## FOURTEENTH NATIONAL ORGANIC

CHEMISTRY SYMPOSIUM

#### of the

### AMERICAN CHEMICAL SOCIETY

AUSPICES OF THE DIVISION OF ORGANIC CHEMISTRY OF THE A.C.S.,

#### PURDUE UNIVERSITY

and the Purdue Section

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June 13-16, 1955

# FOURTEENTH NATIONAL ORGANIC CHEMISTRY SYMPOSIUM

### of the

### AMERICAN CHEMICAL SOCIETY

Headquarters and Registration—Purdue Memorial Union,

West Lafayette, Indiana.

Monday, June 13, 8:00 a.m. to 8:00 p.m.

Tuesday, June 14, 8:00 a.m. to 8:00 p.m.

Wednesday, June 15, 8:00 a.m. to 8:00 p.m.

Thursday, June 16, 8:00 a.m. to 10:30 a.m.

Meetings—Hall of Music

## Speakers at the Fourteenth National Organic Chemistry $\mathsf{Symposium}$



J. C. Bailar, Jr.



M. Calvin



A. C. Cope



E. J. Corey



S. J. Cristol



V. du Vigneaud



G. S. Hammond



J. D. Roberts



W. S. Johnson



G. Stork F. H. R. B. Vyilby Begarest F. B.S. J. 11 (1.10) 4-27-64



N. J. Leonard



F. H. Westheimer

SAME ALL AND ALL

## Program

#### Monday

- 1:45 p.m. Welcome. FREDRICK L. HOVDE, President, Purdue University. Response. A. H. BLATT, Chairman, Division of Organic Chemistry, A.C.S.
  2:00 p.m. 1. GILBERT STORK, Columbia University.
- Stereospecific Syntheses.
- 3:00 p.m. Discussion of Paper 1.
- 3:30 p.m. 2. STANLEY J. CRISTOL, University of Colorado. Stereospecific and Non-stereospecific Elimination Reactions.
- 4:30 p.m. Discussion of Paper 2.
- 8:00 p.m. 3. FRANK H. WESTHEIMER, Harvard University. Mechanism of Chromic Acid Oxidation of Alcohols.
- 9:00 p.m. Discussion of Paper 3.

#### Tuesday

- 9:00 a.m.4. JOHN D. ROBERTS, California Institute of Technology. New Small Ring Compounds.10:00 a.m. Discussion of Paper 4.
- 10:30 a.m. 5. ARTHUR C. COPE, Massachusetts Institute of Technology. Recent Advances in the Chemistry of Medium-sized Ring Compounds.
- 11:30 a.m. Discussion of Paper 5.
- 2:00 p.m. 6. NELSON J. LEONARD, University of Illinois. Transannular Nitrogen-Carbonyl Interactions.
- 3:00 p.m. Discussion of Paper 6.
- 6:30 p.m. SYMPOSIUM DINNER. Memorial Union. Introduction by A. H. BLATT, Queen's College.

Guest Speaker—ROGER ADAMS, University of Illinois. "Reminiscences"



RÖGER ADAMS

#### Wednesday

9:00 a.m.	7. GEORGE S. HAMMOND, Iowa State Col-
	lege. Recent Developments in the Chemistry of
	Free Radicals in Solution.

- 10:00 a.m. Discussion of Paper 7.
- 10:30 a.m. 8. MELVIN CALVIN, University of California. The Photosynthetic Carbon Cycle.
- 11:30 a.m. Discussion of Paper 8.
- 2:00 p.m. 9. JOHN C. BAILAR, JR., University of Illinois. The Stereochemistry of Some Replacement Reactions in Inorganic Complexes.
- 3:00 p.m. Discussion of Paper 9.
- 8:00 p.m. 10. E. J. COREY, University of Illinois. The Structure of Friedelin.
- 9:00 p.m. Discussion of Paper 10.

#### Thursday

9:00 a.m.	11. WILLIAM S. JOHNSON, University of
	Wisconsin. Steroid Total Synthesis Studies.
10:00 a.m.	Discussion of Paper 11.
10:30 a.m.	12. VINCENT DU VIGNEAUD, Cornell
	University Medical College. Hormones of the
	Posterior Pituitary Gland: Oxytocin and Vas-
	opressin.
11 00	

11:30 a.m. Discussion of Paper 12.

