TWENTY-FIFTH NATIONAL ORGANIC CHEMISTRY SYMPOSIUM

of the

AMERICAN CHEMICAL SOCIETY

AUSPICES OF THE DIVISION OF
ORGANIC CHEMISTRY
and
WEST VIRGINIA UNIVERSITY

June 19-23, 1977
Morgantown, West Virginia

SPEAKERS AT THE TWENTY-FIFTH NATIONAL ORGANIC CHEMISTRY SYMPOSIUM

J. I. Brauman

D. J. Cram

S. Danishefsky

D. A. Evans

M. Jones, Jr.

Y. Kishi

A. I. Meyers

M. F. Semmelhack

K. B. Sharpless

R. B. Woodward

PROGRAM

SUNDAY, June 19

Registration: Towers Conference Center, 1:00-10:00 P.M.

MONDAY, June 20

Registration and Meetings: Creative Art Center

9:00 A.M.	Welcome. RAY KOPPELMAN, Provost for Research and Graduate Studies, West Virginia University. Response. E. C. TAYLOR, Chairman, Division of Organic Chemistry, ACS.
9:30 A.M.	A. I. MEYERS, "Asymmetric Syntheses Using Chiral Lithium Reagents."
11:00 A.M.	MARTIN F. SEMMELHACK, "Arene-Metal Complexes in Organic Synthesis."
8:00 P.M.	D. J. CRAM, "Complexation of Ground and Transition States."

TUESDAY, June 21

9:00 A.M.	YOSHITO KISHI, "Synthetic Studies Toward Mytomycins."
10:30 A.M.	SAMUEL DANISHEFSKY, "New Strategies for the Stereospecific Synthesis of Natural Products."
8:00 P.M.	WILLIAM S. JOHNSON, Roger Adams Award Address, "The Evolution of Synthetic Strategy and the Cortisone Problem."

WEDNESDAY, June 22

9:00 A.M.	MAITLAND JONES, JR., "Gas-Phase Carbene Reactions."
10:30 A.M.	JOHN I. BRAUMAN, "Nucleophilicities and Kinetic Basicities in the Gas Phase."
8:00 P.M.	R. B. WOODWARD, "Recent Advances in the Chemistry of Natural Products."

THURSDAY, June 23

9:00 A.M.	DAVID A. EVANS, "New Concepts in the Catalysis of Sigmatropic Rearrangements."
10:30 A.M.	K. BARRY SHARPLESS, "Atom Transfer Oxidations of Olefins."

THE ROGER ADAMS AWARD IN ORGANIC CHEMISTRY

The Roger Adams Award in Organic Chemistry has been established with joint sponsorship by the American Chemical Society, Organic Reactions, Inc., and Organic Syntheses, Inc. 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 medal and an honorarium of ten thousand dollars. The presentation of the award is made at the biennial National Organic Chemistry Symposium of the Division of Organic Chemistry of the American Chemical Society, and the recipient delivers a lecture as part of the program of the Symposium.

The award recognizes the distinguished career of Roger Adams who played such a vital role in each of the three organizations sponsoring the award, having been Chairman of the Board of Directors as well as President of the American Chemical Society and co-founder of Organic Syntheses and Organic Reactions.

The recipient of this year's award is Professor William S. Johnson of the Department of Chemistry at Stanford University. His award address is entitled "The Evolution of Synthetic Strategy and the Cortisone Problem."

ORGANIZING COMMITTEES

The plans and program for the 25th National Organic Chemistry Symposium have been developed by the members of the Executive Committee of the Division of Organic Chemistry who have served during the past two years.

	1975-76	1976-77
Chairman	H. E. Simmons	E. C. Taylor
Chairman-elect	E. C. Taylor	H. Hart
Secretary	E. M. Burgess	E. M. Burgess
Secretary-elect		P. A. Beak
National Symposium Executive Officer	J. C. Martin	J. C. Martin
Executive Committee	J. E. Baldwin O. L. Chapman J. P. Freeman H. L. Goering N. A. LeBel A. I. Meyers J. H. Prager A. J. Speziale H. J. Shine J. Smuszkovicz A. M. Trozzolo	J. E. Baldwin O. L. Chapman H. L. Goering C. H. Heathcock N. A. LeBel A. I. Meyers H. J. Shine H. E. Simmons J. Szmuszkovicz B. M. Trost A. M. Trozzolo

The local arrangements at West Virginia University have been made by a committee consisting of W. R. Moore (Chairman), G. B. Fodor, D. W. H. MacDowell, C. G. McCarty, C. W. Muth, and A. Winston who are members of the Department of Chemistry of West Virginia University.

