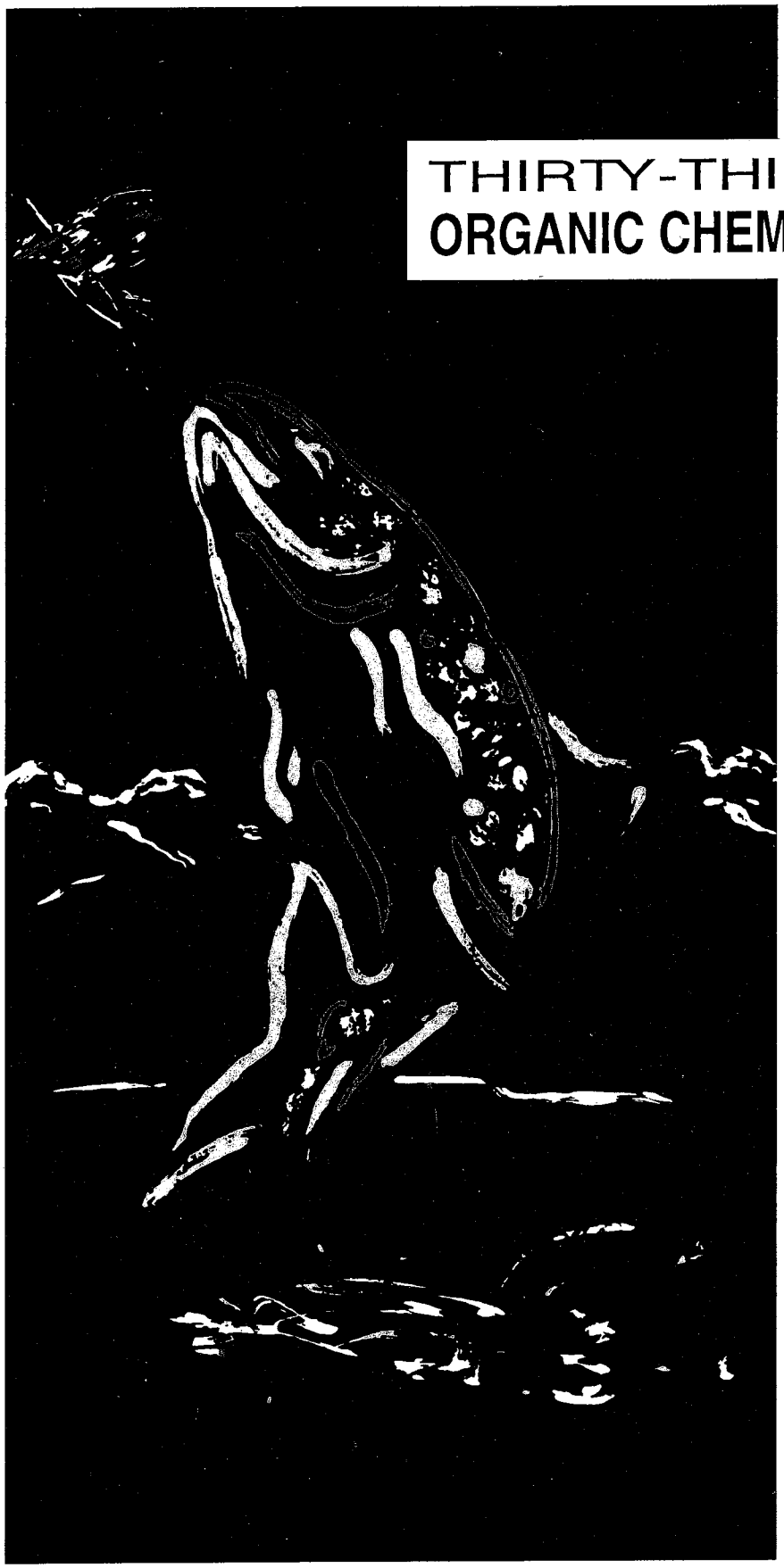

THIRTY-THIRD NATIONAL ORGANIC CHEMISTRY SYMPOSIUM

JUNE 13-17, 1993
MONTANA STATE UNIVERSITY
BOZEMAN, MONTANA

Program and Abstracts

TABLE OF CONTENTS

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Strand Union Graphics
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33RD NATIONAL ORGANIC CHEMISTRY SYMPOSIUM

June 13-17, 1993
Montana State University
Bozeman, Montana

Sponsored by

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OF THE AMERICAN CHEMICAL SOCIETY

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SYMPOSIUM PROGRAM

All lectures are scheduled to take place in the Strand Union; all Poster Sessions are scheduled to take place in the North Gym.

Sunday	
1:00 pm - 9:00 pm	Registration in the Strand Union
8:30 pm - 12:00 am	Opening Mixer and Poster Session A in the North Gym
Monday morning	Presiding: **Amos B. Smith, III,** *Symposium Executive Officer*
7:30 am - 12:00 pm	Registration in the Strand Union
8:30 am - 8:50 am	Opening Remarks
8:50 am - 9:00 am	Welcome by **Robert J. Swenson,** *Vice President for Research and Creative Activities, Montana State University*
9:00 am - 10:00 am	**Larry E. Overman** *Charge as a Key Component in the Design of New Cyclization Reactions*
10:00 am - 10:15 am	Questions
10:15 am - 10:45 am	Break
10:45 am - 11:45 am	**James D. White** *Total Synthesis of Macrolide Antibiotics. A Route to Rutamycin B*
11:45 am - 12:00 pm	Questions
Monday evening	Presiding: **P. W. Jennings,** *Local Committee Co-Chairman*
7:30 pm - 8:30 pm	**Andrew G. Myers** *Mechanistic and Synthetic Studies of the Enediyne Antibiotics*
8:30 pm - 8:45 pm	Questions
8:45 pm - 9:45 pm	**Yoshito Kishi** *Natural Product Chemistry: Palytoxin*
9:45 pm - 10:00 pm	Questions
10:00 pm - 12:00 am	Mixer and Conclusion of Poster Session A in the North Gym
Tuesday morning	Presiding: **Arnold Craig,** *Local Committee Co-Chairman*
9:00 am - 10:00 am	**Louis S. Hegedus** *Synthesis of Amino Acids and Peptides Using Photolytic Reactions of Chromium Carbene Complexes*
10:00 am - 10:15 am	Questions
10:15 am - 10:45 am	Break
10:45 am - 11:45 am	**Cynthia J. Burrows** *Oxidation of Hydrocarbons and DNA Using Nickel Catalysts*
11:45 am - 12:00 pm	Questions

Tuesday evening		Presiding: **Michael P. Doyle**, *Chairman, Organic Division of ACS*
7:30 pm	8:45 pm	**Elias J. Corey**, Roger Adams Award Address: *Studies on Enantioselective Synthesis*
9:00 pm	12:00 am	Mixer and Poster Session B in the North Gym
Wednesday morning		Presiding: **Amos B. Smith, III**, *Symposium Executive Officer*
8:30 am	9:30 am	**Donald A. Tomalia** *Starburst™/Cascade Dendrimers: Fundamental Building Blocks for a New Nanoscopic Chemistry Set*
9:30 am	9:45 am	Questions
9:45 am	10:30 am	Break
10:30 am	11:30 am	**Fred Wudl** *Synthesis and Determination of Exotic Properties of the Methanofullerenes and Fulleroids: Periconjugation and Quasi Shift Reagent Effects*
11:30 am	11:45 am	Questions
11:45 am	12:45 pm	**Jean-Marie Lehn** *Perspectives in Supramolecular Chemistry: From Molecular Recognition Towards Self-Organization*
12:45 pm	1:00 pm	Questions
Wednesday evening		
5:30 pm	7:30 pm	Western Bar-B-Que
7:30 pm	10:00 pm	College National Finals Rodeo
10:00 pm	12:00 am	Mixer and continuation of Poster Session B in the North Gym
Thursday morning		Presiding: **Thomas R. Hoye,** *1995 National Organic Symposium Executive Officer*
9:00 am	10:00 am	**Christopher T. Walsh** *Studies on the Molecular Mechanism for Vancomycin Resistance in Enterococcus faecium BM4147*
10:00 am	10:15 am	Questions
10:15 am	10:45 am	Break
10:45 am	11:45 am	**Stuart L. Schreiber** *Cell Cycle Signaling Pathways Sensitive to Immunophilin-Ligand Complexes*
11:45 am	12:00 pm	Questions
12:00 pm		Closing Remarks

