TENTH NATIONAL ORGANIC CHEMISTRY SYMPOSIUM of the

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AMERICAN CHEMICAL SOCIETY

Auspiges of the Northeastern Section and the Division of Organic Chernistry

> June 12/14, 1947 Boston, Massachuseus



## Headquarters—Hotel Statler.

Meetings — New England Mutual Hall and Charter Room, 225 Clarendon Street.

Wednesday, June 11. Open House and Registration. Harvard

University, Chemical Laboratory, 12 Oxford Street, Cambridge, Massachusetts. 4:00 p.m. to 5:30 p.m. and 8:00 p.m. to 10:00 p.m.

Thursday, June 12. Registration. New England Mutual Hall. 8:30 a.m. to 5:00 p.m.

Friday, June 13. Registration. New England Mutual Hall. 9:00 a.m. to 12:00 m. and 1:30 p.m. to 5:00 p.m.

Saturday, June 14. Registration. New England Mutual Hall. 9:00 a.m. to 12:00 m.

## Speakers at the Tenth National Organic Chemistry Sympos



Richard T. Arnold



H. E. Carter



William S. Johnson



H. R. Snyder



Paul D. Bartlett



Arthur C. Cope



Melvin S. Newman



C. M. Suter



Herman A. Bruso



Louis F. Fieser



Charles C. Price



A. L. Wilds

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Price

# Program

## Thursday Morning

	9:00`A.M.	Welcome. James B. Conant, Harvard University.
Bruson		Response. Roger Adams, University of Illinois.
	9:30 A.M.	I. Charles C. Price. Influence of Substituents
1	•	on Polarity in the Benzene Ring.
+	10:30 A.M.	2. Louis F. Fieser. Naphthoquinones.
	11:30 A.M.	Discussion of papers 1 and 2.
		Paper 1—New England Mutual Hall.
		Paper 2-Charter Room.

## Thursday Afternoon

1:30 P.M.	3. Melvin S. Newman. The Behavior of Or	ganic
	Compounds in Sulfuric Acid Solution.	

- 2:30 P.M. Discussion of paper 3. Charter Room.
- 3:00 P.M. 4. Paul D. Bartlett. Recent Studies on Steric Effects.
- 4:00 P.M. Discussion of paper 4. Charter Room.
- 4:30 P.M. 5. H. R. Snyder. Alkylation by Amines and Amine Derivatives.
- 5:30 P.M. Discussion of paper 5. Charter Room.

## Thursday Evening

7:30 P.M. to 10:00 P.M. Apparatus Exhibit. Massachusetts Institute of Technology, Department of Chemistry, Room 4-440, 77 Massachusetts Avenue, Cambridge, Massachusetts.

## Friday Morning

9:00 A.M.	6. H. E. Carter. Chemistry of the Sphingolipids.
10:00 A.M.	Discussion of paper 6. Charter Room.
10:30 A.M.	7. Arthur C. Cope. Synthesis of Unsaturated
	and Bridged Eight - Membered Ring Com-
	pounds

11:30 A.M. Discussion of paper 7. Charter Room.

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### Friday Afternoon

- 1:30 P.M. 8. William S. Johnson. The Stobbe Condensation and the Synthesis of Fused Ring Systems
- 2:30 P.M. Discussion of paper 8. Charter Room.
- 3:00 P.M. 9. A. L. Wilds. The Synthesis of Some Com pounds Related to the Female Sex Hormones
- 4:00 P.M. Discussion of paper 9. Charter Room.
- 4:30 P.M. 10. C. M. Suter. Some Sulfur Containing Amines.
- 5:30 P.M. Discussion of paper 10. Charter Room.

#### Friday Evening

7:00 P.M. Symposium Dinner (informal). Hotel Statler Ballroom. Not included in registration fee. Ad mission by ticket which may be secured at registration until noon Friday, June 13. Speaker: James B. Conant, President of Harv ard University.

#### Saturday Morning

- 9:00 A.M. 11. Herman A. Bruson. Chemistry of Cyclo pentadiene Polymers and Adducts. 10:00 A.M. Discussion of paper 11. Charter Room.
- 10:30 A.M. 12. Richard T. Arnold. The Stereochemistry of Five- and Six-Membered Rings.
- 11:30 A.M. Discussion of paper 12. Charter Room.

