***Jan-Erling Bäckvall*** (Stockholm University, Sweden). Müller then pleased the audience by testifying that next year's conference will also be held at the Bürgenstock, although from April 13–19, 2002, due to restoration of the hotels.

Excellent lectures, the high level of scientific discussions, and beautiful scenery would be reason enough to apply for the conference next year. However, the meeting would not be *the* Bürgenstock conference if it were not for the comforting and friendly atmosphere that surrounded the whole summit. The unique blend of people, comprising scientists in all ages, from different disciplines and countries, working in either academia or industry, certainly made the conference interdisciplinary. Furthermore, the calm, quiet, and isolated location of the Bürgenstock, together with the relaxed program indeed encouraged interaction between the participants. Thus, it is to anticipate that this year's meeting again laid a good foundation for new advances in chemistry, just as the thirty-five preceding ones have done!

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Case Histories of Drug Design

Mini-Symposium, May 10, 2001, Basel, Switzerland*
Division for Medicinal Chemistry (DMC) of the Swiss Chemical Society (SCS)

Keywords: Angiogenesis inhibitor · Angiotensin-II inhibitor · Drug design · Glycine antagonist · Triglyceride lipolysis inhibitor

The Division for Medicinal Chemistry organized this minisymposium at the University of Basel with the support of the Swiss Chemical Society and the companies F. Hoffmann-La Roche AG, Novartis AG, Basel and Serono SA, Geneva. The meeting was well attended and appreciated by medicinal chemists and students. The content of the four lectures is summarized below.

Design and Structure Activity Relationship of a New Class of Vascular Endothelial Growth Factor Receptor Tyrosine Kinase Inhibitors

Laurent F. Hennequin, *Astra Zeneca, Centre de Recherche, Z.I. La Pompelle, France*

Angiogenesis is essential for the progression of a number of pathological disorders (*e.g.* rheumatoid pannus, retinopathies and solid tumour growth) and occurs in limited physiological processes in the adult (female reproductive cycle and wound healing) [1]. There is evidence that vascular endothelial growth factor (VEGF) has a key role in angiogenesis and may also contribute to tumour progression by increasing vascular permeability in tumours [2]. Two high affinity receptors for VEGF are found on endothelial cells; the fms-like tyrosine kinase receptor, flt-1 and the kinase insert domain-containing receptor, KDR.

To abrogate VEGF signalling, we developed small molecular weight inhibitors of VEGF receptor tyrosine kinase (RTK) activity that were compatible with chronic oral administration. We have previously reported that anilino-quinazolines are potent inhibitors of KDR [3]. ZD6474 is a small molecular weight compound that inhibits KDR and possess satisfactory physicochemical properties, bioavailability and pharmacokinetics in mouse, rat and dog (Fig. 1). It shows selectivity for KDR, *versus* other receptor tyrosine kinases (*e.g.* PDGFR, FGFR-1, IGF-1R *etc.*) and serine/threonine kinases (CDK2, AKT, *etc.*) [4].

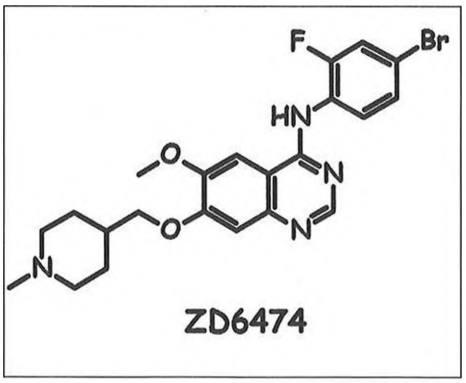

Fig. 1

This compound is active against a panel of human tumour xenograft (Colon, Lung, Ovarian, Prostate, Breast, *etc.*) following once-daily oral administration, and against syngeneic tumour models.

It produces a dose-dependent hypertrophy of the femoro-tibial growth plates of young growing rats [4]. This is consistent with the inhibition of angiogenesis which is a critical step in the conversion of cartilage to bone during growth.

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Glycine N-Methyl-D-Aspartate Antagonists: The Discovery of UK 240,455 and UK 315,716

Alan Stobie, *Discovery Chem. Dep., Pfizer Global Research and Development, Sandwich, Kent, UK*

This talk covered the discovery of potent, soluble and blood brain barrier penetrant quinoxalinedione based glycine site antagonists, with potential utility in treating stroke.

The design criteria were laid out and it was shown how manipulation of acidic pKa and logD led first to a series of hydroxyquinolones *e.g.* UK-148,475 which had activity *in vivo,* but were limited by high-unbound clearance and low functional potency. Applying the same principals aqueous solubility, coupled to good functional potency and blood brain barrier penetration were then introduced into the insoluble and low potency quinoxalinedione template, giving the prototype candidate UK-240,455. The discovery synthesis of this candidate and the process route, which involved a dynamic resolution to give a single atropisomer

*Organised by Dr. Rudolf Giger
Novartis Pharma AG
WSJ-507.7.03-A
CH-4002 Basel
Tel.: +41 61 324 81 95
Fax: +41 61 324 42 36
E-Mail: rudolf.giger@pharma.novartis.com

were then described. Finally the back-up programme, addressing the need for greater aqueous solubility to allow a lower dose volume, leading to the discovery of the clinical candidate UK-315,716, was discussed (Fig. 2).

It was also demonstrated, by comparing *in vivo* and early clinical data, that these compounds are capable of testing the utility of glycine antagonist in treating stroke.

The Case History of Xenical®

Paul Hadváry,
Hoffmann-La Roche AG, Basel

Xenical® is the first and only representative of digestive lipase inhibitors clinically used for inhibition of dietary fat absorption. It represents the only non-centrally acting treatment of obesity and has clinically proven beneficial effects on related metabolic disorders such as type II diabetes, hyperlipidemia and hypertension.

The β-lactone of the active substance orlistat (tetrahydrolipstatin, THL) reacts with the active site serine 152 of pancreatic lipase and forms a 1:1 adduct which is essentially irreversible during the time of the digestive process in the gastrointestinal tract. The parent compound lipstatin was isolated from the culture broth of Streptomyces toxytricini in a microbial broth screening for lipase inhibitors using a specially developed robotic system allowing automated titration of the liberated fatty acids. The success of this screening effort was dependent on the use of *in vitro* test conditions mimicking the composition of the intestinal lumen (emulsified triolein in the presence of bile acids and phospholipids) thus avoiding unspecific detergent effects and the titrimetric assay system allowed to test very high initial concentrations of the broth extracts which was a prerequisite to detect a minor component such as lipstatin (initially < 100 ng/ml broth).

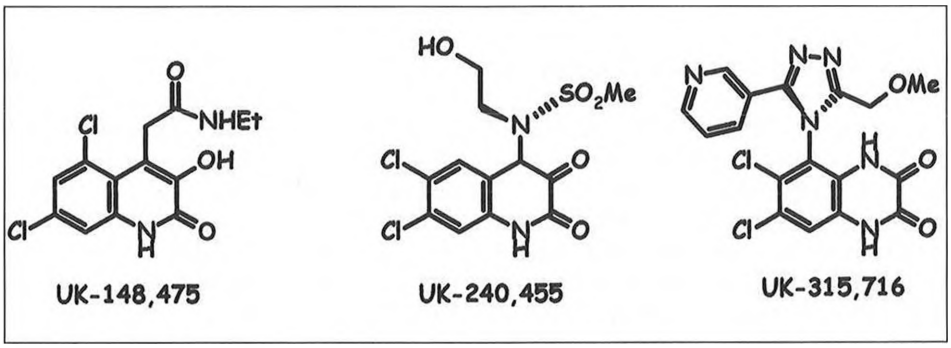

Fig. 2

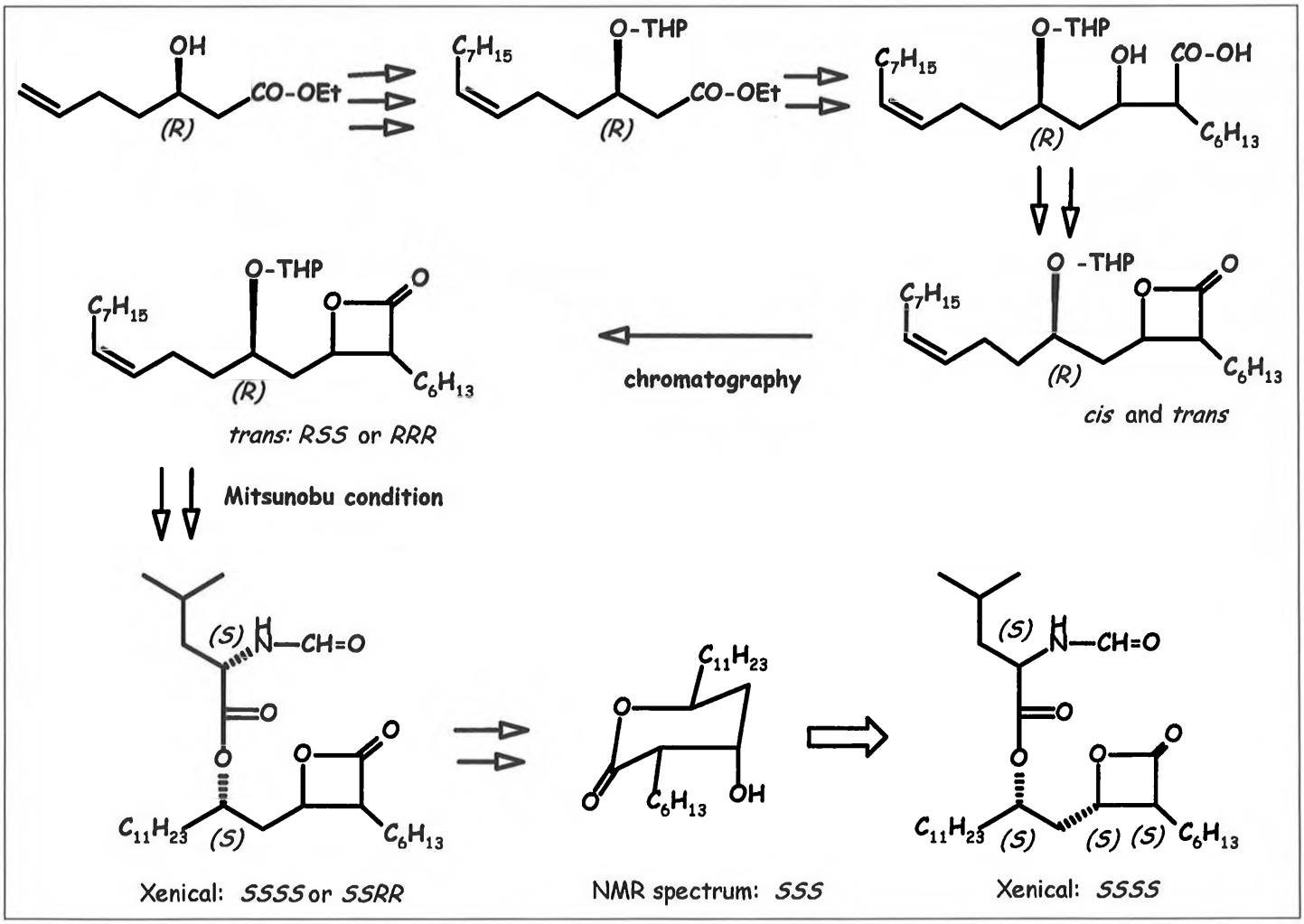

Fig. 3

Both absolute structure determination and structure-activity evaluations were dependent on the establishment of a total synthesis, see Fig. 3.

It could be shown that the stereochemistry of the backbone in the natural compound lipstatin (*S,S,S*) and the (N-formyl-(*S*)-Leu) substitution result in the most potent inhibitors. Shorter aliphatic chains can result in higher *in vitro* potency but *in vivo* they lose activity due to degradation.

Clinical development of Xenical® showed that the effect is limited to inhibition of triglyceride lipolysis with a plateau at about 30% excretion of the dietary fat load with the current galenical formulation.

The Case History of Diovan®

Peter Bühlmayer,
Novartis Pharma AG, Basel

The renin angiotensin system (RAS) produces Angiotensin II (Ang-II), a very potent vasoconstrictive and volume-retaining hormone which is partly responsible for regulation and maintenance of blood pressure. Blockers of the RAS such as angiotensin converting enzyme (ACE) inhibitors have successfully been introduced into the market for the treatment of hypertension and congestive heart failure. However, blocking the system with specific antagonists of Ang-II may turn out to be a more suitable way for blood pressure control.

Starting from structure-activity data (SAR) obtained with peptides, a three-dimensional model (CAMM) of the pentapeptide Tyr-Ile-His-Pro-Ile and the structure of DuP-753, a series of new and highly potent antagonists have been designed where the imidazole moiety of the Du Pont compound has been replaced by an N-acylated aminoacid residue [1]. Valsartan® (CGP48933, (*S*)-N-Pentanoyl-N-{[2'-(1H-tetrazol-5-yl-)biphenyl-4-yl]methyl}-valine), was synthesized initially in 1989 and reached the market in July 1996 (Fig. 4).

