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CHIMIA

Fall Meeting 2000
Assemblée d'automne 2000
Herbstversammlung 2000

NEUE SCHWEIZERISCHE CHEMISCHE GESELLSCHAFT
NOUVELLE SOCIETE SUISSE DE CHIMIE
NEW SWISS CHEMICAL SOCIETY

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and its Sections

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und
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SGPP	Swiss Soc. of Photochemistry and Photophysics	SGPP	Schweiz. Ges. für Photochemie und Photophysik
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VSN	Swiss Association of Science Teachers	VSN	Verein Schweiz. Naturwissenschaftslehrerinnen und -lehrer

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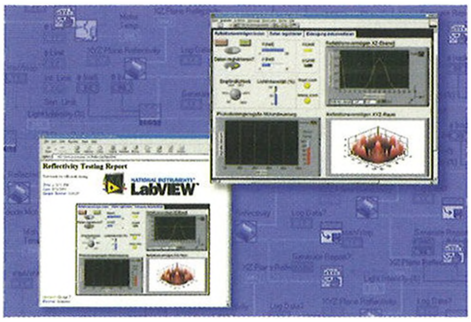

LabVIEW 6i: Internet-optimiertes intelligentes Messen – und mehr!

Mit der Vorstellung seiner neuesten Version von LabVIEW knüpft National Instruments abermals an seine Tradition der Revolution der Mess- und Automatisierungstechnik an. LabVIEW 6i bietet viele neue Funktionen und ermöglicht die blitzschnelle Anbindung ans Internet, so dass Ingenieure und Wissenschaftler noch effektiver arbeiten können als bisher. In dieser Version steht den Anwendern der neue LabVIEW Player™ zur Verfügung – ein WebBrowser-Plug-in, mit dem sie Steuerapplikationen an Kollegen übermitteln, aber auch Daten im Internet veröffentlichen oder ihrem gesamten Unternehmen im Handumdrehen zugänglich machen können.

Zusätzlich können LabVIEW-Anwender die in der neuesten Version eingebettete Mess- und Steuerungsintelligenz nutzen und ihre Anwendungen viel schneller und mit weniger Aufwand entwickeln als bisher. Dabei beinhaltet das Konzept der Mess- und Steuerungsintelligenz die automatische Konfiguration der Mess- und Steuerungshardware, so dass die Produktivität der Anwender um ein Vielfaches gesteigert wird.

'LabVIEW 6i ist eine der umfassendsten Entwicklungsumgebungen, aber gleichzeitig leicht zu handhaben.', so Tim Butterfield, Senior Software Engineer bei Lucent Technologies. 'Mit Hilfe von LabVIEW 6i können wir die Entwicklungszeit von Prüfanwendungen erheblich reduzieren, da es nun viele Funktionen bietet, die wir bislang immer selbst programmieren mussten.'

Fortsetzung auf Seite A490

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CHIMIA-REPORT

CHIMIA 2000, 54, No. 7/8

EDITORIAL

Invitation to Attend the Fall Meeting of the New Swiss Chemical Society in Lausanne, Thursday, October 12, 2000

On behalf of the New Swiss Chemical Society (NSCS) and the Local Organizing Committee, it is our pleasure to invite you to attend the 2000 Fall Meeting of the NSCS. This is the second of the Fall Meetings in the new cycle involving a biennial rotation between the major linguistic regions of Switzerland. This year it is organized in Lausanne in the comfortable facilities of the Collège Propédeutique and the Ecole de Pharmacie of the University in Dorigny.

The Fall Meeting of the NSCS 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.

The scientific program starts with the opening ceremony and two lectures by the two Werner Prize laureates for 2000 as the only plenary session, followed by the parallel sessions in Analytical Chemistry, Medicinal Chemistry, Inorganic and Coordination Chemistry (minisymposium), Organic Chemistry (three parallel sessions), Physical Chemistry, and Computational Chemistry.

In addition to this program of oral presentations there will be poster sessions in all disciplines in the Main Hall of the Collège Propédeutique. In addition, the main authors of the posters in Organic Chemistry will describe their work in three-minute presentations.

The best oral communication and the best poster in each discipline will be rewarded with a prize.

In addition, this meeting is, by tradition, a nice occasion to meet friends and colleagues and to develop or strengthen social and scientific connections. Experience has shown that many fruitful collaborations between research groups have been initiated by discussions in front of a poster or after an oral communication at the Fall Meeting. We therefore look forward to well-attended and lively sessions and to welcome you in Lausanne and hope you will enjoy the 2000 Fall Meeting of the New Swiss Chemical Society.

PD. Dr. Roland Wenger
Chairman of the
Section Chemical Research of the NSCS

Professor André Merbach
Chairman of the
Local Organizing Committee

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SECTIONS	SECTIONS	SEKTIONEN
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CHEMICAL RESEARCH	RECHERCHE CHIMIQUE	CHEMISCHE FORSCHUNG
MEDICINAL CHEMISTRY	CHIMIE THERAPEUTIQUE	MEDIZINISCHE CHEMIE

Fall Meeting 2000
Assemblée d'automne 2000
Herbstversammlung 2000

Thursday, October 12, 2000
Jeudi, 12 octobre 2000
Donnerstag, 12. Oktober 2000

Lausanne

Université de Lausanne, Dorigny
Collège Propédeutique
Ecole de Pharmacie

Organizing Committee

André Merbach (Chairman) – University of Lausanne
Claude Daul – University of Fribourg
Jean-Luc Marendaz – University of Lausanne
John Robinson – University of Zürich
Jean-Luc Veuthey – University of Geneva

Jean-Claude Bünzli – University of Lausanne
Rudolf Giger – Novartis Pharma AG, Basel
Martin Quack – ETH Zürich
Daniel Stahl – EPF Lausanne
Roland Wenger – Wenger Chemtech, Riehen

Secretary: Fabienne Gottofrey, Secrétariat Section de Chimie, Université de Lausanne-BCH, CH–1015 Lausanne, Tel.: +41 21 692 38 52, Fax: +41 21 692 38 55, E-Mail: fabienne.gottofrey@icma.unil.ch

Informations

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

Les étudiants membres de la NSSC peuvent demander le remboursement des frais de voyage sur la base du billet de train Lausanne et retour, 2^e classe, ½ 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 NSSC– Madame *Lilly Etter*, c/o Ciba K-1354.3.06, CH–4002 Bâle.

Lunch: Des sandwiches, boissons et cafés seront offerts près des posters. Les restaurants universitaires sont à proximité.

Pauses café: Des pauses café seront organisées de 15.00 à 15.45 (*Ecole de Pharmacie, Hall*) et de 15.30 à 16.15 (*Collège Propédeutique, Main Hall*).

Informationen

Keine Anmeldung erforderlich, der Eintritt ist frei.

Studierende, die Mitglied der NSCG sind, erhalten folgende Reisekosten zurückerstattet: Bahnbillett nach Lausanne, 2. Kl. ½ 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 – wenn möglich unter Beilage eines Einzahlungsscheines beim Sekretariat der NSCG, Frau *Lilly Etter*, c/o Ciba K-1354.3.06, CH–4002 Basel, einzureichen.

Lunch: Sandwiches, Café u.s.w. werden in der Nähe der Posters zur Verfügung stehen. Es hat auch Verpflegungsmöglichkeiten in nahegelegenen Restaurants der UNIL.

Kaffeepausen: Kaffeepausen finden statt von 15.00 bis 15.45 (*Ecole de Pharmacie, Hall*) und von 15.30 bis 16.15 (*Collège Propédeutique, Main Hall*).

Transportation

By train: from Basel (BS), Bern (BE), Fribourg (FR) and Zürich (ZH); do not exit the train in Lausanne, but continue to Renens (next stop after Lausanne). From Geneva (GE), exit the train in Renens (one stop before Lausanne). From the Renens train station, take the tram (TSOL) to the University of Lausanne (tram stop: UNI/Sorge).

Unfortunately this option does not apply for people coming from Neuchâtel (NE). In this case, exit the train in Lausanne, then take the subway from Lausanne train station to Place du Flon and then the tram (TSOL) to UNI-Sorge.

Morning: Tram Stop Renens→UNI/Sorge (every 10 min)			**Evening**: Tram Stop UNI/Sorge→Station Renens		
Train from	Departure	Arrival Renens/Lausanne	Departure Renens/Lausanne	Arrival	Train to
BS	7.04	9.43	17.49	20.38	BS
BE	8.22	9.43	17.47	19.13	BE
FR	8.45	9.43	17.48	18.47	FR
GE	8.40	9.15	17.47	18.50	GE
NE	8.01	9.04	17.49	18.58	NE
ZH	7.03	9.43	17.47	20.26	ZH

By car: Follow the direction of Lausanne-Sud, take the exit UNIL-EPFL, then turn to the right at the sign EPFL/UNIL. Parking facilities will be available at the Collège Propédeutique.

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Programme of the Fall Meeting 2000
Programme de l'assemblée d'automne 2000
Programm der Herbstversammlung 2000

10.00–10.40 Opening Ceremony

Collège Propédeutique: Auditorium B
Presentation of the Werner Prize Laureates for 2000
Dr. H.L. Senti

Lectures of the Werner Prize Laureates 2000
Dr. ***Stefan Pitsch***
Laboratorium für Organische Chemie,
ETH Zentrum, Zürich
'Towards a Total Synthesis of Aminoacylated t-RNAs'
Abstract 1

Dr. ***Thomas Wirth***
Institut für Organische Chemie, Universität Basel, Basel
'New Chiral Electrophilic Reagents'
Abstract 2

10.50–16.50 Analytical Chemistry

10.50–11.05 General Assembly of Members:
Ecole de Pharmacie, Auditorium C

11.10–12.50 Lectures: *Ecole de Pharmacie, Auditorium C*
Abstracts 3–7

13.00–15.00 Poster Session: *Collège Propédeutique, Main Hall*
Abstracts 8–55

15.00–16.50 Lectures: *Ecole de Pharmacie, Auditorium C*
Abstracts 56–59

10.50–16.20 Medicinal Chemistry

10.50–11.00 General Assembly of Members:
Ecole de Pharmacie, Auditorium B

11.05–12.25 Lectures: *Ecole de Pharmacie, Auditorium B*
Abstracts 60–63

13.00–14.00 Poster Session: *Collège Propédeutique, Main Hall*
Abstracts 64–67

14.00–16.20 Lectures: *Ecole de Pharmacie, Auditorium B*
Abstracts 68–73

10.45–17.00 Chemical Research

10.45–10.55 General Assembly of Members:
Collège Propédeutique, Auditorium B

11.00–17.00 Inorganic and Coordination Chemistry

11.00–14.00 Poster Session: *Collège Propédeutique, Main Hall*
Abstracts 74–163

14.00–17.00 Minisymposium: Molecular Magnetism:
Collège Propédeutique, Auditorium D
Abstracts 164–166

11.00–16.40 Organic Chemistry

11.00–12.00 Short Presentation of the Posters:
Collège Propédeutique, Auditoriums A, B, C

12.00–14.00 Poster Session: *Collège Propédeutique, Main Hall*
Abstracts 167–224

14.00–16.40 Lectures: *Collège Propédeutique, Auditorium A*
Abstracts 225–232

14.00–16.20 Lectures: *Collège Propédeutique, Auditorium B*
Abstracts 233–239

14.00–16.40 Lectures: *Collège Propédeutique, Auditorium C*
Abstracts 240–247

11.10–16.40 Physical Chemistry

11.10–12.10 Lectures: *Ecole de Pharmacie, Auditorium A*
Abstracts 248–250

12.10–13.40 Poster Session: *Collège Propédeutique, Main Hall*
Abstracts 251–278

13.40–16.40 Lectures: *Ecole de Pharmacie, Auditorium A*
Abstracts 279–286

11.10–17.00 Computational Chemistry

11.10–13.20 Poster Session: *Collège Propédeutique, Main Hall*
Abstracts 287–299

13.20–17.00 Lectures: *Collège Propédeutique, CP 321*
Abstracts 300–310

17.05 Awards for the Best Oral and Poster Presentations

Collège Propédeutique, Main Hall

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 poster
Jury: *J.-C. Bünzli, C. Piguet, T. Ward*

Organic Chemistry:
3 posters and 3 oral presentations
Jury: *R. Haener, H. Heimgartner, E.P. Kündig, J. Lacour, P. Müller, J.A. Robinson, G. Tuchscherer, P. Vogel, H. Wennemers*

Physical Chemistry:
1 poster and 1 oral presentation
Jury: *S. Leutwyler, T. Rizzo, D. Stahl*

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

DETAILED PROGRAMME OF THE FALL MEETING 2000

Analytical Chemistry

10.50–11.05 General Assembly of Members:
Ecole de Pharmacie, Auditorium C

Lectures
11.10–12.50 *Ecole de Pharmacie, Auditorium C*
Abstracts 3–7
Chairpersons: *J.-L. Veuthey, R. Zenobi*

11.10–11.30 ***W. Bernhard,*** *P. Regenscheit, B. Aebi*
Institute of Forensic Medicine, University of Bern
'Ion Mobility Spectrometry (IMS) for Trace Detection of Drugs of Abuse in Forensic Chemistry and Forensic Toxicology'
Abstract 3

11.30–11.50 ***D. Günther,*** *I. Horn*
Laboratory of Inorganic Chemistry, ETH Zürich
'Laser Ablation-Inductively Coupled Plasma Mass Spectrometry – New Strategies for Trace and Ultra Trace Element Analysis in Solids'
Abstract 4

11.50–12.10 ***P. Salaün,*** *N. Parthasarathy, G. Lagger, M. Martin, J. Buffle*
Chimie Analytique et Biophysicochimie de l'Environnement, Université de Genève
'Speciation and Detection Capabilities of PLM Devices'
Abstract 5

12.10–12.30 ***S. Brombacher,*** *S. Kölliker, M. Oehme*
Organic Analytical Chemistry, University of Basel
'Ion Trap Multiple Mass Spectrometry Coupled to LC: A Powerful Method for Structure Elucidation and Quantitative Analysis of Carbonyls in Ambient Air'
Abstract 6

12.30–12.50 ***S. Friess,*** *R. Zenobi*
Laboratory of Organic Chemistry, ETH Zürich
'Protein Structure Information by Mass Spectrometry: STARS (Selective Titration of Arginine Residues by Sulfonates)'
Abstract 7

Poster Session
13.00–15.00 *Collège Propédeutique, Main Hall*
Abstracts 8–55
Chairpersons: *J.-L. Veuthey, R. Zenobi*

Lectures
15.00–16.50 *Ecole de Pharmacie, Auditorium C*
Abstracts 56–59
Chairpersons: *J.-L. Veuthey, R. Zenobi*

15.00–15.50 ***Prof. W. Lindner***
Institute of Analytical Chemistry, University of Vienna, Austria
'Reflections on Selectivity in Separation Sciences and in Analytical Chemistry'
Abstract 56

15.50–16.10 ***S. Rudaz,*** *E. Varesio, D. Ortelli, K.-H. Krause, J.-L. Veuthey*
Laboratory of Pharmaceutical Analytical Chemistry, University of Geneva
'Nano-LC and Capillary Electrophoresis Coupled to Electrospray Ionisation Mass Spectrometry for the Detection of Amyloid-ß Peptide Variants'
Abstract 57

16.10–16.30 ***M. Biedermann***
Kantonales Labor, Zürich
'Die Visualisierung des Verdampfungsprozesses in der heissen Verdampferkammer des klassischen Split und Splitlosen GC-Injektors'
Abstract 58

16.30–16.50 ***J. Ferrari,*** *C. Terreaux, J.-L. Wolfender, K. Hostettmann*
Institut de Pharmacognosie et Phytochimie, Université de Lausanne
'Stop-Flow Time Slice LC/NMR and LC/MS^n of *Gnidia Involucrata*: a Rational Approach for a Rapid Chemical Screening'
Abstract 59

Medicinal Chemistry

10.50–11.00 General Assembly of Members:
Ecole de Pharmacie, Auditorium B

Lectures
11.05–12.25 *Ecole de Pharmacie, Auditorium B*
Abstracts 60–63
Chairperson: *R. Giger*

11.05–11.25 ***W. Froestl,*** *B. Bettler, H. Bittiger, J. Heid, K. Kaupmann, S.J. Mickel, D. Strub*
Novartis Pharma AG, Research Department, Basel
'Ligands for the Isolation of $GABA_B$ Receptors'
Abstract 60

11.25–11.45 ***S. Röver,*** *G. Adam, A.M. Cesura, F.M. Dautzenberg, F. Jenck, S. Kolczewski, J. Wichmann*
Hoffmann-La Roche Ltd., Pharma Research, PRBC, Basel
'ORL1 Receptor Ligands: Structure-Activity Relationships of 8-Substituted 1-phenyl-1,3,8-triazaspiro[4.5]decan-4-ones'
Abstract 61

11.45–12.05 ***Y.P. Auberson***
Novartis Pharma AG, Basel
'AMP397A, a Novel Broad Spectrum Anticonvulsant with Potential Benefit for Therapy-resistant Epileptic Patients'
Abstract 62

12.05–12.25 ***R. Masciadri,*** *C. Apfel, D. Banner, D. Bur, M. Dietz, C. Hubschwerlen, H. Locher, M.G. Page, W. Pirson, J.-L. Specklin, T. Hirata*

Pharma Division, Preclinical Research, F. Hoffmann-La Roche Ltd., Basel
'Hydroxamic Acid Derivatives as Peptide Deformylase Inhibitors and Antibacterial Agents'
Abstract 63

Poster Session
13.00–14.00 *Collège Propédeutique, Main Hall*
Abstracts 64–67
Chairpersons: *R. Giger, W. Froestl*

Lectures
14.00–16.20 *Ecole de pharmacie, Auditorium B*
Abstracts 68–73
Chairperson: *W. Froestl*

14.00–14.20 ***K.-H. Altmann,*** *A. Flörsheimer, G. Caravatti, G. Bold, M. Wartmann*
Novartis Pharma AG, TA Oncology Research, Basel
'Chemistry and Biology of Epothilones – Fully Synthetic Analogs and Semi-Synthetic Derivatives'
Abstract 68

14.20–14.40 ***B. Büttelmann,*** *A. Alanine, M.-P. Heitz, E. Pinard, S. Röver, R. Wyler*
Pharma Division, Preclinical Research, F. Hoffmann-La Roche Ltd., Basel
'Tetrahydroisoquinolines as NMDA-NR2B Subtype Selective Antagonists'
Abstract 69

14.40–15.00 ***C. García-Escheverría,*** *P. Chène, M.J.J. Blommers, P. Furet*
Oncology Research and Core Technologies, Novartis Pharma AG, Basel
'Antagonists of the Association of hdm2 with the Tumor Suppressor p53 as New Antitumor Agents'
Abstract 70

15.00–15.20 ***F. Gasparini,*** *P. Flörsheim, A. Pagano, D. Ott, N. Stoehr, M. Heinrich, I. Vranesic, P.J. Flor, R. Kuhn*
Nervous System Research, Novartis Pharma AG, Basel
'Characterisation of the Non-Competitive Binding Site of the Group I Metabotropic Glutamate Receptors Using Subtype Selective Ligands'
Abstract 71

15.20–15.40 *Coffee Break*

Chairperson: *R. Giger*

15.40–16.00 ***A. Marzinzik,*** *R.A. Falchetto, S. Moss*
Novartis Pharma AG, Core Technology Area, Basel
'Application of the One-Bead-One-Compound Approach in Drug Discovery'
Abstract 72

16.00–16.20 ***O. Zerbe,*** *R. Bader, G. Folkers, A.G. Beck-Sickinger*
Institute of Biochemistry, University of Leipzig, D-4103 Leipzig; Institute of Pharmaceutical Sciences, Department of Applied Biosciences, ETH Zürich
'Describing Hormone-membrane Interactions by NMR'
Abstract 73

Chemical Research

10.45–10.55 General Assembly of Members:
Collège Propédeutique, Auditorium B

Inorganic and Coordination Chemistry

Poster Session
11.00–14.00 *Collège Propédeutique, Main Hall*
Chairpersons: *J.-C. Bünzli, C. Piguet, T. Ward*

A: Catalysis	Abstracts 74–92
B: Solid State	Abstracts 93–102
C: Bioinorganic	Abstracts 103–123
D: Fundamental Aspects	Abstracts 124–163

Minisymposium
14.00–17.00 **Molecular Magnetism (in honor of the late Olivier Kahn)**
Collège Propédeutique, Auditorium D
Chairperson: *J.-C. Bünzli*

14.00–14.15 *Prof.* ***Henri Kagan***
Université de Paris sud, Orsay, France
'The Distinguished Career of Olivier Kahn'

14.15–15.00 *Prof.* ***Dante Gatteschi***
Università di Firenze, Italia
'Physical Methods for the Investigation of Molecular Magnets'
Abstract 164

Chairperson: *C. Piguet*

15.00–15.45 *Prof.* ***Michel Verdaguer***
Université de Paris 6, France
'Molecular Magnetism, Achievements and Prospects: a Tribute to Olivier Kahn'
Abstract 165

15.45–16h15 *Coffee break*

16.15–17.00 *Prof.* ***Karl Wieghardt***
Max-Planck Institut für Strahlenchemie, Mülheim, Deutschland
'The Electronic Structure of Linear Thiophenolate-Bridged Heterotrinuclear Complexes: Localized *versus* Delocalized Models'
Abstract 166

Organic Chemistry

Posters: Short presentations
11.00–12.00 *Collège Propédeutique, Auditoriums A, B, C:*
The results described in each poster will be presented by the main author: 2 slides, 3 min max. for each presentation

Auditorium A: Chairperson: *J.A. Robinson*
D. Joester, B. Pfeiffer, E. Freund, Y. Berger, M. Wilming, A. Iffland, R. Damoiseaux, M. Oberhuber, K. Kloiber, W. Fieber, C. Schenkels, G. Klein, L. Gartenmann, E. Bernal-Méndez,

L. Signor, M.-O. Ebert, C. Bauer, H. Wennemers, A. Blaser, O. Lohse
Abstracts 167–186

Auditorium B: Chairperson: *H. Wennemers*
N. Zimmermann, G. Albano, F. Viton/M. Gardiner, L. Vial, H. Ratni, S. Pache, C. Benhaim, O. Corminboeuf, R. Chuard, B. Becattini, T. Wirth, P. Nury, P. Nury, C. Boléa, B. Sesto, N. Künzle, W.-R. Huck, A. Gsponer, A. Gisler, C. Beck
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I. Calderón, P. Waridel, G. Raoelison, E.F. Queiroz, A. Marston, C. Ollivier, T. Kovac, C. Helgen, V. Hebbe, A. Tomassini, G. Trevitt, P. Müller, K. Meilert, F. Monnat, E. Couché, R.A. Breiten-Moser, M. Blagoev, A. Gebert, T. Netscher
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Chairperson: *G. Tuchscherer*

14.00–14.20 ***J.-P. Bourgeois****, M. Fibbioli, P. Seiler, E. Pretsch, L. Echegoyen, F. Diederich*
Laboratorium für Organische Chemie, ETH Zürich
'Regioselective Synthesis of *trans*-1 Fullerene-C_{60} Bis-Adducts Directed by Crown Ether'
Abstract 225

14.20–14.40 ***A. Renard****, L. Jiang, J.A. Robinson*
Organisch-chemisches Institut, Universität Zürich
'Synthesis of a Library of Cyclic Hairpin Mimetic Peptides Conjugated to a Phospholipid as Potential Synthetic Vaccine Candidates Against *Plasmodium falciparum*'
Abstract 226

14.40–15.00 *D. Banfi, M. Mutter,* ***L. Patiny***
Institute of Organic Chemistry, University of Lausanne
'Evolutionary Principles for Generating Protein Mimetics: Directed Assembly of Peptide Loops on Topological Templates'
Abstract 227

15.00–15.20 ***A. Biland****, M. Nakazono, M. Spichty, B. Giese*
Department of Chemistry, University of Basel
'Parameters that Influence the Electron Transfer in DNA'
Abstract 228

15.20–15.40 ***R. Bertolini****, R. Tona, J. Hunziker*
Department of Chemistry and Biochemistry, University of Bern
'Sugar-Modified Oligodeoxynucleotides: Synthesis and Pairing Properties'
Abstract 229

15.40–16.00 *N-Q. Nguyen-Trung,* ***P. Strazewski***
Institute of Organic Chemistry, University of Basel
'Puromycin Analogs: Synthesis, Bioactivity and Conformation'
Abstract 230

16.00–16.20 ***D. Ackermann****, S. Pitsch*
Laboratorium für Organische Chemie, ETH Zürich
'Synthesis and Pairing Properties of p-RNA Analogues'
Abstract 231

16.20–16.40 ***N. Bensel****, J.-L. Reymond*
Department of Chemistry and Biochemistry, University of Bern
'New Efficient Catalytic Antibodies for the Hydrolysis of Pivalate Prodrugs'
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14.00–14.20 ***C. Adlhart****, C. Hinderling, P. Chen*
Laboratorium für Organische Chemie, ETH Zürich
'Mechanistic Studies of Olefin Metathesis by Ruthenium Carbene Complexes using ESI-MS'
Abstract 233

14.20–14.40 ***M. von Arx****, T. Mallat, A. Baiker*
Laboratorium für Technische Chemie, ETH Zürich
'Heterogeneous Enantioselective Hydrogenation of Trifluoromethyl Ketones'
Abstract 234

14.40–15.00 *P. Barthazy, A. Togni,* ***A. Mezzetti***
Laboratorium für Anorganische Chemie, ETH Zürich
'Ruthenium(II)-Mediated C–F Bond Formation. Catalytic Nucleophilic Fluorination of Activated Aliphatic Bromides'
Abstract 235

15.00–15.20 *R. Cannas, K.P. Kaliappan, E. Peter Kündig,* ***A.R. Pape****, S. Tchertchian*
Département de Chimie Organique, Université de Genève
'Enantioselective and Diastereoselective Dearomatisation of Arene Chromium Tricarbonyl Complexes and Synthetic Applications'
Abstract 236

15.20–15.40 ***B. Acar****, T. Damiano, F. Glarner, V.M.F. Cardona, U. Burger*
Département de Chimie Organique, Université de Genève
'The Photochemical Contraction of Pyridinium Salts. A New Approach towards Aminocyclopentitols'
Abstract 237

15.40–16.00 *L. Andrau,* ***L. Feray****, N. Kuznetsov, P. Renaud*
Institut de Chimie Organique, Université de Fribourg
'Diastereoselective 1,5-Hydrogen Transfer as a New Tool in Asymmetric Synthesis'
Abstract 238

16.00–16.20 ***V. Narkevitch**, P. Vogel*
Institut de Chimie Organique, Université de Lausanne
'A New Asymmetric Carbon–Carbon Bond Forming Reaction: Four-Component Stereoselective Synthesis of Methyl Sulfones'
Abstract 239

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14.00–16.40 *Collège Propédeutique, Auditorium C*
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Chairperson: *R. Haener*

14.00–14.20 ***C. Allemann**, T.A. Jenny*
Institut de Chimie Organique, Université de Fribourg
'A Novel Chiral Fp Analogue used as Cyclization Catalyst'
Abstract 240

14.20–14.40 ***R. Hilgraf**, M. Schönleber, A. Pfaltz*
Department of Chemistry, University of Basel
'Chiral TADDOL-Phosphite- and Bis(*N*-Tosylamido)-phosphine-oxazolines as Ligands in Asymmetric Catalysis'
Abstract 241

14.40–15.00 ***D. Renneberg**, H. Pfander, C. Leumann*
Department of Chemistry and Biochemistry, University of Bern
'Total Synthesis of Coraxeniolide-A'
Abstract 242

15.00–15.20 ***S. Gerber Lemaire-Audoire**, S. Ainge, C. Glanzmann, P. Vogel*
Institut de Chimie Organique, Université de Lausanne
'Toward the Total Synthesis of Sporeamicin A and Analogues'
Abstract 243

15.20–15.40 ***N. Soldermann**, R. Neier*
Institut de Chimie, Université de Neuchâtel
'Application of the Novel Tandem-Process Diels-Alder Reaction/Ireland-Claisen Rearrangement to the Synthesis of (+)-Juvabione and (+)-Epijuvabione'
Abstract 244

15.40–16.00 ***A. Rieder**, C.S. Sheehan, B. Kräutler*
Institute of Organic Chemistry, University of Innsbruck, Austria
'Loading a Porphyrin with Fullerenes'
Abstract 245

16.00–16.20 ***M. Bänziger**, J. Cercus, W. Stampfer, U. Sunay*
Novartis Pharma, Basel
'New Synthesis to 'Obeline' Intermediates for NS Active Compounds'
Abstract 246

16.20–16.40 ***M.-E. Schwenter**, P. Vogel*
Institut de Chimie Organique, Université de Lausanne
'A New, Non-iterative Asymmetric Synthesis of Long-Chain 1,3 Polyols'
Abstract 247

Physical Chemistry

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Chairperson: *D. Stahl*

11.10–11.30 ***T. Bally**, B. Müller, F. Williams, R. Pappas*
Institut de Chimie Physique, Université de Fribourg; Department of Chemistry, University of Tennesse, Knoxville, USA
'The Surprising Fate of [1.1.1] Propellane on Ionization'
Abstract 248

11.30–11.50 ***S. Choua**, H. Sidorenkova, T. Berclaz, M. Geoffroy, P. Le Floch*
Laboratoire Hétéroéléments et Coordination, UMR CNRS 7653, Ecole Polytechnique Palaiseau, France; Département de chimie physique, Université de Genève
'Etude par RPE/ENDOR du radical anion de la biphosphinine et du complexe de Nickel(0) associé'
Abstract 249

11.50–12.10 ***D.C. Lührs**, I. Fischer*
Laboratorium für Organische Chemie, ETH-Zentrum, Zürich
'Excited-state Proton Transfer in 1-Naphthol / Ammonia Clusters: Wavelength-dependence of the Pump-probe Spectra'
Abstract 250

Poster Session
12.10–13.40 *Collège Propédeutique, Main Hall*
Abstracts 251–278
Chairpersons: *S. Leutwyler, T. Rizzo, D. Stahl*

Lectures
13.40–16.40 *Ecole de Pharmacie, Auditorium A*
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Chairperson: *S. Leutwyler*

13.40–14.00 ***D. Ferri**, T. Bürgi, A. Baiker*
Laboratorium für Technische Chemie, ETH-Zentrum, Zürich
'*In situ* ATR-IR Spectroscopy Study of CO Adsorption on Pt and Pt/Al_2O_3 Thin Films at the Solid-liquid Interface'
Abstract 279

14.00–14.20 ***M.S. Schneider**, R. Wandeler, N. Künzle, T. Mallat, A. Baiker*
Laboratorium für Technische Chemie, ETH-Zentrum, Zürich
'Phase Behavior of Supercritical Fluid Mixtures: Application in Heterogenous Catalysis'
Abstract 280

14.20–14.40 ***S. Glaus**, G. Calzaferri*
Department of Chemistry and Biochemistry, University of Bern
'Quantum Chemical Investigations of Metal/Semiconductor Contacts'
Abstract 281

14.40–15.00 ***F. Rota***, *R. Prins*
Laboratory of Technical Chemistry, ETH-Zürich
'Stereochemistry in the Hydrodenitrogenation of *o*-Toluidine and Methylcyclohexylamine over Sulfided $NiMo/\gamma\text{-}Al_2O_3$'
Abstract 282

15.00–15.20 *Coffee break*

Chairperson: *T. Rizzo*

15.20–15.40 ***C. Martinez***, *A. Neuner, A.M. Braun, E. Oliveros*
Lehrstuhl für Umweltmesstechnik, Engler-Bunte-Institut, Universität Karlsruhe, Deutschland
'Polarity Effects on the Quantum Yield of Singlet Oxygen ($O_2(^1\Delta_g)$) Production by Fluorenone'
Abstract 283

15.40–16.00 ***D. Stadler***, *M.J. Rossi*
Laboratoire de Pollution de l'Air et du Sol, Département Génie Rural, EPF Lausanne
'HONO Formation by Heterogeneous Interactions of NO_2 and Soot Particles'
Abstract 284

16.00–16.20 ***D. Rueda***, *O.V. Boyarkin, T.R. Rizzo, A.Chirokolava, D.S. Perry*
Institut de Chimie Physique Moléculaire, EPF-Lausanne; Department of Chemistry, University of Akron, Ohio, USA
'Infrared Spectroscopy of Vibrationally Excited Methanol and Some of its Isotopomers'
Abstract 285

16.20–16.40 ***C. Zwahlen***, *D. Früh, J.R. Tolman, S.J.F. Vincent, G. Bodenhausen*
Section de Chimie, Université de Lausanne; Nestlé Research Center, Vers-chez-les-Blanc, Lausanne
'Protein Motions Studied by NMR'
Abstract 286

Computational Chemistry

Poster Session
11.10–13.20 *Collège Propédeutique, Main Hall*
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Chairpersons: *C. Daul, J. Weber*

Lectures
13.20–17.00 *Collège propédeutique, Salle CP 321*
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Chairperson: *C. Daul*

13.20–13.40 ***M. Bruschi***, *H.P. Lüthi*
Laboratory of Physical Chemistry, Zürich
'Molecular and Electronic Properties of Polytriacetylene Oligomers'
Abstract 300

13.40–14.00 ***J. Vande Vondele***, *A. Laio, U. Röthlisberger*
Laboratory of Inorganic Chemistry, ETH Zentrum, Zürich
'The Structure of Cu^{2+} Binding Sites in the C-terminal Domain of the Murine Prion Protein: A Mixed *ab initio* – Classical Molecular Dynamics Study'
Abstract 301

14.00–14.20 ***G. Wipff***
Laboratoire MSM, Institut de Chimie, Université de Strasbourg, France
'Importance of Interfacial Phenomena in Liquid-Liquid Extractions: Molecular Dynamics Investigations'
Abstract 302

14.20–14.40 ***T.A. Wesolowski***, *A. Goursot, J. Weber*
Département de Chimie Physique, Université de Genève
'Theoretical Studies of CO in ZSM5 Zeolite. Applications of a DFT Method Based on Electron Density Partitioning'
Abstract 303

14.40–15.00 ***J.-F. Fuchs***, *J. Mareda*
Department of Organic Chemistry, University of Geneva
'Computational Study of Solvolysis Reactions of Strained Bridgehead Substrates'
Abstract 304

15.00–15.20 ***F.P. Rotzinger***
Institut de chimie physique, EPF, Lausanne
'Electron Self-Exchange of the Hexaaqua Cobalt(II)/(III) Couple'
Abstract 305

15.20–15.40 ***T. Heine***, *A. Goursot, J. Weber*
Département de chimie-physique, Université de Genève
'Calculating ^{29}Si NMR Chemical Shifts – from Silanes to Zeolites'
Abstract 306

15.40–16.00 ***S. Portmann***, *A. Inauen, S. Leutwyler, H.P. Lüthi*
Laboratory of Physical Chemistry, Zürich; Departement für Chemie und Biochemie, Universität Bern
'Chiral Discrimination in Hydrogen-bonded Complexes'
Abstract 307

16.00–16.20 ***S. Rey***, *M. Rabii, G. Caron, G. Ermondi, P. Gaillard, A. Pagiara, P.-A. Carrupt, B. Testa*
Institut de Chimie Thérapeutique, Université de Lausanne
'Development and Applications of Molecular Hydrogen Bonding Potentials (MHBPs)'
Abstract 308

16.20–16.40 ***A. Laio***, *J. Vande Vondele, U. Röthlisberger*
Laboratory of Inorganic Chemistry, ETH Zentrum, Zürich
'Towards a Consistent Electrostatic Coupling Scheme for Mixed Quantum-Classical Calculations'
Abstract 309

16.40–17.00 ***C. Lehmann***
Institute of Organic Chemistry, University of Lausanne
'Molecular Modelling: Indispensable Tool at the Interface between Structural Analysis and Molecular Design'
Abstract 310

Organic Chemistry **1**

Towards a Total Synthesis of Aminoacylated t-RNAs

Stefan Pitsch

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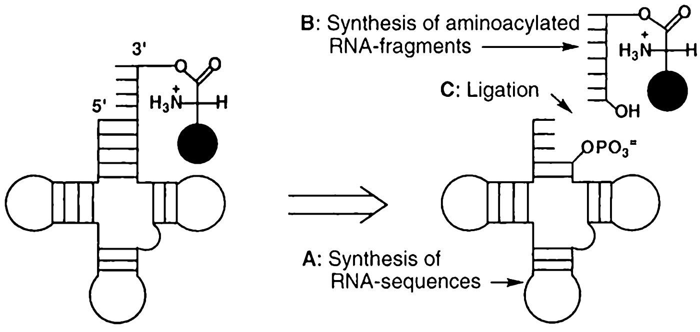
In the ribosomal biosynthesis of proteins, the aminoacylated t-RNAs serve as carriers of the amino acids. A total synthesis of these biological key-compounds would allow the site-specific incorporation of modifications within the t-RNA and attachment of any desired amino acid. Such analogues are useful tools for structural and functional studies, and for the incorporation of unnatural amino acids into proteins.



Our retrosynthetic scheme for the preparation of aminoacylated t-RNAs is shown above. It includes the synthesis of truncated t-RNAs (**A**), the synthesis of aminoacylated RNA-fragments (**B**), and their subsequent ligation (**C**). Our approaches toward the realization of these three tasks will be presented.

Organic Chemistry **2**

New Chiral Electrophilic Reagents

Thomas Wirth [+]

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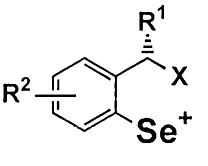
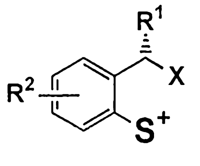
The stereoselective functionalization of non-activated double bonds is still an attractive goal. For this purpose various chiral electrophilic reagents have been developed.

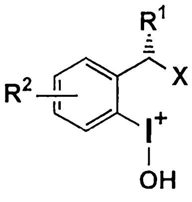
Selenium, sulfur and iodine based chiral electrophiles of type **1** – **3** have been synthesized. We are reporting very efficient reactions with these reagents and their application in total synthesis. First developments towards polymer-bound reagents will be discussed as well.



1



2



3

X= OR, NR_2

U. H. Hirt, B. Spingler, T. Wirth, *J. Org. Chem.* **1998**, *63*, 7674 – 7679.
T. Wirth, *Angew. Chem.*, in press.

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Analytical Chemistry **3**

Ion Mobility Spectrometry (IMS) for Trace-Detection of Drugs of Abuse in Forensic Chemistry and Forensic Toxicology

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Bern Switzerland

A short review of the analysis principle of IMS will be presented. Trace amounts of drugs (Heroin, Cocaine, Amphetamines, LSD, Hashish, and others) are adsorbed on dust particles on clothes, in cars, mobile phones and other items of evidence. Of special interest is also the screening for drug traces on hands, nose smear of death or living persons. The samples are collected on a membrane filter and directly introduced into the ion mobility spectrometer. Drug traces are detected by IMS in approx. 4 seconds. Positive results are confirmed by GC-MS, instrumental TLC or HPLC-DAD.

For the special testing of street drugs the screening is done in our laboratory by IMS. Applications of the method at the crime scene and in forensic toxicology (nose smear, finger nail dirt) will be discussed.

Key Words: Ion Mobility Spectrometry, IMS, Mass Spectrometry, street drugs, trace analysis,

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Analytical Chemistry **4**

Laser Ablation-Inductively Coupled Plasma Mass Spectrometry – New Strategies for Trace and Ultra Trace Element Analysis in Solids

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Laser Ablation-ICP-MS has become a powerful analytical technique for the determination of major, minor and trace elements, which has successfully been demonstrated on a wide variety of solid materials [1]. The combination of a 193 nm ArF excimer laser and a newly designed 266 nm laser ablation system with a homogenized optical set up, using lens arrays, a condensor lens and an aperture (imaging optic) allows the controlled ablation with a crater diameter between 4 and 120 μm. These ablation systems achieve a constant fluency (adjustable between 2 and 40 J/cm^2 using an attenuator) on the sample surface for the different spot sizes, which is sufficient for a controlled ablation of highly and opaque samples. Sensitivity and reproducibility for the determination of trace elements in solid samples mainly depend on the mass ablated per shot (i.e crater diameter), and the mass fraction that is transported into the ICP-MS. Using Helium as the carrier gas improved aerosol formation and transport efficiency of the technique by a factor of 5. Especially for short transient concentration-variable signal acquisition (e.g. inclusion analysis) a reduction of the cell volume leads to less dispersion of the signal and improves the signal to background ratio drastically. The quantification of trace elements carried out using external non-matrix matched calibration standards leads to good agreement to results obtained by other techniques. Homogeneous samples allow an RSD better 5 % for elements above 1 μg/g.

[1] D. Günther, S. E. Jackson, H. P. Longerich, Laser ablation and arc spark solid sample introduction into inductively coupled plasma mass spectrometers. Spectrochim. Acta. Rev. 54B (1999) 381 – 409.

Analytical chemistry **5**

SPECIATION AND DETECTION CAPABILITIES OF PLM DEVICES

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The permeation liquid membrane (PLM) is very well suited for both speciation and preconcentration of trace metal ions in natural waters. It is a simple, selective and non-perturbing technique. PLM is based on uphill transport of metal ions by means of neutral carrier-aided transport through a hydrophobic membrane impregnated with an organic solvent. The flux is diffusion limited from a source solution to a so-called "strip" solution which contains a strong complexant. Speciation is achieved by setting up the permeability criterion π which depends on physical parameters such as carrier concentration or diffusion layer thickness. Depending on the conditions, either free metal ions or labile hydrophilic complexes or even lipophilic complexes can be determined.

Another major advantage for metal analysis is the PLM capability of performing large preconcentrations when using very small volume of strip solution compared to the source solution one. PLM devices have been built with or without coupling sensitive detectors. One of these, a voltammetric microfabricated thin film mercury coated iridium microelectrode array which is placed in the strip solution, will be presented. The microelectrodes are protected with an agarose gel containing C-18 modified particles in order to prevent adsorption of organic solvent leached from the PLM onto the electrode surface. The strip volume is 0.75 µl and the distance between PLM and the microelectrode is ca. few microns which allows to get fast response time. Measurement of the initial flux from PLM is proportional to the metal species concentration of interest and hence time of measurement can be shortened.

Analytical Chemistry **7**

Protein Structure Information by Mass Spectrometry: STARS (Selective Titration of Arginine Residues by Sulfonates)

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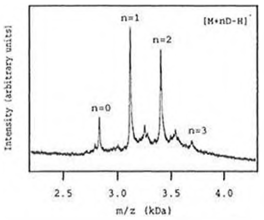
Noncovalently bound complexes between basic sites of peptides/proteins and sulfonates have been studied using Matrix Assisted Laser Desorption Ionization (MALDI) Mass Spectrometry. Reactive sulfonate dyes such as Cibacron Blue F3G-A are known to bind to protonated amines on the exterior of a protein [1]. In this work, we examined a wide range of other sulfonates with distinctly simpler structure and more predictable reactivity. Naphtalene-1,5-disulfonic acid (NDA) was shown to bind to Arginine only, as opposed to expected binding to all basic sites. We developed detailed control experiments to exclusively confirm this selectivity to Arginine.

The MALDI spectra show that the number of complex adducts found reflects only the accessible Arginine sites on the surface of folded peptides and proteins, also including the N-terminus. Residues with sterically hindered access do not show any complexation.
MALDI-MS can therefore provide useful and fast information about the structure of the examined biomolecules.
STARS might be an interesting application for screening of recombinant proteins or biogenetics such as structural screening of prions.



Negative ion mode MALDI mass spectrum of Melittin (M) and NDA (D). The number of adducts corresponds to the number of accessible Arginine sites plus the N-terminus.

[1] B. Salih, R. Zenobi, *Anal. Chem.* **1998**, 7, 1536.

Analytical Chemistry **6**

Ion trap multiple mass spectrometry coupled to LC: A Powerful Method for Structure Elucidation and Quantitative Analysis of Carbonyls in Ambient Air

Stephan Brombacher, Stephan Kölliker and Michael Oehme

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Much attention has been paid to carbonyl compounds in air pollution studies because of their formation by photochemical degradation of hydrocarbons. Their influence on the formation of radicals and ozone is well known. Sampling by solid phase adsorbent with simultaneous conversion into 2,4-dinitrophenylhydrazone derivatives (DNPH) has become a standard procedure widely applied in air monitoring programmes.

Ion trap multiple mass spectrometry combined with atmospheric pressure chemical ionization in the negative ion mode was most suitable for these carbonyl derivatives. A structure elucidation scheme for these compounds of was established [1]. Compound quantities around 50 pg were sufficient for detection in mass chromatograms generated from full scan records. Amounts of around 1 ng allowed to elucidate structures completely or partially. Some examples will be given concerning the identification of compounds in ambient air samples.

Furthermore, this technique is well suitable for quantification. 23 important carbonyl-DNPH derivatives were quantified within one chromatographic run of 40 min employing an internal standard method. The limit of quantification (LOQ) varied between 0.1 to 3 ng. This corresponds to carbonyl concentrations of 0.1 to 0.8 µg/m^3, respectively, in ambient air. These values are comparable to other quantification methods for such as HPLC-UV detection. Quantitative results for eight ambient air samples will be presented and compared with results obtained by HPLC/UV analysis.

[1] S. Kölliker and M. Oehme, Anal. Chem. 70, 1979-1985 (1998).

Analytical chemistry **8**

Selection of basic test compounds for the characterization of RP-HPLC stationary phases

UNIVERSITÉ DE GENÈVE

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[1]Laboratory of Pharmaceutical Analytical Chemistry-University of Geneva, 1211 Geneva 4
[1]Laboratory of Pharmaceutical Organic Chemistry-University of Geneva, 1211 Geneva 4

Basic 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. Reversed phase high performance liquid chromatography (RP-HPLC) is currently the method of choice for the analysis of these compounds. However, secondary interactions between the analyte and residual silanols with traditional silica packings produce peak tailing which affect resolution, sensitivity and reproducibility. In order to overcome this kind of problem, new stationary phases have been developed.

In order to characterize and evaluate properties of these packings several tests are proposed in the literature, which can be divided in two main categories: general tests and particular tests (i.d. tests for basic compounds). 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 14 basic test compounds was selected, combining compounds proposed by McCalley [1] with other basic compounds selected in our laboratory. From a data set of chromatographic parameters (k', As, N) on different LC columns (Supelcosil ABZ Plus, Discovery RP Amide, etc.), Principal Component Analysis (PCA) was applied to ensure that selected molecules present pertinent properties to characterize a stationary phase.

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

Analytical Chemistry **9**

Analysis of oligomeric and polymeric tannins of grape berries by LC/ESI-MS/MS^n

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

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

Tannins are highly polar, water soluble and thermally labile compounds witch are difficult to ionize. Therefore, mass spectrometry becomes very helpful for the structural elucidation of such compounds. A sensitive method based on liquid chromatography coupled with mass spectrometry has been developed in our laboratories for the identification of tannins composition in grape berries (var. Gamaret). The potential of an IT/MS (ion trap), equipped with ES (electrospray) interface, permit us to develop multiple stage fragmentation (MS^n) providing more structural information. This technique has been applied on a mixture of proanthocyanidin and proanthocyanidin gallates oligomers (B-type) generating identical ion sequences for each parent ion. Sensitive detection is obtained in the negative ion mode by post-column addition of alkaline buffer, generating intense deprotonated molecular ion.

Crude extract of tannins has been fractionated on Toyopearl HW-40s. MS experiments have been directly performed after HPLC separations by the use of the sequential scan event of the IT instrument.

Analytical chemistry **10**

Use of borate complexation for the analysis of non UV-absorbing natural compounds by capillary electrophoresis

K. Bekkouche[1], Y. Daali[2], S. Cherkaoui[2], P. Christen[2] and J-L. Veuthey[2]
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In the last ten years, a number of nitrogen-containing polyhydroxylated heterocyclic compounds has been isolated from plants. These natural products have been found to be competitive inhibitors of various glycosidases, presumably because the structure similarity with carbohydrates. The more potent of them are used for the treatment of diseases including diabetes, cancer, and viral infections[1]. Among these compounds, a new class of nortropane polyhydroxylated alkaloids, called calystegines, has been recently isolated from different species belonging to the Solanaceae, Convulvulaceae and Moraceae [2] and has shown promising therapeutic properties.

As calystegines present similar structures and do not possess any chromophore, their analysis by capillary electrophoresis (CE) coupled to UV detection was carried out using complexation between borate ions and calystegine hydroxy groups. The effects of borate buffer pH and concentration as well as temperature were investigated to optimize the electrophoretic conditions. Successful results were obtained with a conventional fused silica capillary, 80 mM borate buffer (pH 9) at 50 °C and UV detection at 191 nm. Finally, the described method was applied to the qualitative analysis of calystegines in plant extracts.

[1] G.S. Jacob, Current Biology, 5 (1995) 605-611.
[2] R.J. Molyneux, R.J. Nash, N. Asano, in Alkaloids : Chemical and biological perspectives (1996) vol 11, William Pelletier, Pergamon Press (Chapter 4) p 303.

Analytische Chemie **11**

Application of Graphite-Assisted Laser Desorption/Ionization Mass Spectrometry to Art Conservation

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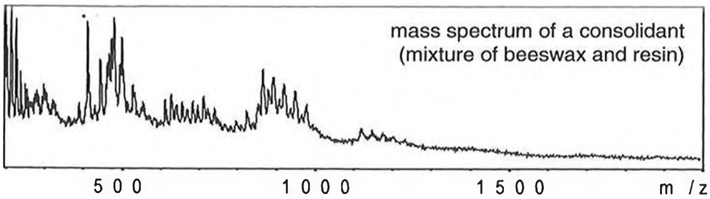
In technical art history studies as well as in art conservation, often only a small sample may be taken for chemical analysis. At the same time, the material to be studied is generally a complex mixture, which also has been altered by ageing. Graphite-assisted laser desorption/ionization mass spectrometry (LDI-MS) has proved to be an advantageous tool for the study of such small complex samples, particularly terpenoid resins. It provides a detailed picture of the range of substances present and requires only a relatively small sample.

In addition to resins, the method has recently been extended to various organic binding media, and was used to investigate samples from art objects. Compared to infrared spectroscopy (FT-IR), graphite assisted LDI-MS was much more effective in differentiating between media of various types.

It has been possible so far to characterize consolidants (mixtures of beeswax and resins) and picture varnishes (mixtures of drying oil and resins or synthetic varnishes). The materials were identified either by the molecular masses of characteristic substances or by specific distributions of molecular masses.



Analytical Chemistry **12**

Can Binding Constants of Noncavalent Complexes be Determined by Soft Ionization Mass Spectrometry?

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Matrix-assisted laser desorption/ionization (MALDI) and electrospray ionization (ESI) are widely used soft ionization methods in mass spectrometry. Not only high molecular weight compounds, but also noncovalent complexes have become accessible for mass spectrometric analysis. A recurring question is whether the strength of a noncovalent interaction can be measured by ESI-MS or MALDI-MS [1]. While ESI generates ions directly from solution, the relation of typical MALDI data to the solution chemistry is less obvious. To overcome this problem, we employed two-phase MALDI, a method where the analyte is dissolved in liquid glycerol and dispersed onto solid graphite particulates.

We are developing methods to determine association constants masss spectrometrically. We considered collision-induced dissociation (CID) of complex ions in the mass spectrometer, direct determination of the association constant via measurement of the solution-to-gas phase transfer coefficients, mass spectrometric analoga of a melting curve, and titration type experiments. A promising method for metal ion – crown ether complexes employed competition of several metals for the same ligand, followed by iterative fitting of relative ESI ion signals for a range of relative metal ion/ligand concentrations [2]. Advantages and disadvantages of the different methods will be discussed, and quantitative/semiquantitative data on the binding strength of selected noncovalent complexes will be shown.

[1] F. Dubois, R. Knochenmuss, R. Zenobi, *Eur. Mass Spectrom.* **1999**, 5, 267.
[2] D. Giraud, O. Laprévote, B.C. Das, *Org. Mass Spectrom.* **1994**, 29, 169.

Analytical chemistry **13**

Turbulent flow capillary LC/MS for fast analysis of methadone in serum

UNIVERSITÉ DE GENÈVE

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Laboratory of Pharmaceutical Analytical Chemistry, University of Geneva

Over the last ten years capillary LC is increasingly used for applications were sensitivity is important and the amount of sample is limited. The main advantage of using smaller I.D. columns is the increase in sensitivity, and especially its compatibility with electrospray-MS detection.

Although the most successful application of capillary LC is in proteomics field, there is a growing interest for capillary LC in bioanalysis.
The pressure to carry out e.g. pharmacokinetic studies with smaller test animals (i.e. lower sample amounts), is a driving force to look for more sensitive analysis methods. Another need of today's bioanalysis is high throughput. Analysis methods that eliminate the time consuming sample preparation steps are therefore of increasing importance.

In this poster the use of high flow rates in capillary LC for the direct analysis of serum samples under turbulent flow conditions using MS detection is presented.
Beside a substantial reduction in the solvent consumption compared to its conventional counterpart (i.e. from 4 ml/min down to 150 µl/min for the 1.0 mm and 180 µm I.D. columns, respectively), a substantial increase in detection sensitivity is inherent with high flow rate capillary LC.
This allows for the determination of ppb-level concentrations of methadone and its primary metabolite in crude serum and an unrivalled sample throughput.

Analytische Chemie **14**

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

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Since the 1960s less toxic and less persistent insecticides have been developed. N-methylcarbamates, such as carbaryl and methomyl, constitute a class of insecticides which combat pests in an great variety of crops. Today they are widely used in agriculture. As a consequence their residues are frequently encountered in fruit and vegetables. Swiss legislation regulates the use of these insecticides and defines maximum residue limits in food.
Numerous publications about residue analysis of carbamates in food have been issued in the last years. The lack of a chromophore in the molecule and the thermolability of several carbamates are the reasons why the research focused on the determination with HPLC and fluorescence detection after post-column derivatisation of the carbamates.
The aim of the present work was to develop a robust method with LC/MS after a single extraction with ethyl acetate, which is commonly used in our laboratory for pesticide analyses [3]. The determination of 10 carbamate insecticides and several metabolites in vegetables and fruit were performed with a high pressure liquid chromatograph coupled with an ion trap mass spectrometer. The analytes were separated on a 2 mm Prodigy 3μ C18 column and ionized with the atmospheric pressure chemical ionisation technique (positive mode, m/z 50-450). The working range was between 0.02 to 10 mg/kg (resp. 50 pg to 10 ng per μl of injected sample extract) depending on the analyte.
Recoveries in vegetables (aubergine, zucchetti, winter salads) and fruit (pineapple, apple, kiwi, kaki) ranged from 63 to 133 % with a mean value of 94 - 123 % recovery depending on the matrix and the analyte.

[1] Ch. Wäfler, V. Glatt und W. Meier, Mitt. Gebiete Lebensm. Hyg. **72**, 22-30 (1981).

Analytical Chemistry **15**

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

Jürg M. Daniel, Günther Nicolussi, Renato Zenobi

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Electrospray is a very soft ionization method that allows to generate intact protein ions from solution [1]. Under certain conditions it is even possible to detect protein ions in their native conformation [2].

Interactions between selected protein-inhibiting ligands and their protein targets have been studied with electrospray time-of-flight mass spectrometry (ESI-TOF-MS). The formation of such complexes is shown by the shift in mass of the protein-ligand complex relative to the mass of the bare protein. In order to verify the performance of the technique both a protein inhibitor known to bind covalently as well as a non-covalently binding inhibitor were employed in the experiments. Complexes of thrombin with PPACK (H-D-Phe-Pro-Arg-$CH_2Cl.2HCl$) and apo-myoglobin with haem were utilized to study interactions of covalent and non-covalent origin, respectively.

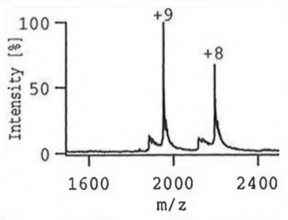

Figure 1: Mass spectra of native Myoglobin with a non-covalently bound haem group.

[1] R. D. Smith, J. A. Loo, C. G. Edmonds, C. J. Barinaga, H. R. Udseth, *Anal. Chem.* **1990**, *62*, 882.
[2] K. J. Light-Wahl, B. E. Winger, R. D. Smith, *J. Am. Chem. Soc.* **1993**, *15*, 5869.

Analytical Chemistry **16**

Dutch Elm Disease: Isolation and Identification of Secondary Metabolites Investigation of some infected wood by LC-ESI-MS^n

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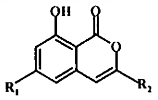
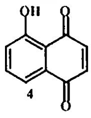
Cerato-ulmin [1], which is a wilting toxin of *Ceratocystis ulmi* (= *Ophiostoma ulmi*) is responsible for the Dutch elm disease. The main vector of this disease is two bark beetles species [2] named as *Scolytus scolytus* and *Hylurgopinus rufipes*.

The chemical compositions of the culture medium of an anamorph *Pesotum ulmi* have been investigated. We isolated and identified ten compounds from the phytotoxic fractions obtained from the ethyl acetate extract. Bioassays carried on Dutch elm leaves showed that compounds **4**, **5**, and **6** were the most toxic metabolites.



1 R_1=OH R_2=CH_2OH
2 R_1=OMe R_2=CH_2OH
3 R_1=OH R_2=$CH_2CHOHCH_3$



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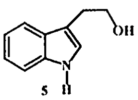

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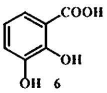

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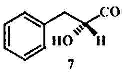

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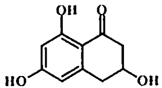

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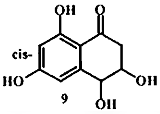

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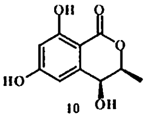

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We also searched for these toxic metabolites in some healthy and infected woods using LC-ESI-MS^n, in order to determine if these compounds could be involved in the disease.

[1] B. Temple, P.A. Horgen, *Mycologia* **2000**, 92(1), 1-9.
[2] R.N. Coulson, *Ann. Rev. Entomol.* **1979**, 24, 417-447.

Analytical Chemistry

17

On-line differentiation of isomeric flavonoid C-glycosides by various CID MS/MS techniques

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LC-MS is a powerful tool for the dereplication of known natural products in crude plant extracts and for the localisation of potentially new molecules. However LC-MS alone generates mainly molecular ions and more detailed structural information must be obtained by complementary MS-MS experiments [1]. Flavonoid C-glycosides are widespread in the plant kingdom; these molecules occur in different isomeric forms which are difficult to distinguish. In this study, the potential of LC-MS-MS and LC-MS^n with atmospheric pressure ionisation techniques (API) for the identification of flavonoid C-glycoside isomers is discussed. Single stage MS-MS on a triple quadrupole (TSQ) is compared to multiple stage MS^n experiments on an ion-trap (LCQ). Analysis of orientin, isorientin, vitexin and isovitexin proves that discrimination between 8-C- and 6-C-glycoside isomers is possible for both analytical systems. However the fragment ions involved for the discrimination of the pairs of isomers may differ in both types of MS-MS collision cells. These differences and their influence on the fragmentation pattern are discussed as a function of the collision energy used in the different mass analysers. LC-MS-MS is very useful for the unambiguous dereplication of flavonoid C-glycosides and it has been successfully applied to the screening of various plant extracts.

[1] G. Rath, A. Touré, J.-L. Wolfender, K. Hostettmann, *Chromatographia* **1995**, 41, 332.

Analytical Chemistry

19

Comparison of recent extraction techniques with conventional extraction method of plant material. Application to cocaine from coca leaves.

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Liquid-solid extraction is usually the conventional method used to extract secondary metabolites from plant material. Because this extraction method is time consuming and requires relatively large quantity of solvent, it is worthwhile to develop rapid, simple and selective extraction methods with low solvent consumption.

Three recent extraction techniques : supercritical fluid extraction (SFE), accelerated solvent extraction (ASE) and focused microwave assisted extraction (MAE), will be briefly presented and compared with conventional liquid-solid extraction. Advantages and disadvantages of each technique will be discussed through a particular application of cocaine extraction from coca leaves.

SFE of cocaine has been optimised taking into account the variation of pressure, temperature, percentage of polar modifier in carbon dioxide and its composition (mixture of water and methanol) by means of a central composite design. Results showed that a large quantity of polar modifier in CO_2 was needed to achieve comparable recoveries. Thus, ASE with different solvents was then investigated. Recovery and precision will be compared.
Finally, focused MAE at atmospheric pressure was carried out. Extraction time of cocaine was considerably reduced by applying microwave energy which facilitates the breaking of analyte-matrix bond. A comparable recovery of cocaine with an excellent precision was obtained. MAE at atmospheric pressure appears to be a promising alternative to conventional extraction techniques.

Analytical chemistry

18

High throughput analyses using a monolithic bed column in liquid chromatography

UNIVERSITÉ DE GENÈVE

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University of Geneva, 1211 Geneva 4

Reduction in analysis time is required in various areas, such as pharmacology, quality control, toxicology, combinatorial chemistry in order to increase the sample throughput. Liquid chromatography (LC) is now recognized as the method of choice in pharmaceutical industry. However, with standard procedures, the analysis time varies from 5 to 30 min depending on matrix complexity and on the nature of the compounds.

Recently, a new generation of monolithic bed columns appeared for high throughput LC analyses. These columns are packed with one rod of continuous monolithic porous silica which can operate at higher flow rate with lower back pressure than conventional columns.

In the present work, an analytical method for quality control of prilocaine injectable solutions has been developed, with an analysis time of less than one minute per sample. Method validation, according to SFSTP procedure, has been achieved in less than 30 min for testing repeatability, linearity and accuracy. Thus, the complete validation procedure was conducted in half a day instead of three days when using a conventional LC column.

20

DETERMINATION OF SALICYLATE AND ITS MAJOR METABOLITES IN HUMAN URINE BY CAPILLARY ELECTROPHORESIS WITH FLUORESCENCE DETECTION

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Acetylsalicylic acid (Aspirin) is rapidly metabolized to salicylate and other fluorescing compounds, including gentisic acid and salicyluric acid. Monitoring of salicylate and its metabolites is of toxicological interest. A competitive binding, electrokinetic capillary-based immunoassay was developed and is shown to be capable of recognizing the presence of salicylate and gentisic acid in urine. In this approach, urines and immunoreagents are combined and analyzed by capillary electrophoresis (CE) with laser induced fluorescence (LIF) detection. Differentiation of the two compounds, however, is not possible. CE with direct urine injection and LIF detection is shown to permit the determination of salicylate, gentisic acid and salicyluric acid. Identification of these compounds is shown to be best performed using wavelength resolved LIF detection. The CE techniques with fluorescence detection have been applied to toxicological patient urines and urines collected after ingestion of 500 mg acetylsalicylic acid.

This work was supported by the Swiss National Science Foundation.

Analytical Chemistry **21**

Occurrence of Macrolide Antibiotics in the Aquatic Environment

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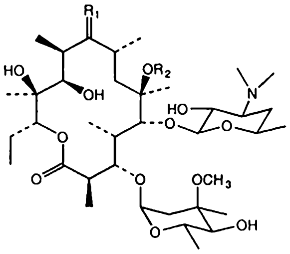
This poster presentation reports on an ongoing research program investigating occurrence and behavior of pharmaceuticals in different compartments of the aquatic environment.

Relatively persistent and non-adsorptive macrolide antibiotics were chosen for this study (see Figure). The objectives were to follow the exposure routes of macrolides, to determine the amounts reaching ambient waters, to study the environmental behavior of these substances and to provide information for environmental risk assessment. An analytical method was developed based on solid phase-extraction followed by separation and quantification with LC-MS.

erythromycin:
R_1=O, R_2=H
clarithromycin:
R_1=O, R_2= CH_3
roxithromycin:
$R_1=NOCH_2O(CH_2)_2OCH_3$, R_2=H



Initial studies on effluents of municipal wastewater treatment plant as well as on river and lake water show the occurrence of clarithromycin, the main metabolite of erythromycin and roxithromycin. Maximum concentrations of 0.13 µg/L were found in mechanically-biologically treated wastewater effluents, whereas concentrations in surface waters were 2-10 times lower.

Chimie analytique **22**

Analyse de résidus d'érythromycine dans la viande et le poisson par extraction sur phase solide échangeuse de cations

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22, quai Ernest-Ansermet, 1211 Genève 4

L'érythromycine appartient à la famille des macrolides, importante classe de composés antibactériens, utilisée aussi bien en médecine humaine que vétérinaire. Par conséquent des résidus peuvent être retrouvés dans la viande, les abats (foie et rognons), les œufs et le lait.

Une procédure fiable et sensible est présentée pour l'analyse de l'érythromycine dans la viande et le poisson. La méthode est basée sur une purification par extraction sur phase solide avec une cartouche échangeuse de cations, d'une dérivatisation en mode pré-colonne et sur une séparation par chromatographie liquide avec détection fluorimétrique.

La procédure est caractérisée qualitativement et quantitativement. La sélectivité est satisfaisante pour des matrices variées et complexes, comme la viande et le poisson. Du point de vue quantitatif, si les recouvrements sur toute la procédure sont relativement faibles (> 50 %), l'utilisation d'un standard interne (l'oléandomycine) permet de parfaitement compenser les pertes. Dans ces conditions la répétabilité, la linéarité, les limites de détection et de quantification, mais surtout l'exactitude sont satisfaisantes.

Analytical chemistry **23**

Analyse de l'indinavir dans les cheveux par chromatographie liquide haute performance (CLHP) et commutation de colonnes

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L'indinavir est un inhibiteur spécifique de la protéase du virus de l'immunodéficience humaine (HIV), une enzyme nécessaire à la maturation et à la réplication du virus.

L'indinavir est considéré comme étant un des agents thérapeutiques les plus efficaces à l'heure actuelle pour traiter les infections à HIV.

L'analyse des cheveux permet d'observer la consommation de certaines drogues sur une longue période suivant la longueur de la mèche. C'est pourquoi une analyse de l'indinavir dans les cheveux devrait permettre un meilleur suivi thérapeutique.

Une méthode CLHP utilisant la commutation de colonnes (column switching) a été développée pour la détermination rapide et quantitative de l'indinavir dans les cheveux.

Après incubation des cheveux, lavés et broyés, dans 1 ml de méthanol pendant 2h. à 45°C, l'échantillon est centrifugé et la phase organique évaporée sous azote. L'extrait sec est reconstitué dans 100 µl de phase mobile constituée de tampon phosphate et d'acétrontrile (70 :30).

L'échantillon est alors injecté et extrait par une technique de commutation de colonnes utilisant une colonne Bio Trap 500 MS. Le méthylclonazepam est utilisé comme standard interne. L'analyse se fait par CLHP en phase inverse à l'aide d'un détecteur à barrette de diodes et l'indinavir est mesuré à une longueur d'onde de 254 nm. La droite de calibration est linéaire dans un domaine de concentration entre 3 et 20 ng/mg. Les coefficients de variation à basse et à haute concentrations sont de 13% et 9% respectivement. Le rendement d'extraction est supérieur à 95% pour tout le domaine de calibration.

Title: Determination of Aromatic Compounds in Aerosol from an Indoor Smoking Environment by Two Step Laser Desorption/Ionization Mass Spectrometry (L2MS)

24

Brad Morrical and Renato Zenobi*

Department of Organic Chemistry, ETH Zurich
CH-8092 Zurich

Cigarette smoking is a major cause of indoor aerosol pollution in Europe. Determination of exposure to environmental tobacco smoke (ETS) aerosol is critical to understanding health effects. Using two step laser desorption/ionization (L2MS) to analyze aerosol collected from a smoking area in a university building, the determination of ETS tracers on aerosols and the „aging" of ETS over the course of a day is examined. Additionally, the spatial distribution of aerosol from the smoking lobby is examined to see what effect distance from the source has on the mass spectrum observed.

L2MS has been proven to be an effective technique for the selective ionization of polycyclic aromatic compounds (PAC) and other polyaromatic compounds. Results from the analysis of ETS show that several unique m/z ions are present in the mass spectrum when compared to other combustion sources, such as automobiles and diesel trucks. In particular, ions at m/z 118, 132, 146, and 160 are consistently present and are not found in other sources. For the indoor environment, where chemical transformation is much less rapid than in the outdoor environment, these ions were found to be present as soon as the first smokers appeared and persisted over the course of the day.

Aerosol sampled during the early part of the day revealed a prominence of ions due to aerosol from other combustion sources, namely automobiles and or road dust suspended by vehicle motion. These enter the building through ventilation and the opening of doors.

The mass spectra of samples taken throughout the building indicate that down some hallways the ETS signature was quite clear, while in others the mass spectrum resembled the outside PAC distribution. The transport of the ETS throughout the building appears to be dependent on the ventilation patterns in the building.

Analytical Chemistry **25**

Untersuchung der thermischen Stabilität von Bis-(Methylbenzyliden)-sorbitol sowie Bestimmung des Diffusionsverhaltens eines seiner Zersetzungsprodukte in Polypropylen.

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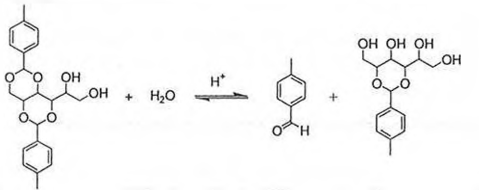
Hochschule für Technik und Architektur Freiburg
Vincent Dudler
Bundesamt für Gesundheit Bern

Bis-(Methylbenzyliden)-sorbitol wird als Nukleationsagenz zur Erhöhung der optischen Transparenz bei der Herstellung von Polypropylen-(PP)-folien eingesetzt. Derartige PP-Folien werden unter Anderem auch als Lebensmittelverpackungen verwendet. Die Prozesstemperaturen bei der Fabrikation von PP-Folien liegen, wie die durchgeführten thermogravimetrischen Messungen zeigten, im Bereich der Zersetzungstemperatur des Nukleationsadditivs (250°). Das Massenspektrum der Zerfallsprodukte zeigte, dass *p*-Toluylaldehyd gebildet wird.



Da dieses Zersetzungsprodukt bereits bei Konzentrationen von 50 ppb geschmackliche Veränderungen in Nahrungsmitteln bewirkt, wurde in der Folge sein Diffusionsverhalten in PP untersucht. Dazu wurde eine reine PP-Folie auf beiden Seiten mit einer an *p*-Toluylaldehyd gesättigten PP-Folie in Kontakt gebracht und bei konstanter Temperatur gelagert. Die Konzentration des migrierenden *p*-Toluylaldehyd in der mittleren Folie wurde IR-spektroskopisch in Funktion der Zeit verfolgt. Unter Zuhilfenahme der Lösung der entsprechenden Fick'schen Gleichung wurde durch nichtlineare Regression die Diffusionskonstante bestimmt. Bei 40°C liegt die Diffusionskonstante von *p*-Toluylaldehyd in PP bei $2.53 \cdot 10^{-9}$ cm^2s^{-1}. Die bei weiteren Temperaturen bestimmten Diffusionskonstanten lassen die Berechnung der Arrheniusparameter für den Diffusionsvorgang zu. Die Aktivierungsenergie liegt bei 49 $kJmol^{-1}$, der präexponentielle Faktor bei 0.4 cm^2s^{-1}.

Chimie analytique **27**

ESTIMATION DE LA MISE EN DANGER PAR DES SITES CONTAMINES

Roxane Boudoux, Michäel Bensimon* et Claude Rohrbasser**

*M. Dr Michäel Bensimon, Geolep, EPFL, CH-1015 Lausanne
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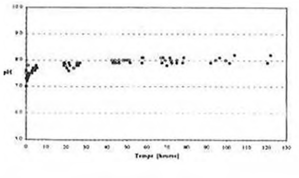
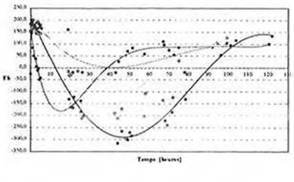
Une nouvelle ordonnance sur l'assainissement des sites pollués (OSITES) a été récemment adoptée par le Conseil fédéral. Cette ordonnance règle les modalités d'assainissement des sites susceptibles de causer des atteintes nuisibles à l'environnement. Pour évaluer ce risque de pollution, une procédure basée sur l'analyse des métaux dans un essai de lixiviation sur colonne en laboratoire est recommandée en annexe de l'ordonnance. Ce travail consiste à mettre au point l'essai de lixiviation selon la directive OSITES et de tester l'installation sur des cas réels.

Pour évaluer la fiabilité de la méthode, certains paramètres physico-chimiques comme la reproductibilité, le débit, la charge de la colonne et autres ont été optimisés. Cette procédure est comparée avec la méthode plus ancienne, mais plus facile à mettre en place, décrite dans l'ordonnance sur le traitement des déchets (OTD). L'acquisition des paramètres physico-chimiques (pH, eH, conductivité) est effectuée en ligne à l'aide du programme LabView. Les analyses des éléments en trace sont réalisées par la spectrométrie de masse à haute résolution couplée à un plasma (HR-ICP-MS).





Au vu des résultats obtenus, on peut affirmer que cette méthode apporte une bonne reproductibilité et fiabilité. La comparaison des deux méthodes proposées mène à la conclusion que le test OSites se rapproche plus des conditions naturelles que le test OTD qui lui se déroule dans des conditions plus agressives.

Analytical Chemistry **26**

Characterisation of optical chemical sensors by combined absorbance and impedance spectroscopy

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An interesting example of a chemical sensor is an NO_2 gas sensor that is based on the Nile Blue derivative ETH 5418 and an aquacyanocobalt(III) cobyrinate derivative [1]. Nitrogen dioxide is presumed to be bound by the cobyrinate and causes an absorbance change of ETH 5418 due to its protonation. The mechanism in the gas phase – in contrast to the situation in solution [2] – is very poorly understood.

Interdigitated gold microelectrodes on glass offer the possibility to study the membrane reactions by absorbance and impedance spectroscopy simultaneously. „Invisible" reactions such as water uptake which have little effect on the UV/VIS-spectra can be monitored by impedance spectroscopy. This complements the knowledge of the membrane reactions needed to elucidate the mechanism.

[1] T. Nezel, A. Fakler, G. Zhylyak, G. J. Mohr and U. E. Spichiger-Keller, *accepted by Sensors and Actuators B* (2000).
[2] C. Demuth and U. E. Spichiger, Analytica Chimica Acta **355**, 259-268 (1997).

Analytical Chemistry **28**

Environmental Hazard of Superplasticizers: Analytical Methods and Field Study

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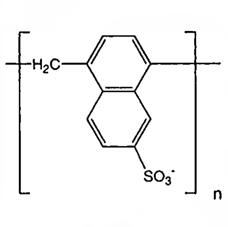
Modern concrete technology uses increasing amounts of concrete admixtures, which are mostly synthetic organic compounds. Most superplasticizers are based on sulfonated naphthalene-formaldehyde-condensates (SNFC). The technical SNFC-product consists of several mono- and disulfonated monomers and their condensated oligomers. SNFC are well soluble in water and not easily biodegraded. Due to these properties they are expected to be mobile and persistent in the aquatic environment.



n = 5-10

An analytical method was developed based on fluorescence spectroscopy for a quick and simple determination of the total SNFC-concentration in environmental samples. A major advantage of this method is that the measurements can be performed without prior enrichment.

Groundwater samples have been analyzed from an aquifer through which a railroad tunnel is being built. The maximum concentrations ranged from 2 to 4 µg/L. The samples were also analyzed using an HPLC-method [1] with fluorescence detection, giving information on the oligomer distribution of the SNFCs. Only the disulfonated monomers, which are less biodegradable than the monosulfonated ones, and the dimers were found in the groundwater.

[1] C. Wolf, Ph.D. Thesis, University of Karlsruhe, 1999.

Analytical Chemistry **29**

Occurrence and Behaviour of Fluoroquinolone Antibiotics in Municipal Wastewater Treatment

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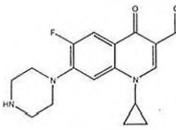
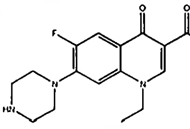
Fluoroquinolones (FQs) are among the most important groups of synthetic antibiotics used in human and veterinary medicine. Because metabolization rate of FQs is generally less than 25%, an important percentage of the administered drug is excreted mainly via urine as the parent compound.

The occurrence of these antibiotics in the effluents of several municipal wastewater treatment plants was studied using solid-phase extraction and liquid chromatography with fluorescence detection. FQ identification was carried out by liquid chromatography tandem mass spectrometry and by acquiring the fluorescence spectrum.

The two FQs mostly used in human consumption, Ciprofloxacin (**1**) and Norfloxacin (**2**), were found in mechanically treated effluents (100-400 ng/L) and biologically treated effluents (20-150 ng/L). Therefore, even though a relatively efficient elimination during the treatment process occurs (60-80%), (**1**) and (**2**) are emitted into surface waters. The fact that no veterinarian FQ was detected in municipal wastewaters indicates that for veterinary antibiotics a different exposure route prevails, normally via manure dispersion and animal excretion on soils.


(1)


(2)

Analytische Chemie **30**

Rückverfolgbarkeit chemisch-analytischer Messungen auf das SI

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Das Ziel von Messungen ist, mit Hilfe eines bestimmten Messverfahrens, den Wert einer wohldefinierten Messgrösse zu ermitteln. Mit dem Konzept der ***Rückverfolgbarkeit*** der Messungen auf universell anerkannte Einheiten wird der Messwert unabhängig von Ort und Zeit, d.h. vergleichbar und verifizierbar. Jeder Messwert ist aber untrennbar mit einer ***Messunsicherheit*** behaftet. Diese allgemeinen Prinzipien der Metrologie gelten grundsätzlich auch für chemisch-analytische Messungen. Die Vielzahl chemischer Stoffe und die beschränkte Zahl von primären Messmethoden und Referenzmaterialien machen es aber oft schwierig oder sogar unmöglich, die Messwerte durch eine ununterbrochene Kette von Messungen mit bestimmbarer Messunsicherheit auf die Basiseinheiten des SI zurückzuführen.
Mit dem Ziel, die metrologischen Prinzipien auf dem Gebiet der chemischen Analytik zu fördern, haben das EAM und die EMPA eine Vereinbarung zur Zusammenarbeit für die Bereitstellung und Weitergabe genauer Messwerte und Referenzmaterialien in der chemischen Analytik getroffen. Aufgrund von Kontakten mit Organisationen und Firmen sowie durch das Studium der relevanten Bundesverordnungen wurde eine Standortbestimmung in Bezug auf das chemische Messwesen vorgenommen und der Bericht mit dem Titel "***Studie und Strategievorschlag: Metrologie der Stoffmenge und Referenzmaterialien in der Schweiz***" verfasst. Es zeigt sich, dass auf verschiedenen Gebieten noch grosse Anstrengungen unternommen werden müssen, um die Resultate von Stoffmengenmessungen auf SI-Einheiten zurückzuführen. Die vorgeschlagene Strategie soll beitragen, die Qualität chemischer Messungen in der Schweiz weiter zu verbessern.

Analytical Chemistry **31**

New Potentiometric Ion Sensor for Monitoring of Pb^{2+} in Environmental Water Samples

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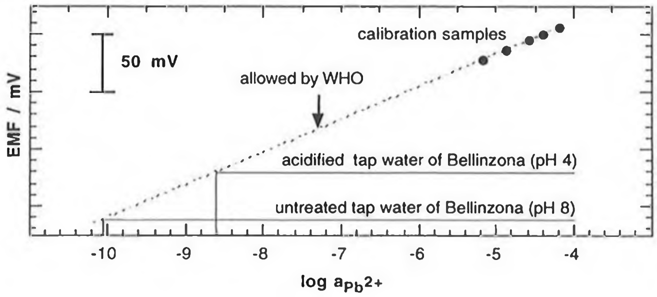
Insufficient lower detection limits and selectivities have been the main obstacles to applying ion-selective electrodes (ISEs) in environmental heavy metal trace analyses. Recently, we showed that the achievable lower detection limits and inherent membrane selectivities of already existing ISEs are often better by many orders of magnitude than hitherto assumed. The key to improving these characteristics for a better performance of such sensors is to avoid biases caused by leaching of primary ions into the aqueous surface layer of the ISE membranes.
The composition of the polymeric menbrane and the internal solution as well as the measurement protocol have been optimized in order to obtain fast and unbiased responses. This allowed the detection of Pb^{2+} activities down to 10^{-9} M in acidified (pH 4.0) and below 10^{-10} M in untreated (pH 7.0-8.5) tap water samples. The method can be used for the trace level detection of other ions for which sufficiently selective ionophores are available.



Analytical Chemistry **32**

Fluorogenic Reactands: A New Concept to Sense Neutral Molecules

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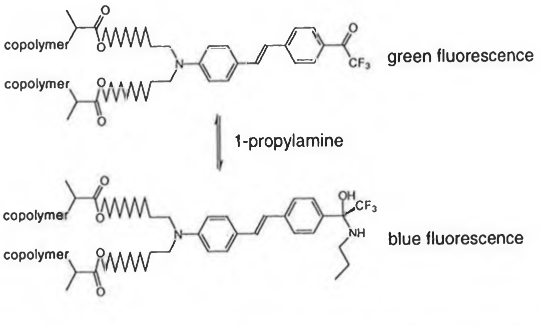
Fluorogenic reactands are presented that perform a reversible chemical reaction with aqueous aldehydes, and give strong changes in fluorescence. Using plasticized poly(vinyl chloride) as the polymer matrix, optical sensor layers for acetaldehyde and propionaldehyde are obtained.

In order to improve the operational lifetime of the sensor layers, reactand copolymers for amine-sensing are synthesized where the reactand is linked covalently to the polymer backbone by a methacrylate group. The change in fluorescence of the copolymer is based on the nucleophilic reaction of the analyte (1-propylamine) with the trifluoroacetyl group of the reactand.



The mechanism of the chemical recognition as well as the sensitivity and selectivity of the new sensor layers for amines and aldehydes are discussed.

Analytical chemistry **33**

Short-end capillary electrophoresis: Method validation for the determination of fentany citrate

UNIVERSITÉ DE GENÈVE

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Fentanyl citrate is a widely used synthetic analgesic with strong anesthetic properties. Validated methods to quantify fentanyl are necessary for pharmaceutical purposes. Capillary electrophoresis (CE) is an analytical alternative method to liquid chromatography (LC) in the area of quantitative drug analysis. Advantages of CE include fast method development, high resolution and low cost of operation. Furthermore, by using the short-end capillary injection, rapid analyses are obtained due to the reduced effective length (8.5 cm).

