

Le Laboratoire de Chimie Organique à l'EIA-FR

Jean-Marc Bourgeois*

Practical Organic Chemistry at the University of Applied Science at Fribourg

Abstract: We describe some aspects of practical organic chemistry at the EIA-FR. To motivate the students, we let them carry out their laboratory work like research projects in synthetic organic chemistry. To provide some guide lines, we propose the following general reaction scheme: 2,6-di-(hydroxymethyl)-phenols are prepared and, after dehydration, brought to reaction with nucleophiles such as alcohols or activated aromatics. Within this reaction scheme, students start with the Reissert reaction to prepare substituted indols, which they will then try to connect to the 2,6-di-(hydroxymethyl)-phenols by substitution of the hydroxyl part. During this practical work we hope the students will learn how to observe, how to analyse and how to understand organic reactions. Furthermore we hope that through this kind of continued laboratory projects, the students will get a realistic impression of the fascinating work of a synthetic organic chemist.

Keywords: Hydroxymethylation · Indols · Laboratory · Phenols · Practical work

1. Introduction

La chimie organique doit faire partie de la culture générale de l'ingénieur. Présente dans tous les domaines de la chimie, elle se montre indispensable, tant pour comprendre certains chapitres de la chimie physique que pour fournir des dérivés à la chimie analytique ou développer des procédés de génie chimique. Un enseignement de base est donc donné pendant les deux premières années de la formation, suivi d'un cours spécialisé en troisième année. Les étudiants suivent le laboratoire de chimie organique durant la deuxième année après révision de la chimie structurale (chaîne carbonée et fonctions) et parallèlement à l'étude des mécanismes de réaction et de l'analyse spectrale (IR, RMN, MS).

2. Organisation

L'organisation du travail pratique de chimie organique se heurte à divers problèmes:

- la dotation horaire (6h/semaine),
- la disparité des formations qui s'échelonnent d'une pratique nulle à une bonne pratique de laboratoire,
- l'adéquation au cours théorique,
- l'apprentissage des méthodes d'analyse spectrale en vue de la caractérisation des produits,
- l'apprentissage du travail bibliographique.

Tout cela doit être mené dans un contexte écologiquement correct, financièrement modeste, en assurant une sécurité maximum à chaque participant.

Pour les étudiants peu au courant des techniques de laboratoire (environ 20%),

nous avons établi quelques programmes de base classiques leur permettant de découvrir les manipulations importantes et les grands types de réactions.

3. Sujet de recherche

Pour motiver les autres, nous avons établi un sujet de recherche et développement original auquel chacun apportera sa contribution. Ainsi, nous avons préparé une série de 2,6-di-(hydroxyméthyl)-phénols. Certains sont bien connus comme le 4-méthyl- ou le 4-chloro-2,6-di-(hydroxyméthyl)-phénol, d'autres sont plus ou moins originaux comme l'acide 4-hydroxy-3,5-di-(hydroxyméthyl)-benzoïque ou le 4-acétamido-2,6-di-(hydroxyméthyl)-phénol. L'une des propriétés intéressantes de ces phénols est l'élimination d'eau sous catalyse acide (schéma 1):

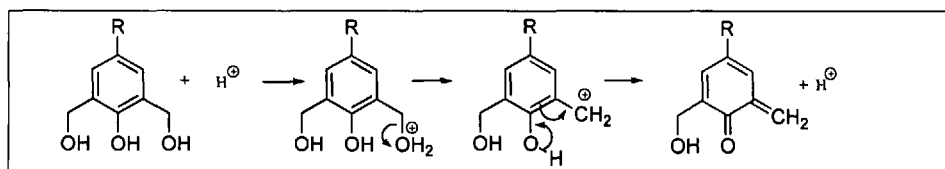


Schéma 1

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La déshydratation se produit aussi par simple chauffage à une température supérieure à 100 °C (schéma 2):