## Purdue Committees

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Purdue University and the Purdue Section of the American Chemical Society are acting as hosts.

#### Committees in Charge

GeneralE. T. McBee
HousingWilliam E. Truce
Registration Nathan Kornblum
Dinner ArrangementsR. A. Benkeser
PublicityHerbert C. Brown and C. W. Roberts
RecreationG. B. Bachman

#### Division of Organic Chemistry

The plans and program of the Fourteenth 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.

1953-54	1954-1955
ChairmanMax Tishler	A. H. Blatt
Chairman-elect A. H. Blatt	Nelson J. Leonard
Secretary Nelson J. Leonard	William E. Parham
Frank McGrew	Ted Cairns
Melvin S. Newman	n James Cason
John D. Roberts	Frank C. McGrew
Frank H. Westhei	mer John D. Roberts

#### An Invitation to Organic Chemists who are not members of

#### the Division of Organic Chemistry

The Executive Committee of the Division of Organic Chemistry extends to you a cordial invitation to become a regular member of the division.

Each of the divisions of the American Chemical Society serves a field of specialization and the Organic Division endeavors to serve organic chemists by furthering organic chemistry. To that end, it wishes to have associated with it as many organic chemists as possible.

The requirements for divisional membership are: (1) membership in the American Chemical Society, (2) active interest in organic chemistry, and (3) payment of annual dues of \$1.50. These dues are used to pay the expenses involved in the activities of the division which are:

- 1. Mailing of notices and forms for the presentation of papers at the Spring and Fall Meetings of the A.C.S.
- 2. Lithoprinting and distributing to members abstracts of the papers to be presented, in advance of the national meetings.
- 3. Arranging for National Symposia on organic chemistry. These are held every two years and the speakers and program are determined by the members of the Organic Division.
- 4. Establishing and promoting policies vital to the advancement of organic chemistry.

If you wish to become a regular member of the Organic Division, all that is necessary is to give or send your name, mail address, and \$1.50 to:

> WILLIAM E. PARHAM, Secretary Organic Division, A.C.S. Department of Chemistry University of Minnesota Minneapolis 14, Minnesota

Extra copies of this Symposium Abstract Booklet can be obtained at \$1.00 each from the Secretary. Abstracts of the 13th Symposium, held at Ann Arbor, Michigan in June, 1953, are also available at the same price.

#### STEREOSPECIFIC SYNTHESES

#### Gilbert Stork

Examples of attempts to control the steric course of syntheses will be discussed, using illustrations from the author's laboratory.





allo and 3-epiallo yohimbane

with R. K. Hill, JACS, 76, 949 (1954)

Steric Determination







with E.E. Van Tamelen, L. J. Friedman and A.W. Burgstahler, JACS, <u>75</u>, 384 (1953)

#### STEREOSPECIFIC AND NON-STEREOSPECIFIC ELIMINATION REACTIONS

#### Stanley J. Cristol



S. J. Cristol, J. Am. Chem. Soc., <u>69</u>, 338 (1947); S. J. Cristol, N. L. Hause and J. S. Meek, ibid., <u>73</u>, 674 (1951).

If these two mechanisms are correct, then calculations have shown that (a) is ordinarily more exothermic than the rate-determining step in (b) and that (a) should normally proceed at higher rate and with lower activation energy. This accounts for the normal preference of trans elimination over cis elimination in acyclic and non-rigid cyclic systems. The preference for trans elimination over cis elimination should be minimized or disappear (1) when the carbanion process (b) is markedly stabilized by the formation of a stable carbanion, i.e., when a group is present on the carbon beta to Y which can accommodate the negative charge developing on that carbon atom or (2) when the geometry of the system is restricted so that the face of the tetrahedron of the alpha carbon atom opposite to Y is not in a position to be attacked by the electron pair being liberated by X, i.e., when Walden inversion is not possible or when atoms X, C, C and Y may not readily assume a trans coplanar conformation. Tests related to each of these factors have been made.

#### THE MECHANISM OF THE CHROMIC ACID OXIDATION OF SECONDARY ALCOHOLS

F. H. Westheimer

#### Introduction

The chromic acid oxidation of simple secondary alcohols probably proceeds according to the mechanism:



The further reactions of the unstable tetravalent chromium compound, HCrO3, have also been elucidated.