CONTENTS

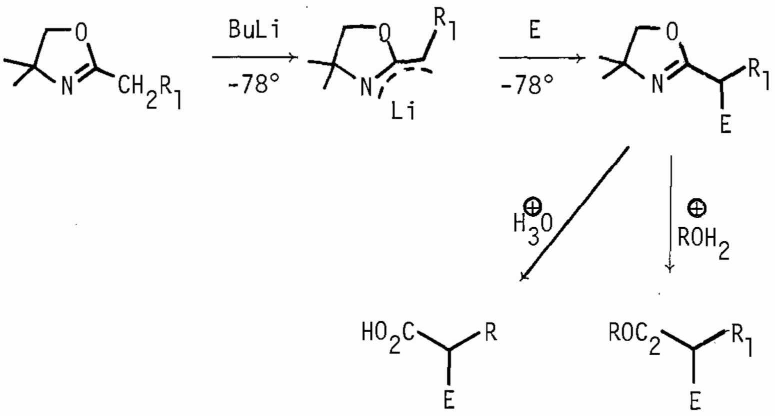
ASYMMETRIC SYNTHESES USING CHIRAL LITHIUM REAGENTS

A. I. Meyers

Colorado State University
Fort Collins, Colorado

In 1970, we reported the use of 2-oxazolines as precursors to elaborated acetic acids (1). The method involved low temperature metallation of the α-proton followed by alkylation with various electrophiles (E).

Scheme 1



Hydrolysis or alcoholysis, under acidic conditions, gave the α-substituted carboxylic acids or their esters (Scheme 1). A number of acids were prepared in this manner including α,β-unsaturated and aromatic derivatives (2).

Due to the low temperatures used and the alkylation efficiency observed (~90%), it was felt that this system could provide a route to chiral carboxylic acids if the appropriate chiral oxazoline could be readily obtained. In 1973, we prepared the chiral oxazoline from a readily available precursor which proved to be rather useful in achieving our goal (Scheme 2).

ARENE-METAL COMPLEXES IN ORGANIC SYNTHESIS

Martin F. Semmelhack

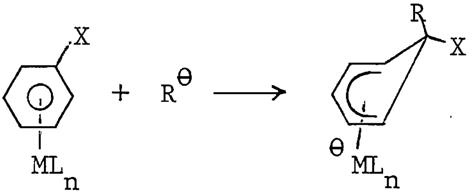
Cornell University
Ithaca, New York

ARENE-METAL COMPLEXES IN ORGANIC SYNTHESIS

Martin F. Semmelhack

Coordination of an aromatic ring with a transition metal via π-bonding can perturb strongly the usual reactivity of the ring. Evidence has accumulated from many laboratories over the past twenty years to establish five distinct effects, some of which are now beginning to be exploited in organic synthesis. The metal can exert a powerful steric effect, blocking one face of the arene ligand and controlling the orientation of reaction at nearby substituents. Positive charge at the benzylic position is stabilized by a factor of ca 10^5 due to metal complexation. Negative charge at the benzylic position is also stabilized. The hydrogen substituents on the arene ligand show enhanced acidity, and the arene ring becomes a reactive electrophile.

This last effect allows nucleophilic reactants to add to a carbon of the arene ligand to form π-(cyclohexadienyl) complexes (e.g., 1), parallel with the first step in classical nucleophilic aromatic substitution (which produces Meisenheimer complexes). Our work has been con-



1

COMPLEXATION OF GROUND AND TRANSITION STATES

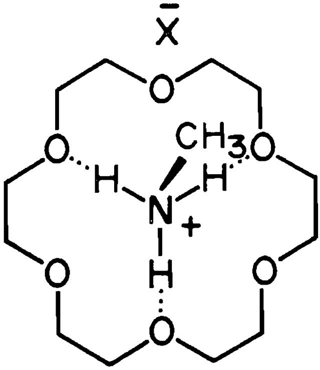
D. J. Cram

University of California
at Los Angeles
Los Angeles, California

Complexation of Ground and Transition States

By D. J. Cram, Department of Chemistry, University of
California at Los Angeles, Los Angeles, California 90024

Structured complexation between organic hosts and guests in ground and transition states are central to genetic, enzymatic, immunologic, transport and control phenomena of the biological world. We report the study of synthetic hosts with binding sites and steric barriers designed to be complementary to selected guests, particularly amino acids and their derivatives. Criteria for structural and chiral recognition of host and guest for one another have been developed.



