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II Semester 1934-35


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The Stereochemistry of Triarylmethyl Radicals

G. Karagunis and G. Drikes, Z.physik. Chem., 26B, 428-38 (1934)

(Authors located at the University of Athens and have had no previous publications.)

Until now experiments intended to determine the steric configuration of free triarylmethyl radicals have been unsuccessful.

The irradiation of asymmetric radicals with circularly polarized light during treatment with halogens gave a mixture of halides which was optically active. A mechanism was postulated as follows: The radicals are of tetrahedral form and exist as a mixture of the two possible antipodes. Irradiation results in the activation of one of the forms, causes chlorination of it, and consequent optical activity.

By using $Me(4,MeC_6H_4)(p\text{-}EtC_6H_4)C$- with circularly polarized light of wavelength 4300Å and introducing $Cl_2$ at 0°C, a maximum rotation of 0.2° was obtained. For the compound, $Ph(PhC_6H_4)(\alpha C_{10}H_7)C$-, rotations up to 0.1° with light of 5390Å were given. The phenomenum was anisotropic, i.e. with light polarized to the right, rotation occurred in one direction and with light of the same frequency but polarized ~~in the opposite~~ to the left, the rotation was in the opposite direction.

Seminar Report

M.F.Roy

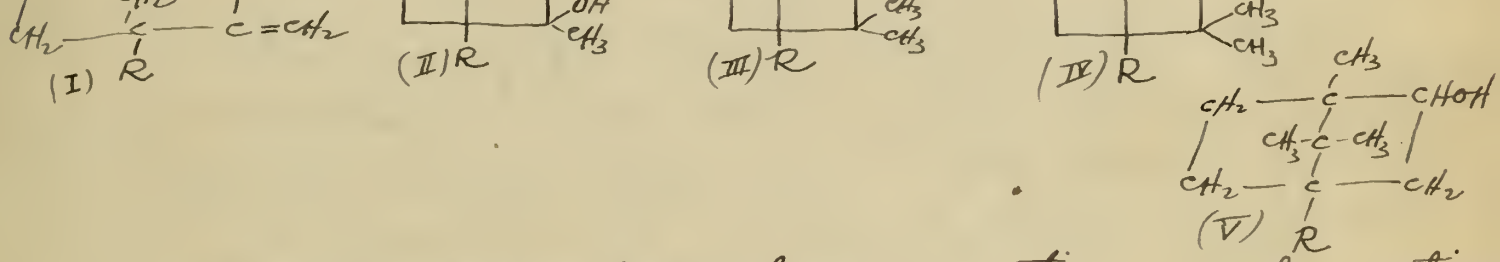
March 24, 1935.

Organic Seminar, May 15, 1935. Reported by Poe Liang

"A New Series of Homologs of the Camphor Group"

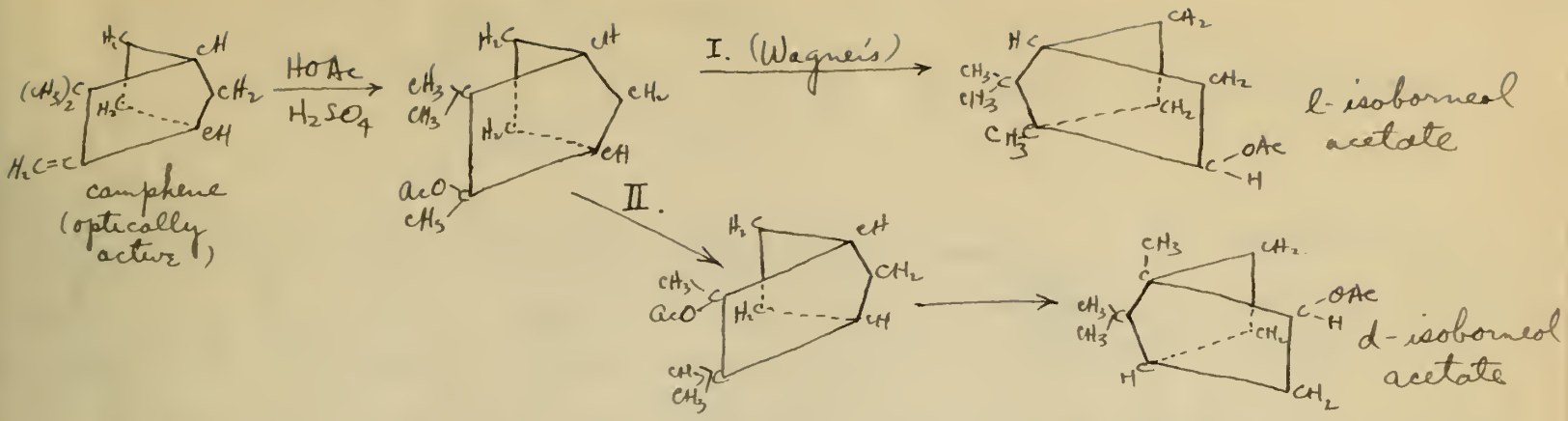
Cf. S. S. Nametkin and coworkers, Ann., 516, 199 (1935); J. pr., [2] 124, 144 (1930); Ann., 459, 144 (1927).