The influence of experimental parameters on migration time precision and method accuracy were studied in a pre-validation step. Capillary rinse procedures and electrolyte alteration both were found to have an incidence on precision of migration time, while ionic strength of samples influenced accuracy. After optimization of the operating conditions, the total time between two injections was set at 3 minutes.

Method validation and robustness were performed following the SFSTP procedure [1], using procaïne as internal standard. The short-end injection CE method was found to be accurate and precise for the quantitative determination of fentanyl citrate in injections.

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

Analytical Chemistry **34**

A rationally designed oligopeptide shows significant conformational changes upon binding to sulphate ions

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In recent years, a number of proteins that selectively interact with anions have been characterized. Substrate-binding sites of enzymes may serve as promising models for the development of ionophores. Our work aimed at designing synthetic oligopeptides on the basis of molecular recognition sites of oxoanions found in enzymes.

The design of the peptide ionophores was based on the enzyme Purine Nucleoside Phosphorylase (PNP). The amino acids involved in the complexation of oxoanions were linked through flexible spacer residues. These spacers were chosen such that the relative orientation of the interacting amino acids was conserved. A number of peptide sequences was pre-selected based on intermolecular H-bond frequencies. These frequencies were calculated from molecular dynamics trajectories of the corresponding peptide-anion complexes and used to score the binding properties of the peptides. The most promising peptides were prepared using solid phase peptide synthesis.

Anion binding of the peptide ionophores was screened using circular dichroism (CD) and confirmed by NMR spectroscopy. CD measurements performed in methanol revealed a significant conformational change of a linear undecapeptide upon binding to sulphate ions. 2D-NMR experiments confirmed that a conformation with high helical content is formed in the presence of sulphate ions. These conformational changes induced by the anion stimulate the development of new transduction mechanisms in chemical sensors.

Chimie analytique **35**

Structural characterization of aquatic biopolymers by capillary electrophoresis and fluorescence correlation spectroscopy

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Based on their physicochemical nature, their origin, and their concentration in the water column, organic biopolymers (humic substances, polysaccharides and proteins) are expected to play a major role in a majority of physicochemical reactions in aquatic systems.
In order to understand better their behaviour under different physicochemical regimes, the influence of ionic strength and pH was systematically studied by capillary electrophoresis (CE) and fluorescence correlation spectroscopy (FCS).

CE was used to determine the electrophoretic mobilities, which are proportional to the ratio of the charge to hydrodynamic diameter whereas FCS provided information about the diffusion coefficients and hydrodynamic sizes of the molecules. Both the mobilities and sizes of the aquatic biopolymers were in line with theoretical predictions for a polyelectrolyte for variable pH and ionic strength. For example, the IHSS fulvic acid showed a sigmoidal curve for the variation of mobility as a function of pH. Small, but significant decreases in the diffusion coefficients with decreasing pH were observed and could be attributed to the formation of small aggregates. The effect of ionic strength (0 – 400 mM) was in most cases small or insignificant.

Analytical chemistry **36**

ENANTIOMERIC SEPARATION OF PHARMACEUTICALS USING ON-LINE CAPILLARY ELECTROPHORESIS-ELECTROSPRAY IONISATION MASS SPECTROMETRY

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Because of its high efficiency, flexibility and very high resolution, capillary electrophoresis (CE) has revealed an enormous potential for drugs analysis. In particular, CE exhibits excellent results in the field of optical isomer separations. However, the main disadvantage of CE with on-column UV detection resides in its relatively low sensitivity which is due to the short optical path-length afforded by the small internal diameter of capillaries. On-line coupling of chiral CE with electrospray mass spectrometry (CE-ESI-MS) is a promising combination of two analytical techniques. While CE provides high separation efficiency per unit of time, MS affords high sensitivity and selectivity as well as molecular structural elucidation.
Enantiomeric separation by CE is generally performed in direct separation mode, with a chiral selector in the background electrolyte (BGE). However, when CE is coupled with MS there is a risk of source contamination by non volatile additives such as cyclodextrins. Counter current partial filling technique is generally recommended to avoid the chiral selector entrance into the MS ion source, which induces a detrimental effect on sensitivity. This technique requires filling a discrete portion of the capillary with a buffer containing a suitable amount of chiral selector. The latter possesses a charge opposite to that of the analyte, and thus creates a counter current process where chiral selector and analyte migrate in opposite direction.
This contribution describes the successful application of CE-ESI-MS in the enantiomeric separation of basic compounds of pharmaceutical interest (tramadol, venlafaxine and their metabolites, methadone, etc) in biological matrices (serum, plasma, etc.). For this purpose, the use of negatively charged cyclodextrins combined with the partial filling technique is investigated.

Analytical Chemistry

37

Lipophilic, Redox-Active, Self-Assembled Monolayer as a Novel Solid Contact for Ion-Selective Electrodes

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Krisanu Banyopadhyay, Shen Gao Liu, Luis Echegoyen, Department of Chemistry, University of Miami, Coral Gables, FL 33124, USA

Philippe Bühlmann, Department of Chemistry, University of Minnesota, 207 Pleasant St., SE, Minneapolis, MN 55455, USA

Solid-contacted ion-selective electrodes (SC-ISEs) have long been known to show drifting signals or erratic, sudden potential changes due to the lack of a controlled redox equilibrium at the membrane/metal interface and to the uptake of water eventually leading a third phase between membrane and metal electrode. Here, we report a new methodology to fabricate SC-ISEs using self-assembled monolayers of a lipophilic redox-active compound and a traditional solvent polymeric membrane. The redox property of these compounds garantees a stable potential, while their lipophilicity prevents the formation of an aqueous layer between membrane and metal electrode. This novel approach leads to improved potential stability and prevents redox or O_2 interference SC-ISEs.

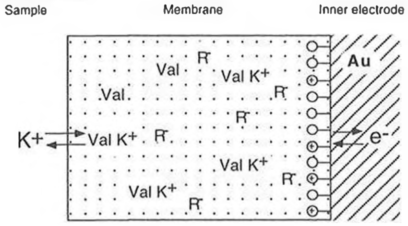

Figure 1. Working principle of the solid-contact ISEs with a redox-active self-assembled monolayer.

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ELECTROPHORETIC SEPARATIONS IN PMMA CAPILLARIES WITH UNIFORM AND DISCONTINUOUS BUFFER SYSTEMS

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Polymethylmethacrylate (PMMA, Plexiglass) is a moderately hydrophilic polymer that has been employed successfully over many years in the manufacturing of separation chambers for large scale electrophoretic free fluid instruments. Recently, PMMA capillaries of 50 to 75 µm I.D. were proposed as an alternative to fused-silica capillaries with a deliberately applied polymeric wall coating. Despite the lower thermal conductivity and lower optical transparency of PMMA compared to fused-silica, PMMA capillaries were found to permit high-resolution zone electrophoretic separations of proteins. The basic phenomena occurring within PMMA capillaries under the conditions of zone electrophoresis and isotachophoresis have been explored in our laboratory. Electroosmotic and electrophoretic properties observed in PMMA capillaries are compared to those characteristic for untreated fused-silica capillaries. The use of an imposed co-flow for the performance of bidirectional isotachophoresis is also discussed.

This work was supported by the Swiss National Science Foundation.

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ANALYSIS OF URINARY CODENOIDS BY AN ELECTROKINETIC CAPILLARY IMMUNOASSAY AND CAPILLARY ELECTROPHORESIS-ION TRAP MASS SPECTROMETRY

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Screening for and confirmation of drugs of abuse in human urine is a timely topic in which capillary separation techniques play a key role. Capillary electrophoresis (CE) represents the newest technology employed in this field of analysis. A competitive binding, electrokinetic capillary-based immunoassay is shown to be capable of recognizing the presence, but not the identity, of urinary codeinoids. In this approach, aliquots of urine and immunoreagents are combined and analyzed by CE with laser induced fluorescence detection. Confirmatory testing was performed by electrophoresis-ion trap mass spectrometry which permitted identification of dihydrocodeine, codeine and their glucuronides. The assay is based upon solid-phase extraction followed by analysis of the extract using the LCQ mass spectrometer with electrospray ionization. MS^n ($n \geq 2$) is shown to be capable of properly identifying the codeinoids on the 300 ng/mL concentration level.

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

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ANALYSIS OF FUROSEMIDE IN HUMAN URINE BY CAPILLARY ELECTROPHORESIS WITH OPTICAL AND MASS SPECTROMETRIC DETECTION

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Furosemide is a diuretic drug that is used in the pharmacotherapy of a range of diseases, including congestive heart failure, hypertension and some types of oedema. Based on its promotion of urine excretion, it is also a drug that is frequently employed to conceal the presence and misuse of performance enhancing substances and it is thus considered as a doping agent in sports. Analysis of furosemide in human urine by capillary electrophoresis with UV absorbance detection, laser induced fluorescence detection and ion-trap mass spectrometry was investigated. Having direct urine injection, the latter two detection principles were found to permit the ppm recognition of urinary furosemide. Unambiguous access to sub-ppm concentrations is obtained after extraction only. Capillary electrophoresis is shown to represent a simple and rapid screening and confirmation approach for furosemide in urine.

This work was supported by the Swiss National Science Foundation.

Analytical Chemistry **41**

Na⁺ and K⁺ affinities of common MALDI matrices

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Besides protonated ions, sodiated and potassiated analyte molecules are often observed in MALDI mass spectra. Therefore, cationization is considered a prevalent pathway for ion formation in MALDI [1] influenced both by the interaction between metal ions and analyte molecules and the metal ion affinity of the matrix. To study cationization at a fundamental level, we determined thermochemical values including cation basicities and affinities of MALDI matrices.

The gas-phase metal ion basicities(e.g. for Na: GNaB) of various MALDI matrices (M) were determined in a Fourier transform ion cyclotron resonance mass spectrometer (FT ICR MS) by a method closely related to the equilibrium bracketing method [2]. This method is based on monitoring the competition of a reference compound (with known gas phase sodium or potassium basicity) and a MALDI matrix for sodium and potassium ions, respectively .

$$[M+Na]^+ + R \xrightleftharpoons{\Delta G} [R+Na]^+ + M \quad -\Delta G = \mathrm{GNaB(R)-GNaB(M)}$$

Reactant species were generated by laser desorption or introduced through a leak valve. In addition, theoretical calculations were performed at the B3LYP/6-31G* level in order to substantiate the experimental findings.

Absolute values of metal ion basicities were obtained from this method. The gas-phase metal ion affinities of MALDI matrices are much lower (by a factor of 10) than their gas-phase proton affinities. For example, the sodium ion affinities for common matrices lie between 100 and 200 kJ mol^{-1}. In the cases studied so far, the potassium ion basicities are ca. 30% lower than sodium ion basicities.

[1] K. Breuker, R. Knochenmuss, R. Zenobi, Int. J. Mass Spectrom. 184 (1999) 25-38
[2] Zenobi R. and Knochenmuss R., 1998, Mass Spectrom. Rev. 17 (1998) 337-366

Analytical Chemistry **42**

Capillary electrophoresis-diode array detection-electrospray mass spectrometry for the analysis of selected tropane alkaloids in plant extracts

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Tropane alkaloids are widely distributed in the Solanaceae and related families. The principal alkaloids of medicinal interest in this group are (-)-hyoscyamine, its racemate atropine, and scopolamine which have widespread activities such as spasmolytic and mydriatic effects. The synthetic production of these alkaloids is more expensive than their extraction from plant material and they are therefore currently industrially isolated from various solanaceous plants belonging to genera *Atropa, Duboisia, Datura* and *Hyoscyamus*. Because of the complexity of the extracts and the therapeutical value of the compounds, there is a need to develop rapid, sensitive and accurate analytical methods for the analysis of these alkaloids, both in pharmaceutical preparations and in plant extracts. In this context, the on-line coupling of capillary electrophoresis with mass spectrometry (CE-MS) is a promising combination of two analytical techniques : while CE provides high separation efficiency per unit of time, MS affords high sensitivity and selectivity, as well as molecular structural information.

A capillary zone electrophoresis, coupled to UV and interfaced with electrospray mass spectrometry (CE-ESI-MS), is described for the simultaneous analysis of hyoscyamine and scopolamine as well as their biosynthetic precursors, namely tropine, littorine and 6β-hydroxyhyoscyamine. Under optimized conditions, including CE and ESI-MS parameters, both alkaloids were resolved in a short time and with a very high sensitivity. Moreover, up front collision induced dissociation (CID) is also presented to differentiate hyoscyamine and its positional isomer littorine, commonly encountered in plant material. Finally, the developed method was applied to the analysis of these alkaloids in Belladonna leaf extract, in *Datura candida x D. aurea* and *Hyoscyamus muticus* hairy root extracts.

Analytical Chemistry **43**

Nonaqueous Capillary Electrophoresis - Mass Spectrometry

Pharmaceutical applications

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Recently, widening the application range of capillary electrophoresis (CE) by using nonaqueous buffers has encountered growing interest. Compared to aqueous buffers, the different chemical and physical properties of organic solvents (viscosity, dielectric constant, polarity, auto-protolysis-constant, electrical conductivity, etc.) considerably improve selectivity, which is a challenging task in the science of separation, and reduce Joule heating. Moreover, organic solvents proved to be useful in analyzing hydrophobic compounds as well as drugs and metabolites which are difficult to separate in aqueous buffers. Very high efficiency and resolution, short analysis time and the possibility to increase analyte solubility are the main reasons for this fast breakthrough. Last but not least, the use of organic solvent containing volatile electrolyte presents a high MS compatibility due to the improved evaporation of the electrospray droplets.

In this presentation, the potential of nonaqueous CE is discussed for the fast separation of pharmaceutical drugs, which have similar structure as well as charge to mass ratio. Sub-minute drug separations are reported using short length capillaries and appropriate organic solvent composition. Advantages of nonaqueous media are also highlighted for the on-line coupling to an electrospray ionization mass spectrometer.

Analytical Chemistry **44**

Microemulsion electrokinetic chromatography and high performance liquid chromatography for the analysis of withanolides in plant extract

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Withanolides are polar C28 steroidal α,β-unsaturated -lactones occurring almost specifically in the Solanaceae family. Several interesting biological activities have been attributed to these steroids, such as antibacterial, virostatic, immunomodulating or antifeedant activities. A number of withanolides has been isolated from the leaves of *Iochroma gesnerioides* (Kunth) Miers, the most abundant being withaferin A, withacnistin and iochromolide.

Recently, capillary electrophoresis (CE) has become an interesting alternative to conventional chromatographic techniques for the analysis of natural products. Alternatively, microemulsion electrokinetic chromatography (MEEKC) has emerged as a new electrokinetic technique in which analytes interact with moving oil droplets present in a microemulsion buffer.

A MEEKC method is developed for the simultaneous determination of withanolides. The effects of buffer pH, SDS concentration, capillary temperature and voltage are systematically studied. Optimal resolution is obtained with a microemulsion consisting of 70 mM octane, 800 mM butanol, 100 mM SDS and 10 mM phosphate-borate buffer (pH 7) using a fused-silica capillary operating at 25 kV and 40°C. The separation by MEEKC is compared to that obtained with reversed phase liquid chromatography and showed similar retention order, indicating the analogy of the retention mechanism of both techniques. Finally, the described method is applied to the qualitative analysis of withanolides in a *Iochroma gesnerioides* plant extract

CHIMIA 2000, 54, No. 7/8

Chimie analytique **45**

CONFORMATIONAL TRANSITIONS OF SUCCINOGLYCAN AS OBSERVED BY ATOMIC FORCE MICROSCOPY

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Succinoglycan is an extracellular bacterial polysaccharide which has a high molecular weight and which can undergo disorder to order transitions with increasing ionic strength. Atomic force microscopy (AFM) has been used to study the conformation of this polysaccharide as a function of ionic strength. Aliquots of a 10 mg.l^{-1} succinoglycan solution, in water, in 0.01 M KCl and in 0.5 M KCl were deposited on freshly cleaved mica and observed using tapping mode AFM under ambient conditions (50 - 60 % relative humidity).

AFM images revealed that (i) succinoglycan may exist both as double helical structures and as individual single chains in water, and that (ii) an increase in the ionic strength of the medium resulted in an increase of the intrinsic rigidity of the macromolecules, via the formation of a single helix. Furthermore, at higher ionic strength (0.5 M KCl), succinoglycan chains were observed to form a gel. Measurements of the variation of bending angles of the succinoglycan chains on the mica surface yielded a persistence length of 19 ± 7 nm for the flexible chains in water and 36 ± 13 nm for the flexible chains in 0.01 M KCl. The values obtained in water are higher than the persistence length determined from ligth scattering on succinoglycan in the disordered conformation and indicated that the succinoglycan chains were not equilibrated with the mica surface in these experimental conditions ; this suggested that the surface influenced the rigidity of the chains. In 0.01M KCl solution, the persistence length agrees quite well with that determined in solution on the ordered conformation showing a better interaction with the mica surface in presence of salt excess.

Analytical Chemistry **46**

Individually addressable gel-integrated microelectrode array for high resolution measurements concentration profile at Interfaces

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Neuchâtel

Since the thickness of chemical strata of sediment is only a few millimeters, measurements with high spatial resolution are an analytical prerequisite to model diagenetic processes, calculate fluxes of nutrients and electron acceptors through the boundary layer and enable a clear understanding the biogeochemical processes at sediment-solution interface.

A novel voltammetric probe, which consists of gel-integrated, Hg-plated, Ir-based microelectrode array with 64 individually addressable lines, has been developed. This is the first reported system which allows simultaneous recording of 64 complete voltammograms with fast dynamic techniques. The capability of this system for real-time, high spatial resolution concentration profile measurements have been tested at well-controlled liquid-liquid and solid-liquid interfaces with steep concentration gradients. The individually addressable microelectrode array was placed at the interface of the liquid-liquid system; the concentration profiles were recorded as function of time and the effective diffusion coefficients were calculated. The novel sensor arrays was used to monitor the diffusion processes of Tl(I) and Pb(II) at the solid-liquid interface. The influences of porosity, geometry of the porous media and complexation, on the diffusion processes have been studied. All of these results show that this novel microsensor arrays is capable of measuring the correct real-time diffusion profiles of solutes at interfaces with a 200 μm resolution.

Analytical Chemistry **47**

Gas adsorption studied by pulse thermal analysis

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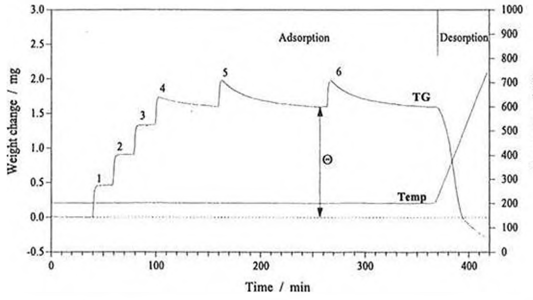
The potential of pulse thermal analysis (PulseTA®) [1] for measuring gas adsorption is studied. PulseTA® is based on the injection of a given amount of the adsorptive gas into a carrier gas stream and monitoring of changes in mass, enthalpy and gas composition, occurring as a result of adsorption-desorption phenomena. The method allows to study adsorption at atmospheric pressure and temperatures above 30°C. The desorption rate of physisorbed species is shown to depend on carrier gas flow and thickness of the sample bed. An important advantage of PulseTA®, compared to classical volumetric methods, is that pretreatment of the adsorbent, determination of the kind and amount of preadsorbed gases, as well as temperature programmed desorption can all be carried out in the same experimental set-up. The efficiency and reliability of PulseTA® for gas adsorption studies is demonstrated by comparing ammonia adsorption measurements on zeolites ZSM-5 and mordenite with corresponding volumetric measurements.



[1] F. Eigenmann, M. Maciejewski, A. Baiker, *Thermochim. Acta*, in press.

Analytical chemistry **48**

Near-Field UV Raman Spectroscopy: New Tool of Detection

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and R. Zenobi

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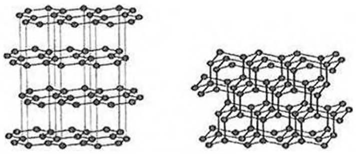
Near-Field Raman spectroscopy is a powerful tool for getting information on the structural characteristics of a compound. With excellent spatial resolution (≤100nm), it allows measurements in different environmental conditions (see for example [1]).
However, Raman spectroscopy has some limitations that come from the small scattering cross section and from the luminescence signal that can completely obscure the weak Raman bands of certain materials. An improvement can be achieved by Resonant Raman Scattering (RRS) using UV radiation for excitation [2].
UV near-field Raman spectra of chemical vapor deposited (CVD) diamond will be obtained as a first step. It is straightforward to distinguish between sp^2 and sp^3 hybridization which is responsible for the different structures of graphite and diamond (see figure below). This preliminary study will show the feasibility of such approach, as a starting point towards getting an insight, for example, into crystal growth.



[1] J.P. Fillard, *Near-Field Optics and Nanoscopy*, **1996**, Singapore: World Scientific.
[2] P.C. Stair, C. Li, *J. Vac. Sci. Technol. A* **1997**, 15, 1679.

Analytische Chemie **49**

Cross-Sections of Vanadium Oxide Nanotubes Characterised by Transmission Electron Microscopy and Electron Spectroscopic Imaging

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The recently discovered vanadium oxide nanotubes [1-2] represent a further example of the steadily growing family of inorganic nanotubes [3]. Although a wealth of information about morphology and wall structure can already be obtained from TEM images of the tubes in longitudinal projection, an observation along the tube axis is necessary in order to characterise the structure within the tube walls comprehensively. This projection could now be achieved by modifying a cross-sectional preparation method for TEM specimens.

In the TEM images, the structure inside the walls appears as a pattern of alternating dark and bright lines. Elemental maps of V and C, obtained by means of the electron spectroscopic imaging technique, show that V is located at the sites that appear with dark contrast in the TEM image whereas the amine molecules are embedded between these VO_x layers.

The systematic investigation of a multitude of cross-sections reveals the presence of different types of tubes. 'Ideal' tubes with tubes walls built up by concentric, closed cylinders are rarely found. A larger fraction consists of scrolls with 1-4 VO_x layers. The tube walls quite often contain both types, scrolled and cylindrical layers, simultaneously. Furthermore, defects such as gaps in the layers occur. This observed variety actually indicates a disturbed growth of the nanotubes.

[1] F. Krumeich, H.-J. Muhr, M. Niederberger, F. Bieri, B. Schnyder, R. Nesper, J. Am. Chem. Soc. **1999**, *121*, 8324.
[2] H.-J. Muhr, F. Krumeich, U. P. Schönholzer, F. Bieri, M. Niederberger, L. J. Gauckler, R. Nesper, Adv. Mater. **2000**, *12*, 231.
[3] W. Tremel, Angew. Chem. Int. Ed. **1999**, *38*, 2175.

Analytical Chemistry **50**

COUPLING OF MICRO VOLTAMMETRIC CELL WITH PLM FOR TRACE METAL SPECIATION IN WATER

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A newly emerging technique is permeation liquid membrane (PLM) based on one step membrane species selective separation and preconcentration technique. The membrane wall separates two aqueous solutions, the sample or the source solution containing the analyte of interest on the outside of the membrane and a strip solution containing a complexant to back extract the metal extracted by the tubular or hollow fibre membrane. The flux of cations is proportional to the concentration of metal in the source solution. By using large volume of sample and small volume of strip high enrichment factors can be obtained within short preconcentration time e.g. enrichment factors of ca. 300 and 1000 for Cu and Pb after 30 minutes preconcentration. The concentration of metals in the preconcentrated sample was determined by flame or graphite furnace atomic absorption spectroscopy. In this poster, we will demonstrate the speciation capabilities of PLM method using simple synthetic ligands (e.g. Sulphosalicylic acid), macromolecular ligands often used as model of humic substances and natural ligands i.e. Suwannee river fulvic acid. In addition, for real time measurements, on line voltammetric coupling of PLM device with a microliter volume flow through electrochemical cell incorporating iridium-mercury microelectrode will be presented. To date, such a coupling has not been reported.

Optimisation of the coupled device will be described and applications of this system to on line determination of free lead and copper in River Arve water will be presented.

Analytical chemistry **51**

Near-Field Raman Spectroscopy on Catalytically Active Substrates

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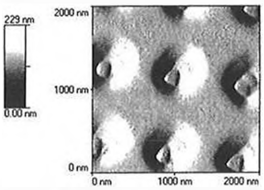
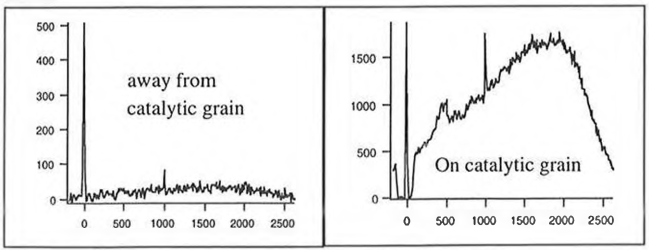
Vibrational spectroscopy has been established as a valuable tool for the investigation of catalytic reactions. The application of surface enhanced Raman scattering (SERS) improves the sensitivity by many orders of magnitude and even allows sensitve detection of molecular monolayers [1]. We used scanning near-field optical microscopy (SNOM) in combination with SERS for an online monitoring of a heterogeneous catalytic reaction with excellent spatial resolution (≤100 nm).



As a model reaction system, we chose the Pd-assisted hydrogenation of benzene to cyclohexane. To obtain information about the size and distance dependence of the catalytic sites we used highly defined nano-structured metal particle arrays [2].

Below preliminary spectra of benzene adsorbed on catalyst are shown.



Near-field Raman spectroscopy applied to catalytically active substrates will add to our understanding of catalytic mechanisms on a molecular scale.

[1] D. Ziesel, V. Deckert, R. Zenobi, and T. Vo-Dinh, *Chem. Phys. Lett.* **1998**, 283, 381.
[2] R. Prins, M. Schildenberger, Y.C. Bonetti, and J. Gobrecht, *Chimia* **1998**, 54, 63.

Chimie analytique **52**

Développement d'une méthode rapide d'identification de chlorophénols et chloroanisoles dans les vins

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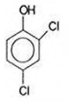
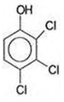
La qualité des vins peut être altérée par des « mauvais goûts ». Des accidents de type « goût de bouchon » sont parfois constatés et ont été attribués à la présence de composés organochlorés. Divers constituants de cette famille chimique sont mis en évidence dans les bouchons mais également dans les matériaux présents dans les caves.

Plusieurs centaines de constituants ont été identifiés et le développement de méthodes analytiques de plus en plus performantes permet d'allonger continuellement la liste. Ces molécules ont la particularité d'être détectées olfactivement à de très faibles concentrations (~ 5 ng/l).

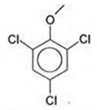
But :détecter, dans la phase vapeur (phase située entre le liquide et le bouchon), la présence de quatre composés, sans ouverture préalable de la bouteille.



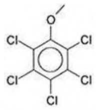
2,4-dichlorophénol



2,3,4-trichlorophénol



2,4,6-trichloranisole



pentachloranisole

Les analyses sont effectuées par GC couplée à des techniques SPME, APS, et une détection ECD, FID ou/et MS. Les détecteurs FID et MS, ne présentent pas toujours la sensibilité nécessaire. Ce n'est qu'avec l'utilisation en série de la SPME, de la GC et de l'ECD que nous avons réussi à détecter jusqu'au ppt les quatre composés dans des vins présentant le „goût de bouchon". Cette méthode est rapide, simple à utiliser et de plus, aucun traitement préalable de l'échantillon n'est nécessaire.

Analytical Chemistry **53**

Chromatographic techniques applied to the determination of UV-Curable inks

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UV technology inks consists of a mixture of acrylic acid esters, and resins of higher molecular weight also originating from acrylate chemistry [1]. After the curing under UV rays (or possibly electron beam), the ink polymerizes on its substrate with help of activators (photo-initiators).
Recent developments in UV formulation make these inks applicable in sensitive markets such as food-packaging. For that particular application, extensive control is undertaken to ensure the accuracy of the curing process and, ultimately, the completion of photo-polymerization.

Analytical assessments are made to ensure :

- The quality of the inks formulated
- The low concentration of residuals (uncured material)
- The complete monitoring of potentially migrant chemicals into food, according to current recommendations [2]
- Sensorial impact of the packaging for the final product

The analytical methods rely on the use of HPLC equipped with a photodiode array detector and a GC equipped with a mass detector. The control of the molecular weight of resins is ensured by size exclusion chromatography (SEC). Sensory analyses are based on « sniff » tests and « Robinson » tests [3,4].

[1] « Photoinitiation , photopolymerization and photocuring », J.P. Fouassier, Hanser publisher, 1995
[2] 90/128/EEC
[3] DIN Norm 10955
[4] ISO Norm 6658-1985 [E]

Chimie analytique **54**

Non-Perturbing fluorescent labeling of a neutral polysaccharide, schizophyllan.

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Rivers and lakes contain several organic macromolecules including humic and fulvic acids, proteins and polysaccharides. These organic biopolymers are known to play different roles in the aquatic environment according to their conformations. Schizophyllan, was used as a model for the aquatic polysaccharides. It consists of linear β-(1$\rightarrow$3)-D glucose residues with a β-(1$\rightarrow$6)-D-glucose side chain every three main chain residues.

Fluorescence Correlation Spectroscopy (FCS) allows the analysis of diffusion coefficients of low concentrations (typically <1 μM) of macromolecules. Because polysaccharides are not naturally fluorescent, their analysis requires that they are first labelled, in as non-perturbing a manner as possible. In this case, a rhodamine derivative, the rhodamine green X-succinimidyl ester hydrochloride (λ_{ex} = 495 nm, λ_{em} = 524 nm), was employed to tag the reducing end of schizophyllan. Diffusion coefficients of the schizophyllan/fluorophore conjugates were then determined by FCS. The hydrodynamic radius was estimated using the Stokes-Einstein equation and polymer length using the Broersma equation.

Size Exclusion Chromatography, using fluorescence and refractive index detectors, confirmed that the derivatization was effective and did not perturb the structure of the polysaccharide. Tapping mode Atomic Force Microscopy was used to characterize the schizophyllan molecules before and after their derivatization with the fluorophore. Polymer contour lengths and persistence lengths, both before and after labelling, were consistent with literature measurements.

Analytical Chemistry **55**

NMR Study of Bacterial Polysaccharides

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and F. Stingele[1]

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Lactic acid bacteria (LAB) are naturally occurring, food grade micro-organisms, which upon fermentation of milk secrete texturizing exopolysaccharides (EPS). This phenomenon is exploited in the production of fermented dairy products such as cheese and yogurts. The EPS structures of different LAB strains have been determined and revealed a large structural diversity. To date, the correlation of the structure of an EPS with its macroscopic rheological properties is not feasible.

In this presentation approaches for the structural investigation of bacterial EPS using chemical methylation analysis and high-resolution NMR spectroscopy will be outlined.

Analytical Chemistry **56**

Reflections on Selectivity in Separation Sciences and in Analytical Chemistry

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Selectivity with regards to an unbiased qualitative and quantitative analysis of analytes in more or less complex sample matrices is one of the most important criteria in analytical chemistry. This, however, cannot be discussed isolated without considering also sensitivity as most striving value taking into account that signals may suffer from interferences thus from “chemical” noise of the detection signal in addition to electronic noise. With other words, selectivity can be related to the analyte selective detection signal but also to selectivity in separation sciences when one takes advantage of analyte selective interactions between a chemo-selective medium (e.g. surface, reaction partner, surfactant, chelating agent and many more chemical entities and compartments) and the analyte(s) in question.
In this context and to stress the point particular emphasis will be given in this lecture towards “enantioselectivity” in separation sciences which has to be considered as a particular case of selectivity which is directed by spatially controlled interactional phenomena. Similar principles are perfectly in place in the various forms of “biorecognition cascades” where high selectivity is of utmost importance to read and to duplicate informations stored by the molecules, by the sequence of macromolecular entities, as e.g. proteins and DNAs, but also by molecule assemblies, including their three dimensional structure and conformation.
During this lecture some of these consideration will be discussed thus reflecting the importance of the selectivity term used in analytical chemistry and sometimes confused with specificity.

Analytical chemistry **57**

Nano-LC and capillary electrophoresis coupled to electrospray ionisation mass spectrometry for the detection of amyloid-β peptide variants

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[1] Laboratory of Pharmaceutical Analytical Chemistry, University of Geneva
[2] Biology of Ageing Laboratory, University of Geneva

Alzeihmer's disease (AD) is a neurodegenerative disorder and the major cause of dementia in the elderly. AD is characterised pathologically by the progressive deposition of a specific form of amyloid in the brain, the amyloid-β peptide (Aβ). Aβ is present in two principal variants, one that contains 40 amino acid residues ($A\beta_{1-40}$) and one extended variant that contains 42 amino acid residues ($A\beta_{1-42}$). The recent identification of Aβ from circulation seems indicate that quantification of Aβ levels in plasma could offer a simple diagnostic for AD.

In this work, nano-LC and capillary electrophoresis (CE) coupled to mass spectrometry (MS) were compared to determine the most appropriate technique to reach the usual Aβ concentration in plasma or serum. Both a 75 µm I.D. nano-LC column or a 50 µm I.D. CE capillary were coupled to a single quadrupole mass spectrometer with the use of a sheath-liquid electrospray (ESI) interface. The latter is the preferred interface for on-line coupling of CE or nano-LC with MS. Its capability to generate ions with multiple charges allows the detection for even large species such as peptides or proteins. Furthermore, *m/z* data of multiple charged ions observed can be mathematically deconvoluted to give original masses of the species.

Even if CE is a powerful separation technique, its main disadvantage remains its low sensitivity due to its limited injection volume. On the other hand, nano-LC with a column-switching setup was found to be a powerful technique allowing detection of Aβ at the ppb level (few femtomoles injected) according to its higher sample loading capability.

Analytische Chemie **58**

Die Visualisierung des Verdampfungsprozesses in der heissen Verdampferkammer des klassischen split und splitlosen GC-Injektors

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Die Kapillar-Gaschromatographie kämpft oft mit nicht reproduzierbaren Ergebnissen. Dabei liegen die Fehlerquellen vielfach schon im Injektor. Der Verdampfungsprozess in der heissen Verdampferkammer war schwer zu erfassen und bot Anlass zu vielen Spekulationen. Mit Hilfe der nachfolgend beschriebenen Versuchsanordnung kann die Verdampfung sichtbar gemacht und die Vorgänge im Injektor beobachtet werden.

Eine Injektorimitation aus Glas wurde in einem Heizbad auf 200 °C thermostatisiert; als Probe wurden Perylenlösungen eingespritzt [1]. Perylen diente als Indikator unverdampfter Probenflüssigkeit: unter UV-Bestrahlung zeigt gelöstes Perylen starke Fluoreszenz, welche nach dem Verdampfen des Lösungsmittels erlischt. Die Experimente wurden gefilmt, auf den Computer übertragen und ausgewertet [2].

Die Videos zeigen wie die Probenflüssigkeit bei unterdrückter Verdampfung in der Spritzennadel diese als Strahl verlässt, Hindernisse umkurven kann, oft am Säuleneingang vorbeischiesst und wilde Bewegung ausführt. Viele der Röhrchen mit eingebauten Hindernissen stoppen die Flüssigkeit nicht zuverlässig. Packungsmaterialien mit geringer thermischer Masse (z.B. Glaswatte) saugen die Probenflüssigkeit auf, weil sie in der Auftreffzone sofort auf den Lösungsmittelsiedepunkt abgekühlt werden. Wird die Spritzennadel auf Injektortemperatur erhitzt, erzeugt partielle Verdampfung in der Nadel einen Thermosprayeffekt: die Flüssigkeit vernebelt und verdampft aus kleinen, in der Gasphase schwebenden Tröpfchen [3].

[1] K. Grob, M. DeMartin, *J. High Resol. Chromatogr.* **1992**, 15, 335.
[2] M. Biedermann, *"Visualization of the Evapotarion Process during Classical Split and Splitless Injection in GC"*, CD-ROM, **2000.**
[3] K. Grob, M. Biedermann, *J. Chromatogr. A*, submitted.

Analytical Chemistry **59**

Stop-flow time slice LC/NMR and LC/MS^n of *Gnidia involucrata*: a rational approach for a rapid chemical screening

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In the course of our investigation of the Thymelaeaceae [1], the methanolic extract of the aerial parts of *Gnidia involucrata* Steud. ex A. Rich., an African species of this family used in the traditional medicine of Zimbabwe, has been studied. In order to obtain a rapid evalutation of the chemical composition of this extract, LC/UV/APCI-MS^n and LC/NMR were performed. This type of approach has indeed already proved its usefulness for the rapid identification of various plant metabolites [2]. The LC/MS analyses of the crude extract gave the molecular weights and useful fragment information for most of the UV-active constituents. LC/^{1}H-NMR in the on-flow mode, however, gave ^{1}H-NMR information only for the four main compounds because of the inherent lack of sensitivity of this method. In order to obtain satisfactory ^{1}H-NMR data on the minor constituents directly in the crude extract, a new procedure was adopted. HPLC conditions were optimised in order to work on an analytical RP-18 separation column with radial compression, allowing a very high loading. With this column, 20 mg of crude extract were separated in a single run without compromising the LC resolution. To enhance sensitivity, a 15-hour "time-slice" LC/NMR experiment was performed. This experiment allowed the acquisition of twenty well resolved spectra. Combination of LC/APCI-MS^n and ^{1}H-NMR spectra led to the partial identification of some of them. Further evaluation of the LC/NMR data is still underway.

[1] J. Ferrari, C. Terreaux, S. Sahpaz, J.D. Msonthi, J.-L. Wolfender, K. Hostettmann, *Phytochem.* **2000**, in press.
[2] J.-L. Wolfender, K. Ndjoko, K. Hostettmann, *Curr. Org. Chem.* **1998**, 2, 575.

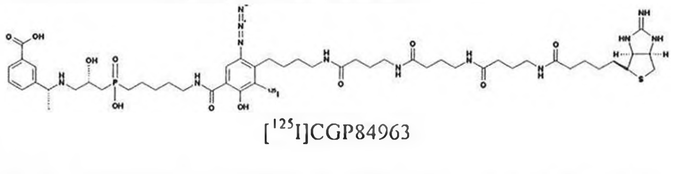
Medicinal Chemistry **60**

Ligands for the Isolation of GABA$_B$ Receptors

Wolfgang Froestl, Bernhard Bettler, Helmut Bittiger, Jakob Heid, Klemens Kaupmann, Stuart J. Mickel and Dietrich Strub

Novartis Pharma AG, Research Department, CH-4002 Basel

In 1997 Kaupmann *et al.* succeeded in cloning two splice variants of the metabotropic GABA$_B$ receptor designated GABA$_B$ R1a (960 amino acids) and GABA$_B$ R1b (844 amino acids) [1]. Although the amino acid sequences are now known, precise information on the three-dimensional environment of the GABA$_B$ R1 binding site is still lacking. Malitschek *et al.* showed that the amino acids of the seven transmembrane helices are not essential for ligand binding as extracellular, soluble GABA$_B$ receptor fragments are perfectly able to bind antagonists [2].
We synthesized affinity chromatography radioligands for the isolation and purification of the recombinantly expressed soluble receptor fragments to obtain crystalline receptor fragment-ligand complexes for X-ray structure determination. The ligand [^{125}I]CGP84963 (K_D = 2 nM) combines, in one molecule, a GABA$_B$ receptor binding part, an azido-salicylic acid as photoaffinity moiety and 2-iminobiotin, which binds to avidin in a reversible, pH-dependent fashion.



[^{125}I]CGP84963

[1] K. Kaupmann, K. Huggel, J. Heid, P.J. Flor, S. Bischoff, S.J. Mickel, G. McMaster, C. Angst, H. Bittiger, W. Froestl, B. Bettler, *Nature* **1997**, 386, 239.
[2] B. Malitschek, C. Schweizer, M. Keir, J. Heid, W. Froestl, J. Mosbacher, R. Kuhn, J. Henley, C. Joly, J.-P. Pin, K. Kaupmann, B. Bettler, *Mol. Pharmacol.* **1999**, 56, 448.

Medicinal Chemistry **61**

ORL1 Receptor ligands: Structure-Activity Relationships of 8-substituted 1-phenyl-1,3,8-triaza-spiro[4.5]decan-4-ones

Stephan Röver, Geo Adam, Andrea M. Cesura, Frank M. Dautzenberg
François Jenck, Sabine Kolczewski and Jürgen Wichmann

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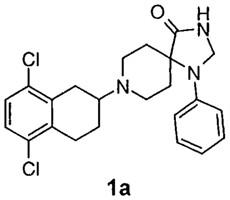
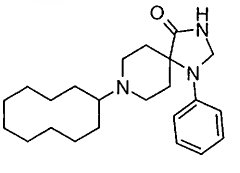
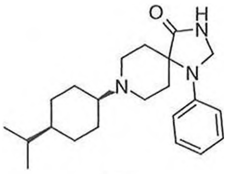
The discovery of 8-(5,8-dichloro-1,2,3,4-tetrahydro-naphthalen-2-yl)-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one, **1a**, as a high affinity ligand for the human ORL1 (Orphanin FQ/nociceptin) receptor led to the synthesis of a series of optimized ligands.


1a

Surprisingly, the unsophisticated and achiral 8-cycloalkyl-1-phenyl-1,3,8-triaza-spiro[4.5]decan-4-ones show remarkable affinity for the ORL1 receptor. Optimizing for selectivity we show that the maximum of affinity for the ORL1 receptor and selectivity vs. the μ, κ and δ opioid receptors is achieved for 8-cyclodecyl-1-phenyl-1,3,8-triaza-spiro[4.5]decan-4-one **2e** and 8-(*cis*-4-isopropyl-cyclohexyl)-1-phenyl-1,3,8-triaza-spiro[4.5]decan-4-one **2q**. The identified compounds (**2e, 2q**) are more or less equipotent to the natural ligand itself, both in the binding assay and in the functional GTPγS assay.


2e


2q

Medicinal Chemistry **62**

AMP397A, a novel broad spectrum anticonvulsant with potential benefit for therapy-resistant epileptic patients

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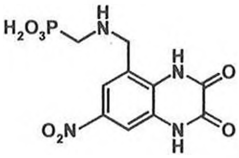
AMP397A, a 5-aminomethylquinoxaline-2,3-dione derivative, is a new type of antiepileptic agent. It is the first competitive AMPA antagonist combining high affinity for the receptor with good *in vivo* potency and oral bioavailability.


AMP397A

[^{3}H]CNQX binding: IC_{50} = 11 nM

AMP397A demonstrated anticonvulsant activity in a wide range of animal models of epilepsy, including electroshock- and chemically-induced seizures in mice, and in genetically epilepsy-prone rats. AMP397A also delayed the development of kindling and diminished seizure severity in fully kindled rats. This animal model reflects complex partial seizures, the largest subtype of therapy-resistant epilepsies. In summary, the novel mechanism of action of AMP397A as compared to marketed antiepileptic drugs, combined with broad-spectrum anticonvulsant efficacy, may offer a unique opportunity for refractory patients of various seizure types, and thus cover an undisputed medical need.

Medicinal chemistry **63**

Hydroxamic acid derivatives as peptide deformylase inhibitors and antibacterial agents

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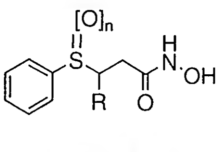
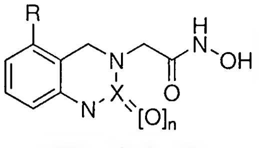
Low molecular weight hydroxamic acid derivatives (**1, 2**) have been synthesized and found to be potent inhibitors of *E. coli* peptide deformylase (PDF). Most of the compounds synthesized and tested displayed antibacterial activities that cover several pathogens found in respiratory tract infections, including *Chlamydia pneumoniae, Mycoplasma pneumoniae, Haemophilus influenzae* and *Moraxella catarrhalis*. The potential of these compounds as antibacterial agents is discussed with respect to selectivity, intracellular concentrations in bacteria, and potential for resistance development.


1 (n=1,2)


2 (X = C; n = 1)
(X = S; n = 2)

Chimie thérapeutique **64**

Convergent Synthesis of a family of (1→3)-*C*-linked Disaccharides starting from Isolevoglucosenone and Levoglucosenone

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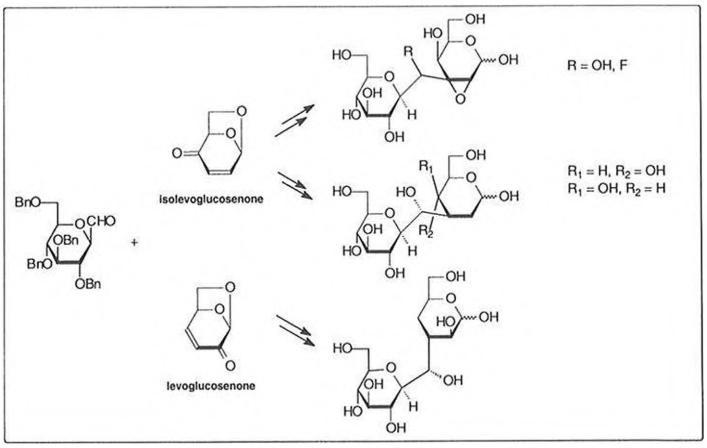
A Oshima Nozaki coupling reaction [1] between an aldehyde and isolevoglucosenone [2] or levoglucosenone provided enones from which five (1→3)-*C*- disaccharides have been synthetised:



These *C*-linked disaccharides are resistant to hydrolytic enzymes and as such, are potential inhibitors of glycosidases and glycosyltransferases.

[1] A. Itoh, S. Ozawa, K. Oshima, H. Nozaki; *Bull. Chem. Soc. Jpn.* **1981**, *54*, 274-278.
Y.-H. Zhu, R. Demange, P. Vogel; *Tetrahedron: Asymmetry* **2000**, *11*, 263-282.
[2] D. Horton, J.P. Roski, P. Norris; *J. Org. Chem.* **1996**, *61*, 3783-3793.

Medicinal Chemistry **65**

Salicylanilides: Potent and Selective ATP-Competitive Inhibitors of the EGF-R Protein Tyrosine Kinase

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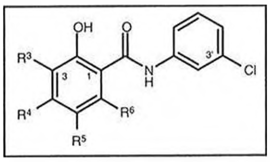
‡ Oncology Research, Novartis Pharma AG, CH-4002 Basel

Epidermal growth factor receptor (EGF-R) protein tyrosine kinase (PTK) is involved in epithelial proliferation and has been strongly implicated in malignant tumor growth. Therefore, the EGF-R PTK was selected as a target for the rational design of selective ATP-competitive inhibitors.

3'-Chlorosalicylanilide showed inhibition of EGF-R PTK (IC_{50}: 10.2 μmol) and was chosen as a lead compound. According to the pharmacophore model [1], which is based on structure-activity relationship studies (SAR) and computer assisted molecular modelling (CAMM), modifications of the structure led to potent and selective inhibitors, such as **1** and **2**.



	R^3	R^4	R^5	R^6	IC_{50} (EGF-R ICD)
1	H	OH	H	OH	32nM
2	H	OMe	OH	H	57nM

[1] P. Furet, G. Caravatti, N. Lydon, J.P. Priestle, J.M. Sowadski, U. Trinks, P. Traxler, *J. Com. Mol. Des.* **1995**, *9*, 465.

Medicinal Chemistry **66**

A Novel Chemical Approach to Glycosylated Sulfopeptides

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[a]Institute of Organic Chemistry, University of Lausanne, CH-1015 Lausanne, Switzerland; [b]Division of Hematology, Centre Hospitalier Universitaire Vaudois (CHUV), CH-1011 Lausanne, Switzerland.

Tyrosine O-sulfation and N- or O- glycosylation are two important posttranslational modifications found in mature proteins, involved in diverse biological functions such as modulation of protein folding, intra- and intercellular trafficking, receptor binding and cell signaling. In the search of potential inhibitors for the first step in the cell adhesion cascade, a novel strategy was developed for the chemical synthesis of glycosylated sulfopeptides resembling a region of P-selectin glycoprotein ligand-1 (PSGL-1), a dimeric membrane mucin involved in selectin mediated cell adhesion. Evidence suggests that the N-terminus of the extracellular mature PSGL-1 is important for high affinity binding to P-selectin with a pivotal role in recognition of at least one tyrosine sulfate residue either at position 46, 48 or 51 and a glycosylated threonine within that segment. Here, we present a straightforward approach to glycosulfopeptides based on a combination of acid labile protecting groups and resin and the chemoselective oxime bond formation for the 'post-synthetic' introduction of the carbohydrate moiety. The sulfated N-terminal peptide sequence was assembled using Fmoc-Tyr(SO_3Na)-ONa as building block and functionalized selectively at ε-NH_2 lysine with an aminooxy acetic acid moiety for the subsequent ligation of a reducing sugar in aqueous solution. In contrast to the inherent heterogeneity of post-translational modifications of recombinant proteins and the intrinsically low quantities of glycosylated sulfopeptides obtained in vitro by the chemoenzymatic approach, this chemical strategy offers several advantages. The insertion of Tyr sulfate residues and glycans is (i) possible at defined positions, (ii) renders complex protection/deprotection schemes superfluous and (iii) allows for the generation of sugar libraries for a systematic investigation of the role of glycans in molecular recognition processes.

Medicinal Chemistry **67**

Functional Mimetics for Molecular Recognition Studies

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Gabriele Tuchscherer,[1]

[1]Institute of Organic Chemistry, University of Lausanne, CH-1015 Lausanne, Switzerland; [2]Division of Hematology, Centre Hospitalier Universitaire Vaudois (CHUV), CH-1011 Lausanne, Switzerland

Despite the progress in design and synthesis of bioactive compounds, the construction of protein-like folding motifs as structurally stable scaffolds for the introduction of 'function' represents one of the major objectives in protein de novo design. As a most versatile concept in drug development, we use topological templates for mimicking essential features of biologically active compounds. In conceptually separating structure and function, we have designed a chimeric 4-helix bundle TASP based on the ROP (repressor of primer) protein and the cell adhesion glycoprotein E-selectin aimed at inhibiting an early stage in the cell adhesion cascade, in particular leucocyte adhesion. To obtain a stable bundle structure, the core residues from the antiparallel homodimeric ROP protein have been taken to ensure optimal internal packing and thus, a defined bundle structure. In a second step, the surface of E-selectin which is covered upon binding to its counterreceptor PSGL-1 has been matched onto the surface formed by two neighboring helices in the TASP molecule, including the Ca^{2+} complexing site. The antiparallel attachment of the helices was achieved via chemoselective ligation using a two-step procedure, i.e. selective thioether bond formation with orthogonally protected Cys residues in the template and the Br-CH_2CO- moiety at the N- or C- terminus of the helices. Conformational studies and in vitro assessment of the potential inhibitory effect of such a chimeric bundle arrangement will be presented.

Medicinal Chemistry **68**

Chemistry and Biology of Epothilones – Fully Synthetic Analogs and Semi-synthetic Derivatives

Karl-Heinz Altmann, Andreas Flörsheimer, Girgio Caravatti, Guido Bold, Markus Wartmann

Novartis Pharma AG, TA Oncology Research

Epothilones A and B (Fig. 1: R = H, CH_3) are naturally occurring microtubule depolymerization inhibitors, which exhibit potent *in vitro* and *in vivo* antiproliferative activity.

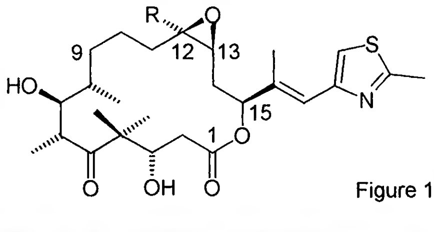

Figure 1

Epothilone B (Fig. 1: R = CH_3) is a 3-30-fold more potent inhibitor of human cancer cell growth than paclitaxel in paclitaxel-sensitive cell lines and in paclitaxel-resistant lines exceeds paclitaxel activity by 10^2 - 10^3-fold. In order to gain a better understanding of the structural requirements for epothilone-mediated cytotoxicity and anti-tumor activity and to discover analogs with similar potency but perhaps better tolerability *in vivo*, we have investigated a series of structural modifications primarily involving the epoxide site (C12 -C13), the C9-C12 region, and the heterocyclic side-chain of epothilones. The synthesis of the corresponding analogs will be presented and the impact of the modifications on tubulin polymerization activity as well as cytotoxicity will be discussed.

Medicinal chemistry **69**

Tetrahydroisoquinolines as NMDA-NR2B subtype selective antagonists

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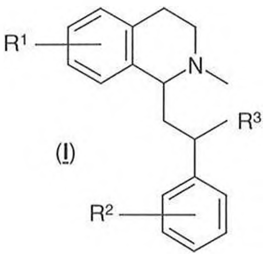
Pharma Division, Preclinical Research, F. Hoffmann-La Roche Ltd., CH-4070 Basel

For the acute treatment of stroke NMDA-NR2B subtype selective antagonists are known to be highly efficacious in animal models. In an ongoing medicinal-chemistry program substituted tetrahydroisoquinolines (I) have been identified as potent ligands of this receptor.

Structure activity relationships and stereochemical aspects will be presented.



(I)

Medicinal Chemistry **70**

Antagonists of the association of hdm2 with the tumor suppressor p53 as new antitumor agents

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[1]Oncology Research and [2]Core Technologies, Novartis Pharma Inc., CH-4002 Basel, Switzerland

The p53 tumor suppresor gene is a multifunctional protein that regulates cell proliferation by induction of growth arrest or apoptosis in response to DNA damage and/or stress stimuli. Among the known mechanisms by which the tumor suppressor functions of p53 can be abrogated, we are interested in the regulation of p53 by the human double minute 2 (hdm2) oncoprotein, which targets p53 for degradation by the ubiquitin pathway. If this pathway operates in tumor cells containing low levels of wild-type p53, the disruption of the p53/hdm2 interaction should result in p53 accumulation and activation of its tumor suppression functions. The disruption of this protein-protein interaction is therefore an attractive approach for cancer therapy because it provides the possibility to regulate the threshold of the p53 response with a therapeutic agent.

As part of our drug discovery program to identify antagonists of the association of hdm2 with p53, we have attempted to determine the amino acid specificities of the binding pockets of hdm2 to establish a pharmacophore model for this protein-protein interactions. Synthetic and phage display libraries allowed to identify an 8-mer peptide as the minimal recognition motif retaining μM affinity for hdm2 (Ac-Phe-Met-Asp-Tyr-Trp-Glu-Gly-Leu-NH_2, IC_{50}= 8.9 ± 0.6 μM). This peptide was used as a molecular framework for mapping the binding pockets of hdm2. Combining conformational constrains as selected by molecular modeling with functional groups that are able to establish additional electrostatic and van der Waals interactions with the hdm2 protein, we have been able to increase the hdm2 binding affinity of our initial 8-mer peptide 1,700-fold (Ac-Phe-Met-Aib-Pmp-*6-Cl*-Trp-Glu-Ac_3c-Leu-NH_2, IC_{50}= 5 ± 1 nM). The new interactions identified and experimentally confirmed in this work could be directly applied to the optimization of non-peptidic leads or incorporated into the *"de novo"* design of antagonists of the p53/hdm2 protein-protein interaction.

Medicinal Chemistry **71**

CHARACTERIZATION OF THE NON-COMPETITIVE BINDING SITE OF THE GROUP I METABOTROPIC GLUTAMATE RECEPTORS USING SUBTYPE SELECTIVE LIGANDS

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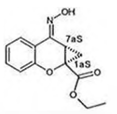
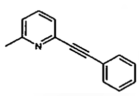
Metabotropic glutamate receptors (mGlu) are G-protein coupled receptors (GPCRs) and constitute with the $GABA_B$, vomeronasal and the Ca^{2+}-sensing receptors a particular subfamily within the GPCRs family of receptors. mGlu1 and mGlu5 receptor subtypes constitute the Group I of the mGlu receptor family. Antagonists acting at these receptors can be classified in two classes: 1) competitive antagonists are amino acid derivatives and interact at the Glu binding site located in the large extracellular domain 2) non-competitive antagonists structurally non-related to amino acid. Recently, two subtype selective antagonists CPCCOEt (2-hydroxyimino-1a,2-dihydro-1*H*-7-oxa-cyclopropa[b]-naphthalene-7a-carboxylic acid ethyl ester) and MPEP (2-methyl-6-(phenylethynyl)pyridine) acting at the mGlu1 and the mGlu5 receptors, respectively have been discovered.



(-)-CPCCOEt



MPEP

Using chimeric/mutated receptors constructs we have found that these antagonists act at a novel pharmacological site located in the trans-membrane (TM). Specific non-conserved amino acid residues in the TM domain have been identified which are necessary for the inhibition by CPCCOEt and MPEP of the mGlu1 and mGlu5 receptors, respectively. Using molecular modeling a model of the TM domain was built for both mGlu1 and mGlu5 receptor subtypes. Docking of CPCCOEt and MPEP into their respective model showed that both antagonists bind to the same microdomain formed by the transmembrane domains TMVII, TMVI and TMIII.

Medicinal Chemistry **72**

Application of the One-Bead-One-Compound Approach in Drug Discovery

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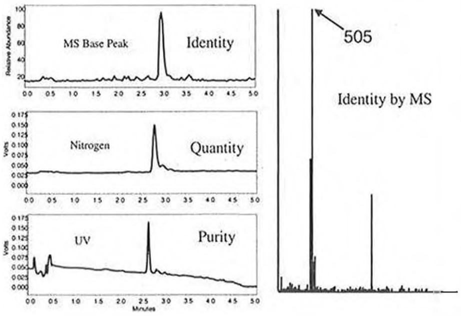
The interest in increasingly efficient, combinatorial chemistry based lead finding approaches led us to the development of methodologies for a closer integration of rapid compound preparation and screening. The perception is that the exploitation of the *Split-and-Mix* process [1], could be maximized by directing the technological progress to the use of beads as carriers of individually distinct chemical entities, while allowing to screen such compounds in solution. At one stage of the screening process the beads are conveyed to separate compartments in order to release single compounds into solution. The availability of uniformly sized beads with a high loading capacity, as well as a broadly applicable and accurate method for the quantification of the released material are both crucial.We devoted particular attention to the analysis of single bead eluates by microanalytical LC/MS in combination with a nitrogen detection system.



[1] A. Furka, F. Sebestyén, M. Asgedom, G. Dibó, in *Highlights of Modern Biochemistry, Proceedings of the 14th International Congress of Biochemistry, Prague, Czechoslovakia, (1988)* (VSP, Utrecht, Netherlands, 1988), vol. 13, p. 47.

Medicinal Chemistry **73**

Describing hormone-membrane interactions by NMR

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Neuropeptide Y (NPY) is a 36 amino acid peptide hormone involved in cardiovascular regulation and control of food-uptake[1]. So far, binding of NPY to the loop regions from five different subtypes of G-protein coupled receptors has been described. Recently, we have developed a selective agonist of NPY at the Y-5 receptor[2]. The structure of this NPY mutant in solution is presented and compared to wild-type NPY.The overall fold is very similar but differences are found in the C-terminal hexapeptide.

Furthermore, we have elucidated the structure of NPY bound to membrane-mimicing DPC micelles by two-dimensional nmr spectroscopy. Residues important for anchoring onto the membrane are identified from studies utilizing doxylstearates as spin labels. ^{15}N relaxation data are recorded to determine the stability of the C-terminal helix in the membrane-bound form. The relaxation data are additionally used to determine whether the flexible N-terminus folds back onto the C-terminal helix.

Similarly, the rigidity of free (dimeric) NPY in solution is characterized. The dimerization interface is described from studies utilizing spin-labels covalently attached to NPY. The residues involved in the intermolecular contacts are compared to those involved in binding of NPY to the membrane.

From these data a three-step model for binding of NPY to its receptor is developed that is based upon the "Compartment Theory" from Schwyzer [3]. The importance of the mode of membrane anchoring for pre-orientation of residues of NPY involved in making contacts to the receptor is discussed. Preliminary results from mutants of NPY in which some of these positions are exchanged are presented. These structural studies may deliver useful input for knowledge-based development of drugs binding to membrane-bound receptors.

[1] A.G. Beck-Sickinger, G. Jung, Biopolymers (Peptide Science) **1995**, 37, 123.
[2] C. Cabrele, M. Langer, R. Bader, H. Wieland, H.N. Doods, O. Zerbe, A.G. Beck-Sickinger, J. Biol. Chem., in press.
[3] R. Schwyzer, Biopolymers **1995**, 37, 5.

Inorganic Chemistry **74**

Hydrodenitrogenation of *o*-Propylaniline by Transition Metal Phosphides

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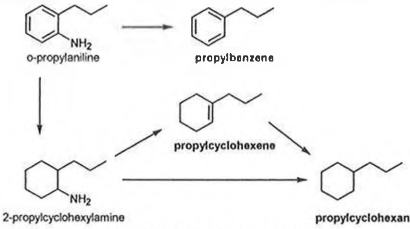
Apart from sulfides, transition metal carbides, nitrides and phosphides are known to act as catalysts in hydrotreating reactions. In contrast to the large body of research on nitrides and carbides [1], research into transition metal phosphides is limited [2].

After a detailed study of molybdenum phosphide MoP as hydrodenitrogenation catalyst [3], we prepared other binary (Co_2P, Ni_2P, WP) and ternary (CoMoP, NiMoP, CoWP, NiWP) transition metal phosphides. All phosphides are easily obtained by reducing a metal oxide/phosphate precursor in a flow of H_2 at elevated temperature. The as-synthesized phosphides were tested in the hydrodenitrogenation of *o*-propylaniline at 643 K and 3 MPa.

All the phosphides were catalytically active and exhibited properties similar to those of conventional transition metal sulfides. We estimated the intrinsic activity of the different catalysts by taking the respective structures into consideration.



HDN reaction network of *o*-propylaniline

[1] 'The Chemistry of Transition Metal Carbides and Nitrides', Ed. S.T. Oyama, Blackie Academic and Professional, London, **1996**.
[2] W. Li, B. Dhandapani, S.T. Oyama, *Chem. Lett.* **1998**, 207.
[3] C. Stinner, R. Prins, Th. Weber, *J. Catal.* **2000**, *191*, 438.

Inorganic Chemistry **75**

Outstanding Catalytic Properties of Ru-silica Hybrid-Aerogel in the Synthesis of N,N-Diethylformamide from CO_2, H_2 and $HN(Et)_2$

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Laboratorium für technische Chemie, ETH Zürich
Universiätstr. 6, CH-8092 Zürich

In previous studies [1-3] we have shown that microporous Ru-Silica xerogels containing Ru with mono- and bidentate phospine ligands exhibit excellent catalytic behaviour (high activity and 100% selectivity) in the synthesis of *N,N*-dimethylformamide from CO_2, H_2 and $HN(Me)_2$. Most favourable behaviour was observed with hybrid xerogels which were synthesized from the bidentate Ru-complex (I) $\{RuCl_2[P_2C_7H_{14}(Si(OEt)_3)_2]_2\}$ and tetraethoxysilane (TEOS) via a sol-gel process leading to a hybrid gel structure. A comparison of the catalytic behaviour of complex (I) in solution with that of the same complex after incorporation in the microporous silica matrix of the xerogel revealed that the heterogeneous catalytic reaction is slowed down by intraparticle diffusion limitations. Intrigued by this observation we prepared corresponding aerogels with mesoporous pore structure using a similar sol-gel process combined with ensuing low temperature supercritical drying with CO_2. The difference in the pore size distributions of the xero- and aerogels had a dramatic effect on their catalytic activity, whereas selectivity (100%) remained unaffected. The turnover frequency (TOF) measured for the xerogel was 2210 h^{-1} which was by far exceeded by the aerogel with a TOF of 18400 h^{-1}. Most striking, the activity of the aerogel was also greatly exceeding that of the bidentate complex (I) in the homogeneous reaction (TOF = 3313 h^{-1}).

[1] O. Kröcher, R.A. Köppel, M. Fröba, and A. Baiker, J. Catal. 178, 284 (1998).
[2] O. Kröcher, R.A. Köppel, and A. Baiker, Chimia 51, 48 (1997).
[3] L. Schmid, O. Kröcher, R.A. Köppel, and A. Baiker, Micro- Mesoporous Mater. 35/36, 181 (2000).

Inorganic Chemistry **76**

Catalytic *ortho*-Alkylation of Benzamide with Chiral Ir(I) Complexes

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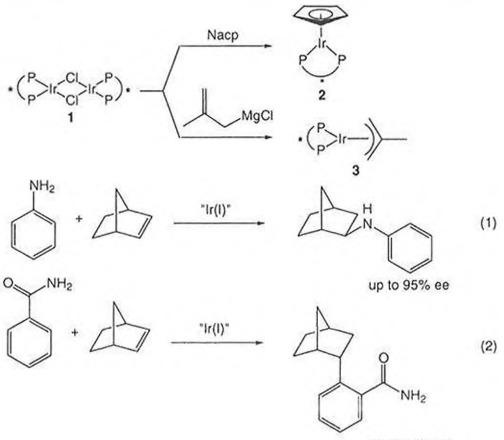
Ir(I) complexes of the type $[IrCl(PP)]_2$ **1** (PP = chiral, bidentate phosphine) are able to activate C—H- , O—H- and N—H-bonds of organic substrates [1], and act as enantioselective catalysts for the hydroamination of olefins [2]. Cleavage of the chloro-bridges of **1** with cyclopentadienyl sodium or 2-(Methallyl)MgCl gives new chiral complexes of type **2** and **3**, respectively.



Results for catalytic reactions (2) and (3) with complexes **1**, **2** and **3** as catalyst precursors will be presented.

[1] Dorta, R.; Togni, A. *Organometallics* **1998**, *17*, 5541.
[2] a) Dorta, R.; Egli, P.; Zürcher, F.; Togni, A. *J. Am. Chem. Soc.* **1997**, *119*, 10857. b) Togni, A. et al. *Pure Appl. Chem.* **1999**, *71*, 1531.

Inorganic Chemistry and Coordination Chemistry **77**

Asymmetric Copper-Catalyzed Cyclopropanations Using Chiral Bipyridine-Complexes

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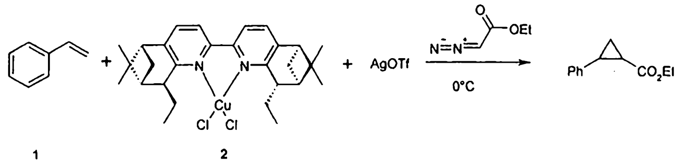
Cyclopropanation of styrene with diazoacetate in the presence of copper complexes was found to give the corresponding *trans*-cyclopropanecarboxylates as major products in good to high optical purity [1]. In our investigations the cyclopropanation of styrene 1 with ethyldiazoacetate in the presence of 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. The inactive dichloro-complex 2 has to be treated with AgOTf and then reduced to the copper(I)-species in situ by ethyldiazoacetate. Other similar copper-complexes gave less favorable results.



This work is supported by the Swiss National Science Foundation.

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[1] T. Katsuki, S. Tabuchi, K. Ito, *Synlett* **1992**, 575.

Inorganic Chemistry **78**

Nitration of Toluene with Nitric Acid and Acetic Anhydride over Zeolites : a Solid-state NMR Study

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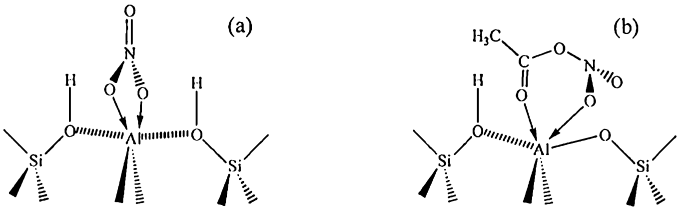
Laboratory of Technical Chemistry, Swiss Federal Institute of Technology (ETH), CH-8092 Zurich, Switzerland

Nitration of aromatic compounds, with particularly high regio-selectivity, can be monitored using zeolite beta as a catalyst and nitric acid in acetic anhydride as a nitrating agent [1]. Based on a comparative study using different zeolites, we concluded that the increased *para*-selectivity in the nitration of toluene is related to sites located in the micropores of the zeolite and originates from steric hindrance induced by adsorption rather than from classical shape selectivity [2]. In order to confirm these conclusions, multi-nuclear solid-state NMR spectroscopy investigations were carried out on zeolite-nitrating agent systems. The reversible transformation of framework aluminum from a tetrahedral into an octahedral environment upon interaction of the zeolite with nitric acid, was revealed by means of ^{27}Al NMR. ^{15}N NMR confirmed that nitric acid, as nitrate species (a), interacts strongly with framework aluminum of the zeolite. Our NMR results show that nitration occurs through surface-bonded acetylnitrate as the reactive nitrating species (b), which is consistent with selectivity being related to the steric hindrance effect, rather than to isolated nitronium ions.



[1] K. Smith, A. Mudsson, G. A. DeBoos, *J. Org. Chem.* **1998**, *63*, 8448.
[2] D. Vassena, A. Kogelbauer, R. Prins, *Stud. Surf. Sci. Catal.* 1999, *125*, 501.

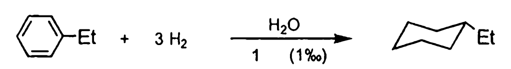
Inorganic and coordination chemistry **79**

Catalytic Hydrogenation of Aromatics under Biphasic Conditions: Isolation and Structural Characterisation of the Cluster Intermediate $[(\eta^6\text{-}C_6Me_6)_2(\eta^6\text{-}C_6H_6)Ru_3(\mu_2\text{-}H)_2(\mu_2\text{-}OH)(\mu_3\text{-}O)]^+$

Matthieu Faure, Ana Vallina Tesouro, Helen Stoeckli-Evans, Georg Süss-Fink *

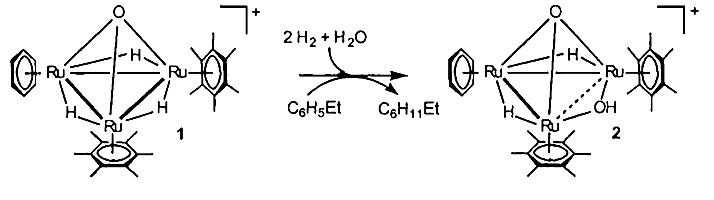
Institut de Chimie, Université de Neuchâtel, Case postale 2, CH-2007 Neuchâtel, Suisse

The warter-soluble cluster cation $[(\eta^6\text{-}C_6Me_6)_2(\eta^6\text{-}C_6H_6)Ru_3(\mu_2\text{-}H)_3(\mu_3\text{-}O)]^+$ (**1**) catalyses the hydrogenation of benzene and benzene derivatives to give the corresponding cyclohexanes under biphasic conditions [1].



110 °C, 60 bar, 15 min

The catalytic activity of **1** depends markedly on the substrate, an extremely high activity being observed for ethylbenzene (catalytic turnover frequency 3413 h^{-1}). The cationic species present in the catalytic mixture of the ethylbenzene hydrogenation could be isolated as the tetrafluoroborate salt and characterised as the cation $[(\eta^6\text{-}C_6Me_6)_2(\eta^6\text{-}C_6H_6)Ru_3(\mu_2\text{-}H)_2(\mu_2\text{-}OH)(\mu_3\text{-}O)]^+$(**2**).



With **2** as the catalyst, the catalytic activity is also much higher for the hydrogenation of other benzene derivatives.

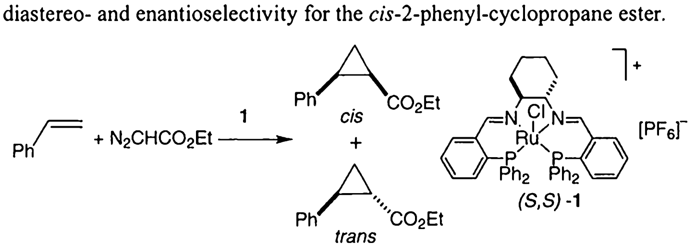
[1] M. Faure, M. Jahncke, A. Neels, H. Stoeckli-Evans, G. Süss-Fink, Polyhedron, 18, (1999), 2679-2685.

Inorganic and Coordination Chemistry **80**

A Ruthenium(II) Catalyst Boosts *cis*-Selectivity and Enantioselectivity of Asymmetric Cyclopropanation

S. Bachmann, M. Furler and A. Mezzetti*
Laboratorium für Anorganische Chemie, ETH Zürich, CH-8092 Zürich

Following our studies on the ruthenium-catalyzed asymmetric epoxidation of olefins with H_2O_2 as oxidant [1], we find now that the cationic ruthenium(II) complex **1** containing a tetradentate PNNP ligand catalyzes the asymmetric cyclopropanation of styrene with extremely high diastereo- and enantioselectivity for the *cis*-2-phenyl-cyclopropane ester.



The system reported here gives, besides excellent enantioselectivity, a cis/trans ratio of 93:7. This is, to the best of our knowledge, the best *cis*-selectivity yet obtained in asymmetric cyclopropanation [2-4].

catalyst	t / h	conv. (%)	cis / trans	ee (cis) (%)	ee (trans) (%)
1 (5 mol %)	20	56	93 / 7	95	23
1 (5 mol %)	2	30	91 / 9	91	36
1 (1 mol %)	2	28	83 / 17	82	4

Investigations with other substrates and PNNP ligands will be described.

[1] R. M. Stoop, A. Mezzetti, *Green Chem.* **1999**, *1*, 39.
[2] T. Aratani, Y. Yomeyoshi, T. Nagase, *Tetrahedron Lett.* **1982**, *23*, 685.
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[4] A. Pfaltz, *Acc. Chem. Res.* **1993**, *26*, 339.

Anorganische Chemie **81**

Flame Synthesis of Vanadia / Titania Nanoparticles for NO Removal

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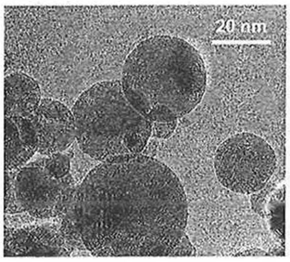
[1] Laboratorium für Technische Chemie, ETH Zentrum, CH-8092 Zürich
[2] Institut für Verfahrenstechnik, ETH Zentrum, CH-8092 Zürich

Vanadia on titania is a widely used catalyst for the selective catalytic reduction (SCR) of NO by NH_3. 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 vanadia/titania nanoparticles prepared in a methane air diffusion flame. The powders exhibit excellent catalytic behaviour in SCR of NO. Turnover frequency and selectivity to N_2 are comparable to those of the best catalysts prepared by wet chemical routes.

Particle producing flame



Well dispersed V_2O_5 on titania

Powders are characterized with high resolution transmission electron microscopy (HRTEM), energy dispersive X-ray fluorescence (EDX), electron spectroscopic imaging, nitrogen absorption (BET), X-ray diffraction (XRD), Laser Raman IR spectroscopy (LRS). Catalytic activity was measured in a continuous flow fixed-bed microreactor in the temperature range 363-663K.

Inorganic Chemistry **82**

Alcohol-induced P-C Bond Splitting in Chiral Ru(II)-Complexes

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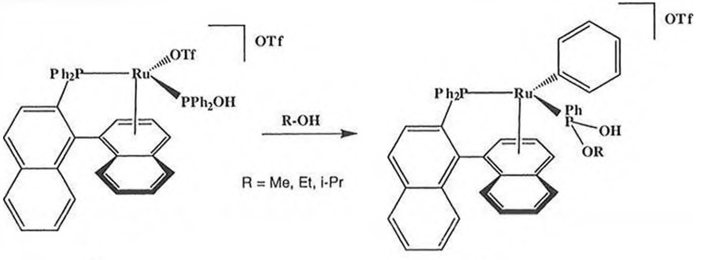
Universitätsstr. 6, CH-8092 Zürich, Switzerland

Recently, the acid-promoted splitting of a P-C bond in Ruthenium(II) complexes was reported upon treatment of a neutral bidentate diphosphine complex with stochiometric amounts of wet triflic acid to form the cationic triflate complex **1**.[1]



1 2

The reaction of the chiral arene-phosphine chelate **1** with simple alcohols affords a product, **2**, which arises from an unexpected P-C bond splitting. Complex **2** posses the a novel P-donor ligand P(OH)(OR)Ph and three different stereogenic centers: i) atropisomerism, i. e. binaphtyl, ii) a stereogenic Ruthenium atom and iii) a chiral phosphine ligand.
The structure of the propyl derivative was determined by X-ray diffraction.

[1] den Reijer, C. J.; Wörle, M.; Pregosin, P. S., *Organometallics* **2000**, *19*, 309

Inorganic Chemistry **83**

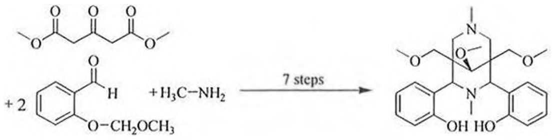
Synthesis of iron- and copper compounds with bispidine-type ligands, and their application in aromatic hydroxylation reactions

Peter Comba and Michael Merz

Universität Heidelberg, Anorganisch-Chemisches Institut, Im Neuenheimer Feld 270, D-69120 Heidelberg

The one-step hydroxylation of phenol and substitued phenoles is a convenient method for synthesizing dihydroxy-benzene derivatives. However, the currently available methods are unattractive because they lead to a low regio-selectivity and low yields. An additional problem is further oxydation of the products under the conditions of currently used methods.
Bispidine-typeligands are very rigid and highly preorganized for various metal ions.. We therefore anticipate that, depending on the metal ion and the substituents on the bispidine backbone, it might be possible to develop corresponding catalysts which lead to hight selectivities and good yields.

The parent ligand with two pyridine substituents (bis-methyl 2,4-pyridin-3,7-diazabicyclo[3.3.1]nonan-9-on-1,5-dicarboxylate) has a rich and interesting copper(II) chemistry but with iron(III) it does not form stable complexes. A substitution of the pyridine pendent groups to phenol was expected to improve this situation (see Figure for the ligand synthsis).

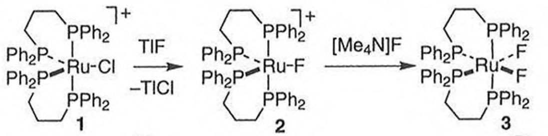


Inorganic and Coordination Chemistry **84**

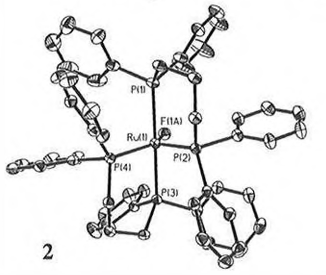
Fluoro Complexes of Ruthenium(II) as Tools for Metal-Mediated C—F Bond Formation

Peter Barthazy, Robert M. Stoop, Michael Wörle, Antonio Togni,* and Antonio Mezzetti*
Laboratorium für Anorganische Chemie, ETH Zürich, CH-8092 Zürich

We have prepared the 16-electron complex **2** and investigated its reactivity. The X-ray structures of **2** and **3** illustrate how the π-donation from the fluoride stabilizes the coordinatively unsaturated **2**.



1 2 3



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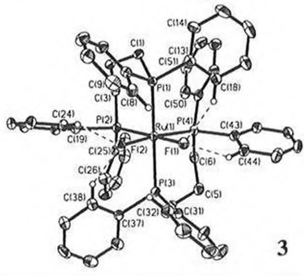
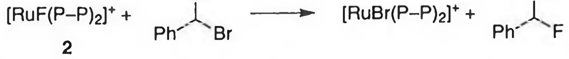


3

Activated alkyl bromides, such as **5**, react with **2** forming the corresponding fluorides:



2

[1] Barthazy, P.; Hintermann, L.; Stoop, R. M.; Wörle, M.; Mezzetti, A.; Togni A. *Helv. Chim. Acta* **1999**, *82*, 2448.
[2] Barthazy, P.; Stoop, R. M.; Wörle, M.; Togni, A. Mezzetti, A. *Organometallics* **2000**, in press.

Chimie minérale et de coordination

85

pH effect on the reactions of catalytically important Rh(I)-phosphine complexes in aqueous solution

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[2]Institut de Chimie Minérale et Analytique, Université de Lausanne, Suisse
Email: Gabor.Laurenczy-Batta@icma.unil.ch

Hydrolysis and hydrogenation of $[RhCl(TPPMS)_3]$, **1** and $[RhCl(CO)(TPPMS)_2]$, **2** was studied in aqueous solutions in a wide pH range (2<pH<11) in the presence of excess TPPMS, *meta*-sulfonatophenyldiphenylphosphine. In acidic solutions hydrogenation of **1** yields a mixture of *cis-mer*- and *cis-fac*-$[RhH_2Cl(TPPMS)_3]$, **3/a-b**, while in strongly basic solutions $[RhH(TPPMS)_3]$, **4**, is obtained, the midpoint of the equilibrium between these hydride species being at pH=8.2. This is the first successful ^1H and ^{31}P NMR characterization of a water soluble rhodium(I)-monohydride (**4**) bearing only phosphine ligands in addition to H^-. Hydrolysis of **2** is negligible below pH=9 and its hydrogenation results in formation of $[Rh(CO)H(TPPMS)_3]$, **5**, an analog to the well known and industrially used hydroformylation catalyst $[Rh(CO)H(TPPTS)_3]$ (TPPTS=*tris*(*meta*-sulfophenyl)phosphine). It was shown by pH-potentiometric measurements that formation of **5** is strongly pH-dependent in the pH 5-9 range and this gives an explanation for the observed but previously unexplained pH-dependence of several hydroformylation reactions. Conversely, the effect of pH on the rate of hydrogenation of maleic and fumaric acid catalyzed by **1** in the 2<pH<7 range can be adequately described by considering solely the changes in the ionization state of these substrates. All these results warrant the use of buffered (pH-controlled) solutions for aqueous organometallic catalysis.

This work was supported by the Office Fédérale de l'Education et de la Science, Suisse (OFES C98.0011) and the research is part of the collaboration within the COST D10/0001 Working Group.