1a

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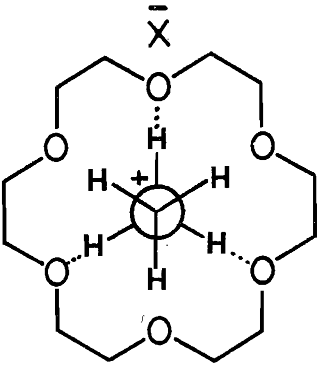


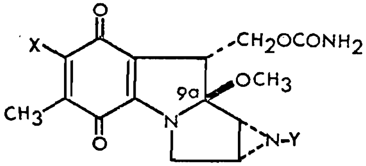
1b

SYNTHETIC STUDIES TOWARD MITOMYCINS

Yoshito Kishi

Harvard University
Cambridge, Massachusetts

The mitomycins (1a-e) are a class of antibiotics with activity against Gram-positive and Gram-negative bacteria and also against several kinds of tumors.[1] Since their structures were first elucidated in 1962,[1] numerous synthetic approaches to the mitomycins have been reported.[2] However, the mitomycins themselves have not yet been synthesized. It seems to us that the most difficult problem in synthesizing the naturally occurring mitomycins is related to introducing the 9a methoxy group since this is known to be the most labile functionality present in the target molecules.[3] We would like to report our synthetic efforts toward the mitomycins, including a total synthesis of deiminomitomycin A (13).



1a : mitomycin A; X=OCH_3, Y=H

1b : mitomycin B; see reference 4.

1c : mitomycin C; X=NH_2, Y=H

1d : porfiromycin; X=NH_2, Y=CH_3

1e : mitiromycin; see reference 5.

NEW STRATEGIES FOR THE STEREOSPECIFIC SYNTHESIS OF NATURAL PRODUCTS

Samuel Danishefsky

University of Pittsburgh
Pittsburgh, Pennsylvania

NEW STRATEGIES FOR THE STEREOSPECIFIC SYNTHESIS OF NATURAL PRODUCTS

Samuel Danishefsky, Robert Doehner, Sarah Etheredge, Kerry Gombatz, Tahashi Harayama, Robert McKee and Rajendra K. Singh.

Department of Chemistry, University of Pittsburgh,
Pittsburgh, Penna. 15260

In this lecture we shall focus on two processes which have been studied in our laboratory over the past five years. The possibilities which these methodologies offer for the solution of problems in the synthesis of natural products will be explored.

The first method draws upon the proclivity of suitably activated cyclopropanes, to suffer ring scission upon reaction with nucleophiles. Our efforts in this area have been directed along two lines.

The first involves intramolecular counterparts of this reaction. We have found that a variety of such activated cyclopropanes bearing intramolecular nucleophiles may be assembled. Furthermore, in contrast to the intermolecular cases, the intramolecular processes occur under mild circumstances and are relatively impervious to substitution on the cyclopropane ring.

Two other findings were central. The first is the heavy, if not exclusive, preference for the spiro mode of opening. This has been demonstrated with a variety of nucleophiles where the choice of ring options is a five-membered ring *via* the spiro mode or a six-membered ring in the fused sense. Similar dominance by the spiro mode is manifested when the ring forming options are spiro → 6 vs. fused → 7.

Furthermore, we have shown that the steric sense of this reaction is that of clean inversion of configuration of the cyclopropane undergoing displacement (*i.e.* ring mutation).