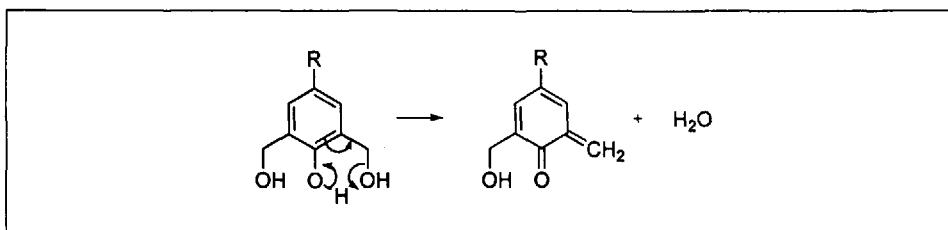


Schéma 2

Le système très réactif formé fixe par addition conjuguée une grande variété de nucléophiles dont les groupements hydroxyles et les noyaux aromatiques actifs (schéma 3):

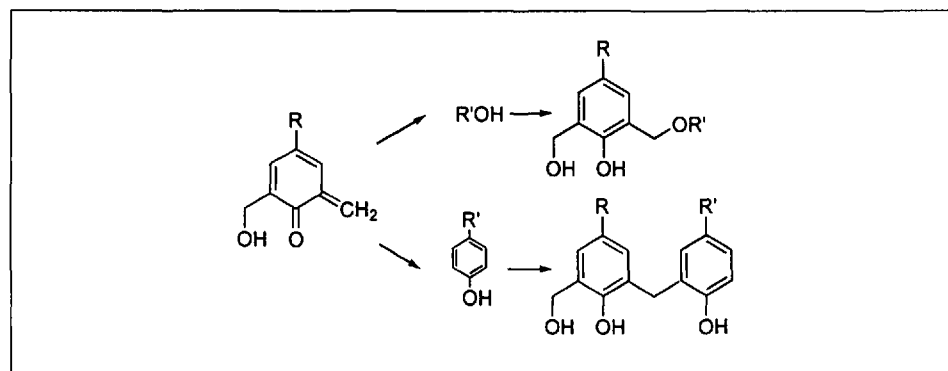


Schéma 3

Ainsi, avec une mise en œuvre extrêmement simple, nos étudiants ont l'occasion de préparer toute une série de produits dont beaucoup sont originaux. Dans le cadre de cette recherche, nous étudions cette année (2000–2001) la synthèse d'indols substitués par la réaction de Reissert puis leur fixation sur un phénol dihydroxyméthylé (schéma 4):

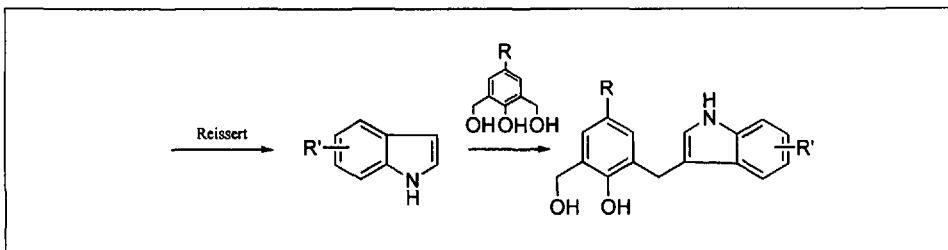


Schéma 4

La réaction de Reissert implique une série d'opérations classiques: nitration, séparation d'isomères de position, condensation dans des conditions anhydres et basiques de type Claisen, réduction, décarboxylation.

La recherche de tous ces procédés dans la littérature est un premier pas qui formera l'étudiant à l'utilisation d'une bibliothèque. La compréhension théorique des divers stades est un second pas qui se fera principalement dans le cadre du cours. Lors de la synthèse de l'indol, pratiquement tous les candidats sont surpris par la différence qui existe entre les affirmations optimistes des auteurs et la réalité du ballon de réaction ainsi que par la difficulté que l'opérateur rencontre à identifier ses substances.