Inorganic and Coordination Chemistry

86

Synthesis and Application of New Cyclic Ferrocenyl Diphosphines

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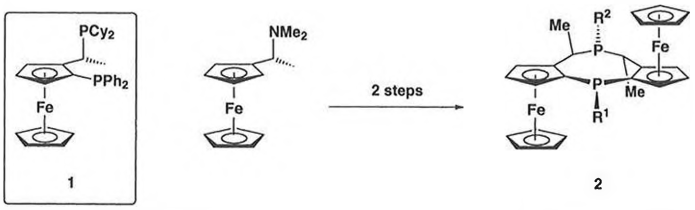
Laboratory of Inorganic Chemistry, Swiss Federal Institute of Technology ,
ETH-Zentrum, CH-8092 Zürich, Switzerland

Chiral ferrocenyl bisphosphines of the Josiphos type (**1**) are known to be powerful ligands in a variety of catalytic enantioselective reactions [1]. Ligands incorporating the phosphorus donor atoms into a cyclic structure are very rare.

With the aim of studying the influence of an enhanced conformational rigidity, we now prepared cyclic derivatives of type **2** in wich the P-atoms are part of an eight-membered ring. Compounds **2** are accessible by a two-step procedure from (*R*)-*N,N*-dimethyl-1-ferrocenylethylamine.



R^1 = Aryl, e.g., Ph
R^2 = Alkyl, e.g., Cy

The structural characterization of the new ligand and their Rh complexes will be presented. Preliminary experiments in catalytic hydrogenation have shown ligands **2** to give high enantioselectivities (92% ee for dimethyl itaconate).

[1] Togni, A. In *Metallocenes. Synthesis. Reactivity. Applications*; Togni, A.; Halterman, R.L., Eds.; VCH: Weinheim, Germany, 1998; pp 685-721.

Inorganic and Coordination Chemistry

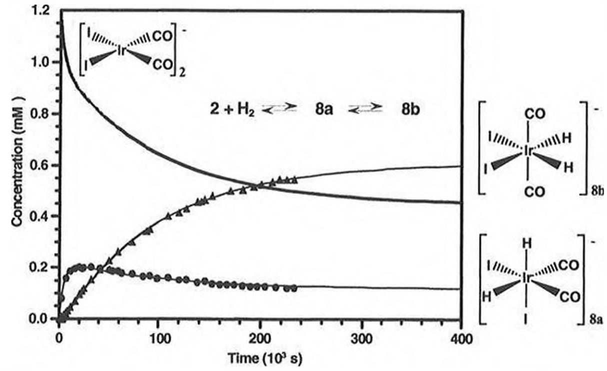
87

Speciation and Kinetics Related to Olefin Carbonylation in the Presence of *cis*-$[Ir(CO)_2I_2]^-$ Under CO and H_2 Pressure.

Raphaël Churlaud, Urban Frey, François Metz and André E. Merbach.

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

NMR and IR, under high pressure of H_2 and CO conditions, allowed us to characterize structurally and kinetically the numerous species involved in olefin carbonylation with *cis*-$[Ir(CO)_2I_2]^-$ catalyst.[1]



For example, H_2 addition to the catalyst is occurring through the kinetically favored species *all-cis*-$[IrH_2(CO)_2I_2]^-$, followed by the formation of the thermodynamically stable species *cis-trans-cis*-$[IrH_2(CO)_2I_2]^-$.

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[1] R. Churlaud, U. Frey, F. Metz, A. E. Merbach *Inorg. Chem.* **2000**, 39, 304.

Inorganic Chemistry

88

Binuclear Iron Species in Fe/ZSM-5 Zeolite Prepared by Chemical Vapour Deposition: a Spectroscopic Characterization

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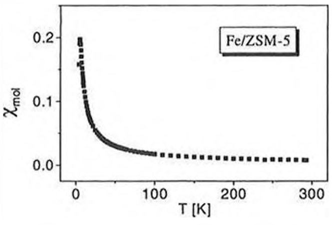
Laboratory for Technical Chemistry, Swiss Federal Institue of Technology
(ETH), CH-8092 Zurich

Fe-exchanged ZSM-5 zeolite is a very promising catalyst for the abatement of nitrogen oxide pollution [1]. The active Fe species, which is introduced into the zeolite cavities through sublimation of $FeCl_3$, has been suggested to be a binuclear $[Fe–O–Fe]^{2+}$ complex located at the ion-exchange positions of the zeolite [2].

We found spectroscopic evidence that such diiron complexes exist through the combined use of EXAFS, Raman, UV-Vis and magnetic susceptibility measurements.

EXAFS analysis unambiguously revealed the presence of binuclear Fe clusters with an average Fe–Fe distance of 3.05 Å and an Fe–Fe coordination number of 1. Vibration modes, typical of [Fe–O–Fe] moieties, were detected by Raman spectroscopy; the magnetic susceptibility showed a temperature dependence (see Figure) typical of binuclear [Fe–O–Fe] species involved in antiferromagnetic coupling.



Magnetic susceptibility vs. temperature.

[1] X. Feng and K. Hall, *J. Catal.* **1997**, *166*, 368.
[2] H.-Y. Chen and W.M.H. Sachtler, *Catal. Today* **1998**, *42*, 73.

Inorganic and Coordination Chemistry **89**

The Cluster Dication $[H_6Ru_4(C_6H_6)_4]^{2+}$ Revisited: The First Cluster Complex Containing an intact H_2 Ligand?

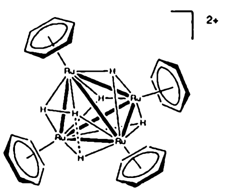
Aline Maisse-François[a], Georg Süss-Fink*[a], Thomas Fox[b], Heinz Berke[b],
Helen Stoeckli-Evans[a], Régis Gautier[c], Jean-Yves Saillard[c]

[a] *Institut de Chimie, Université de Neuchâtel, Case postale 2, CH-2007 Neuchâtel*
[b] *Anorganisch-Chemisches Institut des Universität Zürich, CH-8057 Zürich*
[c] *Université de Rennes I, UMR-6511, F-35042 Rennes Cedex.*

The electron-precise (60e) hexahydrido cluster $[H_6Ru_4(C_6H_6)_4]^{2+}$ (**1**) is in equilibrium with the electron-deficient (58e) tetrahydrido cluster $[H_4Ru_4(C_6H_6)_4]^{2+}$ (2) [1].

$$\underset{(1)}{[H_6Ru_4(C_6H_6)_4]^{2+}} \rightleftharpoons \underset{(2)}{[H_4Ru_4(C_6H_6)_4]^{2+}} + H_2$$

A re-examination of the hexahydrido cluster **1** suggests the dication $[H_6Ru_4(C_6H_6)_4]^{2+}$ to contain an intact H_2 ligand interacting with one of the four hydride ligands over a triangular face of the Ru_4 tetrahedron. Evidence for this is based on low-temperature NMR T_1 data, X-ray crystal data and DFT calculations [2].



Cluster **1** readily transfers H_2 onto other substrates such as olefins or molecular oxygen [1]. Therefore, the equilibrium between **1** and **2** can be used for catalytic hydrogenation reactions.

$$CO_2 + H_2 \longrightarrow HCOOH$$

Thus, cluster **1** was found to catalyse the hydrogenation of carbon dioxide in aqueous solution to give formic acid without the presence of an amine being required.

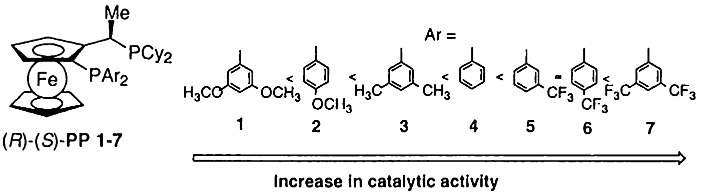
[1] G. Meister, G. Rheinwald, H. Stoeckli-Evans, G. Süss-Fink, J. Chem. Soc., Dalton Trans. (1994), 3215.
[2] G. Süss-Fink, L. Plasseraud, A. Maisse-François, H. Stoeckli-Evans, H. Berke, T. Fox, R. Gautier, J. Y. Saillard, J. Organomet. Chem., in the press.

Inorganic and coordination chemistry **90**

Mechanistic Aspects of the Enantioselective Copolymerization of Propene with CO Catalyzed by Pd(II) Complexes Containing Ferrocenyl Diphosphines

C. Gambs,[b] G. Consiglio, [a,]* and A. Togni [b,]*
[a]*Laboratorium fur Technische Chemie, ETH Zurich, CH-8092 Zurich*
[b]*Laboratorium fur Anorganische Chemie, ETH Zurich, CH-8092 Zurich*

The alternating copolymerization of olefins with carbon monoxide is of great interest due to the potential use of the resulting polymer as new material [1]. We recently reported highly enantioselective alternating copolymerization of propene and CO catalyzed by *in situ* formed Pd(II) complexes bearing chiral ferrocenyl ligands **PP1-7**. Only small variation in stereoregularity (90-97.5 % of *l-diads*) were observed, whereas drastic changes in catalytic activity (productivity from 50 to 1800 $g_{Cop}/g_{Pd}{\cdot}h$) were noted by changing the electronic properties of the PAr_2 substituents [2].



The role of the electronic differentiation of the two binding sites of the ligands **PP1-7** has been studied. We prepared the monocationic palladium complexes $[Pd(CH_3)(NCCH_3)(\textbf{PP1-7})][PF_6]$ and investigated the initial reaction steps of the copolymerization process: (1) CO insertion into the alkyl-Pd bond and (2) olefin insertion into the acyl-Pd bond.

References
[1] a) Drent, E.; Budzelaar, P. H. M., *Chem. Rev.*, **1996**, *96*, 663
b) Bronco, S.; Consiglio, G.; Di Benedetto, S.; Spindler, F.; Togni, A., *Helv. Chim. Acta* **1995**, *78*, 883
[2] Gambs C.; Chaloupka S.; Consiglio G.; Togni A., *Angew. Chem.* **2000**, *112*, in print

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Inorganic Chemistry **91**

Reactions of Dicationic Ru(II) Arene Complexes with Primary Acetylenes

Carolien den Reijer and Paul Pregosin

reijer@inorg.chem.ethz.ch
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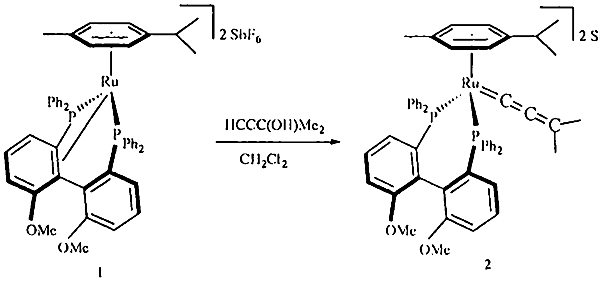
Universitätsstr. 6, CH-8092 Zürich, Switzerland

There is a growing interest in Ru-carbene complexes as these species are potential catalysts for metathesis polymerization. We have been interested in Ru(II) arene systems with the atropisomeric bidentate phosphine ligands, *e.g.* MeO-Biphep. Starting from complex **1**, we have succeeded in preparing several dicationic Ru(II) carbene (*e.g.* **2**) and acetylide species. The synthesis, characterization, structure, and reactivity of these complexes will be described.



Inorganic Chemistry **92**

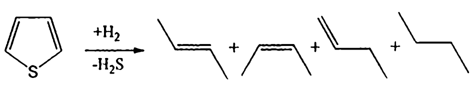
Study of Tungsten Catalysts by Means of EXAFS (Extended X-ray Absorption Fine Structure)

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 [1]. The most frequently used catalyst in industry is $Ni(Co)MoS_2$ on Al_2O_3. W-based catalysts are used less frequently, because they are more costly and less active in the HDS of gasoil. However, W catalysts have excellent hydrogenation properties, making them good catalysts in the HDN reaction [2]. Such properties are necessary for the so-called deep removal of sulfur from gasoil (< 50 ppm) which will be required in Europe by 2005.

In contrast with Mo [3], not much is known about how the oxidic W precursor is transformed into the active catalyst. Therefore, we studied the sulfidation behaviour of Ni-promoted W catalysts by means of EXAFS. We conclude that Ni increases the sulfidability and lowers the sulfidation temperature of the catalysts. We also found that W catalysts have a higher activity in the HDS reaction of thiophene with increasing amount of Ni.



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Inorganic Chemistry **93**

NEW TERNARY RARE EARTH SILICIDES IN THE SYSTEM RE/EA/Si (RE = Ce, La, Nd, Y, Yb; EA = Mg, Sr)

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In the system Sr/La/Si new compounds have appeared. The compound $SrLaSi_2$ (C mcm, a=4.67 Å, b=13.98 Å, c=13.21 Å) could be obtained. The structure contains infinite silicon chains of cis-trans-trans-trans conformation [1].
The new compound $Sr_4La_6Si_8$ (P nma, a=7.91 Å, b=15.83 Å, c=8.18 Å) was characterized. The structure is built of silicon dumb-bells just as another compound, $Sr_5Y_2Si_6$ (P nma, a=7.71 Å, b=23.10 Å, c=8.45 Å) (Fig. 1) [1]. Both structures can be related by a chemical twinning approach and thus fit into a more general concept of understanding solid state structures [2]. Ternary compounds containing dumb-bells like the new compound $Yb_7Mg_2Si_8$ (P nma, a=9.79 Å, b=14.40 Å, c=7.53 Å) and Yb_2MgSi_2 [3] (U_3Si_2-type) or the newly synthesized compounds Ce_2MgSi_2, La_2MgSi_2 and Nd_2MgSi_2 (isotypic to Yb_2MgSi_2) can be included in the same picture.

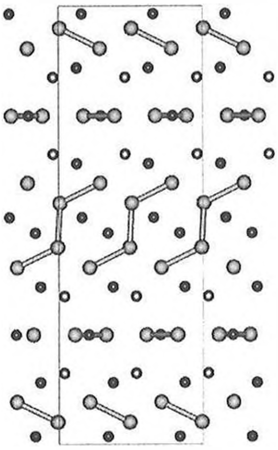

Fig.1: The structure of $Sr_5Y_2Si_6$: layers of dumb-bells are separated from layers of "S"-shaped polyanions: bright grey spheres correspond to silicon atoms, black spheres are strontium atoms and grey spheres correspond to yttrium atoms.

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Inorganic Chemistry **94**

Reactions of the metal carbides with transition metal chlorides in a ball mill.

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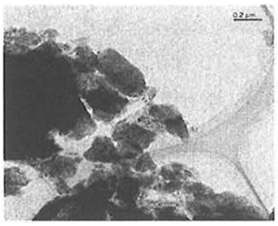
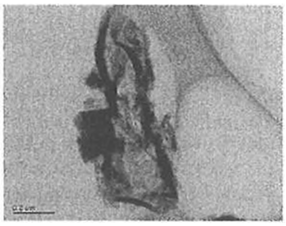
Metal carbides (CaC_2, Li_2C_2) have been reacted with transition metal chlorides ($FeCl_2$, $CoCl_2$, $NiCl_2$) in a planetary mill with use of agate milling tools (3balls, d=20mm, m_{ball}/m_{powder}=1/15, 30 hours reaction time, rotation 400 rpm). The reaction proceeds completely towards Li and Ca chlorides.

In the product metal particles (Fe^0, Co^0, Ni^0) are detected studied by x-ray powder diffraction ($CuK_{\alpha 1}$-radiation). After washing with water and concentrated nitric acid powders were examined by High Resolution TEM. Amorphous carbon is observed containing isolated particles on micro- and nanometer scale.





Inorganic Chemistry **95**

Template-Directed Synthesis of Structured Iron Oxides

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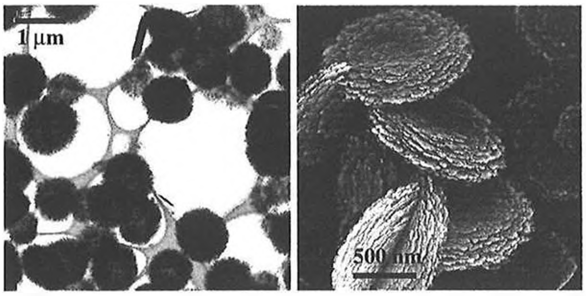
Although many techniques for the preparation of monodispersed colloids have been elaborated [1], it is still rather difficult to produce large quantities of such materials characterized by a narrow size distribution and uniform shapes and compositions.



TEM (left) and SEM (right) images of iron oxide colloids obtained after hydrothermal treatment at 150°C for 3 days.

Here we present the synthesis and characterization of monodispersed iron oxide colloids using the organometallic iron complex $[N(CH_3)_4]_2[OFe_6(H_{-3}thme)_3(OCH_3)_3Cl_6 \cdot MeOH$ (thme = 1,1,1-tris(hydroxymethyl)ethane) [2]. Various synthesis parameters like pH, temperature, aging time, and addition of long-chain surfactant molecules with different functional head groups influence the morphology of the obtained iron oxide particles.

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Inorganic Chemistry **96**

Novel Vanadium Oxide Nanotubes with Double Interlayer Characteristics

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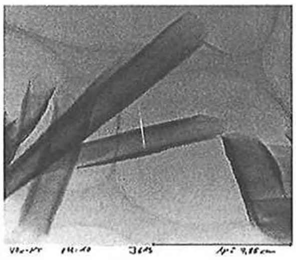
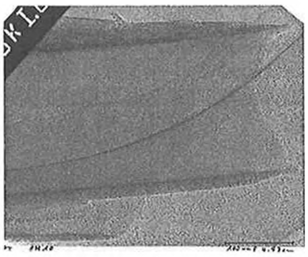
Compared with steadily growing family of nanostructured metal oxides with tubular and/or lamellar structures, the VO_x-NTs found be interesting with their unique morphology and different from the well known structures reported in the literature. The initial pH of the synthesis gel found to be an important parameter in directing the nature of materials formed in this family. Recently, we obtained a novel tube-shaped vanadium oxide with mixed valency using templated synthesis [2].





The high (pH>10) or low (pH< 4) pH ranges, prefer to form crystalline materials with no tubular characteristics and the neutral pH lead to normal vanadium oxide nanotubes. The materials formed at pH 9 and 10 using ammonia found to have a special morphology of alternating double interlayer distances in their tube walls. Such a wall structure is without precedent in any other tubular material.

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Inorganic chemistry **97**

Synthesis of Large-Pore Silica with a Narrow Pore Size Distribution

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Enlarging the pore diameter of MCM-41 by means of the swelling method was reported in the first publications on M41S materials [1, 2]. The products obtained in this way exhibit a broad pore size distribution and a small pore volume. The nature of the micelles is correlated to the geometrical requirements of the used tenside, and swelling agents change these requirements. In addition, the stability of the enlarged structure is lower, and more material is destroyed during calcination.

To overcome the geometrical constraints, we used a mixture of alkyl-trimethylammonium tensides of different alkyl chain length. We adjusted the pH of the synthesis gel during synthesis to improve the stability of the material [3].

The obtained large-pore materials have a large surface area (~1200 m^2/g, BET) and pore diameters up to 80 Å (BJH). Powder XRD and TEM indicated a disordered structure. In addition, the TEM examination showed that almost no amorphous silica was formed.

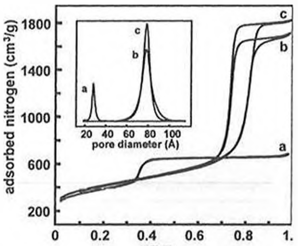

Fig. 1: N_2 adsorption isotherms and BJH plot (inset) of M41S without additive (a), with mesitylene and C_{16}- (b) and C_{16}/C_{12}-surfactant (c).

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Inorganic Chemistry **98**

Alignment and Conductivity Measurements of Vanadium Oxide Nanotubes

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L.-J. Gauckler and R. Nesper
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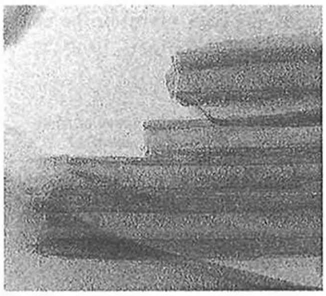
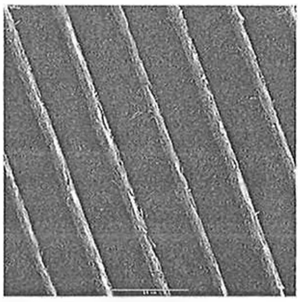
In the course of the present efforts towards miniaturization of electronic devices, structures with a size in the nanometer region have stimulated intensive, world-wide research activities. Among such nanostructures, tubular materials are especially interesting, because of their anisotropic shape which gives reason to anisotropic physical properties.



Vanadium Oxide Nanotubes (VO$_x$-NT's)



Alignment of VO$_x$-NT's

Here we report the alignment of vanadium oxide nanotubes[1] (VO$_x$-NT's) by capillary filling methods and the following measurements of their conductivity behavior by using a four-point-measurement array.

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Inorganic Chemistry **99**

Structural Studies in the Ru-Zn System

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Up to now, in the Ru-Zn system only the binary phase $RuZn_6$ has been synthesized and crystallographically characterized [1]. Another more ruthenium-rich phase was mentioned as a side product.

We reinvestigated the system because we were interested in suboxide studies due to the fact that $RuZn_6$ contains a large number of void positions with 6, 7 and 8 closest Zn neighbors.

The structure is a beautiful chiral interpenetration of three double helices along [1 0 0], [0 1 0], [0 0 1] built from $RuZn_{12}$ icosahedra (Figure 1).

Another new stochiometric phase $RuZn_3$ has been found and characterized from powder diffraction data. The structure derives from the cubic Cu_3Au type by an elongation of the c-axis (c/a=1.032). The structure contains a void at (½ ½ ½) with 6 Zn neighbors at d=1.88 Å (d(Zn-O, ZnO) = 1.97 Å).

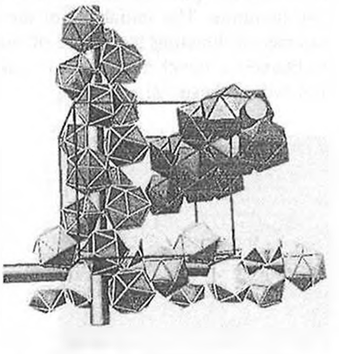

Figure 1: The three double helices in $RuZn_6$

We tried to introduce oxygen by using binary metal oxides, but could not find an indication for suboxide formation. This is supported by calculations of the electron localization function (ELF).

Literature:
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Inorganic Chemistry **100**

Reactivity of Zintl Anions in Salt Melts

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Zintl phases make up a class of solid compounds between metals and semimetals that are electronically located amid intermetallic and insulating valence compounds. They show a rich variety of in some cases completely new homoatomic E14 or E15 arrangements and oligomeric clusters, so called *Zintl anions*, which set up links between classical inorganic and cluster compounds.

In order to explore these rich chemical potential we investigate the reactivity of Zintl phases in organic salt melts (e.g. Immidazoliumbromid/$AlBr_3$) with melting points in the range of -10-140 °C. In the last years these melts have found rising interest with respect to their usage as reaction media for organic as well as inorganic reactions. [1,2] We think these kind of salt melts may overcome the common problems in the solvolysis of Zintl phases. Due to their higher polarizabilities they should be more capable to stabilize or dissolve highly charged polyanions than the classical organic solvents. First investigations on Zintl phases of silicon in melts of 1-Ethyl-2,3-Dimethyl-Immidazoliumbromid show a solvolysis of the Zintl phases leading to interesting new compounds of silicon.

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Inorganic and Coordination Chemistry **101**

LiB$_x$ – An Incommensurate Composite Structure at Low Temperatures

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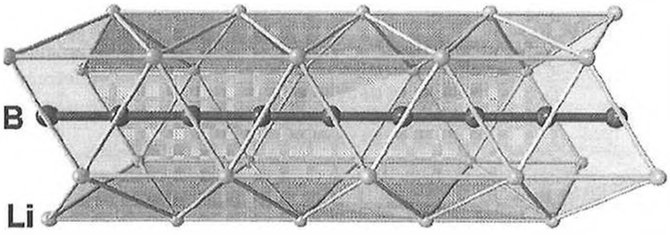
The lithium boride LiB$_x$ (0.82<x<1.0) the first boride known to contain linear boron chains, isoelectronic to carbyne which are embedded and stabilized in a lithium matrix [1]. Indeed, this compound contains a surprising solution to the famous carbyne problem. At room temperature the boron chains are disordered, giving rise to diffuse scattering in the corresponding X-ray and neutron powder diffraction patterns. At about 150 K a second order phase transition takes place which leads finally to the formation of an incommensurate composite structure. The crystal structures at 2 K of both sublattices were determined from the neutron diffraction experiment and refined in the space group P–1(αβγ).



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Anorganische Chemie **102**

LiAlSn: a New Zintl phase with a Distorted Diamond Network

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A new Zintl phase was synthesised in sealed tantalum crucible under argon atmosphere at 1223 K. A small crystal with metallic lustre was found and measured by 4 circle diffractometry.
The structure (Fig. 1) of the new Zintl phase LiAlSn was solved in the tetragonal $I\bar{4}m2$ space group with the cell parameters: a = 466.3(1) pm and c = 653.3(2) pm. The structure is a slightly distorted tetragonal variant of the well known cubic LiAlSi structure, which is also found in the Zintl phase LiAlGe. The distortion is confirmed by powder X-ray diffraction.
Band structure calculations based on LMTO method provide an explanation why this distortion occurs by changing the tetrel atom from germanium to tin.

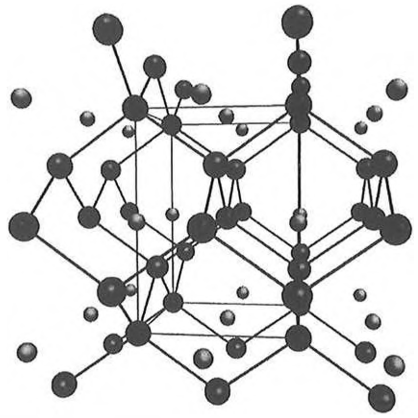

Fig. 1: Li light grey, Al dark grey and Sn black.

Inorganic Chemistry **103**

Peroxynitrite-mediated Nitration of Tyrosine Residues in Hemoglobin and Myoglobin

Michael Exner, Martin Mehl and Susanna Herold

Laboratorium für Anorganische Chemie, ETH-Zentrum, 8092 Zürich

Peroxynitrite (ONOO$^-$), a strong oxidizing and nitrating agent generated *in vivo* from the diffusion controlled reaction between NO$^•$ and O$_2^{•-}$, 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 [1]:

$$\mathrm{HbFeO_2 + HOONO \rightarrow HbFe^{IV}{=}O}$$
$$\mathrm{HbFe^{IV}{=}O + HOONO \rightarrow HbFe^{III}}$$

As the reaction rates for both steps are quite large [1] and as it has been shown that peroxynitrite can easly cross the erythrocyte membrane [2], it is likely that the reaction between HbFeO$_2$ and peroxynitrite takes place *in vivo*. It is thus of interest to find out whether tyrosine residues are modified in the course of this reaction.
We have investigated the both proteins by HPLC-analysis after complete hydrolysis as well as after enzymatic digestion. Additionally, nitrotyrosine was detected with nitrotyrosine antibodies. Our results show that peroxynitrite is able to nitrate the tyrosine residues of hemoglobin as well as myoglobin in a concentration dependent way but in very low yields. When added in equimolar amounts, peroxynitrite nitrates only about 0.4% of the available tyrosine residues.
Furthermore, we show that MbFeO$_2$ protects free tyrosine from peroxynitrite-mediated nitration. About 1/10 of equivalents of MbFeO$_2$ (relative to free tyrosine) are required to inhibit tyrosine nitration (IC$_{50}$).
We conclude that because of its low yield the nitration reaction is not likely to be relevant *in vivo* but that hemoglobin as well as myoglobin may protect against peroxynitrite-mediated nitrations.

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Inorganic Chemistry **104**

Is Nitrotyrosine Formed in the Course of the NO$^•$-mediated Oxidation of Oxyhemoglobin?

Susanna Herold and Michael Exner

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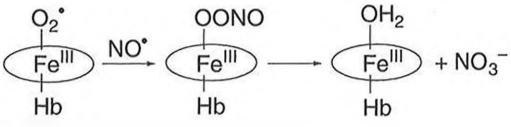
Nitrogen monoxide rapidly oxidizes oxyhemoglobin (HbFeO$_2$) to methemoglobin (HbFe^{III}) in a reaction which is considered to be the major pathway for NO$^•$-depletion in the blood vessels. We have recently shown that, in analogy to the formation of peroxynitrite (ONOO$^-$) by reaction of NO$^•$ with O$_2^{•-}$, this oxidation proceeds *via* an intermediate peroxynitrito-methemoglobin complex (HbFe^{III}OONO) which then decays to HbFe^{III} and nitrate (see Scheme) [1]. Kinetic studies showed that the rate of decay of the peroxynitrito-complex is significantly larger than that of isomerization of free peroxynitrite to nitrate [1].



About 1% of oxyhemoglobin is oxidized daily to methemoglobin either *via* autoxidation or, more likely, *via* the reaction with NO$^•$. Peroxynitrite is known to oxidize amino acid residues and, in particular, to nitrate tyrosine residues. It is thus of interest to find out whether the intermediate peroxynitrito-complex is also capable of nitrating tyrosine residues and whether this reaction is relevant *in vivo*.
We report here that ion chromatographic product analysis indicates that nitrate is formed quantitatively from NO$^•$. Moreover, HPLC-analysis of the amino acids after complete hydrolysis of the protein shows that only negligible amounts of nitrotyrosine are formed. We conclude that the nitration reaction is not likely to have any physiological relevance.

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Inorganic Chemistry **105**

Pd(II)DuPHOS complexes.
Are small chiral ligands "intrusive"?

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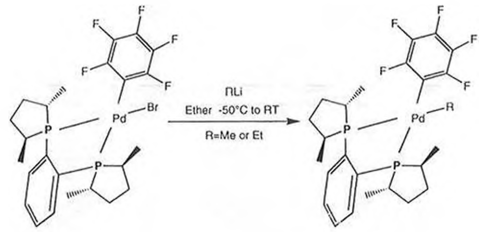
Although the chemistry of Ru- and Rh-DuPHOS complexes is well documented, until recently the Pd chemistry of these "moderately-intrusive" ligands remains widely uninvestigated.

The synthesis, characterisation, structure and reactivity of several pentafluorophenyl, alkyl and allyl Pd(Me-DuPHOS) compounds will be described.



1 2

Reaction scheme for the synthesis of Pd(C_6F_5)alkyl derivatives is shown above. For compounds 1 {PdBr(C6F5) [(R,R)Me-DuPHOS]}, and 2a {PdMe(C6F5) [(R,R)Me-DuPHOS]}, the solid state structures have been solved by X-ray diffraction.

Inorganic and Coordination Chemistry **106**

Unusually Large Water Relaxivity for a Self-Aggregated Gadolinium Podate : Study and Characterisation of the Lanthanide complexes

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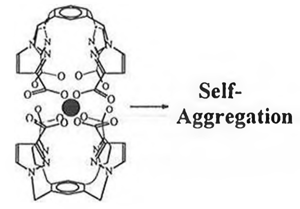
BCH, CH-1015 Lausanne.

Lanthanide(III) poly-aminocarboxylates are widely used as contrast agents for magnetic resonance imaging (MRI).[1] The relaxivity of paramagnetic complexes in the range of 10-100 MHz is mainly limited by their rotation correlation time and their rigidity, which prompted major efforts devoted to build super-nanosized paramagnetic edifices.[2]



We present the coordination properties of a phenyl anchored podand H_4L^1 fitted with four carboxylate-bearing pyrazole arms, programmed for intermolecular interactions. Complexes with 1:1 and 1:2 metal to ligand ratios were synthetized. They self-aggregate in spheric entities at low concentration. The relaxivity properties of Gd-containing self-aggregated nanoparticles at physiological pH and their physico-chemical characterisation are presented.

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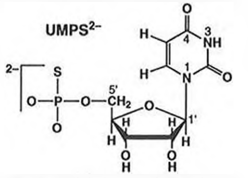
Anorganische Chemie und Koordinationschemie **107**

Complex Formation of Lead(II) in Aqueous Solution with Methylthiophosphate ($MePS^{2-}$) and Uridine 5'-*O*-Thiomonophosphate ($UMPS^{2-}$)

Carla P. Da Costa,[a] Andrzej Okruszek,[b] Wojciech J. Stec,[b] Helmut Sigel[a]

[a]Institute of Inorganic Chemistry, University of Basel, Spitalstr. 51, CH-4056 Basel, Switzerland; [b]Ctr. of Molecular and Macromol. Studies, Dept. of Bioorg. Chemistry, Polish Acad. of Sciences, PL-90-363 Lódź, Poland



The phosphorothioate (PS) group, in which a phosphate O is replaced by an S atom, is employed, e.g., in antisense oligonucleotides [1] and in studies of ribozymes [2]. Therefore we are studying metal ion-thionucleotide interactions [3] in order to learn which factors govern binding. Because of the existence of leadzymes [4] we determined now (pot. pH titrations) the stability constants of the 1:1 complexes (aq. sol.; 25 °C; $I = 0.1$ M, $NaNO_3$) between Pb^{2+} and $MePS^{2-}$ or $UMPS^{2-}$. Preliminary results are given in the Table (column 2) together with the calculated (calcd) constants which are based on the pK_a values of the $H(PS)^-$ species and on log $K^{Pb}_{Pb(R\text{-}PO_3)}$ *vs* p$K^{H}_{H(R\text{-}PO_3)}$ straight-line plots which hold for simple phosphate monoester or phosphonate ligands with a non-coordinating residue R (= R-PO_3^{2-}) [5]. The positive differences between measured and calculated constants, log $\Delta_{Pb/PS}$, prove the expected higher affinity of Pb^{2+} for S compared to O. The data also demonstrate that in Pb(UMPS) no interaction of the thiophosphate-coordinated Pb^{2+} with the nucleobase residue occurs; this corresponds to Pb(UMP) [5]. These results reveal further that the affinity of Pb^{2+} towards a phosphate group increases by a factor of about 250 if an O atom is replaced by an S atom.

PS^{2-}	log K_{exptl}	log K_{calcd}	log $\Delta_{Pb/PS}$
$MePS^{2-}$	4.78±0.07	2.32±0.08	2.46±0.11
$UMPS^{2-}$	4.63±0.05	2.23±0.08	2.40±0.09
p$K^{H}_{H(MePS)}$ = 4.96±0.02;	p$K^{H}_{H(UMPS)}$ = 4.78±0.02		

Supported by the Swiss Nat. Sci. Found. and via COST D8 by the Swiss Fed. Off. for Educ. & Sci. and the State Com. for Sci. Research, Poland.

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Inorganic Chemistry **108**

Synthesis of new cyclic peptides and their copper(II) transition metal complexes

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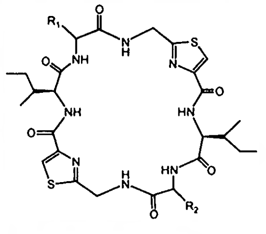
In recent years various families of *Lissoclinum* peptides have been isolated[1]. The family of patellamides from *Lissoclinum patella* has a 24-azacrown-8 structure.

We report the synthesis of three new cyclic peptides, cyclo[(Ile-L-Thr-Gly(Thz))2] (1), cyclo[Ile-L-Thr-Gly(Thz)-Ile-D-Thr-Gly(Thz)] (2) and cyclo[(Ile-L-Ser-Gly(Thz))2] (3). They were obtained by solid phase synthesis, followed by high dilution cyclization of the linear peptides.



(1) R_1: L-Thr, R_2: L-Thr
(2) R_1: L-Thr, R_2: D-Thr
(3) R_1: L-Ser, R_2: L-Ser

It is known that, upon coordination to metal ions, these macrocycles undergo conformational changes. Copper(II) solution studies, involving UV-vis-, CD- and EPR-spectroscopy, combined with empirical force field calculations and spectra simulations,may contribute to a thorough interpretation of the solution structures as a function of the peptide structure and metal ion preferences[2]. Details of the syntheses and characterization of the ligands (1)-(3) will be presented together with spectroscopic data and solution structures of the corresponding dicopper(II) compounds.

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[2] Comba, P.; Cusack, R.; Fairlie, D. P.; Gahan, L. R. ; Hanson, G. R.; Kazmaier, U.; Ramlow, A. *Inorg. Chem.* **1998**, *37*, 26, 6721

Anorganische Chemie

109

Copper(II) Catalyzed Peroxynitrite Decompositions

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Peroxynitrous acid is a substance of biological interest formed by the rapid recombination of nitrogen monoxide and the superoxide ion. It isomerizes rapidly in neutral or acidic solutions, but the anion is more stable. At pH = 9, the decomposition rate is around $1 \times 10^{-2}\ s^{-1}$.

There is earlier work about an accelerating effect of copper(II) on this decomposition [1], but the copper(II) species was not well-defined. We studied the catalysis with the copper(II) nitrilotriacetate (NTA) complex.

The process differs with copper(II)-NTA in excess and peroxynitrite in excess. In the first case, nitrate is the major product, the rate is first order in peroxynitrite and independent on copper(II), and the rate constant is $3.5 \times 10^{-2}\ s^{-1}$. In the second case, the reaction is biphasic. The first phase is of first order in peroxynitrite and of order 0.15 in copper(II). The rate constant is $8 \times 10^{-2}\ s^{-1}$ if the reaction order of copper(II) is forced to zero in the fit. The second phase is identical with the reaction of copper(II) in excess. The major product here is nitrite. We also showed that both reactions involve coordination of peroxynitrite, since the copper(II) d-d absorption bands between 600 and 800 nm display the same temporal changes as the peroxynitrite band at 300 nm. The copper(II) catalyzed reaction is not compatible with homolysis into $NO^{\bullet}$ and $O_2^{-\bullet}$, which should occur at $1.7 \times 10^{-2}\ s^{-1}$ [2]. The peroxynitrite reaction order is consistent with this claim, but the copper(II) complex would then act as a $O_2^{-\bullet}$ scavenger, and the overall rate should be the homolysis rate, which is experimentally exceeded. It could be argued that coordination accelerates homolysis, but then, nitrite should be the main product with all concentration ratios, because $NO^{\bullet}$ and O_2 would be formed as intermediates.

[1] Hughes, M.N., *et al.*.: J. Chem. Soc. A, **1971**, 3722
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Anorganische Chemie

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Oxidation of Nitrite by Peroxynitrous Acid: An Isotope Experiment

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Peroxynitrous acid, a substance of biological interest, is formed by the rapid recombination of nitrogen monoxide and the superoxide ion. Preparations for in vitro studies are usually contaminated with 10-100% of nitrite, a fact which is often neglected in research. Peroxynitrite, however, is a powerful oxidant that could convert nitrite into nitrate. If this occurred, it is obscured by the isomerization of peroxynitrous acid which also yields nitrate. The isomerization is delayed by addition of nitrite in excess [1]. Coddington *et al.* assume that nitrite scavenges radicals released by homolysis of peroxynitrous acid, thus altering the chain reaction [2].

In order to obtain more insight, we carried out the peroxynitrous acid isomerization in the presence of various excesses of $^{15}NO_2^-$. The mixtures were analyzed for the $^{14}NO_3^-/^{15}NO_3^-$ ratio by NMR and electrospray mass spectrometry after the reaction. Total nitrate yields were determined by anion chromatography. Exchange between $^{15}NO_2^-$ and $^{14}NO_2^-$ or $^{14}NO_3^-$ was excluded by control experiments, also the possible radical exchange of $^{15}NO_2^-$ with $^{14}NO_2^{\bullet}$.

We found that $^{15}NO_3^-$ was produced proportionally to the nitrite concentration, and the yield reached 85% of the original peroxynitrous acid at 50-fold excess. The reaction cannot compete with the isomerization at biological concentrations, but the nitrite concentration dependence implies that the isomerization is not a homolysis-recombination reaction. Molecular dynamics calculations favor an oxygen transfer reaction which has no activation barrier in the gas phase. The pathway is maintained in simulations in a water box, however, an activation barrier appears [3].

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Chimie minérale et de coordination

111

The nitrogen-to-metal multiple bond functionnalities : the reaction of calix[4]arene-W(IV) with azides and diazoalkanes

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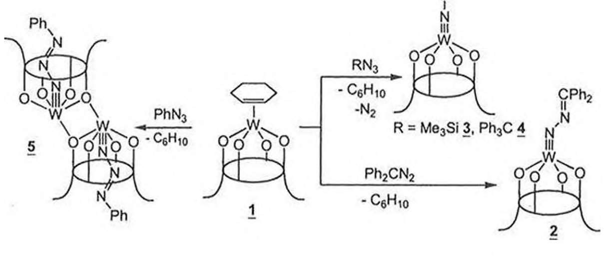
This report concerns the use of a [W(IV)-calix[4]arene]-olefin complex as a source of the d^2-[W(IV)-calix[4]arene]-fragment in the reaction with azides and diazoalkanes. These reactions led, either to the two electron reduction of the substrate or to the cleavage of nitrogen bonds with the formation of metal-imido species. This reactivity has been chosen for its relationship with N_2 reduction and N-N cleavages. The pre-organised O_4 coordination environment which make available at the metal a σ and two π frontier orbitals is a determining factor in such a chemistry.



The reaction of 1 with Ph_2CN_2 led to the formation of 2, where the diphenyldiazomethane has been reduced by two electrons, thus forming a metalla-hemihydrazone. In the case of organic azides, both the cleavage of N-N bonds and the two electron reduction of the RN_3 functionnal group has been observed, depending on the steric and electronic properties of the azide employed : reaction of 1 with Me_3SiN_3 or Ph_3CN_3 led to the exo-metal-imido derivatives 3 and 4, with the loss of dinitrogen, while reaction of 1 with PhN_3 led to metal-bonded azide inside the cavity of the calix[4]arene ligand 5.

Inorganic Chemistry

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Diffusion measurements as a tool for determining the nuclearity of organometallic complexes

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In the identification and characterisation of organometallic compounds one of the first problems to solve is the determination of the nuclearity of the complex. A direct, easy and fast technique, which can be used in most cases, involves the diffusion measurements by NMR spectroscopy using the PGSE sequences[1]. We applied successfully this method to a lot of organometallic compounds[2] of different molecular weight, e. g., to a set of four small arsine Pd(II) complexes, $PdCl_2L_2$, L = $AsMe_XPh_{3-X}$, X = 3, 2, 1, 0, as well as to ferrocene phosphine dendrimers[3]. The results suggest that this tool can be a practical alternative to classical methods used in organometallic chemistry for estimating the molecular size. Another useful application of this method concern the study of ion pairs in solution, e. g., the determination of the dissociation constants

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[3] C. Köllner, B. Pugin, A. Togni, *J. Am. Chem. Soc.*, 120, **1998**, 10274.

Inorganic and Coordination Chemistry **113**

Anisotropic solvation and outer-sphere relaxivity of MRI-relevant Gd(III) chelates

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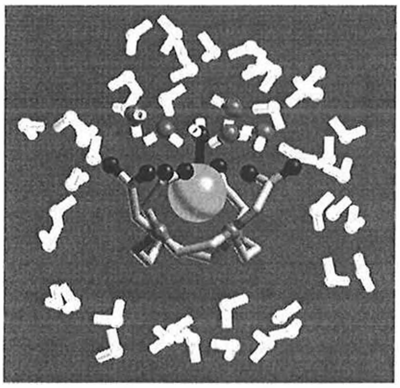
The effectiveness of MRI contrast agents is measured by the water protons magnetic relaxation rate enhancement (*relaxivity*) in their vicinity. It is divided into two contributions, namely inner-sphere (caused by water molecules bound to the metal ion) and outer-sphere (dipolar interaction with bulk water molecules). Molecular dynamics simulations of Gd(III) chelates in solution have revealed the existence of an anisotropic second coordination shell, whose structure and dynamics have been studied extensively.



Numerical calculations have been performed to assess the consequence of these findings on the outer-sphere relaxivity of these compounds.

Inorganic Chemistry **115**

Kinetic and Mechanistic Studies on the Reaction of Ascorbate with Peroxynitrite

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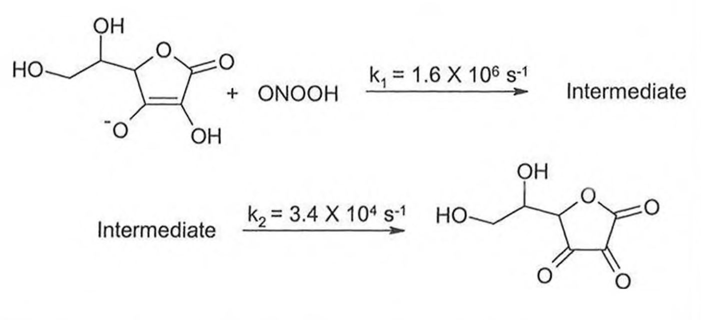
Peroxynitrite is formed *in vivo* from the diffusion-controlled reaction of $NO^{\bullet}$ with $O_2^{\bullet-}$. Peroxynitrous acid (ONOOH) is a strong oxidant and reacts with a wide variety of biomolecules. Kinetic studies carried out by stopped-flow spectroscopy with ascorbate show an intermediate with an absorption maximum at 345 nm. This intermediate is not the ascorbyl radical that has been observed earlier [1]. At low concentrations of ascorbate (< 1 mM) and peroxynitrite (< 25 μM) the formation of the intermediate is first order in peroxynitrite and apparently zero order in ascorbate. The decay of the intermediate is first order in the intermediate. The nature of this intermediate is presently under investigation. The final product is dehydroascorbate.



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Anorganische Chemie und Koordinationschemie **114**

Intramolecular Aromatic-ring Stacking in Mixed Ligand Cu^{2+} Complexes of 1,10-Phenanthroline (Phen) and Adenosine 5'-Diphosphate (ADP^{3-})

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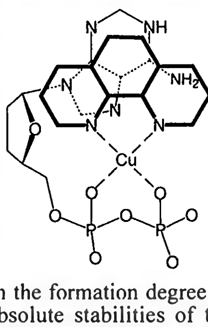

Stacking interactions are essential for the correct positioning of nucleotides, e.g., in the active site of enzymes [1], and their relevance in recognition reactions in nature is evident. Little is known in this regard about nucleoside 5'-diphosphates [2,3]. Therefore we have now studied (pot. pH titrations; aq. solution; I = 0.1 M, $NaNO_3$; 25°C) the formation of intramolecular stacks between the aromatic rings of Phen and the purine residue of ADP^{3-}. The stacked isomer forms not only with $Cu(Phen)(ADP)^-$ (Table), but also in the monoprotonated species, Cu(Phen)(H;ADP), where the proton is at the β-phosphate group. A comparison of the stacking tendency of AMP^{2-} [4], ADP^{3-} and ATP^{4-} [5] in such complexes shows that the length of the phosphate residue has little effect on the formation degree of the stacks (Table; column 3). Of course, the absolute stabilities of the complexes differ but the values of log $\Delta_{Cu/Phen/N}$, which reflect the position of the intramolecular equilibrium between the open and stacked species, are very similar.

Cu(Phen)(N)	log $\Delta_{Cu/Phen/N}$	%$Cu(Phen)(N)_{st}$
Cu(Phen)(AMP)	0.99 ± 0.08	90 ± 2 [4]
$Cu(Phen)(ADP)^-$	0.80 ± 0.08	84 ± 3
Cu(Phen)(H;ADP)	1.25 ± 0.32	94 ± 4
$Cu(Phen)(ATP)^{2-}$	1.07 ± 0.15	91 ± 3 [5]

Supported by the Swiss National Science Foundation.

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[4] S. Massoud, R. Tribolet, H. Sigel, *Eur. J. Biochem.*, **1990**, *187*,387-393.
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Inorganic and coordination chemistry **116**

A new method to analyse the EPR spectra of Gd^{3+} complexes measured at multiple frequencies and temperatures

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[b] DRFMC/SCIB/RIMM, CEA-Grenoble, 38054 Grenoble Cedex 9, France
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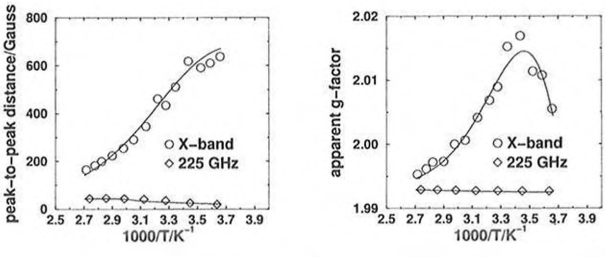
Gd^{3+} complexes are widely used as contrast agents in magnetic resonance imaging. So, the electronic relaxation rates and the dynamics of these complexes are of special interest. A complete theoretical description, which accounts for the isotropic Brownian rotation and vibrations of the complex, is presented. From the measured peak-to-peak distances and dynamic shifts in the paramagnetic resonance spectra, using our model, we estimated the crystal field parameters, the activation energies for the rotation and vibration of the complex, and the corresponding correlation times.



Peak-to-peak distance and apparent g-factor *vs* 1/T at X-band (9.425 GHz) and at 225 GHz for $[Gd(H_2O)_8]^{3+}$. Symbols: experimental points; continuous lines: result from our theoretical model.

The resulting parameters are in good agreement with the Stokes–Einstein model of rotational diffusion and coherent with other measurements on the complexes.

Anorganische Chemie und Koordinationschemie **117**

Comparison of the Extent of Stack Formation in Ternary Complexes Formed with a Heteroaromatic Amine and Adenosine 5'-Monophosphate (AMP^{2-}) or its Analogues 9-[2-(Phosphonomethoxy)ethyl]adenine (PMEA) and 9-(Phosphonobutyl)adenine (dPMEA)

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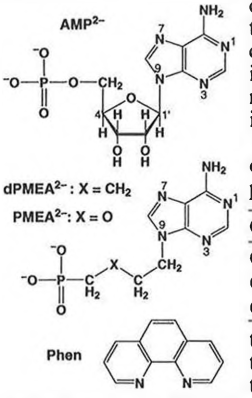

$PMEA^{2-}$ shows antiviral properties in contrast to its carba relative $dPMEA^{2-}$ [1] but both are analogues of (2'-deoxy)AMP^{2-} (Structures), and it was concluded that the ether O is compulsory for the activity of PMEA [1,2]. Since the anchoring process of a substrate in an enzyme cavity often involves aromatic-ring stacking, we are comparing the extent of intramolecular stack formation in the Cu(Phen)(N) complexes, where Phen = 1,10-phenanthroline and $N^{2-} = AMP^{2-}$, $PMEA^{2-}$ or $dPMEA^{2-}$. To this end we determined (pot. pH titration; aq. solution; 25°C; $I = 0.1$ M, $NaNO_3$) the stability constants and calculated [3,4] from the stability increase attributable to stack formation (log Δ; Table) the formation degree of the stacked isomers, $\%Cu(Phen)(N)_{st}$. The results reveal that stacking of $PMEA^{2-}$ and $dPMEA^{2-}$ resembles that of their parent nucleotide AMP^{2-}.

Cu(Phen)(N)	log Δ	$\%Cu(Phen)(N)_{st}$
Cu(Phen)(dPMEA)	0.96 ± 0.12	89 ± 3
Cu(Phen)(PMEA)	(see [3])	92 ± 2 [3]
Cu(Phen)(AMP)	0.99 ± 0.08	90 ± 2 [4]

Supported by the Swiss Nat. Sci. Found. and via COST D8 by the Swiss Fed. Off. for Educ. & Sci. and the Ministry of Educ. of the Czech Rep.

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Inorganic Chemistry **118**

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

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Ferryl, oxoiron(IV)myoglobin ($MbFe^{IV}{=}O$), formed *in vivo* under ischemic conditions by reaction of myoglobin and hydrogen peroxide, has been proposed to be involved in tissue injury resulting from reperfusion and reoxygenation of ischemic myocardium [1]. It has been reported that nitrogen monoxide 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 [2, 3]. In contrast, nitrite dramatically enhances the H_2O_2-mediated toxicity [4]. In order to evaluate the relevance of these reactions *in vivo* we have carried out detailed kinetic and mechanistic studies.

We have determined by stopped-flow spectroscopy that the reaction between $MbFe^{IV}{=}O$ and nitrogen monoxide 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). 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 of the nitrogen-containing species by ion chromatography 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.

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

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

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Inorganic and Coordination Chemistry **119**

Eu(II) Poly(Amino Carboxylate) Complexes: A Possible Route towards Redox Responsive MRI Contrast Agents

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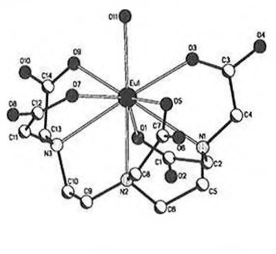
Université de Lausanne BCH ; CH-1015 Lausanne, Switzerland

Paramagnetic Gd^{III} poly(amino carboxylate) complexes have been used as contrast agents in Magnetic Resonance Imaging (MRI). The Eu^{II} is isoelectronic with Gd^{III} which may lead to similar biomedical application. The rates for water exchange, electron spin relaxation and complex rotation have been recently determined for $Eu^{II}_{(aq)}$ [1] and $[Eu^{II}(DTPA)(H_2O)]^{3-}$ [2] complexes. The water exchange rate of these complexes was found to be three orders of magnitude higher than that of Gd^{III} poly(amino carboxylates). Now we have extended these studies for macrocyclic Eu^{II} complexes which have higher redox stability than $[Eu^{II}(DTPA)(H_2O)]^{3-}$. We have performed variable temperature and multiple field ^{17}O NMR, ^1H NMRD and EPR studies in order to get more information on Eu^{II} complexes. [3] Moreover, the first X-ray solid state structure for a Eu^{II} chelate has also been acquired.



[1] P. Caravan, É. Tóth, A. Rockenbauer, A. E. Merbach, *J. Am. Chem. Soc.* **1999,** *121*, 10403.
[2] S. Seibig, É. Tóth, A. E. Merbach, *J. Am. Chem. Soc.* **2000,** *in press.*
[3] L. Burai, É. Tóth, S. Seibig, R. Scopelliti, A. E. Merbach, *Chem. Eur. J.* **2000**, in press.

Inorganic and Coordination Chemistry **120**

Lipari-Szabo approach as a tool for the analysis of polymeric Gadolinium based MRI contrast agents

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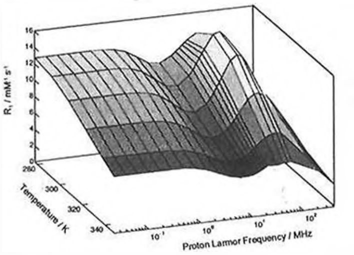
Université de Lausanne, BCH, CH-1015 Lausanne, Switzerland.

Recently, we have shown that the Lipari-Szabo approach can be applied to analyze the water ^{17}O longitudinal relaxation rates in polymeric Gd(III) based potential MRI contrast agents [1]. This approach uses a global correlation time to describe the movement of the entire molecule, and a local correlation time to describe the movements of the Gd-O vector.



Temperature dependence of the NMRD profile of the $[Gd(EGTA\text{-}BA\text{-}C12)]_n^{n+}$ polymer

We present here for the first time a simultaneous analysis of the ^{17}O NMR, EPR and NMRD data, where the Lipari-Szabo approach has been used to describe both ^1H and ^{17}O longitudinal relaxation times. The parameters governing the proton relaxivity of the $[Gd(EGTA\text{-}BA\text{-}C12)]_n^{n+}$ polymer could hence be determined. The polymeric chain is unfortunately short and the relaxivity is limited by the rotation correlation time at the body temperature (Figure).

[1] E. Tóth; L. Helm; K.E. Kellar; A.E. Merbach. *Chem. Eur. J.* **1999**, *5*, 1202-1211.

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Anorganische Chemie und Koordinationschemie **121**

Acid-Base Properties of Ternary Complexes Formed by Coordination of (Diethylenetriamine)Platinum(II) to N1 or N7 of the Adenine Moiety of the Antiviral Nucleotide Analogue 9-[2-(Phosphonomethoxy)ethyl]adenine (PMEA)

Gunnar Kampf,[a,b] Marc Sven Lüth,[a,b] Larisa E. Kapinos,[a] Jens Müller,[b] Antonín Holý,[c] Bernhard Lippert,[b] and Helmut Sigel[a]

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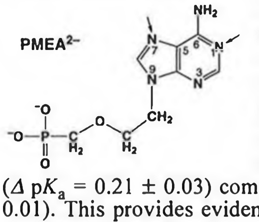
[c]Inst. Org. Chem. & Biochem., Acad. of Sci., CZ-16610 Prague, Czech Rep.

The antiviral PMEA^{2-} is an acyclic-nucleoside phosphonate analogue of (2'-deoxy)adenosine 5'-monophosphate [(d)AMP^{2-}][1,2]. We combined it with Pt(II), which occurs in *cis*-$(NH_3)_2PtCl_2$, an antitumor drug [3], and synthesized the ternary complexes (Dien)Pt(PMEA-*N1*) and (Dien)Pt(PMEA-*N7*). From the acidity constants (Table; aq. solution; 25°C; usually $I = 0.1$ M, $NaNO_3$) follows that phosphonate groups (PMEA^{2-}) are by Δ pK_a = 0.7-0.8 more basic than phosphate groups (AMP^{2-}). Furthermore, deprotonation of -$P(O)_2(OH)^-$ is only slightly affected by N1-coordinated (Dien)Pt^{2+} (Δ pK_a = 0.21 ± 0.03) compared with the N7 derivative (Δ pK_a = 0.44 ± 0.01). This provides evidence that in (Dien)Pt(PMEA-*N7*) in solution an intramolecular outersphere macrochelate forms via H bonds between -PO_3^{2-} and a Pt(II)-coordinated (Dien)-NH_2 group (formation degree about 40%).



Protonated Species	**pK_a**: (N7)H$^+$	P(O)(OH)$_2$	(N1)H$^+$	P(O)$_2$(OH)$^-$
$H_3(AMP)^+$ (see [4])		0.4 ±0.2	3.84±0.02	6.21±0.01
$H_4(PMEA)^{2+}$ (see [2])	–0.35±0.05	1.22±0.13	4.16±0.02	6.90±0.01
H_3[(Dien)Pt(PMEA-*N1*)]$^{3+}$	0.5 2±0.10	1.4 ±0.2		6.69±0.03
H_3[(Dien)Pt(PMEA-*N7*)]$^{3+}$		0.78±0.13	1.80±0.10	6.46±0.01

Supported by the SNSF, the DFG, and within COST D8 by the Swiss Fed. Off. for Educ. & Sci. and the Ministry of Educ. of the Czech Rep.

[1] A. Holý, et al., *J. Med. Chem.*, **1999**, *42*, 2064-2086 and refs therein.
[2] H. Sigel, *Pure Appl. Chem.*, **1999**, *71*, 1727-1740 and refs therein.
[3] B. Lippert (Ed.), *Cisplatin: Chemistry and Biochemistry of a Leading Anticancer Drug*, VHCA, Zürich, and Wiley-VCH, Weinheim, **1999**.
[4] H. Sigel, S. S. Massoud, N. A. Corfù, *JACS*, **1994**, *116*, 2958-2971.

Inorganic Chemistry **122**

Coordination and Decomposition of Peroxynitrite by Titanium

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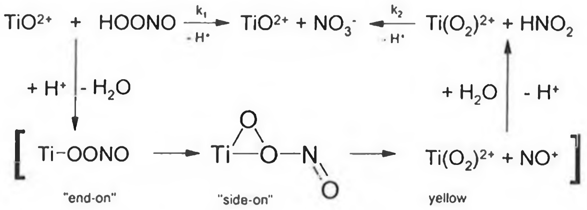
Peroxynitrous acid (ONOOH) isomerizes to nitrate at a rate of 1.2 s^{-1} at 25 °C; its pK_a is 6.5 at low phosphate concentration [1]. Other Lewis acids also catalyze the isomerization of peroxynitrite. However, it is also possible to stabilize peroxynitrite in the coordination sphere of a metal ion [2]. Recently we synthesized a Co(III)peroxynitrito complex that is stable for days. Our present interest is focussed on reactions between peroxynitrous acid and titanyl.

At low pH (pH < 2) titanyl is present as the monomer TiO^{2+}. With hydrogen peroxide a stable orange-red complex $Ti(O)_2^{2+}$ is formed (λ_{max} = 410 nm). Peroxynitrite coordinates first in a fast reaction "end-on" to titanium. A rearrangement from the "end-on" to the typical "side-on" coordination leads to a yellow coloured species. Release of NO^+ and formation of nitrous acid destroy any titanperoxo complex. Nitrous acid is oxidized by $Ti(O)_2^{2+}$ to the final product nitrate (scheme 1).



Scheme 1: $k_1 = 1.2\ s^{-1}$, $k_2 = 7.7\ M^{-1}s^{-1}$

[1] Kissner, R. et al. *Chem.Res.Toxicol.* **1997**, *10*, 1285-1292.
[2] Wick, P.K. et al. *Helv.Chim.Acta* **2000**, *83*, 748-754.

Inorganic and Coordination Chemistry **123**

EPR, ^{17}O NMR and NMRD Study of Gadomer 17, a Promising Dendritic Contrast Agent

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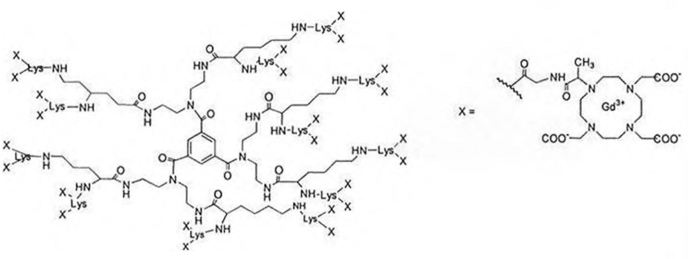
In the last few years, dendrimers, as high molecular weight compounds, appeared as potential blood pool and tissue specific contrast agents for Medical Magnetic Resonance Imaging. One of the candidates is the Gadomer 17 (see below) developed by Schering AG [1].



The different parameters affecting its proton relaxivity have been determined by a multiple field EPR, ^{17}O NMR and NMRD study. The Lipari-Szabo treatment has been used to separate local and global rotational motions [2].

(1) Dong, Q.; Hurst, D. R.; Weinmann, H. J.; Chenevert, T. L.; Londy, F. J.; Prince, M. R. *Investigative Radiology* **1998**, *33*, 699.
(2) Tóth, E.; Helm, L.; Kellar, K. E.; Merbach, A. E. *Chem. Eur. J.* **1999**, *5*, 1202.

Chimie Minérale et de Coordination **124**

IRON(II) AS THERMALLY-ADRESSABLE OPTICAL FILTER IN SELF-ASSEMBLED NON-COVALENT d-f PODATES

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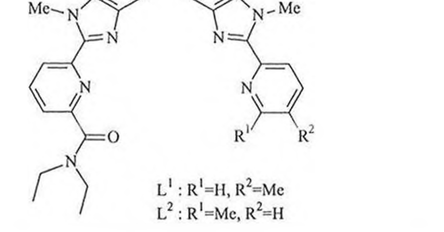
[†]*University of Lausanne, Institute of Inorganic Chemistry, CH-1015 Lausanne, Switzerland*

We have shown that iron(II) can be used in non-covalent tripod $[LnFe(L^1)_3]^{5+}$ to organize nine-coordinate sites around Ln(III) [1]. However, the associated room temperature Fe(low-spin) ↔ Fe(high-spin) spin-crossover behavior completely quenches the luminescence of Eu(III) in $[EuFe(L^1)_3]^{5+}$. The shift of the methyl group to the 6-position in L^2 forces Fe(II) to adopt a pure high-spin configuration that only partially alters the concomitant emission of Eu(III). The structural, magnetic and optical properties of the heterodimetallic d-f triple-stranded helicate $[EuFe(L^2)_3]^{5+}$ will be reported.



[1] C. Piguet; E. Rivara-Minten, G. Bernardinelli, J.-C.G. Bünzli, G. Hopfgartner, *J. Chem. Soc., Dalton Trans.*, **1997**, 421.

Chimie Minérale et de Coordination

125

THE EFFECT OF THE GADOLINIUM BREAK ON PARAMAGNETIC NMR SPECTRA OF LANTHANIDE COMPLEXES

S Rigault and C. Piguet

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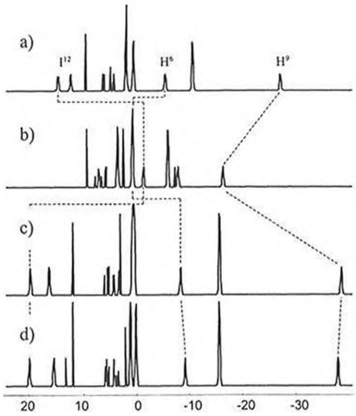

The use of classical crystal field dependent techniques fails to predict and rationalize ^{1}H-NMR spectra for the strongly paramagnetic triple helical lanthanide complexes $[LnCoL_3]^{6+}$ (Ln=Tb-Er) (spectra a ,b: predictions for $[HoCoL_3]^{6+}$; spectrum d: experimental data). Drastic deviations from linearity occur near the middle of the lanthanide series. Such breaks have been erroneously ascribed to structural changes associated with the well-known lanthanide contraction. However, the recent use of a crystal-field independent method [1] establishes the existence of an isostructural series from Ce to Yb [2]. A concomitant variation of the crystal-field parameter and of the hyperfine coupling constants occurs near the middle of the lanthanide series, in line with specific electronic effects associated with the 'Gadolinium break'. The latter technique offers unique perpectives for predicting and assigning NMR spectra as shown for $[HoCoL_3]^{6+}$ (spectrum c: predicted, spectrum d: observed).

[1] C. Platas, F. Avecilla, A. de Blas, C. F. G. C. Geraldes, T. Rodriguez-Blas, H. Adams, J. Mahia, *Inorg. Chem*,. **1999**, 38, 3190.

[2] S. Rigault, C. Piguet, J.-C. G. Bünzli, *J. Chem. Soc., Dalton Trans.*, in press (2000).

126

Kinetics and mechanism of the Cu^{2+} incorporation into the bismacrocycle 3,5-bis(1,4,7-triazacyclonon-1-yl-methyl)pyrazole

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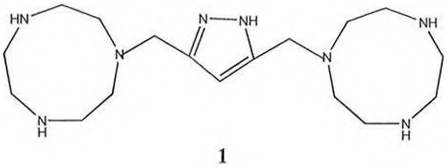
The kinetics and the mechanism of the Cu^{2+} incorporation into the bismacrocycle **1** were studied using the stopped – flow technique, starting either from the free ligand (LH_m) or from the 1:1 species ($CuLH_2$), which is an intermediate in the process.



1

Whereas k_{obs1} was too fast to be measured, log k_{obs2} was linearly dependent from log $[Cu^{2+}]$ and the pH. The results for both processes, i.e. the reactions of excess Cu^{2+} with LH_m or $CuLH_2^{4+}$, were identical. To explain the pH-dependence $CuLH^{3+}$, is postulated as the species which reacts with the second Cu^{2+} ion.

$$LH_m + Cu^{2+} \xrightarrow{k_1} CuLH_2^{4+} \overset{K_H}{\rightleftharpoons} CuLH^{3+} \xrightarrow{k_2} Cu_2LH_m^{2+}$$

The bimolecular rate constant of the second step ($k_2 = 1.4 \cdot 10^4$ $M^{-1}s^{-1}$) is about 200 times lower than the bimolecular rate constant for the Cu^{2+} complexation into 1,4,7-triazacyclononane ($k = 2.4 \cdot 10^6$ $M^{-1}s^{-1}$[1]). This is probably due to the higher charge of $CuLH^{3+}$ compared to that of LH^+ which is the reactive form of 1,4,7-triazacyclononane.

[1] Th. J. Riedo and Th. A. Kaden, *Helv. Chim. Acta* ***1979***, 62, 1089 - 1096.

Coordination Chemistry

127

Synthesis and X-Ray Structure of Chloro(dichloromethyl)(phosphinooxazoline)palladium(II)

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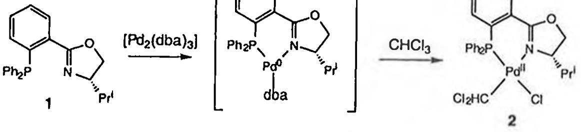
The oxidative addition of the substrate to a Pd^0 species is the first step in many palladium-catalysed reactions. Although bidentate (P,N) ligands have been successfully applied as catalysts in insertion [1], *Heck* [2] or copolymerisation reactions [3], little is known about the pathway of the oxidative addition to the $[Pd^0(P,N)]$ catalyst.



Chloro(dichloromethyl)(phosphinooxazoline)palladium(II) (**2**) was obtained by the reaction of $CHCl_3$ with $[Pd^0(dba)(1)]$.

The X-ray structure of **2** reveals that the chlorine ligand is positioned *trans* to the phosphorus. The dichloromethyl ligand is disordered. The two conformers differ in the orientation of the $CHCl_2$ moiety. Distorsion of the square-planar coordination geometry indicates steric strain in both conformers.

NMR spectroscopic investigations suggest the presence of a single isomer in solution confirming the high regioselectivity of the oxidative addition [1,3b].

[1] H. A. Ankersmit, B. H. Loken, H. Kooijman, A. L. Spek, K. Vrieze, G. Van Koten, *Inorg. Chim. Acta* **1996**, *252* and references therein.

[2] a) O. Loiseleur, M. Hayashi, N. Schmees, A. Pfaltz, *Synthesis* **1997**; 1338; b) E. P. Kündig, P. Meier, *Helv. Chim. Acta* **1999**, *82*, 1361.

[3] a) A. Aebi, G. Consiglio, *Helv. Chim. Acta* **1998**, *81*, 35; b) E. K. van den Beuken, W. J. J. Smeets, A. L. Spek, B. L. Feringa, *Chem. Commun.* **1998**, 223.

Inorganic Chemistry

128

Synthesis and magnetic properties of some high spin dendrimers

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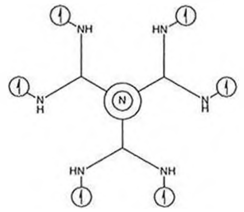
During the last few years, building new molecular species and addressing their architecture in order to control their physical properties, has been a topic for many research groups. The field of molecular magnetism has by essence of its supramolecular nature, benefited from advances in the field of supramolecular chemistry[1].

One field of current interest is dendrimer chemistry because these molecules can be specifically functionalized at the periphery, and as a consequence, they have useful application in materials chemistry [2]. The functionalization of such highly branched molecules with stable organic free radicals [3] to create a high spin dendrimer will be presented.



[1] O. Kahn, *Molecular Magnetism*, **1993**, VCH Press: Weinheim, Germany.

[2] K. Tsuda, F. C. De Schryver & al., *J. Am. Chem. Soc.*, **2000**, *122*, 3445-3452.

[3] G. Francese, F. M. Romero, A. Neels, H. Stoeckli-Evans & S. Decurtins, *Inorg. Chem.*, **2000**, *39*, 2087-2095.

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Inorganic Chemistry **129**

Novel molecular magnetic 3-dimensional network compounds, based on the molecular unit $[Nb^{IV}(CN)_8]^{4-}$

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A novel series of isostructural molecular 3-dimensional network compounds of the type $[Nb^{IV}\{\mu\text{-}(CN)_4M^{II}(H_2O)_2\}_2] \cdot 4H_2O$ are obtained by the reaction of Mn^{2+}, Fe^{2+} and Co^{2+} ions with the octacyano-metallate $K_4[Nb^{IV}(CN)_8]$. The bridging cyanides connect the Nb^{4+} ions with the transition-metal ions, which are coordinated by four cyanides of two different $[Nb(CN)_8]^{4-}$ units and two water molecules to complete the coordination sphere (Figure 1).

The magnetic coupling of the paramagnetic octacyano-niobate and the paramagnetic transition-metal ions is favored by the bridging cyanides. In this class of materials the coupling leads to cooperative magnetic ordering below a critical temperature, which rises in the series $M^{II} = Co^{2+}$, Fe^{2+} and Mn^{2+} from 13 to 43 to 50 K. With respect to the coercive field the tendency is reversed. Here the Co^{2+} derivative has the highest (160 Gauss at 5 K) and the Mn^{2+} the lowest (4 Gauss at 2 K) coercive field, respectively.

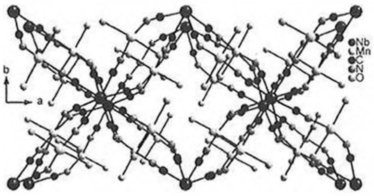

Figure 1: 3-dimensional network of $[Nb^{IV}\{\mu\text{-}(CN)_4M^{II}(H_2O)_2\}_2] \cdot 4H_2O$

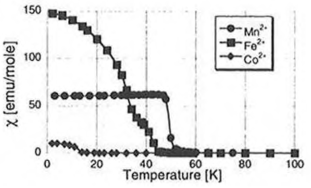

Figure 2: Magnetic susceptibility vs. T at 50 Gauss

Inorganic Chemistry **130**

New high-spin molecules

Federica Bonadio and Silvio Decurtins

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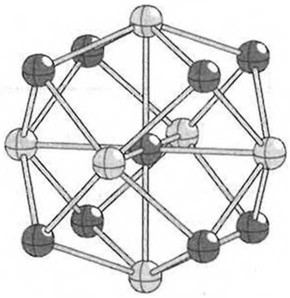
The synthesis and investigation of magnetic properties of novel molecular clusters containing paramagnetic transition metal ions is currently attracting a great deal of interest.
Recently we presented a novel cyano-bridged Mn_9^{II} Mo_6^{V} molecular cluster with a S=51/2 ground state, e.g. of formula $[M\{M(MeOH)_3\}_8(\mu\text{-}CN)_{30}\{M'(CN)_3\}_6] \cdot 5MeOH \cdot 2H_2O$, where M is Mn^{II} and M' is Mo^{V}.[1]
Here we present two novel molecular cluster compounds with an analogous formula, where M is Co^{II} and M' is Mo^{V} or W^{V}.



[1] Joulia Larinova, Mathias Gross, Melanie Pilkington, Hanspeter Andreas, Helen Stoeckli-Evans, Hans U. Güdel, and Silvio Decurtins, *Angew. Chem. Int. Ed.* **2000**, 39, 1605-1609

Inorganic and Coordination Chemistry **131**

Chiral ligands containing sulfonic groups: synthesis and characterisation

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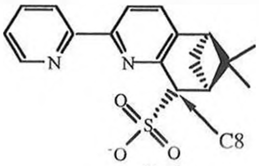
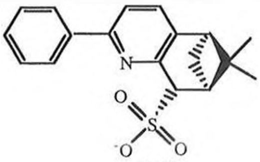
The synthesis of chiral ligands and their metal complexes has been the subject of widespread interest in coordination chemistry over recent years.[1]

Pyridine and bipyridine ligands can be used to synthesize coordination compounds in which the stereochemistry at the metal center is predetermined by the configuration of the ligands. An important feature of the molecules of the pinene-phenyl-pyridine and pinene-2,2'-bipyridine series is their ability to bind stereoselectively another groupe at one center(C8) of the pinene.[2]

We are investigating the sulfonated forms of chiral pinene bipyridine and pinenepyridine derivatives such as 5,6-pinenebipy (L1) and pinene-phenyl-py (L2), in order to prepare uncharged chiral metal complexes.



(L1)



(L2)

[1] U. Knof, A. von Zelewsky, *Angew. Chem.*, **1999**, 111, 312.
[2] H. Muerner, P.Belser, A. von Zelewsky, *J. Am. Chem. Soc.*, **1996**, 118, 7989.

This work is supported by the Swiss National Science Foundation.

Inorganic Chemistry **132**

TRANSITION METAL COMPLEXES OF 1,10-PHENANTHROLINE-5,6-DIONE AND SOME OF ITS DERIVATIVES

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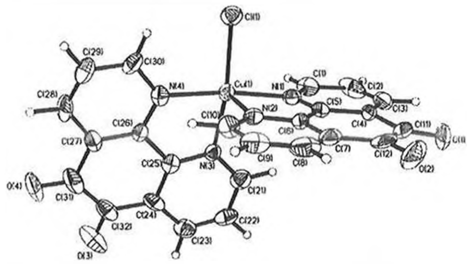
The use of transition metal complexes of bridging ligands to construct predictable, multi-dimensional networks has been the subject of intensive research over recent years.

We have focused our attention on 1,10-Phenanthroline-5,6-dione (Phendione) because this ligand has the ability to form stable complexes with a wide variety of metal ions and carries an *o*-quinone moiety with pH-dependent electro-activity.

We will report our preliminary findings on the co-ordinating properties of Phendione and some of its derivatives.



X-ray crystal structure of $[CuCl(Phendione)_2](PF_6)_2 \bullet 2H_2O$

Coordination Chemistry **133**

Synthesis and studies of new photonic devices

Vincent Adamo and Peter Belser

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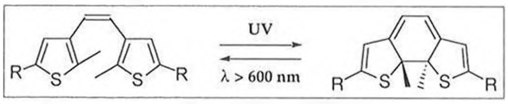
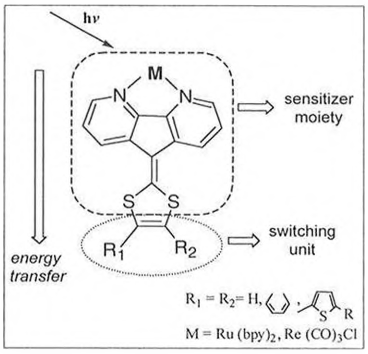
Lehn and Irie [1] have independently developed a reversible photonic device based on a dithienylethene system. The closed and open form of the system corresponds to a conducting or non-conducting bridge. To change the wavelength of the closing process from *UV* to *VIS* light, we are in progress to introduce a metal complex to the switching unit, that can act as a sensitizer.



In the present work we discuss the synthesis of this metal complex. The coupling step to combine the sensitizer with the switching unit, is a *Wittig-Horner* reaction between a phosphorus 1,3-dithiol-2-ide carbanion and diazafluorenone [2].

UV-VIS absorption, electrochemical and emission measurements are planned to prove the properties of this new switching molecule.



$R_1 = R_2 =$ H, ,

M = Ru $(bpy)_2$, Re $(CO)_3Cl$

[1] A. Fernandez-Acebes, J.-M. Lehn, *Chem. Eur. J.* 1999, *5*, 3285;
T. Yamada, M. Irie, *J. Am. Chem. Soc.* 2000, *122*, 1589.
[2] K. Kloc, J. Mlochowski, Z. Szulc, *J. Prakt. Chem.* **1977**, *319*, 959.

Inorganic and co-ordination chemistry **134**

Synthesis of New Oligopyridil-pyrazine Ligands for the Self Assembly of Circular Helicates - The Role of Stereocontrol at Metal Centres

Thomas Bark and Alex von Zelewsky

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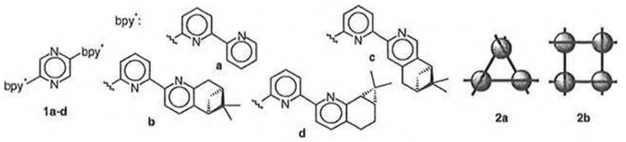
2,5-Bis-(2,2'-bipyridin-6-yl)-pyrazine (1a) and chiral, terpene annellated derivatives of it have been synthesised. Their co-ordination to middle and late first row transition metals ($Cr^{2+/3+}$ - Cu^{2+}) and to Zn^{2+}, Cd^{2+} and Pb^{2+} has been examined.

We are interested in pyrazine containing ligands that can serve as bridging ligands in self assembled, supramolecular co-ordination species. Such complexes are potentially interesting materials for electrochemical and magnetic studies due to the linking pyrazine moiety.[1]
The ligand 2,5-Bis-(2,2'-bipyridin-6-yl)-pyrazine (**1a**) has been designed to yield chiral, cyclic, oligonuclear complexes (**2**) (so-called circular helicates) with octahedrally co-ordinated metal ions.



Formation of such rings instead of polymeric chains demands metal ions of the same configuration. In order to predetermine the configuration at the metal centres, the chiral, enantiopure derivatives (**1b – d**) are used as ligands

[1] M. Graf, H. Stoeckli-Evans, A. Escuer, R. Vicente, *Inorg. Chim. Acta*, **1997**, *257*, 89.
[2]- A. von Zelewsky, O. Mamula, *Dalton Transactions*, **2000**, 219.

This work is supported by the Swiss National Science Foundation.

Coordination Chemistry **135**

The High-Spin $^5T_2$ State in $[Ru(bpy)_3]^{2+}$

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The excited state electronic structure of the $[Ru(bpy)_3]^{2+}$ (bpy = 2,2'-bipyridine) is well known. Its famous orange luminescence, originating from the lowest excited state ^{3}MLCT, is thermally quenched above 200 K. This behaviour has been explained as being due to the thermal population of a close-lying ligand-field state, namely the $^3T_1(t_{2g}{}^5e_g{}^1)$ d-d state [1]. We have determine the activation volume for the thermal quenching of the ^{3}MLCT luminescence, by doping the complex into inert host lattices of Zn(II) and Cd(II), in which the difference in internal pressure is known [2].
The resulting activation volume of ~20Å^3 is too large to correspond to the $(t_{2g}{}^5e_g{}^1)$ configuration. **We therefore reassign the d-d quencher state in $[Ru(bpy)_3]^{2+}$ to the high-spin $^5T_2(t_{2g}{}^4e_g{}^2)$ state.**

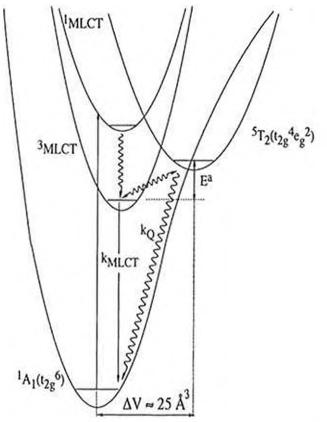

Fig.1: model for the excited state potentials of $[Ru(bpy)_3]^{2+}$.

[1] J. Van Houten, R. J. Watts, *J. Am. Chem. Soc.*, **98** (1976) 4853.
[2] S. Schenker, A. Hauser, W. Wang, I. Y. Chan, *Chem. Phys. Lett*, **297** (1998) 281.

Inorganic and Coordination Chemistry **136**

Synthesis of Macrocycles and Catenanes Based on (-)bis-5,6-pinene-bipyridine

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Chiral bipyridine ligands annelated with terpenes have been used to predetermine the configuration of many structures : octahedral and tetrahedral complexes, linear and circular helicate.[1]

Non-covalently interlocked molecules such as rotaxanes and catenanes are of current interest as models for molecular recognition and as precursors to molecular devices or molecular machines.[2]

Our aim is to integrate our chiralized bipyridines into macrocycles or interlocked molecules such as the catenane shown in **Fig. 1**.