Nametkin and coworkers have shown that transformation of hydrocarbons of camphor type into alcohols of isoborneol type as well as the reverse process do not proceed in only one direction (camphene rearrangement of type I, or Wagner's rearrangement), but may also be accompanied by an isomerization of another manner (camphene rearrangement of type II). This latter type of rearrangement may be illustrated by the following scheme for the transformation of α-substituted camphenes (I) to the corresponding 4-substituted isoborneol (IV-V):




To serve as proof for this proposition may be mentione some recent work by other investigators in which the above scheme proposed by Nametkin for the rearrangement of camphene was applied with success for the explanation of an extremely interesting attendant phenomenon of this reaction, namely that of the partial or complete racemization.

This phenomenon which takes place during the transformation of camphene into isoborneol can be easily explained if we assume that the rearrangement which results with isobornyl acetate may proceed following course I as well as course II according to the proposed scheme:



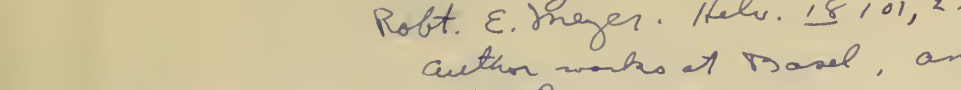

The isoborneols thus formed according to the different courses of the rearrangement are mirror images of each other and may therefore under proper conditions in which they are formed simultaneously and in equal quantities give a racemic mixture. But if the process is carried out under rigorous conditions, the reaction will proceed in only one specific direction with the result of the formation of an optically active end-product.

The course of formation of 4-propyl-isoborneol from d-propyl-bornyl alcohol is discussed in detail with reference to the corresponding methyl compounds. The structure of the various intermediates and end-products are supported by sound experimental evidences.