Pour la fixation de l'indol substitué au phénol dihydroxyméthylé, c'est à l'étudiant lui-même de trouver des conditions opératoires. Il est dès lors confronté à diverses questions:

- quelles quantités mettre en jeu?
- quel solvant utiliser?
- à quelle température travailler?
- comment savoir si la réaction se fait?
- comment savoir si la réaction est finie?
- faut-il un catalyseur?
- comment isoler et purifier le produit final?
- comment identifier le composé formé?

Pour y répondre, il devra trouver des méthodes analytiques sensibles et rapides qui lui révéleront, dans le meilleur des cas, une série de problèmes nouveaux:

- le phénol dihydroxyméthylé peut réagir avec lui-même ou avec le solvant ou se décomposer,
- il fixe successivement 2 indols à des vitesses proches,
- un catalyseur trop acide entraîne la décomposition des deux réactifs,
- etc.

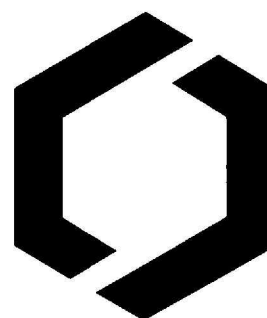
A la fin du laboratoire de semestre, bien peu de candidats auront préparé le produit demandé mais nous espérons qu'ils auront appris à se poser les bonnes questions et qu'ils auront progressé dans leur façon d'aborder un problème de synthèse organique, qualité essentielle pour leur mission de recherche et développement.

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KT 1 GC-Kopplungen mit IR und MS**Referenten**

Dr. Hans-Ulrich Gremlich, Novartis Pharma AG; Prof. Dr. Michael Oehme, Universität Basel

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Zürcher Hochschule, Winterthur
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QS 5 Praxisnahe Qualitätskontrolle in der organischen Rückstands- und Spurenanalytik**Referent**

Prof. Dr. Michael Oehme, Universität Basel

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Fachhochschule Aargau, Brugg/Windisch
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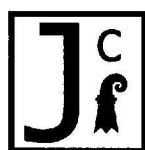
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Firstly, we aim to organise a series of presentations by young chemists from industry, academia, venture capital companies, consultancies and national research institutions in order to give students an insight into the careers available to chemists. Of course, we aim to cover all relevant fields of work in the chemical industry such as research, production, documentation and marketing. A chance for informal discussion after these talks will be available during a reception. We would welcome any offers from the readers of CHIMIA to give a presentation in Basel!

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Dipl.-Chem. Sebastian P. Smidt

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Deadline for Submission of Abstracts:

Tuesday, 29th May 2001

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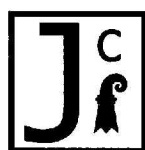
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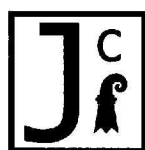
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INFORMATION

News

Novartis Venture Fund on the Path of Success

Basel, 19 February, 2001 – The Novartis Venture Fund can already look back on four years of successful operation. Today sees the publication of its fourth annual report. The number of new companies established with the support of the Novartis Venture Fund has risen to 83. And by the end of the year 2000, the Fund had provided a total of CHF 96 million for these start-ups. The number of jobs either created or preserved in these companies runs to about 1000.

Of the new companies to benefit from the support of the Novartis Venture Fund, five grew out of Swiss universities, six were spin-offs from Novartis, and four others involve former Novartis employees. Six of the companies are engaged in pharmaceutical research and eight are service companies, four of them providing services to the pharmaceutical industry. Three others are engaged in the marketing of products. Eleven of the companies are operational in Switzerland, three in the USA, and one each in France, Ireland, The Netherlands and Kenya.