Adjournment,

## **Boston Committees**

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The Northeastern Section of the American Chemical Society is acting as host for the organic chemists.

atler	Honorary Chairman	James B. Conant
Ad- lat	General Committee	Paul D. Bartlett Arthur C. Cope
arv-	Registration	Walter J. Gensler
-	Room and Dinner Arrangements	Warren C. Lothrop
clo-	Apparatus Exhibit	John C. Sheehan

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## Division of Organic Chemistry

The plans and program of the Tenth National Organic Chemistry Symposium have been developed by the Executive Committees of the Division of Organic Chemistry who have served during the past two years.

Chairman Secretary 1944-46

1946-47

S. M. McElvain Ralph W. Bost Paul D. Bartlett Arthur C. Cope Walter M. Lauer Arthur C. Cope Ralph W. Bost Paul D. Bartlett S. M. McElvain Ralph L. Shriner

## An Invitation to Organic Chemists who are not members the Division of Organic Chemistry

The Executive Committee of the Division of Organic Chen istry extends to you a cordial invitation to become a regula member of the division.

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

The requirements for divisional membership are: (1) men bership in the American Chemical Society, (2) active intere in organic chemistry, and (3) payment of annual dues of 1.00These dues are used to pay the expenses involved in th 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.
- Lithoprinting and distributing to members abstracts of the papers to be presented, in advance of the national meetings.
- Arranging for National Symposia on organic chemistr These are held every two years and the speakers an program are determined by the members of the Organ Division.
- 4. Establishing and promoting policies vital to the advance ment of organic chemistry.

If you wish to become a regular member of the Organi Division, all that is necessary is to give or send your name, ma address and \$1.00 to:

## RALPH W. BOST, Secretary

Department of Chemistry University of North Carolina Chapel Hill, North Carolina :TS

INFLUENCE OF SUBSTITUENTS ON POLARITY IN THE BENZENE RING.

Charles C. Price

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Relation of Rate and Equilibrium to Free Energy.

 $k = \lambda e^{-\Delta F/RT} \text{ or } K = e^{-\Delta F/RT}$  $\Delta F = \Delta E + T \cdot \Delta S$  $\Delta E = \text{"resonance energy"} + \text{"electrical energy"}$ 

It seems that, because of the peculiar symmetry and rigidity of the benzene ring, the factors involving entropy and resonance are sufficiently insensitive to substitution so that, except for the ortho positions, the influences of substituents may be largely ascribed to "electrical" effects.

It is obvious that ionic reactions in general, for example, the usual electrophillic substitution reactions, should be subject to important electrical effects.

 $Br_{2} + FeBr_{3} \implies Br^{+} FeBr_{4}^{-}$   $RC1 + AlC1_{3} \implies R^{+} AlC1_{4}^{-}$   $HONO_{2} + 2H_{2}SO_{4} \implies NO_{2}^{+} + H_{3}O^{+} + 2HSO_{4}^{-}$ 



#### NAPHTHOQUINONES

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#### Louis F. Fieser

Collaborators; Harvard: E. Berliner, F. J. Bondhus, F. C. Chang, W. G. Dauben, M. G. Ettlinger, G. Fawaz, M. Fields, M. Fieser, C. Heidelberger, H. Heymann, A. M. Seligman, W. R. Vaughan, A. G. Wilson, E. Wilson, Mao-i Wu; <u>Abbott Laboratories</u>: M. T. Lef K. E. Hamlin, E. J. Matson, E. E. Moore, M. B. Moore, H. E. Zaugg

The clue that hydrolapachol possesses mild antimalarial acti in the suppression of <u>P. lophurae</u> in the duck led to the investig of nearly three hundred 2-hydroxy-3-alkyl-1,4 naphthoquinones. Assays in ducks by A. P. Richardson show that in any series the activity rises with increasing size of side chain to a maximum an, then falls off.



## HE BEHAVIOR OF ORGANIC COMPOUNDS IN SULFURIC ACID SOLUTION

by Melvin S. Newman, The Ohio State University

The concept of carbonium ions as reaction intermediates is based largely on convincing explanations of experimental facts. Little concrete evidence bearing in the existence of carbonium ions for a finite time has been obtained. For the most part they are thought of is transient stages of extremely short life.