Replacements of the imidazole part of the Du Pont compound by other heterocycles have been published in literature and patents. In contrast, we have designed a novel series of orally active derivatives in which the heterocycle of losartan has been replaced by an acylated aminoacid. We speculated that the imidazole mimics a peptide bond and the tetrazole mimics the C-terminal carboxylic function of Ang-II ('amide hypothesis'). Extensive comparative analyses of energy minimized conformations of losartan and the C-terminal pentapeptide Tyr-Ile-His-Pro-Ile of [Sar(1),Ile(8)]Ang-II were undertaken to check this idea. Overall *ca.* 600 designed analogues have been prepared based on the 'amide idea' resulting in the identification of two development compounds.

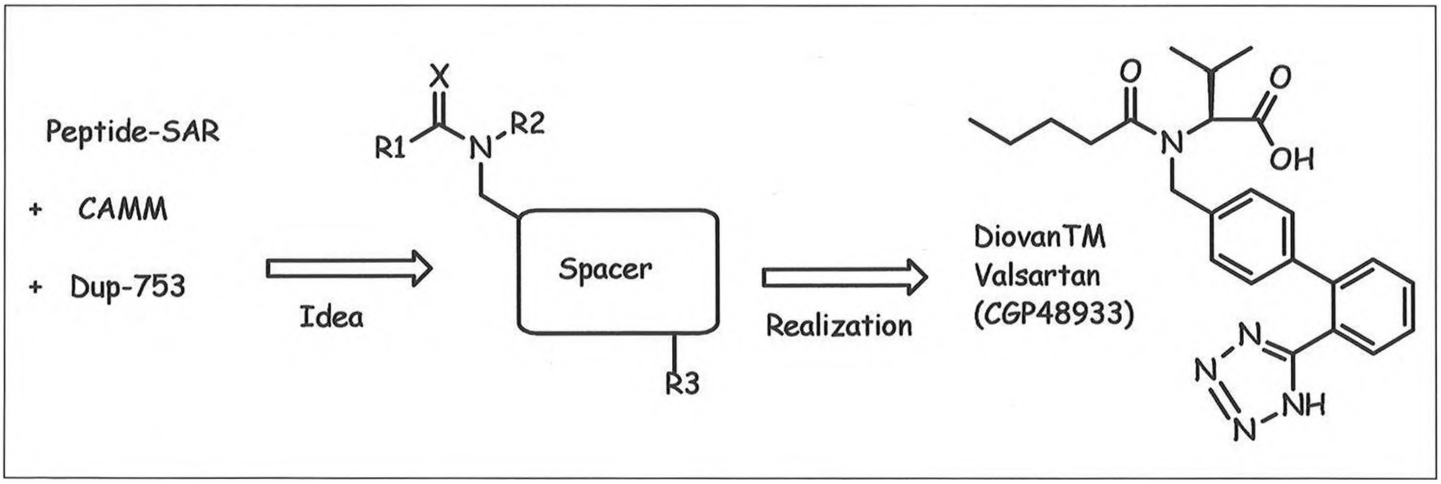

Fig. 4

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De nouveaux moyens analytiques pour la filière de Génie Chimique de l'école d'ingénieurs de Genève (EIG)

Dominique Robin*

New Analytical Tool for the Chemical Engineering Course at the University of Applied Sciences of Geneva

Abstract: With regard to the rearrangement of competences within the HES-SO, the chemical engineering course at the University of Applied Sciences of Geneva has opted to focus on the study of environmental protection procedures. For this purpose the University of Applied Sciences of Geneva has acquired an ICP-MS (Ion Coupled Plasma Mass Spectrometry), as a first step.

Keywords: Chemical engineering · ICP-MS · University of Applied Sciences of Geneva

Dans le cadre de la nouvelle répartition des compétences à l'intérieur de la HES-SO, la filière de Génie Chimique de l'école d'ingénieurs de Genève s'oriente vers l'étude des procédés touchant à la protection de l'environnement. Dans cette perspective, il est indispensable de s'équiper de moyens modernes d'analyse tant pour l'étude des métaux lourds sous forme de traces ou d'ultra-traces que pour la mesure des composés organiques tels que les dioxines, furanes ou PCB.

Dans cette optique l'EIG s'est dotée dans un premier temps d'un ICP-MS (Plasma à Couplage Inductif relié à un Spectromètre de Masse). Cet appareil permet l'analyse de métaux dans des solutions aqueuses à des concentrations de l'ordre du ppb ou moins encore selon les éléments.

Cet achat s'inscrit dans la perspective des nouvelles tâches des HES plus particulièrement pour les projets de Ra&D mais également dans le cadre de prestations pour tiers.

Plusieurs appareils ont été évalués et notre choix s'est porté sur celui d'Agilent type 7500 (voir photo).

Son principe de fonctionnement, qui est le même pour tous les fabricants est dans un premier temps de former avec l'échantillon à analyser, un spray de micro gouttelettes dans une atmosphère d'argon. Plusieurs types de nébuliseurs peuvent être utilisés selon les volumes disponibles et selon les propriétés des so-

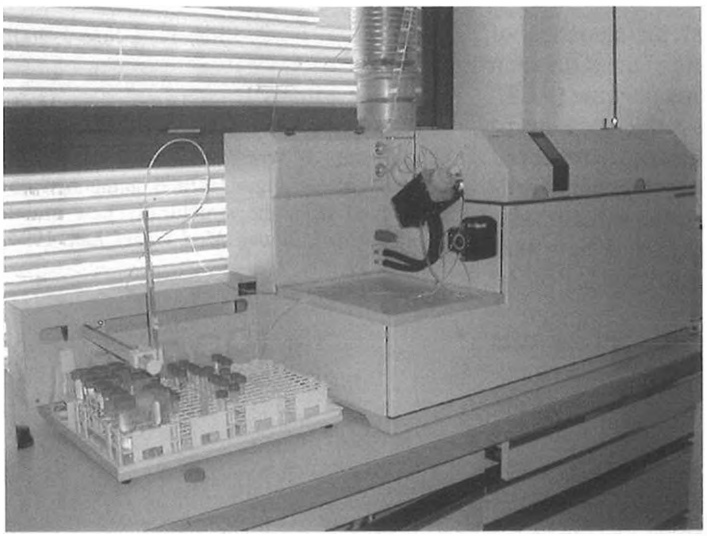

Fig. 1. ICP-MS

*Correspondance: Prof. Dr. D. Robin
Ecole d'ingénieurs de Genève
Laboratoire de génie chimique
Rue de la Prairie 4
CH–1202 Genève
Tel.: +41 22 338 04 95
Fax: +41 22 338 04 10
E-Mail: robin@eig.unige.ch

lutions à analyser. Cette partie est très importante car seul un faible pourcentage de la solution à analyser arrive dans le plasma. Ce dernier est alimenté par un bobinage de quatre spires parcouru par un courant de radiofréquence oscillant à 27,12 mégahertz. Les oscillations entraînent des collisions entre les atomes d'argon et les électrons prisonniers de l'intense champ oscillant. Ces collisions ionisent l'argon.

Les ions formés, pris à leur tour dans le champ oscillant provoquent d'autres collisions et entretiennent l'ionisation jusqu'à former et entretenir un plasma d'argon. Au centre de ce plasma la température varie de 8000 à 10 000 degrés. Le plasma d'argon est une bonne source d'ions positifs mono chargés et montre une bonne efficacité d'ionisation pour les autres éléments présents dans le plasma. Les ions ainsi formés sont extraits de ce dernier et dirigés vers le premier étage du système de vide à travers l'orifice ménagé dans le cône avant de la chambre à vide. Les ions sont extraits de l'interface, accélérés et focalisés par un système d'optiques ioniques. Diverses astuces permettent d'éliminer les photons par déviation du flux de particules.

Le vide est maintenu par une pompe turbo moléculaire dans cet étage intermédiaire. Les ions passent ensuite dans le quadripôle constitué de quatre longs barreaux métalliques alimentés par un mélange de potentiels continus et alternatifs à radiofréquences. En ajustant ces potentiels convenablement, les barreaux se comportent comme des filtres de masse qui ne laissent passer que les ions pourvus d'un rapport de masse sur charge (m/z) spécifique. Tous les autres ions viennent heurter les barreaux. Une variation adéquate et rapide des potentiels permet de balayer la gamme des masses élémentaires.

Les ions sont détectés par un multiplicateur d'électrons et l'ensemble est maintenu sous vide par une seconde pompe turbo moléculaire. Le comptage des masses est linéaire sur huit à neuf ordres de grandeurs soit de quelques dizaines de ppt jusqu'aux g/l. Dans la réalité les effets mémoires engendrés par de fortes concentrations pour certains éléments ne permettent pas de tester facilement ces performances.

Cet appareil a été installé dans le laboratoire de chimie nucléaire de notre école, qui est un laboratoire de type B. Nous pouvons ainsi analyser des isotopes radioactifs. Pour les éléments de longues périodes la sensibilité de l'ICP-MS est meilleure que les méthodes traditionnelles utilisées en radiochimie (spectroscopie de type alpha ou gamma).

L'appareil est également pourvu d'un système permettant de réaliser un plasma 'froid' pour l'analyse du fer 56 à des concentrations de l'ordre du ppb. En effet pour certains éléments l'utilisation d'un plasma d'argon crée des interférences qui faussent les résultats. Dans le cas de la masse 56 en plus du fer on retrouve par exemple le composé ArO^+ qui présente la même masse; en jouant sur la température du plasma on peut minimiser la proportion de ArO^+, ce qui permet l'analyse du fer à de très faibles concentrations (<ppb).

D'autres interférences existent, par exemple l'analyse du chrome à la masse 62 dans une solution contenant du carbone sous forme organique ou minérale on retrouve le composé ArC^+ qui a la même masse. Pour l'analyse de l'arsenic (100% masse 75) dans un milieu chargé en chlore, le composé $ArCl^+$ présente deux masses 75 et 77 selon l'isotope du chlore. Connaissant le rapport isotopique de cet élément on peut par soustraction déduire la proportion d'$ArCl^+$ ce qui nous permet ainsi de déterminer celle de l'arsenic. Ce ne sont que quelques exemples qui montrent que la plupart des problèmes d'interférences peuvent être résolues mais qu'ils nécessitent une attention pour toute nouvelle situation d'analyse.

En plus des analyses de solutions aqueuses l'analyse de composés solides ou de composés organiques est possible après minéralisation. Celle-ci s'effectue par attaque acide à pression atmosphérique ou en bombe fermée par chauffage micro ondes.

La sensibilité et la rapidité d'analyse font de cet appareil un moyen indispensable pour les mesures de métaux en général et plus particulièrement pour les métaux lourds ou traces dans l'environnement.

Reçu le 28 Juin 2001

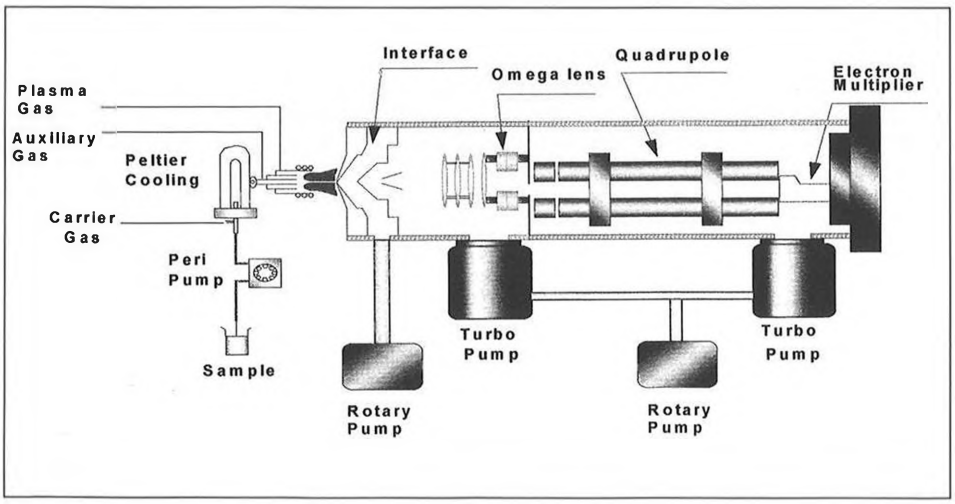

Fig. 2. Schéma de l'appareil (Source Agilent)

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SCHWEIZERISCHE CHEMISCHE GESELLSCHAFT
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DIC Division Industrielle Chemie

Kurzbericht zur Mitgliederversammlung 2001 mit Firmenbesuch vom 04.05.2001 bei der Firma Carbogen/Neuland in Hunzenschwil

Visp, 10.07.2001

Liebe Mitglieder der Division Industrielle Chemie

Zur Jahresversammlung 2001 der Division Industrielle Chemie trafen sich 34 Mitglieder bei der Firma Carbogen/Neuland in Hunzenschwil. Wir wurden durch die Herren Dr. Beer und Dr. Küenburg herzlich in den rund vor einem Jahr neu bezogenen Räumlichkeiten Willkommen geheissen.

Nach Eintreffen der Teilnehmer wurde die Firma Carbogen von Dr. Beer kurz präsentiert und anschliessend durch den Präsidenten der DIC H.R. Dettwiler die Mitgliederversammlung um 10.30 gemäss folgender Traktandenliste eröffnet und abgewickelt.