33RD NATIONAL ORGANIC CHEMISTRY SYMPOSIUM: ORGANIZATIONAL RESPONSIBILITIES

Overall management:

Amos B. Smith, III, *National Organic Chemistry Symposium Executive Officer*

Local arrangements:

P. W. Jennings, *Local Co-Chairman*
Arnold Craig, *Local Co-Chairman*
Melanie J. Stocks, *Conference Services*
Carol Carpenter, Darcy Van Beek, Lori Gibson, Amy McCubbin, *Conference Services*
Kathy Kohlbeck, Sue Edgmond, Chris Hallock, Devon Baker, Bill Brown, *Strand Union Graphics*
Montana Travel, *Travel and Tour Arrangements*

General oversight:

ACS Division of Organic Chemistry:

	1992	1993
Chairman	James A. Marshall	Michael P. Doyle
Chairman-Elect	Michael P. Doyle	Franklin A. Davis
Past Chairman	Joseph J. Gajewski	James A. Marshall
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	Steven D. Burke	William A. Nugent
	Thomas R. Hoye	Homer L. Pearce
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	James D. White	Peter J. Stang
	Kathlyn A. Parker	Michael P. Doyle
	Peter J. Stang	Victor Snieckus
Alternate Councilors	David M. Lemal	Peter Beak
	Peter Beak	Marye Anne Fox
	Marye Anne Fox	Cynthia A. Maryanoff
	Cynthia A. Maryanoff	Dennis P. Curran

THE ROGER ADAMS AWARD IN ORGANIC CHEMISTRY

The Roger Adams Award in Organic Chemistry is sponsored jointly by the American Chemical Society, Organic Reactions, Inc., and Organic Synthesis, Inc. The award recognizes the distinguished career of Roger Adams, who played a vital role in each of these three organizations. He was Chairman of the Board of Directors as well as President of the American Chemical Society, and he co-founded *Organic Syntheses* and *Organic Reactions*.

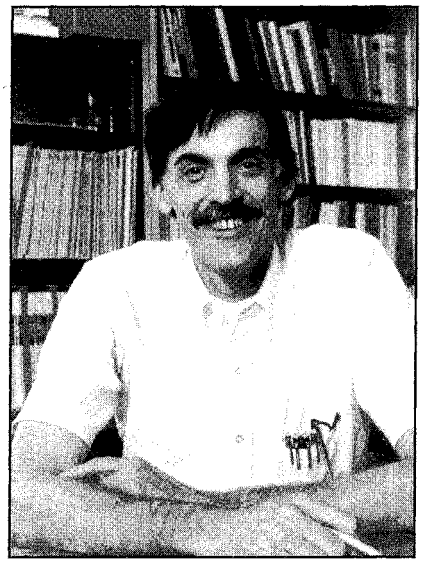
The award is made biennially to an individual, without regard to nationality, for outstanding contributions to research in organic chemistry. The award consists of a gold medal, a sterling silver replica of the medal, and an honorarium of twenty-five thousand dollars. It is presented at the biennial National Organic Chemistry Symposium of the Division of Organic Chemistry of the American Chemical Society. The awardee is a featured lecturer in the program of the Symposium.

The recipient of this year's Roger Adams Award is Professor Elias J. Corey of Harvard University. Professor Corey was cited "for his many contributions to the logic, planning, methodology, and execution of complex chemical synthesis." His award address entitled *"Studies on Enantioselective Synthesis"* will be delivered on Tuesday evening, June 15, 1993.

E.J. Corey

Speakers

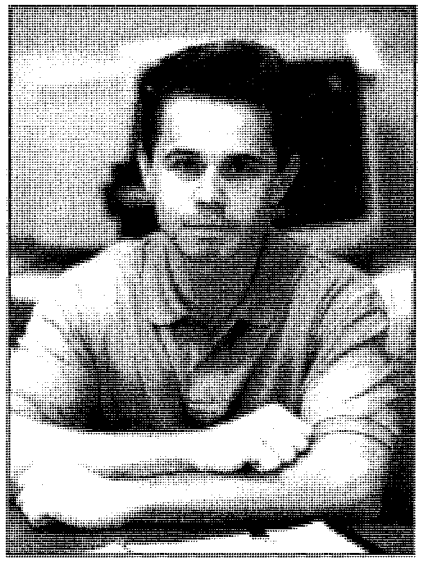
Cynthia J. Burrows



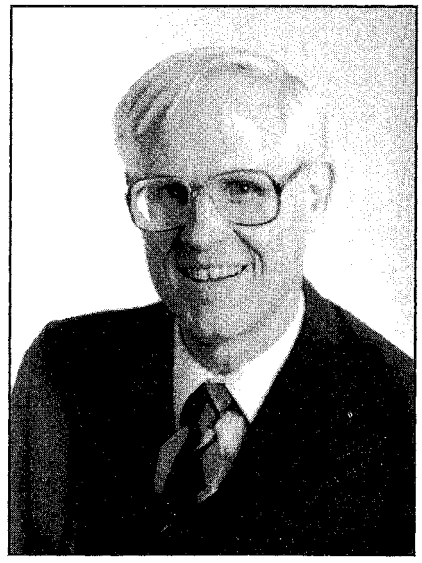
Louis S. Hegedus

Yoshito Kishi

Jean-Marie Lehn

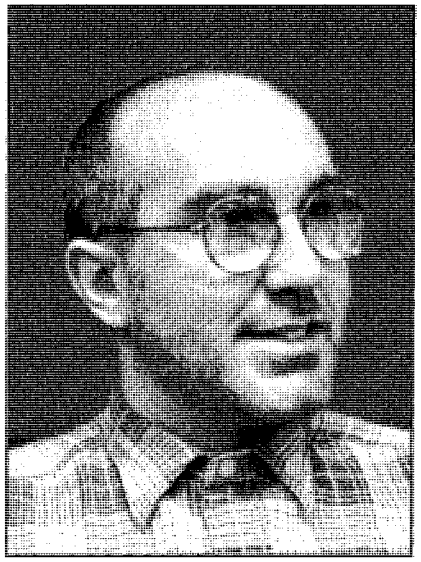


Andrew G. Myers



Larry E. Overman

Speakers



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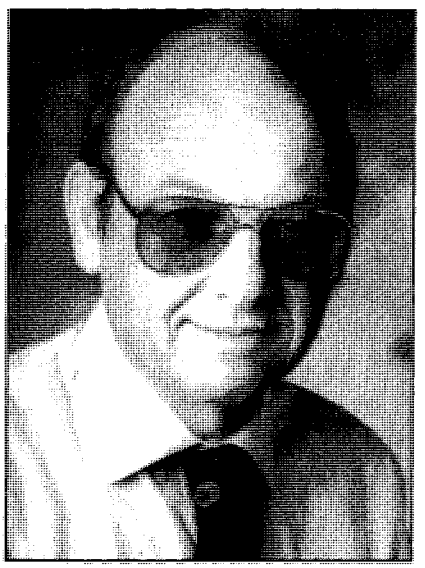

Fred Wudl

GRADUATE FELLOWS AND SPONSORS

Listed below and on the following page are the names of the twenty-four advanced graduate students who won Division of Organic Chemistry Graduate Fellowships during the past two years. Also listed are the names of their institutions, their faculty research advisors, and the companies that sponsored these awards. The Division of Organic Chemistry is pleased to honor these extraordinary students and to acknowledge with gratitude the financial support provided by these outstanding companies.