The Novartis Venture Fund can look forward to a secure future. Thanks to the successful business operations of some of the companies in its portfolio, it was able to book its first major capital repayments and will thus be

in a position to continue its investment activities. In so doing, the Fund remains faithful to the unique positioning of its organization. Unlike other providers of venture capital, its investment decisions do not focus exclusively on profit considerations. 'The creation of jobs continues to be an important concern of the Fund,' explains François L'Eplattenier, President of the Supervisory Board. The prospects which the companies have of successfully implementing their scientific results in an economic setting represent another important criterion.

The annual report of the Novartis Venture Fund (in English), which summarizes the activities of the Fund and describes some examples of newly founded companies, can be ordered from the following address:

Dr. Rudolf Gyax
Portfolio- and Business-Manager
Novartis International
WSJ-200.225
CH-4002 Basel
E-Mail: rudolf.gyax@group.novartis.com

Further information on the Fund can be found on the internet at <http://www.venture-fund.novartis.com>.

Honors/Ehrungen

Prof. Jack Dunitz, Laboratorium für Organische Chemie, ETH Zürich, wurde zum Honorary Fellow of the Royal Society of Chemistry ernannt.

Lectures

Basler Chemische Gesellschaft

Donnerstag, 17.30 Uhr
Institut für Organische Chemie, Kleiner Hörsaal

26. April 2001 Prof. Dr. Alois Fürstner
Max-Planck-Institut für Kohlenforschung,
Mülheim/Ruhr, D
'Neue Beiträge zur Metathese von Alkenen und Alkinen'

Berner Chemische Gesellschaft

Mittwoch, 16.30 Uhr
Hörsaal EG 16
Departement für Chemie und Biochemie, Freiestr. 3
(Kaffee um 16.10 Uhr vor dem Hörsaal)

4. April 2001 Prof. Luisa De Cola
Institute of Molecular Chemistry,
University of Amsterdam
'Electron Transfer in Multicomponent Systems'

Société Chimique de Genève

Lundi, 17.30 h
Amphithéâtre A 150, UNI Sciences II, 30, Quai E. Ansermet

14 mai 2001 Dr. P. Pottier
Centre National de la Recherche Scientifique, France
'Contributions à la médecine'

Société Vaudoise des Sciences Naturelles

at 5 p.m.
Université de Lausanne UNIL

April 4, 2001 Prof. R. Zenobi
Auditorium A ETHZ, CH
BEP UNIL 'Modern Laser-Based Mass Spectrometry'
Pharmacy

Departement für Chemie und Biochemie der Universität Bern

Seminare in Organischer Chemie und Biochemie
Freiestrasse 3

Dienstag, 3.4.2001 Prof. Pierre Vogel
15.30 Uhr Institut de Chimie Organique, Université de
Hörsaal EG 1 Lausanne
'Spongistatin and Polyketide Synthesis'

Donnerstag, 5.4.2001 Dr. *Mike Shipman*
16.30 Uhr University of Exeter
Hörsaal 379 'Towards an Understanding of the Mechanism of Action of the Azinomycins: Naturally Occuring anti-Cancer Agents'

Montag, 9.4.2001 Prof. *Wolfram Bode*
16.30 Uhr Max-Planck-Institut für Biochemie,
Hörsaal 379 Planegg-Martinsried
'Structural Studies on the Metzincins, a Superfamily of Zinc Endopeptidases'

Montag, 23.4.2001 Prof. *Jonathan L. Sessler*
16.30 Uhr Department of Chemistry and Biochemistry,
Hörsaal EG 16 University of Austin, Austin, Texas
'Spongistatin and Polyketide Synthesis'

Montag, 30.4.2001 Prof. *Amadeo Caflisch*
16.30 Uhr Institut für Biochemie, Universität Zürich
Hörsaal 379 'Protein Folding and Drug Design: Grand Challenges of the Postgenomic Era'

Departement für Chemie und Biochemie der Universität Bern

Seminare in Anorganischer, Analytischer und Physikalischer Chemie
Donnerstag, 11.15 Uhr
Hörsaal S-481
Freiestr. 3