Traktandenliste Mitgliederversammlung 2001:
Rückblick auf das Geschäftsjahr 2000
- Jahresrechnung 2000
- Budget des Geschäftsjahres 2001
- Entlastung des Vorstandes
- Wahl neuer Vorstandsmitglieder
- Wahl neuer Vorstandsmitglieder
- Projekte des Vorstandes
- Varia, Verdankungen, Schluss der Versammlung

Der Bericht zur Mitgliederversammlung 2000 der Division wurde im Rahmen des Rechenschaftsberichtes der SCG in der CHIMIA **2000**, *54*, Nr. 10 veröffentlicht.

Für die laufenden Aktivitäten der DIC äusserte sich der Präsident in seinen rückblickenden und vorausschauenden Ausführungen zu folgenden Themen:

5. Freiburger Symposium 2000 am 28. /29. September 2000.
Themenbereich 'Chemische Produktion in Mehrzweckanlagen'

Dieses Symposium war bezüglich der Teilnehmerzahl (über 200 Personen), der Qualität der Präsentationen und dem sehr positiven Rechnungsabschluss eine ausserordentlich erfolgreiche Veranstaltung. Diese Erfahrung bestätigte uns, dass mit der Wahl aktueller Themen die in der produzierenden Chemischen Industrie tätigen Chemiker und Chemieingenieure immer noch die Zeit für eine Informations- und Weiterbildungsveranstaltung finden können.

Publikationen in CHIMIA Heft 9/2000.

In dieser Ausgabe der CHIMIA konnte zum **Thema 'Green Chemistry/Umweltverträgliche Prozesse'** eine Artikelserie veröffentlicht werden, die ausgewählte Beispiele zu ökologisch sinnvollen Verfahrensverbesserungen präsentierte. Es war dies ein erster Ansatz zur verstärkten Publikation von Fortschritten in der Chemisch/Technischen Entwicklung und Produktion.

Aufnahme der Tätigkeit zur Erarbeitung eines **Skill Inventory.**

Das Skill Inventory bezweckt die gegenseitige Nutzbarmachung der Fachkompetenz der Mitglieder der Division. Mit der Firma Sinka Interactive wurde eine entsprechende Maske für die Erfassung der Kernkompetenzen erarbeitet. Es ist vorgesehen, dass damit jedes Mitglied der DIC sein Fachprofil auf dem System hinterlegen kann und andererseits selbst Zugriff auf die Fachinformation erhält. Das System wurde bereits innerhalb der Vorstandsmitglieder getestet. Es wird über die WEB-Page der SCG verfügbar sein. Wir rechnen mit einer Aktivierung für alle Mitglieder noch in diesem Jahr. Eine entsprechende schriftliche Mitteilung wird folgen.

Aufnahme der Tätigkeit zur **Entwicklung eines Informationskonzepts,** Vereinheitlichung der Homepage innerhalb der SCG.

Die SCG hat ein Projekt zur Überarbeitung des gesamten Kommunikations- und Informationskonzepts der Gesellschaft gestartet.

Mit dem neuen Kommunikationskonzept soll Folgendes erreicht werden:

Durch den Auftritt soll die Schweizerische Chemische Gesellschaft als moderne, auf die Zukunft ausgerichtete und aktive Gesellschaft wahrgenommen werden.

Wegen ihrer ungebundenen Informationspraxis nach innen zu den Mitgliedern und nach aussen zur Bevölkerung sind die Schweizerische Chemische Gesellschaft und ihre Divisionen der bevorzugte Ansprechpartner für nationale und internationale Gremien und Organisationen, für Medien und Mitbürger.

Die DIC wird innerhalb dieser Rahmenbedingungen ihre Informationspraxis überarbeiten und am Konzept der Gesellschaft aktiv mitgestalten.

Vernehmlassung mittels Fragebogen zur **Erhebung der Ausbildungsbedürfnisse** der Mitglieder.

Die DIC hat einen Fragebogen zur Erhebung der Ausbildungsbedürfnisse der Mitglieder in Umlauf gegeben. Die Auswertung der Resultate wird durch den Vorstand anlässlich eines Workshop im Sept. 01 vorgenommen und als Grundlage für weitere Aktionen verwendet werden.

Es besteht neu die Möglichkeit zur Abgabe einer **CD zum Thema 'Thermal Safety Tutorial'** an die Mitglieder. Diese kann über unser Vorstandsmitglied Walter Jucker bezogen werden und ist über eine beschränkte Zeit kostenlos verfügbar.

In der Person von Ch. Buxtorf ist der Vorstand als **Beirat in der Planungsgruppe für das Nachdiplomstudium in chemischer Verfahrensentwicklung und Produktion aktiv** (Hochschule für Technik u. Architektur Fribourg). Dieser Studiengang wird speziell für die Aus- u. Weiterbildung von produktionsorientierten Chemikern von Nutzen sein. Es wird auf einen klaren Praxisbezug grosses Gewicht gelegt. Die DIC unterstützt dieses Ausbildungskonzept und der Vorstand wird seine Position noch weiter präzisieren.

Der **Kassenbericht 2000** wurde in ausführlicher und kompetenter Weise vom Kassier Dr. Kurt Käser erläutert. Der Revisor, Dr. Joyeux, bestätigte die korrekte Rechnungsführung. Die Versammlung konnte damit dem Kassier einstimmig Entlastung erteilen und die Arbeit mit Applaus verdanken. Der erfolgreiche Abschluss des Freiburger Symposium 2000 hat unserer Kasse solide schwarze Zahlen beschert. Dies wird sich insbesondere positiv auf zukünftige Ausbildungsveranstaltungen auswirken. Das

Budget konnte ebenfalls auf das Wohlwollen der Versammlung zählen. Auf die spezielle Präsentation der Zahlen wird an dieser Stelle verzichtet.

Das notwendige **Wahlgeschäft für die Ersatzwahl von drei neuen Vorstandsmitgliedern** konnte speditiv abgewickelt werden. Als neue Vorstandsmitglieder wurden vorgeschlagen:
- Dr. Gérard Gandillon, Givaudan Vernier SA
- Dr. Rolf Pfluger, Syngenta Münchwilen
- Dr. Daniel Roulet, Vantico Monthey

Die Herren wurden durch Akklamation in ihrer neuen Funktionen bestätigt.

Im Anschluss an die Mitgliederversammlung konnte im Rahmen eines ausgezeichneten Mittagessens auch der firmenübergreifenden Fachdiskussion Raum geboten werden.

Geführt durch kompetente Mitarbeiter von Carbogen konnten wir auf einem ausführlichen Rundgang durch Entwicklungs- und Produktionseinheiten das Innenleben der Firma kennenlernen.

Wir verdanken der Firma Carbogen 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

SGMS Swiss group for mass spectrometry

2001 Meeting of the Swiss Group for Mass Spectrometry (SGMS)

Swiss group for mass spectrometry
Schweizerische Gruppe für Massenspektrometrie
SGMS
Groupe suisse de spectrométrie de masse
Gruppo svizzero di spettrometria di massa

October 25th and 26th, 2001
Hotel Chaumont et Golf near Neuchâtel

Plenary Lectures:
'The Swiss Light Source – SLS'
Dr. *Rafael Abela*, Paul Scherrer Institute (PSI), CH-5232 Villigen PSI, Switzerland

'The Effect of Nucleoside Proton Affinity and the Formation of Zwitteironic Oligonucleotides'
Dr. *Giovanni Sindona*, Dipartimento di Chimica, Università della Calabria, via P. Bucci, cubo 15/c I-87030 Arcavacata di Rende (CS), Italy

'APCI-MS for Rapid and Dynamic Measurement of Flavour Release'
Dr. *Andy Taylor*, Division of Food Sciences, University of Nottingham, Sutton Bonington Campus, Loughborough LE12 5RD UK

'Mass Independent Single Molecule Detectors for Mass Spectrometry'
Dr. *Daniel Gerber*, Institut de Physique, Université Neuchâtel, Rue A.-L.Breguet 1, CH-2000 Neuchâtel, Switzerland

Information is available on *http://www.sgms.ch*

New Members

Badine, Michael, 1279 Chavannes de Bogis
Gubler, Ralph, 8008 Zürich
Kansy, Manfred, Dr., 4070 Basel
Severin, Kay, Prof., 1015 Lausanne
Todorova Gubler, Tonya, 8008 Zürich
Wild, Ferdinand, Dr., 8057 Zürich
Zepik, Helmut, Dr., Santa Cruz, CA 95064, USA

INFORMATION

News

Strategames
Kein Spiel – so ist Forschung

3. Juli 2001. Die Pharma Information bietet als innovatives Netucational neue 'Strategames' an: Unter der Internet-Adresse *www.interpharma.ch* müssen interaktiv Strategien entwickelt und knifflige Aufgaben gelöst werden. Mit den Strategames können verschiedene Taktiken wie sie bei der Medikamentenforschung angewendet werden, online ausprobiert werden. Es geht darum, komplexe Systeme zu erforschen und Zusammenhänge aufzudecken, um – wie bei der Medikamentenforschung – in einem Organismus etwas zu bewirken. Strategames ist kein Spiel, sondern macht die Überlegungen eines Forschers nachvollziehbar – eine Art interaktiver Denksport mit verschiedenen Schwierigkeitsstufen.

Auf der Homepage '*www.interpharma.ch*' sind sechs verschiedene Strategames verfügbar, die direkt gespielt oder heruntergeladen werden können. Wer das Eiweiss-Harmonium, den Key-Finder, die Neuro Blackbox, den Copy-Sound und das Wirkstoff-Labyrinth gelöst hat, erhält die Möglichkeit den Effect-Switcher (Bonus Level) zu erforschen. Auf dem Weg zum Bonus Level wurden dabei ähnliche Strategien verfolgt, die ein Forscher nutzt, um neue Wirkstoffe zu entwickeln, um Veränderungen in Eiweissen zu finden, um Abbauwege einer Substanz zu verfolgen oder unbekannte Wirkungsmechanismen zu erkennen und die Signale richtig zu interpretieren.

Für weitere Auskünfte:
Pharma Information, Petersgraben 35, 4003 Basel
Tel.: 061 / 264 34 34, Fax: 061 / 264 34 35
Homepage: *www.interpharma.ch*
E-Mail: info@interpharma.ch

Congresses – Conferences – Workshops

Graduate Summer School of Inorganic Chemistry (séminaire hors-ville du 3e cycle en chimie inorganique) 'ACTIVATION OF ALIPHATIC C-H BONDS', Champéry, 2nd to 6th September 2001

Organized by Prof. *G. Süss-Fink* and *T.W. Ward* (Uni Neuchâtel), the 2001 graduate summer school of inorganic chemistry is directed towards Ph. D. students, post-doctoral fellows and chemists from university and industry interested in recent developments in the area of C-H bond activation.

The catalytic functionalisation of alkanes is a topical issue in organometallic and bioinorganic chemistry. In particular, methane conversion is a challenge for both fundamental and industrial research.

The following distinguished chemists have agreed to present recent advances in this field: Prof. *T. Flood* (University of Southern California, Los Angeles) for organometallic aspects, Prof. *J.-J. Girerd* (Université de Paris-Sud, Orsay) for biomimetic aspects, Prof. *R.A. Periana* (University of Southern California, Los Angeles) for industrial aspects, Dr. *G.B. Shul'pin* (Russian Academy of Sciences, Moscow) for mechanistic aspects, and Prof. *G. Süss-Fink* (Université de Neuchâtel) for the radical approach.

For further information and registration, contact:
Prof. Thomas R. Ward, Institut de Chimie, Université de Neuchâtel, Avenue de Bellevaux 51, CH-2000 Neuchâtel (Tel.: +41 38 23 24 00, Fax: +41 38 23 25 11, E-Mail: thomas.ward@UNINE.CH).

Lectures

Institut de Chimie, Université de Neuchâtel

Lundi	Colloque ERASMUS-SOCRATES
24.09.2001	Prof. *Carlo Scolastico*
Heure à définir	Università di Milano (Italie)
Salle E14	'Le titre sera communiqué plus tard'
Mardi	Colloque ERASMUS-SOCRATES
25.09.2001	Prof. *Carlo Scolastico*
Heure à définir	Università di Milano (Italie)
Salle E14	'Le titre sera communiqué plus tard'
Lundi	Colloque ERASMUS-SOCRATES
24.09.2001	Prof. *Carlo Scolastico*
10h30	Università di Milano (Italie)
Petit Auditoire	'Le titre sera communiqué plus tard'

Molecules

FRONTIERS IN CHEMISTRY IN A GLOBAL SOCIETY

2 NOVEMBER 2001
AT HÖNGGERBERG CAMPUS, ETH ZURICH, SWITZERLAND
INAUGURAL SYMPOSIUM, NEW CHEMISTRY BUILDING

THEME:

With close to 700 members, the Department of Chemistry at the ETH Zürich is one of the largest research institutions in Chemistry worldwide.
The move of the Department into the new Hönggerberg building is a true «centennial» event: The first Chemistry building at ETH was built more than 100 years ago and, with additions and extensions, has been used for teaching and research until today.
As part of the inaugural celebrations, the Department of Chemistry is organizing a one-day Symposium on «Frontiers in Chemistry in a Global Society» with the aim of highlighting some of the most innovative research avenues in chemical sciences as well as providing perspectives and visions for the future role of chemistry in society.

You are cordially invited to join the celebration.