1991-1992	1992-1993
American Cyanamid Company	
Steve Chamberlin *The University of Chicago* *Professor William Wulff*	Stewart L. Fisher *California Institute of Technology* *Professor Barbara Imperiali*
Dow Chemical Company Foundation	
Todd Underiner *University of Wisconsin* *Professor Charles P. Casey*	Kathlynn C. Brown *The University of Texas at Austin* *Professor Thomas Kodadek*
Eli Lilly & Company	
Wendy B. Young *Princeton University* *Professor Edward C. Taylor*	Steve W. Elmore *Ohio State University* *Professor Leo Paquette*
Glaxo Research Laboratories	
Gregory S. Welmaker *University of South Carolina* *Professor James A. Marshall*	Andrew J. Carpenter *University of South Carolina* *Professor Robert Coleman*
ICI Americas Pharmaceuticals	
Jonathan R. Parquette *Stanford University* *Professor Barry M. Trost*	Mark E. Schnute *University of Illinois at Urbana-Champaign* *Professor Scott Denmark*
Merck Sharp & Dohme Research Laboratories	
Michael K. Rosen *Harvard University* *Professor Stuart L. Schreiber*	James L. Leighton *Harvard University* *Professor David Evans*

1991-1992	1992-1993
The Monsanto Company	
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R. W. Johnson Pharmaceuticals	
John Anthony *University of California at Los Angeles* *Professor François Diederich*	Erik J. Sorensen *Scripps Research Institute* *Professor K. C. Nicolaou*
SmithKline Beecham	
Stefan Loren *University of California-Berkeley* *Professor Joel M. Hawkins*	Allan C. Krueger *Wayne State University* *Professor James Rigby*

TRAVEL AWARDS

Travel Awards for Faculty from Undergraduate Institutions
Sponsored by Janssen

Dawood Afzal
Northeast Missouri State University

Jeffrey H. Byers
Middlebury College

D. Scott Davis
Mercer University

Roger A. Egolf
Pennsylvania State University, Allentown

Jeff Frick
Illinois Wesleyan University

Raymond J. Giguere
Skidmore College

Girita Subramaniam
Pennsylvania State University

Phyllis Leber
Franklin & Marshall College

William H. Miles
Lafayette College

Ernest G. Nolen
Colgate University

Leo A. Ochrymowycz
University of Wisconsin, Eau Claire

Kevin E. O'Shea
Florida International University

Tetsuo Otsuki
Occidental College

Michael W. Pelter
Purdue University Calumet

Travel Awards for Undergraduates
Sponsored by the Organic Division of the American Chemical Society

Jennifer Allen
Occidental College

Todd Brugel
Muhlenberg College

Duke Fitch
University of Pennsylvania

Kevin Gardinier
Colgate University

Christina Gardner
Barry University

Amy Geffken
Middlebury College

Eric Kantorowski
California State University, Fullerton

Craig Masse
University of Massachusetts at Lowell

Bonnie May
University of Regina

Brendan O'Leary
Middlebury College

Sari Jayne Paikoff
State University of New York, Stony Brook

Timothy Snowden
Clemson University

Gregory N. Tew
North Carolina State University

MONTANA STATE UNIVERSITY AND RODEO

Rodeo is synonymous with Montana State University. The first MSU rodeo was held in 1957 and the sport has grown steadily since that time. Success has been a key to the MSU rodeo team, with the men winning 14 of the last 16 regional titles and three national championships. The women have won 15 regional championships and one national championship.

The College National Finals Rodeo determines the national team and event champions, and has been held at Montana State University 23 out of the last 24 years.

Rodeo is the only sport in the world to have developed from skills required in an actual working situation. Rodeo's "on the edge" excitement from rough stock events to timed events has enough entertainment for the whole family.

Rodeo found its way into the college ranks in 1949. Due to a growing interest in forming an organization to promote rodeo as a nationally recognized and accepted collegiate sport, representatives from thirteen colleges met and adopted a constitution and bylaws - the beginning of the National Intercollegiate Rodeo Association (NIRA). From thirteen colleges initially, the NIRA has grown to a student organization with 120 member colleges and universities and approximately 2,300 individual student members. The efforts of the founding students of the NIRA, to combine education and rodeo, have certainly been successful.

College National Final Rodeo Schedule of Events

Monday, June 14
Slack at the Brick Breeden Fieldhouse

Tuesday, June 15
Slack at the Brick Breeden Fieldhouse
Inland Empire Shows open south of Brick Breeden Fieldhouse
Noon to Midnight, Tuesday through Sunday
CNFR Parade, Downtown Bozeman - 2:00 pm
CNFR Championship Performance, Brick Breeden Fieldhouse, 7:30 pm

Wednesday, June 16
CNFR Championship Performance, Brick Breeden Fieldhouse, 7:30 pm
Corral West Bull Fight, Brick Breeden Fieldhouse, 9:30 pm

Thursday, June 17
CNFR Championship Performance, Brick Breeden Fieldhouse, 7:30 pm
Corral West Bull Fight, Brick Breeden Fieldhouse, 9:30 pm

Friday, June 18
CNFR Championship Performance, Brick Breeden Fieldhouse, 7:30 pm
Corral West Bull Fight, Brick Breeden Fieldhouse, 9:30 pm

Saturday, June 19
CNFR Championship Performance, Brick Breeden Fieldhouse, 7:30 pm
Corral West Bull Fight, Brick Breeden Fieldhouse, 9:30 pm

Sunday, June 20
CNFR Championship Finals, Matinee Performance, Brick Breeden Fieldhouse, 1:30 pm

LECTURE ABSTRACTS

Oxidation of Hydrocarbons and DNA using Nickel Catalysts

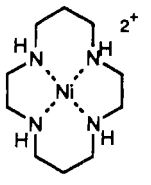
Cynthia J. Burrows

Department of Chemistry, University at Stony Brook

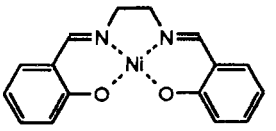
Stony Brook, NY 11794

Curiosity about the mechanisms of biological oxidations and the search for new catalysts for industrial applications have led to exciting discoveries in transition metal-mediated oxidation of organic and biological substrates. As examples, one may cite the stereoselective hydroxylation of steroids by the enzyme Cytochrome P_{450}, the oxidation of DNA using the antitumor agent iron-bleomycin, Sharpless's asymmetric oxidation of allylic alcohols using chiral titanium reagents, and the industrial production of propylene oxide with molybdenum catalysts.

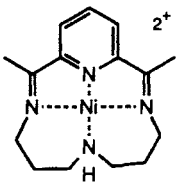
Our interests began with the study of macrocyclic nickel(II) complexes where the inorganic coordination chemistry was known, but applications to catalysis were not. Nickel coordination compounds are well suited to catalytic oxidation chemistry; complexation within a polyazamacrocyclic cavity allows one to oscillate between various coordination numbers (4, 5, or 6), coordination geometries (square planar, tetrahedral, square pyramidal and octahedral) and oxidation states (I, II, or III). Each of these features is tunable and highly sensitive to the structure of the ligand.



NiL¹



NiL²



NiL³

Nickel-Catalyzed Olefin Epoxidation

In 1987, we found that simple tetradentate ligands such as cyclam, $\mathbf{L^1}$, and salen, $\mathbf{L^2}$, render nickel(II) active as a catalyst for olefin epoxidation.[1] We were particularly excited by the discovery that nickel salen complexes utilize a practical oxidant, sodium hypochlorite, and

STUDIES ON ENANTIOSELECTIVE SYNTHESIS

E. J. Corey

Department of Chemistry
Harvard University
Cambridge, Massachusetts, 02138

One of the most interesting and crucial areas of chemical research at present is the development of new catalysts and reagents for enantioselective synthesis. Many laboratories have contributed to the recent flood of important new results in this area. Through their research the science of chemical synthesis has been profoundly altered and enriched. This lecture reviews certain aspects of our work in this area subsequent to that which was described at the 31st National Organic Chemistry Symposium in 1989.[1] Specifically, Part I describes research on catalytic enantioselective Diels-Alder reactions and Part II deals with enantioselective addition of carbon to carbonyl groups.