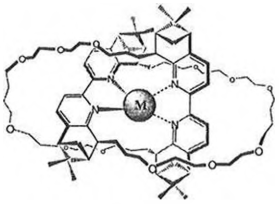

Fig. 1

After the stereoselective grafting of alkyl chains at the pinene groups, we envision to use a metal-templated strategy combined with Ring-Closure Metathesis in order to obtain a catenane or a macrocycle based on (-)bis-5,6-pinene-bipyridine.

[1] A. von Zelewsky, O. Mamula, *J. Chem. Soc., Dalton. Trans.*, **2000**, 219.
[2] Sauvage, J-P; Dietrich-Buchecker, C. *Molecular Catenanes, Rotaxanes and Knots*, Wiley-VCH, **1999**.

This work is supported by the European Union TMR project and the Swiss National Science Foundation.

CHIMIA 2000, 54, No. 7/8

Chimie minérale et de coordination **137**

Spin-crossover in $[Co(bpy)_3]^{2+}$

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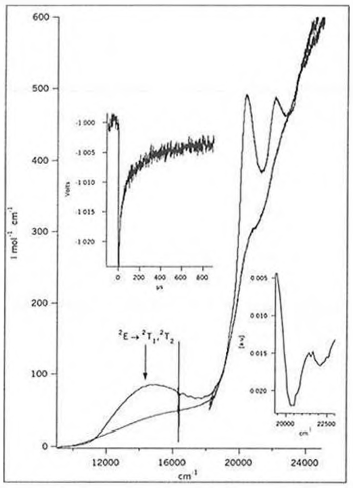
Usually $[Co(bpy)_3]^{2+}$ (bpy = 2,2'-bipyridine) is a d^7 high-spin complex with a $^4T_1(t_{2g}{}^5e_g{}^2)$ ground state, as for instance in the oxalate network compound $[Co(bpy)_3][NaCr(ox)_3]$. Substituting Na^+ by Li^+ reduces the size of the cavities provided by the oxalate backbone. The corresponding chemical pressure destabilises the high-spin state of $[Co(bpy)_3]^{2+}$ sufficiently for the $^2E(t_{2g}{}^6e_g{}^1)$ low-spin state to become the actual ground state. As a result, $[Co(bpy)_3][LiCr(ox)_3]$ and $[Co(bpy)_3][LiRh(ox)_3]$ are spin-crossover systems, as evidenced by magnetic susceptibility measurements, single crystal optical spectroscopy and X-ray structure determination.



At room temperature, the high-spin→low-spin relaxation of Co(II) spin-crossover compounds is typically two orders of magnitude faster than for Fe(II) compounds. At low temperatures this difference is much larger. Whereas the lifetimes of light-induced metastable states of Fe(II) spin-crossover systems are in the range of seconds to hours at 10 K, those for Co(II) compounds are in the microsecond range. The figure shows the temperature dependent absorption spectra of $[Co(bpy)_3][LiRh(ox)_3]$ as well as the transient difference absorption spectrum and decay curve following pulsed laser irradiation at 10 K.

Inorganic and Coordination Chemistry **138**

STUDIES OF OCTAHEDRAL COMPLEXES WITH LIGANDS OF BISBENZIMIDAZOLE PYRIDINE TYPE

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University of Geneva, Quai E. Ansermet
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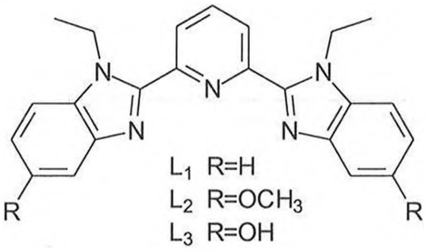
Ligands derived from the well known 2,6-bis(benzimidazol-2-yl) pyridine ligand (L_1, R = H) have been prepared with a view to the incorporation of this binding unit into more complicated systems. The coordination chemistry of these ligands with 3d metals such as manganese(II), iron(II), and cobalt(II) is reported. All form stable pseudo-octahedral complexes of composition ML_2.



The introduction of hydroxy (L_3) or alkoxy (L_2) substituents remote from the metal binding site produces little significant change in physicochemical properties from those observed for L_1. If, however, the phenol groups of L_3 are deprotonated, there are significant changes in the UV-visible spectra and redox chemistry, suggesting a strong interaction between the metal site and the phenol group.

Chimie Minérale et de coordination **139**

The Binding Ability of Iron Bonded to Porphodimethene : Synthesis and reactivity

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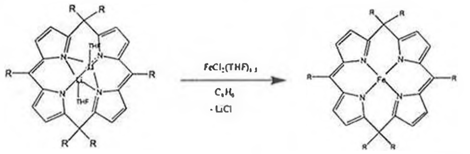
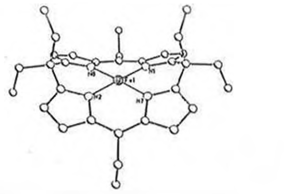
CH-1015 Lausanne

The availability of the parent compound, the meso-hexaethylporphodimethene-iron(II), $[(Et_6N_4)Fe]$, **2**, is due to a novel synthetic methodology making easily available $[Et_6N_4Li_2(THF)_2]^1$, **1**.
A quite recent methodology has made available large scale synthesis of the porphodimethene skeleton in the protic form, as well as a lithium derivative, particulary appropriate for transmetallation reactions. Porphodimethene as a macrocyclic ligand has peculiar features that places it in between porphyrinogen and porphyrin. It would serve to test how much the changes in the aromaticity, in the conformation of the ligand, in the electronic properties, can affect the metal binding ability towards the substrates, which has been so extensively studied in metal-porphyrin chemistry.



We report here the synthesis of **2** which was performed from the transmetallation of **1** in benzene. The reaction led to the formation of green crystals of **2**, which have a magnetic moment of 3.65 BM at 298 K.



The compound **2**, which contains a tetracoordinated iron in a quasi-planar geometry, can add either one or two additional ligands in the axial positions, and to undergo one electron oxidation.

[1] J.-M. Benech, L. Bonomo, E. Solari, R. Scopelliti, C. Floriani, Angew. Chem. Int. Ed., 1999,38,1957

Chimie Minérale et de coordination **140**

Eu^{2+} Ion Hydration Sphere in Aqueous Solution A first XAFS Study

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

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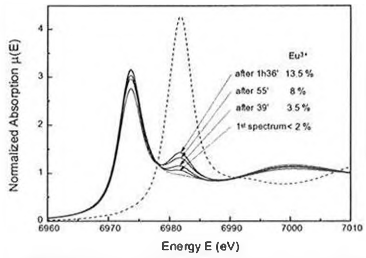
[b] *Institute of Solid State Physics, University of Riga, Latvia*

The Eu^{2+} aqua ion is one of the few cations for which no hydration structure has been established yet [1].

For the first time, a XAFS study is presented for this aqua ion. Eu^{2+} is known not to be stable in aqueous solution as it reacts quickly with oxygen and is slowly oxidized by water [2]. First of all, europium L_3-edge XANES measurements clearly demonstrated that sealed oxygen free samples of Eu^{2+} aqueous solutions are stable in a closed cell for at least 5 h.



Eu^{2+} solution XANES measurements (dotted line) and its progressive oxidation by air (full lines) ; Comparison with a pure Eu^{3+} solution (dashed line).

XAFS data were then interpreted taking into account both theoretical and experimental phases and amplitudes. It allowed us to determine a preliminary RDF - like function as well as an approaching local structure of Eu^{2+} aqua ion.

[1] Richens, D. T., *The Chemistry of Aqua Ions*, Wiley, **1997**, 197-201.
[2] Johnson, D. A., *Adv. Inorg. Chem. Radiochem.*, **1977**, *20*, 1-132.

Inorganic and Coordination Chemistry **141**

New imine-ether ligands for coordination chemistry

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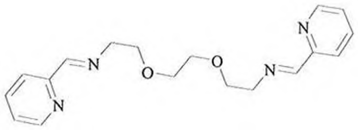
CH-2000 Neuchâtel

One of the main goals today in coordination chemistry is to synthesize molecules with predefined geometry. To do this, it would be useful to have a library of ligands and a database concerning their characteristics as far as coordination to first row transition metals is concerned. In this way, molecular fragments could be assembled to produce a whole variety of compounds with predetermined geometry. While much is known about polypyridil type ligands, less is known about mixed donor ligands incorporating pyridine. The condensation reaction of pyridine-2-carboxaldehyde with primary amines offers an easy and inexpensive way to form a variety of bis-bidentate and bis-tridentate ligands.

Here we present one of a series of such ligands, a new N_4O_2 Shiff base and some examples of its coordination chemistry.



Structural scheme of the ligand. **L.**

Both mono and binuclear complexes of L have been obtained with a variety of transition metals. As expected, the central =NCH2CH2OCH2CH2OCH2CH2N= bridge is found to be very flexible. Incorporating all this information into a dedicated molecular mechanics force field for such compounds could be extremely helpful to predict which geometrical arrangements on coordination are possible. The consequences of reducing or increasing this flexibility will be discussed.

Inorganic and Coordination Chemistry **142**

Synthesis of Coordination Compounds with Predetermined Chirality using Self-assembly Processes

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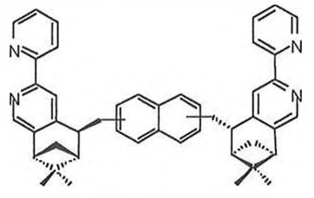
CH-1700 Fribourg (e-mail: marielle.loi@unifr.ch)

The enantiomerically pure CHIRAGEN ligands (linked pineno-2,2'-bipyridines) can be used to synthesize configurationally stable coordination compounds in which the stereochemistry at the metal center is predetermined by the configuration of the ligands [1].



(-)-4,5-Chiragen [DMN]

Several self-assembled silver(I) helicates with controlled chirality have been structurally characterised starting from 5,6-CHIRAGEN-type ligands. [2]

We are investigating the formation of coordination compounds by self-assembly with a new CHIRAGEN ligand family where ten different substitutionnal isomers can be prepared: (-)-4,5-CHIRAGEN-[dimethyl-naphthalene].

[1] P. Hayoz, A. von Zelewsky, H. Stoeckli-Evans, *J. Am. Chem. Soc.*, **1993**, 115, 5111.
[2] A. von Zelewsky, O. Mamula, *J. Chem. Soc., Dalton. Trans.*, **2000**, 219.

This work is supported by the European Union TMR Project and the Swiss National Science Foundation.

Inorganic and Coordination Chemistry **143**

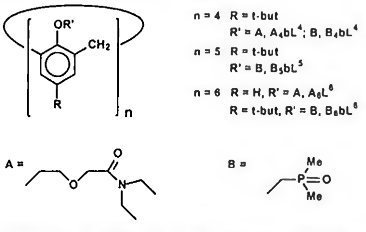
Study of Lanthanide Complexes formed with Functionalized Calix[n]arenes (n= 4-6) with Ether-Amide and Phosphinoyl Pendant Arms

F. de M. Ramírez,[a,b] S. Varbanov,[a,c] R. Scopelliti,[a] C. Cécile,[a] L. J. Charbonnière,[d] and J.-C. G. Bünzli[a]

[a] *Institute of Inorganic and Analytical Chemistry, University of Lausanne, BCH, CH-1015 Lausanne, Switzerland.*
[b] *Instituto Nacional de Investigaciones Nucleares, Departamento de Química, Km 36.5 Carretera México-Toluca, Salazar, Edo. de México D.F., C.P. 52045. México.*
[c] *Institute of Polymers, Bulgarian Academic of Sciences, 1113 Sofia, Bulgaria.*
[d] *Laboratoire de Chimie, Électronique et Photonique Moléculaire, UPRES-A 7008 au CNRS, 25 Rue Becquerel, 67087 Strasbourg, France.*

Calixarenes are amenable to chemical modifications at both the narrow and large rims and can thus be easily transformed into versatile materials with potential applications in extraction, separation and analytical techniques, including biomedical applications and nuclear waste management [1][2].

We report here the syntheses and characterisation of the functionalized calix[n]arenes at the narrow rim (see scheme) as well as stability constant determinations, photo-physical properties and solid state and solution structural data of the resulting complexes with trivalent lanthanide ions.



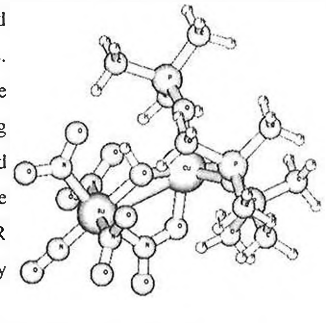
[1] J.-C. G. Bünzli, F. Ihringer and F. Besançon in *Calixarene molecules for separations,* G. Lumetta, A. Gopalan and R.D. Rogers, eds, ACS Symposium Series, ACS, Washington, D.C. 2000, Ch. 14.
[2] L. Le Saulnier, S. Varbanov, R. Scopelliti, M. Elhabiri , J.-C.G. Bünzli, J. Chem. Soc., Dalton Trans., 3919 (1999).

Chimie minérale et de coordination **144**

The calculated gas phase structure of mixed Ru–O–M (M= Cu, Ni, Zn) complexes as a starting point for the interpretation of EXAFS and IR measurements

F.Mariotti[1], C.Daul[1], A.Varnek[2], G. Wipff[2], V. Torgov [3], E. Stoyanov [3] and S. Erenburg [3].
(1) Institut de Chimie Inorganique, Université de Fribourg,
CH–1700 FRIBOURG, Switzerland
(2) UMR 7551 CNRS, Faculté de Chimie, Université Louis Pasteur, 4, rue B. Pascal, Strasbourg, FRANCE
(3) Institute of Inorganic Chemistry of Ac. Sci. Russ., av. Lavrentiev 3,
Novosibirsk, RUSSIA

A new method of Ru extraction based on the formation of the mixed complex $[RuNO(NO_2)_4OH{-}M{-}L_n]$ (where M=Cu,Ni,Zn; L=Oct_3PO, n=2–3) has been developed by Torgov[1, 2]. The characterisation of the structure of the Ru–O–M complexes was attempted by EXAFS and IR spectroscopy [2]. For the purpose of interpretation of the experimental data, the gas phase structure of these complexes was calculated using the DFT (M=Cu) and PM3–tm (M=Cu, Ni, Zn) methods. Calculated DFT and PM3–tm structures are very closed and reveal interesting coordination patterns of metals: Ru is linked to Cu *via* OH and NO_2 bridging groups. The structures fitted from EXAFS and IR spectroscopy in hexane solution are fully consistent with the calculated models.



[1] V.G Torgov, R.S. Schulman, T.V. Us, V.A. Emelianov, T.M. Korda XI Russian Conference on Solvent Extraction, Abstracts, p. 92, Moscow, 21–27 June 1998, Ac. Sci. Russ.
[2] INCO–COPERNICUS project IC15–CT98–0208. Annual Report, 1999.

Coordination Chemistry **145**

On the route to a new photo-switchable system

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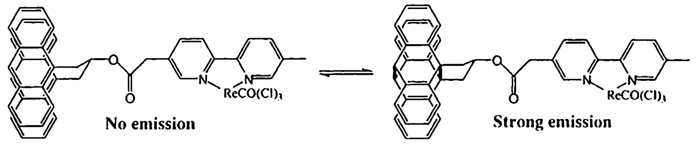
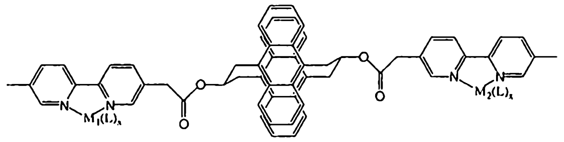
Institute of Inorganic and Analytical Chemistry
University of Fribourg, CH-1700 Fribourg, E-mail: david.mauron@unifr.ch

In a recent work, we have synthesized a switching unit which was able to perform many open-closing cycles without molecular decomposition.[1] The switch was based on two anthracenes moieties linked by an ester bridge to a bipyridine unit. It is well known that two anthracenes molecules can undergo a reversible photocyclisation. Such process converts the aromatic anthracenes moieties into an aliphatic bridged system.



To indicate the state of the switch (open and closed form), we have introduced a rhenium metal center coordinated to the bipyridine ligand. The emission of the rhenium complex can be observed depending on the state of the switching unit (emitting or non-emitting).
To improve the capability of such a photonic device, a dinuclear metal complex with two anthracenes moieties as a bridging ligand is under construction.



With such a molecular device, energy and/or electron transfer reactions can be studied in the aromatic and aliphatic form of the bridge.

[1] P. Belser et al., *Angew. Chem., Int. Ed. Engl.*, **1997**, 36, 2779.

Inorganic Chemistry **146**

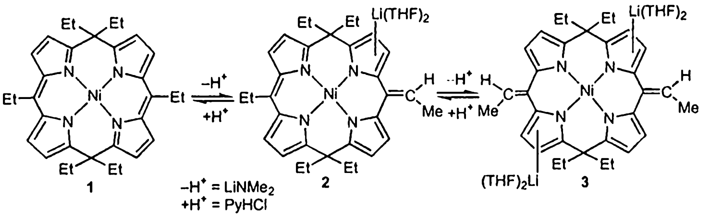
Porphodimethene-Porphyrinogen Relationship: The Generation of Unprecedented Forms of Porphyrinogen

Lucia Bonomo, Euro Solari, Rosario Scopelliti and Carlo Floriani

Institut de chimie minérale et analytique, Université de Lausanne, BCH, CH-1015 Lausanne

The intermediacy of porphodimethenes in the oxidation of porphyrinogen to porphyrin is well accepted. Work on the chemistry of porphodimethene skeleton has suffered, however, for a long time from the absence of a real synthetic methodology, which is now available for exploring its reactivity. Porphodimethenes are the target molecules of this report, since they allow one to enter the field of unprecedented forms of porphyrinogen.

The electrophilic reactivity of the porphodimethene skeleton towards nucleophiles led the establishment of a synthetic methodology to unprecedented forms of porphyrinogen containing the vinylidene substituents as well as other functionalities in the *meso*-positions (see Scheme 1).[1]



Scheme 1

[1] Bonomo, L.; Solari, E.; Scopelliti, R.; Latronico, M.; Floriani, C. *Chem. Commun.* 1999, 2227-2228.

Chimie Minérale et de Coordination **147**

A Density Functional Study of Gaseous Reaction of $CoCl_2$ with Pyridine.

Ilaria Ciofini , Claude A. Daul , Carl-Wilhelm Schläpfer.

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Université de Fribourg, Pérolles, 1700 Fribourg.

The complex formation of $CoCl_2$ with pyridine (py) and 4-picoline (pic) has been studied using Density Functional Theory (DFT) using ADF1999 [1] and Gaussian98 program packages [2] as prototype complex formation reaction.
The experimental data available in literature [3], UV-vis spectra and thermochemical data, were collected for the following reactions

$$CoCl_2 + 2L \leftrightarrow CoCl_2L + L \leftrightarrow CoCl_2L_2 \qquad L = py,\ pic$$

in gas phase and therefore they are especially suitable for a direct comparison with theoretical characterisation.
As a preliminary study, the ground state potential energy surface of $CoCl_2$ has been analysed in detail. The molecule has a degenerate ground state and shows a Renner Teller distorsion.
A complete thermochemical and structural characterisation of the complex with one and two additional ligand was performed and the results compared to the available experimental data.
The effect of pyridine substitution on the complex stability is currently under analysis.

[1] Gaussian98 rev. A.5, Gaussian Inc. Pittsburgh PA, 1998.
[2] a) ADF1999, E J Baerends et al. b) C Fonseca Guerra, J G Snijders, G te Velde, E J Baerends, *Theor. Chem. Acc.* **1998**, 99, 391.
[3] A. C. Daul, F. Emmenegger, M. Minar, M. Piccand *Inorg. Chem.* **1993**, 32, 2992.

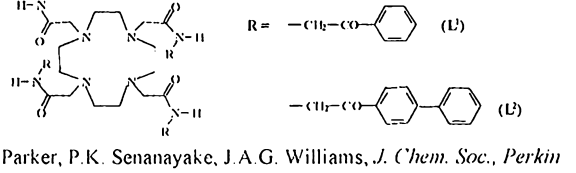
Inorganic and Coordination Chemistry **148**

LUMINESCENCE ENHANCEMENT IN LANTHANIDE CYCLEN-BASED LIGANDS USING PHENACYL MOIETIES

Gaël Zucchi, Rosario Scopelliti, and Jean-Claude G. Bünzli
Institute of Inorganic and Analytical Chemistry, University of Lausanne, BCH, CH-1015 Lausanne

Since the middle of the eighties, lanthanide coordination compounds based on 12-membered macrocyclic ligands have stirred an increasing interest. The first investigations were centered on their potential use as contrast agents in magnetic resonance imaging. In order to take advantage of their high stability for *in vivo* applications, luminescence studies on cyclen-based lanthanide complexes have started to be carry out in the middle of the nineties in view of their application as responsive probes for the analysis of various ions in biological media [1]. The chromophoric group attached to the pendant arms plays an essential role in these processes.

We have recently studied several cyclen derivatives with various arm lengths and chromophoric moieties. In such edifices, the energy transfer from the organic chromophore to the metal ion is a function of both electronic and geometric parameters [2]. We are now pursuing our study with two new ligands incorporating phenacyl groups (L^1 and L^2), targeted for an efficient triplet state-to-metal energy transfer on respectively Tb and Eu ions under physiological conditions, in view of potential applications in fluoroimmunoassays. We describe here both the structural and photophysical properties of such complexes, for which reasonably high quantum yields have been obtained: 23% for Tb (L^1) and 8-9% for Eu (L^2).



[1] D. Parker, P.K. Senanayake, J.A.G. Williams, *J. Chem. Soc., Perkin Trans. 2* 1998, 2129.
[2] G. Zucchi, R. Scopelliti, P.-A. Pittet, J.-C.G. Bünzli, R.D. Rogers, *J. Chem. Soc., Dalton Trans.* 1999, 931.

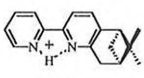
Inorganic and Coordination Chemistry **149**

Protonation of Chiral Bipyridine Ligands

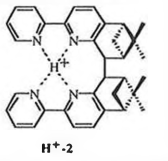
Mathias Düggeli and Alex von Zelewsky

University of Fribourg, Institute of Analytical and Inorganic Chemistry,
Pérolles, 1700 Fribourg, e-mail: Mathias.Dueggeli@unifr.ch

We are interested in the protonated forms of chiral pinene-bipyridine derivatives such as 5,6-pinene-bipyridine (**1**) or 5,6-CHIRAGEN[0] (**2**). Both of these ligands show a large shift of the peaks in the UV-spectrum (2D-graph for ligand **1**) upon protonation with strong acids (hydrochloric acid, trifluoroacetic acid in methanol/water 9/1).



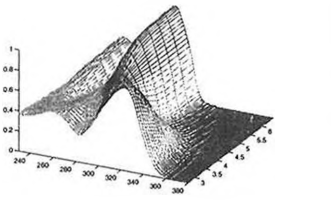
H^+-1

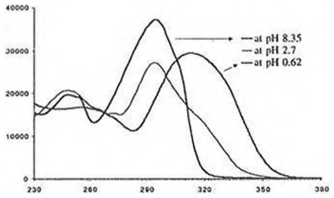


H^+-2

2 can be protonated twice in the pH–range of 10-0 (linear graph). The comparison of the estimated pK-values of the protonated forms $\mathbf{H^+}$**-1** and $\mathbf{H^+}$**-2** shows a difference of nearly 1.5 units.

The single-protonated form $\mathbf{H^+}$**-2** is stabilized by a chelating effect, in which the proton interacts with all four nitrogen atoms. This hypothesis can be corroborated by CD-spectroscopy.





This work is supported by the Swiss National Science Foundation.

Inorganic Coordination Chemistry **150**

Inorganic H-bonded polymers of different dimensionality based on alkaline earth metal halides –A supramolecular approach

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

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[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.

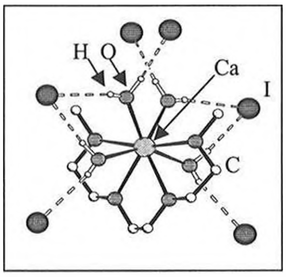

Figure 1

It will also be shown how the preorganization of a ligand can improve the structure prediction. The results of these investigations will be presented on behalf of the examples derived from CaI_2 and oxygen donors, leading to $\{[Ca(DME)_2(H_2O)_3](DME)I_2 \cdot DME\}_{1/\infty}$, $\{[Ca(DME)_2(H_2O)_4]I_2\}_{3/\infty}$ and $\{[Ca(CH_3(OC_2H_4)_3OCH_3]I_2\}_{3/\infty}$ (Fig. 1) [1].

[1] K. M. Fromm, G. Bernardinelli, H. Goesmann, *Polyhedron*, in press

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Inorganic chemistry **151**

Synthesis of novel mixed heterometallic-ligand clusters

E. Gueneau and K. M. Fromm

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Quai E. Ansermet 30, CH-1211 Geneva 4
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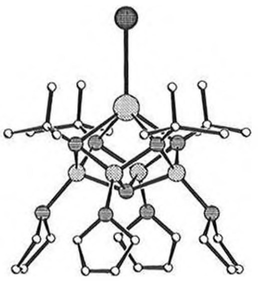
Due to their valuable properties as precursors for the preparation of metal oxide systems (i.e. MOCVD methods) alkaline earth metal alkoxides still spark a growing interest.

We report here the synthesis and characterization of new mixed heterometallic-ligand aggregates. $\mathbf{[BaI(O\mathit{t}Bu)_4Li_4(THF)_4(OH)]}$ (1) was made from a bulky lithium alkoxide as reacting block with alkaline earth halide in etheral solution.

$$\boxed{BaI_2 + LiO\mathit{t}Bu \xrightarrow[THF]{} \underline{1}:}$$



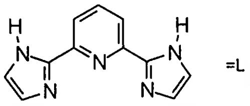
Inorganic and Coordination Chemistry **152**

Modulation of metal reduction potential by deprotonation of an imidazol moiety

G.Stupka, A. F. Williams

University of Geneva
Dept of Inorganic, Analytical and Applied Chemistry
Quai Ernest-Ansermet, 30
CH-1211 Genève 4

Deprotonation of the coordinated imidazol of the ligand 2,6-bis(imidazol-2'-yl)pyridine modified the reduction potential of coordinated metal (Fe, Co, Ni).The ligand was synthetised via a Negishi type cross-coupling. Deprotonation of the ML_2 complex in air led to complete oxidation of the coordinated Fe(II) and Co(II) respectively to Fe(III) and Co(III). With Ni(II) only partial oxidation to Ni(III) takes place. For example the reduction potential of the iron complex were switched from +0.920 V to -0.460 V.[1]



1. R. F. Carina, L. Verzegnassi, G. Bernardinelli and A. F. Williams, *Chem. Commun.*, **1998**, 2681.

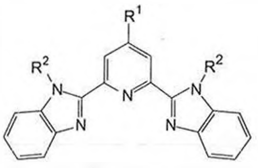
Inorganic and Coordination Chemistry **153**

STABILITY, SOLUTION STRUCTURE AND LUMINESCENCE OF LANTHANIDE TRIPLE HELICAL COMPLEXES

N. André,[a] C. Platas Iglesias,[b] R. Scopelliti,[a] C. Piguet[c] and J.-C. G. Bünzli[a]

[a] *Institute of Inorganic and Analytical Chemistry, University of Lausanne, BCH 1403, CH-1015 Lausanne, Switzerland*
[b] *Departamento de Quimica Fundamental e Industrial, Universidade da Coruña, Campus de A Zapateira s/n 15071 A Coruña, Spain*
[c] *Dept. of Inorganic, Analytical and Applied Chemistry, University of Geneva, CH-1211 Geneva-4, Switzerland*

Derivatives of bis(benzimidazole)pyridine form triple helical complexes with Ln^{III} ions in acetonitrile solution the stability of which is influenced, among other factors, by the substitution at the 4-position of the central pyridine ring. We present here a study of the role of the electron donor substituent, diethylamino, on the stability of the $[Ln(L^1)_3]^{3+}$ complexes using a competitive potentiometric titration with Ag^+.



$R^1 = H$, $R^2 = Me$: mbzimpy
$R^1 = H$, $R^2 = NEt_2$: L^1

Furthermore, the solution structure of the triple helical edifices is investigated in deuterated acetonitrile by means of a paramagnetic NMR investigation (lanthanide induced shifts): the complexes are shown to be isostructural and the results are compared to the structure determined by X-ray crystallography for Tb^{3+}.

A photophysical study of the energy transfer processes in the Eu^{3+} and Tb^{3+} complexes shows L^1 to provide an efficient ligand to metal energy transfer. However, but an inefficient intersystem crossing within the ligand leads to weak quantum yields. High resolution luminescence spectra of $[Eu(L^1)_3]^{3+}$ indicate a distorted D_3 symmetry around Eu^{3+}.

[1] S. Petoud, J.-C. G. Bünzli, F. Renaud, C. Piguet, K. Schenk, G. Hopfgartner, Inorg. Chem., **36**, 5750 (1997)
[2] C. Platas, F. Avecilla, A. de Blas, C. F. G. C. Geraldes, T. Rodriguez-Blas, H. Adams, J. Mahia; Inorg. Chem., **38**, 3190 (1999).

Chimie de Coordination **155**

Calixarene-like Cyclophanes: Improved Synthesis and Alkaly Metals Binding by Hexahomotrioxacalix[3]arene trianion.

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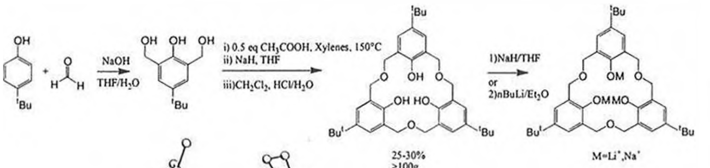
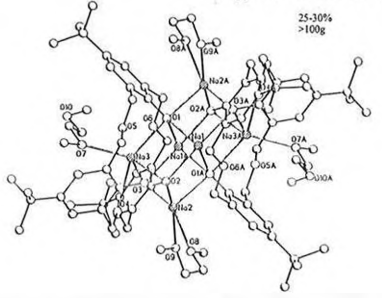
CH-1015 Lausanne

The condensation of p-Bu^t-Phenol and paraformaldehyde yields a series of cyclic oligomers. Under certain conditions a homologue containing three arene rings and three extra oxygens can also be isolated [1,2].
Despite the emerging interest for this class of cyclophanes, the lack of a high-yield and large-scale synthesis is limiting a systematic investigation. This note is concerned with the new preparation in hundred-grams scale of p-Bu^t-Hexahomotrioxacalix[3]arenetriol and the complexation of Li^+ and Na^+ cations in the C3 symmetry scaffold provided by the ligand trianion.





[1] Dhawan, B.; Gutsche, C. D. *J. Org. Chem.* **1983**, *48*, 1536-1539.
[2] Hampton, P. D.; Bencze, Z.; Tong, W.; Daitch, C. E. *J. Org. Chem.* **1994**, *59*, 4838-4843.

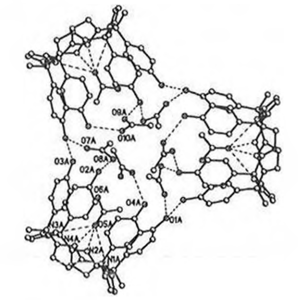
Inorganic Chemistry **154**

A Cylindrical Cavity with Two Different Hydrogen-Binding Boundaries: the Calix[4]arene Skeleton Screwed onto the *meso*-Positions of the Calix[4]pyrrole

Lucia Bonomo, Euro Solari, Gülsen Toraman, Rosario Scopelliti, and Carlo Floriani

Institut de chimie minérale et analytique, Université de Lausanne, BCH, CH-1015 Lausanne

There has been a recent explosive development in the realm of molecular recognition of polar, and often uncharged, multifunctional organic molecules in which multi-point hydrogen bonds provide stabilization.
Multi-point hydrogen bonding molecules are appropriate devices for the maintenance of the function and structure of complex biomolecules. Many of them are bifunctional molecules, *i.e.* aminoacids, steroids, all requiring bifunctional hosts which have two chemically different binding areas.
We deal here with the discovery of a class of compounds particularly appropriate to play a role in multi-point or multi-site host-guest interactions [1] (see side figure).



The acid-catalyzed condensation of pyrrole with p- or m-hydroxyacetophenone led to the formation of *meso*-tetramethyltetrakis(hydroxyphenyl)calix[4]pyrroles occurring in three isomeric forms, with the cone conformer displaying topologically variable multi-site or multi-point surfaces for binding neutral or anionic substrates.

[1] Bonomo, L.; Solari, E.; Toraman, G.; Scopelliti, R.; Latronico, M.; Floriani, C. *Chem. Commun.* **1999**, 2413-2414.

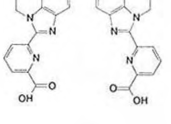
Inorganic and Coordination chemistry **156**

Emission Quantum Yield and Energy Transfer Processes in Lanthanide-Containing Bimetallic Triple Helicates

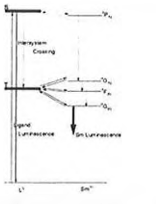
F. R. Gonçalves e Silva[a], O. L. Malta[b], C. Piguet[c] and J.-C. G. Bünzli[a]

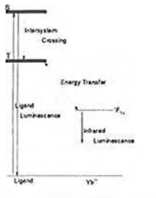
[a] *Institute of Inorganic and Analytical Chemistry, University of Lausanne, BCH, CH-1015 Lausanne, Switzerland.* [b] *Deptº de Química Fundamental-UFPE, 50740-540 Recife, PE-Brazil.* [c] *Department of Inorganic Chemistry, University of Geneva, CH-1211 Geneva-4, Switzerland.*

The photophysical properties of L^C [1] and $[Ln_2(L^C\text{-}2H)_3]xH_2O$ (Ln = Nd, Sm, Dy, Yb) are investigated in H_2O and D_2O at pH = 7-12. Upon UV excitation ($\lambda_{exc} \approx 360$ nm), L^C sensitises the luminescence of Nd^{3+}, Sm^{3+} and Yb^{3+} but the ligand-to-Ln^{3+} energy transfer is not complete resulting in residual ligand emission. The intensity of the ligand luminescence decreases upon formation of the helicates, because of the enhancement of the intersystem crossing. The metal-centred luminescence of the Nd, Sm and Yb helicates and the lifetime of the Sm $^4G_{5/2}$ level increase in D_2O. We propose a quantitative treatment of the following energy transfer processes.



L^C





The direct and exchange Coulomb interaction models [2] are used to determine the energy transfer rates between the ligand and Ln^{3+} levels. The Sm complex has higher energy transfer rates than the Yb helicate, since $\Delta E(^3\pi\pi^* - {}^4G_{5/2}) < \Delta E(^3\pi\pi^* - {}^2F_{5/2})$.

[1] M. Elhabiri, R. Scopelliti, J.-C. G. Bünzli and C. Piguet, J. Am. Chem. Soc. **121**, 10747 (1999).
[2] F.R.G. e Silva and O.L. Malta, J. Alloys and Comp., **250**, 427 (1997).

CNPq

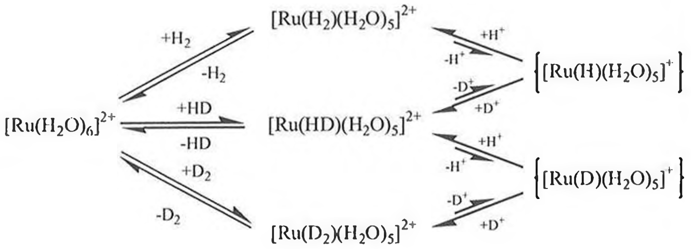
Inorganic and Coordination Chemistry **157**

The first dihydrogen aqua complex: in situ characterization and isotope exchange

Pascal Grundler, Alain Porquet, Nicolas Aebischer, André E. Merbach

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

The product of the reaction between $[Ru(H_2O)_6]^{2+}$ and pressurized H_2 in water is $[Ru(H_2)(H_2O)_5]^{2+}$ whose nature was unambiguously demonstrated by ^1H and ^{17}O NMR and which is the first characterized dihydrogen aqua complex [1].



An interesting feature of this complex is that it catalyses the H/D exchange between the dissolved gas, H_2, and the NMR solvent, D_2O.

A kinetic study at variable pH of this system was performed by ^1H and ^2H NMR and UV-Vis spectroscopy under H_2 pressures up to 740 bar. These measurements provided the formation, dissociation and isotope exchange rates for the $[Ru(H_2)(H_2O)_5]^{2+}$ complex.

On the base of our results we propose a mechanism for the isotope exchange reaction with an hydride as intermediate.

[1] N. Aebischer, U. Frey, A. E. Merbach, *J. Chem. Soc., Chem. Commun.*, **1998**, 2303.

Chimie minérale et de coordination **158**

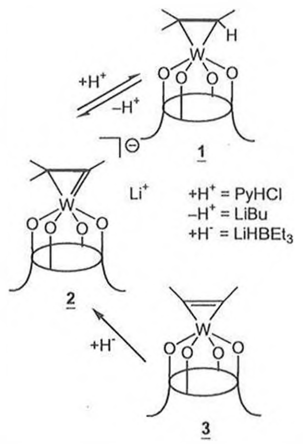
Alkene- and Alkyne-Reactivity over a Metal-oxo Surface Modelled by Calix[4]arene-Tungsten(IV) : the Formation of η^2-Vinyl and Alkylidene Complexes

Geoffroy Guillemot, Euro Solari, Carlo Floriani
Institut de Chimie Minérale et Analytique, BCH, Université de Lausanne, CH-1015 Lausanne, Switzerland.

Some fundamental steps of alkene and alkyne rearrangements over a metal-oxo surface can be nicely modeled by the use of metalla-{*p*-Bu^t-calix[4]arene} (Cal). Such mononuclear complexes maintain some of the pecularities of a metal-oxo surface : (i) a quasi-planar oxo environment for the metal ion, making available frontier orbitales appropriate for the stabilization of M-C multiple bond ; and (ii) the bifunctionality of the extended structure, making available two reaction sites, the acidic (metal ion) and the basic (oxo group) one.

Thus, we report here the general synthesis of **CalW(η^2-alkene)** 1 and **CalW(η^2-alkyne)** 3 complexes, which have been converted into the **CalW(η^2-vinylidene)** 2 specie (which pave the way to metalla-alkylidynes) by either deprotonation of the alkene or addition of hydride to the alkyne.

The reactivity of these cyclic metalla-alkylidenes with electrophiles led to unprecedented substituted alkenes by the assistance of the basic O-donor atoms, while formation of dinuclear metalla-alkylidenes was obtained with one electron oxidizing agents.

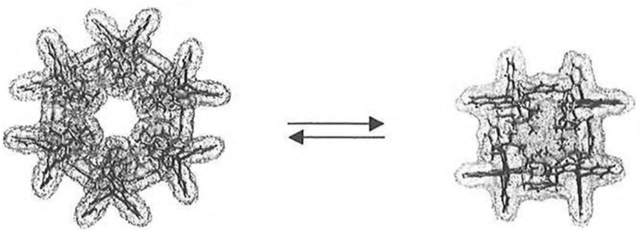


Inorganic and Coordination Chemistry **159**

High Pressure ^1H NMR and ^{109}Ag NMR Study of Hexanuclear Circular Helicate in Solution

Florence J. Monlien, Alain Porquet, André E. Merbach
Institute of Inorganic and analytical chemistry, University of Lausanne, BCH; CH-1015 Lausanne (Switzerland)
Olimpia Mamula, and Alex Von Zelewsky
Institute of Inorganic Chemistry, University of Fribourg, Perolles, CH-1700 Fribourg (Switzerland)

In our last communication on a circular helicate,[1] we observed that some proton signals of $[Ag(C_{42}H_{42}N_4)]_6(PF_6)_6$ were broadened significantly at room temperature. Spectra taken at low temperature (down to 233 K in CD_3CN) show distinct sharpening of the NMR signals leading eventually to a splitting into sets of signals of unequal intensity. We have now investigated silver helicate solutions by ^{109}Ag NMR and by ^1H NMR. This behaviour is attributed to the existence of two exchanging species in solution $[Ag_6L_6]^{6+}$ and $[Ag_4L_4]^{4+}$.



Variable temperature, concentration and variable pressure[2] studies were undertaken and the ΔH°, ΔS°, ΔV° parameters obtained thereof.

[1] Mamula, O.; Von Zelewsky, A.; Bernardinelli, G. *Angew. Chem. Int. Ed.* **1998**, *37*, 3, 290

[2] Cusanelli, A.; Nicula-Dadci, L.; Frey, U.; Merbach, A. E. *Inorg. Chem.* **1997**, *36*, 10, 2211 ; Frey, U.; Helm, L.; Merbach, A. E.; Roulet R. *Advanced Applications of NMR to Organometallic Chemistry* **1996**, John Wiley & Sons Ltd .

Inorganic and Coordination Chemistry **160**

SYNTHESIS OF NEW CHIRAL BUILDING BLOCKS BASED ON METALLOCENE AND APPLICATIONS IN SUPRAMOLECULAR CHEMISTRY

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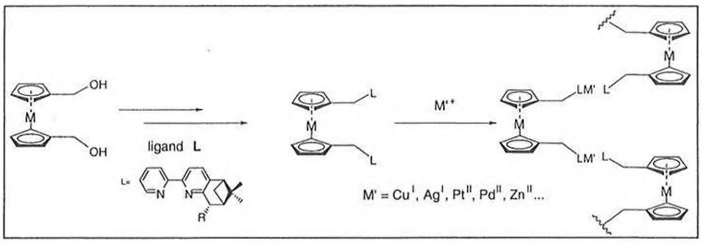
Institute of Inorganic and Analytical Chemistry, University of Fribourg, CH-1700 Fribourg, Switzerland

Recently, chiral building blocks have been synthesised, based on CHIRAGEN type ligands, to predetermine the chirality in metal complexes.[1] The aim of our project is to synthesise a new category of CHIRAGEN derivatives, containing metallocenes as bridges.



This work is supported by the Swiss National Science Foundation

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

CHIMIA 2000, 54, No. 7/8

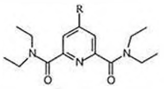
Inorganic Chemistry **161**

LANTHANIDE TRIPLE HELICAL COMPLEXES WITH CHIRAL LIGANDS

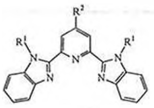
G. Muller,[a] B. Schmidt,[b] C. Maupin,[c] J. P. Riehl,[c] C. Piguet[d] and J.-C. G. Bünzli[a]

[a] Institute of Inorganic and Analytical Chemistry, University of Lausanne, BCH, CH-1015 Lausanne, Switzerland. [b] Novartis Pharma AG, CNS, 4002 Basel, Switzerland. [c] Michigan Technological University, Department of Chemistry, Houghton, MI 49931-1295, USA. [d] Department of Inorganic Chemistry, University of Geneva, CH-1211 Geneva-4, Switzerland

Previous studies with ligands derived from bis(benzimidazole)pyridine have shown that substituents R^1 strongly influence the stability and structure of the final complexes. Substituents R^2 on the other hand mainly affect the electronic and photophysical properties. [1]



R = -CH₂-$\overset{*}{C}$H(COOMe)(NHCOOCMe₃) L^A



R^2 = -COOCH₂-$\overset{*}{C}$HMeEt L^B

We report here on the effect of introducing chiral substituents in the 4-position of the related bis(benzimidazole)pyridine and 2,6-bis(N,N'-diethylcarboxamide)pyridine frameworks. $\mathbf{L^A}$ and $\mathbf{L^B}$ form helical 1:3 complexes with Ln^{III} ions. Stability constants have been measured in acetonitrile by spectrophotometric titrations. Photophysical properties have been examined in the solid state and in solution and the quantum yields of both the ligand- and the metal-centred emissions are reported along with lifetimes of the excited $^5D_0$(Eu) and $^5D_4$(Tb) ions. The influence of the chiral substituent on the helicity of the complexes and the polarisation of the emitted light will be discussed.

[1] S. Petoud, J.-C. G. Bünzli, F. Renaud, C. Piguet, K. J. Schenk, G. Hopfgartner, *Inorg. Chem.*, **1997**, 36, 5750. F. Renaud, C. Piguet, G. Bernardinelli, J.-C. G. Bünzli, G. Hopfgartner, *Chem. Eur. J.*, **1997**, 3, 1646.

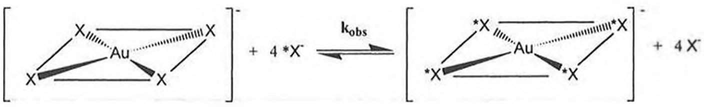
Inorganic and Coordination Chemistry **162**

Variable temperature and variable pressure NMR study of ligand exchange on $[AuX_4]^-$ (X^-= Cl^-, Br^-) in aqueous solution.

Florence Monlien, Amira Abou-Hamdan, Lothar Helm, André E. Merbach

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

The chemical exchange of chlorine and bromine on square planar gold(III) complexes in aqueous solution was studied by chlorine-35 /chlorine-37 and bromine-79/bromine-81 NMR relaxation. The exchange rates were measured as a function of anion concentration, temperature and pressure (up to 2000 bars) from broadening of Cl^- or Br^- resonances due to chemical exchange. Signals of bound chlorine and bromine are to broad to be observed.



The study of the linewidths of pairs of isotopes allows separation of quadrupolar relaxation (depending on the square of the electric quadrupole moment) from broadening due to chemical exchange (independent of the properties of the isotopes). The observed exchange rate was found to be the sum of two contributions: one term, k_1, which is independent on concentration of X^- and a second term, $k_2[X^-]$, which varies linearly with anion concentration.

Inorganic and Coordination Chemistry **163**

η^3-Allyl Palladium(II) Complexes with Chiral Bipyridine Ligands : Synthesis and Characterization

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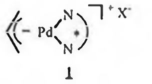
Pérolles, 1700 Fribourg (E-mail : Sarah.Richard@unifr.ch)

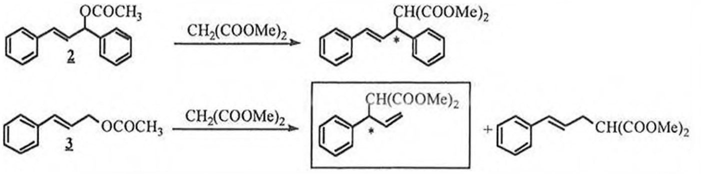
Allyl palladium complexes with chiral N-N ligands have been prepared. The natural products (1*S*)-(-)-α-pinene and (1*R*)-(-)-myrtenal have been used as sources of chirality. Various counterions (X^- = Br^-, PF_6^-, $CF_3SO_3^-$) lead to different solubility properties and determine the catalytic activity of the complexes (1) in allylic alkylation.

The complexes have been characterized by ^{1}H- and ^{13}C-NMR, mass spectrometry, elemental analysis and some of them by X-ray crystallography.



1

Palladium-catalyzed allylic alkylation is one of the most useful carbon-carbon bond forming reactions [1]. In order to test for enantioselectivity and regioselectivity in this reaction type, we examine the alkylation of 1,3-diphenyl-2-propenyl acetate (2) and cinnamyl acetate (3) with dimethylmalonate using the chiral Pd(II) complexes as catalysts.



[1] For a review see: B.M. Trost, D.L. Van Vranken, *Chem. Rev.* **1996**, *96*, 395.

This work is supported by the Swiss National Science Foundation.

164

Physical Methods for the Investigation of Molecular Magnets

Dante Gatteschi
Department of Chemistry, University of Florence
Florence, Italy

Molecular magnetism is a multidisciplinary area where the need for a large number of sophisticated techniques is very high. The transformation from magnetochemistry to molecular magnetism, in which the role of Olivier Kahn cannot be overestimated, has indeed seen a huge increase in the number of physical techniques which must now be routinely mastered in order to satisfactorily characterize the molecular magnets. I will cover here some relatively new techniques, showing with some examples the fundamental information which can be obtained through their correct use. In particular I will show the role of neutron techniques, of anisortropic magnetic measurements, and of magnetic resonance techniques.

Inorganic Chemistry : minisymposium **165**

Molecular magnetism, achievements and prospects, a tribute to Olivier Kahn

Michel Verdaguer

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The lecture will be devoted to some aspects of molecular magnetism impulsed by late Olivier Kahn and to the results obtained either by himself and his team or by his former students and coworkers [1-3].
A particular focus will be on the step: start from an idea to achieve a given (magnetic) property, synthesize, characterize (structure and magnetism), propose a phenomenological description, go to fundamental theory and then to the next idea, fed by experience. This trivial step, applied with enthusiasm, allows to convince that "it works" and that it is rewarding to build the expected magnetic solid from molecules and to get useful devices. Examples will give an overview of some corner-stones in molecular magnetism in the two last decades and propose some dreams for the future:

1) The foundations, lying on ligand field, quantum and symmetry theories
   - tuning of ligand field for tunable spin cross-over;
   - orbital model of exchange interaction;
   - antiferromagnetism and overlap [μ-oxalato copper(II) complexes];
   - ferromagnetism and orthogonality [Cu(II)-VO(IV) complex];
   - molecular ferrimagnetism : [Cu(II)-Fe(III) complex].
2) The creative chemistry with frameworks of increasing sophistication:
   - one-dimensional homometallic chains : Cu(II), Ni(II);
   - bimetallic ferrimagnetic chains and molecule-based magnets;
   - spin cross-over at room-temperature with wide hysteresis;
   - design of photomagnetic and optically active compounds.
3) The devices which can be designed and realized from these new materials.

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Inorganic Chemistry **166**

The Electronic Structure of Linear Thiophenolate-Bridged Heterotrinuclear Complexes: Localized *versus* Delocalized Models

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The electronic structure of a series of linear heterotrinuclear complexes containing six thiophenolato bridges has been established by magnetochemical methods and complementary spectroscopies (electron paramagnetic resonance (EPR), X-ray absorption spectroscopy (XAS), ^{57}Fe Mössbauer). The complexes $[LFeCrFeL]^{1+/2+/3+}$, $[LFeCoFeL]^{2+/3+}$, and $[LFeFeFeL]^{2+/3+}$ contain the same ligand matrix comprising two 1,4,7-tris(4-*tert*-butyl-2-mercaptobenzyl)-1,4,7-triazacyclononane (L^{3-}) ligands. Their electronic structures are discussed in terms of superexchange mechanisms for localized oxidation states and by double exchange for delocalized systems. The isoelectronic systems (low spin d^5 d^6 d^5) $[LFeCoFeL]^{3+}$ and $[LFeFeFeL]^{2+}$ are shown to have different electronic structures despite a common $S_t=1$ ground state. A consistent qualitative model is discussed.

In addition, the electronic structures of compounds of the isostructural series $[LFeMFeL]^{2+/3+}$ (M = Ge, Sn, Pb) are discussed.

Organic Chemistry **167**

Self-Assembling Amphiphilic Dendrimers for Gene Delivery

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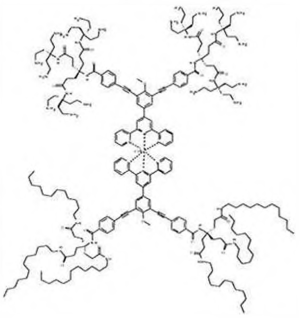
Gene therapy has the potential to provide a therapeutic revolution [1]: for the first time in the history of medicine DNA/RNA are viewed as drugs. However, the actual delivery of DNA to the target cells is still the limiting factor. Synthetic vectors have several advantages over the use of recombinant viruses, especially regarding safety issues and overall production cost. Unfortunately their efficiency is about 1000 fold lower.

Recently dendrimers have been shown to have good vector properties [2, 3]. So far only simple, commercially available dendrimers (PAMAM, PEI) have been studied in detail. We are working on amphiphilic dendrimers, relying both on the high surface charge and buffering capacity of polyamine-functionalized dendrimers and the spontaneous self assembly of amphiphiles which is well characterized for small molecules.

We report here the synthesis of new dendron building blocks of hydrophilic and hydrophobic character and their attachment to a terpyridine core, which in turn was used to assemble functional dendritic amphi-philes *via* a ruthenium complex.



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Organic Chemistry **168**

Synthesis of (*2S, 3R*) 3-Aminoproline and its Application in a Cyclic Peptide Mimicking the Immunodominant Region of the Circumsporozoite Protein of *P.falciparum*

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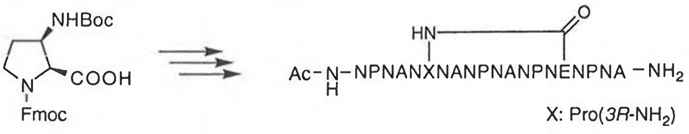
The immunodominant site on the circumsporozoite (CS) protein has been extensively studied for the design of a potential synthetic malaria vaccine [1]. This site consists of a tetrapeptide motif, NPNA, tandemly repeated 37 times [2]. In an attempt to mimic the secondary structure of this central repeat region of the CS protein, a sidechain to sidechain cyclised peptide designed using MD simulations was synthesized containing the nonproteinogenic amino acid (*2S,3R*) 3-aminoproline.



1 **2**

We first describe here the synthesis of aminoproline **1** and its use in the synthesis of the cyclic peptide **2** consisting of five tandemly repeated NPNA motifs with Pro^6 replaced by **1** and Ala^{16} replaced by Glu. The linear assembly of the chain was carried out on solid support using standard Fmoc chemistry. After cleavage and deprotection the linear precursor were successfully cyclized in solution.

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Organic chemistry **169**

Synthesis of Linear Heptapeptides Containing Epimerisation Prone Phenylglycines as Potential Intermediates in Vancomycin Biosynthesis.

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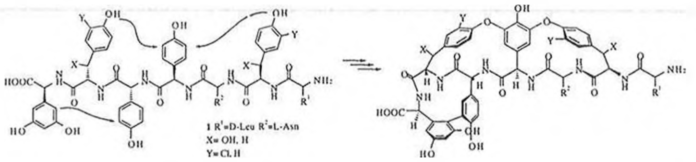
The proposed biosynthesis of vancomycin[1] starts with the assembly of a linear heptapeptide, which should be cyclised at the side chains and finally glycosylated. Three P_{450} enzymes were shown to be responsible for the oxidative phenol coupling reactions which form the tricyclic skeleton of the molecule[2].
In this work, linear heptapeptides 1 containing highly epimerisation prone phenylglycines were synthesised on a solid phase, using the Alloc chemistry for chain elongation[3]. The P_{450} enzymes were expressed in *E. coli* and purified. The conversion of the linear peptides with these enzymes was investigated to establish their role in vancomycin biosynthesis. By synthesising similar peptides, the sequence of steps during the biosynthesis can be elucidated. With this method access could be gained to novel glycopeptide antibiotics using the biosynthetic enzymes, to transform novel substrate analogues.



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Organic Chemistry **170**

Ethylene Glycol and Amino Acid Derivatives of 5-Aminolevulinic Acid as New Photosensitizing Precursors of Protoporphyrin IX in Cells

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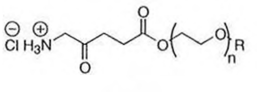
Protoporphyrin IX (PpIX) is used as a photosensitizing agent in photodynamic detection (PDD) and therapy (PDT) of cancer and is synthesized intracellularly from aminolevulinic acid (ALA) precursors. However, extracellularly added ALA is poorly taken up by cells. The lipophilic better cell-permeant ALA esters possess a better cell-permeability but are not cell-type specific and display cytotoxicity. In order to obtain information on the possibility to specifically target ALA-derivatives to defined cells, we have synthesized and characterized ethylene glycol esters **1** and amino acid pseudodipeptide derivatives of ALA **2**, as potential specific substrates for cellular esterases and aminopeptidases, respectively. The PpIX formation induced by these products was investigated using cultures of human and rat cell lines of carcinoma and endothelial origins. The cytotoxicity of these components in the absence of light was also controlled. The results have shown that ethylene glycol esters **1** can induce high levels of PpIX and are useful at concentrations below their cytotoxicity threshold.



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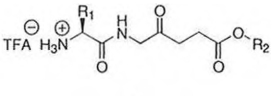

2

Organic Chemistry **171**

Structural investigations on the catalase-peroxidase KatG, the activator of the antitubercular drug isoniazid *in vivo*.

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The heme-containing mycobacterial catalase-peroxidase KatG activates the frontline antitubercular drug isoniazid *in vivo* [1]. Despite its essential role in the way of action of the drug less is known about the structure-function relationship of KatG.

Bacterial catalase-peroxidases like the dimeric KatG are gene-duplicated members of the plant peroxidase superfamily, including the monomeric yeast cytochrome c peroxidase (CCP). Both termini of KatG can be modeled into the high-resolution crystal structure of CCP [2]. Sequence alignment with CCP suggests that the N-terminus of KatG is responsible for heme binding whereas the C-terminal half might play an essential role in isoniazid binding and/or metabolism [3].

We are using the yeast 2-hybrid system to study the specific interactions within KatG:
A very strong interaction was determined between two N-terminal domains. Furthermore, a less intense interaction could be shown between the N- and C-terminus, whereas no interaction was detected between two C-terminal domains. Several smaller segments of KatG with no direct homology to CCP are under current investigation to get further insight in dimerization and mechanistic details of this important class of enzymes.

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Organic Chemistry **172**

Molecular Evolution of Cytochrome *C* Peroxidase

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In order to study the structure-function relationship of cytochrome *c* peroxidase (CCP) from *Saccharomyces cerevisiae*, the enzyme was subjected to directed molecular evolution to generate mutants with increased activity against the classical peroxidase substrate guaiacol, thus changing the substrate specificity of CCP from the protein cytochrome *c* to a small organic molecule. After three rounds of DNA shuffling and screening, mutants were isolated which possessed a 300-fold increased activity against guaiacol and up to a 1000-fold increased specificity for this substrate relative to the natural substrate. In all of the selected mutants the distal arginine (Arg48), which is fully conserved in the superfamily of peroxidases, was mutated to histidine, showing that this mutation plays a key role in the significant increase in activity against phenolic substrates. The results suggest that, in addition to stabilizing the reactive intermediate compound I, the distal arginine plays an important role as a gatekeeper in the active site of CCP, controlling the access to the ferryl oxygen and the distal histidine. The results illustrate the ability of directed molecular evolution technologies to deliver solutions to biochemical problems that would not be readily predicted by rational design.

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Organic Chemistry **173**

The *in vitro* selection of novel DNA repair enzymes

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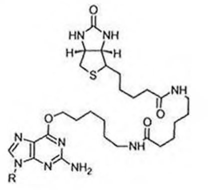
The O^6-alkylation of guanine in DNA plays an important role in mutagenesis and carcinogenesis. O^6-alkylguanine allows the incorporation of either T or C during DNA replication, resulting in possible G-C to A-T mutations.[1] Consequently, mammals and bacteria posses O^6-alkylguanine-DNA alkyltransferases, which repair these lesions. A cysteine of the suicidal alkyltransferase reacts with the alkyl group in a S_N2 manner, resulting in an irreversibly alkylated "enzyme".[2] We are pursuing in the *in vitro* selection of O^6-alkylguanine-DNA alkyltransferases with novel substrate and sequence specificities from phage display libraries. Towards this end, we have synthesized various oligonucleotides containing O^6-alkylguanine derivatives such as **1** and **2**. By attaching a biotin covalently to the alkyl group a link between activity and recovery is created: Upon incubation of the alkyltransferase libraries with these oligonucleotides, proteins with alkyltransferase activity will be biotinylated and can be selected from the library for subsequent amplification. The generation of these compounds and the results of the *in vitro* selections using Fab libraries for the generation of artificial alkyltransferases as well as model selections using the human O^6-alkylguanine-transferase on phage-λ display system will be presented. Furthermore, the use of these oligonucleotides as highly specific probes in clinical diagnostics will be discussed.



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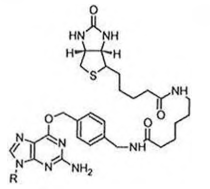

2

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Organic Chemistry **175**

Studies of Protein Dynamics through Differential Multiple-Quantum Relaxation arising from Cross-Correlated Time-Modulation of Isotropic Chemical Shifts

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Many proteins exhibit conformational changes on a μs-ms time-scale that often control biological processes. Here we demonstrate that cross-correlated time modulation of isotropic chemical shifts leads to differential relaxation of double- and zero-quantum coherences, respectively, inducing interconversion between the two-spin coherences $2I_xS_x$ and $2I_yS_y$. The extent of the effect is illustrated with an application to $^{13}C,^{15}N$ -labeled quail CRP2(LIM2), by studying ^{15}N-$^1H^N$ multiple-quantum relaxation. Significant cross-correlated fluctuations of isotropic chemical shifts were observed for residues which are part of a disordered loop region connecting two β-strands in CRP2(LIM2). Differences in $^1H^N$ and ^{15}N exchange contributions to multiple-quantum relaxation observed at these sites illustrate the complex interplay between hydrogen bonding events and conformational reorientations in proteins.

Organic Chemistry **174**

Title: Synthetic Studies on Colourless Chlorophyll Catabolites

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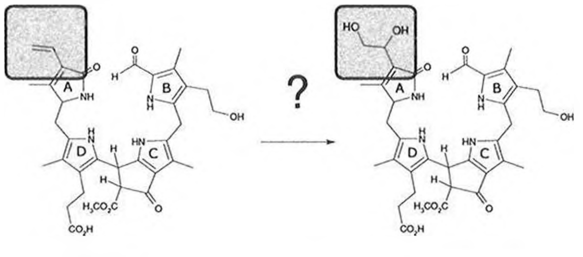
In spite of the remarkable progress in the chemistry of chlorophyll catabolism during the past 10 years [1] the nature of the biochemical transformations is still subject of further experimental investigations. Aspects of the stereochemistry and of the peripheral functionalization are of particular interest. We are interested in the chemical correlation of different chlorophyll catabolites as may be achieved by chemical modification of specific peripheral functionalities.

The chemical constitutions of the colourless chlorophyll catabolites from barley, *Hv*-NCC-1 **(1)** [2], and from *Cercidiphyllum japonicum*, *Cj*-NCC **(2)** [3], differ in the side chain at ring A only. Therefore we applied OsO_4-dihydroxylation to *Cj*-NCC **(2)** to obtain compounds with identical constitution as *Hv*-NCC-1 **(1)**, which were compared with *Hv*-NCC-1 **(1)** by modern spectroscopic methods and HPLC analysis. The results of this work are to be presented here.



Cj-NCC **(2)** *Hv*-NCC-1 **(1)**

This work was supported by the *Austrian National Science Foundation* (FWF, project P-13503).

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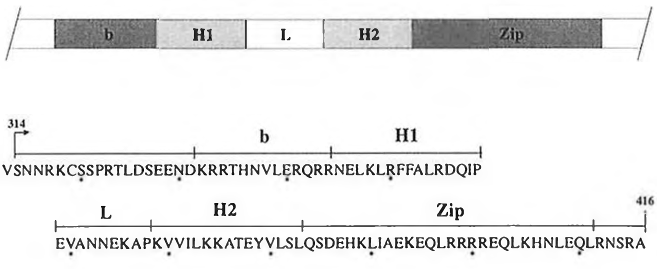
Organic Chemistry / Biochemistry **176**

Solution Structural and Dynamic Properties of the DNA-Binding/Dimerization Domain of the Transcription Factor Myc

Wolfgang Fieber[‡], Martin Schneider[§], Theresia Matt[§], Klaus Bister[§], Robert Konrat[‡] and Bernhard Kräutler[‡]

[‡]Institute of Organic Chemistry and [§]Institute of Biochemistry
University of Innsbruck, Austria

The protein product (c-Myc) of the protooncogene c-*myc* is a transcriptional regulator playing a key role in cellular growth and differentiation. Deregulation of c-*myc* leads to oncogenic activation and cell transformation. The carboxyterminal domain $p15^{v\text{-}myc(314\text{-}416)}$ of v-Myc, the viral analogue of c-Myc, was expressed in bacteria and purified. This segment comprises the characteristic b-HLH-zip (basic / helix-loop-helix / leucine-zipper) motif, which is responsible for DNA-binding and dimerization, respectively. Multi-dimensional NMR spectroscopy has been used to characterize the solution structural and dynamic properties of this transcription factor.



Organic Chemistry **177**

Stable analogs of phosphohistidine containing peptides

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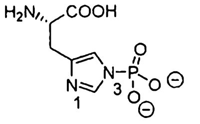
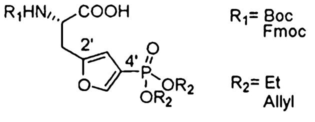
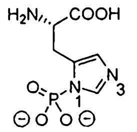
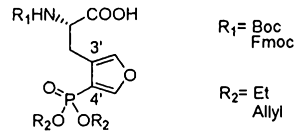
Phosphorylation on histidine residue is commonly represented in signal-transduction pathways in prokaryotes as well as in eukaryotes. In relation to our interest in bacterial phosphotransferase system (PTS system) we have become interested in studying the mode of action of peptides that become phosphorylated at histidine residue [1].
We report here the synthesis of non-hydrolysable stable analogs of 1- and 3-phosphohistidine suitable for peptide synthesis. Biological activity of some stable peptides analogs are investigated within the PTS system.


3-phosphohistidine


(4'-phospho-2'furyl)alanine


1-phosphohistidine


(4'-phospho-3'furyl)alanine

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Organic Chemistry **178**

High Throughput Screening of Catalytic Antibody Libraries using Enantioselective Fluorogenic Assays

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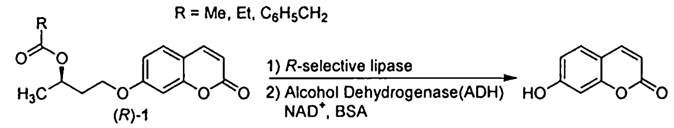
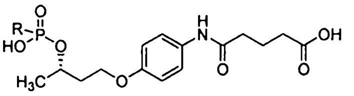
The majority of commerically available lipases selectively hydrolyze only (*R*)-**1**, which is a fluorogenic substrate when coupled with ADH [1]. We have investigated whether catalytic antibodies against optically pure transition state analogs (*S*)-**2** might provide the complementary *S*-enantioselective hydrolytic activity. We report our investigations on high throughput screening of monoclonal antibody libraries for such hydrolytic activities using (*S*)-**1** as fluorogenic substrates.




(S)-2

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Organic Chemistry **179**

Improved Synthesis of Aminocyclopentitols with β-*Gluco* Configuration and Use as Hapten

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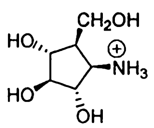
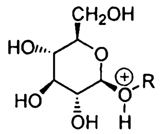
Aminocyclopentitol **1** is an anomer selective inhibitor of β-glucosidases (K_i(**1**) = 0.18 μM for *Caldocellum saccharolyticum*)[1], and may be considered as a mimic of the protonated β-glucoside **2**. We report an improved large scale synthesis of **1** and its functionalization at the nitrogen for conjugation to carrier proteins in view of raising catalytic antibodies with β-glucosidase activity.


1·H⁺


2·H⁺

Acknowledgement. L.G. gratefully acknowledges the Roche Research Foundation for financial support.

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Organic Chemistry **180**

A combinatorial approach for defining base- and backbone sequence effects in DNA triple helix formation.

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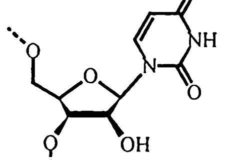
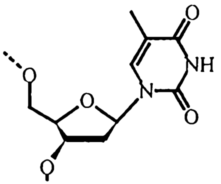
The ability of a triplex forming oligonucleotide (TFO) to bind with its target DNA double helix depends strongly on its backbone conformation, that is correlated to the base sequence [1]. In order to better understand these sequence and conformational effects, we prepared a mixed RNA/DNA TFO library in wich the bases as the principal recognition units remained unchanged whereas, at each nucleotide, deoxyribo- or ribo-sugars were permuted in order to introduce maximum conformational heterogeneity. This combinatorial library was then screened for strong binding TFOs by temperature dependent affinity chromatography on the corresponding DNA target sequence that was immobilized on solid support (Fig.1).Weak and strong binding fractions were deconvoluted by a combined HPLC, ESI-MS, PAGE, UV and CD spectroscopic approach in order to identify individuals. The results obtained so far show an unexpected variation of thermal stability *vs.* the distribution of ribo- and deoxyribonucleotides in the TFO.

Double helix: ●-AAAAGAGGAGGG
3'-TTTTCTCCTCCC

TFO library: 5'-ΓΓΓΓκΓκκΓκκκ-3'
Γ = dT or rU
κ = dC or rC


Uridine


Deoxythymidine

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Organic Chemistry **181**

Axial coordination chemistry of coenzyme F430

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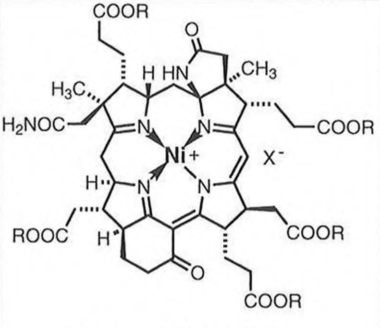
Coenzyme F430 (**1**) is the prosthetic group of methyl coenzyme M reductase (MCR), the enzyme catalysing the last step of biological methane formation in methanogenic *archaea.*[1] The cosubstrates of MCR are the methyl thioether coenzyme M (CH_3SCoM) and a thiol (coenzyme B, HS-HTP) which are converted into methane and the heterodisulfide of coenzymes M and B (CoM-SS-HTP).

The mechanism of this reaction and the role of the nickel center of coenzyme F430 are still unknown although it is known that the active enzyme is in the nickel(I) valence state. Recent X-ray structures of the enzyme in its inactive Ni(II) state show ligands such as coenzyme M coordinated to the nickel in the axial position.[2] We have investigated the coordination chemistry of the penta methyl ester F430M (**2**) in non coordinating solvents and found that thioethers and thiols do not coordinate to the Ni(II) center whereas thiolates form both, pentacoordinate and hexacoordinate complexes.



1 Coenzyme F430 (R = H)
2 F430M (R = CH_3, X = ClO_4)

In the poster we present the results of thermodynamic studies of the coordination of thiolates and thiolate-thioether bidentate ligands to F430M.

[1] B. Jaun, *Metal Ions in Biological Systems*, **1993**, 29, 287.
[2] U. Ermler, W. Grabarse, S. Shima, M. Goubeaud, R.K. Thauer, *Science*, **1997**, 278, 1457.

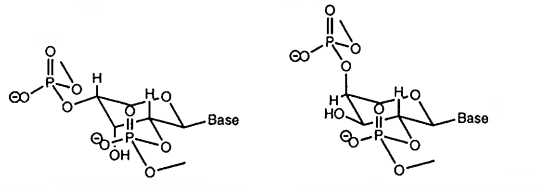
Organic Chemistry **182**

Determination of the solution structure of α-L-arabinopyranosyl(4′-CGAATTCG-2′)$_2$ by NMR

Marc-Olivier Ebert and Bernhard Jaun
Laboratorium für Organische Chemie, ETH Zürich,

H. Huynh, A. Luther, M. Beier, R. Krishnamurti and A. Eschenmoser
The Scripps Research Institute, San Diego

In the course of the exploration of alternative nucleic acid structures [1], both, β-D-ribopyranosyl-NA ("p-RNA") and α-L-arabinopyranosyl-NA were shown to form Watson-Crick pairing systems. For p-RNA, the postulated conformational type has been confirmed by a detailed NMR study on the solution structure of a short duplex [2]. However, for α-L-arabinopyranosyl-NA qualitative analysis neither offers a rationale for the fact that it pairs even more strongly than p-RNA nor does it predict its propensity to cross pair with the latter (Fig.1).



β-D-Ribo-NA, " p-RNA " (confirmed by NMR)   α-L-Arabino-NA (structural hypothesis)

Fig.1.: Idealized conformations of two alternative nucleotides [3]

Here we present a NMR study of the self complementary duplex α-L-arabinopyranosyl(4′-CGAATTCG-2′)$_2$ and discuss the difference between its structure and that of the corresponding p-RNA duplex.

[1] A. Eschenmoser, *Science*, **1999**, 284, 2118.
[2] I. Schlönvogt, S. Pitsch, C. Lesueur, A. Eschenmoser, B. Jaun, R. M. Wolf, *Helv. Chim. Acta*, **1996**, 79, 2316.
[3] A. Eschenmoser, M. Dobler, *Helv. Chim. Acta,* **1992**, 75, 218.

Organic Chemistry **183**

Computational modeling and synthesis of derivatives of coenzyme F430 with covalently attached axial ligands.

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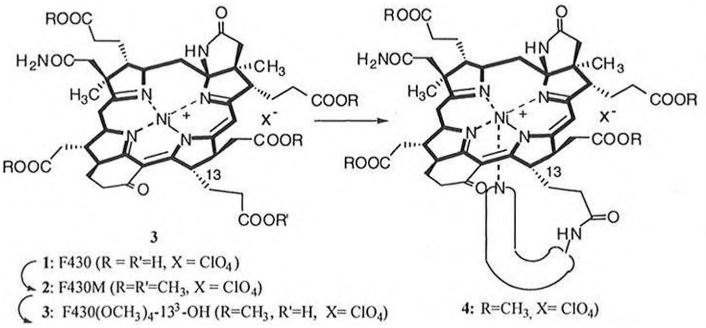
Coenzyme F430 (**1**), the prosthetic group of methyl coenzyme M reductase (MCR), catalyses the last step of biological methane formation in methanogenic *archaea* [1]. X-ray structures of inactive MCR containing F430 in the Ni(II) oxidation state [2] show a glutamine sidechain occupying one of the axial coordination sites of the nickel ion. In order to create more realistic models of the enzyme active site, we have synthesized the five posible tetra-esters of coenzyme F430 (e.g. **3**) and developped methods to covalently attach a spacer with a potential ligand function at its end to the sidechain with the free carboxylate. The structure of the spacer was selected using forcefield calculations and extensive conformational search techniques. In our poster we discuss the design, synthesis and characterization of such a derivative with a pyridine group attached to the C(13)-propionic acid side chain of coenzyme F430 (**4**).



3

1: F430 (R = R′=H, X = ClO_4)
2: F430M (R=R′=CH_3, X = ClO_4)
3: $F430(OCH_3)_4$-13^3-OH (R=CH_3, R′=H, X= ClO_4)

4: R=CH_3, X= ClO_4)

[1] Jaun B., *Metal Ions in Biological Systems* **1993**, *29*, 287-337. [2] Ermler, U., Grabarse, W., Shima, S., Goubeaud, M., Thauer, R. K., *Science* **1997**, *278*, 1457-1462.

Organic Chemistry **184**

Sequence-selective Binding of Small Peptides by Two-armed Receptors

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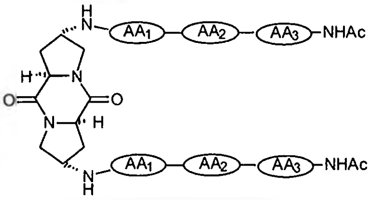
Institute of Organic Chemistry, University Basel, St. Johanns Ring 19, 4056 Basel

Synthetic receptors that recognize small peptides selectively have widespread applications for e.g the development of new therapeutics, studies in molecular recognition or the development of sensors.

We have employed encoded combinatorial chemistry [1] as a tool for the development of a novel class of two-armed receptors that are based on a rigid diketopiperazine template and have variable "arms" consisting of amino acids AA$_n$.



two-armed receptors

The screening of several dye-marked receptor-prototypes against a tripeptide library revealed that the two-armed receptors are not only able to bind to peptides but that small structural differences lead to significant changes in their binding selectivities towards peptides.

[1] M.H.J. Ohlmeyer, R.N. Swanson, L.W. Dillard, J.C. Reader, G. Asouline, R. Kobayashi, M.H. Wigler, W.C. Still, *Proc. Natl. Acad. Sci. USA* **1993**, *90*, 10922.

Organic Chemistry **185**

Stereoselective Synthesis and Inhibition Properties of Aminocyclopentitol Analogs of α- and β-L-Fucose

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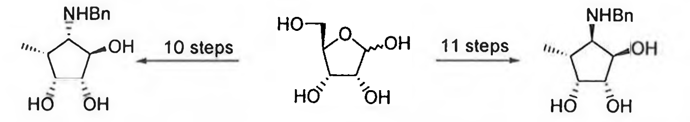
Freiestrasse 3, CH-3012 Bern

Glycosidase inhibitors can be used for treating diabetes, cancer, and viral (HIV, influenza) and bacterial infections and as insecticides. We report the stereoselective synthesis of trans- and cis-aminocyclopentitol derivatives **1** and **2** starting from D-Ribose [1]. Inhibition properties of **1, 2** and related compounds were investigated [2].



1
K_i = 110 μM
α-L-fucosidase from
Bovine Kidney

D-Ribose

2
K_i = 0.68 μM
α-L-fucosidase from
Bovine Kidney

2 is further functionalized for conjugation to carrier proteins in view of preparing catalytic antibodies with α-L-fucosidase activity. The structural analogies between **2** and the transition state of fucoside cleavage will also be discussed.

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[1] Blaser, A.; Reymond, J.-L. *Helv. Chim. Acta* **1999**, *82*, 760; Blaser, A.; Reymond, J.-L. *Synlett* **2000**, *6*, 817
[2] Blaser, A.; Reymond, J.-L. *Org. Lett.* **2000**, in press

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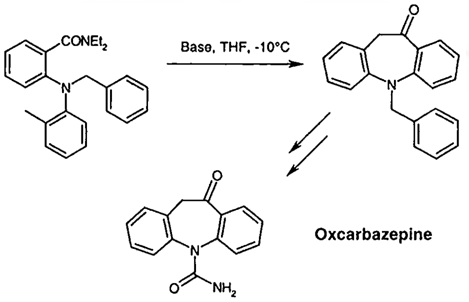
Organic Chemistry **186**

New Synthesis of the Dibenzazepinone, Oxcarbazepine via Directed Remote Metalation of Protected N-*o*-Tolyl-Anthranilamide Derivatives

Olivier Lohse, Ulrich Beutler, Peter Fünfschilling, Pascal Furet,[§] Julien France,[§] Daniel Kaufmann, Gerhard Penn and Werner Zaugg

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

Epilepsy, a syndrome of different cerebral disorders of the central nervous system, affects approximately 50 million people worldwide.[1] Carbamazepine (Tegretol®) is the most widely prescribed antiepileptic drug for the treatment of partial and generalized tonic-clonic seizures.[2] In an effort to improve the tolerability profile of carbamazepine without affecting its antiepileptic potency, the keto-analog Oxcarbazepine (Trileptal®) was developed.
We will report a new and efficient synthesis of Trileptal based on the directed ortho and remote metalation of benzyl and allyl protected N-*o*-tolyl-anthranilamides. The key precursors of the ring closure were efficiently prepared by Buchwald-Hartwig C-N cross coupling reactions, followed by protection of the nitrogen. After ring formation, deprotection of the nitrogen and introduction of the carbamate group furnished a new and efficient synthesis of the antiepileptic drug Trileptal®.



[1] *Epilepsy, A Comprehensive Textbook, Volume II*; Engel J. Jr.; Pedley, T. A., Ed.; Lippincot-Ravens Publishers, Philadelphia, 1998.
[2] *Intractable Epilepsy*; Johannessen, S. I.; Gram, L.; Sillanpää, M.; Tomson, T., Ed.; Wrighston Biomedical Publishing, Petersfield, 1995.

Organic Chemistry **187**

Kinetic Investigations on the Hydrogenation of Olefins with Iridium-PHOX Complexes as Catalysts

Nicole Zimmermann[a], Andreas Pfaltz[a]*, Martin Studer[b], Hans-Ulrich Blaser[b]

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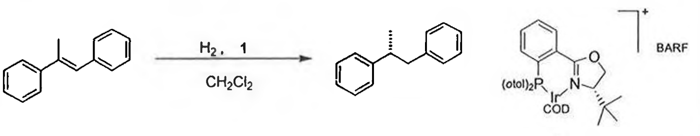
[b] Solvias AG, Klybeckstrasse 191, CH-4002 Basel

Iridium phosphinooxazoline (PHOX) complexes are highly effective catalysts for the hydrogenation of unfunctionalized olefins.[1,2] With unfunctionalized trisubstituted 1,2-diaryl-olefins *ee*'s of more than 99% could be achieved using catalyst loadings as low as
0.025 mol%. Encouraged by these results we wanted to gain further insight into these reactions by kinetic measurements. The hydrogenation of *trans*-α-methylstilbene with iridium-PHOX-complex 1 was chosen as standard reaction.



1

We studied the dependence on the catalyst and alkene concentration, and the influences of the hydrogen pressure and the temperature on the reaction rate and were able to determine the overall rate law for this reaction.

[1] Lightfoot, A.; Schnider, P.; Pfaltz, A. *Angew. Chem. Int. Ed.* **1998**, *37*, 20, 2897.
[2] Blackmond, D.G.; Lightfoot, A.; Pfaltz, A.; Rosner, T.; Schnider, P.; Zimmermann, N. *Chirality* **2000**, 12, in press.

Coordination Chemistry **188**

DFT Calculations for Planning the Synthesis of more Efficient Devices Performing Artificial Photosynthesis

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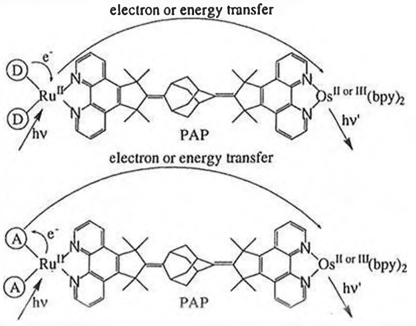
University of Fribourg, CH-1700 Fribourg, gabriella.albano@unifr.ch

Energy and electron transfer processes are very important since they are at the base of many biological phenomena, such as photosynthesis in green plants. The system showed below (D and A = substituted bpy) is an example of an inorganic device performing efficient photoinduced energy and electron transfer processes (k_{en} = 5.2 x 10^7 s^{-1}, k_{el} = 7.2 x 10^6 s^{-1} [1,2]). The introduction of appropriate donor (D) and acceptor (A) units on the Ru(II) center can improve the lifetime of the charge/energy transfer state, resulting in a much longer and efficient storage of energy.