PROGRAM:

9:00
Welcome
Prof. Olaf Kuebler
(President ETHZ)
9:15
Dr. Daniel Vasella
(CEO, Novartis):
«Does a Country's Policy on Higher Education Influence the Success of its Industry?»
10:30
Dr. Stefan Marcinowski
(Chairman, Fonds der Chemischen Industrie):
«Challenges for Academic and Industrial Chemistry in Europe»
11:15
Prof. Richard Lerner
(Scripps Research Institute):
«Antibodies Catalyze the Oxidation of Water»
14:15
Prof. Ahmed Zewail (California Institute of Technology):
«Chemistry and Biology at New Limits»
15:00
Prof. Ronald Breslow
(Columbia University):
«Frontiers in Organic and Bioorganic Chemistry»
16:15
Prof. Martin Jansen
(Max-Planck-Institut für Festkörperphysik):
«Rational Design or Combinatorial Approach: Where is the Future in Inorganic Materials Synthesis?»
17:00
Prof. Gerhard Ertl
(Fritz-Haber-Institut):
«Heterogeneous Catalysis: Towards Atomic Understanding»

LOCATION:

Building HCI, lecture halls G3 and G7

The Symposium is free of charge and registration.

For further information, please refer to the website at www.chem.ethz.ch/symposium

Sponsors
The companies of the KGF: Ciba – Novartis – Roche – Serono – Syngenta
BASF (Schweiz), CarboGen, Cilag, EMS Chemie, Givaudan, Lonza, Merck (Schweiz)

ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

CHIMIA 2001, 55, No. 7/8

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!

Humidity News – Feuchtemessung weltweit

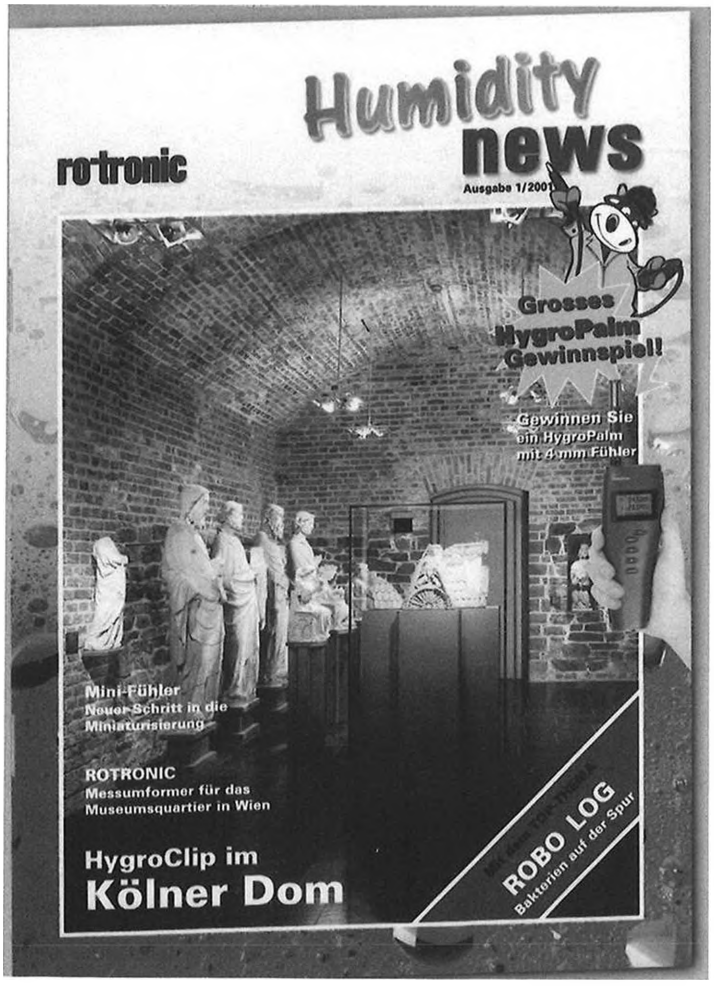
Ein immer strafferes Qualitätsmanagement und ein bedeutendes Energiesparpotential in Produktionsprozessen, lassen Feuchte- und Temperaturmessgeräte immer wichtiger werden. Das hat die Firma Rotronic dazu motiviert, diesem Spezialgebiet eine eigene Zeitschrift zu widmen. Nachdem die ersten zwei Ausgaben Humdity News auf grosses Echo gestossen sind, ist jetzt die dritte Ausgabe in noch höherer Auflage erschienen. Diese Ausgabe steht im Zeichen der digitalen Generation von Feuchte- und Temperatur-Handmessgeräten, dem HygroPalm. Dreissig Jahre Erfahrung und Know-how in Entwicklung und Produktion von genauesten Feuchte- und Temperatur-Handmessgeräten stehen hinter diesen neuesten Handmessgeräten aus dem Hause Rotronic.

Neben vielen interessanten, internationalen Anwendungen wird der weltweit kleinste Feuchtefühler mit 4 mm Durchmesser vorgestellt.

Sichern Sie heute noch Ihr persönliches Exemplar bei Rotronic AG.

- Rotronic AG
  Postfach 451
  CH-8303 Bassersdorf
  Tel. 01-838 11 11
  Fax 01-836 44 24
  E-Mail: rotronic@rotronic.ch
  Internet http://www.rotronic.ch

Leserdienst Nr. 2



Thermo Finnigan statt Thermo Quest

ThermoQuest™ wird Thermo Finnigan

Wir möchten Sie gerne über einige strategische Veränderungen bei unserer Mutterfirma Thermo Electron (www.thermo.com) informieren.

Thermo Electron ist eine börsennotierte, weltweit operierende Technologiegesellschaft (NYSE: TMO).

In diesem Jahr wurde die wichtige strategische Entscheidung getroffen, sich ausschliesslich auf das Kerngeschäft zu konzentrieren: Messinstrumente und Regeltechnik und damit verbundene Komponenten und Systeme. Bis zum Jahre 2001 werden viele Geschäftsbereiche von Thermo Electron ausserhalb dieses Kerns verkauft oder ausgegliedert sein. Es entsteht somit ein 2,2 Milliarden Dollar-Unternehmen mit klarem Marktschwerpunkt und verbesserter technologischer Synergie um bessere Wachstumsmöglichkeiten zu schaffen.

Um weltweit anerkannte Markennamen wie 'Finnigan', 'Nicolet', 'Hypersil', 'LabSystems' etc. mit Thermo Electron in Verbindung zu bringen, wurde das Präfix **'Thermo'** zu all unseren bestehenden Markennamen hinzugefügt.

Im ganzen Unternehmen werden Markenidentitäten nach einem neuen 'Thermo-Markenformat' standardisiert. Es ist das Ziel, den Wert dieser Namen zu bewahren und gleichzeitig eine engere Bindung an Thermo Electron zu schaffen.

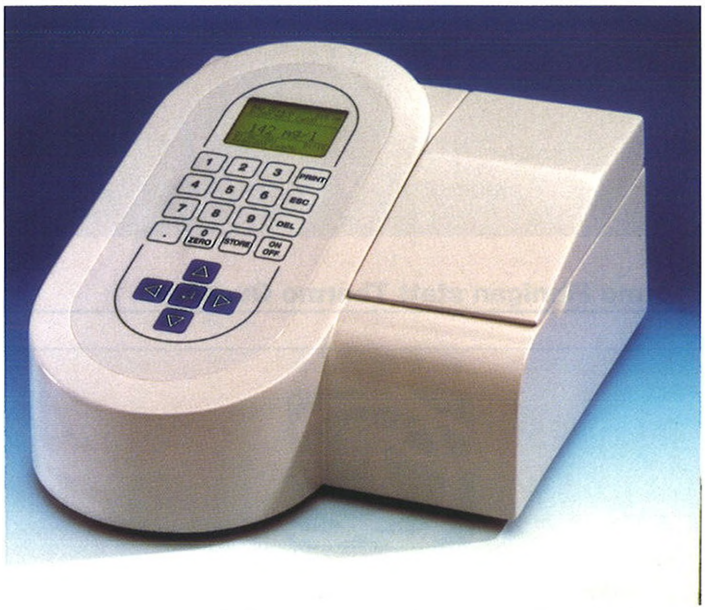
Wir sind fest davon überzeugt, dass dies unseren Kunden ermöglichen wird, die enorme Bandbreite unseres Produktangebots in Märkten, die von Biowissenschaften über Telekommunikation bis hin zur Prozesssteuerung reichen, besser zu nutzen. Die neue Identität wird bald in Werbung, Anzeigen und auf den Produkten sichtbar sein.

Thermo Electron hat sich zum Ziel gesetzt, *das* führende Messgeräteunternehmen der Welt zu werden. Wir sind zuversichtlich, mit Ihrer Unterstützung dieses Ziel erreichen zu können und freuen uns auf eine weiterhin gute Zusammenarbeit.

- Thermo Finnigan
  Hegenheimermattweg 65
  CH–4123 Allschwil
  Tel.: 061 / 487 84 00
  Fax: 061 / 487 84 01
  E-Mail: info@thermofinnigan.ch

Leserdienst Nr. 3

Neues Spektralphotometer PCSPECTRO für die Wasseranalyse



Das neue Lovibond® **PC**SPECTRO ist ein modernes Spektralphotometer, das speziell für die Bedürfnisse der Wasseranalytik entwickelt wurde. Das **PC**SPECTRO verfügt über eine Vielzahl vorprogrammierter Wasseranalytik-Testmethoden, wie z.B.:

- CSB 0–150 mg/l, 0–1500 mg/l, 0–15.000 mg/l
- Ammonium
- Chlor
- Nitrat
- Gesamtstickstoff
- Chlorid
- Mangan
- Eisen, etc.

Die Aktualisierung der Software bei Weiter- und Neuentwicklungen von Testmethoden erfolgt über das Internet. Alle Testmethoden basieren auf der bewährten Palette der Lovibond® Küvettentests, Reagenztabletten und Flüssigreagenzien. Das **PC**SPECTRO ist ideal für den routinemässigen Einsatz im Labor geeignet und bietet dem Benützer zusätzlich Funktionen für anwenderspezifische Anforderungen, z.B.:

- Absorption
- Transmission
- Konzentration
- Zeitverlaufsfunktion (Kinetik)
- Mehrfachwellenlängenfunktion
- Spektrenaufnahme
- Anwender-Kalibrierung (Linear-Polynomisch)

Neben den technischen Features bietet das Preis-/Leistungs-Verhältnis des **PC**SPECTRO viele Vorteile.

- Tintometer AG
  Hauserstrasse 53
  CH–5210 Windisch
  Tel.: +41 56 442 2829
  Fax: +41 56 442 4121
  e-mail: tintometer@bluewin.ch

Leserdienst Nr. 4

EN 149:2001: Erhöhte Anforderungen an Partikelmasken

In der europäischen Norm EN149 sind die Anforderungen an partikelfiltrierende Halbmasken (Einweg-Staubmasken) festgelegt. Diese Norm ist nun revidiert worden. Feinstaubmasken müssen jetzt strengere Kriterien erfüllen. Mit 3M Partikelmasken ist der geforderte Atemschutz voll sichergestellt, ohne dass Eingeständnisse beim Komfort gemacht werden.

Die EN149 umschreibt die 'Anforderungen, Prüfung, Kennzeichnung von filtrierenden Halbmasken zum Schutz gegen Partikel'. Die erste Fassung erschien im Jahr 1990 und blieb bis jetzt unverändert in Kraft.

Die Revision 2001 hat die Anforderungen massiv gesteigert. Sämtliche Einweg-Staubmasken, welche die Zulassung nach EN149:2001 erhalten möchten, müssen neu die Prüfkriterien gegen feste und flüssige Aerosole erfüllen. Somit entfallen die bisherigen Unterteilungen 'S' (gegen feste Partikel) und 'SL' (gegen feste Partikel und flüssige Aerosole). Es bleiben nur noch die Schutzstufen FFP1, FFP2, und FFP3. Die Wahl der richtigen Schutzstufe wird dadurch wesentlich vereinfacht.

3M Atemschutzmasken erfüllen die EN149:2001

Im Hinblick auf die neuen Leistungsanforderungen entwickelte 3M das neue Filtermaterial *3M™ Advanced Electret Material*. Diese Filtertechnologie verbindet die Vorteile eines mechanischen und elektronischen Filters: höhere Leistung bei gleichzeitg verringertem Atemwiderstand. Das Filtermaterial ist dünner als das für die meisten herkömmlichen Atemschutzmasken. Es bietet erhöhte Filterleistung ohne zusätzliche Filtermaterialschichten, welche den Komfort beeinträchtigen würden.

Alle 3M Partikelmasken erfüllen die Anforderungen der EN149:2001. Ab Herbst 2001 werden die 3M Atemschutzmasken mit der neuen Kennzeichnung ausgeliefert.

- 3M (Schweiz) AG
  Eggstrasse 93
  Postfach
  CH–8803 Rüschlikon
  Telefon 01 724 90 90
  Telefax 01 724 91 55
  www.3m.com/ch/safety

Leserdienst Nr. 5

Focus Katalog – Feuchtemessung für jedermann

Die Firma Rotronic stellt im Bereich Feuchtemessung einen neuen auf die meist verwendeten Produkte 'fokussierten' Bestellkatalog vor. Der Focus Katalog deckt wie der bewährte Hauptkatalog 2000/2001 die gesamte Produktepalette im Bereich Feuchtemessung ab.