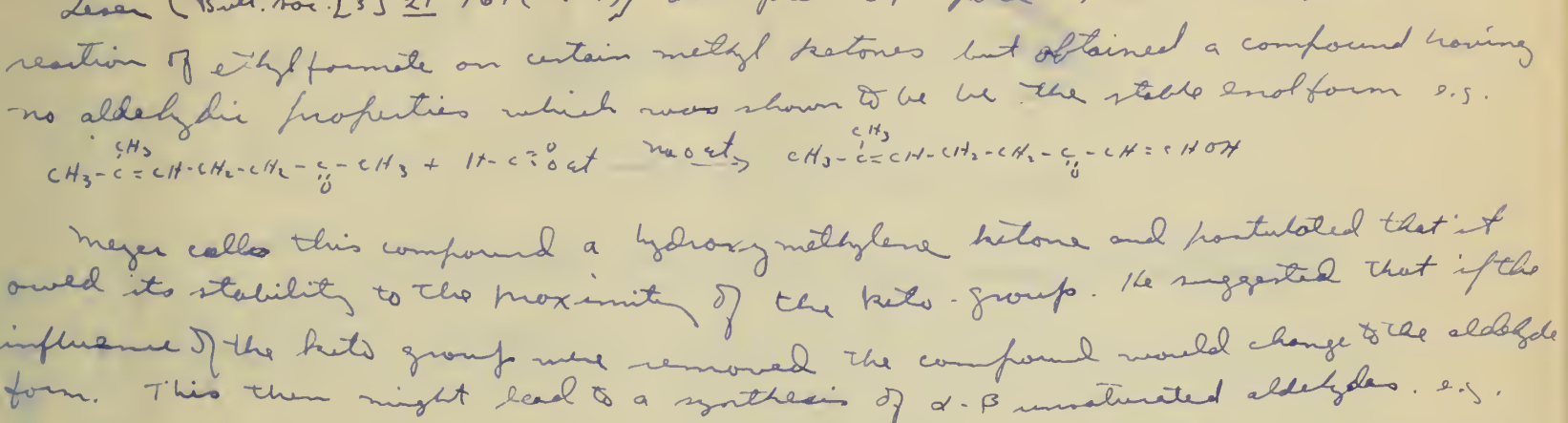
# Reaction of the Grignard Reagent on Hydroxymethylene Ketones.

Robt. E. Meyer. Helv. 18 101, 279, 282, 305, (1935)
author works at Basel, anstalt für anorganische chemie
Field: Terpenes.

Lesser (Bull. Soc. [3] 21 967 (1899)) attempted to prepare 1,3 keto aldehydes by the reaction of ethylformate on certain methyl ketones but obtained a compound having no aldehydic properties which was shown to be the stable enol form e.g.

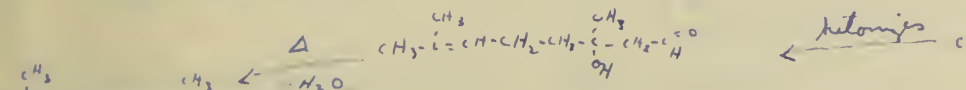


Meyer calls this compound a hydroxymethylene ketone and postulated that it owed its stability to the proximity of the keto-group. He suggested that if the influence of the keto group were removed the compound would change to the aldehyde form. This then might lead to a synthesis of α-β unsaturated aldehydes. e.g.

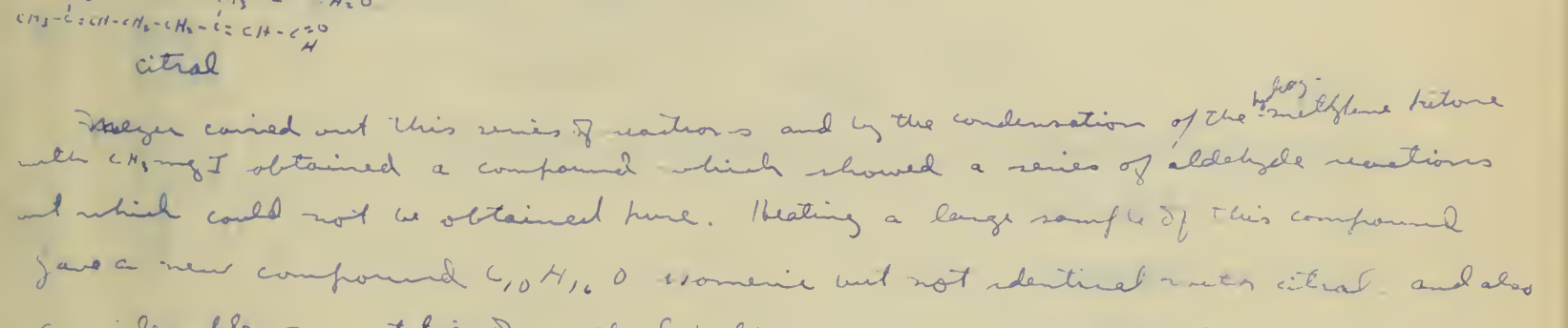



Meyer carried out this series of reactions and by the condensation of the hydroxymethylene ketone with $CH_3MgI$ obtained a compound which showed a series of aldehyde reactions and which could not be obtained pure. Heating a large sample of this compound gave a new compound $C_{10}H_{16}O$ isomeric but not identical with citral and also considerable quantities of methyl heptenone and acetaldehyde.