Part I

Earlier research in our group on the use of the 8-phenylmenthyl group as a chiral controller for Diels-Alder reaction of acrylate esters[2] nurtured the idea that neighboring aromatic π-groups could influence transition-state energies in such a way as to enforce high stereoselectivity.[3] Thus, the $AlCl_3$-catalyzed Diels-Alder reaction shown in Fig. 1 afforded a major adduct (*ca.* 97 : 3 diastereoselectivity) which could be transformed into the optically pure lactonic prostaglandin precursor **1b** with recovery of 8-phenylmenthol. We supposed that the catalytically active species is the *s*-trans ester–$AlCl_3$ complex **1a** and that the aromatic ring stabilizes both the complex and the transition state by proximity with the electron deficient carbonyl carbon; acrylate face selectivity is then a consequence of the steric screening by the aromatic ring. It is important to recognize that electron deficiency in the Lewis-acid complexed carbonyl is preserved even in the Diels-Alder product, so it must exist in the transition state for the reaction, as well as in the initial complex of $AlCl_3$ with the dienophile. The idea that π-aromatic units could be used both to stabilize specific transition-state geometries and to provide stereoselectivity through facial

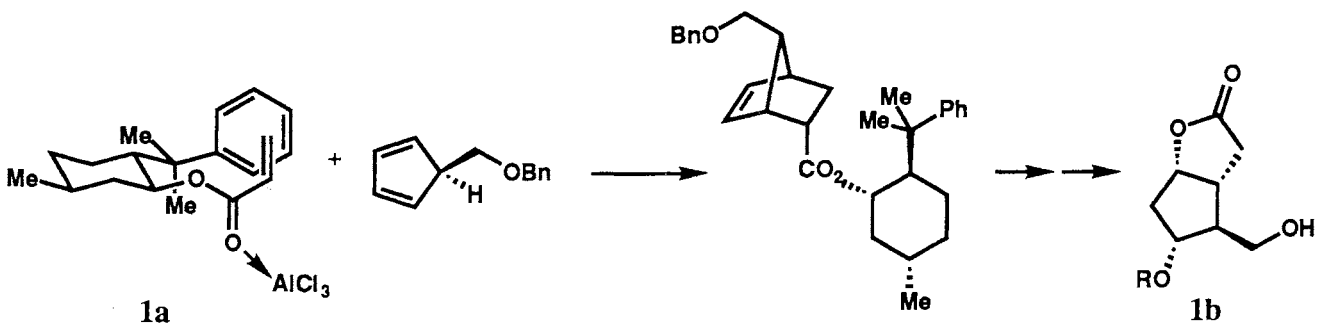


Figure 1. Enantioselective route to prostaglandins using the 8-phenylmenthol controller.

Synthesis of Amino Acids and Peptides Using Photolytic Reactions of Chromium Carbene Complexes

Louis S. Hegedus, Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523

Introduction

α-Amino acids occupy a prominent position in current organic chemistry, and many new synthetic methods for their preparation have been developed.[1] A major impetus for this activity is to provide routes to unnatural α-amino acids for incorporation into small peptides, with the intent of altering the stability, bioavailability or bioselectivity of these peptides.[2]

Modern synthetic approaches to optically active α-amino acids are many and varied (Figure 1). They include (a) alkylation of optically active glycine enolate equivalents with carbon electrophiles; (b) alkylation of electrophilic optically active glycine equivalents with carbon nucleophiles; (c) amination of acid derivative enolates with "electrophilic" nitrogen; (d) amination of α-haloacids with nucleophilic nitrogen; (e) α-carboxylation of amines. It is an unusual variation of this last approach that forms the basis of this lecture.

Results

Over ten years ago, Mike McGuire, at that time a graduate student in my research group, made the remarkable observation that photolysis of Fischer type chromium carbene complexes produced species that had ketene-like reactivity (Eq. 1). Thus, photolysis of heteroatom stabilized "Fischer" carbenes in the presence of alkenes gave cyclobutenones, in the presence of imines gave β-lactams, and in the presence of alcohols or amines gave α-heteroatom carboxylic acid derivatives. In principle, photolysis of *amino*carbene complexes in the presence of alcohols should produce α-amino acid esters. The challenge was to

NATURAL PRODUCT CHEMISTRY: PALYTOXIN

Yoshito Kishi
Department of Chemistry, Harvard University
Cambridge, Massachusetts 02138

Palytoxin, the toxic principle isolated from marine soft corals of the genus *Palythoa*, is the most poisonous substance known to date except for a few naturally occurring proteins found in bacteria and plants [ref. 1]. The gross structure of palytoxin was elucidated in 1981 by two groups independently, the one led by Professor Hirata at Nagoya in Japan [ref. 2a] and the other by Professor Moore at Honolulu in the United States [ref. 2b]. Thus, it became evident palytoxin to be uniquely distinct from molecules, which organic chemists previously dealt, in terms of magnitude of molecular size and of structural complexity. Shortly after the gross structure was elucidated, we decided undertaking investigations on this extraordinary natural product; our interests were primarily two-fold, chemical synthesis and conformational analysis. However, we realized that the information given by the gross structure was not sufficient enough to address our questions properly. For this reason, the very first step of this project was to establish unambigously the complete structure of palytoxin, and we decided to depend principally on organic synthesis to do so. On the basis of extensive efforts approximately for two years, we succeeded in elucidating the complete structure of palytoxin in 1982 [ref. 3]. In this presentation, we shall review our efforts on the chemical synthesis and conformational analysis of palytoxin.

1. Total Synthesis

By the summer of 1985, we developed the syntheses of the eight key building blocks. Each synthesis was improved and polished up to the level satisfactory in terms of overall efficiency and practicability. For example, before the current route developed, the C.8-C.22 segment had been synthesized by four different routes. Each of the syntheses had provided numerous opportunities to discover exciting and intriguing chemistry, which is, in our view, worth for its own sake. However, we should emphasize the fact that the progress beyond this stage critically depended on the availability of these building blocks. In this respect,

PERSPECTIVES IN SUPRAMOLECULAR CHEMISTRY: FROM MOLECULAR RECOGNITION TOWARDS SELF-ORGANISATION

Jean-Marie LEHN
Université Louis Pasteur, Strasbourg and Collège de France, Paris

Supramolecular chemistry has relied on more or less preorganised molecular receptors for effecting molecular recognition, catalysis and transport processes. A step beyond consists in the design of systems undergoing *molecular self-organisation*, i.e. systems capable of spontaneously generating a well-defined supramolecular architecture by *self-assembling* from their components in a given set of conditions.

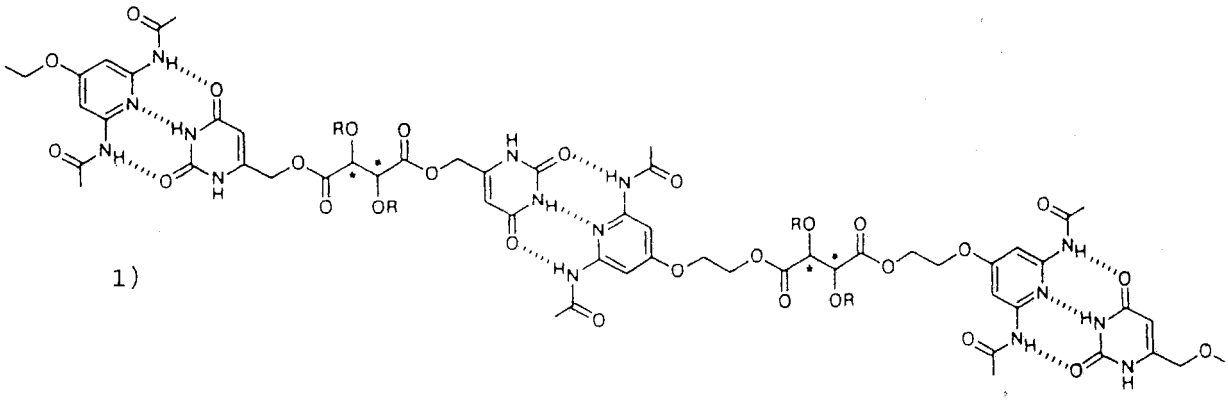
The *molecular information* necessary for the process to take place must be stored in the components and acts through selective molecular interactions. Thus, these *programmed supramolecular systems* operate via molecular recognition.