Durch die Beschränkung auf die meist eingesetzten Produkte im jeweiligen Sortiment, eine übersichtliche Darstellung und die vereinfachte Bestellcodierung ist die Auswahl des richtigen Gerätes auch für sporadische Anwender einfach.

Der 32-seitige Focus Katalog deckt trotz der seiner kompakten Darstellung einen umfassenden Teil im Bereich Feuchtemessung ab.

Sichern Sie sich noch heute Ihr persönliches Exemplar bei Rotronic AG.

- Rotronic AG
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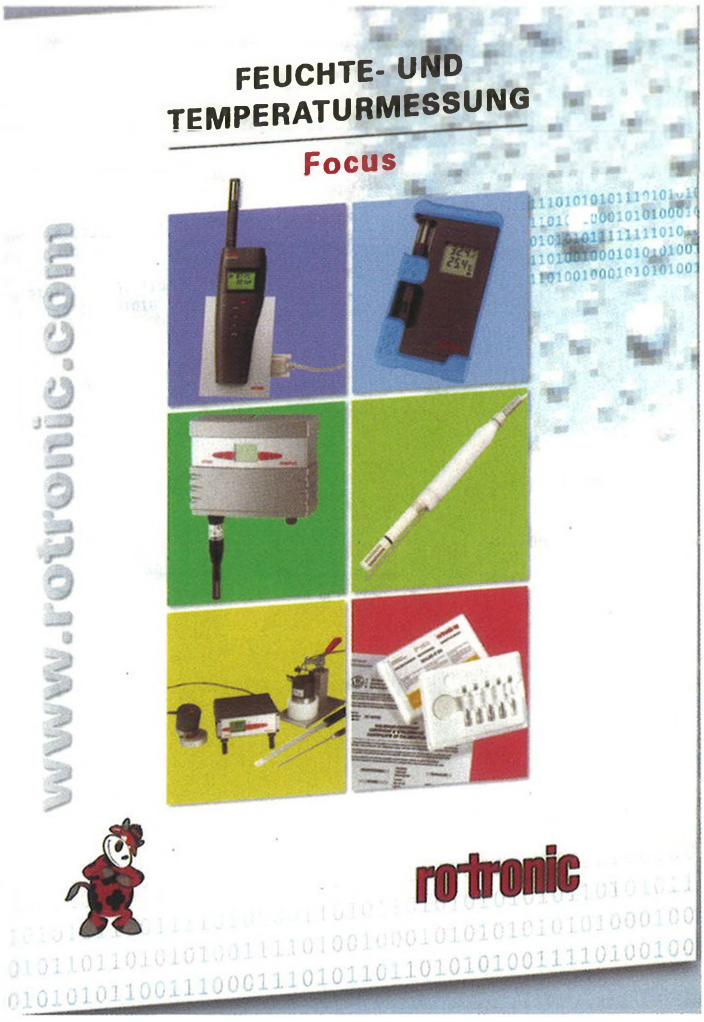
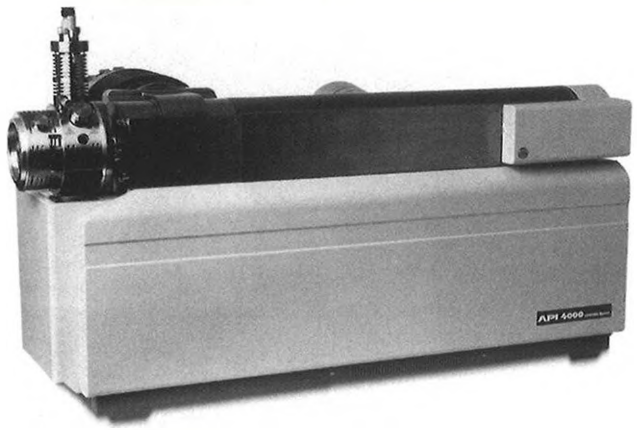
  CH-8303 Bassersdorf
  Tel. 01-838 11 11
  Fax 01-836 44 24
  E-Mail: rotronic@rotronic.ch
  Internet http://www.rotronic.ch

Leserdienst Nr. 6



Pharmaunternehmen profitieren vom neuen LC/MS/MS-System

Die Einführung des neuen Hybrid-Flüssigkeitschromatographie-Massenspektrometrie-Systems von Applied Biosystems ist auf dem besten Wege, eine bedeutende Auswirkung auf den Marktbereich Pharmakokinetik des Arzneimittelmetabolismus zu haben. Das API 4000 LC/MS/MS-Tripel-Quadrupol-System bietet eine bis zu 10fach höhere Empfindlichkeit, die den in der Forschung tätigen Wissenschaftlern die Identifikation und Quantitation von Arzneimittelkandidaten bei niedrigeren Konzentrationen als zuvor ermöglicht. Damit wird Pharmaunternehmen die Möglichkeit geboten, die Markteinführung von Arzneimitteln wesentlich zu beschleunigen.



Die Ionisationsmodi für die Ionenquelle des API 4000 können umgeschaltet werden, während nur ein einzelnes Ionenquellengehäuse verwendet wird. Hierbei handelt es sich um ein einzigartiges Merkmal, mit dem sich die Fähigkeiten und die Produktivität des Systems steigern lassen. Die Benutzer können ohne weiteres von Elektrospray-Ionisation auf chemische Ionisation bei Atmosphärendruck übergehen, indem sie lediglich eine einzelne Sonde umschalten.

Hochgradige Automatisierung und die ausgezeichneten Datenverarbeitungsfähigkeiten der Analyst™-Software stellen einen hohen System-Throughput sicher, während fortschrittliche Software-Pakete, wie zum Beispiel Information Dependent Acquisition (IDA) und Automatisierung den Throughput durch Maximierung der von einem einzelnen LC/MS-Durchlauf erfassten Informationen noch weiter steigern.

Das API 4000-System trägt zur Erweiterung der Familie der integrierten LC/MS-Systeme von Applied Biosystems bei. Robuste Ionenquellen und zuverlässige Hardware machen diese Systeme zu den empfindlichsten Instrumenten, die den Forschern zur Erfassung quantitativer wie auch qualitativer Daten zur Verfügung stehen.

Applera Corporation setzt sich für die Bereitstellung von weltweit führender Technologie und Informationen für auf dem Gebiet der Life Sciences tätige Wissenschaftler ein. Die aus den Unternehmen Applied Biosystems und Celera Genomics bestehende Applera Corporation verpflichtet sich nicht zur Veröffentlichung der Ergebnisse von gegebenenfalls erforderlichen Revisionen prognostischer Angaben, die in dieser Mitteilung gemacht oder impliziert wurden, wenn diese aufgrund von Ereignissen oder Umständen nach diesem Datum oder das Eintreten nicht vorhergesehener Ereignisse möglich wären. Die in dieser Mitteilung enthaltenen Angaben sind entsprechend zu bewerten.

Weitere Informationen erhalten Sie durch Kontaktaufnahme mit:

abdirect@eur.appliedbiosystems.com
oder

- Applied Biosystems
  Birchwood Science Park North
  Warrington WA3 7PB, UK
  Telefon +44 (0) 1925 825650
  Telefax +44 (0) 1925 282502
  Internet:
  www.appliedbiosystems.com

Leserdienst Nr. 7

3M Jupiter™ Gebläseeinheit: Der neue Massstab für Gebläse-Atemschutz

Die 3M Jupiter Gebläseeinheit ist äusserst kompakt und leicht. Sie setzt neue Massstäbe bezüglich Tragekomfort, Sicherheit, Flexibilität und Wartung.

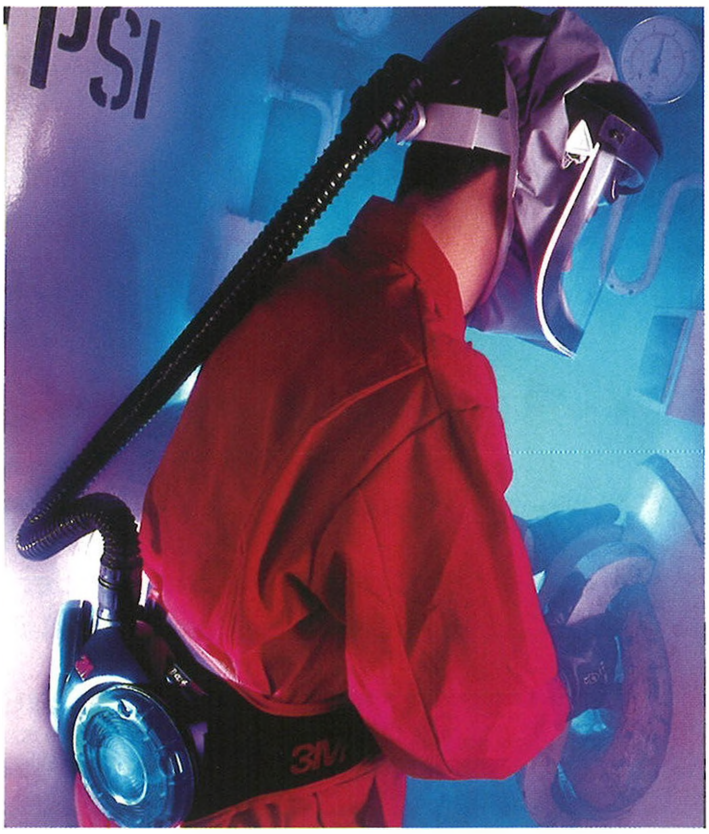
Die 3M Jupiter Gebläseeinheit ist ein leistungsstarkes Gerät. Dank der integrierten Batterie ist es zu einem kleinen, kompakten, eng anliegenden Gesamtsystem zusammengefasst. Der gepolsterte Gürtel bleibt auch nach stundenlangem Tragen formstabil und bietet allerhöchsten Tragekomfort. Das kompakte Gesamtsystem erlaubt grosse Bewegungsfreiheit auch in beengten Arbeitsbereichen und ermöglicht ermüdungsfreies Arbeiten über eine längere Zeitdauer hinweg. Die glatte Formgebung des Gehäuses erschwert das Absetzen von Schmutz und erleichtert die Reinigung.

Der Luftstrom wird elektronisch überwacht. Das Gerät gibt akustische und visuelle Alarmsignale bei abfallendem Luftstrom oder niedriger Batterieladung. In Kombination mit der 'Ex-Batterie' wird die ganze Einheit zu einem exgeschützten Atemschutz-System.

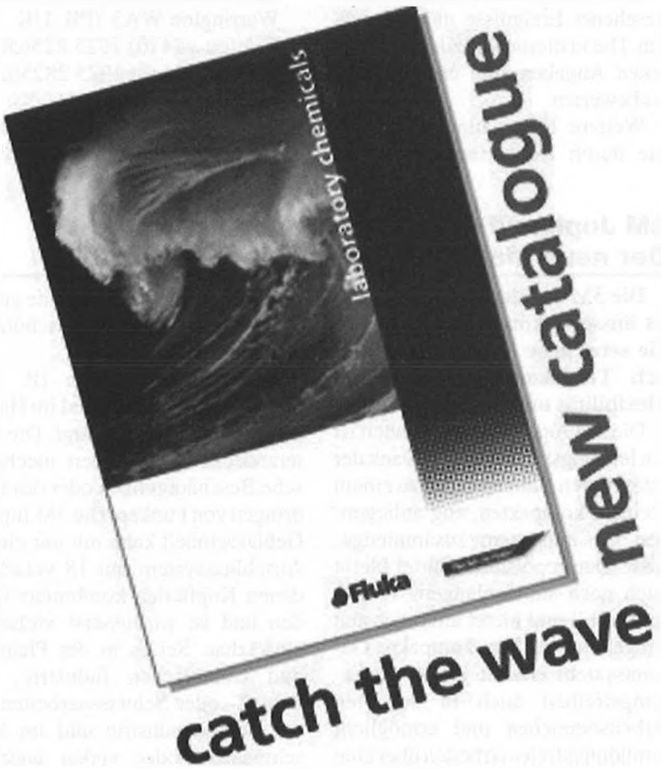
Die fünf Filtertypen (P, AP, ABEP, KP, ABEKP) sind im Handumdrehen sicher befestigt. Die Filterabdeckung verhindert mechanische Beschädigungen oder das Eindringen von Funken. Die 3M Jupiter Gebläseeinheit kann mit nur einem Anschlusssystem mit 18 verschiedenen Kopfteilen kombiniert werden und ist so äusserst vielseitig einsetzbar. Sei es in der Pharma- und Chemischen Industrie, bei Schleif- oder Schweissarbeiten, in der Schwerindustrie und im Maschinenbau oder vielen anderen Branchen und Anwendungen.

- 3M (Schweiz) AG
  Eggstrasse 93
  Postfach
  CH–8803 Rüschlikon
  Telefon 01 724 90 90
  Telefax 01 724 91 55
  www.3m.com/ch/safety

Leserdienst Nr. 8



Catch the wave of innovative products: New Fluka / Riedel-de Haën Catalogue 2001/02



The 2 Brands Fluka and Riedel-de Haën are presenting a wave of new innovative products in their second Joint Catalogue 2001/02. 1900 new products for Organic and Analytical Chemistry and Biochemistry.

With these new additions both brands have reinforced already strong areas of expertise as well as introduced new groups like Protein Sequencing Reagents, BCR®/ IRMM Reference Materials, LC-MS Standards, Ionic Standards and Electronic Chemicals. Other important product groups e.g. Certified Trace Analysis Standards, Fluorescent Probes and Labels, Pestanal Standards for Residue Analysis and Peptide Synthesis Reagents has been substantially enlarged.