Ab initio (DTF) calculations were made in order to predict the appropriate donor and acceptor ligands for the synthesis of the target molecules.
Synthetic work is on the way for comparison with the theoretical results.

[1] V. Balzani et al., J. Phys. Chem. **1996**, *100*, 16786.
[2] L. De Cola, Chimia **1996**, *50*, 214.

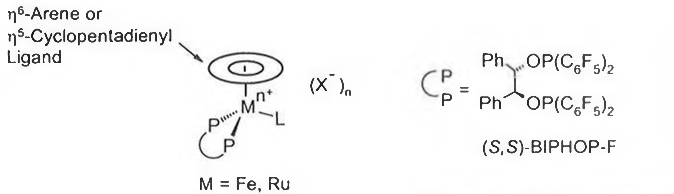
Organic Chemistry **189**

Development and Applications of Chiral Iron and Ruthenium Lewis Acids

E. Peter Kündig*, Florian Viton, Mihaly Gardiner and
Christophe M. Saudan
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]. An attractive feature of this family of Lewis acid catalysts is their well defined structures and electronic properties. Interpretation of observed enantioselectivities is thereby placed on firmer ground than those advanced for in situ prepared catalysts.

We here compare the isostructural iron(II) [CpFe(BIPHOP-F)L][X] and ruthenium(II) [CpRu(BIPHOP-F)L][X] complexes. The poster will also report on ongoing work on chiral arene ruthenium complexes [2] and progress in the field of asymmetric catalytic 1,3-dipolar cycloaddition reactions.



X = TFPB, SbF_6, PF_6, BF_4, OTf

[1] a) E. P. Kündig, C. M. Saudan, G. Bernardinelli, *Angew. Chem. Int. Ed.* **1999**, *38*, 1220. b) M. E. Bruin, E. P. Kündig, *Chem. Commun.* 1998, 2635.
[2] J. W. Faller, J. Parr, *Organometallics* **2000**, *10*, 1829.

Organic Chemistry **190**

New Chiral Bipyrazolyl Ligands for the Asymmetric Epoxidation of Unfunctionalized Alkenes.

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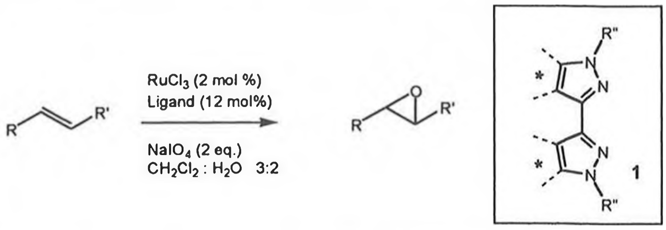
Département de Chimie Organique, Université de Genève, 1211 Genève 4

Enantioselective epoxidation of unfunctionalized alkenes constitutes an appealing strategy for the synthesis of useful enantioenriched intermediates or products. An interesting catalytic method ($RuCl_3$ 2 mol%, phen 12 mol%, $NaIO_4$, CH_2Cl_2 : H_2O) has been reported by Balavoine in 1984 [1]. Its transformation into an enantioselective process was recently achieved using a C_2-symmetric bisozalamides (e.e. up to 62%) [2].



It appeared to us likely than other chiral C_2-symmetric diimine could be efficient asymmetric ligands. In this context, we have developed a short two-step synthetic route to enantiopure 1,1'-dialkyl or 1,1'-diaryl-1H,1'H-[3,3']bipyrazolyl compounds (**1**) from chiral ketones, dimethyloxalate and monosubstituted hydrazines. Herein, we report the initial epoxidation experiments with tri-, bi- and monosubstituted prochiral olefins.

[1] a) G. Balavoine, C. Eskenasky, F. Meunier, H. Rivière, *Tetrahedron Lett.*, **1984**, *25*, 3187; b) G. Balavoine, C. Eskenasky, F. Meunier, H. Rivière, *J. Chem. Soc. Chem. Commun.*, **1985**, 1111.
[2] N. End, A. Pfaltz, *Chem. Commun.*, **1998**, 589.

Organic Chemistry **191**

Planar Chiral Arene Chromium Complexes: Methodology and Application to the Synthesis of Lythraceae Alkaloids

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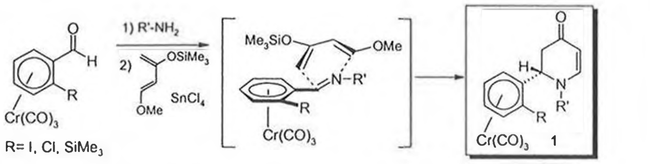
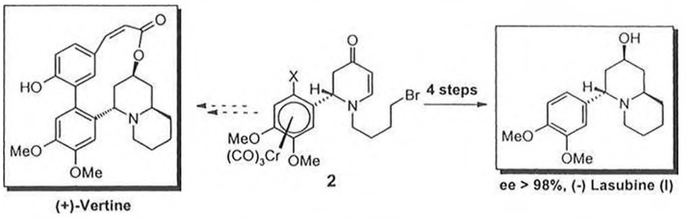
30 Quai Ernest Ansermet, CH-1211 Genève 4

Enantiopure aryl hydropyridinone complexes (e.g. **1** and **2**) are readily accessible via an aza-Diels-Alder reaction between enantiopure *o*-substituted arylaldehyde imine complexes and Danishefsky's diene [1]. The $Cr(CO)_3$ group serves both as steric control element and as activating group.



de > 98%

In this poster we report on the application of this methodology to the synthesis of Lythraceae alkaloids. We have recently completed a synthesis of (–)-Lasubine (I) via the planar chiral complex **2** [2]. The communication will report on our progress towards the first total synthesis of (+)-Vertine using this approach.



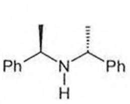
[1] E. P. Kündig, L. H. Xu, P. Romanens, G. Bernardinelli, *Synlett*, 1996, 270.
[2] H. Ratni, E. P. Kündig, *Org. Lett.*, 1999, *1*, 1997.

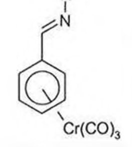
Organic Chemistry **192**

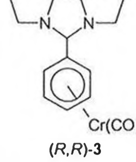
Synthesis of Planar Chiral *o*-substituted Benzaldehyde Chromium Complexes *via* Enantio- and Diastereoselective Lithiations

Sandrine Pache, E. Peter Kündig*,
Rina Aav, Axel Tomassini and Alexandre Alexakis*
Département de Chimie Organique, Université de Genève, 1211 Genève 4

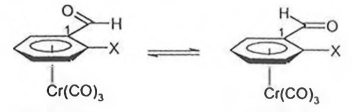
Planar chiral [(η^6-arene)$Cr(CO)_3$] complexes are finding wide application in organic synthesis, both as chiral building blocks and as ligands in asymmetric catalysis. Strategies developed independently in our two laboratories focus on the asymmetric directed *ortho*-lithiation and include both diastereoselective and enantioselective methods.[1] This communication reports on two new approaches to *ortho*-substituted benzaldehyde complexes. Enantioselective lithiation of imines **2a** and **2b** with Li-**1**, and diastereoselective lithiation of the chiral aminal [2] (*R,R*)-**3** with *n*BuLi, afford, after hydrolysis, *o*-substituted benzaldehyde complexes (*1S*)-**4** (X=Me, $SiMe_3$, $SnMe_3$, CO_2Me, etc.) in ee's of up to 90%.


(*R,R*)-**1**


2a: R=cyclohexyl
2b: R=phenyl


(*R,R*)-**3**

Unusual chiroptical properties of complexes **4** (X=$SnMe_3$, $SiMe_3$), are ascribed to the existence of two aldehyde conformations and these studies will be detailed in the poster.



(+)-(*1S*)-**4**
anti

(-)-(*1S*)-**4**
syn

[1] (a) A. Quattropani, G. Bernardinelli, E. P. Kündig, *Helv. Chim. Acta* **1999**, *82*, 90. (b) S. Pache, C. Bothua, R. Franz, E.P. Kündig, J. Einhorn, *Helv. Chim. Acta* **2000**, submitted. [2] See poster A. Tomassini

emistry **193**

Enantioselective conjugate addition of organozincs onto various nitro-olefins

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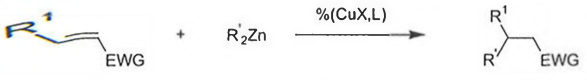
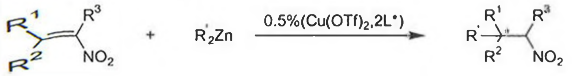
Université de Genève, Département de chimie organique,
Quai Ernest-Ansermet 30, CH-1211 Genève 4

The copper catalysed 1,4 conjugate addition of diorganozincs nts to α,β insaturated system is a good way to introduce new carbon n bond.[1]



EWG = CO-R, NO_2, CN

The enantioselective version has been studied with numerous sphorus ligands on different types of enones[2]. As nitro-olefins are very d Michael acceptor, we became interested in these substrates. Thus, we ort here the copper catalysed asymmetric conjugate addition of ganozincs onto various nitro-olefins with excellent results:



Yield: 66-100%
ee: 0-94%

Alexakis, A.; Frutos, J.; Mangeney, P. *Tetrahedron: Asymmetry* **1993**, *4*, 2427; Alexakis, A.; Vastra, J.; Mangeney, P. *Tetrahedron: Asymmetry* **1997**, *38*, 7745-7748. Alexakis, A.; Vastra, J.; Burton, J.; Mangeney, P. *Tetrahedron: Asymmetry* **1997**, *8*, 3193; Alexakis, A.; Burton, J.; Vastra, J.; Mangeney, P. *Tetrahedron: Asymmetry* **1997**, *8*, 3987; 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.

Organic Chemistry **195**

A RADICAL ALTERNATIVE TO THE OXY-COPE REARRANGEMENT

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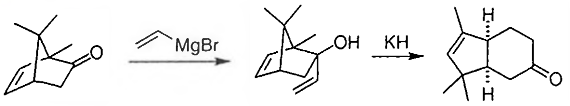
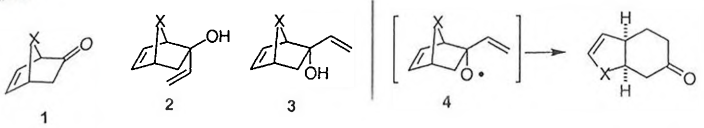
Institut de Chimie Organique de l'Université de Fribourg
CH-1700 Fribourg

The anionic oxy-Cope rearrangement[1] is a well established procedure for the preparation of advanced intermediates in natural product synthesis. For instance, conversion of a camphor derivative into a bicyclo[4.3.0] system is easily accomplished according to the following scheme.[2]



However, starting from simple systems such as norbornenone 1 (X = CH_2) and and 7-oxanorbornenone 1 (X = O) has not found many applications due to the difficulty in preparing *endo* vinyl derivatives of type 2.[3] Indeed, addition of vinyllithium or vinylmagnesium bromide to ketone 1 always occurred from the *exo* face leading to the *endo* alcohol 3. Since the oxy-Cope rearrangement is not feasible with 3, we have developed a radical mediated alternative using the fragmentation of the alkoxyl radical 4 as key step.



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(1) R. K. Hill in "Comprehensive Organic Synthesis", B. M. Trost, I. Fleming Eds; Pergamon, Oxford 1991, p. 785.

(2) J. H. Hutchinson, D. L. Kuo, T. Money, B. Yokoyama, *J. Chem. Soc., Chem. Commun.* 1988, 1281.

(3) W. L. Brown, A. G. Fallis *Can. J. Chem.* **1987**, *65*, 1828.

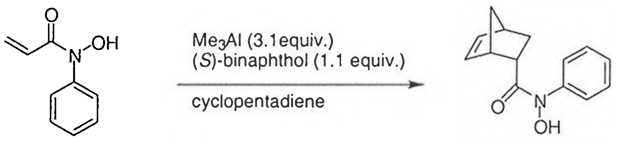
Organic Chemistry **194**

Diels-Alder Reactions of *N*-Hydroxy-*N*-Phenylacrylamide

O. Corminboeuf and P. Renaud

Université de Fribourg, Institut de Chimie Organique, Pérolles
CH-1700 Fribourg, Switzerland

The choice of the template for chiral Lewis acid catalyzed reactions is crucial. We describe here the use of *N*-hydroxy-*N*-phenylacrylamide for aluminum promoted Diels-Alder reactions. Hydroxamic acids form stable and covalent complexes with aluminum Lewis acids. The effect of the aluminum/chiral ligand ratio on the selectivity has been examined. Interestingly, the highest selectivity was observed with a Me_3Al/(*S*)-binaphthol 3.1:1 ratio.



96% yield, 88% ee

Organic Chemistry **196**

Regio-, Stereo- and Enantioselective Hydroboration for the Preparation of Radical Precursors

Barbara Becattini, Cyril Ollivier and Philippe Renaud*

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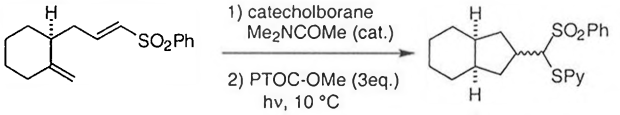
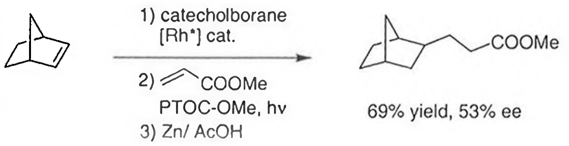
Recently, we have reported a modified version of the Brown-Negishi reaction [1] where hydroboration with catecholborane and radical addition to enones and enals were performed in a one-pot procedure [2]. Other classical radical traps such as unsaturated esters, amides and sulfones react also efficiently in the presence of a chain transfer reagent [3].

We present here further developments of these reactions taking advantage of the high regio- and diastereoselectivity of the hydroboration step (Eq. 1). The first examples of catalytic enantioselective hydroboration followed by a radical reaction will also be presented (Eq. 2).



Eq. 1

58% yield, 4:4:1:1 dr



Eq. 2

69% yield, 53% ee

[1] H. C. Brown, E. Negishi, *J.Am. Chem.Soc.* **1971**, *93*, 3777-3779.
[2] C. Ollivier, P. Renaud, *Chem. Eur.J.* **1999**, *5*, 1468-1473.
[3] C. Ollivier, P. Renaud, *Angew. Chem. Int. Ed.* **2000**, *39*, 925-928.

Organic chemistry **197**

Cu-catalyzed desymmetrization of *N*-sulfonylaziridines with methylmagnesium halides

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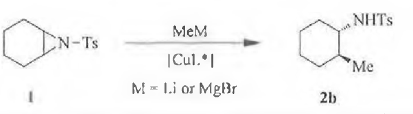
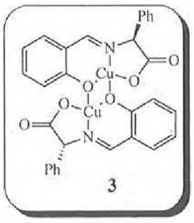
The ring-opening of *meso*-epoxides is a well known synthetic procedure and has been extensively investigated. On the other hand, only a few procedures for ring-opening of aziridines are known. In this account, we report a new route for desymmetrization. Cyclohexene *N*-*p*-toluenesulfonylimine (**1**) undergoes enantioselective ring-opening to (**2**) upon treatment with methyl magnesium halides or MeLi in presence of an asymmetric Cu-catalyst [1].



Lewis acid activation of the aziridine is not required. Enantioselectivities of up to 91 % have been observed under optimized conditions with the chiral imine catalyst (**3**) derived from phenylalanine.



[1] P. Müller and P. Nury, *Org. Letters* **1999**,1 (3), 439-441.

Organic chemistry **198**

Enantioselective nucleophilic ring opening of 2-substitued 1,3-dioxolanes by organolithimum reagents

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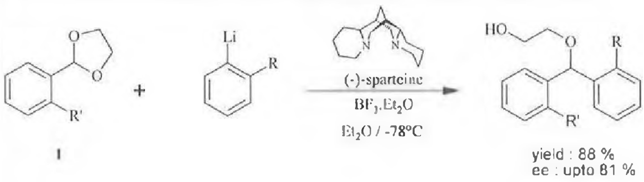
Acetals are established protecting groups preventing nucleophilic attack on carbonyl compounds. They are normally unreactive towards organometallic reagents, such as organolithium, Grignard or organocopper compounds. However, replacement of alkoxy substituents of acetals by alkyl group is possible in the presence of Lewis acids such as BF_3 or $TiCl_4$. Although enantioselective ring-opening of meso-1, 3-dioxolanes in the presence of a chiral Lewis acid catalyst has been reported [1], no efficient combination of an organometallics with an external chiral ligand has so far been developed. In this account, we describe an enantioselective nucleophilic ring-opening of 2-substitued 1,3-dioxolane (**1**) by a (-)-sparteine / organolithium reagent.



The *ortho*-substituents R of the phenyllithium reagent and R' of the dioxolane exert a determining influence on the enantioselectivity of the reaction. So far, the best results were obtained with R = ethyl and R'= isopropyl.

[1] M.Kinugasa, T.Harada, A. Oku, *J. Org. Chem.* **1996**, 61, 6772-6773.

Organic chemistry **199**

Asymmetric Cu-catalyzed cyclopropanations and insertions with iodonium ylides

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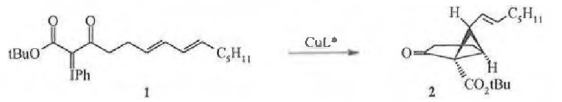
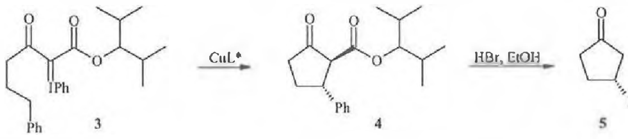
The transition metal-catalyzed decomposition of phenyliodonium ylides was investigated with regard to applications in asymmetric carbenoïd reactions [1]. The intramolecular cyclopropanation of iodonium ylide (**1**), in the presence of an asymmetric Cu-catalyst, proceeds with 68% e.e., which is unprecedented [2].



The intramolecular insertion into the benzylic C-H bond of (**3**), with a Cu-catalyst, affords ketoester (**4**) in 52% yield. Hydrolysis and decarboxylation, under acidic conditions, leads to the cyclopentanone (**5**) with an ee of 72%.



[1] P.Müller, D. Fernandez, P. Nury and J-C. Rossier, *Journal of Physical Organic Chemistry* **1998**, *11*, 321.
[2] P.Müller, C. Boléa, *Synlett* **2000**, 826.

Organic Chemistry **200**

Highly Stereo- and Regioselective CO/Propene Copolymerisation Induced by New Achiral Diphosphine Ligands

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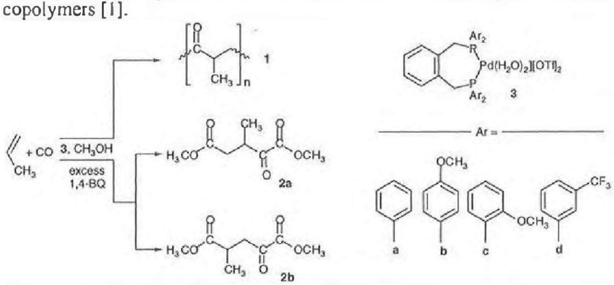
Poly[propene-*alt*-CO] **1** can be efficiently synthesized from propene and carbon monoxide using cationic Pd(II)-complexes modified by diphosphine ligands. Basic diphosphine allow the control of the regiochemistry whereas chirality of the ligand causes the formation of stereoregular isotactic copolymers [1].



Compounds **3** were found to be active catalysts precursors for this copolymerisation reaction, surprisingly showing pronounced properties of regio- and stereocontrol. In particular, both **3b** and **3d** gave essentially regioregular copolymers with a stereoregularity close to 94 and 96% (expressed as concentration of *l*-diads), respectively. However, the two catalyst precursors display essentially reversed regiochemistry for propene insertion as demonstrated when the carbonylation reaction is carried out in the presence of excess 1,4-benzoquinone [1,4-BQ]. Under these conditions the regioisomeric 2-oxoglutarates **2a** and **2b** form in a molar ratio close to 19/81 and ~100/0, respectively. The highly stereoselective copolymer formation should arise by chain end control that causes preference of *l*-insertion independent of the regiochemistry of the insertion. The prevalence of the achiral conformation of the ligand system is probably responsible for the high stereoselectivity. Note that secondary insertion of the olefin causes formation of syndiotactic copolymers in the related styrene copolymerisation.

[1] S. Bronco, G. Consiglio, *Macromol. Chem. Phys.*, **1996**, *197*, 355.

Organic Chemistry **201**

Continuous Enantioselective Hydrogenation of Activated Carbonyl Derivatives

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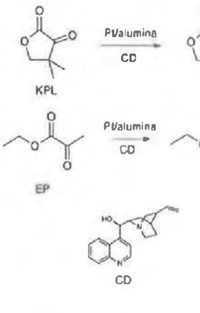
The heterogeneously catalyzed enantioselective hydrogenation of activated ketones is an efficient route to produce chiral alcohols [1]. The catalyst of choice is a Pt hydrogenation catalyst chirally modified by adsorbed cinchona alkaloids. These studies have been made in batch reactors. Here we report the continuous hydrogenation in a fixed bed reactor.



The reactants ethylpyruvate (EP) or ketopantolactone (KPL), and minute amounts of cinchonidine (CD) were continuously fed to a platinum/alumina catalyst. Both reactions resulted in good enantioselectivities (KPL: 83.4 % ee and EP: 89.9 % ee) and productivity rates (KPL: 94 mmol/g_{cat}·h, EP: 23 mmol/g_{cat}·h) [2].

In order to simplify the separation of the solvent after the reaction, it was also investigated whether the liquid solvent (toluene) can be replaced by a supercritical solvent such as ethane.

[1] A. Baiker, *Curr. Opin. Solid St. M.*, **1998**, 3, 86.
[2] N. Künzle, R. Hess. T. Mallat, A. Baiker, *J. Catal.*, **1999**, 186, 239.

Organic Chemistry **202**

Enantioselective Hydrogenation of a Hydroxymethylpyrone over Pd. The Application Limit of Cinchona Alkaloid as Chiral Modifiers.

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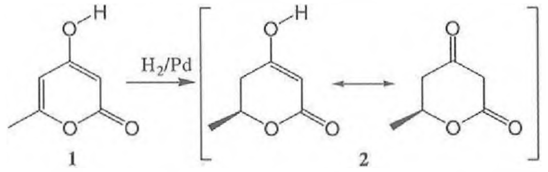
The structure of 2-pyrone and its hydrogenation products are present in many natural compounds and can be used as chiral intermediates, for example in the synthesis of tetrahydrolipstatin, a potent antiobesity drug [1]. The enantioselective hydrogenation of 4-hydroxy-6-methyl-2-pyrone **1** afforded up to 85% ee to the (*S*)-enantiomer of the corresponding 5,6-dihydropyrone **2**, under mild conditions (1 bar, rt). The catalyst was Pd/Al_2O_3 or Pd/TiO_2, chirally modified by adsorbed cinchonidine. This is the highest enantioselectivity achieved in the heterogeneous catalytic hydrogenation of a C=C-double bond, demonstrating the potential of this cinchona-modified Pd. A complicating feature of this reaction is the limited stability of cinchonidine under reaction conditions, which results in a decline of ee with reaction time. Continuous feeding of minute amounts of cinchonidine during reaction allows to maintain the high initial ee with an overall substrate/modifier ratio of ca.20.



[1] Schmid, R., Broger, E. A., Cereghetti, M., Crameri, Y., Foricher, J., Lalonde, M., Müller, R.K., Schoettel, G., Zutter, U., *Pure Appl. Chem.*, **68**, 131 (1996)

Organic Chemistry **203**

Steric Control in the Synthesis of Poly[1-phenyl-2-oxo-propane-1,3-diyl] with Pd(II)-Catalysts

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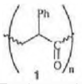
Laboratorium für Technische Chemie
Eidgenössische Technische Hochschule, ETH-Zentrum, CH-8092 Zürich

Since the discovery that poly[1-oxo-2-phenyl-propane-1,3-diyl] **1** formed in the copolymerization reaction of styrene with carbon monoxide using cationic palladium catalysts of the type $[(N^\wedge N)Pd(S)_2](X)_2$ (N^N is 1,10-phenanthroline or 2,2'-bipyridine **2a**, S is a solvent molecule and X a weakly coordinating anion) has a overwhelmingly syndiotactic structure (triad ratio *ll/ul* and/or *lu/uu* ~0/0.12/0.12/1) [1] arising from chain end control, numerous attempts were made to influence in a different manner the stereochemical outcome of the copolymerization process. We present a comparison of the copolymerization results obtained using the complexes $[(L^\wedge L')Pd(H_2O)_2](CF_3SO_3)_2$ **2-5** (where L^L' is **2a-5a**) in order to better focus on the factors involved in the stereo-discrimination processes.



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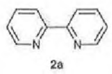
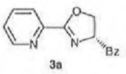
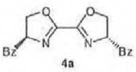


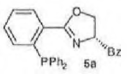
2a



3a



4a



5a

Both catalyst precursors **4** and **5** gave prevailingly isotactic copolymers. In spite of the C_1-symmetry, **5** is more stereoselective than **4** (triad ratio ~1/0.07/0/0 vs. ~1/0.04/0.04/0). The higher stereoregularity is also indicated by the higher molar ellipticity ($\Delta\varepsilon$ =-10.3 vs. –8.5) of the band corresponding to the n-π* transition of the carbonyl chromophore. Remarkably, catalyst precursor **3** gives a copolymer with a prevailingly syndiotactic structure (triad ratio ~0.04/0.18/0.18/1). Due to the presence of *l*-diads the copolymer shows some optical activity ($\Delta\varepsilon$ = -1.7). The same sign of the ellipticity observed with the homochiral catalysts precursors **3-5** is in keeping with the same mechanism for enantioface discrimination of styrene. Therefore, the different stereochemical bias displayed by the two C_1-symmetric ligands is probably caused by a different site selectivity for the olefin coordination preceding insertion. MALDI-MS spectroscopy has allowed us to identify, at least for **3**, β-hydrogen elimination as the most important reaction for chain termination.

[1] P. Corradini, C. De Rosa, A. Panunzi, G. Petrucci, P. Pino, *Chimia*, **1990**, *42*, 52-54.

Organic Chemistry **204**

Epoxidation with Titania-Silica Aerogels Modified by Polar Organic Functional Groups

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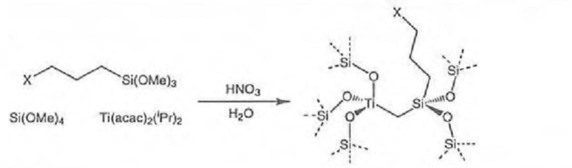
ETH-Zentrum, CH-8092 Zürich, Switzerland

Titania-silica aerogels are among the best solid catalysts for the epoxidation of bulky olefins. Unfortunately, their performance is moderate in the epoxidation of sensitive allylic alcohols due to non-oxidative acid-catalyzed side reactions. We have shown recently that modification of the silica matrix by polar organic functional groups is an efficient tool for for fine tuning the acidity of titania-silica.

Here we report the modification by mono- and bidentate amino-alkyl and acetoxy-alkyl functional groups. The materials were synthesized by the solution-sol-gel method and dried in supercritical CO_2. The corresponding



X-alkyl trimethoxysilane precursors were used to achieve covalent incorporation of the modifier. Modification of titania silica aerogels led to higher activities and enhanced epoxide yields.

[1] C.A. Müller, M. Maciejewski, T. Mallat, A. Baiker, *J. Catal.*, 1999, **184**, 293.

Organic Chemistry **205**

Heterogenous Catalytic Oxidation of Olefins to Allylic Alcohols via the Epoxide

Carsten Beck, Tamas Mallat and Alfons Baiker

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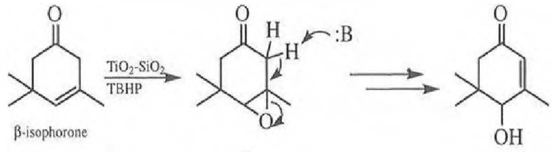
Allylic oxidation of olefins is an essential process in synthetic organic chemistry affording valuable α,β-unsaturated alcohols and carbonyl compounds. Unfortunately, the choice of truly heterogenous catalysts for allylic oxidation of complex molecules is strongly limited. An industrially relevant example is the oxidation of isophorone to ketoisophorone, which cyclic alkenone is a demanded intermediate in the synthesis of carotenoids and fragrances.

We report here the allylic oxofunctionalization of β-isophorone (**1**) in a two-step, one-pot synthesis involving epoxidation and consecutive base-catalyzed isomerization to 4-hydroxy-isophorone (**2**). Epoxidation was catalyzed by hydrophilic and hydrophobic titania-silica aerogels in the presence of tert-butylhydroperoxide (TBHP), and some inorganic or organic base was added to the reaction mixture to promote epoxide ring opening [1]. Addition of solid bases such as CaO, Na_2CO_3 and KF/CaF_2 accelerated the rearrangement and up to 77.5 % selectivity at 83 % conversion was achieved in 3 h.



1 2

[1] Hutter, R., Mallat, T., Peterhans, A., and Baiker, A., *J. Mol. Catal. A* **138**, 241 (1999).

Organic Chemistry **206**

A new methylated isoflavone from *Henriettella fascicularis*

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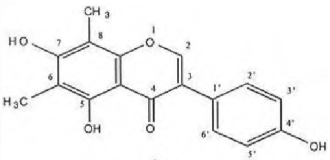
[a]Institut de Pharmacognosie et Phytochimie, Université de Lausanne, 1015 Lausanne, Switzerland, [b]Center for Pharmacognostic Research on Panamanian Flora (CIFLORPAN), College of Pharmacy, University of Panama, Panama, Republic of Panama

Phytochemical investigation of the branches of the Panamanian plant *Henriettella fascicularis* (Sw.) C. Wright (Melastomataceae) has led to the isolation of the new 4',5,7-trihydroxy-6,8-dimethylisoflavone (**1**) together with the known compounds β-sitosterol, palmitic acid, betulinic acid, pinoresinol and a rare methylated xanthone (**2**) which commonly occurs in lichens [1,2]. In addition, it is the first time that either an isoflavone or a xanthone is reported in the Melastomataceae family. Fractionation of the dichloromethane extract was achieved by a combination of silicagel colum chromatography and reversed-phase MPLC. The structures were established by spectroscopic methods, including 2D-NMR heteronuclear correlation experiments.



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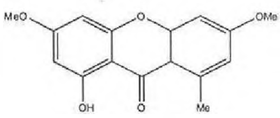

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[1] C. Jiménez, M. Marcos, M.-C Villaverde, R. Figueroa, L. Castedo, F.Stermitz, *Phytochemistry* **1989**, 28, 1992.
[2] Y. Asahina, H. Nogami, *Bull. Chem. Soc. Japan* **1942**, 17, 202.

Organic Chemistry **207**

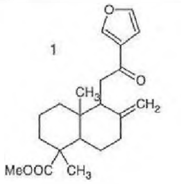
Diterpenes from a freshwater macrophyte *Potamogeton pectinatus*

P. Waridel[a], J.-L. Wolfender[a], J-B. Lachavanne[b] and K. Hostettmann[a].

[a]Institut de Pharmacognosie et Phytochimie, Université de Lausanne, 1015 Lausanne, Switzerland, [b]Laboratoire d'Ecologie et de Biologie Végétale Aquatique, Université de Genève, ch. des Clochettes 18, 1206 Genève, Switzerland

Contrary to higher terrestrial plants, aquatic macrophytes have rarely been investigated under a phytochemical viewpoint. Because of their peculiar habitat, in-between aquatic and terrestrial life, these plants should produce secondary metabolites with original chemical or biological features.
In order to evaluate the type of constituents produced by aquatic macrophytes, a widespread hydrophyte from *Léman's* Lake, *Potamogeton pectinatus* L. (Potamogetonaceae), was investigated. Isolation of the major constituents of its dichloromethane extract yielded several diterpenes. A furanoid labdane diterpene was characterised as a methyl ester of 12-oxo lambertianic acid (**1**). Other labdanes of the same type are still under investigation. A rare linear diterpene, 1,6,10,14-phytatetraen-3-ol (**2**), was also identified, it can be considered as a possible biogenetic precursor of cyclic diterpenoids [1]. These diterpenes are characteristic of plants from the *Potamogeton* genus since LC/UV/MS analyses of several other species also revealed their presence. The occurrence of these compounds under the influence of different exogenous factors, such as stress caused by pollutants, will be the topic of further ecotoxicological studies.

1



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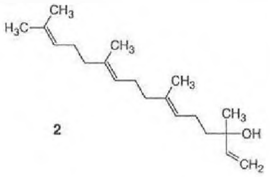

[1] N.V. Avdyukova, E.N. Shmidt, V.A. Pentegova, *Chem. Nat. Compd.* **1971**, 7, 820.

Organic Chemistry **208**

Absolute configurations of two new 6-substituted 5,6-dihydro-α-pyrones

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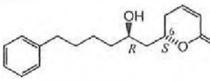
[a]Institut de Pharmacognosie et Phytochimie, Université de Lausanne, 1015 Lausanne, Switzerland. [b]Laboratoire de Pharmacodynamie, Université d'Antananarivo, B.P 906, Ankatso, 101 Antananarivo-Madagascar

The stem bark dichloromethane extract of *Ravensara crassifolia* Danguy *(syn. Cryptocarya crassifolia* Baker) [1] showed antifungal activity against the phytopathogenic fungus *Cladosporium cucumerinum* in bioautographic TLC assays.
The two new antifungal α-pyrones **1** and **2** were isolated and identified by spectral methods (NMR, MS) . The absolute configurations of the hydroxylated carbons were established by chemical methods (formation of Mosher's esters and synthesis of the acetal derivative) [2,3] while stereochemistry of carbon 6 of the pyrone ring was determined by circular dichroism.



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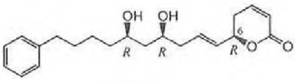

2

Interestingly, it is the first report of the occurrence of pyrones with opposite configuration at C-6 in the same plant.

[1] Kostermans, A. J. H.. *In : F. Didot. Les flores de Madagascar et des Comores, 81 ème famille.* **1950**, 46. Paris.
[2] Dale, J. A., Mosher, H. S., *J. Am. Chem. Soc.* **1973**, 95, 512.
[3] Queiroz, E. F., Silva, E. L. M., Roblot, F., Hocquemiller, E., Figadère, B., *Tetrahedron Letters*. **1999**, 40, 697.

CHIMIA 2000, 54, No. 7/8

Organic Chemistry **209**

Antifungal Prenylated Isoflavonoids from *Erythrina vogelii* Hook. F.

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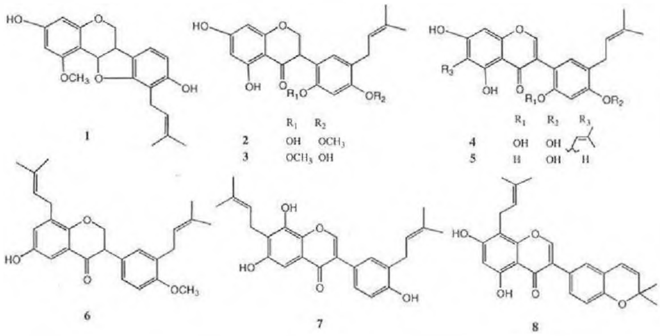
Screening of medicinal plants from the Ivory Coast for antifungal and antibacterial activity [1] indicated strong activities for the extracts of the roots of *Erythrina vogelii* Hook. F. (Leguminosae). In a preliminary biological evaluation, the MeOH and CH_2Cl_2 extracts were found to display antifungal properties [1]. The isolation of the antifungal compounds was monitored by inhibition of growth of *Cladosporium cucumerinum* in a direct TLC bioautographic assay [2]. This strategy led to the isolation of a series of prenylated isoflavonoids. The structures of these compounds were elucidated by spectroscopic techniques and confirmed by chemical methods.



[1]. Atindehou, K. K., Koné, M., Terreaux, C., Traore D., Hostettmann K., Dosso M., *Phytotherapy Res.*, **2000**, Submitted.

[2]. Homans, A.L, Fuchs, A. *J. Chromatogr.*, **1970**, 51, 327.

Organic Chemistry **210**

Saponins from *Glinus oppositifolius* (Aizoaceae)

A. Marston[a], D. Diallo[a,b], C. Terreaux[a] and K. Hostettmann[a]

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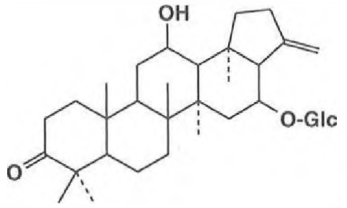
[b]CNRST NUFU Plantes Médicinales, Bamako, Mali

Initial screening of eleven medicinal plants [1] from Mali for molluscicidal, fungicidal and larvicidal activities led to the selection of *Glinus oppositifolius* (Aizoaceae; sometimes assigned to the Molluginaceae family) for further study because of the strong snail-killing properties of a methanol extract of the whole plant.

A combination of silica gel open-column chromatography, centrifugal partition chromatography, low-pressure liquid chromatography on RP-18 supports and gel filtration on Sephadex LH-20 gave 10 saponins. Their structures were elucidated by means of mass spectrometry (electrospray and fast atom bombardment) and NMR (1D and 2D techniques), combined with hydrolysis experiments. Several of the saponins (e.g. **1**) are hopane-type glycosides.



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[1] D. Diallo, A. Marston, C. Terreaux, Y. Touré, B. Smestad Paulsen, K. Hostettmann, *Phytother. Res.*, **2000** (in press).

Organic Chemistry **211**

Inter- and Intramolecular Tandem Radical Addition-Azidation Processes

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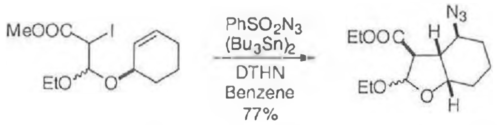
As we have reported recently, secondary and tertiary alkyl iodides and dithiocarbonates can be transformed into the corresponding azides by reaction with ethanesulfonylazide in the presence of dilauroyl peroxide (DLP) as radical initiator[1]. An extention of this methodology to inter- and intramolecular radical additions followed by azidation trapping will be presented.



[1] C. Ollivier and P. Renaud *J. Am. Chem. Soc.* **2000**, *122*, in press.

Organic Chemistry **212**

Preparation of the Podophyllotoxin Framework via Radical Cascade Cyclization

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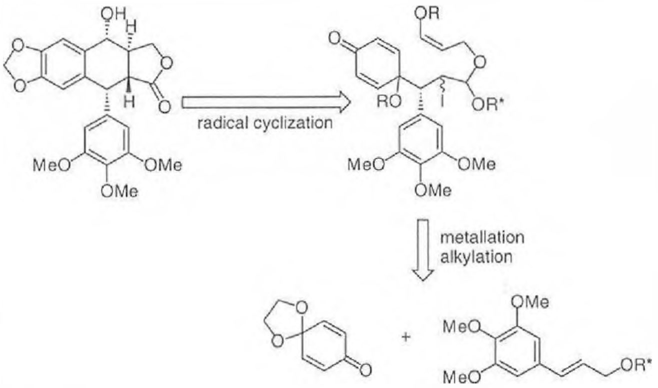
CH-1700 Freiburg

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 based on a radical cascade reaction. The general retrosynthesis is depicted below.



[1] R.S. Ward, *Nat. Prod. Rep.*, **1999**, *16*, 75

Organic Chemistry **213**

Photochemical acylation and its wavelength dependence

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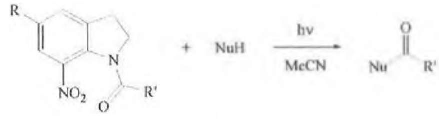
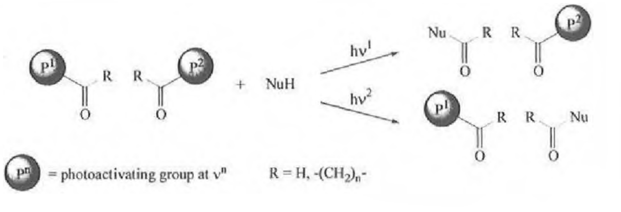
Université de Genève, Département de chimie organique,
Quai Ernest-Ansermet 30, CH-1211 Genève 4

Photocleavable protecting groups have been known for several decades, and many of them are described in the literature. Their contribution in a chemical transformation is mainly passive: upon irradiation, bonds are broken leading to the recovery of the initial functional group. A more interesting feature would be a true activation, *e.g.* towards nucleophiles. In this process, creation of new bonds on the substrate and deprotection would occur simultaneously. Such photoactivating groups are currently being investigated, according to the following scheme:



The reaction rate shows a strong wavelength-dependence. We report kinetic studies at various irradiation wavelengths. Such dependence opens the prospect of group differentiation by the use of selective wavelengths.



Organic and Inorganic Chemistry **214**

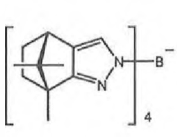
Synthesis of Novel Chiral Pyrazolylborates Anions

Virginie Hebbe and Jérôme Lacour*

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

Pyrazolylborate anions, first introduced by Trofimenko in 1967, have been widely used in different fields of chemistry for their ease of synthesis and efficient coordination properties [1]. Chiral derivatives **1** and **2** – and their application in asymmetric cyclopropanation reactions – were recently reported by Brunner and Tolman [2].

1



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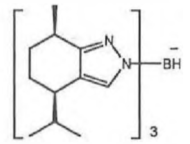
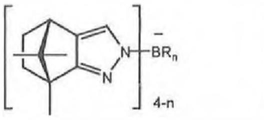
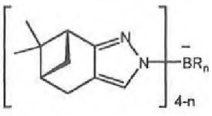


In the context of our continued interest in the asymmetric discriminations occurring between chiral anions and – prochiral or chiral - cations, we decided to investigate the use of enantiopure pyrazolylborate as chiral anionic auxiliaries. We here report on the synthesis of novel bis- and tetrapyrazolylborate anions made in three-four steps from camphor or β-pinene. Preliminary studies on the applications of these compounds as chiral ligands and/or anionic auxiliaries will be reported on this poster.





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[1] a) S. Trofimenko, *J. Am. Chem. Soc.*, **1967**, *86*, 6288; b) S. Trofimenko, *Chem. Rev.*, **1993**, *93*, 943.
[2] a) H. Brunner, *J. Organomet. Chem.*, **1993**, *43*, C16; b) W. Tolman, *Organometallics*, **1998**, *17*, 1984.

Organic Chemistry **215**

A new efficient synthesis of an interesting chiral 1,2-diamine with C_2 symmetry

Tomassini A., Alexakis A., Bernardinelli G.

Université de Genève, Département de chimie organique,
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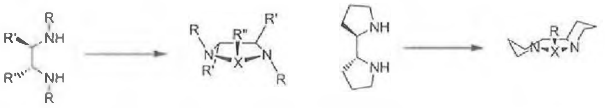
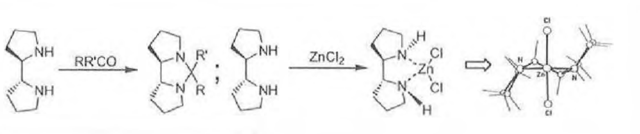
Chiral C_2 symmetrical 1,2-diamines emerged as versatile auxiliaries or ligands in many asymmetric reaction with excellent results. To anderstand why corresponding chiral diamines were so efficient, one has to examine the particular conformation under which they react. In all aminals now studied, the preferred conformation is the one having N-substituent (R) located *trans* to the substituent on the next carbon (R'). In such a conformation, each nitrogen becomes a stereogenic center with different chelation ability, since one lone pair participates to an anomeric effect whereas the other one does not, and therefore is more basic. To know if this conformation is necessary, Bis-pyrrolidine was synthesised by a short, diastereoselective and simple method.¹ The different conformations are shown in the following scheme.



Aminal² and zinc complexes were formed, where the substituent on the next carbon and the N-substituent are *cis* instead of *trans*, as shown below.



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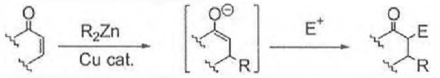
¹ Alexakis A., Tomassini A., Chouillet C., Roland S., Mangeney P., Bernardinelli G., Submitted for publication.
² See poster of Sandrine Pache.

Organic Chemistry **216**

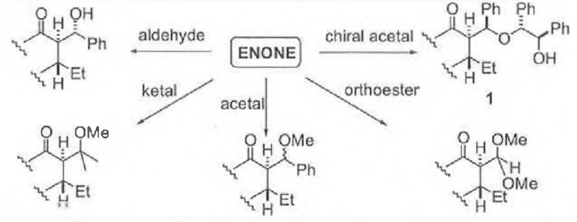
Tandem Asymmetric Michael Addition-Aldol Reactions

Dr. G. Trevitt *Universtité de Genève* Prof. A. Alexakis
Departement de Chimie, Quai Ernest-Ansermet 30, CH-1211, Genève

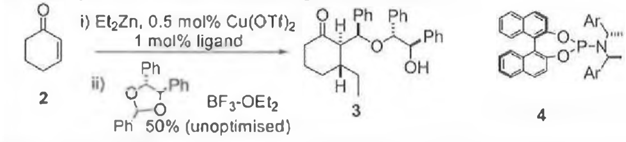
Recent work has focused on studying the chemical behavior of the zinc enolate intermediate formed in the course of the copper catalysed addition of organozincs to Michael acceptors.



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 have shown that benzyl protected alcohols of type **1** can be formed as a single diastereomer. Using chiral ligand **4** in the first step, **3** was formed from **2** in a single transformation with complete control of three contiguous stereocentres.



The scope of this reaction, its optimization and the use of alternative electrophiles are currently under investigation.

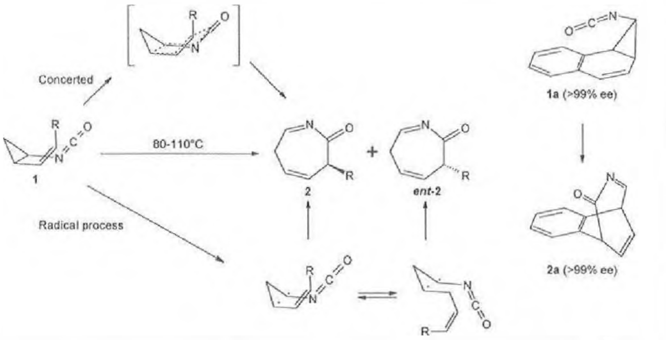
Organic Chemistry **217**

On the Stereochemical Course of the 2-Aza-divinylcyclopropane Rearrangement

Paul Müller, Hassan Imogai and Jean-Louis Toujas

Department of Organic Chemistry – University of Geneva
30, quai Ernest Ansermet, CH-1211 Geneva 4

Vinylcyclopropane isocyanates (**1**) afford chiral dehydroazepinones **2** *via aza*-Cope rearrangement under mild thermal conditions. Mechanistic and stereochemical aspects of this rearrangement are still in discussion. Two mechanisms may be envisaged: a concerted process *via* a *pseudo*-boat transition state, which would give stereoselectively **2**, or a mechanism involving biradicalar intermediates. In the latter case, racemic **2** should be obtained from enantiopure **1**.



We here report the first rearrangement of enantioenriched chiral *cis*-vinyl cyclopropane isocyanates [1,2], which provides new evidence in favour of the concerted mechanism. We observed that benzonorcaradiene isocyanate **1a** (≥99% *ee*) rearranged stereospecifically into **2a** with the configuration predicted from the *pseudo*-boat transition state. These results further open new synthetic perspectives for the *aza*-Cope rearrangement.

[1] P. Müller, H. Imogai, *Helv. Chim. Acta* **1999**, *82*, 315.
[2] P. Müller, J.-L. Toujas, G. Bernardinelli, *Helv. Chim. Acta*, **2000**.

Organic Chemistry **218**

Synthetic studies of Spongistatins : enantioselective approach of the spiroketal units through [4+3] cycloaddition

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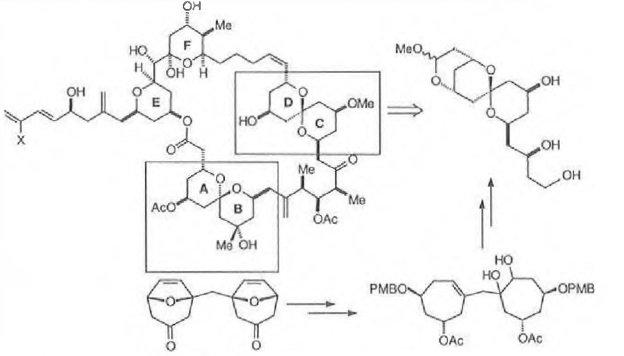
Institut de Chimie Organique, Université de Lausanne, BCH-Dorigny
CH-1015 Lausanne

Since their isolation in 1993 from marine sponges,[1] the spongistatins have become one of the most challenging target for organic chemists. Due to their unique activity against highly chemoresistant tumor cell lines (sub nanomolar growth inhibition), these macrolides have generated a considerable interest in the field of chemical biology and medecine. The spiroketal units seem to play a crucial role in the activity of spongipyrans.[2]

We report here a study toward the synthesis of these spiroketal fragments starting from the double bicycloadduct **1** which can be obtained by a double [4+3] cycloaddition. The key steps for the further elaboration are S_N2' bridge opening, desymmetrisation and spiroacetalisation.



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[1] G. R. Pettit, Z. A. Cichacz, F. Gao, M. R. Boyd, J. Hooper, J. M. Schmidt, C. L. Herald, *J. Org. Chem.* **1993**, *58*, 1302.
[2] F. M. Uckun, C. Mao, A. O. Vassilev, S. T. Jan, He Huang, *Bio. & Med. Chem. Lett.* **2000**, *10*, 541.

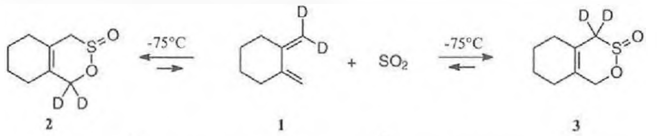
Organic Chemistry **219**

THE *HETERO* DIELS-ALDER REACTION OF SO_2 TO 1,2-DIMETHYLIDENECYCLOHEXANE IS ASYNCHRONOUS

Frédéric Monnat and Pierre Vogel*

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

Most 1,3-dienes add to SO_2 giving the corresponding sultines[1-6] under conditions of kinetic control (low temperature, acidic catalyst). They give the corresponding more stable sulfolenes under conditions of thermodynamic control, at higher temperature. With the dideuterated diene **1**, we have been able to show that the *hetero* Diels-Alder reaction is concerted but asynchronous, the C-S bond being formed to a larger extend that the C-O bond in the transition state.



$$\frac{k_H}{k_{D,2}} = 0.99 \pm 0.04 \qquad \frac{k_H}{k_{D,3}} = 0.89 \pm 0.03$$

The reactions rates have been measured by quantitative ^{13}C-NMR spectroscopy.

[1] Heldeweg, RF; Hogeveen, H *J. Am. Chem. Soc.* **1976**, *98*, 2341.
[2] Durst, T; Tétreault-Ryan, L *Tetrahedron Lett.* **1978**, 2353.
[3] Deguin, B; Vogel, P *J. Am. Chem. Soc.* **1992**, *114*, 9210.
[4] Fernandez, T; Suarez, D; Sordo, JA; Monnat, F; Roversi, E; de Castro, AE; Schenk, K; Vogel, P *J. Org. Chem.* **1998**, *63*, 9490.
[5] Fernandez, T; Sordo, JA; Monnat, F; Deguin, B; Vogel, P *J. Am. Chem. Soc.* **1998**, *120*, 13276.
[6] Roversi, E; Monnat, F; Schenk, K; Vogel, P; Braña, P; Sordo, JA *Chem. Eur. J.*, **2000**, 6, 1858.

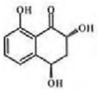
Organic Chemistry **220**

Enantioselective synthesis of natural Tetralone : 2,4-dihydro-2,4,8-trihydroxy-1-(2H)-naphtalenone.

E.Couché, A.Fkyerat, R.Tabacchi.

Institut de Chimie de l'Université de Neuchâtel,
Avenue de Bellevaux, 51, CH-2000 Neuchâtel

In our search for phytotoxic substances produced by *Ceratosystis fimbriata* sp. *Platani* [1], fungi responsible for the disease of plane tree, we have reported the isolation and structural elucidation by spectroscopic methods of cis and trans 2,4-dihydro-2,4,8-trihydroxy-1-(2H)-naphtalenone **1** and **2**.



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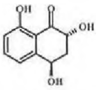
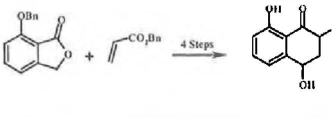


2

These naturals naphtalenones was already known from *Penicillium diversum* var. *Aureum* [2]. Their structures were confirmed by the synthesis from juglone, by Fujimoto and al., using a method with moderate yield without regioselectivity and without enantioselectivity.

Here, we report the total enantioselective synthesis of these products only in four steps from phthalide annulation followed by hydroxylation using chiral N-sulfonyloxaziridine.



[1] N.Bürki, Thèse de l'Université de Neuchâtel, **1996**.
[2] Fujimito Y., Satoh M., *Chem.Pharm.Bull.* ,**1986**, 34(11), 4540-4544.

Organic Chemistry **221**

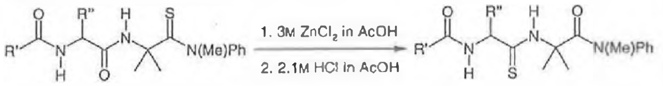
Scope and Limitation of an Acid Catalyzed Isomerization of Aib-Containing Thiopeptides

Roland André Breitenmoser and Heinz Heimgartner

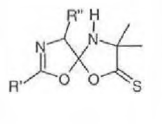
Organisch Chemisches Institut, Universität Zürich
CH-8057 Zürich

Peptides with backbone modifications are of considerable interest. Among them are endothiopeptides with one or more peptide bonds replaced by thioamides within the peptide chain and peptides containing 2,2-disubstituted glycines. The reaction of 3-amino-2*H*-azirines with amino thioacids combined with a novel isomerization [1] offers a convenient synthetic access to prepare peptides with a combination of these two backbone modifications.

We synthesized a variety of Aib-containing dipeptide thioanilides. By treatment with $ZnCl_2$ in AcOH followed by HCl-saturated AcOH, the thiocarbonyl group shifted from the last to the penultimate amino acid in high yields and without epimerization.



It could be established that a mechanism *via* spirocyclic intermediates [2] is conceivable for this isomerization. Moreover, we showed that our methodology to build up longer epimerically pure endothiopeptides containing the thiocarbonyl group next to the bulky Aib is quite versatile as long as a carbonyl group next to the *N*-terminus of the penultimate aminoacid is present.



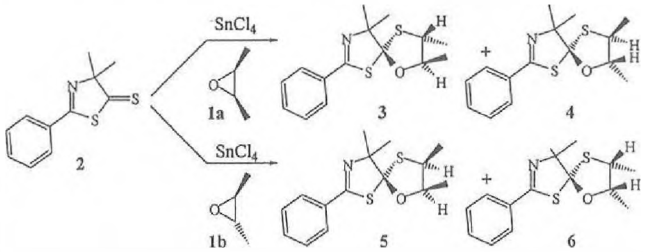
[1] J. Lehmann, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **1999**, *82*, 888.
[2] R.A. Breitenmoser, H. Heimgartner, *Helv. Chim. Acta*, in preparation.

Organic Chemistry **222**

Studies on the Mechanism of the Reaction between Thiocarbonyl Compounds and Oxiranes

M. Blagoev, A. Linden, and H. Heimgartner*
Institute of Organic Chemistry, University of Zurich
Winterthurerstr. 190, CH - 8057 Zurich, Switzerland

In our recent papers we reported on the formation of spirocyclic 1,3-oxathiolanes, *via* the reaction of oxiranes and thiocarbonyl compounds in the presence of a *Lewis* acid [1]. In order to further investigate the mechanism of this reaction stereochemically defined *cis*- and *trans*-2,3-dimethyloxiranes **1a** and **1b**, respectively, were allowed to react with 4,4-dimethyl-2-phenyl-1,3-thiazole-5(4*H*)-thione **2** and some thioketones.



The structures of the corresponding pairs of products **3**, **4** and **5**, **6** were established by means of NMR-experiments as well as by X-ray crystallography. The inversion at one of the oxirane C-atoms confirms our proposal, that the intermediates in the reactions are resulting from an S_N2 attack of the thiocarbonyl S-atom at the complexed oxirane.

[1] M. Blagoev, A. Linden, and H. Heimgartner, *Helv. Chim. Acta*, 1999, **82**, 1458; *ibid.*, 1999, **82**, 2312.

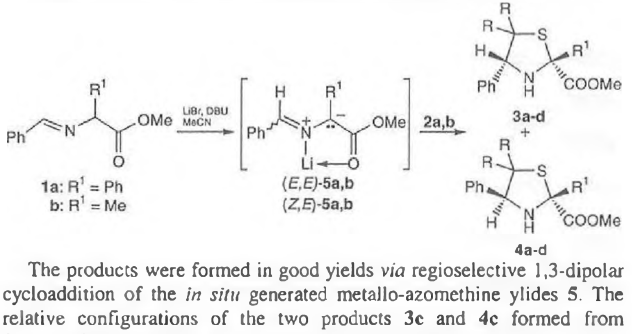
Organic Chemistry **223**

1,3-Dipolar Cycloaddition of Azomethine Ylides from *N*-Benzylidene α-Amino Acid Esters with Aromatic Thioketones

A. Gebert, A. Linden and H. Heimgartner

Institute of Organic Chemistry, University of Zürich

A few years ago, *Grigg et al.* developed the generation of azomethine ylides *via* 1,2-prototropic rearrangement of α-amino acid imines **1**, which offers a way to synthesize pyrrolidines which are not substituted at the *N*-atom [1,2]. The reaction of *N*-benzylidene phenylglycine methyl ester (**1a**) and *N*-benzylidene alanine methyl ester (**1b**) with thiobenzophenone (**2a**) and fluorene-9-thione (**2b**) in acetonitrile in the presence of lithium bromide and DBU yielded for each example a mixture of two corresponding diastereoisomeric 1,3-thiazolidines **3** and **4**.



The products were formed in good yields *via* regioselective 1,3-dipolar cycloaddition of the *in situ* generated metallo-azomethine ylides **5**. The relative configurations of the two products **3c** and **4c** formed from fluorene-9-thione (**2b**) and **1a** were established by X-Ray crystallography.

[1] R. Grigg, V. Sridharan, *Adv. +Cycloaddition* **1993**, *3*, 161.
[2] D. A. Barr, M. J. Dorrity, R. Grigg, S. Hargreaves, J. F. Malone, J. Montgomery, J. Redpath, P. Stevenson, M. Thorton-Pett, *Tetrahedron* **1995**, *51*, 273.

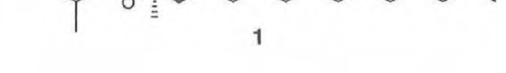
Organic Chemistry **224**

First Total Synthesis of (2*R*,4'*R*,8'*R*)-δ-Tocopherol

Thomas Netscher, Patrick Bohrer, Stéphanie Specht, and Pierre Fechter

Vitamin Research and Technology Development
F. Hoffmann-La Roche Ltd, CH-4070 Basel, Switzerland

(*R*,*R*,*R*)-δ-Tocopherol (**1**) is a major vitamin E component of several economically relevant edible oils, e.g. from soybeans [1]. The first total synthesis of this biologically important antioxidant is described. Key-steps of the sequence are the formation of a racemic chroman unit from a monoprotected hydroquinone, an optical resolution by chromatographic separation of diastereomeric esters [2], and a transition-metal catalyzed C-C coupling of a perfluoroalkylsulfonic ester [3] with an isoprenoid Grignard reagent [4] whose chiral centers originate from enantioselective hydrogenation. In addition, selected unnatural diastereoisomers of **1** for analytical assignment have been obtained accordingly. This allows the quantitative determination of all eight possible stereoisomers of δ-tocopherol by a combination of HPLC on a chiral and GC on an achiral phase [1,5].



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[1] Th. Netscher, *Chimia* **1996**, *50*, 563-567, and references cited therein.
[2] Cf. Th. Netscher, I. Gautschi, *Liebigs Ann. Chem.* **1992**, 543-546.
[3] Cf. Th. Netscher, P. Bohrer, *Tetrahedron Lett.* **1996**, *37*, 8359-8362.
[4] Th. Netscher, P. Bohrer, *Chimia* **1993**, *47*, 295.
[5] W. Walther, Th. Netscher, *Chirality* **1996**, *8*, 397-401.

CHIMIA 2000, 54, No. 7/8

Organic Chemistry **225**

Regioselective Synthesis of *trans*-1 Fullerene-C_{60} Bis-Adducts Directed by Crown Ether.

Jean-Pascal Bourgeois,[a] Monia Fibbioli,[a] Paul Seiler,[a] Ernö Pretsch,*[a] Luis Echegoyen,*[b] François Diederich,*[a]

[a] *Laboratorium für Organische Chemie, ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich, Switzerland.*
[b] *Department of Chemistry, University of Miami, Coral Gables, FL 33124, USA.*

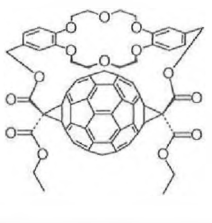

Figure. The *trans*-1 C_{60} bis-adduct (±)-**1**.

We present the first regioselective *Bingel* macrocyclization of C_{60} with a bis-malonate containing a novel dibenzo[18]crown-6 (DB18C6) tether which yields up to 55 % of the planar-chiral *trans*-1 bis-adduct (±)-**1**. [1] We have show that the DB18C6 tether in (±)-**1** is a true template which can be readily removed, thereby providing a versatile entry into diverse fullerene molecular scaffolding. Starting from this compound the synthesis of novel highly symmetrical hexa, hepta and octa-adducts of C_{60} will be presented. We have also demonstrated in extensive electrochemical studies with (±)-**1** that, for the first time, cation complexation strongly affects the redox potentials of C_{60} as a result of the close proximity of the ionophore-bound cation to the fullerene surface.

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Organic Chemistry **226**

Synthesis of a Library of Cyclic Hairpin Mimetic Peptides Conjugated to a Phospholipid as Potential Synthetic Vaccine Candidates Against *Plasmodium falciparum*

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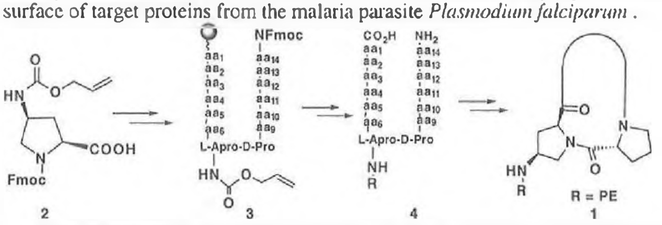
Small synthetic, conformationally constrained peptides are of great interest for the development of new drug or vaccine candidates. We previously showed that cyclic peptides containing the heterochiral D-Pro-L-Pro unit represent an interesting class of β-hairpin protein epitope mimetics [1-3]. Here we explore the use of such peptidomimetics to mimick B-cell epitopes on the surface of target proteins from the malaria parasite *Plasmodium falciparum* .



The design and the synthesis of a library of 35 14-mer cyclic peptides (**1**) derived from the AMA-1 protein of *P. falciparum* and their conjugation to phosphatidyl ethanolamine (PE) are described. We first present an efficient synthesis of the modified amino acid **2**. The linear precursors **3** incorporating **2** were successfully assembled on a solid support using the Fmoc chemistry. We finally describe the obtention of the final conjugate **1** using a key cyclization of **4** in solution.

[1] J. A. Robinson, *Synlett*, **1999**, 4, 429
[2] M. Favre, K. Moehle, L. Jiang, B. Pfeiffer, J. A. Robinson, *J. Am. Chem. Soc.* **1999**, 121, 2679
[3] J. Späth, F. Stuart, L.Jiang, J. A. Robinson, *Helv. Chem. Acta*, **1998**, 81, 1726

Organic Chemistry **227**

Evolutionary Principles for Generating Protein Mimetics : Directed Assembly of Peptide Loops on Topological Templates

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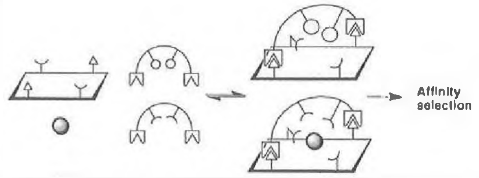
The use of topological templates proves to be a versatile concept in protein design and mimicry[1,2]. In separating the structural and functional part of a protein receptor, the attachment of ligand binding peptide loops to regioselectively addressable template molecules gives access to protein mimetics (Tasp) exhibiting essential features of native receptors[3]. In exploring novel methodologies for the reversible condensation of peptide libraries to chemoreactive templates, the principles of combinatorial chemistry are applied for generating a new class of protein mimetics. To this end, topological templates, e.g. cyclic decapeptides of type c[proGlyLys(Y1)AlaLys(Y2)]$_2$ are reacted with a library of peptide loops, e.g. X1-Xaa$_6$-X2 (X1, X2, Y1, Y2 = chemoselectively addressable groups) in the presence of ligands, e.g. metal ions (Figure), resulting in a library of ligand binding Tasp molecules.



Due to the reversibility of the assembly process, the ligand directed selection of metal coordinating peptide loops results in the formation of Tasp of maximal metal binding affinity. The potential of this concept will be exemplified for the ligand directed assembly of a number of metalloprotein mimetics, focussing on the elucidation of the chemical and structural parameters of the evolutionary process.

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[1] Tuchscherer, G.; Scheibler, L.; Dumy, P.; Mutter, M. *Biopolymers* **1998**, *47*, 63-73.
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Organic Chemistry **228**

Parameters that Influence the Electron Transfer in DNA

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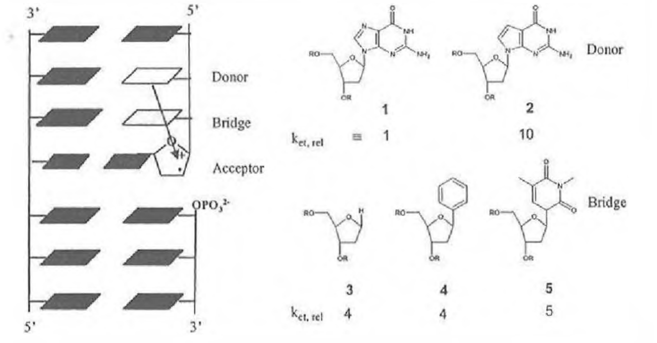
St. Johannsring 19, CH-4056 Basel

Electron transfer through DNA depends upon several parameters, among them: a) the distance between donor and acceptor [1], b) the difference of their redox potentials [2] and c) the structure of the bridge.

Measurements in double stranded DNA showed an increase of the electron transfer rate by a factor of 10 if the donor guanin (**1**) is replaced by 7-deazaguanin (**2**), which has a 0.4eV lower oxidation potential than **1** [3]. Exchanging the bridge by the unnatural base analogs **3-5** results in a faster electron transfer by a factor of 4-5. This is presumably evoked by the increased flexibility of the DNA double strand due to the reduced distance between the donor and acceptor.



[1] B. Giese, E. Meggers, D. Kusch, M. Spichty, U. Wille, *Angew. Chem. Int. Ed.* **1998**, *37*, 460
[2] B. Giese, E. Meggers, A. Dussy, T. Schäfer, *Chem. Eur. J.* 2000, *6*, 485
[3] calculated on the B3LYP/6-31G** level

Organic Chemistry **229**

Sugar-Modified Oligodeoxynucleotides: Synthesis and Pairing Properties

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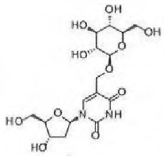
Freiestrasse 3, 3012 Bern

Glycosylated nucleosides such as **1** or **2** are found in the DNA of certain *E. coli* bacteriophages or in *Trypanosoma brucei* – a protozoan causing African sleeping sickness.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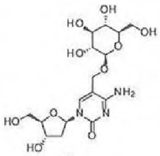
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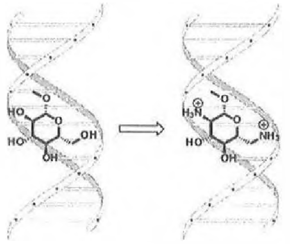

The glucose residues of DNA containing **1** reside within the major groove and protect the DNA from degradative enzymes. Replacing the 2- and 6-hydroxy groups of the glucose by ammonium groups should result in increased thermal stability.

The synthesis of phosphoramidite building blocks containing glucose and aminoglucose modifications will be reported as well as their effects on oligonucleotide pairing properties [1,2].

[1] J. Hunziker, *Bioorg. Med. Chem. Lett.* **1999**, *9*, 201.
[2] R. Tona, R. Bertolini, J. Hunziker, *Org. Lett.* **2000**, *2*, in print.

Organic Chemistry **231**

Synthesis and Pairing Properties of p-RNA Analogues

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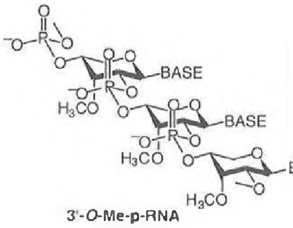
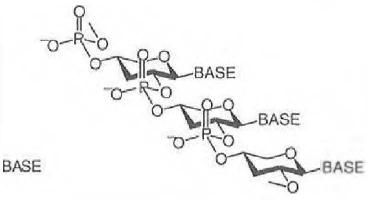
p-RNA oligonucleotides (based on ribopyranose) are much stronger and more selective pairing systems than the corresponding RNA oligonucleotides (based on ribofuranose). Furthermore, these two pairing systems are completely orthogonal to each other [1].

We will present an efficient, large-scale syntheses of 3'-*O*-methyl- and of 3'-deoxy ribopyranosyl phosphoramidites and the pairing properties of oligonucleotides derived therefrom (*Figure*).


3'-*O*-Me-p-RNA


3'-Deoxy-p-RNA = p-DNA

[1] S. Pitsch, S. Wendeborn, B. Jaun, A. Eschenmoser, *Helv. Chim. Acta* **1993**, *76*, 2161; S. Pitsch, R. Krishnamurthy, M. Bolli, S. Wendeborn, A. Holzner, M. Minton, C. Lesueur, I. Schlönvogt, B. Jaun, A. Eschenmoser, *Helv. Chim. Acta* **1995**, *78*, 1621; R. Krishnamurthy, S. Pitsch, M. Minton, C. Miculka, N. Windhab, A. Eschenmoser, *Angew. Chemie* **1996**, *108*, 1619; I. Schlönvogt, S. Pitsch, C. Lesueur, A. Eschenmoser, B. Jaun, R.M. Wolf, *Helv. Chim. Acta* **1996**, *79*, 2316.

Organic Chemistry **230**

PUROMYCIN ANALOGS: SYNTHESIS, BIOACTIVITY AND CONFORMATION

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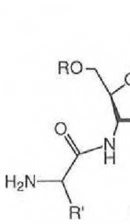
St. Johanns-Ring 19, CH – 4056 Basel

Several derivatives of **1** and **2**, structural analogs of the natural antibiotic and potent inhibitor of ribosomal protein synthesis *puromycin*, have been synthetised and tested for their *in vitro* protein release activity in a reconstituted *E. coli* translation system.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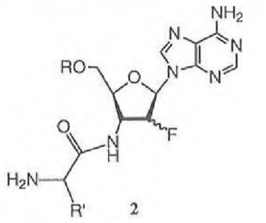
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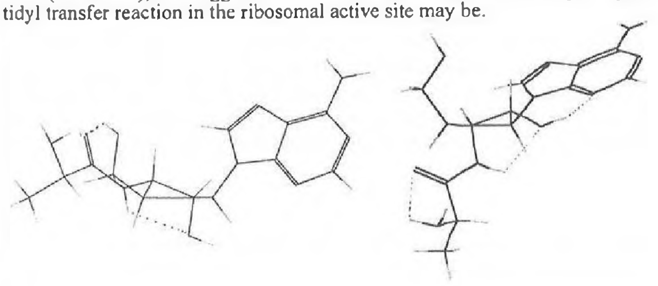
In addition, pH- and temperature-dependent ^{1}H NMR data of aqueous solutions of puromycin and analogs together with *ab initio*-calculated conformers (MP2/6-311++G**//B3LYP/6-311++G**) of the simplest derivative reveal the pK_a value of the nucleophilic α–amino group, the preferred conformations (see below), and suggest what the active conformations during the peptidyl transfer reaction in the ribosomal active site may be.



Organic Chemistry **232**

New efficient catalytic antibodies for the hydrolysis of pivalate prodrugs

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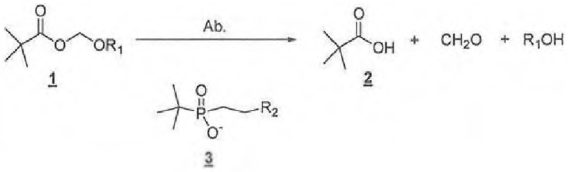
Freiestrasse 3, CH-3012 Bern

One important part of the medicinal chemistry is the use of prodrugs. They can be very useful to solve stability or toxicity problems. We report here a general strategy for the cleavage of pivalate prodrugs using catalytic antibodies. [1]



12 catalytic antibodies were isolated by HTS of antibodies obtained from mice immunized with phosphonate type haptens such as 3. These antibodies cleave prodrugs 1 that are otherwise resistant to esterases.

We will present the THS [2] strategy employed for isolation of catalytic antibodies, their substrate specificity, and the mechanism of action. Possible applications of these catalytic antibodies to specific prodrugs will also be discussed.

---

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[2] N. Bensel, N. Bahr, M.T. Reymond, C. Schenkels, J-L. Reymond *Helv. Chem. Acta*, **1999**, 82, 44.

Organic Chemistry **233**

Mechanistic Studies of Olefin Metathesis by Ruthenium Carbene Complexes using ESI-MS

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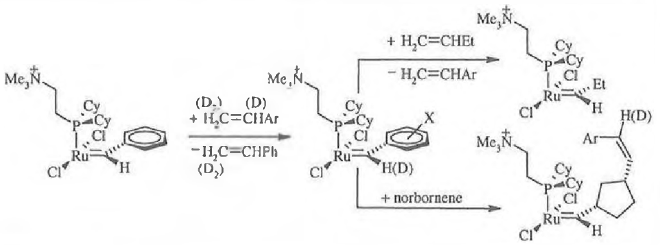
CH-8092 Zürich

The olefin metathesis reaction of the Grubbs ruthenium carbene complex [1] has been investigated in the gas phase by electrospray ionization tandem mass spectrometry. Relative rates of reaction for substituted ruthenium benzylidenes and alkylidenes after removal of one phosphine ligand were interpreted with aid of linear free energy analysis and kinetic isotope effect.



The experimental observations are consistent with a reaction profile in which the metallacyclobutane structure is a transition state rather than an intermediate, although alternative explanations cannot be wholly ruled out. Electron-withdrawal on the carbene moiety is found to accelerate the metathesis reaction when only the metathesis step itself is examined.

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Organic Chemistry **234**

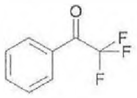
Heterogeneous Enantioselective Hydrogenation of Trifluoromethyl Ketones

M. von Arx, T. Mallat, A. Baiker

Laboratorium für Technische Chemie, ETH-Zentrum, CH-8092 Zürich

The asymmetric hydrogenation of trifluoromethyl ketones provides a direct route to the synthesis of valuable α,α,α-trifluoromethyl alcohols [1]. We have shown recently [2] that cinchona-modified Pt affords good enantioselectivity in the reduction of trifluoroacetophenone **1**.

Testing a series of trifluoromethyl ketones possessing different functional groups allowed us to discriminate between steric and electronic influences on the hydrogenation of activated ketones. The low enantioselectivities obtained with some trifluoromethyl ketones (e.g. trifluoroethylpyruvate **2** or 1,1,1-trifluoroacetone **3**), as well as the very high enantioselectivity obtained with ethyl trifluoroacetoacetate **4** (90 % ee using O-methyl-cinchonidine as modifier) can be explained by this way.



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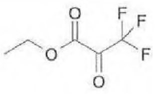

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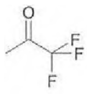

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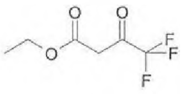

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Further investigation of the hydrogenation of **1** and **4** revealed some significant differences compared to the behaviour of other activated ketones such as α-ketoesters. Even though the mechanism of these reactions is not understood yet, the findings are not consistent with the existing models for enantioselective hydrogenation of α-ketoesters with the platinum-cinchona system.

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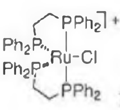
Organic Chemistry **235**

Ruthenium(II)-Mediated C–F Bond Formation. Catalytic Nucleophilic Fluorination of Activated Aliphatic Bromides

P. Barthazy, A. Togni* and A. Mezzetti*
Laboratorium für Anorganische Chemie, ETH Zürich, CH-8092 Zürich

The five-coordinate fluoro complex $[RuF(dppp)_2]^+$ is known to react with organic bromides R–Br to give R–F and $[RuBr(dppp)_2]^+$ [1]. We find now that the reaction becomes catalytic using **1** or **2** as catalysts and TlF as the fluoride source. The aliphatic halides **3** and **4** give the corresponding R–F in fair yield. The chiral catalyst **2** fluorinates (*rac*)-**4** with kinetic resolution. PhMeCHF is formed with 16% ee at 1% conversion, which suggests metal involvement, but the ee drops to 3% at 100% conv. The Tl-adduct $[Tl(\mu\text{-}F)_2Ru(dppe)_2]^+$, the main species in solution during catalysis, was isolated and characterized.



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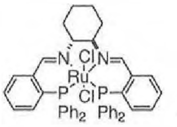

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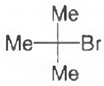
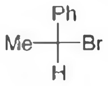


$Me_3C\text{–}Br$

3



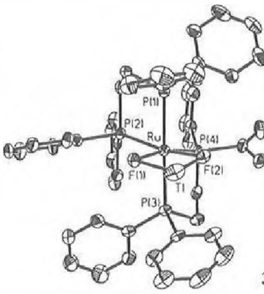
$PhMeCH\text{–}Br$

4

$$\underset{(\mathbf{3}\text{ or }\mathbf{4})}{R\text{–}Br} + TlF \xrightarrow[\text{CHCl}_3,\ \text{RT}]{\mathbf{1}\text{ or }\mathbf{2}} R\text{–}F + TlBr$$

subst.	cat. (mol%)	t / d	yield (%)
3	1 (10%)	5	63
4	1 (1%)	8	34
3	2 [a] (10%)	5	50
4	2 [a,b] (1%)	1	49

[a] $Tl[PF_6]$ (1 equiv) is added. [b] In CH_2Cl_2.



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Organic Chemistry **236**

Enantioselective and Diastereoselective Dearomatisation of Arene Chromium Tricarbonyl Complexes and Synthetic Applications

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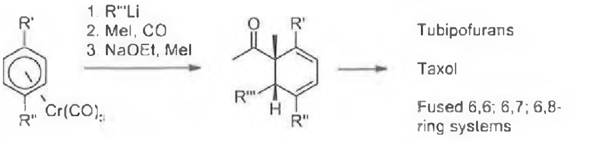
Département de Chimie Organique, Université de Genève
30 Quai Ernest Ansermet, CH-1211 Genève 4.

Dearomatisation of arenes via temporary complexation to the electrophilic $Cr(CO)_3$ group yields highly functionalized alicyclic molecules [1]. The use of arene bound chiral auxiliaries, chiral nucleophiles and planar chiral arene chromium tricarbonyl complexes has enabled the synthesis of compounds with high enantioenrichment [2].



R' = H or OMe; R'' = oxazoline, cyclohexylimine or R(S)AMP hydrazone;
R''' = methyl, phenyl, n-butyl, propargyl, vinyl, ethoxy vinyl, or allyl.

The efficiency of the above methodology, which enables the regio- and stereoselective addition of up to three carbon units across an arene double bond in a one pot transformation, has prompted its application to advanced synthetic targets. Here we report a total synthesis of (-)-acetoxy tubipofuran, a novel approach towards taxol and rapid access to 6,6-, 6,7- and 6,8-fused ring systems.

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Organic Chemistry **237**

The Photochemical Contraction of Pyridinium Salts A New Approach towards Aminocyclopentitols

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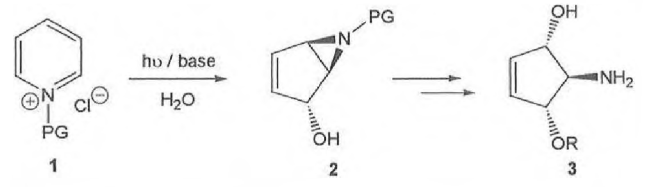
The photohydration of N-substituted pyridinium salts in alkaline medium proceeds smoothly to give bridged aziridines in good preparative yield [1]. An enantiopure aziridine can be prepared when starting from α-D-glucopyranosyl pyridinium chloride (**1**, PG = α-D-Glc) [2]. We report on regio- and stereospecific aziridine opening and face selective transformations.



PG = MEM or Glc ; R = Bn, Ac

[1] E.A. Acar, F. Glarner, and U. Burger, *Helv. Chim. Acta* **1998**, *81*, 1095-1104.

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Organic Chemistry **239**

A New Asymmetric Carbon-Carbon Bond Forming Reaction: Four-Component Stereoselective Synthesis of Methyl Sulfones

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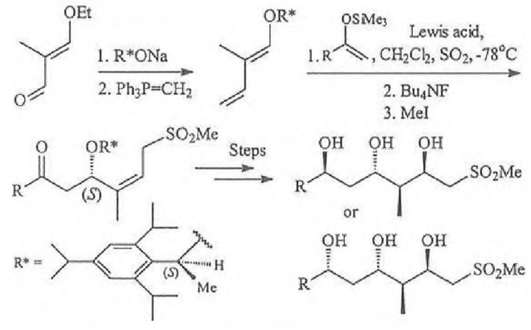
Section de Chimie de l'Université de Lausanne, BCH-Dorigny
CH-1015 Lausanne

In the presence of a Lewis acid, 1-alkoxy-1,3-dienes can be combined with enoxysilanes and sulfur dioxide to generate (Z)-6-oxo-4-oxyalk-2-ene sulfinates, which react with methyl iodide (S-alkylation) to afford the corresponding methyl sulfones [1].
We report here an asymmetric version of this new carbon-carbon bond forming reaction that can be used to construct polyketide fragments stereoselectively [2].