Several approaches to self-assembling systems have been pursued:

1) the generation of *mesophases* and *liquid crystalline polymers* of supramolecular nature from complementary components, amounting to macroscopic expression of molecular recognition;
2) the molecular recognition directed formation of *ordered solid state structures*;
3) the *self-assembling of inorganic species* based on ligand design and on the use of suitable coordination algorithms as expressed in
   a) the formation of helical metal complexes, the *double-stranded and triple-stranded helicates*, that result from the spontaneous organisation of two or three linear polybipyridine ligands respectively into a double or a triple helix by binding of specific metal ions;
   b) the self-assembling of different ligands into a single structure;
   c) the spontaneous generation of a closed cage structure from two different ligands and metal ions in a process involving the self-assembling of 11 particles !

The design of molecular information controlled, "*programmed*" and functional self-organising systems represents new horizons in supramolecular chemistry towards "*intelligent*", functional supramolecular materials, network engineering and polymolecular patterning.

- Lehn, J.-M. *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 89; **1990**, *29*, 1304 and references therein.
- Gulik-Grzywicki, T.; Fouquey, C.; Lehn, J.-M., *Proc. Natl. Acad. Sci. USA* **1993**, *90*, 163.
- Baxter, P.; Lehn, J.-M.; DeCian, A.; Fischer, J. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 69.



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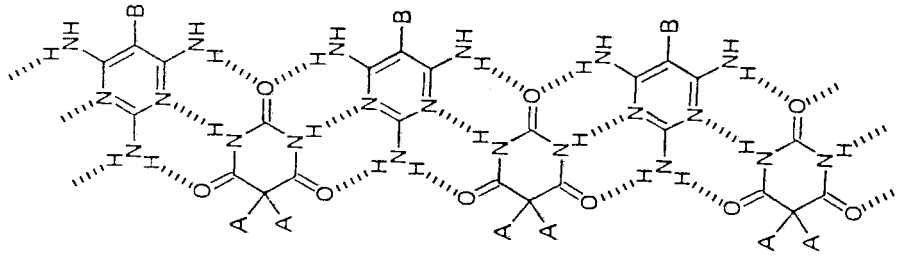

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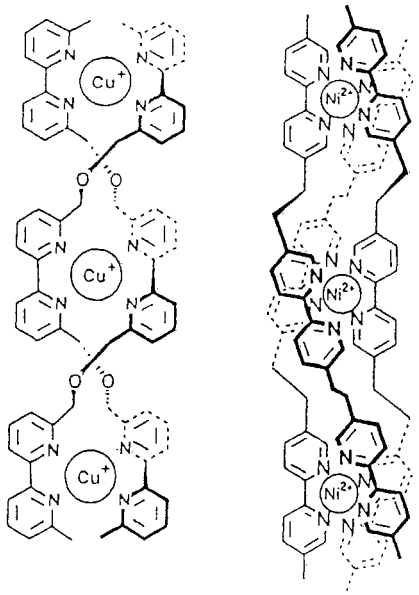
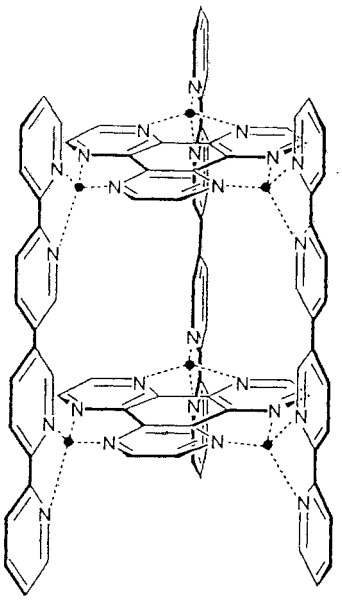


3a)



3c)

Mechanistic and Synthetic Studies of the Enediyne Antibiotics.

Andrew G. Myers

California Institute of Technology

Perhaps more than any class of natural products discovered in recent times, the enediyne antibiotics have provided a wealth of opportunity for discovery in chemistry and biology. The family comprises the structurally unprecedented series of molecules neocarzinostatin chromphore (**1**), esperamicin (**2**), calichemicin (**3**), dynemicin (**4**), and kedarcidin chromophore, for which the structure **5** has recently been proposed.[1,2] These molecules are remarkable from many perspectives. The combination of structural complexity, unique functionality, strain, and chemical instability they exhibit has provided an exciting challenge to synthetic chemists. Their unusual reactivity, most notably a common ability to generate carbon-centered, aromatic 1,4-biradicals, has led to new insights in physical organic chemistry and to the discovery of new biradical-forming organic reactions. Finally, and perhaps most importantly in terms of benefit to mankind, they have revealed a new strategy for the sequence-specific damage of double helical DNA and have provided new leads for the development of chemotherapeutics. Research described in this lecture concerns a series of structural, mechanistic, and synthetic studies of the enediyne antibiotics and nonnatural molecules designed to mimic these agents. The objectives of these studies are (1) to increase our understanding of the detailed mechanisms by which these substances damage DNA and function as antitumor agents; and (2) to provide by chemical synthesis new structures for study as potential DNA cleaving agents and as leads for the design of new antitumor agents.

Charge as a Key Component in the Design of New Cyclization Reactions

Larry E. Overman

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Introduction. Progress in synthetic organic chemistry during the past 30 years has been remarkable.[1] A variety of selective reagents and synthesis strategies have been developed that allow impressively complex target molecules to be assembled.[2] Nonetheless, the science of synthetic organic chemistry is remarkably immature when confronted with the challenge of preparing even relatively simple target molecules in a practical fashion on a large scale. For example, the synthesis of many currently investigated drug candidates, which frequently contain only a few rings and/or stereocenters, often presents formidable problems in spite of their relative lack of complexity.[3]

Future advances in our ability to prepare increasingly complex target structures will come to a large extent from the development of new powerful and selective organic transformations. Although there is no universal definition of a "powerful synthetic reaction," it is most often one that significantly increases chemical complexity, a change that is typically related to increasing the value of the reaction product.[4] Selective reactions are a hallmark of efficient synthetic sequences, since selective reactions produce fewer byproducts and require less protection of potentially competing functional groups. Positional (regioselectivity), stereochemical

Cell Cycle Signaling Pathways Sensitive to Immunophilin-Ligand Complexes[1]

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Cambridge, Massachusetts 02138

Many studies of signal transduction, the process by which an extracellular molecule influences intracellular events, have involved cells of the immune system. For example, the molecular events associated with signaling pathways in T lymphocytes have been illuminated with remarkable clarity during the past several years. As immunologists and cell biologists have now identified many of the molecules that regulate cell function, scientists with a chemical training are well-positioned to achieve the next level of understanding. Chemistry is now able to address a level of complexity that extends beyond the systems studied in classical biochemistry. Thus, the living cell poses a great challenge for organic chemists in the future. How can chemists uniquely approach this problem?

Natural products provide chemists with powerful tools to study molecular aspects of cellular function.[2] Many natural products interfere with specific cellular processes, including growth and division. By studying how the natural products interfere with these processes, the molecular details of the processes themselves can be illuminated. Why haven't cell biologists more regularly adopted this approach? The primary reason is that natural products-based studies of cellular function invariably require the methods of synthetic chemistry, which most biologists are unfamilar with. On the other hand, cell biologists have other powerful tools at their disposal that are unfamilar to many chemists.[3] (Chemists who wish to study cells would be well advised to adopt some of these techniques.) This lecture will focus on a natural products-based study of signal transduction pathways that regulate early events in the cell cycle. I hope to illustrate that the study of natural products together with one simple technique from cell biology, flow cytometry, is a powerful combination for unraveling some of the mysteries of complex cellular processes.