In this new comprehensive Catalogue 2001/02 special fields of reference materials and standards have been presented in complete product group listings. The visually high-lighted sections make the inconvenience of searchnig for standard substances a thing of the past. In addition, blue inserts in the alphabetical section draw your attention to important product groups.

The new Catalogue 2001/02 not only provides a clear survey of the products offered therein, it presents an informative handbook and valuable tool for the customer. Many useful cross references, extensive literature references and structural formulae emphasize the handbook character of this outstanding catalogue impressively.

Guaranteed values for product purity and best service have constituted the foundation for the success of both brands for years. Fluka and Riedel-de Haën offer the user more than 25000 analytical reagents and laboratory chemicals – the most comprehensive supply of product-sever available. Compact and always ready.

Ask for your free copy.
Visit us on the internet:
www.sigma-aldrich.com

- Fluka Chemie GmbH
  Industriestrasse 25
  CH–9471 Buchs/Switzerland
  Tel.: 081 755 25 11
  Fax: 081 756 54 49

Leserdienst Nr. 9

FIZ CHEMIE BERLIN und GDCh vereinbaren neue Kooperation: Strategische Allianz zur Vernetzung der Chemiefachwelt

Berlin, Juni 2001 – Das Fachinformationszentrum Chemie GmbH (FIZ CHEMIE Berlin) und die Gesellschaft Deutscher Chemiker (GDCh) haben eine strategische Allianz zum Aufbau einer technischen und organisatorischen Vernetzung der Chemiefachwelt vereinbart. Dies teilten das FIZ CHEMIE Berlin und die GDCh jetzt in einer gemeinsamen Presseerklärung mit.

'Primäres Ziel der Kooperation ist eine bessere Bündelung der fachlichen Information und Kommunikation im Netz', erklärt Dr. René Deplanque, wissenschaftlicher Geschäftsführer des FIZ CHEMIE Berlin. Professor Dr. Heindirk tom Dieck, Geschäftsführer der GDCh, sieht die aktive Unterstützung des Aufbaus einer vernünftig nutzbaren Informationsinfrastruktur für die Chemie als eine wesentliche Aufgabe der Fachgesellschaft an. 'Es geht darum, die neuen Medien optimal für die Informationsversorgung und die Kommunikation in der Chemie einzusetzen, dabei aber durch kompetente Dokumentation und Strukturierung dafür zu sorgen, dass kein unüberschaubares Chaos entsteht'. Darüber hinaus gelte es, alle beteiligten Fachgruppen zusammenzuführen. Erste Gespräche mit möglichen Partnern seien bereits angelaufen.

Als Methode und Werkzeug für die Bündelung sind fachspezifische Internet-Portale angedacht, über die später auch elektronisch aufbereitete Ausbildungsmodule für die Aus- und Weiterbildung in der Chemie zielgruppengerecht bereitgestellt werden können. Portale vergleichbarer Art hat das FIZ CHEMIE Berlin bereits mit dem 'Chem Guide', dem 'PublishersGuide' und dem 'MedPharmGuide' im Internet (http://www.chemistry.de – Stichwort: Datenbanken).

Das FIZ CHEMIE Berlin ist ein non-profit Informations- und Dokumentationszentrum mit Schwerpunkt in Entwicklung, Produktion und Bereitstellung von elektronischen Informationsdiensten (Suchmaschinen, online und inhouse Datenbanken, Web-based teachware) und gedruckten Diensten für Wissenschaftlerinnen und Wissenschaftler, die in allgemeiner Chemie, organischer Chemie und Synthese, chemischer Technik, Kunststoffchemie, Pharmakologie oder Sicherheit tätig sind. Es ist auch ein Service-Institut der Wissenschaftsgemeinschaft Gottfried Wilhelm Leibniz.

Die GDCh mit fast 30 000 Mitgliedern, überwiegend promovierten Chemikern und Chemikerinnern, ist die grösste derartige Fachorganisation auf dem Europäischen Kontinent. Ihre vielfältigen Aktivitäten spiegeln sich in zweiundzwanzig Fachgruppen und über sechzig Regionalvertretungen. Sie hat erfolgreich Europäische Kooperationsstrukturen aufgebaut und gibt für weitere die Richtungen vor und befördert damit eine auch im Weltmassstab wettbewerbsfähige European research area. In Fragen der Fachinformation und der modernen elektronisch unterstützten Lehre bilden die beiden Partner die stärkst mögliche Allianz.

- FIZ CHEMIE Berlin
  Franklinstrasse 11
  D–10587 Berlin
  Inernet: www.chemistry.de
  E-mail: info@fiz-chemie.d

Leserdienst Nr. 10

cc-markets und chemplorer fusionieren zu cc-chemplorer

Zwei führende Internet-Marktplätze fur die Chemie- und Life Science-Industrie nun unter einem Dach vereint.

Stetige Ausweitung des Angebots soll Position von cc-chemplorer als erste Adresse für One-Stop-Procurement stärken / Marktplatz will auch international führend werden.

Die Fusion zwischen cc-markets und chemplorer, den beiden führenden Internet-Marktplätzen für die Chemie- und Life Science-Industrie, ist jetzt perfekt: Derzeit bieten etwa 200 Lieferanten insgesamt 1,6 Mio. Produkte und Dienstleistungen in standardisierten Katalogen an. Der Marktplatz ist spezialisiert auf sogenannte indirekte Güter, d.h. alles ausser Rohstoffen, für die Chemie-, Life Science-Industrie und chemienahe Branchen. 'Durch ihre Fusion läuten cc-markets und chemplorer die in der Branche erwartete Konsolidierungsphase ein', erklärte Christian Rast, Geschäftsführer von cc-chemplorer und Sprecher der Unternehmensgruppe, auf einer Pressekonferenz anlässlich der Fusion vor internationalen Journalisten in Frankfurt am Main.

cc-chemplorer werde als international aufgestelltes Unternehmen zu den wenigen starken Playern gehören, welche die E-commerce-Ernüchterung überleben und zu Informations- und Prozessdrehscheiben ihrer Industrie würden.

'Der Marktplatz', so sagte er, 'verbindet die Expertise der Old Economy mit den modernen Technologien und Organisationsformen der New Economy.' Zu den Erfolgsfaktoren, die der Marktplatz mitbringe, gehöre die klare Fokussierung auf Zielmarkt und Kernkompetenz. 'Eine vagabundierende Strategie gibt es bei cc-chemplorer nicht', erklärte er. Statt dessen sei die konsequente und kontinuierliche Ausweitung des Dienstleistungsangebots und eine Verstärkung der internationalen Präsenz geplant, um die Position cc-chemplorers als erste Adresse für elektronische Beschaffung in der Chemie- und Life Science-Industrie zu stärken.

Potentiale für Einkäufer und Lieferanten gleichermassen

cc-chemplorer bietet Einkäufern ein beträchtliches Potential zur Verschlankung ihrer Bestellprozesse und damit zur Einsparung von Beschaffungskosten, die im Verhältnis zur bestellten Ware oft unverhältnismassig hoch sind. Mit Hilfe von standardisierten Produktkatalogen und effizienten Suchmaschinen können die Angebote verschiedener Anbieter schnell und bequem miteinander verglichen und das günstigste Angebot ermittelt werden. Auch die sogenannten E-negotiation-Tools von cc-chemplorer – Ausschreibungen und Auktionen auf Online-Basis, die auf den beiden fusionierten Marktplätzen bereits mit wachsendem Erfolg eingesetzt wurden – helfen dabei, das günstigste Angebot zu finden.

Aber auch für Lieferanten eröffnet der Marktplatz grosse Potentiale. Lieferanten erreichen ohne aufwendige Vertriebsaktionen über cc-chemplorer einen wesentlich grösseren und vor allem internationalen Kundenkreis.

One-Stop-Procurement umfasst Mehrwertdienste

cc-chemplorer versteht sich als Rundumanbieter. Neben Produkten und Dienstleistungen für das operative Geschäft werden auch Services angeboten, die Marktplatzteilnehmern, und zwar Einkäufern wie Lieferanten gleichermassen, die tägliche Arbeit erleichtern. In diesem Rahmen werden auf der elektronischen Plattform verschiedene Mehrwertdienste wie der Zugriff auf internationale Unternehmens- und Wirtschaftsinformationen oder die Aufbereitung von Marktplatz- und Unternehmensdaten angeboten.

- cc-chemplorer Service GmbH
  Eduard-Pflüger-Strasse 55
  D–53113 Bonn
  Tel. +49 228 6195 0
  Fax +49 228 6195 100
  E-Mail: info@cc-chemplorer.com

Leserdienst Nr. 11

Sterilisation, Pasteurisation, Lagerung und Transport
Zuverlässige Temperatur- und Drucküberwachung

Die vielseitige Logger-Baureihe **EBI 1** von ebro Electronic in Ingolstadt deckt eine riesige Vielfalt an spezifischen Anwendungen ab. Die Messbereiche der Ausführungen **EBI-85 A** und **EBI-125 A** reichen von –40....+85 °C bis zu –40... +125 °C sowie von 0...2/5110/20 bar. Mit externen Fühlern sind sogar Temperaturen –50... +150 °C und –50...+400 °C messbar. Für das Programmieren und Auslesen dieser Logger hält ebro die Standard-Schnittstelle EBI-AE-S bereit. Die Software EBI-WINLOG 2000 ermöglicht die grafische und numerische Auswertung. Der integrierte Formel-Editor erleichtert die Berechnung von temperatur- oder druckabhängigen Grössen.

Zu den wichtigsten Anwendungsgebieten zählen die Autoklavierung in Medizin und Chemie, Sterilisierung und Validierung im Krankenhaus nach DIN EN 554/285, F- und PE-Wert-Berechnung, Überwachung von Lebensmitteltransport, Blutbanken und Prozessbedingungen in der Chemie. Hinzu kommen Bowie-Dick-Test, Flaschenreinigung, Messung von Temperatur und Druck sowie CO_2-Messung in Brauereiwirtschaft und Getränkeindustrie.

Mit den absolut wasserdichten Loggern (IP 68) der Serien EBI-85 A und EBI-125 A für Flaschen und Dosen bietet ebro ein intelligentes System zur Temperaturmessung bei der Wärmebehandlung von Lebensmitteln und pharmazeutischen Produkten. Zur Befestigung der Logger mit Fühlerlängen von 135 bis 300 mm für Flaschen bzw. 125 bis 150 mm für Dosen gibt es spezielle Adapter. Die Logger haben eine Speicherkapazität von 18 000 Messwerten und eine Batterie-Lebensdauer von 5 bis 8 Jahren.

• MBV AG
Microbiology & Analytic
Bahnhofstrasse 8
CH–8712 Stäfa
Tel.: (01) 928 30 80
Fax: (01) 928 30 49
E-mail: h.zingre@mbv.ch

Leserdienst Nr. 12

Wenn Multimedia-Strategie für Kundendienst steht: Eine Premiere auf dem chemischen Sektor

Als Marktführer auf dem Gebiet der Entwicklung von hochleistungsfähigen Polyurethan- und Epoxydharzen baut das französische Unternehmen **AXSON** gegenwärtig seine Kommunikations- und Kundendienststrategie aus. In diesem Zusammenhang wurde eine originelle und interaktive Website erstellt, die zur raschen und systematischen Aktualisierung der Produktfiles mit einer CD gekoppelt ist. Dies stellt im Bereich der Spezialchemie eine absolute Premiere dar. Die in französischer (www.axson.fr) und englischer (www.axson.com) Fassung vorliegende Website ist ab sofort abrufbar. Die CD sowie die italienische, spanische und deutsche Version der Website wird in wenigen Monaten verfügbar sein.

Benutzerfreundlich und leistungsfähig bieten diese Tools für den Anwender erheblichen Zeitgewinn und hohe Effektivität. Sie ermöglichen es, die Erwartungen der Kunden und Handelsvertreter besser zu erfüllen, bieten dem weltweiten Vertriebsnetz günstigere Voraussetzungen und dienen darüber hinaus als Informationsquelle für Institutionen und Medien.