Mosher and Whitmore (J. Am. Chem. Soc., <u>70</u>, 2544 (1948)) discovered that chromic acid partially oxidizes methyl t-amyl carbinol to the corresponding ketone, and partially cleaves it according to the equation:



A similar cleavage has now been investigated, and has been shown to result from the attack on the carbinol of an unstable compound of pentavalent chromium. The study has led to methods for maximizing or for eliminating the cleavage.

#### NEW SMALL-RING COMPOUNDS

John D. Roberts.



RECENT ADVANCES IN THE CHEMISTRY OF MEDIUM-SIZED RING COMPOUNDS

Arthur C. Cope

Formation of non-vicinal glycols from cyclic olefins and performic acid, or hydrolysis or solvolysis of the corresponding epoxides ("transannular reactions").

> A. C. Cope, S. W. Fenton and C. F. Spencer, J. Am. Chem. Soc., 74, 5884 (1952).



- (1) Pyrolysis of the diacetate formed a mixture of dienes, which was hydrogenated quantitatively to cyclooctane.
- (2) Oxidation formed a mixture of acids, from which adipic and oxalic acids were isolated.
- (3) Was not oxidized by periodic acid, and was different from the known cis- and trans-1,2-cycloöctanediols.
- (4) Oxidation distinguished between the structures possible from these data (1,4- and 1,5-cyclooctanediols).



m.p. 85-86.5°

#### TRANSANNULAR NITROGEN-CARBONYL INTERACTIONS

Nelson J. Leonard

#### Development of the Idea

"In cryptopine and protopine, the weakened basic character of the-NMe- group may well be due to the existence of the arrangement

which at the same time explains the loss of reactivity observed in the carbonyl group itself."

- W. O. Kermack and R. Robinson, J. Chem. Soc., 121, 427 (1922).



Vomicine



- Absence of normal ketone reactions.
- (2) Low basicity toward MeI.

- R. Huisgen, H. Wieland, and H. Eder, Ann., 561, 193 (1949).



Triethanolamine Borate (m.p. 236.5-237.5°, m.w. and anal. indicate C<sub>6</sub>H<sub>12</sub>BNO<sub>3</sub>)

- Reaction with MeI proceeds at 1/ 1700 the rate of N(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>3</sub>.
- (2) Slow neutralization, independent of acid concentration in water.
- (3) Slow neutralization with CH<sub>3</sub>SO<sub>2</sub>OH in nitrobenzene.

- H. C. Brown and E. A. Fletcher, J. Am. Chem. Soc., 73, 2808 (1951).

6:30 p.m. SYMPOSIUM DINNER. Memorial Union. Introduction by A. H. BLATT, Queen's College.

Guest Speaker-ROGER ADAMS, University of Illinois. "Reminiscences"



ROGER ADAMS

#### RECENT DEVELOPMENTS IN THE CHEMISTRY OF FREE RADICALS IN SOLUTION

#### George S. Hammond

The production of free radicals by thermal decomposition of peroxides and azo compounds poses several important questions as to detail.

Dialkyl peroxides  $(Me_3CO-)_2 \longrightarrow 2Me_3CO\cdot$  Unambiguous primary process followed by,  $Me_3CO\cdot \longrightarrow Me_2CO + Me \cdot$   $Me_3CO\cdot + AH \longrightarrow Me_3COH + A \cdot$ Diacyl peroxides  $(C_{6H_5CO_2-})_2 \longrightarrow 2C_{6H_5}CO_2 \cdot$   $C_{6H_5} \cdot + C_{6H_5}CO_2 \cdot + CO_2$ , an ambiguous primary process CN NC  $Me_2C-N=N-CMe_2 \longrightarrow 2Me_2CCN + N_2$   $Me_2CCN + Me_2CCN$  $Me_2CON + Me_2CCN$ 

Ambiguity has been suggested to account for anomalous behavior as a polymerization initiator. Primary process in  $Bz_2O_2$  decomposition is determined by scavenging first fragments with iodine.