STARBURST*/CASCADE DENDRIMERS: FUNDAMENTAL BUILDING BLOCKS FOR A NEW NANOSCOPIC CHEMISTRY SET

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Chemistry is not just a science involving the study of electron movement to rearrange and connect atoms--it is a philosophy, it is a way of thinking about the world, about how matter is constructed, organized and how it functions throughout the dimensional hierarchy of the universe, from the simplest atoms to the most complex phenomena--namely life itself. The adventure I would like to share with you in this lecture evolved from just such a philosophical perspective. It deals to a large extent with the *analysis and interpretation of some simple, but pervasive patterns observed in Nature.*

Historically, the origin of our "first chemistry set," that based on atomic building blocks, dates back to the publication in 1789 of "The Elements of Chemistry" by Antoine Lavoisier (1743-1794). At that time, these building blocks were defined empirically as the "actual terms whereat chemical analysis had arrived" and consisted of 23 authentic building blocks (elements) as revealed by Lavoisier. This new science described a totally different vision of compound materials which were characterized by constant, well defined elementary compositions, as opposed to physical mixtures of indefinite composition. The objectives of its disciples were to prepare new substances and materials with new properties. These new

*Trademark of the Michigan Molecular Institute

Studies on the Molecular Mechanism for Vancomycin Resistance in *Enterococcus faecium* BM4147

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The vancomycin group of glycopeptide antibiotics, used to treat a wide variety of infections due to gram-positive bacteria, acts by complexation with the peptidyl-D-Ala-D-Ala termini of the peptidoglycan of growing bacterial cell walls. Despite being used clinically for more than 30 years, bacterial resistance to vancomycin has arisen only recently. In *Enterococcus faecium* BM4147, the plasmid pIP816 confers an inducible resistance to vancomycin that requires five gene products. The functions for some have been inferred from the predicted amino acid sequences based on the DNA sequence determined by P. Courvalin's Group (Institut Pasteur, Paris). These gene products were overproduced and biochemically characterized in this laboratory. The first gene product whose function was determined, VanA, was initially identified as a 38 kDa membrane-associated protein, whose synthesis was inducible by vancomycin. Surprisingly, VanA shared 28 to 36% sequence similarity at the amino acid level with D-Ala-D-Ala ligases, which are responsible for synthesis of the D-Ala-D-Ala dipeptide, to which vancomycin binds. By overproduction and purification of VanA, it has been shown that VanA has D-Ala-D-Ala ligase activity with an altered substrate specificity for depsipeptides. These results imply that the cellular role for VanA may be to synthesize a novel D-Ala-X dipeptide that does not bind vancomycin but is still cross-linked and incorporated into the peptidoglycan. It has also been shown that VanH is a dehydrogenase that probably leads to synthesis of a precursor for the depsipeptide. The function of VanX is unknown.

Two additional gene products, VanR and VanS, comprise a two-component regulatory system based on sequence homologies to other proteins. By using

Total Synthesis of Macrolide Antibiotics. A Route to Rutamycin B

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Summary. A new method for the synthesis of macrolactones based on tin(IV)-mediated cyclization of ω-hydroxy trifluoroethyl esters is presented. The reaction is catalytic in the tin reagent and is believed to involve an ω-stannyloxy intermediate. An approach to the synthesis of the macrolide antibiotic rutamycin B is outlined in which four principal subunits are constructed. Two of these are coupled to assemble the linear polypropionate segment. Stereocontrol is exercised in these synthetic sequences through the application of crotylboronate and crotylstannane addition to aldehydes, and by aldol condensation with chiral ketone enolates.

Macrocyclic lactones ("macrolides") are ubiquitous in nature, occurring in a very wide variety of organisms including marine species. Many members of the family possess antibiotic activity and a few, such as erythromycin, are highly valued for their medicinal properties. As a structural class, macrolides surpass even the steroids in their spectrum of biological activities. Not surprisingly, there has been a great deal of interest in the synthesis of macrolide antibiotics, with the result that many innovative strategies have been developed for assembling the complex architecture of these substances [1].

Two issues of paramount importance must be faced when considering the synthesis of a complex macrolide. These are, first, the systematic creation of multiple chiral centers, some of which may be subject to stereomutation en route to the target and, second, the closure of a seco acid to a highly functionalized, often labile lactone at or near the final stage of the synthesis. Our studies of lactonization methodology in general and of synthetic routes to the antibiotic rutamycin B (**1**) in particular have addressed these dual problems with interesting, and sometimes unexpected results.

Of the two most frequently employed techniques for macrolactone synthesis from ω-hydroxycarboxylic acids (scheme I), that invoking carbonyl activation is by far the most common [2]. Hydroxyl activation, as in the Mitsunobu lactone synthesis, is a useful but more limited alternative. Methods in which both termini of the chain bear activating groups, have not been systematically

Synthesis and Determination of Exotic Properties of the Methanofullerenes and Fulleroids: Periconjugation and Quasishift Reagent Effects

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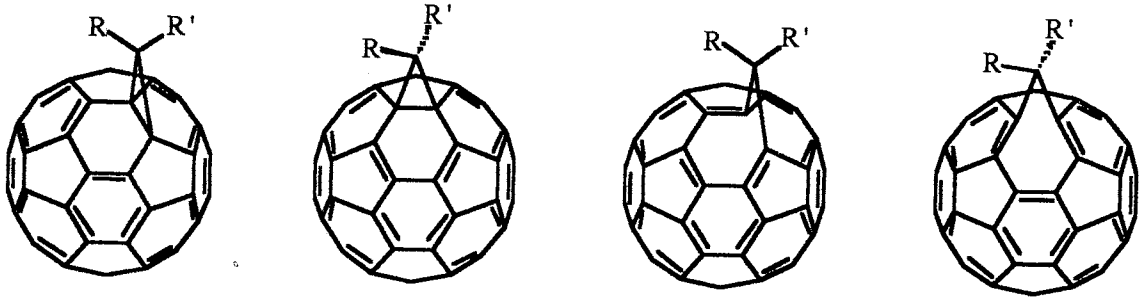
Santa Barbara, California 93106

Buckminsterfullerene C_{60}[1], the molecular allotrope of carbon with a truncated icosahedral symmetry contains six double bonds linking twelve pentagons. These are the most reactive sites of the molecule. The reaction of organic diazo compounds with C_{60} affords stable, characterizable derivatives of formal carbene addition[2] and represents a versatile way of functionalizing fullerenes[3,4]. Many isomers with very similar frameworks can be generated[2,3a] and the assignment of the correct structure to these adducts is critical

In principle, the single addition of a symmetric carbene moiety (R=R') to a double bond of C_{60} can produce up to four different isomers: the norcaradienic structures 1 and

Chart 1



1 2 3 4

2 (*methanofullerenes*)[5], with the three-membered ring spanning over a 6,6 and a 5,6

GENERAL INFORMATION

Welcome to the 33rd National Organic Chemistry Symposium. A special welcome to Bozeman is extended to you. We hope you will enjoy the Symposium and your stay in Bozeman.

Abstract Booklets: A copy of this Program and Abstract Book may be obtained by sending a check for $15.00 (payable to the ACS Division of Organic Chemistry) and a self-addressed 10" x 13" envelope to William R. Roush, Secretary-Treasurer, ACS Division of Organic Chemistry, Department of Chemistry, Indiana University, Bloomington, IN 47405.

Alcoholic Beverages: Please be advised that the Montana drinking age is 21, and state law stipulates that establishments serving alcohol see proof of age before serving. The same policy will be in effect during the mixers and barbecue. Montana State University must abide by Montana state policy, and will not be allowed to serve alcohol to anyone under 21 years of age.

Banking: There are two ATM machines located in the Strand Union. If you need to change American Express foreign travelers checks, please contact Montana Travel at 587-1188. Their office is located at 209 S. Willson and their hours are 8:00 am - 5:30 pm Monday through Friday.