12. April 2001 *Ralph Schenker* (Dissertationsvortrag)
Universität Bern, im Hause
'Exchange Interactions in Cr³⁺ and Fe³⁺ Dimers: An Optical Spectroscopic and Magnetic Study'

19. April 2001 Prof. Dr. *Jean-Claude G. Bünzli*
Section de Chimie, Université de Lausanne
'Designing Functional Supramolecular Edifices Containing Lanthanide Ions'

24. April 2001 Prof. Dr. *Roman Boca*
Dept. of Inorganic Chemistry, Slovak Technical University,
Bratislava, Slovakia
'Spin Crossover Systems'

Institut de Chimie, Université de Neuchâtel

Mercredi Colloque ERASMUS-SOCRATES
4 avril 2001 Prof. *Mike Shipman*
10h30 Université d'Exeter (Royaume-Uni)
Petit Auditorio 'The Use of Strained Molecules in the Synthesis of Enantiomerically Pure Natural Products I'

Jeudi Colloque ERASMUS-SOCRATES
5 avril 2001 Prof. *Mike Shipman*
8h15 Université d'Exeter (Royaume-Uni)
Salle E14 'The Use of Strained Molecules in the Synthesis of Enantiomerically Pure Natural Products II'

Vendredi Colloque ERASMUS-SOCRATES
6 avril 2001 Prof. *Mike Shipman*
10h15 Université d'Exeter (Royaume-Uni)
Salle E14 'The Use of Strained Molecules in the Synthesis of Enantiomerically Pure Natural Products III'

Mardi Colloque du 3^{ème} cycle
24 avril 2001 Prof. *J. Sessler*
Heure à définir Université ?
Salle à définir Le titre sera annoncé plus tard

Mercredi Colloque d'institut
25 avril 2001 Prof. *D. Sinou*
10h30 Université Claude Bernard de Lyon (France)
Petit Auditorio 'Catalyse organométallique en milieux non usuels: Avantages et inconvénients'

Jeudi Colloque ERASMUS-SOCRATES
26 avril 2001 Prof. *Herfried Griengl*
16h00 Technische Universität Graz (Autriche)
Salle E14 'The Enzyme-Catalysed Synthesis of Cyanohydrins – from Laboratory Scale to Industrial Realisation'

Vendredi Colloque ERASMUS-SOCRATES
27 avril 2001 Prof. *Herfried Griengl*
8h15 Technische Universität Graz (Autriche)
Salle E14 'Selective Hydroxylation of Organic Compounds Using Biocatalytic Methods'

Laboratorium für Organische Chemie der ETH Zürich

Montag, 16.30 Uhr
Hörsaal CHN A 31
Universitätsstrasse 16, 8092 Zürich

2. April 2001 Prof. Dr. *Rudolf Glockshuber*
ETH Zürich / CH
'Circular Permutation as Tool to Study Protein Folding'

9. April 2001 Dr. *Gavin MacBeath*
Harvard University, Cambridge / USA
'Extending Microarray Technology to Study Protein Function'

Anorganisch-chemisches Institut der Universität Zürich

Freitag, 17.00 Uhr
Seminarraum 34 F 48, UZI
Winterthurerstrasse 190, Zürich-Irchel

5. April 2001 *Sohrab Kheradmandan*
Donnerstag Universität Zürich
'Redoxaktive phosphansubstituierte mono-, di- und trinukleare Mangan-Acetylid-Komplexe: Synthese, Charakterisierung und magnetisches Verhalten'

20. April 2001 Dr. *Christian Bärlocher*
ETH Zürich
'Pushing the Limits of Crystal Structure Analysis Using Powder Diffraction Data'