Le does not react directly with Bz<sub>2</sub>O<sub>2</sub> /with L.M. Soffer/

Alternative Rout to BZO• (1)  $(C_{6H_{5}})_{3}C$ • +  $Bz_{2}O_{2}$  benzene  $\rightarrow$  BzOT + BzO (2) BzO• + T•  $\rightarrow$  BzOT (3) BzO• + T• + ArH  $\rightarrow$  BzOH + Ar-T (tetraphenyl methane in benzene solution)

This presents an enigma since benzoyloxy radicals produced in aromatic solvents by thermal decomposition of benzoyl peroxide undergo extensive decarboxylation before (or concurrently with) their reaction with solvent. This indicates that formation of benzoic acid <u>requires</u> the cooperation of another radical such as

#### THE PHOTOSYNTHETIC CYCLE

#### Melvin Calvin

A cyclic sequence of transformations, including the carboxylation of RuDP (ribulose diphosphate) and its reformation has been deduced as the route for the creation of reduced carbon compounds in photosynthetic organisms. With the demonstration of RuDP as substrate for the carboxylation in a cell-free system, each of the reactions has been carried out independently in vitro. Further purification of this last enzyme system has confirmed the deduction that the carboxylation of RuDP leads directly to the two molecules of PGA (phosphoglyceric acid) involving an internal dismutation and suggesting the name "carboxydismutase" for the enzyme. As a consequence of this knowledge of each of the steps in the photosynthetic COp reduction cycle, it is possible to define the reagent requirements to maintain it. The net requirement for the reduction of one molecule of COp is four equivalents of [H] and three molecules of ATP. These must ultimately be supplied by the photochemical reaction.

The requirement of four equivalents of [H] and three molecules of ATP for the reduction of each molecule of CO<sub>2</sub> in the photosynthetic carbon reduction cycle suggests the possibility that respiration may contribute some of the energy required for photosynthesis by supplying some of the ATP. This possibility was studied by measuring the quantum requirement of photosynthesis at various ratios of photosynthesis rate to respiration rate. Both corrected and uncorrected quantum requirements approach an experimental value of 7.4 with increasing photosynthetic rates, while the corrected rate approached 4 as the photosynthetic rate approaches zero. A study of the effect of light intensity on the appearance of radiocarbon in a number of pools directly associated with the tricarboxylic acid cycle has implicated thioctic acid in a step very closely related to the photochemical act. Direct experiments designed to determine just how close that association is have been performed. These involve the observation of increased quantum yield for photosynthesis and oxygen production under a variety of conditions. They have led to a new conception of the nature of the photochemical act as it occurs in the lamina of the subchloroplast structural units (grana). The suggestion is that the absorption of light creats within the chlorophyll-containing layer conduction electrons, one per quantum, which are separated from the remaining "holes" because of the structure of the lamina. The holes are trapped by donation of electrons from water molecules, or their close relatives, while the electrons are accepted by the sulfur atoms of a thioctic acid-like compound to produce a dithiol which, in turn, can pass its hydrogen on to other carriers, ultimately to PGA.

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#### THE STEREOCHEMISTRY OF SOME REPLACEMENT REACTIONS IN INORGANIC COMPLEXES

John C. Bailar, Jr.

The stereochemistry of the tetrahedral carbon atom represents only one phase of the whole field of stereochemistry, which will be quickly reviewed.

Stereochemic	al Forms for Seve	ral Coordination 1	Numbers
2 Linear [AgCl <sub>2</sub> ] -	3 Planar CO <sub>3</sub> =	4 Planar [Pt(NH <sub>3</sub> ) <sub>2</sub> Cl <sub>2</sub> ]	5 Triangular Bi <sub>,</sub> pyramidal
Angular	Pyramidal	Tetrahedral	$LFe(CO)_5$
H <sub>2</sub> O	NH <sub>3</sub>	CH <sub>4</sub>	
6 Octahedral [Co(NH <sub>3</sub> ) <sub>6</sub> ] <sup>+++</sup>	7 Pentagonal Bipyramidal IF <sub>7</sub> Prismatic [TaF <sub>7</sub> ] <sup>=</sup>	8 Cubic [Sr(H <sub>2</sub> O) <sub>8</sub> Anti prism [TaF <sub>8</sub> ] <sup></sup> Dodecahed [Mo(CN)	] <sup>++</sup> atic  Hral 8] <sup>-4</sup>

The stereochemistry of coordination number 4 and that of coordination number 6 are subject to study by the methods of classical organic chemistry, as well as by physical methods. Metals showing a coordination number of 4 can be either planar (e.g.,  $Pt^{+2}$ ) or tetrahedral (e.g.,  $Be^{+2}$ ). Complexes of both types are known for Ni<sup>+2</sup>.