By a series of reactions Meyer proved that the compound $C_{10}H_{16}O$ was



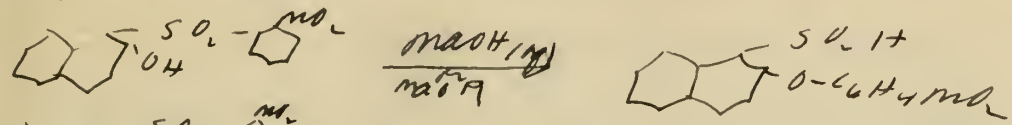
which would be formed by 1:4 addition of the Grignard reagent to the hydroxymethylene ketone. e.g.

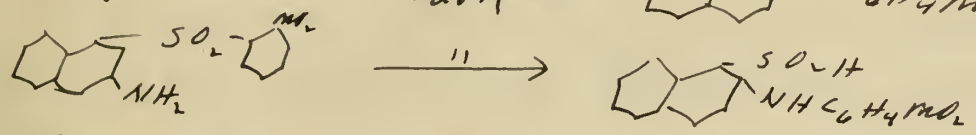



So far as the author could find 1:4 addition took place exclusively, so he concludes that α.β unsaturated aldehydes of the ~~ketone~~ citral type cannot be made by this method. The hydroxymethylene ketones from dihydro pseudo-ionone and β-ionone were likewise shown to give 1:4 additions of the Grignard reagent.

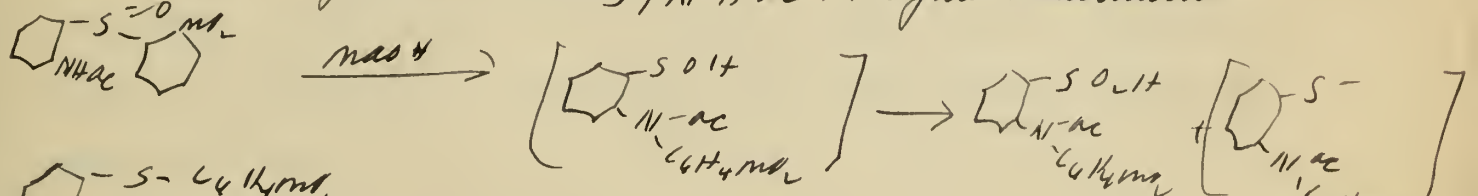
Smiles, S. Rearrangement of O Substituted Sulfones, Sulfoxides, + Sulfides. J.C.S. 1931, 171. (an abstract of seminar report given Apr. 3, 1935.)

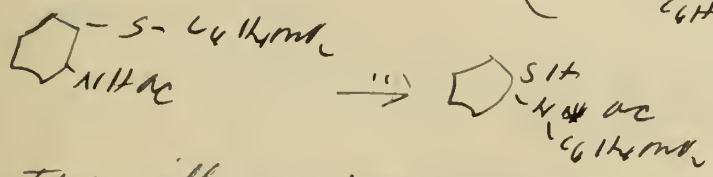
A. Types of Rearrangements observed:

1. 

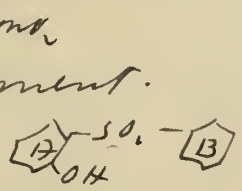
2. 

For $NH_2$ the groups $NHCH_3^+$, NHac may be substituted

3. 

4. 

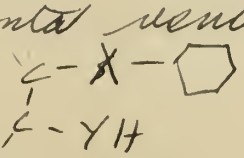
B. Factors influencing rearrangement.

1. For O OH sulfones. – 

a. O or P negative substitution in B facilitates rearrangement.
b. m " " " " inhibits "
c. P. (to OH) " " " A facilitates "
d. " " positive " " " inhibits "
e. m. " negative " " " " "
f. nature of medium.