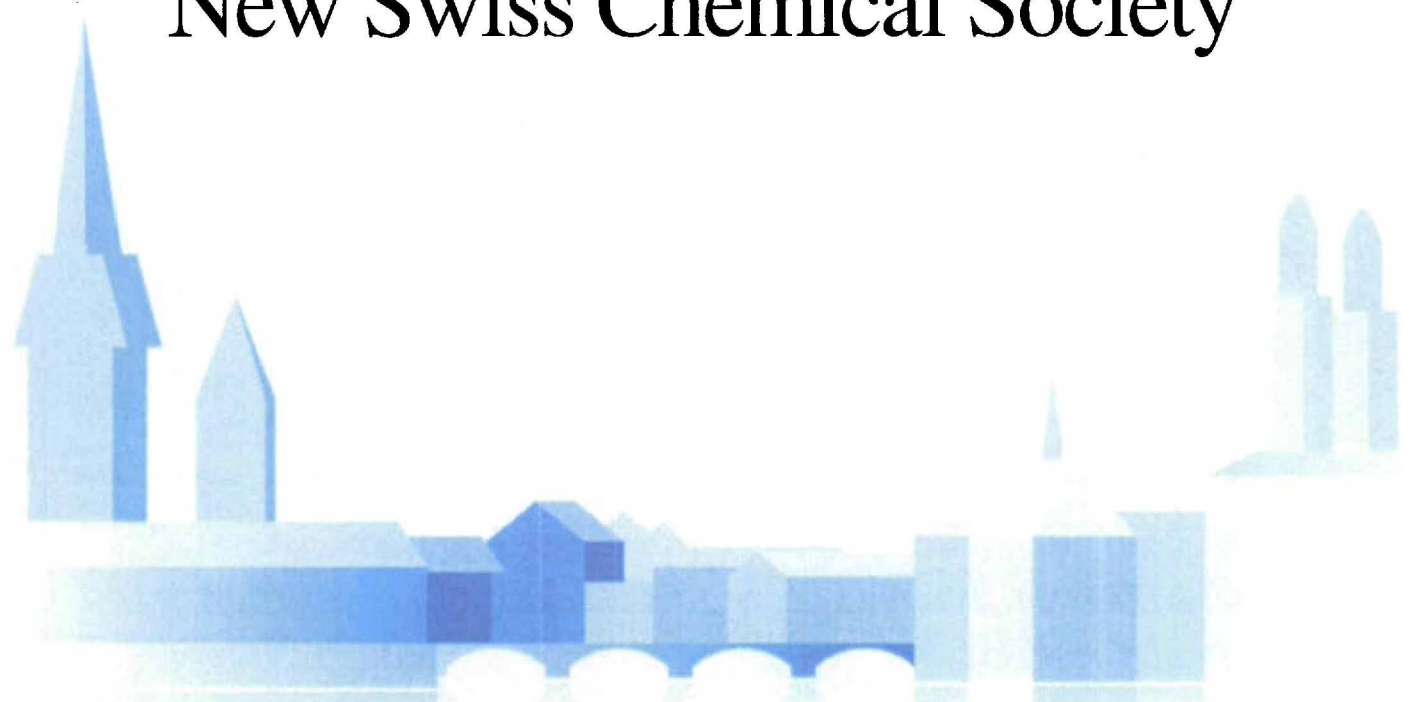
27. April 2001 Prof. *Peter Maitlis*
University of Sheffield
'Why Study Metal Catalysed CO Hydrogenation when Oil is Cheap Again?'

Novartis-Chemistry Lectureship 2000/2001

Location: Novartis Pharma AG, Auditorium Horburg, WKL-430.3.20
Müllheimerstr. 195, CH-4057 Basel
Time: 10.30 am ('Get Together': 10.00 am)

April 4, 2001 *Masakatsu Shibasaki*
University of Tokyo, Japan

New Swiss Chemical Society



FALL MEETING 2001 – ZÜRICH

Friday, 12th October, 10.00 – 17.00

University of Zürich – Main Building

Invitation to Present a Scientific Communication

In Analytical Chemistry, Medicinal Chemistry,
Inorganic and Coordination Chemistry, Organic
Chemistry, Physical Chemistry, and
Computational Chemistry

Organized by Prof. H. Berke (Uni. ZH) and the Section of Chemical
Research of the New Swiss Chemical Society.