A theory to account for the behavior of certain rganic compounds in sulfuric acid has been developed ind is summarized in Hammett's "Physical-Organic hemistry" pg 45-49, 54-56, 278-281. This theory is based largely on cryoscopic measurements and assumes that certain types of carbonium ions are stable in sulfuric acid solution. Thus, evidence for the finite existence of carbonium ions exists. This evidence will be reviewed and new applications of the theory to reaction mechanisms will be discussed.

Apparatus Used for Cryoscopic Determinations



#### RECENT STUDIES ON STERIC EFFECTS

#### Paul D. Bartlett

Definition - For the purpose of this discussion, steric effects a those due only to spatial relations between atoms or groups, and dependent of the chemical or electrical character of such atoms o groups.

#### Classification of Steric Effects

- 1. Equilibrium shifted by steric effects:
  - a. Crowding in reaction product, at seat of reaction (e.g., du quinone oxime)
  - b. Crowding in reaction product, elsewhere than at seat of reaction ("B-strain" in trimethylammonium ion)
  - c. Steric hindrance favors one electronic structure over anoth at equilibrium (e.g., basic strength of dimethylpicramide)
  - d. Shift of equilibrium through dielectric effect of alkyl gro (e.g., second ionization constant of tetramethylsuccinic ac
- 2. Physical properties affected by steric hindrance (e.g., electr moments of durene derivatives)
- 3. Rate decreased by steric effects
  - a. Due to crowding at seat of reaction (neopentyl halides)
  - b. Due to damped resonance in transition state (triptycene)
  - c. Due to constraints on bond angles (chloroapocamphane)
- 4. Rate increased by steric effects (solvolysis of branched terti chlorides)

Examples of steric effects on equilibrium:



(Kehrmann, Ber., 21, 3315 (1888); J. prakt. Chem., <u>39</u>, 392 (1889); <u>40</u>, 188, 257 (1889)



(Brown, Bartholomay, and Taylor, J.A.C.S., 66, 435 (1944))

## ALKYLATION BY AMINES AND AMINE DERIVATIVES

### By H. R. Snyder



## CHEMISTRY OF THE SPHINGOLIPIDS

#### H. E. Carter

Janet Crosby, F. J. Glick, C. G. Humiston, W. E. Ledyard, Olga Nalbandov, W. P. Norris, G. E. Phillips, and W. Poggemeier have contributed to the research work discussed below.

Lipids of Nerve Tissue

- Phospholipids (30 per cent) Α.
  - Lecithins 1.
  - Cephalins 2.
  - Phosphatidyl serine 3.
  - Acetal phospholipid 4.
  - Lipositol 5.

Β.

- 6. Sphingomyelins
  Sphingolipids (15-20 per cent)
  1. Cerebrosides (10-15 per cent)
  - Sphingomyelins (4-6 per cent) 2.
  - Gangliosides 3.
  - Other components not completely characterized 4.

Cholesterol and cholesterol esters (10 per cent) C.

Hydrolysis products of Sphingomyelins, Cerebrosides and Gangliosides

Sphingomyelins	<b>→</b>	Sphingosine Fatty acid Choline Phosphoric acid
Cerebrosides	$\rightarrow$	Sphingosine Fatty acid Galactose (glucose)
Gangliosides	$\rightarrow$	Sphingosine

spningosine Fatty acid Glucose Galactose Neuraminic acid

### SYNTHESIS OF UNSATURATED AND BRIDGED EIGHT-MEMBERED RING COMPOUNDS

#### by Arthur C. Cope

The synthesis of cyclobctatetraene from pseudopelletierine reported by Willstätter and Waser, Ber., 44, 3423 (1911) and Willstätter and Heidelberger, Ber.,  $\overline{46}$ , 517 (1913) has assumed the remarkable status of a questionable classic in synthetic organic chemistry. Some physical and chemical properties reported for their cyclooctatetraene correspond closely to properties of styrene, and the opinion has been expressed that their product may have been styrene. Studies of open chain "model compounds" resembling intermediates in the synthesis from pseudopelletierine have been interpreted as casting serious doubt on the structure of cyclooctatetraene.