THE EVOLUTION OF SYNTHETIC STRATEGY AND THE CORTISONE PROBLEM

William S. Johnson

Stanford University
Stanford, California

The strategy for the total synthesis of polycyclic natural products, e.g., cortisone, has most generally involved step-by-step annelations, i.e., each new ring is formed in a separate step. The biomimetic approach to total synthesis, on the other hand, entials the formation of a number of rings stereospecifically in a single step via an intramolecular telomerization of an acyclic chain having appositely placed trans olefinic bonds. The biomimetic cyclization is analogous to the enzymatic conversion of squalene into polycyclic triterpenoids, e.g., lanosterol, in the key step in the biogenesis of steroids from acetate as outlined in Figure 1.[1]

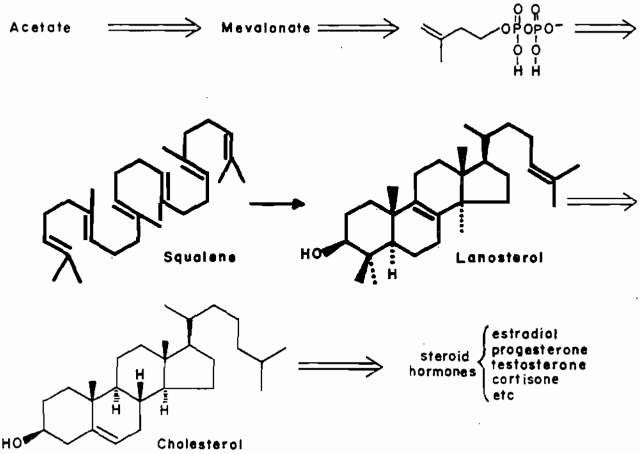


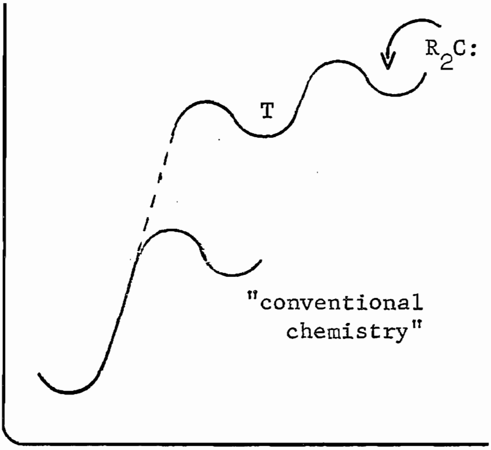
Fig. 1. Flow sheet summary of the biogenesis of steroids from acetate, emphasizing the conversion of squalene to lanosterol.

GAS-PHASE CARBENE REACTIONS

Maitland Jones, Jr.

Princeton University
Princeton, New Jersey

Why should one bother to look at reactions of relatively large carbenes in the gas phase? Even though it may seem odd at first sight, the reason is that we think it may be possible to synthesize interesting molecules that cannot be made by more conventional methods. In a sense, what we want to do is to use the carbene as an energy source. If a physical organic chemist wants to make some target molecule (T), it is probably because T has some unusual structural feature that warrants investigation, and this in turn often means that T will be very high in energy. Thus it may be difficult to climb up in conventional fashion into the potential energy well in which T lies simply because other chemistry is likely to intervene. What one would like to do is to approach T from above - from some species even higher in energy. Then the problem would be to hold it in its potential well, but at least one might have an easier time of making it. It seemed to us that carbenes would be ideal molecules provided one could design them so that formation of the target molecules could be expected.