DEADLINE FOR SUBMISSION OF ABSTRACTS

TUESDAY, 29th May, 2001

For more details see <http://www.unizh.ch/aci/nscs-fallmeeting-01>

INFORMATION

News

Novartis Venture Fund on the Path of Success

Basel, 19 February, 2001 – The Novartis Venture Fund can already look back on four years of successful operation. Today sees the publication of its fourth annual report. The number of new companies established with the support of the Novartis Venture Fund has risen to 83. And by the end of the year 2000, the Fund had provided a total of CHF 96 million for these start-ups. The number of jobs either created or preserved in these companies runs to about 1000.

Of the new companies to benefit from the support of the Novartis Venture Fund, five grew out of Swiss universities, six were spin-offs from Novartis, and four others involve former Novartis employees. Six of the companies are engaged in pharmaceutical research and eight are service companies, four of them providing services to the pharmaceutical industry. Three others are engaged in the marketing of products. Eleven of the companies are operational in Switzerland, three in the USA, and one each in France, Ireland, The Netherlands and Kenya.

The Novartis Venture Fund can look forward to a secure future. Thanks to the successful business operations of some of the companies in its portfolio, it was able to book its first major capital repayments and will thus be

in a position to continue its investment activities. In so doing, the Fund remains faithful to the unique positioning of its organization. Unlike other providers of venture capital, its investment decisions do not focus exclusively on profit considerations. 'The creation of jobs continues to be an important concern of the Fund,' explains François L'Eplattenier, President of the Supervisory Board. The prospects which the companies have of successfully implementing their scientific results in an economic setting represent another important criterion.

The annual report of the Novartis Venture Fund (in English), which summarizes the activities of the Fund and describes some examples of newly founded companies, can be ordered from the following address:

Dr. Rudolf Gyax
Portfolio- and Business-Manager
Novartis International
WSJ-200.225
CH-4002 Basel
E-Mail: rudolf.gyax@group.novartis.com

Further information on the Fund can be found on the internet at <http://www.venture-fund.novartis.com>.

Honors/Ehrungen

Prof. Jack Dunitz, Laboratorium für Organische Chemie, ETH Zürich, wurde zum Honorary Fellow of the Royal Society of Chemistry ernannt.

Lectures

Basler Chemische Gesellschaft

Donnerstag, 17.30 Uhr
Institut für Organische Chemie, Kleiner Hörsaal

26. April 2001 Prof. Dr. Alois Fürstner
Max-Planck-Institut für Kohlenforschung,
Mülheim/Ruhr, D
'Neue Beiträge zur Metathese von Alkenen und Alkinen'

Berner Chemische Gesellschaft

Mittwoch, 16.30 Uhr
Hörsaal EG 16
Departement für Chemie und Biochemie, Freiestr. 3
(Kaffee um 16.10 Uhr vor dem Hörsaal)

4. April 2001 Prof. Luisa De Cola
Institute of Molecular Chemistry,
University of Amsterdam
'Electron Transfer in Multicomponent Systems'

Société Chimique de Genève

Lundi, 17.30 h
Amphithéâtre A 150, UNI Sciences II, 30, Quai E. Ansermet

14 mai 2001 Dr. P. Pottier
Centre National de la Recherche Scientifique, France
'Contributions à la médecine'

Société Vaudoise des Sciences Naturelles

at 5 p.m.
Université de Lausanne UNIL

April 4, 2001 Prof. R. Zenobi
Auditorium A ETHZ, CH
BEP UNIL 'Modern Laser-Based Mass Spectrometry'
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