Barbecue: A limited number of extra tickets for the barbecue are available for $15. These will be available at the registration desk on Monday only from 7:30 am until noon. No additional tickets will be available after that time.

Bookstore: The MSU Bookstore in the Strand Union serves as the University's main source for books, clothing, gifts, and novelty items with the Montana State University logo. In addition, you can find a variety of items ranging from computer software to wrapping paper and art supplies. Hours of operation are Monday through Friday, 7:45 am to 4:30 pm.

Conference Information & Registration: A representative from Conference Services will be available at the registration desk on Sunday, June 13 from 1:00 pm to 9:00 pm and Monday, June 14 from 7:30 am until noon in the Strand Union. The office of Conference Services in the Strand Union is open 7:00 am to 5:00 pm Monday through Friday.

Emergency: To report a serious injury, illness, or fire, call University Police at 2121. This is a 24 hour number.

Messages: Telephone messages can be left during regular office hours, 7:00 am to 5:00 pm at Conference Services, (406) 994-3333. Messages can also be left with the ASK US Information Center in the Strand Union from 6:30 am to 11:00 pm at (406) 994-4636. There will be a message board at the registration table during symposium general session hours.

Name Tags: Please wear your name tag to ALL scheduled functions. A colored line on your tag indicates to Symposium staff that you are a guest.

Parking: You may park without a special permit in areas designated for staff, students, or visitors (S,B,or E). Do not park in posted restricted areas such as handicapped, emergency, loading zones or H (24-hour reserved). There is also a pay ($1 per day) parking lot located just south of the Strand Union.

Phones: The phones in the University Residence Halls can be used for unlimited on-campus and local phone calls. To call on-campus numbers, just dial the last four digits of the phone number. For off-campus local calls, dial 9, listen for the dial tone, and place your call. To reach a long-distance operator for charge and collect calls, dial 9, 0, followed by the number you are calling.

Post Office: There is a postal drop and a Federal Express drop box located on the first level of the Strand Union. Stamps may be purchased from the ASK US Information Center located in the Strand Union. Fax services are available through the office of Conference Services.

Recreation: If you have a name tag, the athletic facilities on campus may be used free of charge during the symposium. The Health, Physical Education, and Recreation Complex contains indoor and outdoor running tracks, exercise bicycles, basketball courts, weight rooms, tennis and racquetball courts and an indoor swimming pool. Regular building hours for the complex are 6 am to 7 pm.

The Strand Union has a Recreation Center located on the first level. Enjoy pool tables, video games, bowling, and more. Use of the facilities is free of charge but youth must wear name tags (available at the registration desk) to be allowed to enter. The Recreation Center hours are Noon - 10:00pm.

Bozeman has three fine golf courses, two bowling facilities, additional tennis courts, an outdoor swimming pool, and a hot springs. There is a wealth of hiking trails of all levels of difficulty. Blue-ribbon trout fishing, white-water rafting, and leisurely float trips are available on three rivers. There are also numerous dude ranches in the area.

Restaurants: Please see separate listing.

Shuttles: Shuttle service will be provided for those Symposium registrants staying in motels downtown. Schedules will be available at the registration desk.

Sightseeing Around Town: Please see Bozeman Area Chamber Visitor Guide.

Smoking: Montana State University has smoking policies which severely limit smoking in public areas. Please check to see that you are in a designated smoking area before you smoke.

Taxis: Bozeman is served by one taxi service, City Taxi. They can be reached at 587-2341.

TOURS

Tour #1 Yellowstone Park

Departure will be early this morning for travel through the Paradise Valley to the north entrance of Yellowstone National Park. The first stop will be Mammoth Hot Springs, famed for its steaming, multicolored mineral terraces. Traveling next to Norris Geyser Basin, you will have the opportunity to visit Yellowstone's most active thermal area where numerous geysers, fumaroles (steam vents), and hot springs actively display their uniqueness. Arriving in the Old Faithful area at lunchtime, you will have free time to eat your picnic lunch, witness the eruption of Yellowstone's most well known geyser, and explore the adjacent thermal area. The next of Yellowstone's natural wonders is the Grand Canyon of the Yellowstone where you will have extraordinary views of the canyon and its waterfalls from Artist Point and the Upper Falls. Your route will continue over the scenic Dunraven Pass (8859 ft.) and on to Tower Falls for a brief visit before exiting Yellowstone, once again by the north gate.

Includes: Transportation, sack lunch, park admission, tour escort.
Dates: June 12, 13 & 18, 1993
Time: 7:00 a.m. - 7:00 p.m.
Price: $32.00/person

Tour #2 Virginia City & Mining Memories

"One of the most delightful outcroppings of art in public places you could hope to find. Virginia City theater is alive, professional, and well." - Design Magazine. "One of the most exhilarating evenings I spent in theater last year was in Virginia City, Montana." - Village Voice. A mid-afternoon arrival in Alder Gulch, site of historic Virginia City, of gold rush and vigilante day fame, will give you several hours to explore the numerous entertaining museums and exhibits in both Virginia City and Nevada City. Exhibits such as the Nevada City Railroad Museum and the Old Music Hall, complete with a wonderful collection of old player pianos and organs, will remind you of the spirit of the Old West! You will enjoy an early evening buffet dinner at the Wells Fargo Coffee House before arriving at the Virginia City Opera House for an 8 o'clock curtain of an exhilarating performance of the Virginia City Players - a perfect way to end your stay with us in Montana.

Includes: Transportation, tour escort, buffet dinner, Opera House admission.
Date: June 17, 1993
Time: 2:00 p.m. - 12:00 a.m.
Price: $40.00/person

Tour #3 Lewis & Clark Caverns - Missouri Headwaters

Today will be full of history and outdoor activities. Our first stop in the historic Gallatin Valley will be at the Madison Buffalo Jump, the site of the stampeding of buffalo by local Indian tribes in the 1800's. Your lesson will range from Montana Indian history to the explorations of the Lewis & Clark Expedition, as we stop for a visit at the Missouri Headwaters State Park in Three Forks which was established to commemorate Lewis & Clark's discovery of the confluence of the Jefferson, Madison, and Gallatin Rivers forming the Missouri River. From here we will continue to the largest known limestone caverns in the Northwest, the Lewis & Clark Caverns. Upon arrival you will begin your approximately two-hour tour of these spectacular caves. As the caves are naturally air conditioned, please bring a sweater or jacket. Comfortable walking shoes are also advised as there is considerable walking involved in the tour.

Includes: Transportation, tour escort, cavern admission.
Date: June 14 & 15, 1993
Time: 1:00 p.m. - 5:00 p.m.
Price: $15.00/person

Tour #4 Helena and the Gates of the Mountains

This morning you will travel through the rolling hills of Montana farming country en route to Helena, capitol of Montana since 1875. A driving tour of Helena will include the State Capitol, the original Governor's Mansion, and the Cathedral of St. Helena, before continuing to the Gates of the Mountains, only 15 miles north of the city. Here you will board a scenic cruiser for a striking two hour boat trip on the Missouri River and through the spectacular gorge named by Captain Lewis of the Lewis & Clark Expedition. You will be able to enjoy your sack lunch leisurely while on board. Return to Bozeman is by late afternoon.

Includes: Transportation, tour escort, lunch, all admissions.
Date: June 18, 1993
Time: 8:00 a.m. - 5:00 p.m.
Price: $30.00/person

Tour #5 Gallatin Canyon, Big Sky of Montana

Travel the scenic route through the winding Gallatin Canyon to Big Sky of Montana. Experience the gondola ride to the peak of Lone Mountain.

Includes: Transportation, tour escort, gondola ride.
Date: June 16, 1993
Time: 1:00 p.m. - 5:00 p.m.
Price: $21.00/person

Tour #6 Self-Guided Walking Tour

Maps are available for your walking tour. Visit historical museums and beautiful homes along with unique boutiques in downtown Bozeman.