Isomers of Some Planar Compounds of Platinum (II)





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#### THE STRUCTURE OF FRIEDELIN

#### E. J. Corey

#### **Collaborators**

Structural work - J. J. Ursprung

<u>Isolation and intermediates</u> - H. C. Huang, D. F. Joesting and R. G. Schultz

Deuterium exchange - R. A. Sneen

X-ray analysis - I. H. Riley

#### Previous Work on Friedelin

<u>Separation from cork</u> - Chevreul (1807), admixed with cerin ( $\alpha$  - hydroxyfriedelin).

<u>Salient chemical properties</u> - N. L. Drake et al (1935-1941), see Abstracts Ninth Organic Symposium for summary:

- 1. pentacyclic saturated ketone, C<sub>30</sub>H<sub>50</sub>O
- forms carbonyl derivatives, can be reduced to two epimeric alcohols, C<sub>30</sub>H<sub>52</sub>0.
- 3. can be oxidized to a keto acid,  $C_{30}H_{50}O_3$ .
- 4. can be obtained from cerin,  $C_{30}H_{50}O_2$ , by removal of the ahydroxyl group; oxidation of cerin produces a dicarboxylic acid  $C_{30}H_{50}O_4$ , which by pyrolysis furnishes a norketone  $C_{29}H_{48}O_4$ .
- dehydrogenation of friedelanol with Se at 315-325° affords 1,2,7-trimethylnapthalene, 1,2,8-trimethylphenanthrene and 1,8-dimethylpicene.

L. Ruzicka, O. Jeger et al (1942-1949):

1. presence of  $-CH - CH - CH_2 - CH_2 - unit:$ norfriedelanone [O] norfriedelenone [O] norfriedelendione  $C_{29}H_{48}O$   $C_{29}H_{46}O$   $C_{29}H_{44}O_2$ 

2. oxidation of norfriedelendione, (a) to a tetracyclic saturated ketone,  $C_{25}H_{44}0$ ,  $(H_20_2$  followed by  $0_3$ ) and, (b) to a tetracyclic  $\beta$ ,  $\gamma$  - unsaturated acid,  $C_{26}H_{42}0_2$ ,  $(H_20_2 + 0H^-)$ .

#### TOTAL SYNTHESIS OF TESTOSTERONE

William S. Johnson

A phase of the steroid total synthesis study underway at the University of Wisconsin is considered. The work discussed was performed in collaboration with <u>Brian</u> <u>Bannister</u>, <u>Raphael Pappo</u>, J. E. <u>Pike</u>, <u>Edgar R. Rogier</u>, and J. <u>Szmuszkovicz</u>.





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#### HORMONES OF THE POSTERIOR PITUITARY GLAND: OXYTOCIN AND VASOPRESSIN

Vincent du Vigneaud

Slide

- I. Sequence of amino acids in oxytocin.
- II. Structure of oxytocin.
- III. Structure of arginine-vasopressin.
  - IV. S,S'-Dibenzyloxytocin.
  - V. Proposed intermediate for the synthesis of oxytocin.
- VI. <u>L-Prolyl-L-leucyl-glycine</u> ethyl ester.
- VII. Bis-carbobenzoxy-<u>L</u>-cystinyl-bis-(<u>L</u>-prolyl-<u>L</u>-leucylglycine).
- VIII. S-Benzyl-L-cysteinyl-L-prolyl-L-leucyl-glycine.
  - IX. S-Benzyl-L-cysteinyl-L-prolyl-L-leucyl-glycinamide.
  - X. <u>L</u>-Glutaminyl-<u>L</u>-asparagine.
  - XI. Tosyl-<u>L</u>-isoleucyl-<u>L</u>-glutaminyl-<u>L</u>-asparagine.
- XII. Synthesis of the heptapeptide amide.
- XIII. Synthesis of the protected nonapeptide amide; its reduction and subsequent oxidation.
- XIV. S-Benzyl-L-cysteinyl-L-prolyl-L-arginyl-glycinamide hydrobromide.
  - XV. Synthesis of the protected pentapeptide, N-carbobenzoxy-S-benzyl-L-cysteinyl-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparagine.
- XVI. Synthesis of the protected nonapeptide amide for vasopressin; its reduction and subsequent oxidation.