Reports of the synthesis of cyclooctatetraene from acetylene by a group of chemists headed by W. J. Reppe at the I. G. Farbenindustrie laboratories in Ludwigshaven in 1940 have renewed interest in cycloöctatetraene and in the validity of the Willstätter synthesis. We have reinvestigated the synthesis from pseudopelletierine, which presumably had not been repeated because the alkaloid was not available.

Propercie	s of Cyclooct	aterraene and S	cyrene
	Styrene	Willstätter product	Reppe product
<b>m</b> .• <b>p</b> .•	-33 <sup>0</sup>	-27 <sup>0</sup>	-7 <sup>0</sup>
20 44	0.907	0,925	0.9206
20 D	1.5450	1.5389	1.5290
b.p. (17 mm.)	43 <sup>0</sup>	42.2-42.4 <sup>0</sup>	42.0-42.5 <sup>0</sup>
Dibromide m.p. (C <sub>8</sub> H <sub>8</sub> Br <sub>2</sub> )	72-73 <sup>0</sup>	70-71.5 <sup>0</sup>	710

#### THE STOBBE CONDENSATION AND THE SYNTHESIS OF FUSED RING SYSTEMS

#### William S. Johnson

The alkoxide-catalyzed reaction between a succinic ester and a ketone was discovered by Stobbe in 1893 to proceed by an aldol rather than an acetoacetic ester type of condensation:



In work carried out at Wisconsin it has been found that the use of potassium t-butoxide in the Stobbe condensation Senerally gave higher yields and purer products during shorter reaction periods than were obtained with sodium ethoxide. In the sodium ethoxide-catalyzed Stobbe condensation with ~-tetralone, for example, the best yields (83%) were obtained only after five days, and the product was dark and semi-crystalline. With potassium t-butoxide, nowever, yields as high as 94% of colorless crystalline half-ester were realized after a reaction period of forty minutes. Similar results have been obtained with a number of ketones.



#### THE SYNTHESIS OF SOME COMPOUNDS RELATED TO THE FEMALE SEX HORMONES

#### A. L. Wilds

With Lloyd W. Beck, Warren J. Close, James A. Johnson, Jr. and Thomas L. Johnson





estrone

#### equilenin

Synthesis of compounds having a 16-keto group

ethod of cyclization developed by Paal (1884) and by Borsche (1906-8):





Extension to polynuclear compounds:













#### SOME SULFUR-CONTAINING AMINES BY C. M. SUTER

The experimental basis for this discussion was furnished by the work of N. F. Albertson, R. K. Bair, C. J. Cavallito, R. O. Clinton, G. M. Fohlen, W. Huber, M. E. Jackman, S. C. Laskowski, U. J. Salvador and others.

For many years amino alcohols have served as intermediates for the synthesis of more complex compounds having value as medicinal agents. Recently we have explored some aspects of the chemistry of the amino thicls and their derivatives; new compounds in this group have been prepared, methods of synthesis have been devised or improved and the various sulfur-containing amines have then been converted into more complex products for testing. Interest in the chemistry of aminothicls is enhanced by the biological significance of cysteine and its derivatives. Penicillamine (dimethylcysteine) has come into prominence recently because of its relationship to the penicillins.

C<sub>6</sub>H<sub>4</sub>(CO)<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>Br  $\xrightarrow{\text{KSH}}$  C<sub>6</sub>H<sub>4</sub>(CO)<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>SH  $\xrightarrow{\text{HCl}}$  NH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>SH<sub>•</sub>HCl 8 hrs. m.p.70-72° Gabriel, Ber. 22, 1137 (1889); 24, 1110 (1891).

Product contaminated with  $(NH_2CH_2CH_2)_2S \cdot 2$  HCl.  $C_{6H_4}(CO)_2NCH_2CH_2Br \xrightarrow{(NH_2)_2CS} C_{6H_4}(CO)_2NCH_2CH_2SC(NH_2)_2Br \xrightarrow{(NH_2)_2CS} alc. 67\%$  yield

C6H2(CO)2NCH2CH2SH

CO-S-CH<sub>2</sub>

Clinton, Suter, Leskowski, Jackman and Huber, J.Am.Chem.Soc., <u>67</u>, 594 (1945).