$NaOC_2H_5$ > NaOEt > NaOMe > NaOH. – arranged in decreasing order of ease of promoting rearrangement.

C. Summary of experimental results:

In the cpd. of type 

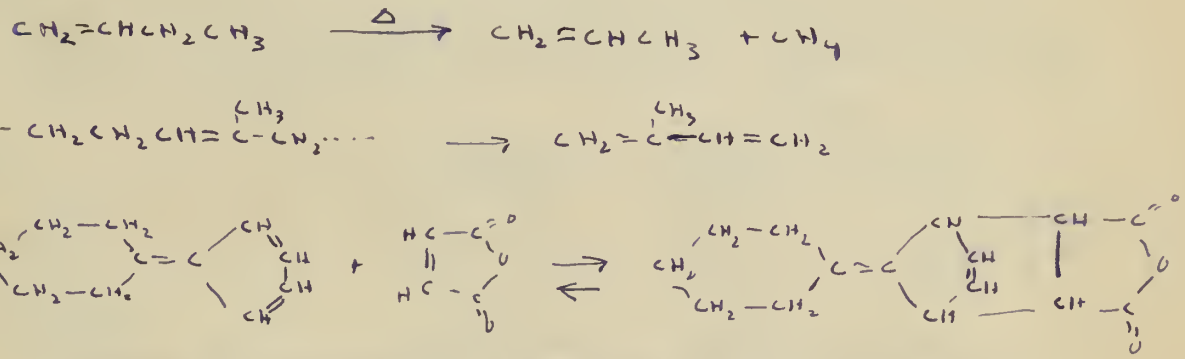
If YH = NHAc, then X may be $SO_2$, SO, or S + Rearr. will take place
" " = OH (aliphatic) " " " $SO_2$, or SO.
" " = $NH_2$ (arom.) " " " $SO_2$ or SO.
" " = OH ( " ) " " " $SO_2$ or SO.
" " = SH " " " O

E.D. Farley.

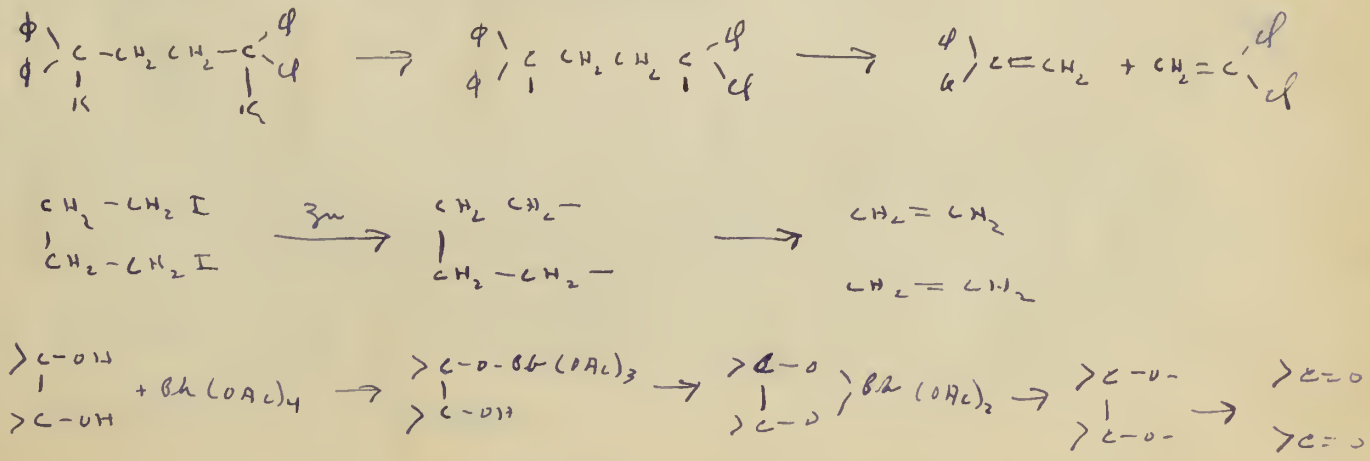
# THEORIES CONCERNED WITH THE SPLITTING OF THE CARBON CHAIN

Seminar report, May 22, 1935. By M. A. Spielman

Otto Schmidt of the Ludwigshafen Laboratory of the I-G Dye Trust has revived the old theory of alternating polarity and applied to it the mechanics of Heitler and London. As a result of his calculations he arrived at the following rule: In the splitting of a compound containing a double bond, or one in which a double bond is formed as a prelude to splitting, the break takes place between atoms 3 and 4. Examples are given.