Eine breite Palette von Dienstleistungen

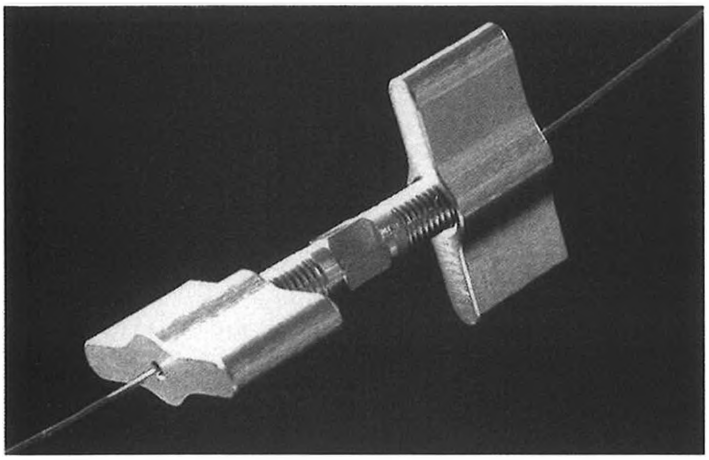
- **AXSON** stellt den Internetnutzern Informationen über die Aktivitäten der Untemehmensgruppe, die Produkte von **AXSON** und ihre Anwendung sowie über das weltweite Vertriebsnetz zur Verfügung.
- Die innovative Lösung des Unternehmens besteht darin, dass dem Kunden bzw. Handelsvertreter im Online-Modus technische Hilfestellung, ein Diskussionsforum zu technischen Problemen sowie ein Vorbestellungsmodul (noch ohne Geschäftsabschluss) für die am häufigsten angewandten **AXSON**-Produkte angeboten wird.
- Eine Suchmaschine ermöglicht es dem Kunden oder Handelsvertreter, ein spezielles **AXSON**-Produkt zu finden, welches genau auf dessen Tätigkeitsbereich, die gewünschte Anwendung oder auf dessen Produktpalette zugeschnitten ist.
- Mit Hilfe eines spezifischen CD-Moduls ist ein rasches Update der auf der Festplatte des Anwenders gesicherten technischer Dokumente durch Herunterladen von der Website möglich.
- Die Schaffung eines über Passwort zugänglichen Partner-Workspace bietet den Mitarbeitern des weltweiten Vertriebsnetzes die Möglichkeit zur Information, zur Weiterbildung und zum Informationsaustausch. So können diese zahlreiche Dokumente, wie z.B. Module für die Schulung zu Produkten und Technologien, Unterweisungen zu neu eingeführten Produkten sowie Fotos herunterladen. Dieser Workspace ist ein hervorragendes Mittel zur Kommunikation, welches auch mit Unterstützung durch die allgemeine Globalisierung die Beziehungen zwischen den Mitarbeitern des Vertriebsnetzes von **AXSON** weiter vertiefen wird.
- Unter der Rubrik 'Neuigkeiten' können Internetnutzer und vor allem Journalisten die Entwicklung der Unternehmensgruppe und ihrer Erzeugnisse mitverfolgen.
- Nicht zuletzt haben alle Besucher der Website die Möglichkeit zur sofortigen und kostenfreien Information per E-mail über sie interessierende Neuheiten oder Veränderungen der Website. Dazu genügt es, ein einfaches Formular auszufüllen (Mailing-Liste).

Die Einführung einer solchen multimedialen Strategie stellt eine absolute Premiere auf dem Gebiet der Spezialchemie dar und ist Teil des Programms zur ständigen Verbesserung des **AXSON**-Kundendienstes.

• Jenny Co. AG
General-Guisan-Strasse 11
CH–8401 Winterthur
Telefon +41 (0) 52 212 94 94
Telefax +41 (0) 52 212 89 42
E-mail: info@jenny.ch

Leserdienst Nr.13

Titanium-Connector



The Titanium-Connector for joining two fused silica capillaries is small, rugged and essy to handle. Thanks to the special design no tools are needed for installation. Its heart is a deactivated PressFit connector granting a chemically inert joint – free of dead volume. The connector is additionally tightened and mechanically stabilized against the titanium body by two Vespel™/ Graphite Ferrules. The low thermal mass rules out the formation of cold spots even during fast temperature programming.

Vespel is a Trademark of E.I. du Pont de Neumours & Co., Inc.

• BGB Analytik AG
Laufrainweg 139
CH–4469 Anwil
Tel. +41 61 991 00 46
Fax +41 61 991 00 25
E-mail sales@bgb-analytik.ch

Leserdienst Nr. 14

Die Laborzeitschrift von Kendro ab jetzt weltweit mit neuem Namen!

Mit einer Rekordauflage von 100 000 Exemplaren erschien die Ausgabe 1/2001 der Labor-Kundenzeitschrift von Kendro gleichzeitig mit ihrem neuen Namen Kendro Scope. Jeder Interessierte kann sie kostenlos bei Kendro Laboratory Products anfordern oder unter http://www.kendro.de im Internet herunterladen. Neben Informationen über neue Produkte erfahren die Leser Nützliches zu konkreten Anwendungen.

Unter den Neuheiten wird unter anderem der Heraeus HERAcell 240 CO_2-Inkubator von Kendro mit einem Innenraumvolumen von 240 l vorgestellt. Dieses Gerät eliminiert zuverlässig Mykoplasmen und andere Keime mit seiner hochwirksamen Dekontaminationsroutine ContraCon. Die Heraeus CO_2-Inkubatoren HERAcell (150 l) und HERAcell 240 eignen sich für den Einsatz in der Zellbiologie, in der Reproduktionsmedizin sowie der Klinischen Forschung.

Zum Thema Industrielles Bioprocessing wird die neue Powerfugen-Linie von Carr präsentiert. Mit der Übernahme der amerikanischen CARR Separations Inc. konnte Kendro den Bereich Bioprocessing zukunftsweisend erweitern.

Aus diesem Gebiet stammen auch die Anwenderreportagen, die u.a. zu den Themen 'Von der Zelle zur Anlage' und 'Produktivitätssteigerung von schwierigen Zell-Linien' von den vielseitigen Einsatzgebieten der Kendro Produkte vor Ort berichten.

• Kendro Laboratory Products AG
Räffelstrasse 32, Postfach
CH–8045 Zürich
Telefon 01/454 12 12
Telefax 01/454 12 99
e-mail:
kendro-ag@swissonline.ch

Leserdienst Nr. 15

Neue Vertretung von Honsberg

Per 1. Juli 2001 hat die Firma Fahrer AG von der Roshard, Maschinen- und Apparatebau in Küsnacht, die Vertretung der Firma Honsberg für die Schweiz übernommen.

Honsberg ist als führender Hersteller von Mess- und Überwachungsgeräten für Durchfluss, Niveau, Druck- und Temperatur tätig. Die Geräte werden seit vielen Jahren mit grossem Erfolg im Maschinenbau, der Prozesstechnik und im industriellen Anlagebau eingesetzt.

Anwendungsbeispiele:
- Hydrauliküberwachung von Spannzylindern
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- Überwachung von Werkzeughydraulik, Transferstrassen
- Niveauüberwachung/-messung in hydraulischen Maschinen
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Auskünfte erhalten Sie unter:

• Fahrer AG
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CH-8309 Nürensdorf
Telefon 01 888 69 65
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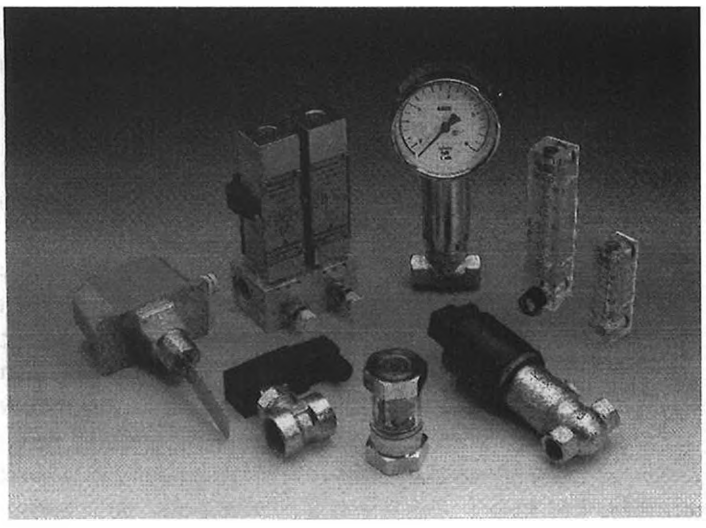
info@fahrer.ch
www .fahrer.ch

Leserdienst Nr. 16



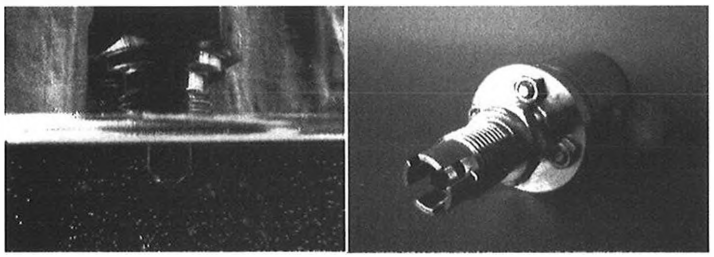
Füllstand messen von –268 °C bis +400 °C

Von 0 bis 25 Mpa mit einem Sondertyp

Dies kann derzeitig nur mit dem Optoelektronischen Füllstandsensor abgedeckt werden. Dieser universelle Sensor kann somit zum Beispiel für die Flüssigkeitsgrenzstandmessung in Kälteanlagen ebenso eingesetzt werden, wie für den Trockenlaufschutz in Hochdruckpumpen. Die zu erfassende Flüssigkeit kann auch leicht trüb oder undurchsichtig sein. Weitere Vorteile des Messprinzips sind die Unabhängigkeit von Mediumseigenschaften wie Dichte, Dielektrizitätskonstante oder Leitfähigkeit. Es sind keine beweglichen oder vibrierenden Teile im Sensor. Aufgrund der Zulassung für die Zone 0 und Überfüllsicherung nach WHG hat sich die Sonde inzwischen einen festen Platz unter den herkömmlich messenden Füllstandsonden erobert.

- WISAG
  Oerlikonerstrasse 88
  CH–8057 Zürich
  Tel.: 01 / 317 57 57
  Fax: 01 / 317 57 77
  Internet: www.wisag.ch
  E-Mail: info@wisag.ch

Leserdienst Nr. 17



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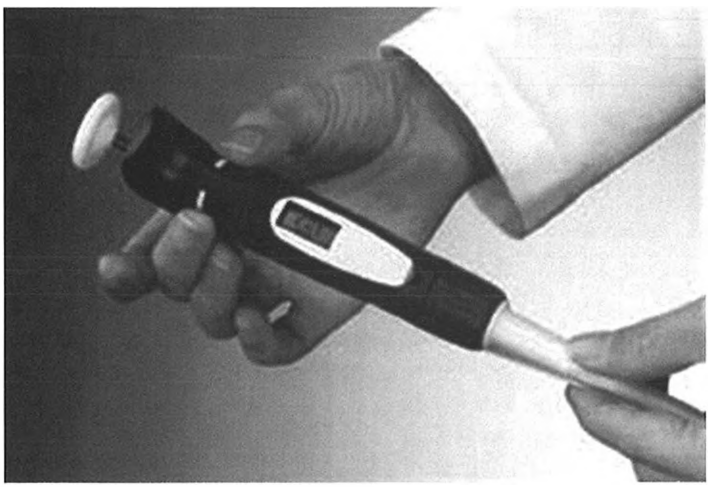

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Leserdienst Nr. 18

Ismatec SA: Berndt Goldmann neuer Geschäftsführer

Per 1. Juni 2001 übernahm Berndt Goldmann die Geschäftsleitung der Ismatec SA. Der studierte Ingenieur kommt aus der Energiebranche, wo er als Managing Director tätig war. Berndt Goldmann wird in seiner Funktion als Geschäftsführer sowohl für die Ismatec SA in der Schweiz als auch übergeordnet für Belange der deutschen Tochterfirma Ismatec Laboratoriumstechnik GmbH verantwortlich sein. Das Schweizer Stammhaus bedient direkt den Markt Schweiz sowie weltweit 50 Distributoren.

Der Markt Deutschland wird durch die Ismatec Laboratoriumstechnik GmbH mit Sitz in Wertheim bedient.

Die Forschung, Entwicklung und Produktion der Ismatec SA umfasst Schlauchpumpen und Antriebe zu Keramikkolbenpumpen- und Zahnradpumpenköpfen. Das 1964 gegründete Unternehmen wurde im April 2000 im Rahmen der Nachfolgeregelung des Gründerehepaars Fritz und Anita Ackermann zu 100 Prozent an die amerikanische IDEX Corporation verkauft. In der Schweiz vertritt Ismatec SA als Kälte- und Wärmespezialist verschiedene international tätige Firmen wie Revco, Virtis, MMM, Infors, Liebisch, Liebherr oder Thermolyne.

- ISMATEC AG
  Feldeggstrasse 6
  Postfach
  CH–8152 Glattbrugg
  Telefon 01 874 94 94
  Fax 01 810 52 92

Leserdienst Nr. 19

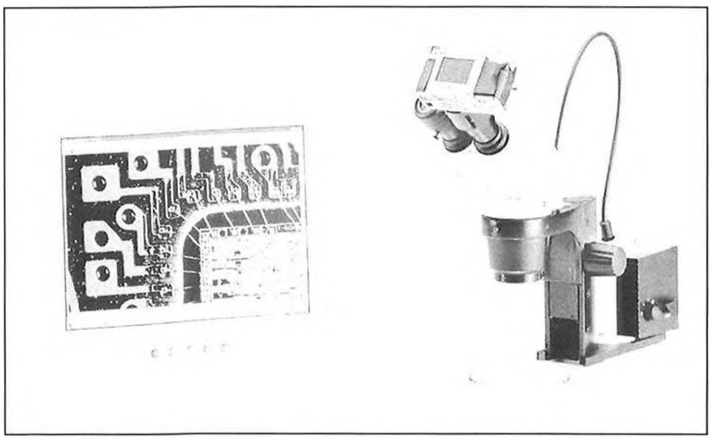
Leica DC 150 – 3.3 Megapixel-Kamera für die professionelle Mikroskopie

Leica Microsystems, Spezialist für Mikroskopie, digitale Bildaufnahmesysteme und Bildmanagementprogramme, erweitert das Programm um die exzellente Digitalkamera Leica DC 150 für private und berufliche Zwecke. Adaptiert an ein Mikroskop, mit oder ohne Fototubus, eignet sich die 3.34-Megapixel-Kompaktkamera mit 6,6-Megapixel-Shift-Technologie für fast alle Anwendungen in Industrie, Bildung und Forschung und liefert bestechende Bilder mit einer Auflösung von 2032x1536 Pixel.