 $C_{6H_4}(CO)_2NCH_2CH_2Br \xrightarrow{KSCSOEt} C_{6H_4}(CO)_2NCH_2CH_2SCSOEt \xrightarrow{HBr} d_{*}=1.78$ 

Hydrolysis difficult.

Gabriel and Colman, Ber., <u>45</u>, 1643 (1912).

 $\begin{array}{c} {}^{\mathrm{CH}_2 - \mathrm{S}}_{\mathrm{CH}_2 - \mathrm{N}} \xrightarrow{\mathrm{HCl}}_{\mathrm{reflux}} \xrightarrow{\mathrm{CH}_2 \mathrm{SH}}_{\mathrm{CH}_2 \mathrm{NH}_3 \mathrm{Cl}} + \mathrm{CH}_3 \mathrm{C00H} \\ {}^{\mathrm{CH}_2 - \mathrm{N}}_{\mathrm{CH}_2 - \mathrm{N}} \xrightarrow{\mathrm{CH}_2 - \mathrm{S}}_{\mathrm{CH}_2 \mathrm{NH}_3 \mathrm{Cl}} + \mathrm{CH}_3 \mathrm{C00H} \\ {}^{\mathrm{CH}_2 \mathrm{OH}}_{\mathrm{CH}_2 - \mathrm{N}} \xrightarrow{\mathrm{CH}_2 - \mathrm{S}}_{\mathrm{CH}_2 - \mathrm{N}} \xrightarrow{\mathrm{CH}_2 \mathrm{CH}}_{\mathrm{CH}_2 \mathrm{CH}_2 \mathrm{SH} \cdot \mathrm{HCl}} \\ {}^{\mathrm{CH}_2 \mathrm{NH}_2 - \mathrm{CH}_2 - \mathrm{N}}_{\mathrm{CH}_2 - \mathrm{N}} \xrightarrow{\mathrm{CH}_2 \mathrm{CH}}_{\mathrm{CH}_2 \mathrm{SH}} \xrightarrow{\mathrm{S0\%}}_{\mathrm{SH}} \times 50\% \\ {}^{\mathrm{Cavallito; Gabriel and Leupold, Ber. 31, 2837 (1898).} \end{array}$ 

#### Chemistry of Cyclopentadiene Polymers and Adducts

Herman A. Bruson

Heat polymerization of cyclopentadiene produces crystalline polymers (A). Catalytic polymerization with  $BF_3$ , SnCl<sub>4</sub>, SbCl<sub>5</sub>, TiCl<sub>4</sub>, FeCl<sub>3</sub> produces rubber-like non-crystalline polymers (B). In absence of catalysts cyclopentadiene plus acrylonitrile give Diels-Alder adduct (C), but if trace of strong alkali is present product (D) is obtained.

Folymers (A) notably dicyclopentadiene and tricyclopentadiene readily add  $H_2O$ , HX, HSCN, R-COOH, R-OH, R-SH to only one double bond.



**Proof** that hydration of dicyclopentadiene does not occur in cyclopentene ring and that rearrangement takes place.

#### THE STEREOCHEMISTRY OF FIVE- AND

SIX- MEMBERED RINGS

#### Richard T. Arnold

The stereochemistry of five- and six-membered rings has many facets. This lecture confines itself to a discussion of three of these, namely:

- a) heterocyclic rings which are easily formed and readily broken,
- b) the role of quasi ring intermediates in organic reactions, and
- c) the stereochemistry of five- and sixmembered rings when attached to aromatic nuclei.

Oxidative cleavage of 1,2-glycols to carbonyl compounds by Pb(OAc)<sub>4</sub>, HIO<sub>4</sub>, Ag<sup>+++</sup>, and NaBiO<sub>2</sub> has been reviewed by Purves and coworkers<sup>1</sup>.

H - c - o - H H - c - o - H	$ \rightarrow \begin{array}{c} H - c - 0 \\ H - c - 0 \\ R \\ \end{array} $
	ţ
H - c = 0	H - c - 0 *
H - c = 0	← H - c - 0*
•	1

They list four properties all of which the oxidiz-

 Central atom R of oxidant must have a diameter of 2.5 - 3.0 x 10<sup>-8</sup> cm. which is required to bridge the gap between oxygen atoms in 1.2-glycols.