[1] B. Deguin, J-M. Roulet, P. Vogel, *Tetrahedron Lett.* 1997, *32*, 6197-6200; J.-M. Roulet, G. Puhr, P. Vogel, *Tetrahedron Lett.* 1997, *38*, 6201-6204.

2] V. Narkevitch, K. Schenk, P. Vogel, *Angew. Chem. Int. Ed.* **2000**, *39*, 06-1808.

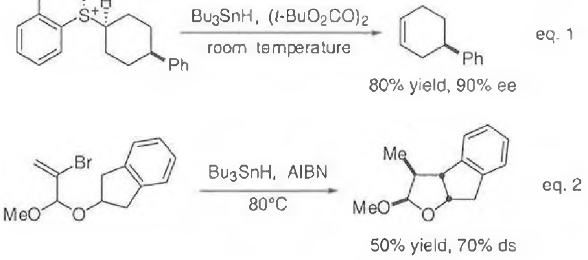
Organic Chemistry **238**

Diastereoselective 1,5-Hydrogen Transfer as a New Tool in Asymmetric Synthesis

Laura Andrau, Laurence Feray, Nikolaï Kuznetsov, and Philippe Renaud*

Institut de Chimie Organique, Pérolles
CH-1700 Fribourg

Diastereoselective 1,5-hydrogen atom transfers are known [1] but the stereoselectivity of these processes has never been investigated in a systematic way.
We report here that stereocontrolled hydrogen transfers represent a new efficient tool in asymmetric synthesis.
Two reactions have been investigated: the fragmentation of sulfoxides [2] (eq. 1) and the cyclization of acetals (eq. 2).



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Organic Chemistry **240**

A novel chiral Fp analogue used as cyclization catalyst

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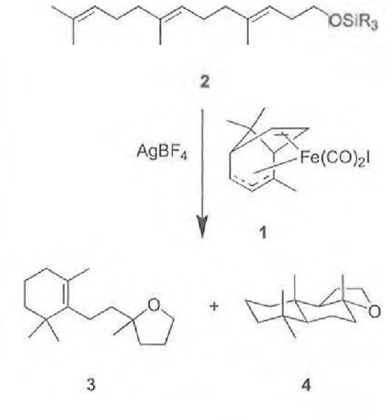
CH-1700 Fribourg

A new catalyst, the dicarbonyliode[η^5-(2,8,8)-trimethylbicyclo[3.2.1]-oct-3,6-dien-2-yl]iron **1** [1], has been developed for the effective cyclization of protected homofarnesol **2**.

We report here on the investigation of the reactivity of the iron complex **1** as a catalyst for olefinic cyclization reactions of protected homorfarnesol **2** affording a mixture of carbocycles including a derivative of β-ionone (**3**) and Ambrox® (**4**), one of the most important commercial substitute for ambergris due to its olfactive and fixative properties [2].



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Organic Chemistry **241**

Chiral TADDOL-Phosphite- and Bis(*N*-Tosylamido)-phosphine-oxazolines as Ligands in Asymmetric Catalysis

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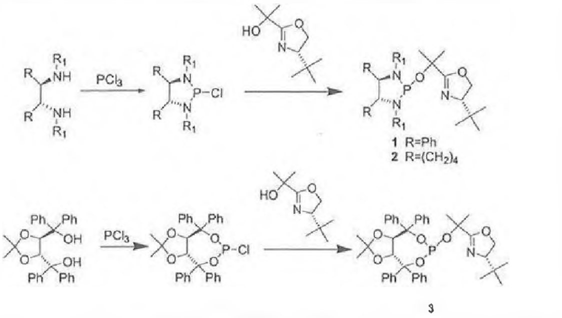
CH-4056 Basel, Switzerland, e-mail: Robert.Hilgraf@unibas.ch

A series of *P,N*-ligands containing a chiral oxazoline ring and a chiral bis(*N*-tosylamino)- or bis(*N*-tolyl) phosphine group derived from 1,2-diamines[1] **1** and **2** or a chiral cyclic phosphite group derived from TADDOL[2],[3] **3** has been prepared.

The synthesis of these new ligands is modular and straightforward:



3

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

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Organic Chemistry **243**

Toward the Total Synthesis of Sporeamicin A and Analogues

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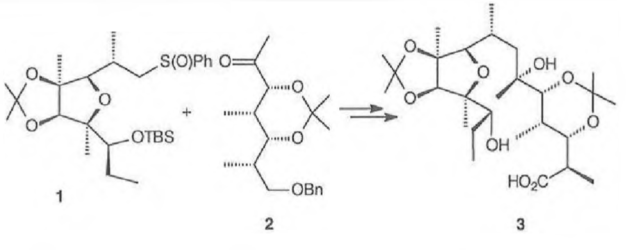
The urgent need for new antibiotics [1] has stimulated the search for new microorganism metabolites and chemically modified known antibiotics. Sporeamicin A was isolated from *Saccharopolyspora* sp. and characterized by Morishita and coll in 1992. [2] This compound revealed a strong activity against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

We report here our approach of the aglycon part of Sporeamicin A which should be obtained through macrolactonisation of compound 3. This seco-acid resulted from the coupling of methyl ketone 2 with sulfoxide 1. The polysubstituted furane ring was prepared by stereoselective functionalization of 7-oxabicyclo[2.2.1]hept-5-ene-2-one derivatives. [4]



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Organic Chemistry **242**

Total Synthesis of Coraxeniolide-A

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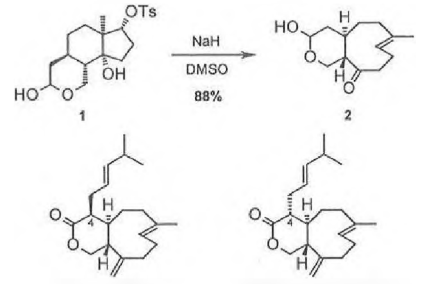
Freiestrasse 3, CH-3012 Bern

Coraxeniolide-A is a naturally occurring diterpene that was isolated from a pink coral [1]. It belongs to the xeniolides, a subclass of xenicanes which exhibit among others interesting antiinflammatory activity [2].

We report here the first total synthesis of optically active coraxeniolide-A and 4-epi-coraxeniolide-A. A keyreaction in the 29 step synthesis was the *Grob*-fragmentation of **1**, with which the nine-membered ring containing the *E*-double bond was elaborated.



Coraxeniolide-A 4-Epi-coraxeniolide-A

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Organic chemistry **244**

Application of the Novel Tandem-Process Diels-Alder Reaction/Ireland-Claisen Rearrangement to the Synthesis of (+)-Juvabione and (+)-Epijuvabione.

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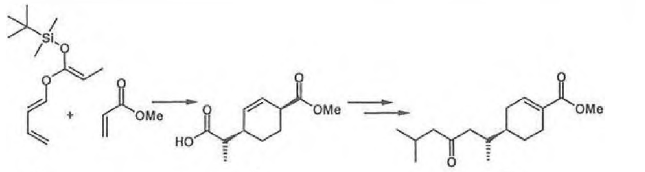
The length of a synthesis is determinated by the increase of complexity achieved per synthetic operation. Combining several transformations into a one-pot reaction has proven to be an excellent strategy to increase the efficiency of organic synthesis [1]. In our group a new tandem process Diels-Alder reaction/Ireland-Claisen rearrangement starting from O-butadienyl-ketene-acetals **1** has been developed [2].

This process shows a high diastereoselectivity for the Ireland-Claisen rearrangement starting from the *endo*-product of the Diels-Alder reaction. Based on this mechanistic knowledge the novel tandem-process could be applied to a short synthesis of Juvabione 3 and Epijuvabione with good overall yield [3].



1 2 3

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Organic Chemistry **245**

Loading a Porphyrin with Fullerenes

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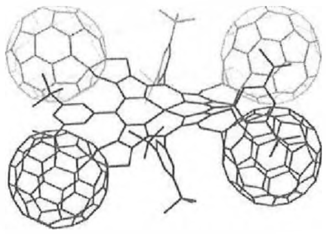
A-6020 Innsbruck, Austria

A complete set of (five) zinc-fullereno-porphyrinates, with one to four fullerene-units covalently attached at the periphery, was made accessible by a new synthetic strategy using a symmetric zinc-tetrasulfoleno-porphyrinate [1] as starting material. The numbers of fullerene-units bound and the sites of their attachment to the porphyrin core was secured by UV/Vis-, FAB-mass- and NMR-spectroscopy. The [60]-fullerene-moieties are indicated to be bound to nonplanar porphyrins. The novel tetrafullereno-porphyrin represents a unique molecular reservoir of electro-and photo-active units.



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Organic Chemistry **247**

A New, Non-iterative Asymmetric Synthesis of Long-Chain 1,3-Polyols.

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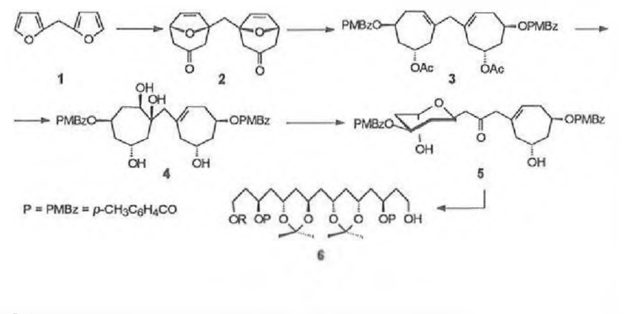
CH-1015 Lausanne

The polyene macrolide antibiotics belong to a large class of natural products incorporating conjugated polyenes and polyol sequences made up of 1,3-diols most commonly.

We present here a new approach to the enantioselective synthesis of pentadeca-1,3,5,7,9,11,13,15-octols and derivatives (**6**). It is based on the Sharpless asymmetric dihydroxylation of meso bis(4-methoxybenzoate) **3** derived from oxa-bridge opening of diketone **2**. The latter was prepared through a double [3+4]-cycloaddition of 1,1,3-trichloro-2-oxyallyl cation with 2,2'-methylenedifuran (**1**). The 1,2-diol **4** obtained in 98.4 % e.e. was cleaved into the hemiketal **5**. Combining the Evans' *anti* and Nasaraka's *syn* reductions of the aldol **5** with S_N2 inversion reactions, all the diastereomeric pentadecaoctols and analogues can be obtained, in principle, with high enantio- and diastereoselectivities [1].



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Organic Chemistry **246**

New Synthesis to „Obeline" intermediates for NS active compounds

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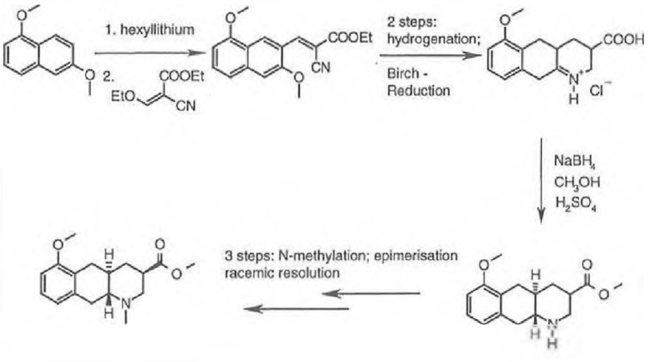
Novartis Pharma (4002 Basel) PDPM-TRD-CHAD-PRD

A new synthetic route to the class of the „obelines" (octahydrobenzo[g]quinolines) is presented. The **„obeline"- building block A** is used for several research NS-candidates as a key intermediate. The synthesis is linear and starts from the cheap starting materials 1,6-dimethoxynaphthalene and ethoxymethylene cyanoaceticacid ethylester.

The key steps are the Birch - reduction and the sodiumborohydride reduction.



"obeline"- building block A

We report the development of the research to the multi kg pilot plant synthesis .

Physical Chemistry **248**

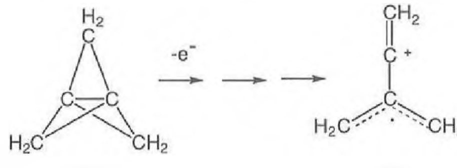
The Surprising Fate of [1.1.1] Propellane on Ionization

Beat Müller,[a] Thomas Bally,[a] Ffrancon Williams,[b] and Rob Pappas[b]

[a] Institut de Chimie Physique de l'Université de Fribourg, 1700 Fribourg
[b] Department of Chemistry, University of Tennessee, Knoxville, TN 37996

Nonwithstanding the fact that ionization of [1.1.1]propellane (**PRP**) occurs from a totally symmetric MO that is essentially nonbonding, the resulting radical cation undergoes spontaneous rearrangement on radiolytic oxidation in cryogenic matrices.

Quantum chemical calculations show that this rearrangement leads via two metastable intermediates to a novel distonic radical cation, dimethylene-allene (**DIA**) that is identified by ESR, IR and UV/Vis spectroscopy.



PRP **DIA**

The reasons for this unexpectedly facile decay of **PRP**, as well as that of the intermediates formed on the way to **DIA** are explored theoretically. Thereby it is found that *vibronic interaction* between the electronic ground state and low-lying excited states are responsible for the pronounced flattening of otherwise steep potential energy surfaces of radical ions.

Other recent examples where this feature allows to understand the surprising chemistry of radical cations will be given.

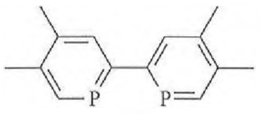
Chimie physique **249**

Etude par RPE/ENDOR du radical anion de la biphosphinine et du complexe de Nickel(0) associé.

Sylvie Choua[1], Helena Sidorenkova[1], Théo Berclaz[1], Michel Geoffroy[1]
Pascal Le Floch[2]

[1] Département de chimie Physique, 30 quai Ansermet, Université de Genève, 1211 genève, Suisse
[2]Laboratoire Hétéroélèments et Coordination, UMR CNRS 7653, Ecole Polytechnique, 91128 Palaiseau Cedex, France.

Le radical anion de tmbp (4,4',5,5'–tetramethyl-2,2'–biphosphinine) a été généré par réaction sur un miroir de potassium à basse température (200K) et étudié par RPE. L'analyse du spectre n'a été possible que grâce à l'obtention d'un spectre ENDOR à 185K. Celui-ci associé aux calculs DFT a permis d'identifier toutes les constantes de couplage des différents protons. L'enregistrement du spectre en solution gelée conduit aux tenseurs hyperfins des deux noyaux de ^{31}P. L'ensemble de ces paramètres RPE montre que l'électron non apparié est essentiellement délocalisé sur le fragment P-C=C-P.
La réduction par voie électrochimique du complexe $Ni(tmbp)_2$ conduit au radical anion. Les spectres en solution liquide et gelée ont permis de déterminer les couplages hyperfins isotropes et anisotropes des quatre noyaux du phosphore. Ces résultats indiquent que l'électron célibataire est fortement délocalisé sur les ligands. Les calculs DFT montrent que la réduction du complexe s'accompagne d'une distorsion vers un système plan carré.



tmbp

Physical Chemistry **250**

Excited- state proton transfer in 1-naphthol /ammonia clusters: Wavelength-dependence of the pump-probe spectra

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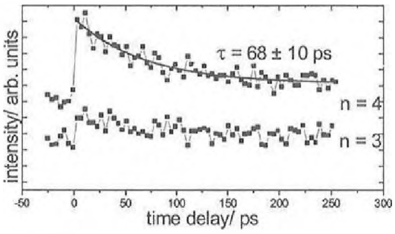
Labor. f. Org. Chemie, ETH Zürich, Universitätstr.16, CH – 8092 Zürich

We investigate the threshold size and time scale for excited-state proton transfer in 1-naphthol/ammonia clusters by picosecond time-resolved photoionization.

The 1-naphthol/ammonia system is the primary model for studying intramolecular excited-state proton transfer (ESPT) and intracluster reactions in general. An important question concerns the size dependence of ESPT: There is still a controversy [1-4] on the minimum number of ammonia molecules solvating the 1-naphthol in order to drive the reaction. Is the threshold size *n* is three or four? We present new data on the ESPT dynamics using time-resolved photo-ionization at various pump and probe wavelengths. The results yield new information on the time scale of intermolecular ESPT and resolve part of the discrepancy between the work of several groups, finding a minimum clustersize n = 4.



[1] O. Cheshnovsky, S. Leutwyler, *J. Chem. Phys.*, **1988**, 88, 4127.
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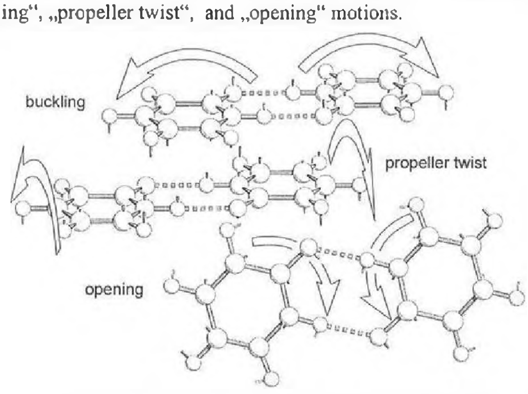
Physical Chemistry **251**

H-bonding analogues for nucleobase pairs

Andreas Müller, Francis Talbot, and Samuel Leutwyler

Departement für Chemie und Biochemie
Freiestrasse 3, 3000 Bern 9

Dimers of substituted pyridines (and their tautomers) are good models for nucleic acid base pairs. They offer the characteristic amide N-H, amino $-NH_2$, and carbonyl groups needed to model the H-bonding interactions in natural nucleobase dimers. Regarding the hydrogen bonding topology, 2-pyridone [1] is a model for uracil (U) or thymine (T), 2-aminopyridine for adenine (A) and 2-amino-6-pyridone for guanine (G).
The intermolecular vibrations of dimers which model the U·U, A·U and G·U interactions were studied in supersonic jets by absorption and emission laser spectroscopic techniques. These intermolecular vibrations are analogous to well-known structural distortion coordinates of base pairs in DNA, such as „buckling", „propeller twist", and „opening" motions.



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Physical Chemistry **252**

Heterogeneous Reactions of Chlorine Compounds on NaCl and KBr Salt Surfaces

Christian Santschi and Michel J. Rossi

Laboratoire de Pollution Atmosphérique, Département de Génie Rural, EPFL, CH-1015 Lausanne

Model and laboratory studies show the importance of halogen compounds in the chemistry of the troposphere. HOCl is considered as an important intermediate in tropospheric as well as in stratospheric chemistry whose reactions with sea salt aerosols lead to a release of gaseous photochemically active halogen compounds such as Cl_2 and Br_2. However, it has not yet been identified in the troposphere.

The reaction of HOCl and its secondary reactions on NaCl and KBr have been studied in a Knudsen cell low pressure flow reactor. The reactions have been investigated on different types of surfaces such on thin film surfaces and powder substrates.

The observed reaction products are Cl_2, Br_2 and BrOCl. In addition, a production of HOCl has been measured. It was found that the reaction kinetics depends strongly on the amount of adsorbed water on the surface. On "dry" surfaces the reactions were much slower than on "humid" surfaces. Saturation effects have been observed as well. By means of SEM-pictures a efficient recrystallization of thin film KBr has been observed upon exposure of those films to Br_2. The interpretation involves a chemical mechanism which needs H_2O in order to proceed.

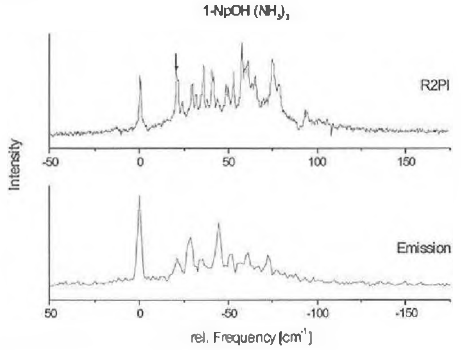
Physical Chemistry **253**

Excited- and Ground-State Spectroscopy of 1-Naphthol/Ammonia Clusters

Christian Tanner, Hans M. Frey and Samuel Leutwyler

Departement für Chemie und Biochemie
Freiestr. 3, CH-3000 Bern 9

Excited-state proton transfer is observed in 1-naphthol-$(NH_3)_n$ clusters with n≥4 [1,2]. The proton transfer events are closely coupled to vibrational motions of the $(NH_3)_n$ solvent cluster. For this reason, the low-frequency intramolecular vibrations of the largest non-proton transferring cluster (n=3) were investigated by laser resonant 2-photon ionization and fluorescence spectroscopy via the $S_1 \leftrightarrow S_0$ electronic excitation. Experimental results are compared to the predictions of ab initio calculations using the SCF and B3LYP density functional methods.



[1] Cheshnovsky, O., Leutwyler, S., *J. Chem. Phys.*, **1988**, 88, 4127.
[2] Knochenmuss, R, *Chem. Phys. Lett.*, **1999**, 305, 233.

Chemical Physics **254**

Properties of the HCl/ice, HBr/ice and H_2O/ice Interface at Stratospheric Temperatures (200K)

Benoît Fluckiger, Laurent Chaix and Michel J. Rossi

Laboratoire de pollution atmosphérique, Département de Génie Rural
Ecole Polytechnique Fédérale de Lausanne
CH-1015 Lausanne

In view of the importance of HCl for atmospheric chemistry, we investigated its kinetic availability involved in heterogeneous reactions, adressing the question of time scale needed to exhaust a given supply of HCl adsorbed on ice, HCl diffusion into ice and the nature of the HCl/ice interface. Bulk, vapor-deposited and single crystal ice has been studied in a Knudsen cell flow reactor in the range 190 to 210 K [1]. Fluxes of surface to bulk loss in ice on single crystal and bulk ice vary from 5×10^{11} to 1×10^{13} and from 5×10^{12} to 5×10^{14} molecule s^{-1} cm^{-2} for HCl and D_2O, respectively. A positive activation energy for diffusional loss of $E_A=3.0\pm0.5$ for HCl/ice and 5.3±0.7 kcal/mol for D_2O/ice has been measured. Complementary measurements ("Dope and Probe" experiments) of the HCl/ice interface region using the titration reaction of $ClONO_2+HCl\rightarrow Cl_2+HNO_3$ allowed the evaluation of the thickness h of the interfacial region, defined as the near surface region of the ice where HCl is immediately available for titration at a high rate. We measured h=100±10 nm for single crystal ice, 200±50 nm for vapor-deposited ice and 1000±200 nm for bulk ice samples. The modeling of our results according to the laws of diffusion leads to values of the HCl diffusion coefficient D_{HCl} ranging from $(4.0\pm1.0)\times10^{-14}$ to $(2.8\pm1.0)\times10^{-12}$ cm^2 s^{-1} for single crystal and bulk ice, respectively.

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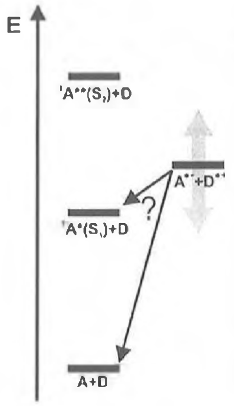
Physical chemistry **255**

Effect of a low-lying electronic excited state on the charge recombination dynamics in a geminate ion pair

P.-A. Muller, E. Vauthey.

Institute of Physical Chemistry, University of Fribourg, CH-1700 Fribourg

Most photoinduced electron transfers (PET) take place from the lowest electronically excited state (S_1 or T_1) of one of the reactant. The charge recombination (CR) of the resulting ions pair (IP) is often slow due to its large exergonicity (Marcus Inverted Region).



Azulene and its derivatives as well as xanthione, are among the few molecules which have a S_2 state with a sufficiently long lifetime to exhibit S_2 fluorescence in solution. We report on our investigation of the CR dynamics in geminate ion pairs (GIP) formed by PET from S_2 state of azulene, benz[a]azulene and xanthione. In these case, the resulting GIP has two possible pathways for CR: to the ground state or to the $^1A^*(S_1)+D$ state.

These systems have been compared to GIPs with similar free energy for CR, but formed upon PET from the S_1 state. It will be shown that the presence of a low-lying excited electronic state lead to a strong acceleration of the CR.

Physical chemistry **256**

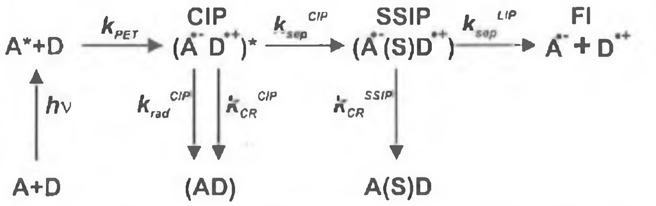
Deuterium isotope effect on the charge recombination dynamics of contact ion pairs formed by electron transfer quenching in acetonitrile

P.-A. Muller [a], E. Vauthey [a], C. Högemann [a], P. Jacques [b], X. Allonas [b].

a Institute of Physical Chemistry, University of Fribourg, CH-1700 Fribourg
b Département de Photochimie Générale, Université de Mulhouse, F-68093 Mulhouse

There is a large controversy concerning the charge recombination (CR) pathway of ion pairs (IP) formed by electron transfer (ET) quenching of 9,10-dicyano-anthracene (DCA) by weak donors.

The primary quenching product is a contact ion pair (CIP) which exhibits a weak exciplexe-like fluorescence.



It has been argued that CR within the CIP is extremely slow and takes place in the solvent separated ion pairs (SSIP), where the interionic distance is larger. We have performed measurements of the deuterium isotope effect on the CIP fluorescence lifetime as well as on the free ion yield. The observed isotope effects can only be explained in a scheme where CR takes place in the CIP and when the SSIP does not play a significant role.

Physical Chemistry **257**

Density Functional Theory Study of the Uracil – Uracil dimer

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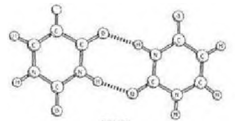
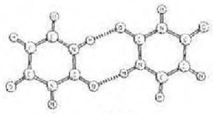
Freiestrasse 3, CH-3012 Bern 9

Two differents structures of the Uracil-Uracil dimer were investigated using Density Functional Theory (DFT). The most stable one is a H-bonded dimer with two N – H ··· O H-bonds, designated HB4[1] it has a binding energy De = -16.20 kcal/mol (corrected for basis set superposition error BSSE) at B3LYP/6-311++G(d,p) level of theory, followed by the isomer HB5 (with De = -10.62 kcal/mol). A biologically relevant U·U dimer, which is called the CALCUTTA[2-3] dimer has a conventional N – H ··· O and an unconventional C – H ··· O. It lies at De = -10.0 kcal/mol above the minimum.

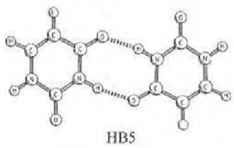
Pontential energy surfaces were calculated in order to obtain the force constant of the counterrotation of the pired bases about thei common axis, i.e., *Propeller Twist* motion.



HB3



HB4



HB5

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Physical Chemistry **259**

Measurement of the Surface Residence Time of NO_2 and H_2O on Different Types of Flame Soot Produced in the Laboratory

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Soot is a substance emitted by combustion processes and its presence in atmosphere is principally due to internal combustion engines especially Diesel motor vehicles. Interactions of some pollutants like NO_2 with soot aerosols as well as the implication of soot particles as condensation nuclei for water vapor in contrails of airplanes or in cirrus clouds constitute our points of interest.

In this work we have obtained both the kinetic parameters and the product spectrum of NO_2 and H_2O interacting with soot samples in terms of surface residence times τ of reacting molecules and uptake rate constants expressed as uptake coefficients (γ_0). 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.

At room temperature, NO_2 interacting with soot generate products like HONO up to a yield of 90% of the injected NO_2 molecules in case of toluene and decane soot, but for acetylene soot no HONO has been observed. We determined initial uptake coefficients γ_0 close to zero for H_2O interacting with soot but up to 0.26 for NO_2 on acetylene soot and an average of 0.1 for NO_2 on decane and toluene soot.

The residence time τ of NO_2 on the different types of soot ranges from 30 ms (toluene, decane) up to 70 ms (acetylene).
H_2O on soot has a residence time between a fraction of and a few milliseconds, which could be long enough to enable condensation of water on soot in airplane contrails.

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Physical Chemistry **258**

The Heterogeneous Reactions of $BrONO_2$ and HNO_3 on Low Temperature Surfaces Relevant to the Lower Stratosphere

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$BrONO_2$, an important halogen and NO_x reservoir, and HNO_3, involved in the formation of polar stratospheric clouds, play both a crucial role in the ozone depletion observed during spring time over Antarctica.

The uptake of $BrONO_2$ and HNO_3 on low temperature surfaces has been investigated in a Teflon-coated Knudsen flow reactor in the temperature range 180 to 210 K using mass spectrometric detection.

The Arrhenius representation of the rate of uptake of HNO_3 on ice shows two distinct regimes. The first at low temperatures (180-190 K) shows a constant uptake coefficient ($\gamma \approx 0.3$), whereas the second at $T > 195$ K corresponds to an activation energy of $E_a = -6.8 \pm 1.0$ kcal/mol. At a fixed temperature a rate law first order in $[HNO_3]$ is observed. The interaction of HNO_3 on H_2SO_4/H_2O frozen solutions has been studied in the concentration range 10 to 98 wt %. When the ice was equilibrated with an external flow of H_2O vapor γ remains constant at $[H_2SO_4] \leq 60$ % at 180 and 200 K. At larger $[H_2SO_4]$ γ decreases. The interaction of HNO_3 with $H_2SO_4/HNO_3/H_2O$ results in a constant value of $\gamma = 0.10 \pm 0.03$ in the temperature range 185-195 K when the composition of the interface was held constant using an external flow of H_2O.

The rate of interaction of $BrONO_2$ with ice is fast in the range 180-200 K with $\gamma = 0.30$ and 0.15, respectively and results in the formation of HOBr(g) and HNO_3(c). Uptake kinetics of $BrONO_2$ on H_2SO_4/H_2O frozen solutions in the temperature and concentration range 180-200 K and 10-70 wt % are similar to the one measured for pure ice. The presence of adsorbed HNO_3 on ice has no effect on γ, nevertheless HOBr appears faster than on pure ice. The presence of adsorbed HBr on the ice results in the production of Br_2 suppressing the formation of HOBr. The uptake kinetics of $BrONO_2$ on HBr-doped ice is the same as on pure ice.

Physical Chemistry **260**

Diffusion kinetics of dye molecules into the channels of zeolite L monitored by Förster energy transfer

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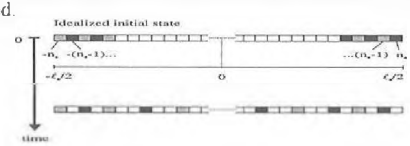
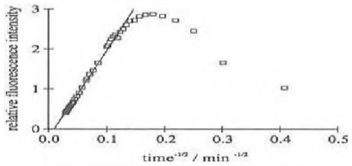
The energy transfer in the channels of zeolite L can be used for measuring the diffusion kinetics [1,2,3]. A situation as illustrated below on the top must be prepared at the beginning of the experiment. Immediately after all dye molecules have entered the zeolite channels maximum energy transfer is observed because the donor to acceptor distance is short. When the molecules diffuse into the channels the donor to acceptor distance increases and hence the energy transfer rate decreases. From this the diffusion kinetics can be derived.



The result of a diffusion kinetics monitored by Förster energy transfer on zeolite L crystals of 1500 nm length is illustrated below.



[1] N. Gfeller, G. Calzaferri, *J. Phys. Chem. B* **101**, 1396-1408 (1997)
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Physical Chemistry **261**

Photoelectrochemical Water Splitting with AgCl as Photoanode?

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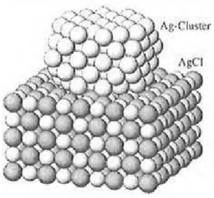
Thin AgCl layers photocatalytically oxidize water to O_2 under appropriate conditions [1]. The photoactivity of AgCl extends from the UV into the visible light region in a process known as self sensitization, which is due to the formation of silver during the photoreaction. This silver can be almost quantitatively reoxidized electrochemically, making it feasible that a thin AgCl layer deposited on a conducting substrate could be used as a photoanode for water splitting if coupled with an appropriate photocathode.

Quantum chemical calculations show that self sensitization is caused by adsorbed silver on the AgCl surface [2]. The silver 5s states decrease the AgCl band gap by about 2 eV. A more complex model where the amount of adsorbed silver atoms is increased is shown in the figure. The properties at the phase boundary between Ag and AgCl, the effects of the silver cluster on the electronic structure of AgCl and the spreading of the interactions within the two materials are objects of our research. The charge distribution and the barrier type in particular will be discussed.



To test its water splitting capability, the AgCl photoanode was combined with other semiconductors suitable as a photocathode. First experimental results will be presented, carried out with an apparatus consisting of two separate compartments connected through a salt bridge. One compartment was used for the AgCl photoanode and the other for the photocathode. Suitable semiconductors for use as a photocathode were selected according to their band edge positions relative to the band edge positions of the photoanode.

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Physical Chemistry **262**

Limitation of the Langmuir-Hinshelwood Model in Kinetic Modelling of the Hydrodenitrogenation of Methylcyclohexylamine over NiMo/Al_2O_3 Catalyst

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The Langmuir-Hinshelwood equation is widely used in the kinetic modelling of heterogeneous catalytic reactions. Various rate equations with different adsorption characteristics have been described in detail by Satterfield [1]. However, if the reaction conditions are not properly selected, the results will be unsatisfactory, even though all the chemical assumptions are met.

In our study of the kinetics of the hydrodenitrogenation of *o*-toluidine, methylcyclohexylamine (MCHA) and the hydrogenation of cyclohexene (CHE), we fitted the experimental data with a Langmuir-Hinshelwood equation and found that the reaction rate constants are always highly accurate. The uncertainty about the adsorption constants, on the other hand, is often considerable with respect to MCHA and *o*-toluidine. A mathematical description has been found that describes the effect of initial partial pressure on the estimation of the parameters.

By carefully choosing the reaction conditions over as large a range of pressure as possible, reliable results can be obtained for the adsorption constants as well.

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Physical Chemistry **263**

EXAFS characterization of Cu/ BEA deNO$_x$ catalyst

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The high and stable catalytic activity of Cu/ZSM-5 zeolite during selective catalytic reduction of NO by C2 and C3 hydrocarbons has aroused interest in catalysis related to deNOx reactions on Cu-exchanged zeolites [1-2].

Different Cu/BEA samples were prepared (Table 1) and treated in oxygen at 400°C and reduced by CO. Their catalytic activity increased in the order S1<S2<S3. XANES spectra provided information on the oxidation state of the Cu, while the structure of the formed species was determined by EXAFS (coordination numbers and inter-atomic distances). Individual types of species present in zeolite BEA after the treatment are summarised in Table 1. It is concluded that isolated Cu(+I) ions are the most active species. It was proven that the type of formed species depends on the zeolite composition.

Table 1 Composition of the sample

	Si/Al	Cu/Al	type of active sites
S1	38	2.2	metal particles + Cu(+I) ions in a minor fraction
S2	17.8	0.69	Cu(+II) as bare ions and (Cu-O-Cu)$^{+II}$ clusters
S3	17.7	0.61	isolated Cu(+I) ions

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Chemical Physics **264**

Photodissociation detection of microwave transitions in highly vibrationally excited molecules. The v_{OH} = 2 and 4 of HOCl.

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We have recently developed a new spectroscopic technique that uses selective photodissociation to detect microwave-induced, pure rotational transitions in highly excited vibrational levels of the ground electronic state. We have applied this technique to the second and fourth excited OH stretching vibration, the (200) and (400) states of HOCl. In addition, we have measured the Stark effect for these excited states, which provides an accurate value of their dipole moment. The (200) $18_{0,18}\rightarrow 17_{1,17}$ transition occurs at 14858.40(1) MHz and the b component of the dipole moment of the (200) state is μ_b=1.515(5) D, while the (400) $16_{1,16}\rightarrow 17_{0,17}$ transition occurs at 27484.33 MHz and the b component of the dipole moment of the (400) state is μ_b=1.560D. This technique is quite general in that the rotational transition can involve levels up to, and exceeding, the dissociation threshold of the ground electronic state.

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Physikalische Chemie **265**

On the Imaging Mechanism of Monatomic Steps in Graphite

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Characterization of mono- and multilayer steps on the atomic scale is of great importance to clarify their reactive nature in terms of their oxidation behaviour at elevated temperature and elucidate their role in metal nucleation processes [1-2]. Studies on the atomic scale can contribute to answering of several longstanding fundamental questions, such as: i) why are multilayer graphite steps oxidized faster than monolayer steps? ii) why are "zig-zag" atoms more reactive than the "arm-chair" atoms? iii) how is a graphite step imaged by STM? iv) is imaging of a graphite step possible without modification? v) does the shape and the atomic arrangement of the imaged step reflect the real structure of the step? The high spatial resolution of STM and the ability to perform measurements under different conditions, without the need of special pretreatment (e.g. decoration), render it a very attractive technique. In this paper we address this phenomena and present an atomically resolved monatomic graphite step. We discuss, for the first time, the origin of the appearance of the imaged features along the step and the shape of the step itself. The interpretation of the STM results are supported with Extended Hückel theoretical calculations. Moreover, we show that due care has to be taken in interpreting STM images of nanotubes deposited on graphite.

[1] F. Atamny and A. Baiker, Appl. Catal. A173 (1998) 201-230.
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Physical Chemistry **267**

VUV (172 nm) actinometry in the gas phase

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The use of xenon excimer lamps is receiving increasing attention in the treatment of waste gases [1,2]. However, the actual methods used to determine in the gas phase the emitted photonic rate of these lamps present some major shortcomings. For instance, oxygen actinometry, as the most frequently cited method, may not be applied in large scale reactors, mainly because of the reactions of ozone with oxygen atoms [3].

This work focuses on the development of a new actinometric method based on the oxidation of ethane. The corresponding reaction sequence implies the reaction between ethane and hydroxyl radicals, the latter being formed upon VUV (172 nm) photolysis of water vapor:

$$H_2O \xrightarrow{172\,nm} HO^{\bullet} + H^{\bullet} \qquad \Phi_{HO^{\bullet}} = 1$$

Kinetics studies of ethane disappearance under different experimental conditions allow to calculate the number of moles of hydroxyl radicals formed per second, being equal to the emitted photonic rate, P_0, of the given light source under appropriate conditions of irradiation. For the light source used in earlier experiments of VUV-induced oxidative degradation in the gas phase [1], a value of P_0 of $4{,}24 \pm 0{,}3 \times 10^{19}$ photons/s was found from which an efficiency of 14,0 ± 1% may be calculated. With respect to photolysis in condensed phase this value is above average and opens a large potential for further developments. The ethane actinometry is a simple and reproducible method, which may be used in the spectral region of 190 to 150 nm.

[1] I. Gassiot, C. Baus, K. Schaber, A.M. Braun, *J. Inf. Recording*, **1998**, 24, 123-132.
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Physikalische Chemie **266**

STM Image Contrast of Monolayer Platinum on Graphite

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Metal particles deposited on carbon supports are used as catalysts in many reactions [1-2]. The microstructure and morphology of supported metal particles play an important role in determining the catalytic activity and selectivity of structure sensitive reactions. Scanning tunneling microscopy (STM) is a local technique with very high spatial resolution enabling studying the local electronic structure on the nanometer scale. Since the modification of the local electronic structure near deposited metal particles are believed to affect the activity and/or selectivity of a catalyst, STM seems to be a very suitable technique to study metal-graphite systems. Knowledge of such local electronic modifications (e.g. the nature of graphite-metal-interaction) is important for understanding the catalytic behavior of metal/graphite catalysts. With this in mind we studied Pt/graphite catalyst addressing the atomic structure of platinum on graphite support. For a better understanding of the Pt-graphite interaction in general and the observed STM images in particular, theoretical calculations were performed. We present results of theoretical calculations of the interaction energies of single Pt atoms at various sites on a graphite surface, and relate the results to the experimental findings. Furthermore, in this report we discuss difficulties associated with the STM image contrast of Pt/graphite systems.

[1] R. Schlögl, in " Handbook of Heterogeneous Catalysis", Eds., Ertl, Knözinger and Weitkamp, Vol.1, (1997) p. 138-191.
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Physical Chemistry **268**

Ultrafast Dynamics of Intermolecular Electron Transfer Reactions in Electron Donating Solvents

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The well known Marcus model of electron transfer (ET) reaction predicts a gaussian relationship between the free energy ΔG^0 and the ET rate constant. The most striking consequence of this model is that at high free energy values, the reaction rate constant decreases as the free energy increases further (Marcus Inverted Region (MIR)).

MIR has been repeatedly observed for charge shift and charge recombination processes, but not for intermolecular photoinduced charge separation reactions. Information on the actual intermolecular ET rate constant is scarce because the overall process is often diffusion limited.

We report here on an investigation of the dynamics of photoinduced charge separation with perylene in electron donating solvents (aniline derivatives). In this case, the diffusional step is eliminated. These ultrafast ET processes were studied with the multiplex transient grating (MTG) technique, which allows the measurement of reaction kinetics by monitoring the disappearance and the formation of reactant and product populations. The free energy dependence of the ET rate constant as well as the effect of steric hindrance will be discussed.

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Physical Chemistry **269**

The spectroscopy and IVR dynamics of HOBr in the ν_{OH}=6 region, probed by infrared-visible double resonance overtone excitation and its comparison with HOCl.

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We use infrared-visible double resonance overtone excitation to prepare HOBr molecules in single, well-characterized rotational levels of high OH stretching states above the dissociation threshold on the ground potential energy surface HOBr → HO + Br. Probing the resulting OH fragments by laser-induced fluorescence (LIF), we are able to monitor the dissociation rates of the initially prepared states. We present here the results obtained in the $6\nu_1$ region of HOBr (about 2000 cm^{-1} above the dissociation threshold) for a large number of rotational (J, K_a) states. The observed dissociation rates are 2 to 4 orders of magnitude lower than predicted by statistical theories, with small state-to-state variations.

Comparison with HOCl $6\nu_1$ (just above the dissociation threshold) shows that the average dissociation rate is similar for the two molecules, while the rates of individual HOCl rotational states exhibit larger, seemingly random, state-to-state variations.

In both cases, the low density of states and weak coupling between the vibrational coordinates give rise to slow intramolecular vibrational energy redistribution (IVR). This, in turn, becomes the limiting step in the dissociation process. Because of the larger excess energy available for HOBr, more product channels are available for dissociation, and individual rates are less likely to show pronounced state-to-state variations.

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Physical Chemistry **270**

Quantum-Sized Silver Sulfide Clusters in Zeolite A

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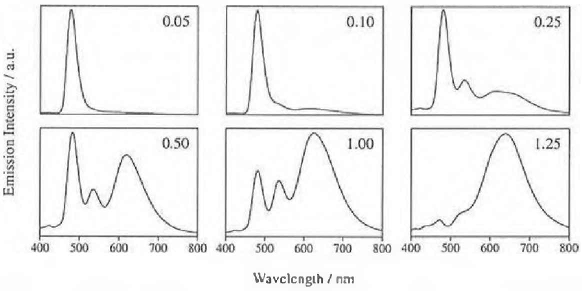
Silver sulfide zeolite A composites can be synthesized by reaction of H_2S with activated Ag^+-loaded sodium or calcium zeolite A (Ag_2S–NaA, Ag_2S–CaA). The optical absorption and emission spectra of samples with different loading densities of silver sulfide suggest the formation of small clusters which are stable under ambient conditions. The composites are colorless (low silver sulfide content) or yellow (high silver sulfide content) and show a wealth of luminescence behaviors. The figure compares the luminescence spectra (measured at 78 K) of six Ag_2S–NaA samples with loading densities ranging from 0.05 to 1.25 silver ions per pseudo unit cell of zeolite A.[1] The excitation spectra indicate that the various luminescence bands can be attributed to silver sulfide species with different dimensions. Samples with low loading densities show a blue-green emission and distinct absorption bands, while samples with high loading densities exhibit a red emission and a continuous absorption reminiscent of a bulk material.



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Physical Chemistry **271**

Influence of fluorination on the sulfidation of alumina-supported tungsten catalysts

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Alumina-supported W catalysts are difficult to sulfide due to the strong interaction between the tungsten phase and alumina [1]. The state of sulfidation is an essential factor in the catalytic performance of hydrotreating catalysts. Catalysts prepared from a sulfidic precursor have a much higher activity than those prepared from an oxidic precursor [2]. Fluorination of the alumina support also increases the hydrodenitrogenation activity of the alumina-supported tungsten catalyst [2]. Temperature-programmed sulfidation and quick extended X-ray adsorption fine structure studies of two series of tungsten catalysts, one made from ammonium metatungstate and the other from ammonium tetrathiotungstate, showed that fluorination of the alumina affects the sulfidation process of tungsten on the alumina-support. The fluorination reduces the number of surface hydroxyl groups and weakens the interaction between the tungsten phase and the alumina. Sulfidation of catalysts prepared from ammonium metatungstate passes through intermediates of W oxysulfides. Fluorination improves the transformation of the W oxysulfides to WS_2 and aids the formation of larger WS_2 particles. With ammonium tetrathiotungstate as the precursor, fully sulfided catalysts can be obtained.

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Physical Chemistry **272**

TRANSIENT EVANESCENT GRATING: A NEW TECHNIQUE FOR INVESTIGATING ULTRAFAST PHOTOINDUCED PROCESSES AT LIQUID-LIQUID INTERFACE

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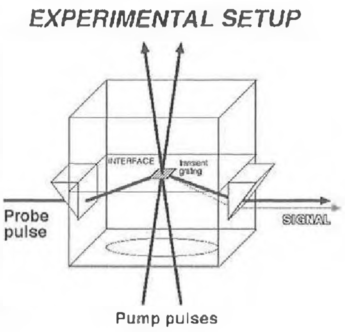
Evanescent waves arise when a beam of light undergoes total internal reflection (TIR) on an interface between two media of different refractive indices. The light coming from the side of higher refractive index is totally reflected if the angle of incidence is greater than the critical angle. In such conditions, a so-called **evanescent wave** is created along the z-direction in the second medium of lowest refractive index. This wave enters perpendicularly to the interface and vanishes exponentially. The penetration depth of this evanescent wave is proportionul to the wavelength and to the angle of incidence of the light.

By crossing two picosecond laser pulses perpendicularly onto the interface of two immiscible liquids, we generate a transient grating (TG) which can now be probed by an evanescent pulsed wave, giving us time-resolved informations about the processes taking place near the interface. This method presents a wide potential of development, like using perpendicularly linear polarised pump pulses to generate a crossed grating (CG), varying the wavelength and the angle of incidence of the probe pulse to change the penetration depth or using a femtosecond pulsed laser to reach an even faster level of kinetics.



Since liquid-liquid interfaces can be considered as simple models of semi-permeable membranes, our new approach might be useful to understand ultrafast phenomena in biological systems.

Chimie physique **273**

EPR studies of the one-electron reduction products of the dimethylsilacalix-[4]-phosphinine Rhodium complex

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Ecole Polytechnique, 91128 Palaiseau Cedex, France

The complex dimethylsilacalix-[4]-1,3-phosphinine-2,4-thiophene Rhodium ($[C_{50}H_{50}P_2S_2Si_4Rh]^+$ $GaCl_4^-$) was shown to undergo a one-electron reduction by electrolysis in situ, in the EPR cavity at 298 K.The liquid solution spectra exhibited hyperfine coupling with two equivalent ^{31}P nuclei and one ^{103}Rh nucleus (nat. Abund.=100%, I=1/2). Spin delocalisation was investigated by simulating the frozen solution spectrum (120 K) : a satisfactory calculated spectrum was obtained by assuming that the unpaired electron is mainly delocalized on the ligands (the spin density on the ^{31}P is only 0.10). The spin density on the metal atom is estimated at ca.7 %.
The reduction of the complex dimethylsilacalix-[4]-phophinine Rhodium was performed both electrochemically and chemically by reaction on a potassium mirror. Liquid solution spectra are characterized by hyperfine couplings with four equivalent ^{31}P nuclei. The identification of the reduction product is discussed .

Physical Chemistry **275**

State-to-state unimolecular reaction dynamics of HOCl near the dissociation threshold: the role of intramolecular energy redistribution probed by time- and eigenstate-resolved spectroscopy

Andrea Callegari, Julia Rebstein, Roman Schmied, Patrice Theulé, [†]Remy Jost, [‡]John S. Muenter and Thomas R. Rizzo

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We use infrared-visible double resonance overtone excitation to prepare HOCl molecules in single, well-characterized rotational levels of the ν_{OH}=6,7,8 vibrational manifolds, above the dissociation threshold on the ground potential energy surface. Combined with time-resolved laser induced fluorescence (LIF) detection of the OH product, this approach allows us to monitor the dependence of unimolecular dissociation rate on the angular momentum (J, K_a, K_c), total energy, and vibrational character of the state of the reactant molecule as well as on the number of dissociation channels available to the OH product. On average, the observed dissociation rates of the parent molecule exhibit an exponential increase with ν_{OH} quantum number but remain much slower than predicted by statistical models. Individual rates exhibit a seemingly random dependence on all other quantum numbers and are scattered on more than three orders of magnitude around the average. Based on our spectroscopic investigation of HOCl and on recent theoretical studies, we propose a simple model Hamiltonian to explain our findings and show that they are all related to the slow intramolecular vibrational energy redistribution of the initially prepared state.

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Physical Chemistry **274**

Imaging the Photodynamics of Atoms and Molecules in Liquid Helium Droplets

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Liquid helium droplets are finite-size quantum systems composed of some 10^3-10^8 atoms and have recently been shown to be superfluid. This poses interesting questions regarding the influence of this remarkable environment on the dynamics of photochemical processes of molecular or atomic species dissolved in or attached to the helium droplets and, vice versa, the influence of these species on the environment.

Details of a new molecular beam machine will be presented which is currently under construction to address some of these questions. The machine will be equipped with a 2-D position sensitive charge detector that can be used in a variety of configurations to gain insight into the dynamics of ionization and photodissociation of molecules in this ultracold environment. When investigating the ionization dynamics the detector can be used either as a photoelectron spectrometer to obtain information on the energy transfer of the electron to the helium cluster or as a streak camera in order to obtain temporal information on the ionization process in liquid helium droplets. When looking at the dissociation dynamics it can be used as an ion-imaging detector to analyze the kinetic energy of the fragments leaving the droplets.

In combination with planned spectroscopic and time resolved pump-probe experiments we expect these investigations to provide detailed information on the photodynamics of molecules in liquid helium droplets.

Physical Chemistry **276**

Conformation of molecules used as chiral modifiers in heterogeneous enantioselective hydrogenation: VCD spectroscopy and ab initio calculations

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Optically active species (chiral molecules) exhibit circular dichroism, i.e. differential absorption of left- and right-circularly polarised light. In the infrared this phenomenon is known as vibrational circular dichroism (VCD) [1]. Due to improvements in instrumentation and theoretical methods in recent years, VCD has become a powerful tool for the investigation of chiral molecules. In combination with quantum chemical calculations the absolute configuration of a chiral compound can unambiguously be determined. VCD spectra furthermore give valuable information about the conformation of a molecule in solution or in the solid state. For intermolecular complexes between a chiral and a non-chiral molecule, VCD activity can also be observed for vibrations associated mainly with the non-chiral molecule. In combination with theory structural information on the interaction complexes can be gained. As such, VCD spectroscopy is a powerful tool for mechanistic investigations of enantioselective reactions.
As an example VCD spectra of several molecules used as modifiers in the heterogeneous enantioselective hydrogenation of α-ketoesters and alkenoic acids over Pt and Pd catalysts were measured and calculated [2].Cinchona alkaloids, the best modifiers found up to now, can be found in several conformations, depending on the solvent. Comparison between calculated and measured VCD spectra allows determining the relative contribution of each conformer, an information, which is difficult to obtain accurately by other methods.

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Physical Chemistry **277**

Artificial Dye-Zeolite L Antenna Systems

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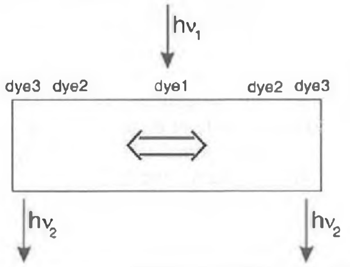
A bi-directional antenna for light collection and transport consisting of three different chromophores was prepared. The main antenna functions known from photosynthetic bacteria or green plants can be realized in such materials, namely light harvesting and fast anisotropic energy transport.[1]
After selective excitation of the organic dye1, the light energy is carried spectrally from blue (dye1) to green (dye2) to red (dye3) and spatially from the crystal center to its top and bottom faces.[2]



The complexity of such host/guest systems affords a careful characterization of the synthesized materials. The role of coadsorbed water, the distribution of molecules between inner and outer surface of the zeolite crystals and the use of Raman spectroscopy and TGA for the characterization of such samples were investigated in detail.[2]

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Physikalische Chemie **278**

Light Harvesting by Pyronine loaded Zeolite L

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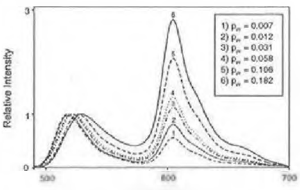
The intercalation of appropriate dyes into zeolites leads to highly anisotropic arrangements in which the dye molecules are present as monomers up to very high concentrations. This knowledge has been used to create an antenna system in which the fluorescent dye pyronine is inserted into the channels of zeolite L. The dye molecules absorb light within the volume of the microcrystals and are able to transport the excitation energy through Förster mechanism. A large spectral overlap between emission and absorption bands, which we found to be temperature independent, allows this energy transport to be very efficient. Thin films of pyronine loaded crystals with oxonine at both ends of the cylindrical nanocrystals on a support were prepared. This system shows extremely fast energy migration along the axis of the crystals. The energy migration was measured as a function of pyronine loading and as a function of the crystal length with constant pyronine loading.



This figure shows the energy migration in pyronine loaded zeolite L microcrystals of about 650 nm length, modified with oxonine at both ends as a function of pyronine loading p_{py}. The oxonine loading p_{ox} is 0.005. this corresponds to one oxonine molecule at both ends of each channel. The relative fluores- cence spectra are shown after specific excitation of pyronine at 470 nm. The maximum of pyronine emission is scaled to the same hight. Its spectral shift from 515 (1) to 530 nm (2) is caused by pyronine-pyronine self-absorption and reemission.

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Physical Chemistry **279**

In situ ATR-IR spectroscopy study of CO adsorption on Pt and Pt/Al_2O_3 thin films at the solid-liquid interface

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Model systems have been designed to study catalytic metal-liquid interfaces using attenuated total reflection (ATR) infrared spectroscopy [1]. Pt and Pt/Al_2O_3 thin films were evaporated on a Ge internal reflection element (IRE) and characterised by XRD, XPS, AFM, STM and IR spectroscopy. Changes within the adsorbate layer of the Pt catalyst surface during cleaning with H_2 and O_2 were followed. After cleaning the catalyst surface was probed by CO adsorption from CH_2Cl_2. The stretching vibration of linearly adsorbed CO showed a coverage dependent frequency shift due to vibrational coupling, thus proving the existence of large clean domains on the reactive catalyst surface even in the presence of an organic solvent. CO adsorption from CH_2Cl_2 was slow before the cleaning process. However, subsequent admission of H_2 resulted in an instantaneous and drastic enhancement of the CO signal. The origin of this enhancement is a structural change of the Pt particles induced by the hydrogen. STM investigations showed sintering of the Pt particles upon hydrogen treatment, resulting in a Surface Enhanced Infrared Absorption (SEIRA) [2]. This hydrogen induced reconstruction of the Pt island film also leads to a change of the effective optical constants of the film, as can be deduced from the dispersive line shape observed after reconstruction and in qualitative agreement with model calculations based on electromagnetic theory. SEIRA together with multiple internal reflection techniques allow adsorbates at coverage far below saturation to be studied at the metal-liquid interface.

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Physical Chemistry **280**

Phase Behavior of Supercritical Fluid Mixtures: Application in Heterogenous Catalysis

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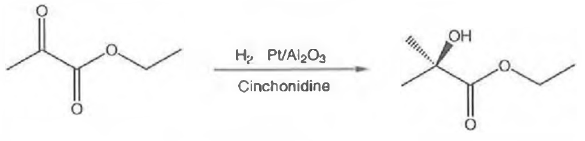
Combination of heterogeneous catalysis and supercritical fluids (as reactant and/or solvent) holds great potential for the optimization of chemical processes [1]. Catalytic reactions will generally involve multi component systems for which the location of the phase border curves in pressure-temperature-composition p,T,x-space may not be known. Knowledge of the phase behavior of the reaction system is a necessary prerequisite to make beneficial use of the supercritical state and for interpreting its effect on the rate and selectivity of a catalytic reaction. Since at this point there is no general equation satisfactorily describing multi component phase diagrams, experimental determination of the phase behavior is indispensable. Therefore we developed a computer controlled high pressure view cell with digital video on-line imaging and recording to examine the phase behavior of such systems by means of optical observation [2].

Here we show the impact of various compositions on the phase behavior and consequently on conversion and selectivity using the example of the platinum-catalyzed enantioselective hydrogenation of ethyl pyruvate.



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Physical Chemistry **281**

Quantum Chemical Investigations of Metal/Semiconductor Contacts

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Although metal/semiconductor contacts were discovered more than 100 years ago, there are still many questions about the behaviour in the region of the boundary layers. The system to be analysed is an Ag/AgCl cluster. Quantum chemical properties of AgCl have recently been investigated [1]. This work tries to answer some questions by means of molecular orbital calculations. i) How large must a system be for inner atoms to be regarded as bulk atoms? ii) Are there localised energy levels in the buffer zone? iii) Do the atoms in the buffer zone show the properties expected for a metal/semiconductor contact? Figure 1 illustrates the cluster we have investigated. The charge distribution was analysed by means of Mulliken population analysis.

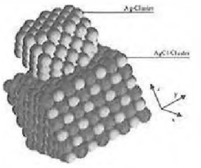

Figure 1: Mixed Ag/AgCl system. The AgCl cluster consists of 384 atoms, the Ag cluster consists of 115 atoms. The shown position of the Ag cluster on the AgCl cluster was calculated as the energy minimum.

To recognise the alteration of electron density several Ag/AgCl cluster distances including the equilibrium distance are calculated. We observe electron transfer from Ag to AgCl in the gap region. An analysis of the electron density along the z-axis shows that directly at the junction a negative charge on the AgCl side and a similar positive charge on the Ag side is observed.

Another concept is the so called metal induced gap states (MIGS). In the gap region a large electron density on the boundary layer was found. These newly formed states are also responsible for the negative charge on the AgCl side of the phase boundary.

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Physical Chemistry **282**

Stereochemistry in the hydrodenitrogenation of o-toluidine and methylcyclohexylamine over sulfided NiMo/γ-Al_2O_3

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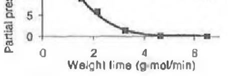
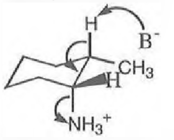
The hydrogenation of the aromatic ring is the rate-determining step in the hydrodenitrogenation (HDN) of many compounds [1,2]. Several studies have focused on the hydrogenation strength of sulfided hydrotreating catalysts in order to understand the hydrogenation mechanism. It was reported that, for o-xylene, cis as well trans hydrogenation is possible [3]. We detected cis-methylcyclohexylamine (cis-MCHA) only during the HDN of o-toluidine (TOL). This suggests a planar adsorption in the hydrogenation of the phenyl ring of TOL. However, if trans-MCHA reacts very fast, before it is detected, then it is still possible that our catalyst produces cis as well trans-MCHA. To study this possibility, we synthesized pure cis- and trans-MCHA. The HDN reactivity of these two diastereomers was completely different: trans-MCHA reacted much slower than cis-MCHA during HDN (see graph). The reason for the difference in the reaction rates of cis and trans-MCHA is that the elimination of NH_3 requires a hydrogen atom in the trans position to the amine group, which is eliminated (see figure).In conclusion, the detection of cis-MCHA only in the HDN of TOL and the slow reaction of trans-MCHA demonstrate that cis hydroge-nation of TOL take place exclusively over sulfidic catalysts.





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Physical Chemistry **283**

Polarity Effects on the Quantum Yield of Singlet Oxygen ($O_2(^1\Delta_g)$) Production by Fluorenone

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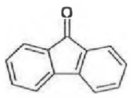
Singlet oxygen ($O_2(^1\Delta_g)$), denoted as $^1O_2$ below), the lowest energy excited singlet state of molecular oxygen, plays a very important role in a large number of chemical reactions of biological, medical, commercial and environmental significance. The quantum yield of $^1O_2$ production (Φ_Δ) is largely dependent on the photophysical properties of the sensitizers and shows a wide range of variation.



Preliminary studies have shown that Φ_Δ of 9*H*-fluoren-9-one (FLU) is influenced by the nature of the solvent [1]. In this work, we have investigated in detail the effect of various media on Φ_Δ of FLU.

Φ_Δ decreases with increasing medium polarity ($E_T(30)$) and proticity as a result of the increase in the rate constant of internal conversion from the singlet excited state, thus diminishing Φ_{ISC} [2]. The influence of ionic and non ionic micellar media and microemulsions on Φ_Δ has also been investigated. We have shown that $^1O_2$ production may be considered as a probe for the localization of FLU in microheterogeneous media.

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Physical Chemistry **284**

HONO Formation by Heterogeneous Interactions of NO_2 and Soot Particles

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Soot particles produced by biomass burning and by combustion engines are expected to be an important source of heterogeneous reaction sites in the atmosphere. The interaction of these sites with NO_2 may result in the formation of gaseous nitrous acid (HONO) which is easily photolyzed to produce OH radicals. Therefore, the NO_2/soot interaction may contribute to start the photochemical reaction cycle in the early morning.

Laboratory soot samples are exposed in a low pressure reactor to a flow of NO_2. By monitoring the gas phase using mass spectrometry we are able to describe the kinetics of both the uptake of NO_2 and its transformation into products such as NO or HONO. It has been revealed that the fuel/oxygen ratio (λ) of the diffusion flame is a key parameter which affects the reactivity of soot towards NO_2 and HONO. A detailed reaction mechanism has been developped showing the differences of the interaction of NO_2 with soot from a lean flame and a rich flame, respectively. Supporting evidence has been acquired by characterizing the different soot types with classical techniques such as SEM, BET and elementary analysis.

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Physical Chemistry **285**

Infrared Spectroscopy of Vibrationally Excited Methanol and Some of its Isotopomers.

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A. Chirokolava, and D. S. Perry
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We have measured spectra of the CH stretch vibrations in jet-cooled CH_3OH from $v_{CH} = 1$ to 5 (~ 3000 to 14000 cm^{-1}). We use Infrared Laser Assisted Photofragment Spectroscopy (IRLAPS) for the detection of the vibrationally excited molecules.

Some of the observed bands have been assigned through model calculations that employ an internal coordinate Hamiltonian and treat the CH stretch–bend Fermi resonance. We have also measured the spectrum of CH_3OD at the energy levels of $v_{CH} = 4$ and 5 to help in the task of assigning the bands of CH_3OH.

The measured spectra show that the CH stretch oscillators approach a local mode behavior with increasing vibrational quantum number.

In our poster, we present the measured spectra and the results of the model calculations.

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Modelling ^{13}C NMR chemical shifts of fullerene derivatives

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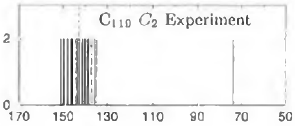
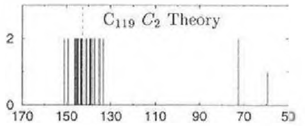
The density-functional tight-binding method (DFTB) [1] is combined with the individual gauge for local orbitals (IGLO) [2] technique to calculate shieldings for large carbon molecules as fullerenes and their derivatives [3]. The model includes one single empirical parameter for a prediction of chemical shifts of those molecules.
On this poster, the IGLO-DFTB method and its application to the 24 isomers of C_{84} [4], to odd-numbered C_{119} fullerenes [5] and C_{70} dimers are presented.





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Physical Chemistry **286**

Protein motions studied by NMR

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Sébastien J. F. Vincent[2], Geoffrey Bodenhausen[1]
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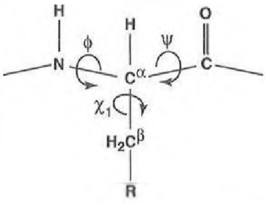
Proteins regulate and perform a wide range of biological processes. Insights into protein function can be gained from structure, as well as from the characterization of local motions. NMR is a method of choice to study protein dynamics in solution.
Local motions modulate chemical shifts, affecting the relaxation properties of the nuclei. Chemical shift of C^{α} and C^{β} carbons in proteins are sensitive to both backbone and side-chain motions. Chemical shift modulation (CSM) may occur in a correlated, i.e. both carbons are affected, or uncorrelated fashion. Correlated CSM is identified from the relaxation rates of $C^{\alpha}C^{\beta}$ multiple quantum coherences.



We present a new NMR experiment to measure the decay rates of multiple quantum coherences. Correlated CSM was identified in regions undergoing conformational exchange, but not in regions presenting unrestrained conformational sampling. This experiment allows one to identify flexible regions, which are often crucial for protein function.

Computational Chemistry **288**

Atomic Properties and Intermolecular Potential using Density Matrix Renormalization Group (DMRG).

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The calculation of intermolecular potential of dimers such as He_2 or Ne_2 is one of the most common benchmark for sophisticated and accurate *ab-initio post*-Hartree Fock techniques [1]. The small energy difference involved and the essential role of electron correlation energy in the determination of the binding energy of such systems, as well as the intrinsic need to use extended basis sets, are a difficult problem to satisfactory treat. In addition 'simple' properties of atoms, such as electron affinities, are, for the same reasons, one of the hardest properties to reproduce at a *post*-HF and DFT level [2].
For these reasons we have decide to compute the intermolecular potential energy surface for He_2 and the electron affinities of selected atoms using Density Matrix Renormalization Group (DMRG) [3].
This method is based on an iterative numerical procedure to diagonalize the Hamiltonian of a full CI expansion in a finite basis set. Therefore we can afford to treat larger systems and we can find the exact solution of the non-empirical molecular Hamiltonian:

$$H = \sum_{i,j,\sigma} h_{ij}^{core} c_{i\sigma}^{\dagger} c_{j\sigma} + \sum_{i,j,k,l,\sigma,\sigma'} \langle ij|kl \rangle c_{i\sigma}^{\dagger} c_{j\sigma} c_{k\sigma'}^{\dagger} c_{l\sigma'}$$

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Computational Chemistry **289**

DFT study of $Ni(tmhd)_2$ complexes

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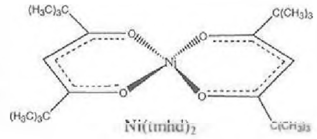
In this work we report the results of DFT calculations on isolated bis(2,2,6,6-tetramethylheptane-3,5-dionato)Nickel(II) ($Ni(tmhd)_2$) and its reaction products with one and two pyridine ligands. Geometry optimisations, frequencies, zero point energies and spectral transitions have been evaluated from *ab initio* principles using the Amsterdam Density Functional (ADF) program package.



The most stable conformation of $Ni(tmhd)_2$ has D_{2h} symmetry (square planar, low spin) and not D_{2d} (tetrahedral). This is in agreement with the X-ray structure [1].

In a first attempt to find the optimised structure of $Ni(tmhd)_2py$, the t-buthyl substituents have been replaced by hydrogens. This has no large influence on the electronic structure of the complex. Then, the t-buthyl groups are reintroduced to estimate the steric effects.

The geometry optimisation of $Ni(tmhd)_2py_2$ was started from the structure of the complex in the crystal [2].

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Computational Chemistry **290**

Theoretical studies of weak intermolecular complexes involving carbazole. Applications of a DFT method based on electron density partitioning.

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The structure and the binding energy of the complexes formed by small molecules (Ne, Ar, CH_4, CO, and N_2) and carbazole have been calculated using a DFT formalism based on partitioning the electron density [1,2]. Such complexes are weakly bound (the disscociation energy falls within the 0.5-1.9 kcal/mol range [3]) and they are known to be difficult to be described by means of conventional DFT methods.

In this study, the partition of the electron density corresponds to two subsystems: a) a small molecule bound to carbazole b) the carbazole molecule.

The calculated binding energies are in an excellent agreement with the experimental data (the differences do not exceeed 15%) showing that the developped formalism based on partitioning of the electron density provides a new opportunity for density functional theory to enter the domain of weak interactions.

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Chimie computationnelle **291**

Theoretical study of the physisorption of water on the MgO(100) surface

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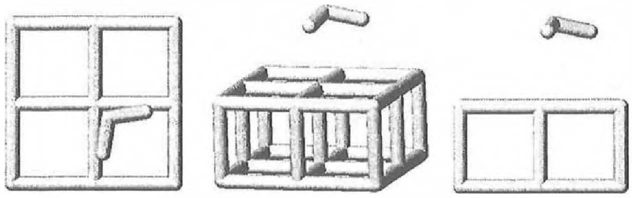
The geometry, the interaction energy, and IR frequencies of the water molecule adsorbed on a cluster representing the MgO(100) surface were investigated using two theoretical methods: (a) supermolecule Kohn-Sham calculations and (b) the recently developed formalism of Kohn-Sham equation with constrained electron density [1].

The IR frequencies are very sensitive to the orientation of the adsorbed water molecule and can be used to determine the adsorption mode. Compared to the free molecule, the frequencies of the two streching vibration modes for both H_2O and D_2O are red-shifted, confirming that the sharp IR peaks observed at 3513 cm^{-1} and 3626 cm^{-1} for H_2O (2597 cm^{-1} and 2676 cm^{-1} for D_2O) [2] can be attributed to the symmetric and asymmetric streching modes of the single water molecule physisorbed on terraces of MgO(100).



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Chimie computationnelle **292**

CAN OCTAHEDRAL t_{2g}^{6} COMPLEXES SUBSTITUTE ASSOCIATIVELY ? THE CASE OF THE ISOELECTRONIC RUTHENIUM(II) AND RHODIUM(III) HEXAAQUAIONS

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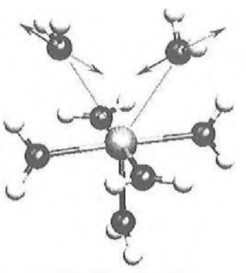
It has been suggested recently in the case of $Ru(OH_2)_6^{2+}$ that the near-zero $\Delta V^{\ddagger}$ value could be due to a bond contraction of the five spectator ligands in an I_d process to reach the transition state, and D. Richens has suggested that in the case of $Rh(OH_2)_6^{3+}$ ($\Delta V^{\ddagger} = -4.2$ cm^3 mol^{-1}) [1] the higher positive charge could promote further volume contraction sufficient in this case to change the sign of $\Delta V^{\ddagger}$ to a negative value for a dissociatively activated process [2]. If true, this would be an example of limitation in the use of the overall activation volume $\Delta V^{\ddagger}$ for a diagnosis of the mechanism.



Transition state (C_2)
$\{[Rh(OH_2)_5\cdots(OH_2)_2]^{3+}\}^{\ddagger}$
for H_2O exchange on $[Rh(OH_2)_6]^{3+}$

Quantum chemical calculations at the Hartree-Fock level including hydration effects have been performed for the water exchange on both aquaions. The resulting energies and bond lengths variations along the reactions pathways confirm the mechanisms assigned from available experimental data : I_d or D pathway for $Ru(OH_2)_6^{2+}$, and I_a pathway (small a character) with retention of configuration for the isoelectronic $Rh(OH_2)_6^{3+}$.

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CHIMIA 2000, 54, No. 7/8

Computational Chemistry **293**

Theoretical Investigations on the Reaction of Peroxynitrous Acid and Nitrite

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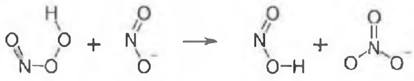
Peroxynitrous acid ONOOH is an important biological oxidant which isomerizes via an unknown mechanism to nitric acid with a lifetime of about 3s at 25 °C and neutral pH. Several hypothetical pathways have been suggested, such as homolysis of the peroxy bond to NO- and OOH-radicals and subsequent recombination to nitric acid [1, 2].

Recently, new experimental observations have raised the possibility of a completely new mechanism via the reaction with nitrite NO_2^-. We have performed DFT calculations in the gas phase and in aqueous solution in order to find a possible reaction pathway and determine activation energies.

Our gas phase calculations suggest a barrierless reaction, exothermic by about 40 kcal/mol, via a transfer of the hydroxy group of ONOOH to the nitrite N, yielding nitrate and nitrous acid as products. Ab initio MD simulations give an estimate for the barrier in aqeuos solution of about 3 kcal/mol. Our studies thus suggest that the reaction of ONOOH with NO_2^- may play an important role in the isomerization of peroxynitrous acid to nitric acid, an alternative that has not been considered so far.



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Computational Chemistry **294**

A density functional study of molecules possessing nonlinear optical properties

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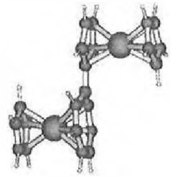
The most important class of nonlinear optical (NLO) compounds are molecules possessing both electron donating and accepting groups which are electronically coupled. In this work, a computational chemistry approach is used to model some nonlinear optical parameters. Using time-dependent DFT as implemented in the Amsterdam Density Functional[1] (ADF) program package, we obtained good parameters for molecules of the family of the para-nitroaniline.

Organometallic donating and accepting groups exhibit interesting features which allow a tuning or even switching of the NLO properties[2]. In a second part, we thus extended our work to the computation of dipolar bimetallic sandwich-like complexes composed of sesquifulvalenes and metal-ligand fragments ML and M'L (M, M'=Fe, Ru; L=C_5H_5, C_5Me_5).



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Computational Chemistry **295**

Comparative Study of Photophysical and photochemical Properties of the $[Fe(CN)_5NO]^{2-}$ and CpNiNO complexes. A Density Functional Theory Investigation.

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The photophysical properties of the nitroprusside complex ($[Fe(CN)_5NO]^{2-}$) have been extensively studied[1]. It has been shown that the process of excitation leads to two long-living metastable states (MS), the first one exhibiting a distorted structure, namely a bended NiNO group of atoms. The second one corresponds to $[Fe(CN)_5ON]^{2-}$, with an inverted NO group of atoms. Contrary to the nitroprusside complex, experiments show that the cyclopentadienylnitrosylnickel complex (CpNiNO) only exhibits one MS, with a bended NiNO group of atoms[2].

We present a comparative DFT investigation of the potential energy surfaces (PES) of both $[Fe(CN)_5NO]^{2-}$ and CpNiNO ground-state complexes. Excited states of these complexes have been calculated using both Slater's Transition State Method and Time-Dependent Density Functional Theory. An interpretation of the absence of experimental evidence of a CpNiON structure is presented.

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Computational Chemistry **296**

The Mechanism of Enantioselective Palladium Catalyzed Hydrosilylation of Olefins with Trichlorosilane: A Theoretical Study.

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Hydrosilylation with trichlorosilane offers a powerful tool for the "one pot" conversion of olefins into alcohols, via oxidation of the alkyltrichlorosilane intermediate by the method developed by Tamao. In this regard hydrosilylation has been widely investigated and efforts have been made to clarify the reaction mechanism(1). The bis(trichlorosilyl) {1-{(R)-1-[(S)-2-(diphenylphosphino-κP)ferrocenyl]ethyl}-3-(2,4,6-trimethylphenyl)-1H-pyrazole-κN}palladium catalyst exhibits in fact an high enantioselectivity with a variety of substrates. Among them styrene shows particularly interesting properties: (a) the regioselectivity on the α-carbon is up to 99%; (b) the enantioselectivity is up to 70%, but there is a reversal due to a remote substituent in the substrate.

In order to examine the reaction pathways we performed DFT and combined quantum mechanics and molecular mechanics (QM/MM) calculations. Our calculations show that the rate determining step of the catalytic cycle is the coordination of the styrene to the central metal.

Our calculations of the Chalk-Harrod mechanism(1) suggest that the insertion of the styrene into the Pd-H bond (Ea=3.6 kcal/mol) is the most likely event. This step is accompanied by η^3-coordination mode of the benzylic intermediate. The formation of the allylic structure stabilizes the insertion product of ~10 kcal/mol and explains also the reason for the observed regioselectivity. Moreover, the formation of the final product proceeds through migration of the silane on the α-carbon and the elimination of alkyltrichlorosilane.

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Computational chemistry **297**

Modelling of the Cation-Olefin Cyclizations by Density Functional and by *Ab Initio* Methods

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The reaction pathways of the highly reactive species carbocations are difficult to control. This is especially true for the olefin-cation cyclizations where the proper alignment of the olefin and cationic center is required. Of particular interest are the reactions involving the olefin-cation cyclizations of 1,2-dimethyl hexene-6-yl cation, which is a suitable model system for cation-olefin cyclization where the protonated cyclopropane was proposed as the key intermediate. This type of cyclization is also proposed in biosynthesis of several natural products.

The electronic structures, energies, and equilibrium geometries of cationic intermediates involved in the cation-olefin cyclizations of 1,2-dimethyl hexene-6-yl cation were studied by means of the *ab initio* calculations at the Moller-Plesset second order perturbation level (MP2) and by density functional theory (DFT) methods. The hybrid functional B3LYP and MP2 methods have been used together with 6-31G* and 6-311G** basis sets. The cyclization step was investigated by means of minimum energy reaction paths. The transition states were located and characterized by vibrational analysis and subsequently the intrinsic reaction paths were computed. Moreover, the pathways by which carbocations are formed and by which they rearrange on the $C_8H_{15}^+$ potential energy surface were explored by DFT methods. The role of alkyl substituents in the stabilization of carbocation intermediates during the cationic cyclization was also evaluated. In addition, we discuss the prominent role of the CC- and CH-hyperconjugative interactions in determining the carbocation conformations during the cyclization step, where the appropriate spatial preorganization of the cationic center with respect to the double bond is necessary.

Computational Chemistry **299**

Application of the ONIOM methods to organometallic compounds

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The ONIOM methods [1-3] have proven to be powerful tools for the treatment of large molecular systems.

The purpose of our study is the investigation of structural and energetical properties of the $(\eta^5\text{-}C_9H_7)Rh\text{-}(P(CH_3)_3)$, $(\eta^5\text{-}C_9H_7)Ru\text{-}(P(CH_2C_6H_5)_3I)$ and $[(\eta^5\text{-}C_9H_7)Ru\text{-}(BIPHOP\text{-}F)]^+$ systems where "BIPHOP" stands for trans-1,2-bis[bis(pentafluorophenyl)phosphinoxy]1,2-diphenylethane.

The calculations have been performed with ONIOM approach, as implemented in the GAUSSIAN 98 program, using two layers. The model system (*i.e.* inner layer + link atoms) has been calculated using DFT at both LDA and/or GGA levels whereas the universal force field (UFF) with the charge equilibration approach has been chosen to treat the outer layer.

The results show that the structural parameters are in good agreement with experimental data. Furthermore, for the rotation of the $\eta^5\text{-}C_9H_7$ ligand, we predict a rotational barrier which deviates by less than 1.0 kcal/mol from experiments [4] (11.45±0.28 kcal/mol).

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Computational Chemistry **298**

Density Functional Modelization of a Mixed Valence Trinuclear Copper Cluster $Cu_3O_2(NH_3)_6|^{3+}$

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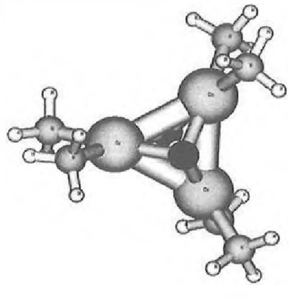

The Magnetic Properties of $Cu_3O_2(L_3)_6|^{3+}$ (L=N-Permethylated (1R,2R)-cyclohexanediamine) have already been experimentally investigated by the ultraviolet absortion spectrum and susceptibility measurements [1] showing that it is a localised system containing 2Cu(II)-Cu(III,l.s.) with ground spin state S=1.

Molecular Properties, of this MV trinuclear copper cluster have been calculated using Density Functional Theory (DFT) with ADF [2] on a model $Cu_3O_2(NH_3)_6|^{3+}$.

The characterisation of the electronic structure of Mixed-Valence (MV) compounds requires the calculation of Spin Hamiltonian parameters which are the Exchange Coupling Constant (J), the Double Exchange interactions (B) and the determination of the frequencies associated to the normal coordinate, responsable for delocalisation/localisation.

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Computational Chemistry **300**

Molecular and Electronic Properties of Polytriacetylene Oligomers

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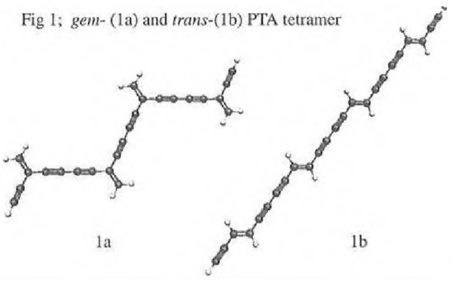
Polytriacetylenes (PTA) are a new class of linearly conjugated polymers with a nonaromatic all carbon backbone. Their molecular properties can be modulated through functionalization with donor and/or acceptors sobstituents. This makes these compounds attractive for a number of applications (photo-electronic devices, NLO, etc.). In this work, we investigate the molecular and electronic properties of (unfunctionalized) *trans*- and *gem*-PTAs (Fig. 1) using different quantum chemical methods.

Fig 1; *gem*- (1a) and *trans*-(1b) PTA tetramer



Based on the structure optimizations of small *trans*- and *gem*-PTA oligomers we were able to derive an extrapolation for the bond length alternation (BLA) to the polymeric limit. These results were compared to those obtained for Polyacetylene and Polydiacetylene.

We also examined the $X^1A_g \rightarrow 1^1B_u$ transition using the ZINDO/S model Hamiltonian and Time Dependent Density Functional Theory (TD-DFT). quantitative relationship between the BLA and the calculated excitation ene gies has been established for *trans*-PTA. We have also developed model culations that are useful in examining the effect of delocalization o conjugation pathway.

Computational Chemistry **301**

The structure of Cu^{2+} binding sites in the C-terminal domain of the murine prion protein
A mixed ab initio - classical molecular dynamics study

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The prion protein, in a modified form, triggers neurodegenerative diseases, such as the mad cow disease (BSE), and is supposed to play a role in a special form of the Creutzfeldt-Jakob disease[1]. The unaltered form, also present in humans, has an unknown biological function. However, the evidence is growing that the prion protein might play a role in the copper metabolism, and EPR experiments suggest that copper binds in the ordered C-terminal domain[2].