Tour #7 Yellowstone River Tour

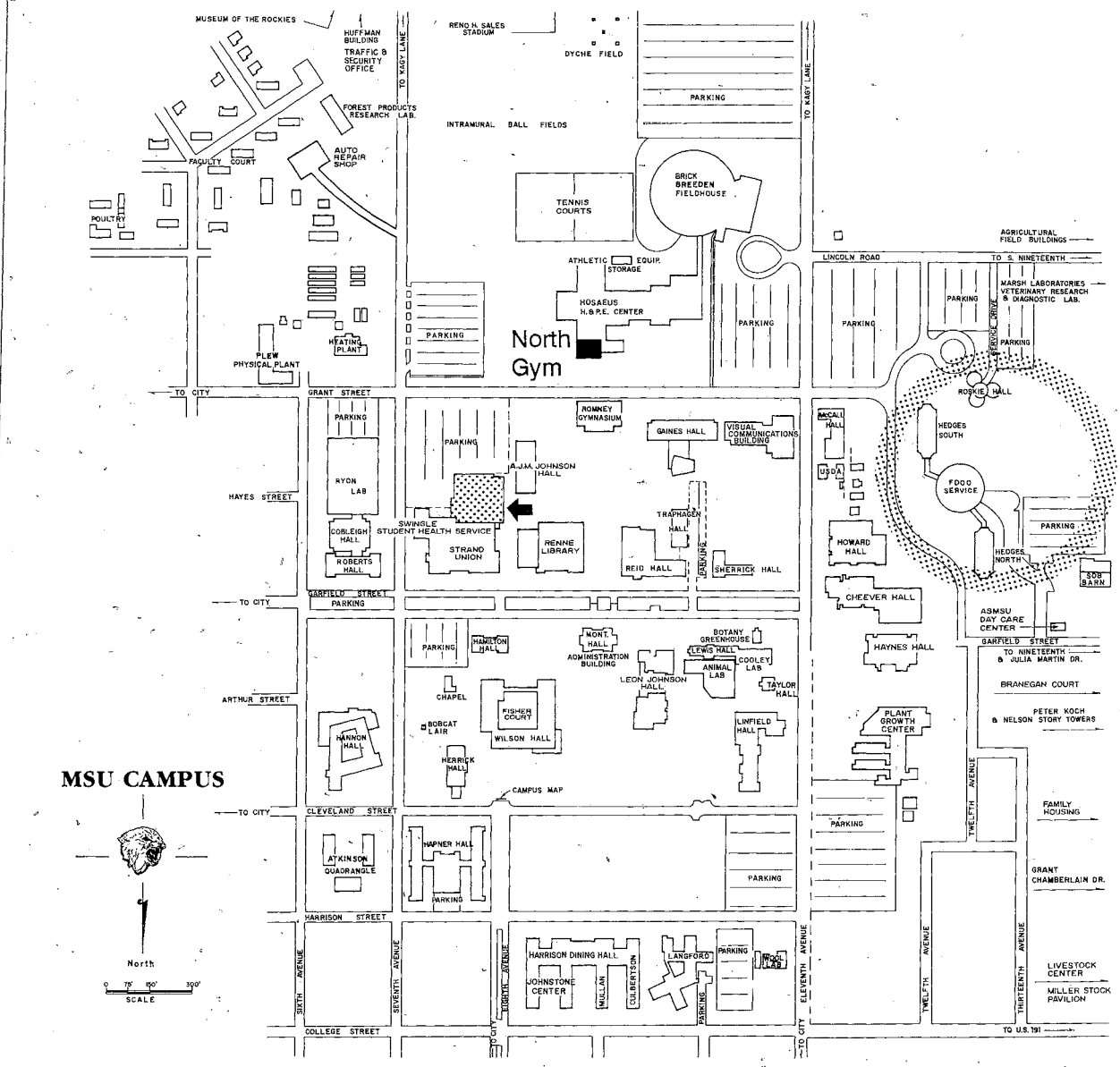
Your day will start with an eight (8) mile journey aboard rafts fully equipped and staffed with a licensed professional. First float through the upper Paradise Valley and then run the many rapids including those in Yankee Jim Canyon. Before continuing through this spectacular valley of the Yellowstone, the last undammed major river in the lower 48 states, you will experience the rich early history of the Yellowstone area's trappers and explorers. Note: A responsibility release is required; this trip is operated by professionals and is recommended for any age (minimum 6 years) whether or not you swim; every member is required to wear a commercially-approved life preserver while on the river; weather and water conditions can affect this itinerary.

Includes: Transportation, professional river guide, sack lunch.
Date: June 12, 17, & 18, 1993
Time: 12:00 p.m. - 7:00 p.m.
Price: $51.00/person

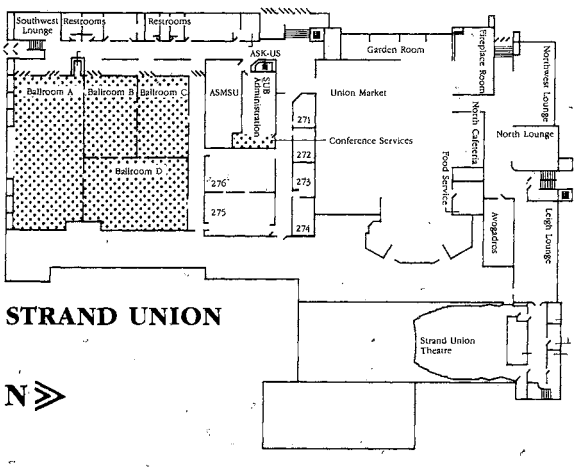
■ R.B. WOODWARD EXHIBIT AT THE 33rd NATIONAL ORGANIC CHEMISTRY SYMPOSIUM ■

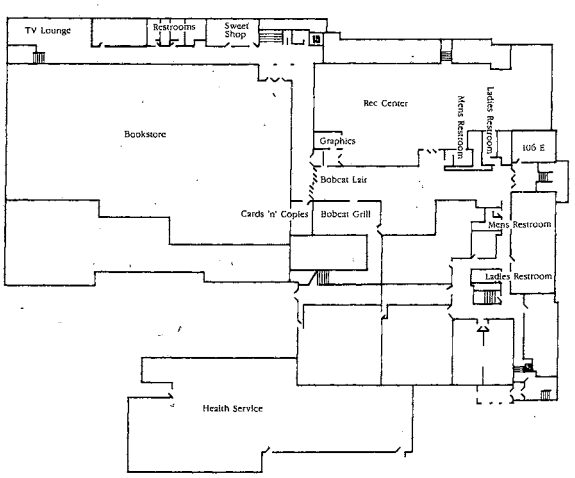
On April 10, 1992, in commemoration of the 75th anniversary of Robert B. Woodward's birth, the Chemical Heritage Foundation unveiled its newest traveling historical exhibit, "R.B. Woodward and the Art of Organic Synthesis."

Robert B. Woodward greatly influenced our understanding of the natural world and our abilities to produce life-saving pharmaceuticals. The Woodward Exhibit on display during all poster sessions details the life and triumphs of this extraordinary man and consummate organic chemist. He is portrayed as a mentor, a creative genius, and a molecular architect. The historical exhibit opens with highlights of Woodward's childhood and college years. After giving a glimpse of the state of organic chemistry before World War II, the 12 panel display focuses on the Nobel Prize-winning research performed by Woodward and his colleagues, including the synthesis of quinine, strychnine, lysergic acid, reserpine, and chlorophyll. The exhibit concludes with the Woodward-Hoffmann Rules for predicting chemical bonding and Woodward's synthesis, in collaboration with a Swiss group led by Albert Eschenmoser, of vitamin B_{12}, "That Mount Everest of Molecules."



Montana State University Campus





THIRTY-THIRD NATIONAL ORGANIC CHEMISTRY SYMPOSIUM

Division of Organic Chemistry
American Chemical Society
June 13-17, 1993
Montana State University
Bozeman, Montana

This program has been facilitated by Conference Services and Strand Union Graphics, Montana State University.