Dabei bedient sich die Leica DC 150 zukunftsweisender Technologien, um die hohe Auflösung, Detailschärfe und Farbreproduktion zu steigern, wie z. B. des 6,6-Mega Pro-Still Modus für ein Höchstmass an Auflösung und Farbtreue: Die Pixel-Shift-Technologie (Doppelbelichtung mit Pixelverschiebung) verdoppelt die Bildpunktzahl auf 6,6-Megapixel. Der DR Pro-Still Modus steigert den Dynamikumfang: Die Daten von verschiedenen Belichtungen mit extrem hohem Kontrast werden kombiniert. Der NR Pro-Still Modus reduziert das elektronische Rauschen: Durch Überlagern mehrerer Kopien entstehen auch bei geringsten Lichtintensitäten hervorragende Bilder. Zu den weiteren Merkmalen der Kamera gehören ein hochwertiges 2.3-fach Zoomobjektiv, Autofokus, die Fähigkeit Videosequenzen aufzunehmen, Mehrfachbelichtungsfunktion, Collage-Funktion, manuelle Belichtungs- und Weissabgleichkorrekturen, vier Empfindlichkeitseinstellungen sowie AE-Programmautomatik mit Blendenpriorität, USB-Schnittstelle, 2"-TFT-Farbmonitor. Im Lieferumfang integriert ist die Image Management Software Leica IM 50.

- Leica Microsystems AG
  Kanalstrasse 21
  CH–8152 Glattbrugg
  Tel. +41 1809 34 34
  Fax +41 1809 34 44
  www.leica-microsystems.com

Leserdienst Nr. 20



Modulares Konzept mit diversen Verstärkern und optionalem Drucker:

Universalmessgerät für fast alle physikalischen Grössen

Unter der Bezeichnung UNIMETER hat ebro Electronic in Ingolstadt ein neuartiges Universalmessgerät auf den Markt gebracht, das aus 3 Modulen besteht: einem Grundgerät mit grosser und grafikfähiger LCD-Anzeige und Funktionstasten für eine einfache, menügeführte Bedienung, einem steckbaren Messverstärker für die entsprechenden Messgrössen und einem optionalen Thermodrucker für Etiketten- oder Endlosdruck. Dadurch lässt sich für jede spezielle Anwendung ein hochgenaues, preiswertes und jederzeit erweiterbares Messgerät zusammenstellen. Zu den wichtigsten Anwendungsgebieten zählen Lebensmittel- und Pharmaindustrie, Grossküchen, Fleisch- und Fischhandel, Chemie, Labors, Elektroindustrie, Maschinenbau, Arbeitssicherheit und Umweltschutz.

Das Gerät ermöglicht 1- oder 2-kanalige Temperaturmessungen mit Thermoelementen des Typs K oder J bzw. Temperaturfühlern Pt 100 oder Pt 1000 sowie Aufzeichnungen mit frei wählbarem Messintervall. Es sind auch ein Barcodeleser mit Typ K sowie ein Infrarot-Vorverstärker lieferbar. In Vorbereitung sind verschiedene Verstärkermodule zur Messung von Strom/Spannung, Druck, relativer

Feuchte, pH-Wert, Leuchtstärke, Lautstärke, Beschleunigung, Strömungsgeschwindigkeit, Vibration, elektrischer Leitfähigkeit, Dehnung sowie Gaskonzentration von CO_2, CO, O_2, Methan, Stickoxid und Ethylen. Das mikroprozessorgesteuerte, akkubetriebene Grundgerät mit Analogausgang 0...1 V ist PC-programmierbar und verfügt über Infrarot-Schnittstelle (RS 232), Min/Max- und Hold-Funktion, Mittelwert- und Delta-Berechnung. Skalierung und Erkennung des Messaufnehmers erfolgen automatisch, die Kalibrierung über das Tastenfeld.

- MBV AG
  Microbiology & Analytic
  Bahnhofstrasse 8
  CH–8712 Stäfa
  Tel.: (01) 928 30 80
  Fax: (01) 928 30 49
  h.zingre@mbv.ch
  Internet: www.ebro.de

Leserdienst Nr. 21

Software zur Überwachung von GMP-Kriterien protokolliert Qualitätskontrollen (QC) und Laufparameter zahlreicher Zentrifugen

Neu: Die Software SORVALL® WatchLog Network Plus™ von Kendro Laboratory Products ermöglicht die zentrale Überwachung und Verwaltung von bis zu 16 gekühlten Zentrifugen der Typen SORVALL® RC3BP™ und RC12BP™ von einem einzigen Desktop-Rechner aus. Das Programm zeigt den Status aller Zentrifugen im Netzwerk in Echtzeit an und zeichnet Informationen zum laufenden Betrieb auf, so dass die GMP-Kriterien (GMP: 'Good Manufacturing Practice', Gute Herstellpraxis) spielend erfüllt werden können.

Die Software verfügt über eine interaktive Benutzeroberfläche, die sich aus verschiedenen farbigen Schaltflächen zusammensetzt, die den Zentrifugenstatus übersichtlich darstellen. Durch Anwahl eines Gerätepiktogramms kann der Bediener in Echtzeit auf die Daten der betreffenden Zentrifuge zugreifen. Zu den abrufbaren Daten gehören QC-Lauf-Status und -Informationen, Programm-Nummer, Set- und Ist-Geschwindigkeit sowie -Zeit und -Temperatur.

Zusammen mit dem Bar Code Scannersystem **BarTrace™** – mit dem Chargen so präzise wie noch nie verfolgt werden können – ermöglicht die Software beim Zentrifugieren eine umfassende Prozesskontrolle.

Sie erfüllt die GMP-Anforderungen und erhöht gleichzeitig die Produktivität.

Der Bediener kann automatische QC-Checks fur jedes gespeicherte Protokoll durchführen. QC-Parameter – z. B. Datum, Bedienername und Seriennummer der Zentrifuge – werden automatisch aufgezeichnet.

Bei der Überwachung von Produktionsabläufen werden zusätzliche Parameter wie Startzeit, maximale und minimaie Temperatur sowie eventuell aufgetretene Fehler protokolliert. Die Daten können auf der Festplatte gespeichert und/oder als Ausdruck ausgegeben werden, wodurch Fehler, die beim manuellen Protokollieren oder durch Unleserlichkeit auftreten können, nahezu ausgeschlossen sind.

- Kendro Laboratory Products AG
  Räffelstrasse 32, Postfach
  CH–8045 Zürich
  Telefon 01 454 12 12
  Telefax 01 454 12 99
  e-mail:
  kendro-ag@swissonline.ch

Leserdienst Nr. 22

CAMAG TLC Scanner 3 mit winCATS – Planar Chromatography Manager

Der CAMAG TLC Scanner 3 ist der optimale Messplatz für die densitometrische Auswertung von Objekten aus den Bereichen Planar-Chromatographie und Elektrophorese.

Wichtigste Merkmale des CAMAG TLC Scanner 3 sind:

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- Gerätequalifizierung via Software (Option)
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*win*CATS, das neue Softwarekonzept für modern Dünnschicht-Chromatographie

- steuert die Geräte
- überwacht den gesamten Arbeitsablauf
- dokumentiert die komplette analytische Methode von der Probendefinition über die Chromatogrammauswertung bis zum Resultat und
- erfüllt die Anforderungen von GMP/GLP

Fordern Sie Unterlagen an oder Infos unter www.camag.com

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  Fax: +41 61 461 07 02

Leserdienst Nr. 23

MWG-Biotech's RoboSmart: The first fully automated system for complete DNA purification up to sequencing reaction

MWG-Biotech announces the official commercialization of the new lab robot RoboSmart. The system is the first robot in the market to completely automate, in one single step on one single robot platform, plasmid or PCR product purification, set up, processing, and subsequent purification of the sequencing reaction.

The RoboSmart is ideally suited to be the fully automated sample preparation system of choice for the several thousand capillary sequenc-

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CHIMIA-Leserdienst
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ers already on the market. In 2001 MWG-Biotech expects to sell circa 20 units of this new robot, which is the latest member of MWG-Biotech's successful lab automation series.

On the new RoboSmart several subsequent process steps have been combined on one single platform to ensure a high degree of automation unprecedented in the market. High process security ensures constant result reliability. At the same time the system is extremely user friendly: it only takes half an hour to completely load the robot. Then more than 768 samples will be processed within 15 hours in a fully automated process without any further user intervention. Thus, the RoboSmart is ideally suited for working overnight, and valuable lab time that is freed for other processes. Due to this fact the complete system will have paid itself off in little over a year.

'We are proud to be the first company in the market to offer complete automation for the most time consuming part of sample preparation. The new RoboSmart represents a long awaited application solution especially for all 96 capillary sequencer users. It is the result of our strategy to develop complete solutions for our customers, so that valuable working time is available for important research work.' said Michael Weichselgartner, CEO of MWG-Biotech AG.

MWG-Biotech is an international innovator of techniques, instruments and services as platform for success in life sciences today and for a better life tomorrow. Further information on MWG-Biotech is available on the company's website at www.mwg-biotech.com.

• MWG-BIOTECH AG
Anzinger Strasse 7a
D–85560 Ebersberg, Germany
Tel.: +49 8092 8289 929
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Leserdienst Nr. 24

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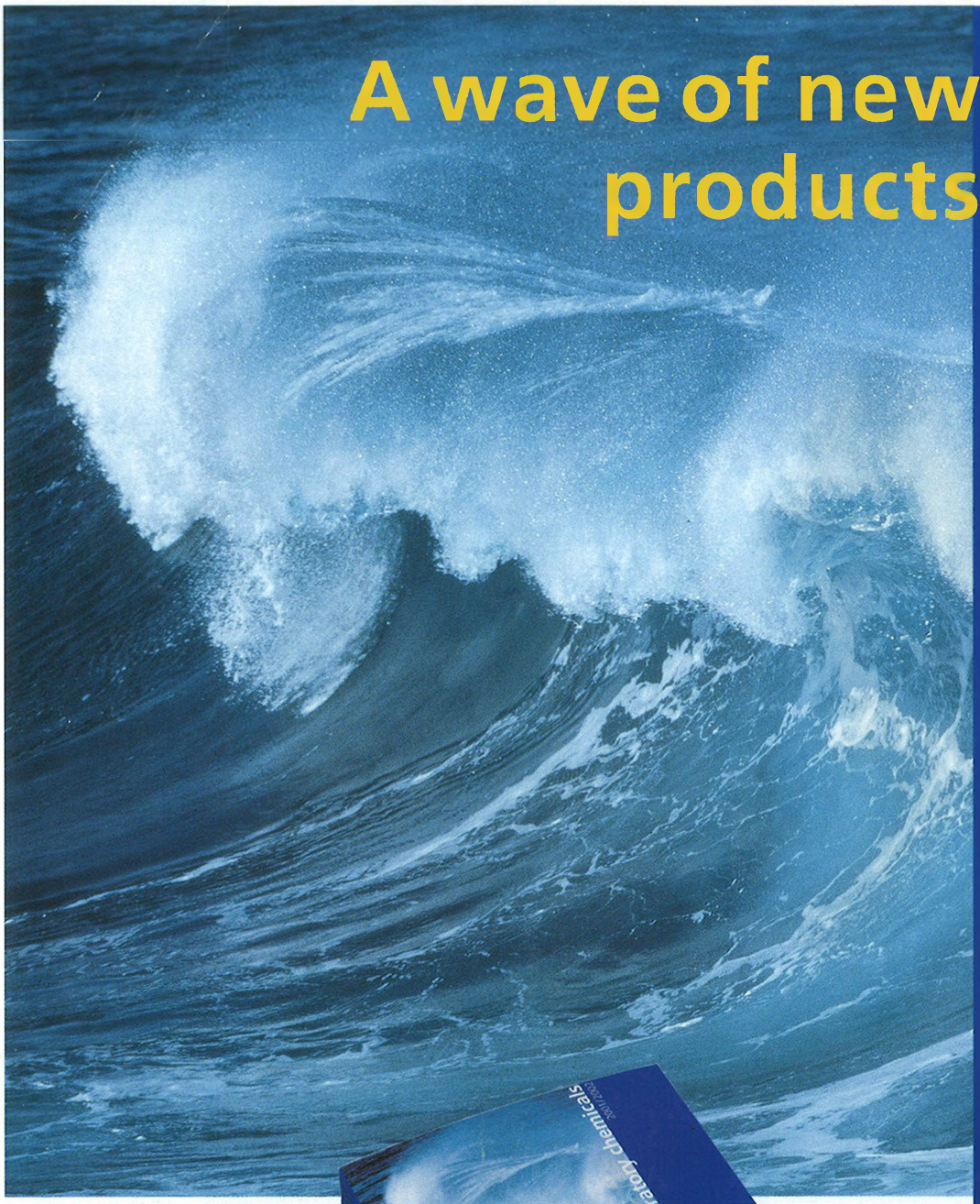

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