NUCLEOPHILICITIES AND KINETIC BASICITIES IN THE GAS PHASE

John I. Brauman

Stanford University
Stanford, California

$$M^{o} \longrightarrow M^{+} + e^{-}$$

$$Li^{o} + Na^{+} \rightleftharpoons Li^{+} + Na^{o}$$

$$\Delta G^{o} = -7 \text{ kcal/mole} \quad (aq)$$

$$\Delta G^{o} = +6 \text{ kcal/mole} \quad (gas)$$

Relative Acidities

Me_3CCH_2OH > t-BuOH > i-PrOH >

EtOH > MeOH > H_2O

all DH°(RO—H) = 104 kcal/mole

Ion - Induced Dipole

$$E = -\frac{1}{2}\,\frac{\alpha z^2 e^2}{\epsilon r^4}$$

RECENT ADVANCES IN THE CHEMISTRY OF NATURAL PRODUCTS

R. B. Woodward

Harvard University
Cambridge, Massachusetts

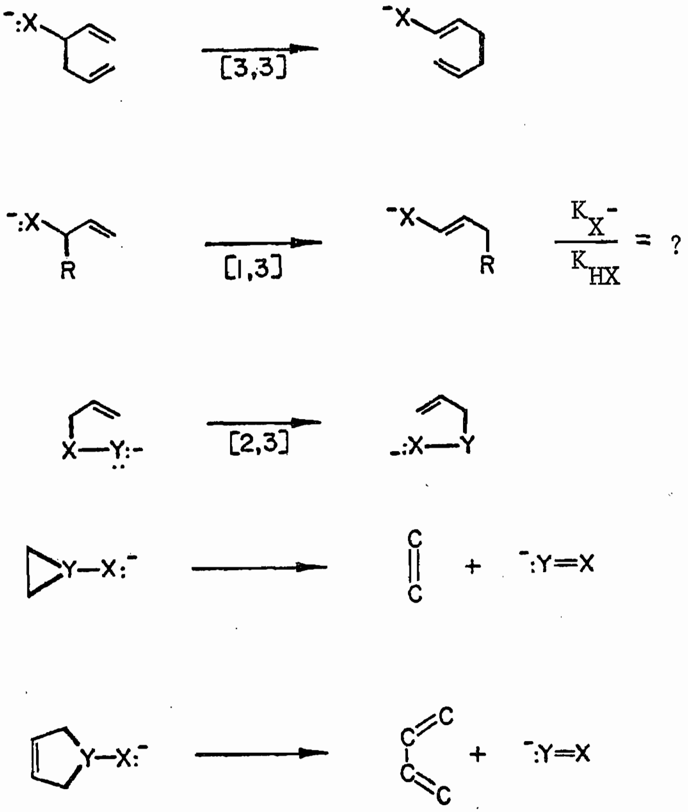
(NOTE: No abstract for RBW appears in the program book.)

NEW CONCEPTS IN THE CATALYSIS OF SIGMATROPIC REARRANGEMENTS

David A. Evans

California Institute
of Technology
Pasadena, California

Sigmatropic rearrangements and related processes constitute an exceptionally useful class of reactions in organic synthesis. For some time my research group has been interested in probing ways in which many of these bond reorganization processes might be accelerated via simple acid-base chemistry. Since the processes



shown above could be anticipated to take place via either a concerted or step-wise mechanism it would be of great interest to have access to

ATOM TRANSFER OXIDATIONS OF OLEFINS

K. Barry Sharpless

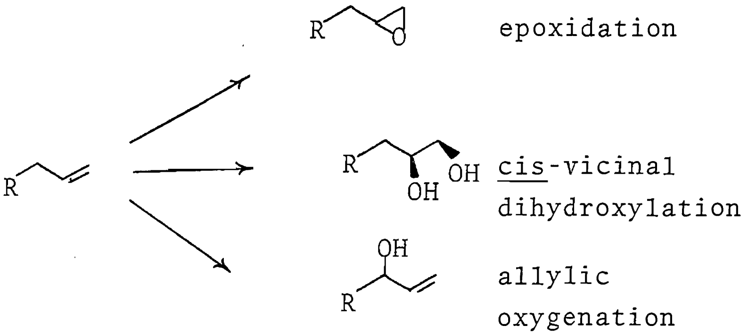
Massachusetts Institute
of Technology

Cambridge, Massachusetts

Atom Transfer Oxidations of Olefins

K. Barry Sharpless
Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

Atom transfer oxidations are among the most useful transformations which olefins undergo. The best known reactions in this class involve transfer of oxygen atoms to the olefinic substrate:



Of these three transformations only epoxidation is regarded as reliable and practical by synthetic organic chemists. By reliable we mean it works for most olefins, and by practical we mean it can be conveniently executed on a large scale (one mole or greater). We have recently developed catalytic procedures for effecting *cis*-dihydroxylation[1] (osmium catalysis) and *allylic* oxygenation[2] selenium catalysis) of olefins which we feel moves these two conversions into the category of reliable and practical. These new procedures will be presented. The inexpensive oxidant *tert*-butyl hydroperoxide is the oxygen atom source in both cases.