The availability of a protein NMR structure[3] allows for detailed atomistic modelling of possible copper binding sites. Our mixed ab initio-classical model uses DFT to describe the binding site, a force field to treat the rest of the protein and solvent, and a consistent way to couple the two systems[4]. We present binding structures that are in agreement with the experimental data, and discuss how a QMMM model was constructed to describe them.

Fig. 1 : protein structure[3]

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Computational Chemistry **302**

IMPORTANCE OF INTERFACIAL PHENOMENA IN LIQUID-LIQUID EXTRACTION: MOLECULAR DYNAMICS INVESTIGATIONS

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Based on MD simulations, we describe the behaviour of ionophores free or complexed, and of salts of hydrophilic, hydrophobic and amphiphilic ions at a water-"oil" interface. The ionophores, although more soluble in the organic phase than in water, are found to display a strong affinity for the interface, as do hydrophobic ions like $AsPh_4^+$, BPh_4^-, dicarbollides, Guanidinium$^+$, Picrate$^-$. The formation of the interface in phase separation processes, the effect of ion and ligand concentration, and the implications concerning the mechanism of ion extraction and recognition are discussed .

Computational Chemistry **303**

Theoretical studies of CO in ZSM5 zeolite. Applications of a DFT method based on electron density partitioning.

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Carbon monoxide belongs to one of the most frequently used probe molecules in IR spectroscopy studies of alkali-ion zeolites. Previous theoretical investigations showed that the complex formed by the cation and CO provides a reasonable model of the CO adsorbed in alkali-ion zeolites. However, the calculated frequency shifts are about two times to large compared to experimental measurements [1].
In this study, the stretching frequency of the CO molecule adsorbed at the alkaline cations (Li^+, Na^+, or K^+) in the ZSM5 zeolite is calculated using a DFT formalism based on partitioning the electron density [1]. The partition of the electron density corresponds to two subsystems: a) one comprising the CO molecule and the alkaline cation and b) another one being the cluster representing the zeolite.
The calculated shifts of the CO stretching frequency are in a very good agreement with experimetal data. The origin of the experimentaly observed blue-shift of the CO stretching frequency is analyzed in detail.

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Computational chemistry **304**

Computational Study of Solvolysis Reactions of Strained Bridgehead Substrates

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The reactivity of bridgehead halides exemplified by bicyclo[n.1.1] heptyl substrates has been posing an intriguing problem to organic chemists. Indeed, these halides solvolyze much more rapidly than would be expected on the basis of the strain accumulated in the corresponding cations. In particular, 1-bicyclo[3.1.1]heptyl derivatives show extraordinary reactivity even under mild solvolytic conditions, leading to a mixture of both rearranged and *un-rearranged* products. These substrates are at least 8 times more reactive than *tert*-butyl bromide, despite the fact that they have been believed to react *via* the intermediacy of highly strained 1-bicyclo[3.1.1]heptyl cation. In order to clarify this problem, we investigated computationally the reaction path for the model solvolysis reaction in which the carbocation intermediate is generated from the protonated alcohol by the departure of the water molecule chosen as the model of the leaving group.

Density functional theory (DFT) and MP2 methods, employing a 6-31G* basis sets, were used to investigate the potential energy surfaces for the heterolytic C-O bond cleavage of protonated 1-bicyclo[3.1.1]heptanol. The DFT methods such as B3LYP and B3P86 were used as they incorporate the correlation energy that is necessary, since cationic species with unusual bonding are involved in this reaction. The computations indicate, indeed, that the initial reaction intermediate of the studied processes is the water complex of unsymmetrical bicyclobutonium cation for which the integrity of bicyclo[3.1.1]heptyl structure is still preserved. The stationary points on the potential energy surface were fully characterized with vibrational analysis to confirm the existence of true energy minima and transition states, respectively. The intrinsic reaction paths were also computed from the solvolysis transition states towards the products and reactants. The results for several water complexes of other $C_7H_{11}^+$ cationic species, which potentially can be formed by the cation rearrangement of the primary intermediate, are also discussed.

Computational chemistry

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Electron Self-Exchange of the Hexaaqua Cobalt(II)/(III) Couple

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The directly measured [1] free energy of activation ($\Delta G^{\ddagger}$ = 70 kJ/mol) for the electron self-exchange reaction of the $Co(OH_2)_6^{2+/3+}$ couple (equation 1) is considerably lower than that ($\Delta G^{\ddagger}$ = 130 kJ/mol) obtained on the basis of cross reactions (equation 2), [2] whereby $M^{II}L$ represents a reductant with a known self-exchange rate and redox potential.

$$Co(OH_2)_6^{3+} + Co(OH_2)_6^{2+} \rightarrow Co(OH_2)_6^{2+} + Co(OH_2)_6^{3+} \quad (1)$$
$$M^{II}L + Co(OH_2)_6^{3+} \rightarrow M^{III}L + Co(OH_2)_6^{2+} \quad (2)$$

The origin of the disparate activation energies for reactions 1 and 2 is not established. Pathways involving thermally excited electronic states of either $Co(OH_2)_6^{3+}$ or $Co(OH_2)_6^{2+}$ were considered and judged unfavorable for reaction 1. Therefore, a water-bridged inner-sphere pathway was suggested as a possible mechanism. [2] Also the possibility, that strong electronic coupling in the transition state lowers its energy was discussed but, in the absence of pertinent data, its relevance could not be assessed. [3]

This study reports on quantum chemical calculations of internal reorganizational energies for the electron self-exchange of the $Co(OH_2)_6^{2+/3+}$ couple. They were performed for reaction 1 proceeding via various electronic states of $Co(OH_2)_6^{3+}$ and $Co(OH_2)_6^{2+}$.

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306

Calculating ^{29}Si NMR chemical shifts - from Silanes to Zeolites

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Calculating NMR chemical shifts can be a powerful tool for predicting structures if accuracies of a few ppm can be achieved. Recently, a tight-binding scheme was combined with the individual gauge for local orbitals (IGLO) technique [1] to calculate ^{13}C NMR chemical shifts of fullerenes [2] and their derivatives [3] (see also poster presentation).
This scheme is expanded to determine ^{29}Si NMR shieldings and therefore applicable to a much wider range of molecules, clusters and solids. It allows to compare some hundreds of isomers and, in combination with the molecular dynamics technique, the study of the dynamical behaviour of the shielding during diffusion processes.
Test molecules include several silane derivatives (e.g. methyl-, aryl, acrylaryl-, methoxy-) which are compared with experimental data and higher-level theory. First applications to zeolites are presented.

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Computational Chemistry

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Chiral discrimination in hydrogen-bonded complexes

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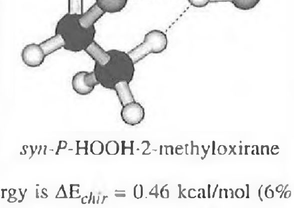
We report an accurate *ab initio* study of the effects of chirality on the intermolecular interactions between two chiral molecules bound by a single hydrogen bond [1]. The methods used are second-order Møller-Plesset theory using canonical (MP2) or localized orbitals (LMP2), as well as density functional theory with a B3LYP functional. The differential interaction energy between two homochiral molecules, e.g. R···R' and the analogous heterochiral molecules R···S' measures the degree of chiral discrimination, termed the chirodiastaltic energy, ΔE_{chir}. The O-H···O hydrogen bond between the chiral hydrogen H-donor HOOH and the chiral acceptor 2-methyloxirane leads to four diastereomeric complexes. There are two qualitative contributions to the chirodiastaltic energies, the diastereofacial contribution which controls the face or side of the acceptor to which the H-bond is formed, and the diastereomeric contribution, which is the energy difference between two complexes formed to the same face. The largest chirodiastaltic energy is ΔE_{chir} = 0.46 kcal/mol (6% of the interaction energy) between the *syn-M-* and *syn-P*-HOOH·2-methyl oxirane complexes. The chiral 2,3-dimethyloxirane acceptor is C_2 symmetric and hence offers two identical faces. Here the chirodiastaltic energy is identical to the diastereomeric energy, and is calculated to be ΔE_{chir} = 0.36 kcal/mol or 4.5% of the interaction energy.



syn-P-HOOH·2-methyloxirane

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Computational Chemistry

308

Development and Applications of Molecular Hydrogen Bonding Potentials (MHBPs)

Sébastien Rey, Mehrva Rabii, Giulia Caron, Giuseppe Ermondi, Patrick Gaillard, Alessandra Pagliara, Pierre-Alain Carrupt and Bernard Testa

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Université de Lausanne, CH-1015 Lausanne

Empirical potentials describing the spatial variation of H-bond properties of solutes was developed using solvatochromic parameters proposed by M. Abraham. A fragmental system Systahl 1.0 was iteratively developed to encode H-bond properties of polyatomic fragments. The donor fragmental values (f_α) are associated to each hydrogen atom in a polar moiety (e.g.,-OH, –NH) and the acceptor fragmental values (f_β) are associated to the pair(s) of free electrons in polar atoms (e.g., –O–, –N=). The total H-bond donor or acceptor capacity of a given compound is obtained by summing of all fragmental constants f_α or f_β.

The H-bond potentials are calculated according the following equation:

$$MHBP_k = \sum_{i=1}^{N} f_i \bullet f(d_{ik}) \bullet f(U)$$

where k is the label of a point in space, i the atom number, N the total number of molecular fragments, f_i the value of α or β of atom i, d_{ik} the distance between the fragment i and the point k, $f(d_{ik})$ the distance function describing how the strength of a H-bond varies with distance and $f(U)$ the angular function since hydrogen-bonds are directional. The effect of intramolecular hydrogen-bonds were carefully examined.

MHBPs are calculated on a suitable molecular surface generating 2
and 3D QSAR parameters useful for the prediction of permeation prope
of drugs. Human oral absorption of a set of therapeutic compounds ha
used to examine the applicability of the MHBPs parameters in quar
structure-activity relationships.

Computational Chemistry **309**

Towards a Consistent Electrostatic Coupling Scheme for Mixed Quantum-Classical Calculations

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A consistent computational scheme for mixed quantum mechanics (QM)-molecular mechanics (MM) calculations on very large molecules in which only a portion of the system undergoes important electronic changes has been developed [1]. The code is based on the merging of CPMD [2] (that calculates the forces and the electronic structure of the quantum subsystem) and GROMOS [3] (that calculates the forces of the classical subsystem).

Within our scheme, the electrostatic coupling between the quantum subsystem and all the rest of the molecule is rigorously kept into account. Moreover, the electrostatic interactions across the MM/QM interface are modified consistently with the definition of the classical force field by a suitable many body-two body mapping.

Satisfying results have been obtained with our scheme for many test systems.

Dotted lines: electrostatic interactions between QM and MM atoms (full and empty circles respectively) that have to be excluded from the Hamiltonian.

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Computational Chemistry **310**

Molecular Modelling: Indispensable Tool at the Interface between Structural Analysis and Molecular Design

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In view of the increasingly growing structural information available in protein as well as small molecule databases (Protein database [1] over 12'000 structures; Cambridge Crystallographic Database [2] over 200'000 entries), the visualization, understanding and treatment of these data by molecular modelling and structure analysis tools become ever more important. The potential of this information for the design of novel compounds is enormous, and by a number of selected structural paradigms, I will illustrate that the laws which govern 3-dimensional conformation are universal - no matter whether we are dealing with macromolecular or low molecular weight compounds. Comparisons of structures in their X-ray crystal or NMR derived solution conformation can be easily carried out with various superposition routines in a molecular modelling suite made recently available for the academic as well as industrial scientific community [3]. Pharmacophore modelling is enhanced by inclusion of a fast 3-d model builder, and conformational trajectories can be generated and analysed with the ultimate goal to develop intrinsic molecular properties into enzyme inhibitors for therapeutic evaluation. De novo designed constitutions are amenable to examination by force fields calibrated against a large number of experimental structures. Important physical paramenters such as the molecular dipole moment can be calculated and are congruent with experimental data. Starting from deductive (analytical) molecular modelling to optimally reflect experimental observation, inductive (synthetical) molecular modelling will be described in fields appearently divergent as much as the chemical etiology of nucleic acids from the development of constitutions potentially useful as new materials.

[1] Protein Database (30 May 2000): http://www.rcsb.org/ pdb
[2] Cambridge Crystallographic Data Centre: http://www.ccdc.cam.ac.uk/ resp. its Zürich mirror: http://sixray.ethz.ch/ csdeth.html
[3] P. R. Gerber: MOLOC - A Molecular Design Software Suite: http://www.moloc.ch

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CONFERENCE REPORTS

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35th ESF/EUCHEM Conference on Stereochemistry
Bürgenstock, April 29–May 5, 2000

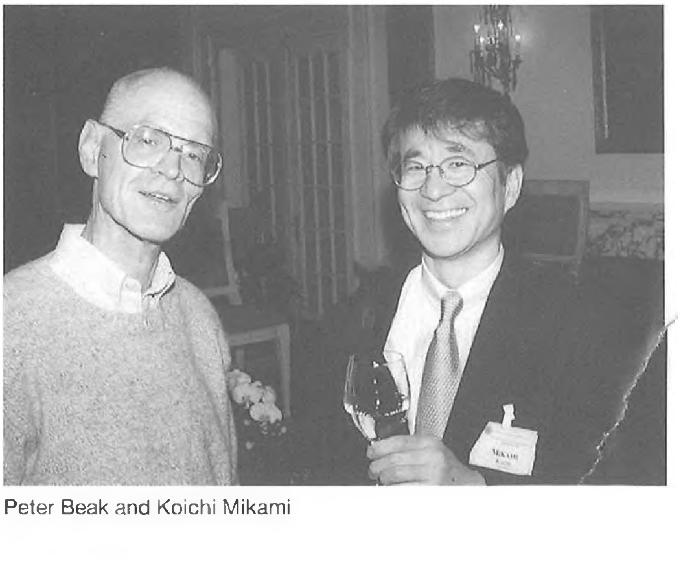
Christian G. Bochet*

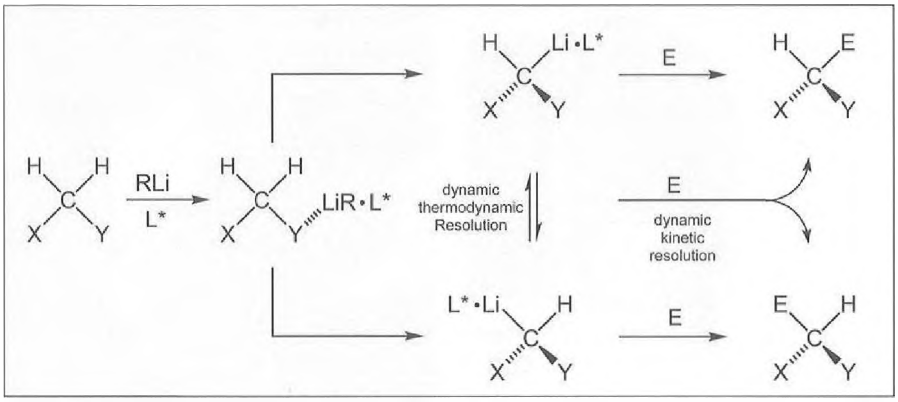
Keywords: Bürgenstock • EUCHEM • Organic chemistry • Stereochemistry

Following tradition, the 35th ESF/EUCHEM conference on stereochemistry took place at the spectacular venue of the Bürgenstock hotel complex, during the first week of May. Although only the organizers knew the conference details, it was clear for everyone that the president ***Jean F. Normant*** (Université Pierre et Marie Curie, Paris, France) would have concocted a delightfully well-balanced program, ranging from polymer science to structural biology, but always with organic synthesis as the centerpiece. ***Henri B. Kagan*** (Université Paris Sud, France) was this year's 'Guest of Honor', and this excellent choice was vigorously applauded by all the participants during the opening dinner on Saturday evening. Also enthusiastically greeted by the audience was the appointment of *Andrea Vasella* (ETH Zürich, Switzerland) as the conference vice-president. As next year's president, he and the organizing committee, composed of *Hans-Beat Bürgi, François Diederich, E. Peter Kündig and Klaus Müller* will organize the 2001 conference.

Javier de Mendoza, introducing ***Peter Beak*** (University of Illinois at Urbana-Champaign, US, 'Regioselective and stereoselective lithiation-substitution reactions: mechanistic pathways and synthetic consequences') opened the first session, which was devoted to organic synthesis. Beak gave a detailed insight into regio-, diastereo- and enantioselective bond formation processes by lithiation-alkylation (Scheme 1). He focused on the powerful combination of butyllithium and (–)-sparteine, which allows the formation of chiral lithium carbanions by deprotonation of *N*-Boc amines. The intrinsic limitation to one enantiomer (indeed, (+)-sparteine is not readily available) was overcome by a clean inversion step using trimethyltin chloride. *N*-Boc-amine-stabilized carbanions were also found to be effective in Michael additions to enones and nitroalkenes, leading to the creation of two chiral centers. Elaboration of the intermediates led to the


Andrea Vasella, Henri B. Kagan and Jean F. Normant (president)


Peter Beak and Koichi Mikami



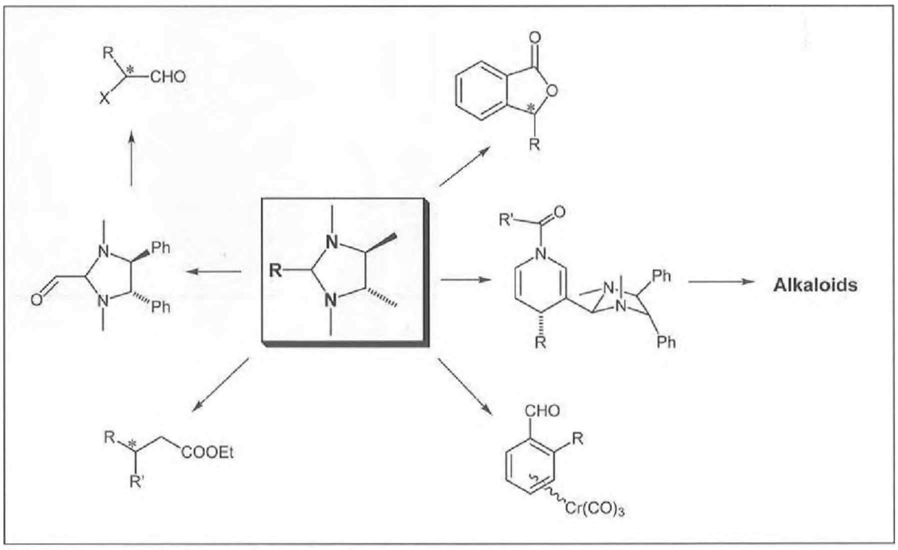
Scheme 1. Pathways for enantioselective lithiation / substitution

synthesis of a series of piperidine and indolizidine alkaloids (*e.g.* coniine, solenopsine, or dihydropinidine) [1].

In the following lecture, ***Alexandre Alexakis*** (Université de Genève, Switzerland, 'New developments in chiral diamine chemistry') showed how his original work with chiral acetals led to the use of chiral *aminals* in asymmetric synthesis. These compounds result from the replacement of the oxygen atoms of acetals with nitrogen atoms. Indeed, optically pure diamines (*e.g.* 1,2-diphenylethylene-diamine), prepared in a very practical fashion, usually react spontaneously with aldehydes to give chiral aminals. When the aldehyde is chiral, a pair of diastereoisomers is then formed, and they can be quantified by NMR (determination of enantiomeric excess (ee)) or chromatographically separated (resolution). Mild acidic hydrolysis liberates the original aldehyde. This new method for measuring ee's was applied to numerous chiral aldehydes; a slight modification on the diamine unit enabled the reaction with ketones. Alexakis then demonstrated how chiral diamine-derived phosphoramides were found to react smoothly with alcohols. Again, when chiral alcohols were used, a pair of diastereoismers was formed, and ^{31}P NMR enabled the ee to be measured accurately. This method was found to be reliable. These diamines are not only limited to analytical applications. Glyoxal-derived mono aminals could be prepared, and diastereoselective manipulation of the remaining aldehyde site was possible (Scheme 2). Alkaloids such as lupinine were prepared by this strategy [2].

The afternoon poster session, chaired by *Hans-Beat Bürgi*, was preceded by five short lectures. *Christian Bochet, Jonathan Clayden, Angelika Fretzen, Lawrence Scott* and *Akira Yanagisawa* briefly presented topics that were then discussed in more detail in front of the posters.

The evening lecture, chaired by *Ilan Marek*, delightfully concluded this first day, with a lecture by ***Koichi Mikami*** (Tokyo Institute of Technology, Japan, 'Asymmetric activation in asymmetric catalysis'). Mikami explained the basis and the application of asymmetric activation in enantioselective catalysis. Hence, a poorly active achiral catalyst is turned into a more active one by the addition of a chiral ligand (the well-known 'chiral ligand acceleration'). But this active catalyst



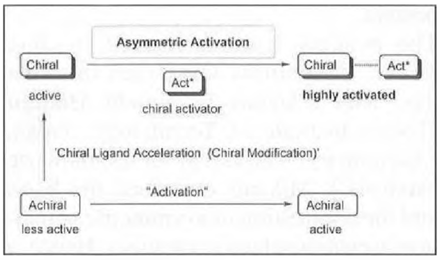
Scheme 2. Chiral aminals as versatile building blocks

Angelo Gavezzotti

Jacques Livage

Andrew Holmes

can itself be turned into an even more reactive one by a chiral activator ('asymmetric activation', Scheme 3). Using the same principle, an undesired catalytic substance can have its activity reduced by the addition of another ligand ('asymmetric deactivation'). A powerful strategy consists in adding simultaneously an activator to promote the desired catalytic reaction, while reducing the activity of the undesired catalytic process with a deactivator. An example of chiral activation was shown with the Ru-catalyzed reduction of acetophenone by a racemic complex of Ru-BINAP, with a chiral diamine (*S,S*-DPEN) as an activator. A spectacular extension of this concept was the 'Super High Throughput Screening' of a library of chiral ligands and chiral activators. In this process, the use of HPLC-CD allowed the direct determination of the ee's by using a simple achiral stationary phase. In the last part of his talk, Mikami demonstrated his broad research interests with some recent progress in liquid crystal chemistry. He detailed how spontaneous enantio-resolution in a fluid liquid crystal phase was observed for the first time [3].



Scheme 3. Strategies for asymmetric catalysis

Peter Wright

André Charette

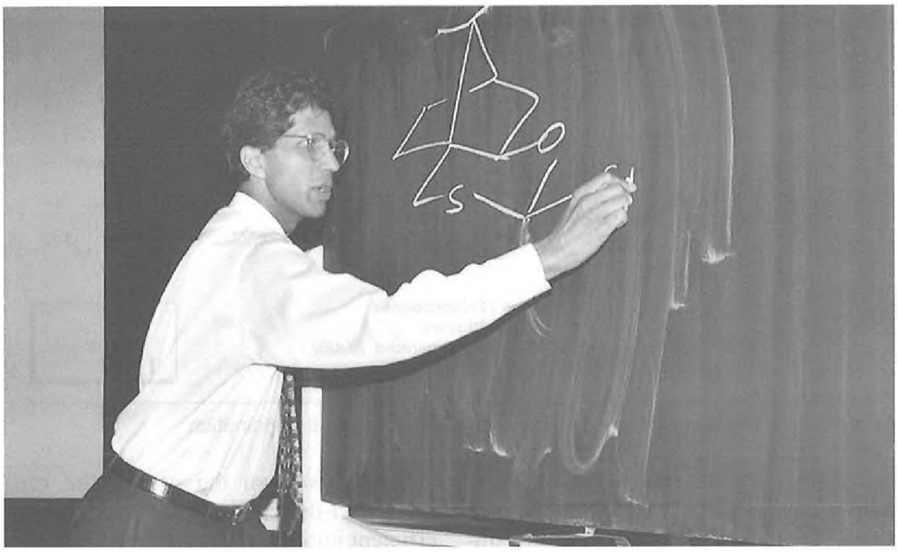
Max Malacria and Alexandre Alexakis

Monday was dedicated to physical chemistry aspects, and started, under the colorful chairmanship of *Jay Siegel*, with the no less colorful lecture of ***Angelo Gavezzotti*** (University of Milan, Italy, 'Crystal packing of organic compounds: reality *versus* computer simulation'). With the aim of predicting the crystal structure of organic compounds using computer calculations, Gavezzotti designed the ZIP-PROMET program 'that even an organic chemist can use'. Not an easy task! He calculated specific examples using his program and compared the results with results from other programs and experimental data. He also detailed the various levels of approximation that have been considered and their physical implication [4].

The audience was then led on a fascinating journey to the world of sol-gel chemistry, with ***Jacques Livage***'s lecture (Université Pierre et Marie Curie, Paris, France, 'From glasses to hybrid materials'). In a very clear fashion, he explained how hybrid organic/inorganic gels were formed. For example, organic dyes can be encapsulated by the condensation of silicic acid (prepared *in situ* by hydrolysis of a silicon alkoxide), in the presence of the dye. The encapsulation process is also compatible with sensitive molecules such as enzymes or even whole cells. Once encapsulated, the substrate retains its original activity. For example, glucose oxidase was encapsulated and used for medical applications (diabetes diagnostics), or Leishmania cells for immunological ELISA assays. This technique was also used for bioartificial organs. Langerhans islets were encapsulated and transplanted into mice; the activity was retained for more than eleven weeks, with the silica matrix protecting against immuno-rejection [5].

The evening lecture was chaired by *Gerald van Koten*, with ***Andrew Holmes*** (Melville Lab. for Polymer Synthesis, Cambridge, UK, 'Seeing polymers in a new light'). In a very lively presentation, Holmes bridged the gap between organic chemistry and material science. Starting from his pioneering work on the electroluminescence of poly(1,4-phenylenevinylene) (PPV), he showed how major issues such as stability, solubility, photoluminescence efficiency, emission wavelength and operating voltages were addressed by the introduction of substituents on the aromatic rings or by the choice of the polymerization process. The use of copolymers was found to have a profound impact on the matching of the electronic properties of the organic material and the electrode. Interesting applications such as flat TV displays were shown, in a nice example of collaboration between industry and academia [6].

Tuesday was devoted to biological aspects of chemistry. The session chaired by *Fritz Winkler* started with a breathtaking lecture by ***Peter Wright*** (The Scripps Research Institute, La Jolla, US, 'Structure and dynamics in protein folding and macromolecular recognition'). Starting from the basics in large biomolecules NMR spectroscopy, where nearly every resonance can be assigned using multidimensional heteronuclear experiments and doubly labeled (^{13}C and ^{15}N) compounds, Wright then showed how intermolecular interaction could be studied by NOE. In a specific example of zinc-finger proteins interacting with DNA, the combination of coherence-transfer and NOE experiments allowed the study of the adduct 3D-structure. Even more impressively, he showed how the determination of nuclear spin relaxation times of all the nuclei gave information on their



Varinder K. Aggarwal

Eichi Nakamura

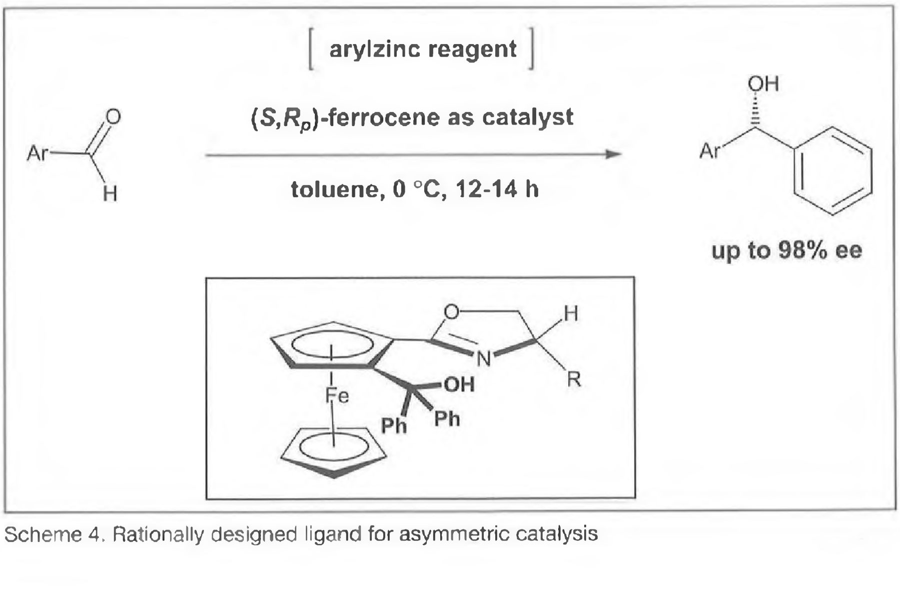
motion. Hence, whereas X-ray diffraction crystallography shows a frozen picture of the structure, NMR is now able to observe the dynamics of the proteins [7].

In the following lecture, ***John A. Katzenellenbogen*** (University of Illinois at Urbana-Champaign, US, 'Steroid receptors: a nexus between chemistry and biology') showed interesting aspects of estrogens and their interaction with their receptors. Indeed, many compounds are estrogens, and they exhibit a quite eclectic structure–activity relationship. The effect of small changes in size and stereochemistry was probed combinatorially, by screening a 96 pyrazole library on solid support [8].

After a memorable dinner at the Bürgenstock club, and a very spontaneous singing performance by *Koichi Mikami, Junzo Otera, Akira Yanagisawa* and *Takushi Kaneko*, with *Eiichi Nakamura* playing the flute, the traditional evening concert featured the Aura String quartet, with a program specially selected by the conference president (Schubert, Mendelssohn, Boccherini and Mozart).

Wednesday was again devoted to organic synthesis, with a strong emphasis on new methods in asymmetric synthesis. Under the chairmanship of *David Grierson*, the first lecture was delivered by ***André Charette*** (Université de Montréal, Canada, 'New reagents for the stereoselective cyclopropanation of unfunctionalized olefins'). After some generalities on the cyclopropanation reaction, Charette detailed all the phases that led to his now famous highly stereoselective cyclopropanation of allylic alcohols. He showed that this is an efficient and general reaction, working equally well with *cis*, *trans*, or tetrasubstituted olefins, with very few limitations. Substituted diazoalkanes could also be transferred, to give *gem*-disubstituted cyclopropanes [9].

Carsten Bolm (RWTH Aachen, Germany, 'Asymmetric catalysis with and without metals: from small molecules to polymers') started his lecture by reminding the audience that the current main challenges in asymmetric catalysis are catalytic activity (fast reactions with long-lived catalysts) and selectivity (stereo- and enantioselectivity). The desired reactions are oxidations, reductions or C–C bond-forming reactions. Among the numerous chiral ligands for such reactions available to date, only a few of them are based on rational design. So Bolm asked the critical question: could one predict which ligand will be best suited for a specific reaction and substrate? A rationally designed catalyst, the (S,R_p)-ferrocene shown in Scheme 4, with a C_2-type symmetry, was tested in a standard reaction (addition of diethylzinc to benzaldehyde). As predicted, the ligand performed better than its diastereoisomer. This ligand was particularly good for the arylation of aldehydes (by addition of diphenylzinc): with amounts as low as 10 mol-% of the (S,R_p)-ferrocene ligand, ee's higher than 90% were consistently obtained (Scheme 4). To improve the catalysts, a polymeric combinatorial approach was considered, based on ring-opening metathesis polymerization. The next challenge that Bolm set forth was the possibility of performing asymmetric catalysis *without* metals. And indeed, cyclic *meso* anhydrides could be efficiently desymmetrized in a complementary fashion by using a stoichiometric amount of quinine and quinidine in the presence of methanol to give optically pure acid/esters in a high yield. In some cases, even a catalytic amount of quinidine gave up to 90% ee. Bolm moved then to the use of

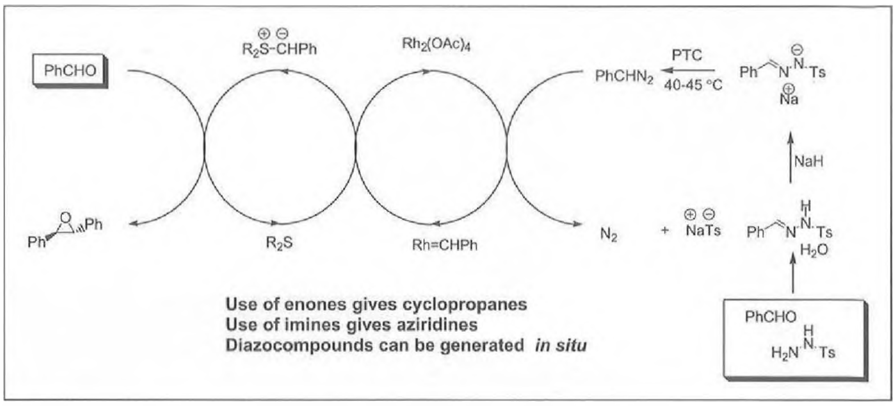


Scheme 4. Rationally designed ligand for asymmetric catalysis

sulfoximines as versatile chiral building blocks, and in particular their use as surrogates for β-amino acids in pseudopeptides [10].

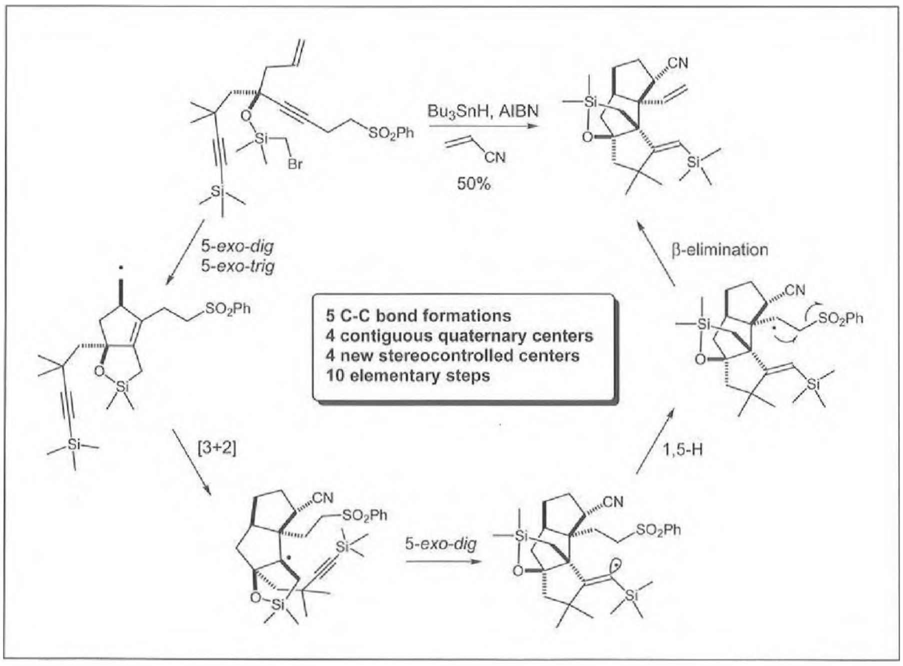
The afternoon session was similar to the Sunday session, with five short lectures. Contributions from *Steven De Feyter, Andreas Gansäuer, Robert Madsen, Nigel Simpkins and Jaroslav Vacek* were followed by a poster session.

Marco Ciufolini chaired the evening lecture by ***Varinder K. Aggarwal*** (University of Sheffield, UK, 'Novel catalyst asymmetric processes for epoxidation and related reactions'). In a very clear and didactic fashion, Aggarwal proved that a good reaction can actually be designed rather than discovered serendipitously. Indeed, after showing his recent progress in the asymmetric epoxidation of unfunctionalized olefins with chiral dioxiranes, he brilliantly exposed the constant upgrades he brought to an apparently simple reaction. An alternative preparation of epoxides results from the addition of sulfur ylids to aldehydes (the so-called Corey homologative epoxidation). To make this reaction enantioselective, the use of a chiral sulfur ylid was a natural choice; but to have a catalytic system, a way of making the ylid *in situ* from a stoichiometric achiral and unreactive (towards the aldehyde) precursor had to be found. Aggarwal chose the copper-catalyzed decomposition of diazoalkanes, known to generate ylids in the presence of a sulfide. After careful screening of several chiral scaffolds, a camphor-derived sulfide was found to give consistently high enantioselectivity (>90%), with a catalyst loading of 20%. At this point, the major drawback was the impracticality of the reaction on a large scale. A remedy would be to also prepare the diazo compound *in situ*. This was done by reacting an aldehyde and tosylhydrazone, with subsequent deprotonation. The impressive net result is that the two halves of the final epoxide arise from two aldehydes, with all the flexibility associated with a convergent step, whereas the only stoichiometric side-product is a sodium sulfinate (Scheme 5). This reaction was extended to prepare optically active aziridines, by replacing the aldehyde by an imine [11].



Scheme 5. Catalytic cycles in aldehyde epoxidation and imine aziridination

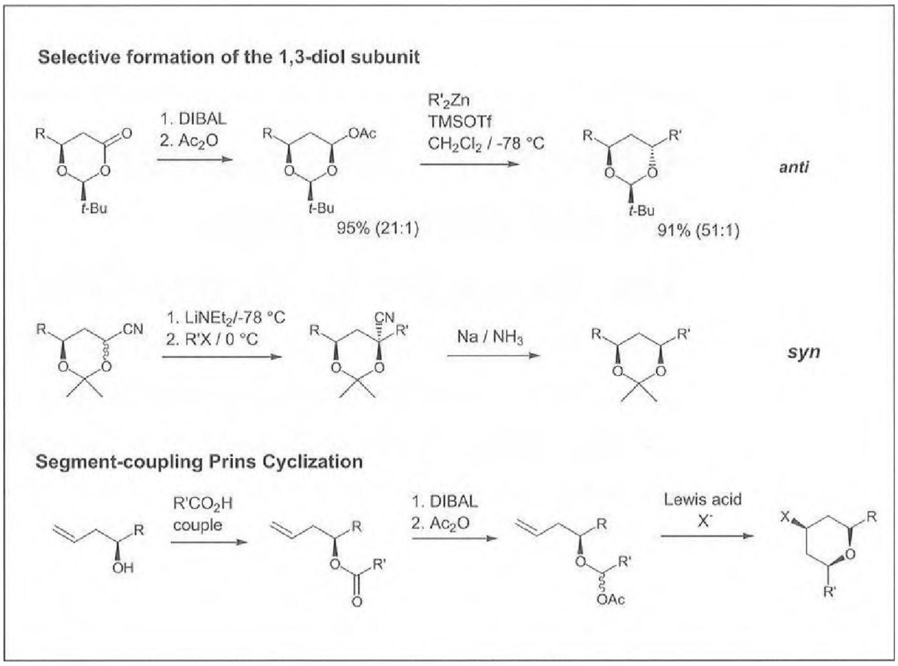
Siegfried Blechert opened the last day's session, with a fascinating lecture by ***Max Malacria*** (Université Pierre et Marie Curie, Paris, France, 'Highly stereoselective radical and transition-metal catalyzed polycyclization reactions'). Malacria focused on the use of the bromomethyl-dimethylsilyloxy group as an efficient initiator for radical cyclizations. After first showing how acyclic polysubstituted allylic alcohols could be prepared from mono- or disubstituted propargylic alcohols, he then demonstrated how cascade reactions cyclizations could form mono- and bicyclic systems. Reactions other than simple additions onto unsaturated compounds were also utilized, such as 1,5-hydrogen shifts or [3+2] annulations. The clever arrangement of suitable functional groups on the precursor opened the possibility for multiple domino reactions. In the culminating example, the linear triquinane skeleton was accessed *in one reaction* (Scheme 6); no less than five carbon–carbon bonds were formed, with four stereocontrolled and four contiguous quaternary centers, in what represent ten elementary steps! A nice application of this multiple cascade reaction in the synthesis of epi-illudol exemplified how powerful this strategy could be. In the last part of his talk, Malacria showed how vinyl sulfoxides were versatile precursors for stereocontrolled radical additions, with an interesting anti-Michael regioselectivity [12].



Scheme 6. Formation of the triquinane skeleton *via* multiple cascade radical cyclizations.

Eichi Nakamura (University of Tokyo, Japan) concluded the morning session with computational studies on the structure of cuprates ('O Copper! Wherefore art thou Copper? Molecular pictures of organocuprates in action'). He presented high-level calculations to offer a better understanding of the degree of aggregation of cuprates in solution, but also to detail their reactivity. In the light of these studies, numerous reaction mechanisms were examined, such as the alkylation, the Lewis-acid acceleration in conjugate addition to enones and the carbocupration of alkynes [13].

The grand finale was given by ***Scott Rychnovsky*** (University of California, Irvine, US, 'Stereochemical consequences of radical and cationic reactions') in the final session chaired by the conference's vice president Andrea Vasella. Applying his now famous 1,3-polyol synthesis, Rychnovsky showed the assembly of the skeleton of many polyene macrolides. In the specific example of Rimocidin, a convergent approach took advantage of the elegant protected cyanohydrin methodology as an acyl-anion equivalent. The reductive decyanation of cyclic ethers was shown to give a *syn* 1,3-diol (Scheme 7). On the other hand, the *anti* 1,3-diol was obtained by the addition of a dialkylzinc to the cation formed by the reaction of a Lewis acid with a-acetoxyethers. Rychnovsky showed how these substrates were prepared by a new method involving the DIBAL reduction/acetylation of protected lactones. A Prins cyclization based on this methodology was particularly efficient to prepare substituted tetrahydropyrans. A key intermediate in the Phorboxazole synthesis was prepared by this strategy [14].



Scheme 7. Strategies for the preparation of macrolide subunits

The meeting was concluded by ***Klaus Müller*** (F.Hoffmann-La Roche AG, Basel, Switzerland), who once again displayed his inclination for geometric and word puzzles. He humorously but very accurately summarized each of the 14 lectures through their most unexpected aspects.

Despite the outstanding scientific level of all the lectures, this meeting wouldn't be *the* Bürgenstock conference without the intense, but relaxed, never-ending discussions between the participants. Indeed, probably stimulated by the fantastic scenery, afternoon hikes or late-night drinks brought together young and older chemists, with very diverse interests. It is certain that many new developments in chemistry found their origin during the previous conferences; and this year's will definitely not be an exception to the rule.

The next Bürgenstock conference will be held on April 28–May 4, 2001, under the presidency of Andrea Vasella; there is no doubt that this week's excitement will be revived at this occasion.

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Chemical Mechanisms of Toxicity Basic Knowledge for Designing Safer Chemicals

Mini-Symposium, May 4, 2000, Basel, Switzerland*

Section for Medicinal Chemistry (SMC) of the New Swiss Chemical Society (NSCS)

Keywords: Chemical toxicity · Medicinal chemistry · SMC · NSCS

Chemical toxicology is the application of organic chemistry to toxicological issues, attempting to understand the underlying chemical mechanisms, and draw relationships between chemical toxic effects of the parent molecule (and/or its metabolites and reactive intermediates) and its physico-chemical properties, shape and reactivity. Chemical toxicology is probably the most complex and least explored chapter of medicinal chemistry. Understanding the origin of chemical toxicity is a great challenge requiring comprehensive interdisciplinary understanding. In order to raise the awareness of chemical toxicity issues (in particular for those which are not related to the pharmacological action of a compound) the Section for Medicinal Chemistry (SMC) of the New Swiss Chemical Society (NSCS) organised a mini-symposium on May 4, 2000, at the University of Basel with support by the Basel Chemical Society and the companies F. Hoffmann-La Roche AG, Lonza AG and Novartis AG, Basel. The meeting was well attended by medicinal chemists, toxicologists and students. John Ashby was asked to moderate the discussion of the four lectures summarised below.

Introductory Remarks

***John Ashby**, Zeneca CTL,*
Alderley Park, Cheshire, UK

It is a great pleasure to be in Basle and to be moderating this meeting. All branches of science are changing rapidly due to the introduction of new technologies and approaches. However, many issues currently faced in medicinal chemistry and in toxicology require answers that are independent of the technology being used at any one time. For example, Zhou *et al.* recently noted that by changing rodent diets one can also change the level of DNA adducts in the rodent liver, thus confirming the growing importance of the conditions under which rodent experiments are conducted (*Mutat. Res.* **2000**, *447*, 137). Likewise, Brinksworth has related the efficiency of malformation induction in neonatal rats, whose fathers were treated with cyclophosphamide before mating, to the levels of male germ cell apoptosis induced by cyclophosphamide (*Mutat. Res.* **2000**, *447*, 148). Such unexpected and enlightening observations indicate the need for provocative experimental designs, as well as the use of advanced technologies. Today our lecturers will fulfil this double need in their presentations.

Mutagenesis: DNA as the Target, DNA Damage, Mutations, Genetic Toxicology

***David M. DeMarini**, Environmental Carcinogenesis Division, US Environmental, Protection Agency, Research Triangle Park, North Carolina 27711, USA*

DNA is the primary target of mutagenesis, and DNA damage is the consequence of exposure to mutagens. Mutagens do not make mutations; mutagens make DNA damage, which is in two general forms: DNA strand breaks or DNA adducts (*i.e.* compounds bound covalently to nucleotides). Mutation is a change in DNA sequence. A change in DNA sequence (*i.e.* mutation) is caused by the cell. In other words, mutagenesis is a cellular process that requires enzymes and, frequently, DNA replication. Mutation spectra are the types of mutations induced by a mutagen or a mutagenic complex mixture. Mutation spectra of complex mixtures or simple binary mixtures have been determined thus far only in Salmonella (the Ames assay). With regard to the particulate organics from urban air and municipal waste incinerator emissions, cigarette smoke condensate, and organic extracts of chlorinated drinking water, the mutation spectrum of the mixture reflects the dominance of one or a few chemical classes within the mixture. The mutation spectra of sunlight and cigarette smoke in Salmonella were similar to those found in the p53 gene of skin or lung tumours in people associated with exposure to these two mutagens. These data provide possible mechanistic links between the types of mutations induced by complex environmental mutagens in an experimental organism (Salmonella) and the types of mutations found in humans exposed to the same environmental mutagens. The primary class of mutation produced by many mutagens within a chemical class (and even among different classes) is frequently the same. These studies indicate that, to some extent, complex mixture-induced mutation spectra can be modelled by the predominant mutagenic chemical class in that mixture and even by a single model compound in that chemical class. Among those mutagens that are mutagenic in a variety of organisms, the primary class of base substitution mutation produced by each compound is the same in each organism. In

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other words, the primary class of base substitution produced by a particular mutagen is the same in bacteria as in mammalian cells in culture, in mice, and in humans. The reason for this is that the DNA repair and replication proteins/machinery is highly phylogenetically conserved across species. Thus, similar cellular mechanisms exist in bacteria and humans to process DNA damage into mutations. Therefore, the molecular data generated in simple laboratory systems have much relevance to humans. Such information should be useful in the interpretation of mutation spectra in experimental organisms in terms of the relevance of such data to human health.

Role of Cytochrome P450 in Chemical Toxicity and Carcinogenicity

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The human body is continuously exposed to a myriad of structurally diverse, lipophilic chemicals, largely naturally-occurring, which it cannot exploit beneficially, and thus endeavours to eliminate. In order to overcome the difficulty of excreting such lipophilic chemicals, the body has developed a number of enzyme systems adept at metabolically converting lipophilic compounds to hydrophilic, readily excretable metabolites. Such metabolism, in most cases, also abolishes any biological activity the chemical may possess. Undoubtedly the most important enzyme system in the metabolism of chemicals are the cytochrome P450-dependent mixed-function oxidases, a ubiquitous system encountered in almost all tissues but which predominates in the liver, which consequently is the principal site of xenobiotic metabolism. It displays unprecedented broad substrate specificity which it achieves by existing as a superfamily of enzymes, which contains a number of families, further subdivided into subfamilies which in turn may contain one or more enzymes, each having its own characteristic substrate specificity.

It is now firmly established that cytochrome P450-mediated metabolism does not always lead to deactivation and excretion, but it may also convert chemicals to reactive intermediates that may interact covalently with DNA and proteins leading to mutations and cancer, cytotoxicity and immunotoxicity. Such reactive intermediates are generated mainly, but not exclusively, in the liver from where they may be also transported to other, metabolically less competent tissues, where they may exert their deleterious effects.

Although a number of cytochrome P450 enzymes may catalyse the metabolism of the same carcinogen, they may effect its metabolism at different sites so that some may direct metabolism through pathways that lead to the formation of inactive metabolites, and consequently deactivation, whereas others facilitate the formation of reactive intermediates, and thus activation. Clearly, the fate of a chemical in the body, whether activation or deactivation, will be determined to a large extent by the nature of cytochrome P450 proteins that are present at the time of exposure. For example, the guinea pig is refractive to the carcinogenicity of 2-acetylaminofluorene because it lacks the enzyme systems capable of catalysing its activation. Similarly, 4-aminobiphenyl is a potent carcinogen in many animal species, all of which can catalyse its cytochrome P450-mediated activation that proceeds through N-hydroxylation. In contrast, no enzyme appears capable of catalysing the N-hydroxylation of the 2-isomer, which is consequently non-carcinogenic.

Of the various cytochrome P450 families, family 1 (CYP1), whose substrates are essentially planar molecules, is the most prominent in the activation of carcinogens. It is only a minor family, comprising less than 5% of the total hepatic cytochrome P450 and, under such circumstances, one would expect that activation of carcinogens is a minor route of metabolism. Many planar carcinogens can, however, on repeated administration, selectively induce the CYP1 family and thus stimulate their own activation, and in this way increase the likelihood of interaction with DNA, leading to mutations and cancer. Therefore, the ability of a chemical to induce its own activation is an important factor in determining its carcinogenic activity. Moreover, such inducers of the CYP1 family also bind avidly to, and activate the Ah receptor, a cytosolic protein that regulates important processes involved in tissue proliferation and differentiation, critical steps in the promotion and progression stages of carcinogenesis.

In summary, toxicity should not be viewed as simply a consequence of the intrinsic molecular structure of the chemical, as it is also determined by the nature of the enzymes present at the time of exposure; these enzyme systems are in turn regulated by genetic factors and by environmental factors, such as diet and previous exposure to chemicals, and the presence of disease.

Structure Toxicity Relationships – How Useful Are they in Predicting Toxicities of New Drugs?

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Several new drugs have either been removed from the market soon after their release, or have been flagged for careful monitoring and restricted use because of severe toxic effects. Although in some cases the parent drug structure may be responsible for the observed toxicities, in most cases reactive metabolites are formed that interact with cellular macromolecules to stress cells directly, and/or more commonly, yield immunogenic products. Since it is the structures of drugs and their metabolites that dictate reactivity and not the metabolic pathways themselves, this presentation focuses on what can be empirically learned from comparisons of structures associated with toxic effects and similar structures that are less toxic.

Some of the most widely used drugs are the NSAIDs. It has been proposed that acyl glucuronide metabolites of arylacetic and arylpropionic acid NSAIDs form immunogens that are responsible for many of the toxic effects associated with these agents. However, it is clear from an examination of several similar drug structures (*e.g.* zomepirac *vs.* tolmetin), and from studies with diclofenac, that other structural moieties must play significant roles in causing toxicities. One substructure that surfaces as a protoxicant in NSAID and several other classes of drugs, is the thiophene moiety; others are the aniline/anilide moieties. These structures are oxidised by cytochrome P450, and sometimes other oxidases, to electrophilic reactive intermediates.

Additional substructures associated with tissue organ damage include furans, nitroaromatics, some halogenated hydrocarbons and halogenated aromatics, and medium chain fatty acids. Oxidation by cytochromes P450 or enzymes of the fatty acid β-oxidation pathway, and reductions by cytochrome P450 reductase and other reductases, appear to generate toxic reactive intermediates from these structures.

Finally, a look at structures of some new drugs (*e.g.* bromfenac and tolcapone) and classes of drugs (*e.g.* COX 2 inhibitors, glitazones and quinolone antibiotics) can provide useful information about structure toxicity relationships. Some examples also show that prediction of toxicities based on our present limited knowledge of structure toxicity relationships is not very reliable because of several factors, including the introduction of new substructures for which little information is available, structural substitution patterns that may markedly alter structure reactivity, low doses of a drug that limit exposure to a drug and/or its reactive metabolites, environmental and genetic factors that modulate rates of reactive metabolite formation and inactivation, immune recognition of macromolecular adducts, and efficiency of macromolecular repair processes. These factors are very problematic for application of even simple semi-empirical approaches to structure toxicity relationships of drugs.

Structure–Activity Relationship Studies and their Role in Predicting and Investigating Chemical Toxicity

***Ann Richard**, National Health and Environmental Effects Research Laboratory, US Environmental, Protection Agency, Research Triangle Park, North Carolina 27711, USA*

Structure-activity relationships (SAR) represent attempts to generalise chemical information relative to biological activity for the twin purposes of generating insight into the mechanism of activity and predicting the potential activities of new chemicals. In addition, assumption of a common mechanism of action or rate determining step, through restriction of chemical class or biological function, is a central guiding assumption that both constrains and enables development of meaningful SAR associations. A wide range of SAR investigations at different levels of resolution are considered. Global SAR models attempt to analyse structurally and mechanistically diverse data relative to a common toxicity endpoint (*e.g.* statistical programs such as CASE and TOPKAT). Since little or no bias or prior knowledge is assumed, these models are useful for data exploration and hypothesis generation. At the next level of resolution are the traditional QSAR or Hansch-type methods which attempt to derive quantitative models of relative potency in relation to structure, with the prior assumption that a common mechanism of action applies to the set of chemicals. The most detailed level of SAR study assumes some molecular-level resolution of the problem, relies on a clear prior hypothesis, and applies computational chemistry techniques to model key reactivity or interaction steps in a putative mechanism of action. Through a series of examples at each level of resolution, this presentation attempted to illustrate the wide range of toxicity problems that can be considered with SAR methods, the nature of the questions, and the types of information that can be gained from such studies. Issues pertaining to the use of global SAR models, such as the commercial toxicity prediction systems CASE and TOPKAT, stress the need to explore the structural basis for predictions and to move beyond statistics to build independent scientific rationale for models and individual predictions. Development of a modified CASE-FDA model for carcinogenicity prediction served to illustrate the strong dependence of the SAR model performance on the composition and size of the training set, the definition of activity, and the model assumptions. An example of developing SAR models for rat nasal toxicity served to illustrate how careful application of quantitative methods can yield useful information even with a small dataset for a chronic *in vivo* endpoint that is seemingly far from the ideal for SAR study. Models relative to haloacetic acids and halogenated alkenes served to illustrate how computational chemistry methods can be brought to bear in a very focused way to explore possible chemical and reactivity mechanisms underlying a biological activity. Finally, modelling of androgen and estrogen receptor binding were offered as examples of receptor-mediated events relying on 3D chemical information, that may or may not pertain to the ultimate toxicity endpoint of concern, and that may or may not require explicit consideration and knowledge of the detailed receptor binding domain and ligand interaction. The talk concluded with a few comments relative to the challenges of applying SAR modelling of toxicity in the pharmaceutical industry, and to the evolving role of SAR in the new era of genomics, as a means for refining our understanding of chemical structure in relation to biology function.

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Lehre, Forschung und Technologietransfer an der Chemieabteilung der HTA Chur

Andreas Kaplan* and Friedemann Haiber

Education, Research, and Technology Transfer at the Department of Chemistry at the HTA Chur
Abstract: The HTA Chur is the only University of Applied Sciences in Switzerland to offer an evening course in chemistry at this level. As teachers and students work during the day in the industry, they can transfer the knowledge gained directly to their companies. Education and applied research and development is concentrated in the fields of polymer chemistry and chemical process engineering. Efforts in the fields of technology transfer and R+D have been intensified since January 2000 by the foundation of a new institute (IFTW). A full-time scientist has been employed for a major research project together with the industry and partly financed by the KTI.

Keywords: Applied research and development · Chemical education · HTA Chur · Technology transfer · University of Applied Sciences

Zu den Aufgaben der Fachhochschule gehören neben der reinen Lehre auch die anwendungsorientierte F + E und der Technologietransfer. Die HTA Chur betreibt die Chemikerausbildung – als einzige Schule in der Schweiz – berufsbegleitend. Wie werden diese Aufgaben an der Chemieabteilung der HTA Chur durchgeführt?

Die Lehre

Einige Besonderheiten der berufsbegleitenden Ausbildung:

Die Dozenten arbeiten nebenamtlich. Hauptamtlich stehen sie voll im Beruf in der Industrie. Sie wissen deshalb genau, welche Fähigkeiten von jungen Chemikern verlangt werden. Beispiele aus dem täglichen Arbeitsumfeld, sowohl der Dozenten als auch der Studenten, machen den Unterricht praxisnah und motivieren die Studenten in ganz besonderem Masse. Aktuelle Fragestellungen und kleinere Probleme in der Industrie werden in Semesterarbeiten bearbeitet. Die Diplomarbeiten beinhalten aktuelle Probleme der Industrie und werden in der Regel auch in der Industrie durchgeführt.

Die Studenten setzen den gelernten Stoff sofort am Arbeitsplatz um. Die Umsetzung der Theorie in die praktische Arbeit ergibt ein tieferes Verständnis für die Zusammenhänge. Durch die Klassen-

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struktur ist auch der Kommunikationsfluss zwischen Studenten in unterschiedlichen Positionen in der Industrie gegeben. Teilweise sind die Studenten bereits Mitglieder des mittleren Kaders.

Technologietransfer

Durch die berufsbegleitende Ausbildung wird somit nicht nur der Stoff praxisnah vermittelt, sondern es kann auch das erworbene Wissen unmittelbar in der täglichen Arbeit angewandt werden. Der Betrieb profitiert von diesem direkten Technologietransfer.

Damit Unternehmen, von Wissen und Erfahrungen der Dozenten und der technischen Einrichtungen der HTA Chur Nutzen ziehen können, wurde an der HTA Chur das 'Institut für Forschung, Technologietransfer und Weiterbildung' – kurz IFTW gegründet. Dieses Institut hat zur besonderen Aufgabe, die Kontakte und die Kommunikation mit der Industrie zu intensivieren. Zusätzlich werden die administrativen Aufgaben im Bereich Forschung, Technologietransfer und Weiterbildung übernommen.

Angewandte Forschung und Entwicklung

Im Bereich der Forschung ist es notwendig, dass hauptamtliche Mitarbeiter eingestellt werden. Forschung ist sehr arbeitsintensiv und erfordert einen hohen Zeitaufwand. Nur so kann eine Konstanz des Know-hows über mehrere Jahre hinweg garantiert werden. Mit der besonderen Unterstützung des KTI ist es jetzt gelungen, für ein gemeinsames Projekt mit der Industrie eine wissenschaftliche Mitarbeiterin zu gewinnen. Der weitere Einsatz von wissenschaftlichen Mitarbeitern und technischem Personal erlaubt eine Ausweitung der Projekte und liefert auch verbesserte Möglichkeiten, Studenten in geführten Arbeiten am Forschungs- und Entwicklungsprozess teilhaben zu lassen. Die ständige Wissenserweiterung und die Vertiefung des Know-hows ist dadurch gegeben, dass sich die Schwerpunkte in Lehre und Forschung auf zwei Vertiefungsgebiete konzentrieren: Die Polymerchemie und die chemische Verfahrenstechnik. Innerhalb dieser Kerngebiete ist der Kompetenzbereich sehr breit angelegt:

- Synthese von Monomeren und Polymeren
- Polymeranalytik und Werkstoffprüfung
- Struktur und Eigenschaften von Polymeren (Polymerphysik)
- Herstellungs- und Verarbeitungsverfahren
- Unit operations
- Mess- und Regeltechnik
- Upscaling
- Umweltschutz und Sicherheit bei chemischen Prozessen

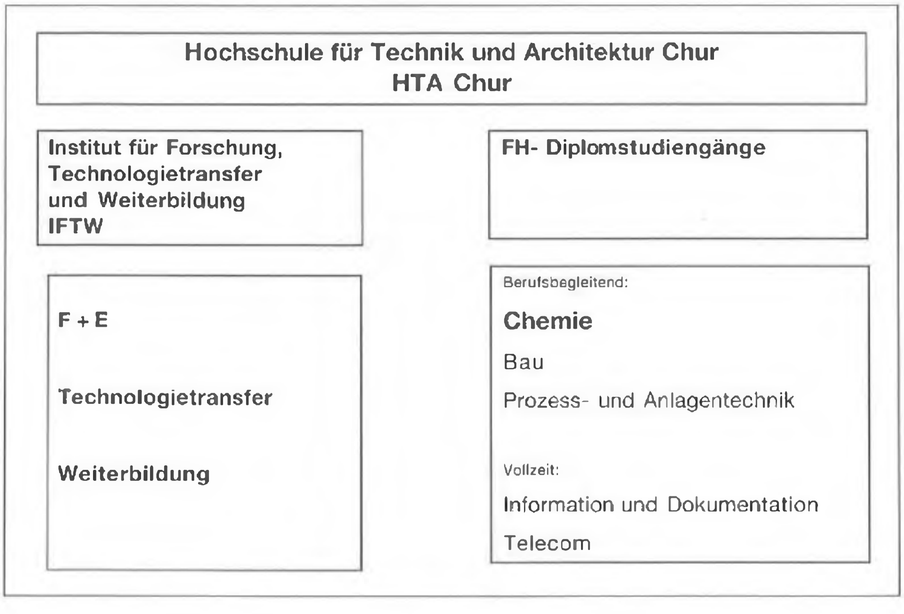
In diesen Bereichen stehen neben der fachlichen Kompetenz auch aufwendige Apparaturen und technische Einrichtungen der Industrie zur Verfügung. Dadurch wird gewährleistet, dass die Forschungseinrichtungen stets dem aktuellen Stand der Technik entsprechen und neben Labor- auch Technikumsdimensionen aufweisen. Mit einer Patentbibliothek im Haus (auf CD-ROM) und dem online-Anschluss an die wichtigsten Datenbanken können zu allen chemischen und verfahrenstechnischen Fragestellungen gezielt die aktuelle Literatur und die relevanten Patente aufgefunden und bewertet werden.

Da das IFTW fachübergreifend aufgebaut ist, können einzelne Projekte auch interdisziplinär ausgestaltet werden und Mitarbeiter von unterschiedlichen Fachrichtungen eingesetzt werden. Durch die kurzen Kommunikationswege können Resultate der anwendungsorientierten Forschung wieder im Unterricht und in Weiterbildungsveranstaltungen eingesetzt werden und die Studenten erhalten einen Einblick in Fachgebiete auch ausserhalb des Unterrichtsstoffs.

Zusammenfassung

Das IFTW an der HTA Chur vermittelt das vorhandene Wissen, die spezifischen Erfahrungen und die technischen Einrichtungen an Industrieunternehmen. Dazu bedarf es nicht nur einer Anhäufung von Wissen und Kompetenzen; es ist auch notwendig dieses Wissen den interessierten Betrieben näher zu bringen und die Kompetenzen zu 'vermarkten'. Kurzfassungen der letzten Diplomarbeiten sind über das Internet unter *www.fh-htachur.ch* abrufbar. Die angewandte F + E und der Technologietransfer verbessern die FH-Ausbildung und die Industrie profitiert von Chemikern, die praxisnah ausgebildet wurden.

Eingegangen am 4. Juli 2000



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SACh Weiterbildung Analytik

Veranstaltungskalender Analytik 2000/2001

Aufgrund der grossen Nachfrage nach unsern Kursen im letzten Jahr hat die Sektion Analytische Chemie (SACh) der Schweizerischen Chemischen Gesellschaft (NSCG) beschlossen mit dem Fachverband Laborberufe (FLB), dem Schweizerischen Chemikanten- und Cheministen-Verband (SCV) und dem Schweizerischen Laborpersonal-Verband (SLV), das vorliegende Aus- und Weiterbildungsprogramm 2000/2001 in Burgdorf, Winterthur, Windisch und neu in Genf zu realisieren.

Im Angebot finden Sie eine breite Palette von Kursen. Wir bieten Ihnen sowohl fachspezifische wie auch fächerübergreifende Kurse an. Die Fachkurse haben wir neu konzipiert und die fachübergreifenden Kurse ausgebaut. Das Angebot reicht vom Grundkurs bis zur Vermittlung von spezifischem Fachwissen. Es ist daher für Einsteiger wie auch für erfahrene Praktiker interessant.

In der Ausschreibperiode 2000/2001 führen wir auch zwei Tagungen durch: Die APPLICA und das Fachseminar PALAB. Die APPLICA ist unsere schweizerische Fachtagung in Instrumentalanalytik mit Ausstellung und integriertem Workshop. Das Fachseminar PALAB behandelt den heute noch zeitaufwendigsten und zugleich messunsichersten Arbeitsschritt in der Analytik, die Probenaufbereitung.

Kurse

Veranst. Nr./Titel	Ort	Datum	Kosten Fr. Mitgl./Nichtmitgl.
1. Chromatographie			
☐ GC 1 Arbeitstechnik in der GC (Französisch)	Genf	30. Nov.–1. Dez. 2000	810/900.–
☐ GC 2 Stand der GC-Technik	Winterthur	26.–28. Feb. 2001	1210/1350.–
☐ GC 3 Fehlererkennung und Fehlervermeidung in der GC	Winterthur	5.–6. März 2001	810/900.–
☐ HPLC 1 Arbeitstechnik in der HPLC (Deutsch)	Burgdorf	13.–14. Nov. 2000	810/900.–
(Französisch)	Genf	11.–12. Dez. 2000	810/900.–
☐ HPLC 2 HPLC-Phasen, -Phasenwahl und -Trennoptimierung	Burgdorf	22.–23. Jan. 2001	810/900.–
☐ HPLC 3 Probleme, Prävention und Fehlersuche in der HPLC	Burgdorf	5.–6. März 2001	810/900.–
2. Kopplungstechniken			
☐ KT 1 GC-Kopplungen mit IR und MS	Winterthur	17.–18. Mai 2001	810/900.–
☐ KT 2 HPLC-Kopplungen mit UV, IR, MS und NMR	Burgdorf	26.–28. Juni 2001	1210/1350.–
3. Bioanalytik (NEU)			
☐ BA 1 Kapillarelektrophorese (Deutsch)	Burgdorf	26. Jan. 2001	450/500.–
(Französisch)	Genf	29. Jan. 2001	450/500.–
☐ BA 2 Einführung in die Chiptechnologie zur Gendetektion	Burgdorf	15. Juni 2001	450/500.–
4. Chemometrie (NEU)			
☐ CM 1 Statistische Auswertung von Messdaten	Winterthur	27.–28. Nov. 2000	860/950.–
☐ CM 2 Optimierungstechniken: Grundlagen/Anwendungen	Winterthur	10.–11. Mai 2001	860/950.–
5. Qualitätssicherung			
☐ QS 1 Aufbau von Qualitätssicherungssystemen	Windisch	4. Dez. 2000	500/550.–
☐ QS 2 Messunsicherheit in der chemischen Analytik	Windisch	5.–6. Feb. 2001	860/950.–
☐ QS 3 Validieren von Analysenverfahren	Windisch	19. März 2001	500/550.–
☐ QS 4 Qualifizieren von Laborgeräten	Windisch	20. März 2001	500/550.–
☐ QS 5 Praxisnahe Qualitätskontrolle in der organischen Rückstands- und Spurenanalytik	Windisch	21. Mai 2001	500/550.–
☐ QS 6 Qualitätssicherung, eine Führungsaufgabe	Windisch	18. Juni 2001	500/550.–
6. Projektmanagement (NEU)			
☐ PM 1 Zeit- und Arbeitsplanung	Burgdorf	25.–26. Okt. 2000	860/950.–
☐ PM 2 Grundlagen des Projektmanagements	Burgdorf	7.–8. Dez. 2000	860/950.–
☐ PM 3 Projekte erfolgreich führen	Burgdorf	1.–2. Feb. 2001	860/950.–

Fachtagungen

Veranst. Nr./Titel	Ort	Datum	Kosten Fr. Mitgl./Nichtmitgl.
☐ FS 1 APPLICA	Zürich	26.–28. Sept. 2000	verlangen Sie
☐ FS 2 PALAB	Windisch	7.–8. Mai 2001	unsere Broschüren

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☐ Senden sie mir unentgeltlich die Weiterbildungsbroschüre 2000/2001

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Telefon: ____________ Fax: ____________ E-Mail: ____________

Zusenden oder übermitteln an:

Fax: 034 426 43 91
Tel.: 076 573 72 23

Sekretariat SACh, Fachhochschule Burgdorf
Abteilung Chemie, Pestalozzistrasse 20
CH–3400 Burgdorf

Anmelden können Sie sich auch über: http://www.sach.ch/formausb.html

APPLICA 2000
Anwendungen und Grenzen moderner Instrumentalanalytik

Die APPLICA 2000 ist ein Fachseminar mit integrierter Ausstellung und darin eingebundener infoExpo. Sie findet vom

26.–28. September an der Universität Zürich-Irchel

statt. Sie knüpft an die APPLICA 98 an und richtet sich an Anwender moderner Analytik.

- Sie zeigt den breiten Einsatz, die Grenzen und Problemlösungen anhand von Anwendungen mit moderner Instrumentierung auf.
- Sie ermöglicht einen Intensiven Erfahrungsaustausch und vermittelt Kontakte mit Wissenschaftlern, Praktikern und Geräteherstellern.
- Sie gibt jungen Lehr-, Fachhochschul- und Hochschulabgängern Gelegenheit, ihr Wissen und Können im Posterwettbewerb zu präsentieren.

Die Schwerpunkte der APPLICA bilden Plenarreferate von geladenen Referenten. Sie werden ergänzt durch Kurzreferate, eine Postersession und die aktive Ausstellung mit Kurzkursen und moderierten Diskussionen.

26. September 2000	27. September 2000	28. September 2000
Session 1	**Session 3**	**Session 5**
ANALYTIK UND KONTROLLE in der Pharmazie und Lebensmittelindustrie	TRENDS, NEU- UND WEITERENTWICKLUNGEN in der Instrumentierung PROBENAUFBEREITUNG	SPURENANALYTIK in der Präklinischen -, Klinischen -, und Gerichtschemie
Poster	Poster	Poster
Session 2	**Session 4**	**Session 6**
LABOR- UND BETRIEBSANALYTIK in der Agro-, Farben-, Chemikalien- und Rohstoffchemie.	QUALITÄTSSICHERUNG	UMWELTANALYTIK
Moderierte Diskussionen und Kurzkurse 1 und 2	Moderierte Diskussionen und Kurzkurse 3 und 4	Moderierte Diskussionen und Kurzkurs 5

Weitere Informationen sowie Anmeldeunterlagen finden Sie im Internet unter www.sach.ch

Anmeldung/Bestellung von Informationsmaterial

☐ Senden sie mir unentgeltlich das 2. Zirkular

Ich melde mich an für:

☐ ganzes Seminar ☐ 26. Sept. ☐ 27. Sept. ☐ 28. Sept.

Teilnahmegebühren

Nichtmitglieder/Mitglieder: Fr. 300.–/270.– / Tag
Fr. 660.–/600.– / 3Tage

Studenten: Fr. 100.– / Tag; Fr. 220.– / 3 Tage

Ich bin Mitglied von: FLB ☐ NSCG ☐ SCV ☐ SLV ☐

Zusenden oder übermitteln an: Fax: 034 426 43 91
Tel.: 076 573 72 23

Name, Vorname:

Firma, Institut:

Abteilung:

Privat:

PLZ/Ort:

Telefon: Fax: E-Mail:

Sekretariat SACh, Fachhochschule Burgdorf
Abteilung Chemie, Pestalozzistrasse 20
CH–3400 Burgdorf

Anmelden können Sie sich auch über Internet: www.sach.ch/applica.html

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FECS Federation of European Chemical Societies

Annual Report 1999

The Federation of European Chemical Societies is a voluntary association, the object of which is to promote cooperation in Europe between those non-profit-making scientific and technical societies in the field of chemistry whose membership consists largely of individual qualified chemists and whose interests include the science and/or practice of chemistry. It was founded in 1970.

A Powerful Voice for Chemists and Chemistry: The Federation of European Chemical Societies (FECS), with the European Communities Chemistry Council (ECCC), through about 50 member societies, together represent some 200 000 individual chemists in academia, industry and government in Europe.

The Structure of FECS: The scientific work of FECS is carried out through its Divisions (Analytical Chemistry, Food Chemistry, Chemical Education, Chemistry and the Environment. Electrochemistry and Organometallic Chemistry) and Working Parties, including the new Working Party on Nuclear and Radiochemistry. The European Communities Chemistry Council (ECCC) was founded in 1973, its primary object being to act in an advisory or representative capacity in matters relating to the science and practice of chemistry, particularly in relation to the European Commission. FECS is an active partner in AllChemE (the Alliance for Chemical Sciences and Technologies in Europe).

The FECS Lecture 'How ATP is made' was given by Prof. Sir John Walker, Director of the Dunn Nutrition Unit of the Medical Research Council, Cambridge, UK, in August, in Berlin, during the Annual Congress of the Gesellschaft Deutscher Chemiker. **The Award for Service to FECS** was presented to Ingenieur Bauke te Nijenhuis, Royal Netherlands Chemical Society, and to Prof. Alberto P. Masia, Royal Spanish Society of Chemistry, in recognition of their services. **The FECS General Assembly** met in September in Helsinki as guests of the Association of Finnish Chemical Societies.

Divisions

Analytical Chemistry

The Symposium 'Analytical Chemistry and Law' was held in September in Vienna and the Workshop 'The Status of Traceability of Chemical Measurement', in September in Bratislava. Plans were made for Euro-analysis XI, to be held in September 2000 in Lisbon.

The first edition of a directory 'Who's Who in Analytical Chemistry in Europe', containing about 800 entries, was completed. Initiatives were undertaken to promote industry input to the Division's activities and to develop an inventory of definitions in order to homogenise analytical terms.

Food Chemistry

The Symposium 'Food and Cancer Prevention III' was held in Norwich, UK, in September. The symposium EUROFOODCHEM X, held in Budapest in September attracted over 350 participants from 40 countries. Plans were made for 'EuroResidue IV' in Veldhoven in May 2000 and for 'Chemical Reactions in Food IV' in Prague in September 2000.

The 2nd edition of 'Who's Who in Food Chemistry', includes consulting/analytical/service laboratories. A 'Handbook of Food Components' will be published as a CD-rom. The Division has supported the candidature of the Division of Food Science, Polish Academy of Sciences, Olsztyn as an INCO Centre of Excellence in Food and Health.

Organometallic Chemistry

The 'XIIIth FECHEM Conference on Organometallic Chemistry' held in Lisbon in August 1999, attracted 426 participants from 35 countries. The booklet 'Organometallic Research Centres in Europe' contains details of over 2000 European organometallic chemists: *http:wwwtw.vub.ac.be/ond/aosc/eoc/default.htm*

Chemistry and the Environment

The 'First International Symposium on Atmospheric Reactive Substances' was held in Bayreuth in April. The '17th International Symposium on Polycyclic Aromatic Compounds (ISPAC)' was held in Bordeaux in October. Initiatives were taken in the areas of Green and Sustainable Chemistry, Education in Environmental Chemistry, and Air Chemistry and Air Pollution/Atmospheric Reactive substances.

Plans were made for the '7th FECS Conference on Chemistry in the Environment, Trace Metal Speciation in the Aquatic Environment', to be held in Porto, 27–30 August 2000, and for a workshop on 'Education in Environmental Chemistry' in 2000.

Chemical Education

The '5th European Conference on Research in Chemical Education' was held in September in Ioannina, Greece, attracting over 140 participants from 23 European countries. The Position Paper on 'Empirical Research into Chemical Education: the Motivation, Research Domains, Methods and Infrastructure of a Maturing Scientific Discipline' is available in Italian, Polish, English and German. A Eurocourse for Chemistry Teaching, supported by Socrates, will be held in Lublin, Poland in June 2000.

Electrochemistry

The 'Eurocurriculum on Electrochemistry' was published and there was collaboration with the European Chemistry Thematic Network on curriculum issues.

Plans were made for a 'Workshop on Electroactive Polymers' to be held in Poraj, Poland in September 2000.

Working Parties

History of Chemistry

A listing of chemical anniversaries being celebrated in 2000 has been compiled, marking events that took place 50, 100, 150, *etc.*, years ago. The 'Third International Conference on the History of Chemistry and Chemical Industry' was held in July in Budapest.

The FECS Millennium Project: 'Celebration of 100 Distinguished European Chemists from the Chemical Revolution to the 21st Century' was published in the magazines of national chemical societies and on the web site *www.chemsoc.org/networks/enc/fecs/100chemists.htm*

Nuclear and Radiochemistry

A new Working Party on Nuclear and Radiochemistry has been created. It will meet during the '5th International Conference on Nuclear and Radiochemistry' in Pontresina, Switzerland 3–8 September 2000. It is expected that this series will seek FECS Sponsorship. The WP will review the need for other symposia and training within nuclear and radiochemistry.

Computational Chemistry

Plans are being made to organise a series of biannual summer schools on computational chemistry, the first being in Perugia, Italy in 1999. A directory of European Computational Chemists can be accessed *via* the FECS web site. The '3rd European Conference on Computational Chemistry (EUCO-CC3)' will be held in Budapest in September 2000.

Chemistry in the Conservation of the Cultural Heritage

A programme has been launched to compile a 'Data Bank on Conservation Procedures of Stone, Metals, Paintings'. Forms for this purpose were published in *Science and Technology for Cultural Heritage* **1997**, *6* (1), edited by CNR, Rome. Data on conservation treatments of monumental buildings are compiled in an interactive data bank.

EUCHEM Conferences

EUCHEM Conferences provide an informal platform to stimulate discussion in emerging areas of chemistry. Meetings are small and time is available for informal discussion. Poster presentations are encouraged. Information presented is not used elsewhere without the approval of the speakers. Plans were made for the EUCHEM Conference 'Bioinformatics, Cheminformatics, Datamining, MQSAR and Chemometrics (BCDC)', in Stockholm in September 2000.

European Communities Chemistry Council

The ECCC comprises national societies, both learned societies and professional associations, representing 150 000 chemists, of whom 50% are under 35 years old.

A dialogue was initiated with the European Commission on the value of the European Chemist designation in connection with the Commission's plans to develop a European research area. A survey of educational materials was begun with a view to sharing information on best practice and adapting successful ideas from other countries. Dialogue with the European Chemistry Thematic Network (ECTN) is continuing in order to assess the support that could be given to the ECTN self-assessment testing programme.

EurChem – the Designation European Chemist

The professional designation, European Chemist (EurChem), is open to members of FECS member societies. About 700 chemists have been awarded the designation. The category-A schedule of qualifications lists the approved academic qualification requirements.
http://www.chemsoc.org/networks/enc/ecccqualifintro.htm

AllChemE

A conference on 'The University/Industry Interface' in June brought together representatives of academia and industry to build on previous workshops in preparation for a publication on 'Chemistry Working for Europe'. The publication sets out how university and industry, working together with governments, can meet the needs of society and promote health and prosperity for the people of Europe. AllChemE projects provide oppor-tunities to harness the expertise of the five member organisations of AllChemE.

The AllChemE report 'Chemistry: Europe and the Future' has been published in English, French, German, Italian and Spanish. Subtitled 'Science and Technology to Improve the Quality of Life in Europe', it illustrates research activity in health and agriculture, new materials, energy and protection of the environment, likely to lead to inventions of high significance. *http://www.allcheme.org*

Obituary

Neue Schweizerische Chemische Gesellschaft

Mit grossem Bedauern müssen wir Ihnen
den Hinschied unseres Ehrenmitglieds

Dr. Roger Firmenich

bekannt geben.

Er ist am 27. Juli für immer von uns gegangen.

Eine ausführliche Würdigung des Verstorbenen
wird in einer späteren CHIMIA-Ausgabe erfolgen.

New Members

Berg, Katja, Dr., 4070 Basel

Cervellati, Rinaldo, 40126 Bologna

Huber, Ulrich, Dr., 4070 Basel

Kendrich, Thomas, 4056 Basel

Leroux, Frédéric, Dr., 1007 Lausanne

Reiss, Gilles, 8050 Zürich

Schweizer, Sacha, 6900 Lugano

Sigel, Roland, Dr., New York, NY 10032

Trinh, Vu Duc, 1005 Lausanne

Wesolowski, Tomasz, A. 1202 Genève

CHIMIA 2000, 54, No. 7/8

INFORMATION

News

Jahresbericht 1999 des Schweizerischen Nationalfonds erschienen: Über 300 Millionen für die Forschung

Bern, 27.6.2000 – 305 Mio. Franken hat der Schweizerische Nationalfonds im vergangenen Jahr für Forschungsprojekte zugesprochen. Unterstützt wurden damit rund 4800 meist junge Wissenschafter und Wissenschafterinnen in sämtlichen Disziplinen. Der Nationalfonds lancierte zudem zwei neue Förderungsinstrumente: die Nationalen Forschungsschwerpunkte (NFS) und die SNF-Förderungsprofessuren.

Da die Gesuche in der Grundlagenforschung im Jahr 1999 erneut anstiegen, ist die Schere zwischen den verfügbaren und nachgefragten Mitteln noch immer weit geöffnet. Der ordentliche Bundesbeitrag an die Förderung der Grundlagenforschung stagniert auf dem Niveau der Jahre 1993/1994. Erneut musste der Nationalfonds zahlreiche als qualitativ gut bewertete Forschungsgesuche kürzen oder gar abweisen.

Grundlagenforschung im Zentrum

Die Nationalfonds-Beiträge flossen im vergangenen Jahr zu 44% in Projekte der Biologie und Medizin, zu 37% in die Mathematik, Natur- und Ingenieurwissenschaften und zu 19% in die Geistes- und Sozialwissenschaften – zum weitaus grössten Teil für Saläre in der nicht orientierten Grundlagenforschung. Drei Viertel der unterstützten Forschenden waren unter 35-jährig und über ein Drittel Frauen.

Forschungsarbeiten in den Nationalen Forschungsprogrammen (NFP) und den vom Nationalfonds betreuten Schwerpunktprogrammen (SPP) wurden 1999 mit rund 37 Mio. Franken gefördert. In den Stipendien- und internationalen Austauschprogrammen zur Nachwuchsförderung konnten rund 560 junge Wissenschafterinnen und Wissenschafter ihre Kenntnisse an ausländischen Forschungsinstitutionen erweitern. Angehende oder fortgeschrittene Forschende unter 35 Jahren wurden mit Stipendien von 21.6 Mio. Franken unterstützt.

Neue Förderungsinstrumente

Erfolgreich lanciert hat der Nationalfonds zwei neue Instrumente der Forschungsförderung: die Nationalen Forschungsschwerpunkte (NFS) und die SNF-Förderungsprofessuren. Eine erste Serie von rund zehn NFS - themenspezifischen Kompetenzzentren mit angeschlossenen Netzwerken – kann nach der definitiven Auswahl Anfang 2001 ihre Aktivitäten aufnehmen. Bereits begonnen haben im Frühling dieses Jahres die Forschungsarbeiten der ersten 26 SNF-Förderungsprofessoren und -professorinnen.

Wichtige Aktivitäten in der Forschungszusammenarbeit mit dem Ausland waren die Ausschreibung der Forschungspartnerschaften mit Entwicklungsländern und die Lancierung des neuen Osteuropa-Programms. Damit setzt der Nationalfonds sein jahrelanges Engagement in der Wissenschaftsförderung auch im internationalen Rahmen fort.

Der soeben erschienene Jahresbericht 1999 des Schweizerischen Nationalfonds enthält eine Übersicht über sämtliche im Berichtsjahr finanzierten Forschungsprojekte. Er kann beim Presse- und Informationsdienst des SNF, Wildhainweg 20, 3012 Bern, bezogen werden (Tel.: +41 31 308 22 22).

Weiter Informationen:
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Cytos Biotechnology Receives CHF 50 Million in Second Round of Venture Capital Financing

Pharma contracts and cash infusion give Swiss biotech added momentum; leaders from biotech industry and scientific community elected to the Board of Directors; management team now in place.

Zurich, Switzerland, 25 July 2000 – Cytos Biotechnology AG, which discovers and develops new protein drugs and innovative therapeutic concepts, has announced the completion of a second round of venture capital financing worth CHF 50 million (USD 32 million). The first round of venture capital financing, completed in 1999, generated CHF 11 million.

The independently managed financing round includes the already existing Cytos shareholders Global Life Science (Germany), Innoventure (a subsidiary of Credit Suisse), and Novartis, plus six new investors: Alta Partners (USA), Aventic (a subsidiary of UBS), Health Cap (Sweden), Lombard Odier (Switzerland), New Medical Technologies (Switzerland), and Private Equity Direct Finance (a subsidiary of Bank Vontobel, Switzerland).

Alix Marduel and Rolf Zinkernagel Join Cytos as Board Members

At the General Assembly held on July 14, 2000 in Zurich, the Cytos shareholders elected Alix Marduel M.D., as a representative of Alta Partners, and Prof. Rolf Zinkernagel M.D., Professor of Experimental Immunology at the University of Zurich, as new Board members.

Having invested in 20 life science companies, including Millennium Pharmaceuticals, Genset, CV Therapeutics and Aviron, Dr. Alix Marduel has very broad experience in the biotechnology industry, both in the United States and in Europe. Prof. Rolf Zinkernagel has been a member of Cytos's Scientific Advisory Board for more than two years. 'His unchallenged expertise in the field of immunology and his vision will continue to be invaluable for our future development', Dr. Renner added.

Management Team Complete

Cytos also announced the completion of its Executive Board with the recent appointment of Lothar Germeroth, PhD, as VP Business Development, and Jakob Schlapbach as Chief Financial Officer. The Executive Board further comprises Martin Bachmann, PhD, as Chief Scientific Officer, and Wolfgang Renner, PhD, as CEO and President of Cytos.

Lothar Germeroth has, in the role of CEO, successfully managed two German biotech companies. As CFO of two publicly quoted companies over the last ten years, Jakob Schlapbach brings with him solid financial experience. He has served as CFO of Ascom in Berne since 1994. Martin Bachmann joined Cytos from the Basel Institute for Immunology where he had the position of a senior member. During his career he has published over 100 articles in internationally renowned scientific journals.

Cytos: Functional Reproduction of the Human Proteome

Cytos is in an ideal position to ride the wave of post-genomics innovation that is revolutionizing the search for new drugs. Its DELphi technology functionally reproduces the 100 000 human proteins and makes this huge pool of potent therapeutic molecules available to pharmaceutical R&D.

In contrast to gene sequence information, which does not deliver therapies, the derived proteins are real drug candidates. The technology developed by Cytos eliminates a critical discovery bottleneck in the post-genomics era. It feeds pharmaceutical companies with the relevant proteins to be used as drugs or targets. Starting from zero in 1982, the market for therapeutic proteins has grown to USD 20 billion in 1999, and is expected to grow at a rate of approximately 20% per year.

Cytos's integrated technology portfolio enables the company to develop its protein drugs and new therapeutic concepts up to clinical trials. Cytos has established a biopharmaceutical product development capability in accordance with current regulatory requirements. In the past few years, this business has been validated through a number of high-value licensing agreements.

Cytos recently signed a major research and option contract with a large pharmaceutical company. This contract is worth USD 1.6 million in R&D support in the first phase and has potential for significant additional research funding and milestone payments plus long-term royalties.

For More Information, Please Contact:
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www.cytos.com

Symyx Technologies and Lonza Group Enter into Discovery and Licensing Agreement for Catalyst Discovery

Basel, July 11, 2000 – Symyx Technologies, Inc. (NASDAQ: SMMX) and Lonza Group (SXW:) today announced that they have entered into a discovery and licensing agreement to develop novel catalysts for the manufacture of chemical intermediates. Chemical intermediates are critical for numerous organic syntheses, including the manufacture of pharmaceuticals and agrochemicals. The catalysts that Symyx seeks to discover in this collaboration would reduce the costs and increase the efficiency of manufacturing processes. Lonza will fund a portion of the research effort, make a milestone payment upon success, and have exclusive rights to use discovered catalysts in their manufacturing processes. In addition, Symyx will receive royalties from the sale of chemical intermediates manufactured using its catalysts. These catalysts could be in commercial use within 12–18 months of discovery.

Symyx is applying its proprietary technologies in chemistry, parallel reactors, high throughput screening and software expertise to the fine and specialty chemicals industry. Symyx has the ability to synthesize and test hundreds to thousands of catalysts at a time and under varying reaction conditions, offering a more cost-effective and productive approach to catalyst discovery and process optimization. In fine chemicals, Symyx has validated chemistry platforms to discover a broad range of catalysts, including chiral chemistry, hydrogenation, aromatic cross-coupling, Friedel Crafts catalysis and selective oxidation.

Lonza Group is a specialty chemicals company headquartered in Switzerland, with sales of CHF 2.2 billion in 1999 and operating 20 facilities in eight countries. It employs 5600 people worldwide and is the leading supplier of active chemical intermediates and biotechnology solutions to the pharmaceutical and agrochemical industries. It also offers a broad catalogue of organic intermediates for a wide range of applications such as pharmaceuticals, agrochemicals, vitamins, food and feedstuff, dyes and pigments, adhesives and fragrances as well as polymers and plastics. Furthermore the Group manufactures specialty biocides and oleochemicals.

Symyx develops and applies combinatorial technologies to the discovery of materials for the life sciences, chemical and electronics industries, through industry collaborations, Symyx Proprietary Materials and Discovery Tools Technology Access.

Symyx was founded by Dr. Alejandro C. Zaffaroni, founder of ALZA, Affymax N.V., Affymetrix and Maxygen, and Dr. Peter G. Schultz, head of the Novartis Institute for Functional Genomics and professor of chemistry at the Scripps Research Institute.

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Brennstoffzellen – eine moderne umweltschonende Energieerzeugung

Brennstoffzellen gelten als Stromerzeuger der Zukunft. Integriert man sie in ein kleines Blockheizkraftwerk, so lässt sich neben dem Strom auch die anfallende Wärme für Heizung und Warmwasser im Haushalt nutzen. Solche Pilotanlagen sind seit 1997 im Betrieb.

Mit explosiver Gewalt vereinigen sich Sauerstoff und Wasserstoff zu Wasserdampf, wenn ein Gemisch der beiden Gase von einem Funken gezündet wird. In der Brennstoffzelle läuft dieselbe Reaktion kontrolliert ab – ohne Knall und Flamme. Dabei fällt nutzbare Energie an. Brennstoffzellen ermöglichen den Bau von effizienten Wärme-Kraft-Kopplungsanlagen. Ihr grosser Vorteil liegt in ihrem emissions- und geräuscharmen Betrieb fast ohne bewegliche Teile und in ihrer Effizienz. Sulzer Hexis AG hat eine Festoxidbrennstoffzelle (SOFC) entwickelt, die 2001 auf den Markt kommt. Ein Brennstoffzellenstapel ist so ausgelegt, dass er den Strombedarf eines Durchschnittshaushalts deckt (1 kW elektrische Leistung).

Im Mai 1997 nahmen die Städtischen Werke Winterthur eine Pilotanlage in Betrieb – *weltweit das erste in der Praxis getestete Miniblockheizkraftwerk, in dem die Energie durch Brennstoffzellen erzeugt wird.* 1998 kamen in Basel, in Deutschland und in Japan weitere Pilotanlagen hinzu.

An der Zürcher Hochschule Winterthur (ZHW) wird seit 1993 Brennstoffzellenforschung in Zusammenarbeit mit Sulzer Hexis und dem Paul Scherrer Institut (PSI) betrieben. Mittlerweile sind drei ZHW Departemente involviert:

- Im Departement Physik und Mathematik werden Stoff-, Wärme- und Ladungstransport, elektrochemische Reaktionen und Fluidströmung innerhalb von Brennstoffzellen simuliert.
- Ein Leittechnikkonzept für eine 3 kW Anlage wird im Departement Maschinenbau und Energietechnik entworfen.
- Im Departement Chemie wird einerseits in Zusammenarbeit mit dem PSI an der Polymer-Elektrolyt-Membran Brennstoffzelle geforscht und andererseits die Aufbereitung von Brennstoffen (insbesondere von Biogas und -ethanol) für die Sulzer-Hexis Brennstoffzelle (SOFC) zur experimentellen Überprüfung von Simulationsmodellen untersucht.

Neben Dozenten, Wissenschaftlichen Mitarbeitern, Assistenten und Angestellten sind auch Studierende und Diplomanden in diese bedarfsorientierte Forschung einbezogen.

Für Rückfragen:
ZHW: Thomas Spielmann,
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thomas.spielmann@zhwin.ch
Sulzer Hexis: Dr. Alex Schuler,
Tel. 052/262 82 97
E-mail: alexander.schuler@sulzer.ch

Wettbewerb mit Prestige

Mit dem Wettbewerb bieten öffentliche und private Sponsoren aus Industrie und Finanzwelt eine Plattform, damit aus technologischen Spitzenleistungen geschäftliche Erfolge werden. Schweizer Innovationen sollen optimale unternehmerische Startchancen erhalten.

Seit diesem Jahr steht der bedeutendste Technologiewettbewerb der Schweiz unter dem Patronat des Staatssekretariates für Wirtschaft (seco) und der Konferenz der kantonalen Volkswirtschaftsdirektoren. Wer mit seiner Innovation puncto Technologie, Originalität und Markpotential die Wettbewerbsjury überzeugt, kann sich auf den Schweizer Gemeinschaftsständen der CeBIT 2001 und der Hannover Messe 2001 dem Fachpublikum aus aller Welt präsentieren.

Das Renommee der Initiative 'Technologiestandort Schweiz' ist einzigartig, auch international. Der Preis hilft den Gewinnern nicht nur bei der Suche nach Partnern und Kunden, sondern gilt erfahrungsgemäss als excellenter Türöffner bei Banken und Behörden. Zuletzt schafften zwei Preisträger den Sprung in den New Market.

Eingeladen zum Wettbewerb sind Unternehmen, junge Technologieunternehmen, start-ups und spin-offs sowie innovative Kooperationsprojekte von Hochschulen und Fachhochschulen mit der Wirtschaft.

Die Ausschreibung läuft noch bis zum 30. September 2000.

Die Ausschreibungsunterlagen und weitere Auskünfte sind erhältlich bzw. *via* Internet abrufbar bei:
Technologiestandort Schweiz
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Untere Sternengasse 2
CH–4504 Solothurn
Tel.: +41 32 627 95 27
Fax: +41 32 627 95 92
E-Mail: urs.stuber@awa.so.ch
URL:
http://www.awaso.ch/arbeitgeber

CHIMIA-REPORT

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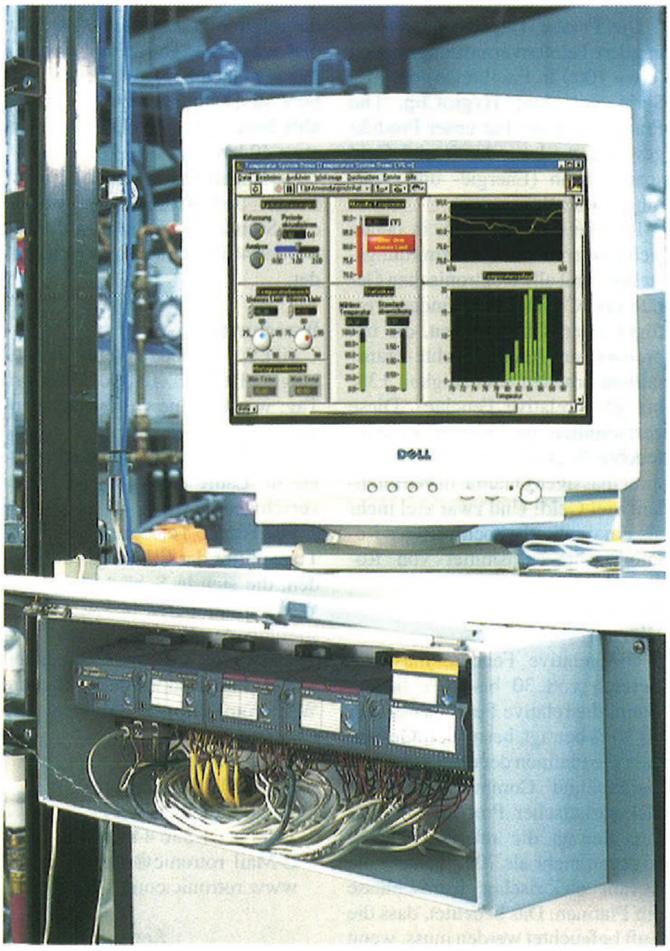
Fortsetzung von Seite A381

Internet-Optimierte Software vereinfacht Datenverteilung

Mit Hilfe von **LabVIEW 6i** und dem neuen LabVIEW Player sind Ingenieure und Wissenschaftler unabhängig von ihrem Aufenthaltsort in der Lage, direkt von Ihrem Web-Browser aus auf VIs zuzugreifen. Dazu müssen die entsprechenden VIs einfach erstellt und die Anwendungen über das Internet zur Verfügung gestellt werden. Anschliessend können die VIs mit Hilfe des LabVIEW Players geöffnet und ausgeführt werden. Der LabVIEW Player ist kostenfrei bei National Instruments unter folgender Internetadresse erhältlich: www.ni.com/labview

Doch nicht nur VIs, sondern auch Mess- und Steuerdaten können sowohl innerhalb eines Unternehmens als auch weltweit über das Internet zugänglich gemacht und genutzt werden. Mit LabVIEW 6i können Anwender die aktuellsten Daten in regelmässigen Abständen publizieren oder sogar automatisch updaten lassen - und das ganz ohne Programmieren. Aktuelle Daten können von der Benutzeroberfläche aus mit einem einzigen Mausklick in das Internet oder in andere Anwendungen übertragen werden.

Mit LabVIEW 6i können Ingenieure und Wissenschaftler Steuerungsanwendungen auch ihrem gesamten Unternehmen transparent zugänglich machen. So können sie beispielsweise die Daten von einem dezentralen Rechner erfassen, von einer leistungsstärkeren Workstation analysieren und die Ergebnisse dann an einem beliebigen Ort im Netzwerk ausgeben lassen.



Intelligente Messung und Steuerung – mit sofortiger Wirkung

Mit LabVIEW 6i führt National Instruments das Konzept der Mess- und Steuerungsintelligenz ein – die Integration von auf die Belange der Messtechnik zugeschnittenen I/Os, Sensoren und Software, mit deren Hilfe verfügbare Mess- und Steuerungskomponenten automatisch erkannt und konfiguriert werden können. Auf diese Weise können die Anwender Steuerungsapplikationen mit wesentlich weniger Programmieraufwand erstellen und so die Entwicklungszeit reduzieren. Zudem bietet LabVIEW 6i eine Vielzahl von Mess- und Steuerungsfunktionen für die Datenerfassung und Gerätesteuerung sowie neue Bibliotheken für die Bilderfassung und Motorensteuerung. Auch mangelt es in dieser neuen Version von LabVIEW nicht an Funktionen, mit denen die Leistungsfähigkeit des Systems und somit die Produktivität der Anwender gesteigert werden kann. So können beispielsweise die Steueralgorithmen in Verbindung mit Einzelpunktmessungen in LabVIEW 6i bis zu 4,7-mal schneller ausgeführt werden als in vorherigen Versionen.

Benutzeroberfläche in neuem Gewand

LabVIEW 6i nutzt hoch entwickelte ComputergrafikTechnologien und kann so mit einfach zu handhabenden dreidimensionalen Steuerelementen für die Benutzeroberfläche aufwarten, mit denen professionelle Steuerungsanwendungen besonders schnell entwickelt werden können. Weiterhin gibt es in LabVIEW 6i auch neue Funktionen zur Darstellung von Daten, wie z. B. Diagramme und Graphen mit mehreren Achsen und einen neuen Digital-I/O-Graphen, mit dem Timing-Daten und Bitmuster veranschaulicht werden können. Ausserdem bietet LabVIEW jetzt auch mehr Microsoft Windows-konforme Steuerelemente, wie etwa Eigenschaftenseiten, mehrspaltige Listenfelder und vom Anwender erstellbare Tip-Strips für Elemente der Benutzeroberfläche.

Weitere Informationen

LabVIEW 6i ist ab Q3 2000 für Windows 2000/NT/9X, Mac OS, Linux, Solaris und HP-UX erhältlich. Die deutsche Version wird in Q4 2000 verfügbar sein. Weitere Informationen über LabVIEW 6i:

- National Instruments
  Sonnenbergstrasse 53
  CH–5408 Ennetbaden
  Telefon 056 / 200 51 51
  Telefax 056 / 200 5155
  E-Mail ni.switzerland@ni.com
  oder National Instruments
  InstrumentationWeb™ unter
  http://www.ni.com/switzerland
  S.A.W., Basel:
  Halle 1.1, Stand A66

Leserdienst Nr. 1

Einzigartiges zweistufiges Desorptionsverfahren für reduzierte Betriebskosten im Labor

Der neue Thermodesorber TurboMatrix von PerkinElmer leistet einen Beitrag zur Reduktion der Betriebskosten im Labor: ein flexibles, einfach zu bedienendes System für genaue, reproduzierbare Ergebnisse, das sämtliche Anforderungen an die Probenvorbereitung erfüllt.

Eine graphische Benutzeroberfläche mit Touch-Screen bietet einfachen Zugriff auf wichtige Informationen , z.B. visuelle Anzeigen des Gerätebetriebes, Setpoints und aktuell eingestellte Temperatur- und Druckwerte. Bei Anwendungen im Bereich der Umweltanalyse, Produktentwicklung, Qualitätskontrolle und Fehler-beseitigung (bei ausserhalb der Spezifikation liegenden Produkten) ersparen TurboMatrix-Thermodesorber aufwendige manuelle Probenvorbereitung.

Ein völlig neuartiges, zweistufiges Verfahren dient zur Desorption von Probenbestandteilen aus dem Probenröhrchen und Refokussierung in einer Kühlfalle mit besonders kleinem Volumen. Anschließend erfolgt ein direkter Transfer der Proben auf die GCSäule. Diese neue Technologie verzichtet auf die Verwendung teuren Flüssig-Cryogens (N2 flüssig) und spart daher Betriebskosten. Weiterhin bietet sie verbesserte chromatographische Ergebnisse und liefert mit einer Heizrate von 400C/Sekunde kleinere Peakbreiten. Analysen über einen breiteren Siedebereich und verbessertes Wasser-Management sind weitere Vorteile.

TurboMatrix-GC-Thermodesorber ermöglichen die direkte Desorption der Probe innerhalb des Gerätes - für die Probenanalyse ist kein Lösungsmittel erforderlich. Da keine Verdünnung durch Lösungsmittelextraktion erfolgt, verbessert sich die Messempfindlichkeit um den Faktor 1000.

- Perkin Elmer (Schweiz) AG
  Bösch 106
  CH–6331 Hünenberg
  Telefon +41 41 785 77 55
  Telefax +41 41 785 77 95

Leserdienst Nr. 2

Immer einige Wellenlängen voraus

Bei Messergebnissen zählt für Sie vor allem eines – Sie müssen sich darauf verlassen können. Die neue Konzeption des Spektralphotometers SPECORD 50 kombiniert den hohen Energiedurchsatz eines Einstrahlphotometers mit der Stabilität eines Zweistrahlphotometers unter Ausnutzung der innovativen Split-Beam Technologie (SBT).

Für Sie bedeutet das: hervorragendes Signal-Rausch-Verhältnis, kurze Messzeit, sehr niedrige Erfassungsgrenze, gute Kurz- und Langzeitstabilität, keine Einlaufphase.

SPECORD 50 erfüllt mit Leichtigkeit die Anforderungen internationaler Vorschriften und Pharmakopöen. Eine quarzvergütete Optik bietet besten Schutz und garantiert eine ausgesprochene Langlebigkeit der optischen Komponenten. Eine Aluminiumguss-Basisplatte ist die Grundlage für hohe optische und mechanische Stabilität. Die minimale Anzahl mechanisch bewegter Teile garantiert Zuverlässigkeit. Sowie die innovative Split-Beam-Technologie und die spannungsstabilisierten Strahlungsquellen ergeben präzise Messwerte.

Der grosszügig dimensionierte Probenraum erlaubt eine schnelle und leicht zu wiederholende Zugabe von Reagenzien und einen zügigen Wechsel von Proben und Zubehör.

Zu dem vielfältigen Zubehör gehören unter anderem ein temperierund rührbarer 6-fach Küvettenwechsler, ein Sippersystem mit Durchflusseinheit, Lichtleiterauskopplung, temperier-und rührbare Einfachküvettenhalter, Mikro- und Halbmikroküvettenhalter, Reflexionsmesseinsätze für Messungen an festen Proben und ein Sipper-Sampler System. Das SPECORD 50 verfügt über eine zweite Probenposition, speziell für trübe Proben.

Für ihre individuellen Applikationen können Sie zwischen der stand-alone Variante und der PC-Variante wählen.

Die menügeführte 32-Bit Software WinASPECT zur GLP gerechten Steuerung des Messprozesses, der Methodenerarbeitung und der Auswertung mit audit-trail Funktion ist ohne lange Einarbeitungsphase zu bedienen.

Die Gliederung der Software ermöglicht eine optimale Anpassung an verschiedene Applikationen wie: Addition, Subtraktion, Peaksuche, Glättung, Ableitung, Kinetik, quantitative Analytik, Schichtdickenmessung, Biologie, Farbmessung, Multikomponentenanalytik sowie Validierung und Makroprogrammierung.

- CONTREC Technologies AG
  Riedstr. 6
  CH–8953 Dietikon
  Telefon 01/746 32 20
  Telefax 01/746 32 29
  E-Mail contrec@bluewin.ch

Leserdienst Nr. 3

FH-Serie bei FRANCE TELECOM

Die France Telecom verwendet in allen Telefonvermittlungsstellen (etwa 1000 in Frankreich) die FH-Serie mit dem HygroClip. Die France Telecom hat unser Produkt gewählt, weil sie damit viel Geld sparen kann (Energie- und Wartungskosten)!

Die meisten Gebäude, in denen sich moderne Telefonvermittlungsstellen (und alle elektronischen Geräte und Computer) befinden, verfügen über Klimaanlagen, die mit preiswerten Relativfeuchte-Transmittern arbeiten (Genauigkeit ±3% bis ±5% relative Feuchte). Diese vermeintlich preiswerten Relativfeuchte-Transmitter kosten wegen ihrer mässigen Qualität in Wirklichkeit viel Geld! Und zwar viel mehr als ein qualitativ hochwertiger Relativfeuchte-Transmitter von Rotronic.

Warum?

Die relative Feuchte muss im Bereich von 30 bis 70% liegen. Wenn die relative Feuchte weniger als 30 % beträgt, besteht die Gefahr, dass die Platinen der elektronischen Geräte und Computer aufgrund elektrostatischer Probleme ausfallen. Beträgt die relative Feuchte dagegen mehr als 70%, besteht die Gefahr elektrischer Kurzschlüsse auf Platinen. Das bedeutet, dass die Luft befeuchtet werden muss, wenn die relative Feuchte auf 31% fällt, und dass sie getrocknet werden muss, wenn die relative Feuchte auf 69% steigt. Solche Systeme haben üblicherweise eine Leistung von etwa 40 kW.

Bedenken Sie: Wenn die Trocknungs- und Befeuchtungssysteme eine Stunde länger laufen als nötig, werden 40 kWh Energie verschwendet.

Berechnung:

40 kWh x 1000 (Telefonvermittlungsstellen) = 40 000 kWh pro Tag; was für eine Geldverschwendung!

Überlegen Sie nur, wieviel Energie im Laufe eines ganzen Jahres verschwendet wird!

Die France Telecom hat sich für Transmitter der FH-Serie entschieden, die sich in Schächten und an Wänden montieren lassen. Die Justierung des HygroClip, die Austauschbarkeit und die Genauigkeit waren die Hauptgründe für die Wahl von RotronicProdukten.

- Rotronic AG
  Grindelstrasse 6
  CH–8303 Bassersdorf
  Telefon 01/838 11 11
  Telefax 01/836 44 24
  E-Mail rotronic@rotronic.ch
  www.rotronic.com

Leserdienst Nr. 4

Klimakammern für die Automobil-Industrie mit Rotronic Transmittern ausgerüstet

Die Leistungen übertreffen die Erwartungen! Die Firma Clive Hurley Environmental Engineering ist einer der weltweit führenden Hersteller von Klimakammern. Eine kürzlich errichtete Anlage in Grossbritanniens führendem Automobilentwicklungszentrum LTC wurde mit dem industriellen Feuchte- und Temperaturtransmitter Rotronic I-2000 ausgerüstet. Bisher arbeitete die Fa. Clive Hurley in der Feuchtemessung stets mit der Trocken- und Feuchtkugelpsychrometrie, aber wegen des breitgefächerten Betriebsbereichs der LTC-Kammer wird neu ein I-2000-Transmitter von Rotronic verwendet.

Dazu erklärte Direktor Andrew Hurley: 'Oberhalb 100° C und unterhalb 0° C sind Feuchtemessungen mit der Trocken- und Feuchtkugelpsychrometrie natürlich nicht durchführbar. Unser Kunde musste aber die Feuchte im gesamten Betriebsbereich der Klimakammer messen können. Der Rotronic I-2000 bot den grössten Temperaturbereich, so dass wir uns natürlich für dieses Produkt entschieden. Nach der Montage waren wir von seiner Genauigkeit, Stabilität und Ansprechzeit wirklich beeindruckt.'

Die LTC-Prüfkammer ist für Fahrzeuge bis zu einer Grösse von Sattelzugmaschinen ausgelegt. Ihre Innenmasse betragen 3,3x4,3x6,3 m, und ihre Tragfähigkeit beträgt 8 Tonnen! Der Temperaturbereich bewegt sich von –40 bis +120° C, wobei die Relativfeuchte im Temperaturbereich von 10 bis 70° C bis zu 99% beträgt. Ausserdem kann starke Sonneneinstrahlung simuliert werden, sodass fast alle Bedingungen der 'realen Welt' geprüft werden können. Zu den Unternehmen, die die LTC-Kammer bereits benutzt haben, gehört auch der Sportwagenhersteller TVR .

Die Rotronic-Transmitter I-2000 sind in zahlreichen Konfigurationen lieferbar, wodurch sie praktisch für alle Anwendungsfälle eingesetzt werden können. Die maximalen Messbereiche betragen 0 bis 100% relative Feuchte und –50 bis +200° C, wobei eine Betriebstemperatur von bis zu –75° C die Sensoren nicht negativ beeinflusst. Der Messfühler des I-2000 ist oben am hinteren Ende der Kammer zu erkennen.

- Rotronic AG
  Grindelstrasse 6
  CH–8303 Bassersdorf
  Telefon 01/838 11 11
  Telefax 01/836 44 24
  E-Mail rotronic@rotronic.ch
  www.rotronic.com

Leserdienst Nr. 5

Neu: Camera Advisor™ von National Instruments

Nutzen Sie die NI-Internetseiten mit ihrer grossen Auswahl an Kameras zur maschinellen Bildverarbeitung und wissenschaftlichen Bildanalyse

Für Ingenieure und Wissenschaftler auf der Suche nach wissenschaftlichen Bilderfassungskameras bietet dieser Teil der Internetseiten von National Instruments nun eine komprimierte Informationsquelle. Unter www. ni. com/ camera kann sich der Anwender vom Camera Advisor Merkmale und Spezifikationen von mehr als 100 Kameras anzeigen lassen und diese miteinander vergleichen. Zudem erklärt der Camera Advisor wie die verschiedenen Kameras mit Hard- und Software von National Instruments kombinierbar sind.

'Das Schöne am Camera Advisor ist, dass er Kameras und Zubehör entsprechend der Bedürfnisse Ihrer industriellen und wissenschaftlichen Applikation vorschlägt.', so John Hanks, National Instruments Vision Produkt Manager. 'Durch die Nutzung des Internets erhalten Sie zahlreiche technische Spezifikationen verschiedener Anbieter. Mit dem Camera Advisor finden Sie dies alles auf einer Webseite.'

Ingenieure und Wissenschaftler, die diese neue Seite auf den Internetseiten von National Instruments besuchen, können sich über die unterschiedlichen Modelle und Funktionen der Kameras wie Zeilen-, Flächen-, Progressive Scan, Digital- und Analogkameras informieren. Mit Hilfe des Camera Advisor können technische Details hinsichtlich der Sensorengrösse, Pixeldichte, Framerate und Pixeltaktrate verglichen werden. Unter den dargestellten Kameras finden sich u.a. Kameras zur maschinellen Bildverarbeitung und wissenschaftlichen Anwendung von Sony, Dalsa, JAI, Kodak, Basler und Pulnix.

Als ersten Schritt fragt der Camera Advisor den Anwender nach den Spezifikationen der Applikation, bevor er geeignete Kameramodelle vorschlägt. Auch bietet er Links zu den Webseiten verschiedener Anbieter, so dass der Benutzer die für seine Applikation optimale Kamera direkt online erwerben kann.

Ingenieure und Wissenschaftler verwenden Kameras oft für optische Messungen und zum automatisieren diverser Aufgaben. Computergestützte Systeme erfassen Bilder von Kameras mit hoher Geschwindigkeit – ideal für die Prüfung von Produkten während der Herstellung. Die Programmierung solcher computerbasierten Systeme kann mit LabVIEW™ von National Instruments erfolgen, dessen grafische Werkzeuge vielen Ingenieuren und Wissenschaftlern vertraut sind.

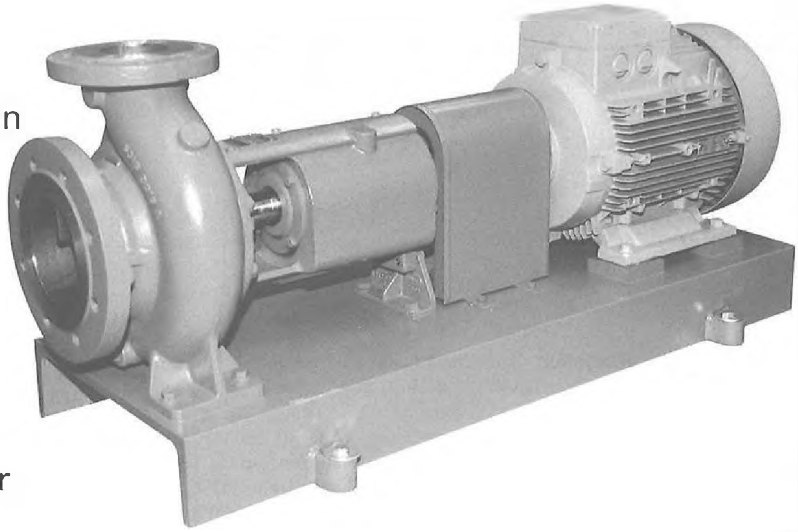
'Die Erstellung eines Bilderfassungssystems erfordert eine genaue Planung.' Erläutert Hanks. 'Man muss berücksichtigen, wie die Kamera und der Computer miteinander kommunizieren sollen. Diese und weitere hilfreiche Informationen liefert der Camera Advisor und erleichtert es Ihnen so, eine kompetente Entscheidung zu treffen.'

Zusätzlich erklärt der Camera Advisor allgemeingültige Bilderfassungs-Begriffe sowie Links zu Leitfäden über die Bilderfassung – auch zu finden auf der Webseite von National Instruments unter

- www.ni.com/camera.
  National Instruments
  Sonnenbergstr. 53
  CH–5408 Ennetbaden
  Telefon 056/200 51 51
  Telefax 056/200 51 55
  E-Mail ni.switzerland@ni.com

Leserdienst Nr. 6

CHIMIA 2000, 54, No. 7/8



DNA-, PCR- oder Vollblutproben sicher Pipettieren?

Kontaminationsfreies Pipettieren mit dem MICROMAN® von GILSON.

Der MICROMAN® ist eine variable Pipette für den Volumenbereich von 0.5 µl bis 1000 µl, die mit einer speziellen Spitze nach dem Direktverdrängungs-Prinzip (positive displacement) arbeitet. Hierdurch wird die Aerosolbildung, eine häufige Ursache für Kontamination (z.B. bei der Amplifikation von Nukleinsäuren) vollständig eliminiert.

Der MICROMAN® erlaubt schnelles, genaues und kontaminationsfreies Pipettieren von schwierigen Flüssigkeiten.

- Einhändige Spitzenaufnahme und -abgabe dank integriertem Spitzenabwurf
- Dank dem ergonomischen Design und dem geringen Gewicht (46 g) ist auch längeres Arbeiten ohne Ermüdung der Hand möglich
- UV-stabil, autoklavierbar und hohe Resistenz gegenüber Säuren und Lösungsmittel
- Spitzen in Racks, wahlweise γ-sterilisiert erhältlich
- Isolierter Griff um Erwärmungseffekte zu verhindern

Wo eine Kontamination nicht riskiert werden darf oder hohe Kosten nach sich zieht (Gerichtsmedizin, Pharmaforschung etc.), ist der MICROMAN® bereits der Standard.

Auch in anderen Industriezweigen erfreut sich der MICROMAN® wachsender Beliebtheit. Dies hat er vor allem seinem weiten Einsatzgebiet zu verdanken. Bei hochviskosen, leichtflüchtigen, gefährlichen oder korrosiven Flüssigkeiten ist der Einsatz von normalen Kolbenhubpipetten eingeschränkt oder unmöglich. Hier bietet der MICROMAN® eine echte Alternative resp. Lösung an.

Der MICROMAN® ist in 6 Ausführungen erhältlich für Volumen von 0.5 µl bis 1000 µl.

- OmniLab Biosystems AG
  Untere Bahnhofstrasse 14
  CH-8932 Mettmenstetten
  Telefon 01 768 22 11
  Telefax 01 768 23 21
  E-Mail omnilab@omnilab.ch

Leserdienst Nr. 7

Analysis of Herbal Drugs

If analysis of herbal drugs is your analytical task, you have good reasons to choose planar chromatography. It is a robust method, tolerating wide variation in sample matrix.

Planar Chromatography is the ideal tool for:

- Identity checks by fingerprints analysis
- Detection of adulteration
- Quantitation of marker compound
- Stability test HMP's

CAMAG offers you:

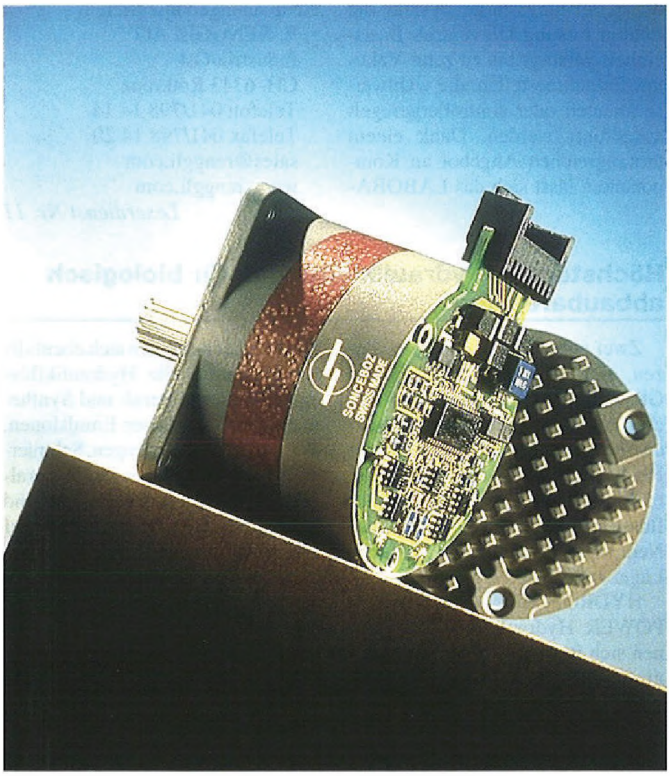
- A complete line of products and consumables for Planar Chromatography
- Methods and training to help optimizing your results
- Contract lab services, including feasibility studies, method development / validation and QC

Request the current list of CAMAG applications on 'natural products, plant ingredients'/new herbal brochure or visit our Homepage www.camag.ch

- CAMAG
  Sonnenmattstrasse 11
  CH-4132 Muttenz
  Telefon +41 61 467 34 34
  Telefax +41 61 461 07 02
  E-Mail info@camag.ch

Leserdienst Nr. 8

Mechatronische Schrittmotorantriebe Serie 8000



Mechatronische Antriebe bestehen aus einer Mechanik für lineare oder rotative Bewegungen, einem Schrittmotor und der Elektronik mit passenden Steuerschnittstellen. Durch die Integration all dieser Elemente in den Motor ergeben sich Antriebssysteme mit vorteilhaften Eigenschaften wie etwa eine optimale Abstimmung von Antrieb und Motor, geringe Abmessungen und sehr gute EMV-Eigenschaften. Für den Anwender wirkt sich dies in Form von höherer Dynamik, geringerem Verkabelungsaufwand und reduziertem Platzbedarf aus.

Dadurch ergeben sich neue Anwendungen wie beispielsweise in Textilmaschinen, in der Hydraulik, in medizinischen Geräten oder auch in der Automatisierung.

Die Antriebe lassen sich über ihre Puls/Drehrichtungsschnittstelle an beliebige Positioniersteuerungen anschliessen. Optional sind auch Feldbusanschlüsse wie z.B. CAN oder RS 485 realisierbar. Mit Drehmomenten bis 0,8Nm, Auflösungen von 1600 Schritten pro Umdrehung oder mehr und Abmessungen in der Grösse eines Tennisballs steht dem Anwender ein miniaturisiertes Kraftpaket für das präzise und zuverlässige Positionieren zur Verfügung.

- Sonceboz SA
  Rue Rosselet-Challandes
  CH-2605 Sonceboz
  Telefon +41 (0)32/488 11 11
  Telefax +41 (0)32/488 11 10
  E-mail info@sonceboz.com
  www.sonceboz.com

Leserdienst Nr. 9

Wärmemessungen mit LabView™

Kostenfreie Zusatz-Software für Lab VIEW und IMAQ™ Vision ist kompatibel mit Infrarot-Kameras von FLIR

National Instruments und FLIR Systems Inc. haben in einem gemeinsamen Projekt Software zur Wärmebilderfassung für die Produkte LabVIEW und IMAQ Vision entwickelt. Um der steigenden Nachfrage nach integrierten Wärmebildmessungen in computerbasierten Mess- und Automatisierungssystemen gerecht zu werden, haben sich FLIR Systems Inc., einer der führenden Hersteller von Wärmebildkameras, und National Instruments als einer der führenden Produzenten im Bereich der computerbasierten Mess- und Automatisierungstechnik zusammengeschlossen.

FLIR entwickelt Infrarot-Kameras für die Industrie, wo der Bedarf an Wärmebilderfassungen im Bereich der Motorenüberwachung und präventiven Wartung stetig wächst. Infrarot-Kameras messen die Abgabe von thermischer oder infraroter Energie, die das blosse Auge nicht erfassen kann. Die beobachteten Objekte geben Wärme als infrarote Energie ab, die die Kamera erfasst und den Unterschied verschiedenfarbig darstellt. Die 'Thermovision InfraRed Machine Vision'-Kameras (IRMV) von FLIR Systems ermöglichen Wärmebildmessungen mit mehr als 76.000 Punkten. In Kombination mit LabVIEW wird es für Ingenieure und Wissenschaftler nun möglich, derartige Wärmebilder mit Hilfe computergestützter Messungen aufzunehmen und auszuwerten. Mit IMAQ Vision können die Qualität und Beschaffenheit beurteilt werden. So würde beispielsweise ein undichtes Rohr durch die Wärmebildänderung auf Grund des austretenden Gases erkannt werden.

'Infrarot-Kameras arbeiten besonders effektiv in Applikationen zur Qualitätskontrolle', erklärt Chris Alicandro, Direktor 'New Business Development' bei FLIR Systems. 'Thermalkameras werden immer günstiger und bedürfen keiner aufwendigen Wartung mehr, so dass Systeme der Wärmebilderfassung mittlerweile in Herstellungsverfahren eingesetzt werden.'

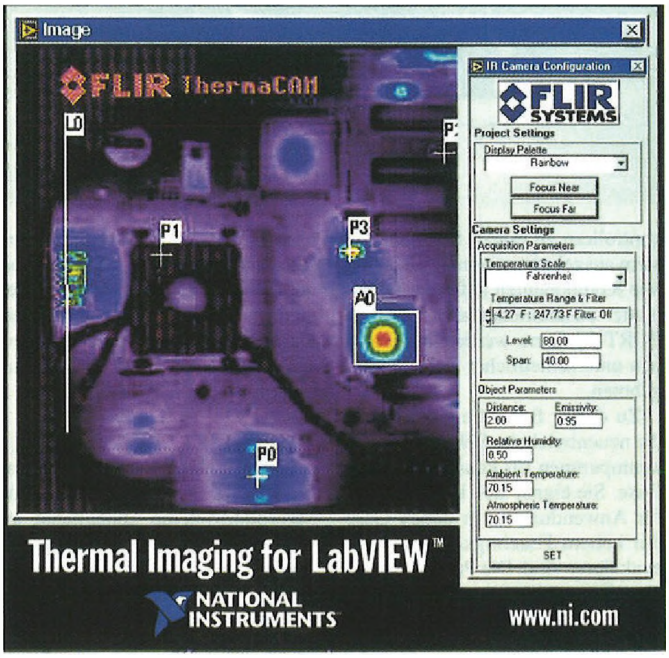
Die Bandbreite der Applikationen, die LabVIEW und die IMAQ Vision-Funktionen der Mustererkennung und Partikel-Analyse zusammen mit Wärmebildkameras verwenden, reicht von der Produktauswertung bis zur Untersuchung elektronischer Komponenten. Die Messung veränderter Temperaturen von elektronischen Komponenten liefert wertvolle Informationen für präventive Wartungsprogramme. 'Solche Applikationen können mit der graphischen Programmierung LabVIEW schnell erstellt werden', so John Hanks, Produktmanager für IMAQ Vision bei National Instruments. 'Die Verwendung von LabVIEW und IMAQ Vision ermöglicht die Erfassung von Wärmebildern und eine schnelle Auswertung der Resultate. Aufgrund der Konnektivität und Leistungsstärke eines PCs kann dann ein Austausch mit Kollegen über das Internet erfolgen. Die Einbindung von Datenerfassungsprodukten und anderen Produkten von National Instruments wie programmierbaren Controllern ermöglicht beispielsweise auch die Überwachung und Steuerung von Prozessen.'

Über das FLIR-System

FLIR entwickelt, produziert und vertreibt weltweit InfrarotBildsysteme für eine Vielzahl von Applikationen. Die Produkte werden in zahlreichen Anwendungen eingesetzt. Im kommerziellen Bereich sind sie z.B. in der Bildübertragung, Zustandsüberwachung, in Sicherheitstests, Forschung und Entwicklung und in der Produktionsüberwachung im Einsatz. Weitere Informationen hierzu sowie die Möglichkeit Virtuelle Instrumente (VI) in LabVIEW zur Steuerung von FLIR-Kameras herunterzuladen erhalten Sie auf der FLIR-Webseite unter www. flir. com.

- National Instruments
  Sonnenbergstr. 53
  CH-5408 Ennetbaden
  Telefon 056/200 51 51
  Telefax 056/200 51 55
  E-Mail ni.switzerland@ni.com

Leserdienst Nr. 10



Project Settings
Display Palette: Rainbow
Camera Settings
Acquisition Parameters
Temperature Scale: Fahrenheit
Temperature Range & Filter: -4.27 F : 247.73 F Filter: Off
Level: 80.00
Span: 40.00
Object Parameters
Distance: 2.00
Emissivity: 0.95
Relative Humidity: 0.50
Ambient Temperature: 70.15
Atmospheric Temperature: 70.15

Vielfalt an Vakuumsystemen

Seit 1998 vertreibt die Firma E. Renggli AG die Labor-Vakuumpumpen von der Firma KNF Neuberger AG exklusiv in der Schweiz. Das Produkteprogramm umfasst drei völlig unterschiedlich aufgebaute Vakuumsysteme, die wiederum in verschiedenen Ausführungen erhältlich sind:

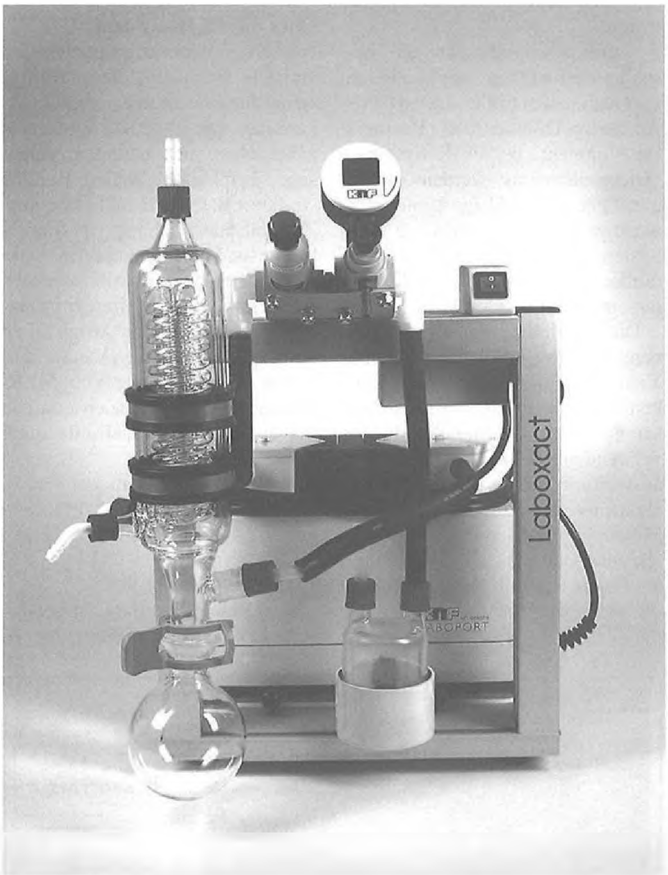
LABOPORT

Der Klassiker ist das modulare Einzelplatz-Vakuumsystem der LABOPORT-Baureihe. Durch einfache Steckverbindungen kann die Membranpumpe je nach Anwendung mit Abscheidern, Hochleistungskondensator und Vakuumcontrollern zu einem flexiblen System ausgebaut werden. Dabei sind alle Komponenten auf einer Basisplatte zusammengefasst. LABOPORT-Systeme werden mit Pumpen unterschiedlicher Leistung angeboten.

Zu dieser Baureihe gehört auch die neuentwickelte Self Drying Vakuumpumpen für kondensathaltige Gase. Sie eignet sich hervorragend für Anwendungen, in denen Gase mit hohem Feuchtigkeitsgehalt zu evakuieren sind. Die Pumpe verfügt über ein ausgeklügeltes Trocknungssystem und lässt sich optimal mit dem Vakuumtrockenschrank Vacucenter Salvis Lab von der Firma Renggli kombinieren.

LABOXACT

Einen völlig neuen und patentierten Ansatz verkörpert das manuelle Vakuumsystem LABOXACT. Es wurde speziell für den Einsatz am Rotationsverdampfer entwickelt und basiert auf einer neuartigen Feinregulierung sowie einem Belüftungsventil zwischen Rotationsverdampfer und Vakuumpumpe. Über das Feinregulierventil lässt sich das Vakuum stufenlos und feinfühlig regulieren, wogegen das Belüftungsventil erlaubt, den Verdampfungsprozess jederzeit zu unterbrechen. Die sichere Kontrolle des Verdampfungsprozesses und eine hohe Rückgewinnungsrate auch bei niedrig siedender Lösungsmittel sind die herausragenden Eigenschaften des neuen LABOXACT-Vakuumsystems.



LABOBASE

Neben Vakuumsystemen für den Einzelplatz gewinnen im Labor Mehrplatzsysteme zunehmend an Bedeutung. Dieser kostengünstigen Variante trägt KNF Neuberger mit dem LABOBASE-Vakuumsystem Rechnung. Besonders für studentische Laboratorien oder Anwendungen, bei denen sich die abzusaugende Gase vermischen dürfen, ist dieses leistungsstarke System die richtige Lösung. Die zentrale Basiseinheit versorgt bis zu zehn Vakuum-Entnahmestellen, die wahlweise manuell oder controllergeregelt ausgeführt werden. Dank einem umfangreichen Angebot an Komponenten lässt sich das LABOBASE-System sowohl in bestehende Laboreinrichtungen als auch bei Neuplanungen integrieren.

- E. RENGGLI AG
  Industrie-Ost
  CH–6343 Rotkreuz
  Telefon 041/798 14 14
  Telefax 041/798 14 20
  sales@renggli.com
  www.renggli.com

Leserdienst Nr. 11

Höchstdruck-Hydraulikleitungen für biologisch abbaubare Öle

Zwei neue Komponenten ergänzen sich: HYDROFLEX® 4SH GREENPOWER Hydraulikschläuche mit ausreisssicheren 4SH Sicherheitsarmaturen. Dieser sichere Höchstdruck-Hydraulikschlauch für biologisch abbaubare Hydraulikflüssigkeiten ist ab sofort in der Nennweite 19 bei Angst + Pfister ab Lager erhältlich.

HYDROFLEX® 4SH GREENPOWER Hydraulikschläuche eignen sich für den Einsatz mit biologisch abbaubaren Hydraulikölen, wie zum Beispiel HTG-, HE- und HPG-Flüssigkeiten. Mit den ausreisssicheren Armaturen HYDROFLEX® 4SH lassen sie sich zu Hydraulikleitungen für höchste Sicherheitsanforderungen konfektionieren.

Die Hydraulikschläuche HYDROFLEX® 4SH GREENPOWER sind in Nominaldurchmessern von DN 19 bis DN 50 und für dynamische Betriebsdrücke von 250 bis 420 bar erhältlich. Sie sind durch vier spiralgewickelte Drahteinlagen höchster Festigkeit verstärkt und lassen sich, je nach Medium, bei Betriebstemperaturen von –40°C bis +100°C einsetzen. Die Schläuche eignen sich ebenfalls für konventionelle Hydraulikflüssigkeiten auf Mineral- und Syntheseölbasis, Öl-Wasser-Emulsionen, Wasser-Glykol-Lösungen, Schmierstoffe auf pflanzlicher und Mineralölbasis sowie für Kühlwasser und Druckluft. Für Flüssigkeiten auf Phosphatester-Basis (HFD) stehen alternative Schlauchqualitäten zur Verfügung. Bei herstellerspezifischen Öl-Zusatzstoffen ist die Eignung vorsichtshalber abzuklären.

Die ausreisssicheren Armaturen 4SH sind nach EN 201 zugelassen. Sie gewährleisten eine dichte, ausreissfeste Verbindung von Schlauch und Armatur. Die Schlauch-Innenschicht muss bei der Konfektionierung nicht geschält werden und bleibt vollständig erhalten. Für den Betriebsdruck steht somit durchgehend die volle Geflechtsfestigkeit zur Verfügung.

- Angst + Pfister AG
  Thurgauerstrasse 66
  CH–8052 Zürich
  Telefon 01 306 61 11
  Telefax 01 302 18 71
  Internet www.angst-pfister.com
  E-Mail ch@angst-pfister.com

Leserdienst Nr. 12

Neuer hochauflösender DNA-Analysekit von Agilent Technologies und Caliper Technologies zur Beschleunigung der Wirkstoffsuche

Agilent Technologies Inc. (NYSE: A) und Caliper Technologies Corp. (NASDAQ: CALP) führten heute den DNA 500 LabChip®-Kit zur automatischen Grössen- und Konzentrationsbestimmung ein. Eingesetzt auf dem Agilent 2100 Bioanalyzer wird dieser Kit den in der genomischen und genetischen Forschung tätigen Biowissenschaftlern eine rasche und bequeme Analyse von DNA-Proben ermöglichen und damit die Suche nach neuen Wirkstoffen beschleunigen.

'Caliper und Agilent sind zurzeit die einzigen Unternehmen, die mikrofluide Lab-on-a-Chip-Produkte, die die Vorteile von Miniaturisierung, Integration und Automatisierung direkt in das Forschungslabor bringen, kommerzialisieren' sagte Dr. Dan Kisner, Präsident und Vorstandsvorsitzender (CEO) von Caliper. 'Wir halten den DNA 500 LabChip-Kit für eine wichtige Erweiterung der (gesamten) LabChip-Produktpalette von Caliper, da er den wachsenden Bedarf an Analysen kleiner DNA-Fragmente zur Erforschung von Krankheiten und neuen Medikamenten stillen kann. Besonderes Interesse werden die(jenigen) Forscher in der pharmazeutischen Industrie und akademischen Forschung daran zeigen, die dringenden Bedarf an höherer Geschwindigkeit, Präzision und Exaktheit in der Nukleinsäure-Analyse haben.'

Basierend auf der mikrofluiden LabChip-Technologie von Caliper kann der DNA 500 LabChip-Kit die Grösse relativ kleiner DNA-Fragmente (25–500 Basenpaare) sehr genau bestimmen. Der Kit ist in erster Linie zur Analyse der kleinen Produkte einer PCR (Polymerasekettenreaktion) bzw. eines Restriktionsenzymverdaus vorgesehen.

Ein wichtiger Anwendungsbereich dieses neuen Kits ist der Nachweis genetischer Mutationen, die mit spezifischen Krankheiten wie z.B. Krebs assoziiert sein können. Wissenschaftler können nun mit einer auf dem Trennprinzip beruhenden Nachweismethode für Mutationen wie der RFLP (Restriktionsfragment-Längen-Polymorphismus), bei der kleine DNA-Fragmente erzeugt werden, eine Vielzahl von Proben effizient screenen und die resultierenden Datendateien rasch analysieren und miteinander vergleichen.

Für den Agilent 2100 Bioanalyzer gibt es drei weitere LabChip-Kits. Im Laufe dieses Jahres wollen Agilent und Caliper noch einen (anderen) LabChip-Kit zur Grössenbestimmung von Proteinen einführen. Dieser Kit wird (dann) die aufwendigen Methoden ersetzen, die aktuell zur Analyse des breiten Spektrums unterschiedlicher Proteinproben aus Forschungslaboratorien und pharmazeutischen Produktionseinrichtungen verwendet werden.

Verfügbarkeit

Der DNA 500 LabChip-Kit ist zurzeit in den USA und in Europa auf dem Markt und kann über ein Agilent-Verkaufsbüro direkt bestellt werden.

Informationen zu den Produkten und Dienstleistungen der Chemischen Analysentechnik von Agilent können Sie im Internet unter folgender Adresse abrufen: www.agilent.com/chem. Informationen zur LabChip-Technologie und den Produkten von Caliper finden Sie unter der Adresse www.calipertech.com.

- Agilent Technologies
  (Schweiz) AG
  In der Luberzen 29
  CH–8902 Urdorf
  Telefon 0848 80 35 60
  Telefax 01 735 97 44
  www.agilent.com

Leserdienst Nr. 13

Die neue Universal-Software HW3

Rotronic hat eine Universalsoftware entwickelt, die zu allen Rotronic-Produkten kompatibel ist. Die Software ist in Visual-Designer-Modulen programmiert und sehr leicht zu bedienen. Sie unterstützt Geräte wie HygroWin, A1H, MOK-03-WIN, BTRS1, I-3000H, HygroLog, AM3 usw. zusätzliche Funktionen.

Das Grafik-Modul kann sowohl Online-Messungen als auch gespeicherte Dateien auf dem Bildschirm darstellen. Es können Grenzwerte gesetzt werden, die optisch dargestellt werden, damit Abweichungen vom Sollwert eindeutig erkennbar sind. Ausserdem werden Abweichungen durch ein akustisches Signal angezeigt.

Das Speichern der Messwerte im PC ist kein Problem. Der Computer kann als Datenerfassungssystem verwendet werden. Die Startzeit, die Stoppzeit und die Aufzeichnungsintervalle können mit Hilfe

der Software frei gewählt werden. Auf Wunsch legt die Funktion Autostore automatisch eine Datei mit allen Messwerten eines Tages, einer Woche oder eines Monats an.

Die HW3-Software überträgt Alarmmeldungen über moderne Kommunikationswege. Sie kann E-Mails oder SMS-Nachrichten an die verantwortliche Person versenden.

Die HW3-Software verfügt über zahlreiche Funktionen wie Absolutfeuchteberechnung, Minimum-, Maximum- und Mittelwertanzeige, automatische Erkennung der angeschlossenen Geräte, Wahl des richtigen Com-Ports, DDE-Funktion (Dynamic Data Exchange), die automatische Erstellung von Kalibrierzertifikaten und die Einbindung des Firmenlogos.

- Rotronic AG
  Grindelstrasse 6
  CH–8303 Bassersdorf
  Telefon 01/838 11 11
  Telefax 01/836 44 24
  www.rotronic.ch
  E-mail rotronic@rotronic.ch

Leserdienst Nr. 14

Low Cost Image Acquisition Workstation

Das kompakte BioDoc-It™ System von UVP wurde speziell für Geldokumentation und Archivierung von Elektrophorese Applikationen im Life Science Bereich entwickelt.

Einfachste Bedienung, günstiger Preis und höchste Qualität sind die Merkmale dieser Neuheit im Bereich Imaging.

Das System benötigt nur zirka 30x30 cm von Ihrem Arbeitsplatz! Flat-Screen Monitor und Disk Drive sind direkt im System integriert.

Das BioDoc-It™ System kombiniert:

- CCD Videokamera
- TFT Active Color Display für live Previews
- Manuelle Touch Pad Steuerung
- Auto-Save mit eingebautem 3¹/₂" Disk Drive
- Platz sparender Benchtop Darkroom
- 302 nm UV Benchtop Transilluminator (Hi/Lo)
- High Quality Thermoprinter

UVP bietet mit dem BioDoc-It™ System eine professionelle und günstige Lösung für Multipurpose User.

Ideal für die Dokumentation von Gelen, fluoreszierenden Gelen, Membranen, Blots Filmplatten und Assays geeignet.

Bei der Bildaufnahme können Integrationszeiten von 0.1 bis 10 Sekunden gewählt werden, um eine optimale Empfindlichkeit zu erreichen. Die im TIFF-Format gespeicherten Bilder können für quantitative Analysen oder für Illustrationen verwendet werden.

Zusammen mit den neuen Chemi-Systemen (digitale high-end Kameras), die für Chemilumineszens-Detektion neue Massstäbe setzen, hat UVP sein Angebot auf die Anwendungen und Bedürfnisse der Zukunft ausgerichtet.

Weitere Informationen finden Sie auf unserer Homepage unter http://www.omnilab.ch, oder nehmen Sie einfach direkt mit uns Kontakt auf. Für ergänzende Auskünfte stehen wir Ihnen gerne zur Verfügung.

- Omni Lab AG &
  OmniLab Biosystems AG
  Untere Bahnhofstrasse 14
  CH–8932 Mettmenstetten
  Telefon 01 768 22 11
  Telefax 01 768 23 21
  E-Mail omnilab@omnilab.ch
  Internet http://www.omnilab.ch

Leserdienst Nr. 15

CF 16 DSP, digitales Signal Processing auf engstem Raum

Trotz Miniaturausführung wurde nicht auf technische Raffinessen verzichtet. Neben der digitalen Signalverarbeitung mit 10 Bit bestimmen automatische Verstärkungs- und Integrationszeitregelung die hervorragenden Gesamteigenschaften der neuen Farb-Miniaturkamera von KAPPA. Die digitale Kantenanhebung sorgt für eine brillante Darstellung auch bei kontrastschwacher Vorlage. Die CF 16 DSP bietet bei 752 x 582 Pixel eine Auflösung von 480 Linien und 50 dB Signalrauschabstand. Die abgesetzte Steuerelektronik ist ebenfalls miniaturisiert. Durch die Auswahl zwischen unterschiedlichen Kameraköpfen (kleinster mit 7 mm Aussendurchmesser) und Objektiven ist hohe Flexibilität und Anpassungsfähigkeit gewährleistet. Optional ist ein RGB Signalausgang integrierbar.

- VIDEAL AG
  Oberstrasse 8
  CH–3360 Herzogenbuchsee
  Telefon 062 961 14 55
  Telefax 062 961 20 41
  www.videal.ch
  E-mail videal@videal.ch

Leserdienst Nr. 16

Tragbares pH-Meter PHM201 von Radiometer

Auch bei der Firma Radiometer, dem bekannten Hersteller von Qualitäts-pH-Metern, Leitfähigkeitsmessgeräten, Titrationssystemen, IUPAC zertifizierten Pufferlösungen, Leitfähigkeitsstandards und Ausrüstungen für die Korrosionsmessung gibt es kostengünstige aber dennoch leistungsfähige pH-Meter.

Das tragbare pH-Meter PHM201 besitzt ein zweizeiliges Display und verfügt über interessante Funktionen, wie z.B. automatische Puffererkennung (IUPAC, DIN, Radiometer) und AUTOREAD. Das Gerät besitzt eine Stabilitätsanzeige für den Messwert, Es können pH-Werte (–9 bis +23), Potentiale (–1999mV bis +1999mV) und Temperaturen (0 bis 99,9°C) mit Auflösungen von 0,01 pH, 1mV, und 0,1° C gemessen werden. Zur Temperaturkorrektur des pH-Wertes kann ein Temperatursensor benutzt werden, oder es kann eine Temperatur eingestellt werden.

Das gesamte Lieferprogramm finden Sie auch im Internet unter www.igz.ch

- IG Instrumenten-Gesellschaft AG
  Räffelstrasse 32
  CH–8045 Zürich
  Telefon 01 /456 33 33
  Telefax 01/456 33 30

Leserdienst Nr. 17

TECAN aids combinatorial library generation

TECAN automated systems are helping a leading European drug discovery company to generate a large number of molecules for its lead-seeking combinatorial chemistry libraries.

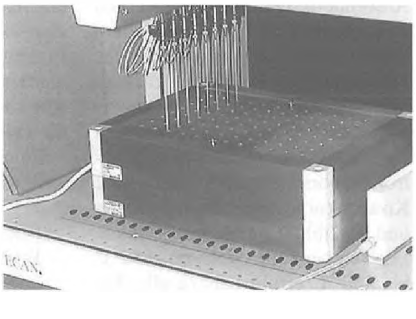
The company is using two TECAN GENESIS CHEMSYSTEMs and a TECAN Workstation to create about 6000 new molecules per system, per day.

According to a spokesperson for the company, one of the most important features of the TECAN systems is flexibility: 'Our needs change all the time and we often need to rewrite procedures. Thanks to a TECAN training course, we are able to customise each system to our requirements. The instrumentation software means that the equipment can be linked together so, for example, GEMINI and FACTS packages are able to communicate with our databases, such as Oracle, via the special drivers created in collaboration with TECAN.'

'Before we decided to purchase the Workstation, TECAN lent it to us for a week to try it out. I have compared many instruments and, in my opinion, TECAN offers the quickest and most user friendly instruments in this sector,' he concluded.

- TECAN AG
  Feldbachstrasse 80
  CH–78634 Hombrechtikon,
  Telefon ++41/55/254 81 11
  Telefax ++41/55/244 38 83
  E-mail tecan@tecan.ch

Leserdienst Nr. 18



FT-IR und FT-NR zur Lösung von Aufgaben in der Qualitätskontrolle

Spectrum One setzt mit seinen vielen intelligenten Merkmalen einen Standard für FTIR-Systeme in der Qualitätskontrolle und hat sich mittlerweile vielfach bewährt. Bisher waren Messungen ausschliesslich im klassischen mittleren IR-Bereich möglich. Das neue Spectrum One NTS (Near-Infrared Testing System) erweitert die Möglichkeiten dieser Gerätefamilie nun auch im NIR-Bereich. Spectrum One-Systeme wurden für die Anforderungen in der Qualitätskontrolle entwickelt, um die Analysen effizienter und kostengünstiger zu gestalten. Die einfach zu bedienende und validierte Software gewährleistet zuverlässigste Ergebnisse, wobei gleichzeitig alle Informationen über die Gewinnung und Bearbeitung der Daten gespeichert und nachvollziehbar sind.

Alle Komponenten – Spektrometer, Software und Probenzubehöre – sind nahtlos integriert und zeichnen sich durch einen gleich hohen Standard aus. Die modularen Probenzubehöre werden über eine serielle Schnittstelle mit dem Spektrometer verbunden. Darüber erfolgen alle notwendigen Verbindungen, werden alle relevanten Parameter übertragen und wird sichergestellt, dass das Zubehör korrekt eingesetzt wurde. Spectrum One erkennt automatisch das Zubehör, stellt die richtigen Parameter ein und führt verschiedene Systemtests durch. Der Wechsel von Zubehören erfordert lediglich Sekunden! Einfach das bestgeeignete Zubehör einsetzen und mit der Analyse beginnen.

- Perkin Elmer (Schweiz) AG
  Bösch 106
  CH–6331 Hünenberg
  Telefon +41 41 785 77 55
  Telefax +41 41 785 77 95

Leserdienst Nr. 19

Das neue Polaroid Sofortbildsystem 1200: 100% beweiskräftig

Zürich, Juni 2000. – Polaroid Sofortbilder als Referenzaufnahmen sind in vielen Berufen nicht mehr wegzudenken. Denn auch im elektronischen Zeitalter ist das Sofortbild dem digitalen Bild um ein entscheidendes Plus voraus: Es ist nicht nur sofort da und sofort überprüfbar, sondern auch ein nicht manipulierbares Unikat und damit 100%ig beweiskräftig.

Als Weiterentwicklung des Image-Systems lanciert Polaroid in der Schweiz jetzt das System 1200 – die Kameramodelle 11200i und 120Osi sowie den 1200er-Film, der 12 statt wie bisher 10 Einzelaufnahmen enthält. Das neue Konzept überzeugt mit einer Reihe von Vorteilen: Der Kunde erhält 20% mehr Filmmaterial, das einzelne Bild ist mehr als 10% preiswerter, und die Filmkassetten müssen weniger oft ausgewechselt werden. Der formatgrösste Integralfilm (74 x 91mm) bietet die bekannt gute Image-Qualität, die sich hervorragend auch zum Einscannen und Weiterbearbeiten am Bildschirm eignet. Der Film wird im Doppelpack mit 2 x 12 Bildern angeboten.

Die formschönen 1200er-Kameras sind mit einem Quintic-Objektiv mit vergüteter Glaslinse, mit Ultraschall-Autofocus und Automatikblitz (Reichweite 4,5m) ausgerüstet. Das Model 1200si besitzt Zusatzfunktionen wie den integrierten Selbstauslöser und die wahlweise Abschaltung von Autofocus und Blitz (z.B. für Aufnahmen durch eine Glasscheibe). Für beide Kameras gibt es Sonderzubehör für Nahaufnahmen, und beide Modelle können auch den bestehenden Image-Filmpack aufnehmen.

Das neue Polaroid System 1200 liefert genau das, was es für perfekte Dokumentationsbilder im Beruf braucht: unkompliziert in der Handhabung, ökonomisch im Einsatz und mit Resultaten, die so beweiskräftig sind, wie es eben nur unmanipulierte Originale sein können.

- Polaroid AG
  Hardturmstrasse 161
  CH–8037 Zürich
  Telefon 01 277 72 72
  Telefax 01 277 72 73
  www.polaroid.com

Leserdienst Nr. 20

Präparative FLASH-Chromatographie mit vorgepackten Kartuschen.

Was bedeutet Ihnen Effizienzsteigerung bei der Chromatographie? Wie zufrieden sind Sie mit der Kapazität, Trennleistung und Reproduzierbarkeit Ihrer präparativen Aufreinigung? Wie oft zerbrechen Sie sich den Kopf über die Übertragbarkeit Ihrer Trennresultate aus Forschung und Entwicklung in den Pilot- oder Produktionsmassstab? Welche Bedeutung hat Sicherheit in Ihrem Labor?

Mit den FLASH-Chromatographiesystemen der Firma Biotage, neu und exklusiv im Programm von BÜCHI Labortechnik AG/GmbH, verschaffen Sie sich in all diesen Fragen einen nennenswerten Vorsprung: In einer Vielzahl von Applikationen bieten die vorgepackten Kartuschen von Biotage bedeutende Zeit- und damit Kostenersparnis. Dank hoher Qualität der Packung und stabilisiertem Chromatographiebett werden Risse und Kanäle effizient vermieden. Dies gewährleistet eine für Flashchromatographie bislang unerreicht hohe Trennschärfe und Reproduzierbarkeit. Die robusten Systeme aus rostfreiem Stahl, Teflonschläuchen und Swagelok-Verbindungen sind bedienerfreundlich und bieten höchste Sicherheit. Das umfangreiche Angebot an stationären Phasen und Kartuschengrössen ermöglicht ein lückenloses Up-scaling vom Forschungs- bis zum Produktionsmassstab im Kilogrommbereich.

Speziell für die parallele Chemie stehen Ihnen die Parallel-FLASH-Chromatographiesysteme Quad4/40 und Quad3 mit individuellen Pumpenköpfen zur Verfügung. Damit lassen sich in kürzester Zeit bis zu 8 bzw. 12 Proben mit maximal 5g bzw. 350 mg Rohmaterial gleichzeitig auftrennen.

- Büchi Labortechnik AG
  Postfach
  CH–9230 Flawil
  Telefon 071 394 63 63
  Telefax 071 394 64 64

Leserdienst Nr. 21

M.U.T. zum ersten Mal mit Begleitkongress

Die M.U.T., die Europäische Messe für Umwelttechnik, die dieses Jahr vom 14. bis 17. November 2000 auf dem Gelände der Messe Basel stattfindet, wartet mit einer attraktiven Neuerung auf Sie: Zum ersten Mal findet parallel zur Messe ein Fachkongress mit 76 hochkarätigen Referenten statt.

Unter der fachlichen Trägerschaft der führenden Schweizer Fachzeitschrift Umwelt Focus organisiert die Mediasec AG (Organisatorin hochstehender Fachkongresse) zum ersten Mal eine Veranstaltung im Umweltbereich: Den M.U.T.-Kongress in Basel. Er bietet den Messebesucherinnen und -besuchern Gelegenheit, ihren Rundgang durch die M.U.T. sinnvoll zu ergänzen und abzurunden.

Der M.U.T.-Kongress ist die grösste Veranstaltung ihrer Art in der Schweiz: 76 hochkarätige Referenten aus allen Umweltbereichen decken das ganze Themenspektrum ab: Ob organisierte Umweltkriminalität, Zukunftsperspektiven der schweizerischen Abfallwirtschaft, Liberalisierung im Wasserbereich oder Umweltschutz in der Praxis: Am M.U.T.-Kongress werden alle Probleme behandelt, mit denen sich Umweltbeauftragte in Firmen, Organisationen und Verwaltungen beschäftigen müssen.

Die Tagung will keinen Konsens schaffen, sondern bewusst verschiedene Standpunkte zur Sprache bringen. Aus diesem Grund geben am M.U.T.-Kongress nicht nur spezialisierte Fachleute ihr Wissen, sondern auch zahlreiche Anwender ihre Erfahrungen weiter.

Das Angebot umfasst mehr als 50 Fachvorträge, die in 11 abgeschlossenen Halbtagsmodulen angeboten worden. Die Halbtage finden zum Teil parallel statt. Aus diesem Grund haben interessierte Teilnehmerinnen und Teilnehmer die Möglichkeit, maximal 6 Halbtage zu besuchen. Der Preis pro Halbtag beträgt CHF 275.–. Im Preis inbegriffen ist die schriftliche Fassung aller Vorträge.

Das detaillierte Tagungsprogramm samt Anmeldeformular ist erhältlich bei:

- Mediasec AG
  Tägernstrasse 1
  CH–8127 Forch
  Telefon +41 1 980 44 66
  Telefax +41 1 980 44 67
  E-Mail: info@mediasec.ch.

Leserdienst Nr. 22

Neuer Dynamisch-Mechanischer Analysator

Shimadzu, weltweit eines der führenden Unternehmen der Instrumentellen Analytik, hat seine Thermoanalyse-Baureihe mit einem Gerät in besonderem Design erweitert: das neue Dynamisch-Mechanische Analysesystems DMA-2000. Auffallend ist das Design des Geräts. Der Messkopf befindet sich in einem Rahmen. Das erleichtert den Anwendern den Zugang zu den Spannzeugen des Geräts. Zudem können sie auch ungewöhnliche Messbedingungen, etwa in Flüssigkeiten, durchführen.

Das DMA-2000 wurde speziell für die Anforderungen von Kontroll-Labors entwickelt, wo robuste Konstruktion, einfache Bedienung und flexible Handhabung zählen. Der Temperaturbereich von –150° C bis 350° C erfüllt nahezu alle Applikationsanforderungen an DMA-Systeme. Das integrierte Kühlsystem garantiert Abkühlzeiten von weniger als 10 min bis –100° C bei einem minimalen Flüssigstickstoffverbrauch von 0,5 Liter. Der Frequenzbereich beträgt 0.001 bis 100 Hz, der dynamische Messbereich erstreckt sich von 1 µm bis 2 mm.

Für die Messung stehen zahlreiche Spannzeuge für Scher-, Druck, Zug- oder Biegeversuche zur Verfügung. Nach jedem Experiment werden automatisch Temperatur, Speicher- und Verlustmodul sowie die Dämpfung berechnet.

- Shimadzu Schweiz GmbH
  Römerstrasse 3
  4153 Reinach
  Telefon 061/717 93 33
  Telefax 061/717 93 30

Leserdienst Nr. 23

STELLENMARKT

SPECTRO eröffnet Internet-Shop

Spectro Analytical Instruments bietet seinen Kunden die Möglichkeit, ihre Einkäufe jetzt auch über das Internet im SPECTRO-SHOP zu erledigen.

Der Zugang zum SPECTRO-SHOP erfolgt über die SPECTRO-Homepage (http://www.spectro-ai.com).

Ausser dem Online-Einkauf von Verbrauchsmaterialien, Ersatzteilen und Zubehör bietet sich hier die Möglichkeit, Applikationsberichte und -methoden oder Prospekte sofort herunterzuladen.

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Tom Blades, Sprecher der Geschäftsführung bei SPECTRO, fügt hinzu: 'Wir haben in den letzen zwei Jahren signifikante Investitionen im Bereich der IT (Informationstechnologie) vorgenommen. In Kürze werden wir die Erweiterung vom Intranet auf das Extranet durchführen, um drei wesentliche Elemente unserer externen Strategie zu realisieren. Zunächst werden wir unseren Kunden die Geschäftsbeziehung im Anschluss an den Gerätekauf erleichtern. Durch den SPECTRO-SHOP reduziert sich der Bestellaufwand für Teile und andere Waren auf einige Mausklicks.'

Zweitens weiten wir unsere Möglichkeiten aus, mit Partnerfirmen zusammen zu arbeiten (B2B, business-to-business), indem wir das Angebot im SPECTRO-SHOP über unsere eigene Produktpalette hinaus ausdehnen. Damit kommen wir den Wünschen unserer Kunden entgegen. Der weltweite Verkauf von mehr als 15000 Systemen in den letzten 20 Jahren ermöglicht uns Zugang zu massgeblichen Kundenkreisen innerhalb der Gruppe der Analysengeräteanwender, die wir mit unseren B2B-Partnerfirmen gemeinsam nutzen können.

Drittens haben wir damit begonnen, ausgewählten 'Beta-Testern' Zugriff auf unser Intranet zu geben, um ihnen über dieses 'SERVICE-NETZ' Anwendungsunterstützung in Echtzeit zu ermöglichen. Dadurch haben wir die Möglichkeit mit Hilfe von Videokonferenztechnologie und einer eingebauten Kamera vor Ort in ein SPECTRO CIROS^{CCD} zu schauen und Ferndiagnose und Fernwartungsmöglichkeiten der Hard- und Software zu verknüpfen. Das bedeutet, wir können einen Kunden Schritt für Schritt bei der Entwicklung einer Methode oder der Fehlerbeseitigung begleiten, wo er sich auch befindet.

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Leserdienst Nr. 24

Sauerstoffwerk Lenzburg AG (SL GAS) Begehrtes Zertifikat ISO 14001 erhalten

SL GAS ist ein führendes, gesamtschweizerisch tätiges Unternehmen für Industriegase und On-Site-Technologien. 1999 war für die traditionsreiche Lenzburger Gase-Firma ein herausragendes Jahr, wurde sie doch mit dem in der Schweiz noch eher seltenen Zertifikat 'Umweltmanagementsysteme' nach ISONorm 14001 ausgezeichnet.

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  www.slgas.ch

Leserdienst Nr. 25

Konferenz: 'Kommerzielle Bedeutung der Molekularbiologie' in Rothamsted

Fortschritte in der Molekularbiologie stehen auf der Agenda der Konferenz 'Bioproducts from Plants and Microbes', die vom 18. bis 20. Oktober 2000 in Rothamsted bei London stattfindet. Als eine Veranstaltung im Rahmen des International BioMarket wird die Konferenz der Frage nachgehen, wie verschiedene Märkte kommerziell von der innovativen Nutzung biologischer Ressourcen profitieren können. Im Mittelpunkt stehen Bereiche wie Pharmazie und Medizin, der Veterinärsektor, Agrobiotechnologie, Lebensmittel und Ernährung, Agrochemikalien und Pflanzenschutz, Feinchemikalien und ökologische Biotechnologie.

Die Veranstaltung richtet sich an führende und innovative Unternehmen aus dem Bereich der Biowissenschaften, an akademische Forschungsgruppen, Schwellenländer, Investoren, Patent/Lizenzorganisationen und Anbieter entsprechender Dienstleistungen. Es besteht Gelegenheit zu vereinbarten Zusammenkünften, zu Präsentationen von Exponaten, Unternehmen, Forschungsgruppen und Ländern sowie zu Gesprächsrunden mit Spezialisten und Beratern.

Rothamsted wurde 1843 gegründet. Mit über 500 Mitarbeitern ist es eines der grössten Zentren für Angewandte Botanik in Europa und verfolgt traditionell die praktische Umsetzung wissenschaftlicher Erkenntnisse. (BN).

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La Faculté des sciences de l'Université de Genève ouvre une inscription pour un poste de

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Les dossiers de candidature doivent être adressés avant le 16 octobre 2000, au professeur Jean-Luc Veuthey, président de la Section de pharmacie, Quai Ernest-Ansermet 30, CH-1211 Genève 4, auprès duquel les renseignements complémentaires peuvent être obtenus. T (022) 702 63 36 – E-mail: Jean-Luc.Veuthey@pharm.unige.ch

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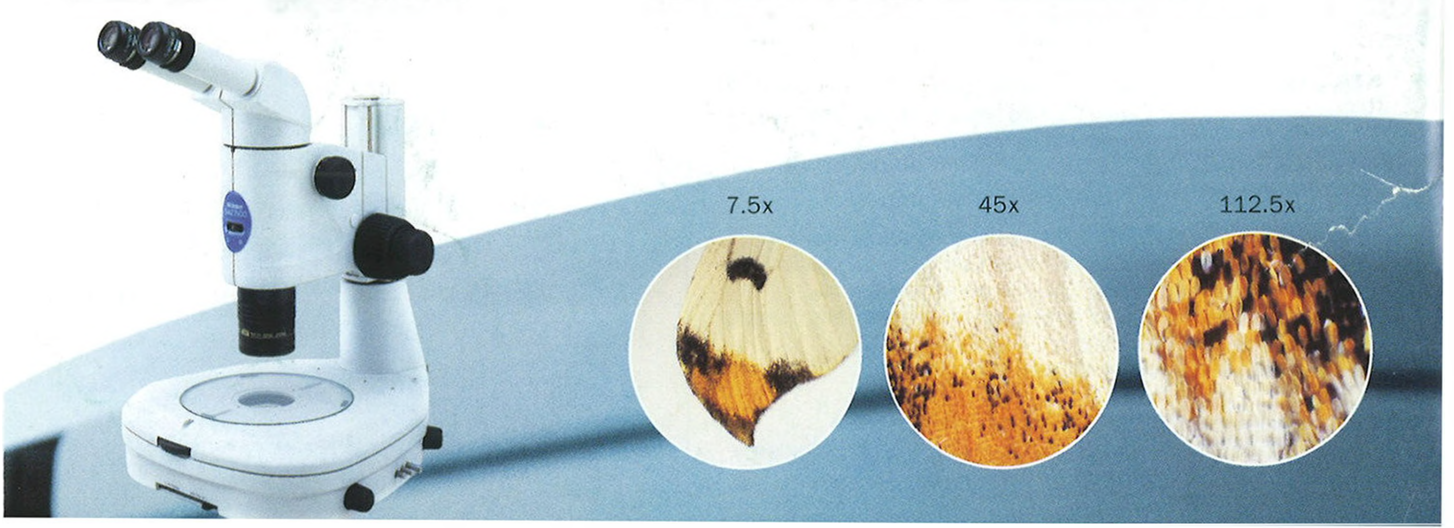
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