Criegee has formulated a different theory: If two mobile groups or atoms are removed from the 1,4-positions of a molecule, a split will take place between atoms 2 and 3. Otherwise stated, the 1,4-diradical is incapable of existence, but stabilizes itself by division between atoms 2 and 3. The following are illustrations.



Schmidt, Ber., 68, 60 (1935).

Criegee, ibid., 68, 665, (1935).

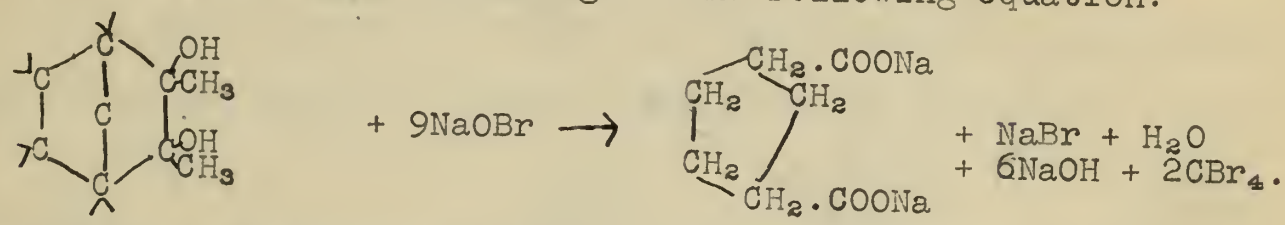
# ORGANIC SEMINAR

## The Action of NaOBr on Dimethylpinacols

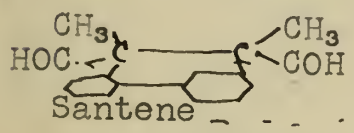
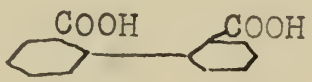
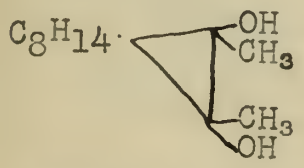
By Baron John Palmen
University of Helsingfors

Reference: Journal für praktische Chemie (2) Vol.141,p.8

Palmen confirmed Semmlers structure of santene by treatment of the glycol with NaOBr according to the following equation:




This reaction gave a 37% yield of acid and an 82% yield of $CBr_4$. For this reason Palmen considered it worth while to perform a series of tests to determine whether or not the $CBr_4$ cleavage of glycols is of general application. His results are summarized in the following table:

| Glycol | PRODUCT | YIELD %$CBr_4$ | YIELD % Acid |
|---|---|---|---|
| $(CH_3)_2COH.COH(CH_3)_2$ | $CH_3COOH$ | 82 | 69 |
| $(C_2H_5)(CH_3)COH.COH(C_2H_5)(CH_3)$ | $C_2H_5COOH$ | 77 | 53 |
| $(C_6H_5)(CH_3)COH.OHC(C_6H_5)(CH_3)$ | $C_6H_5COOH$ | 95 | 90 |
|  Santene |  | 77 | 31 |
| | | 82 | 37 |
|  | $C_8H_{14}(COOH)_2$ | 66 | 63 |

These data indicate that oxidation of the atomic grouping $CH_3.COH.COH.CH_3$ by NaOBr to give an acid and $CBr_4$ is of general character and can be advantageously applied to the structure proof of glycols of this type. The cleavage takes place at room temperature under mild conditions although an excess of alkali is required, for stabilization of the hypobromite. The excess of alkali need not be great since it is produced during the reaction.

No mechanism was suggested.

William Sparks

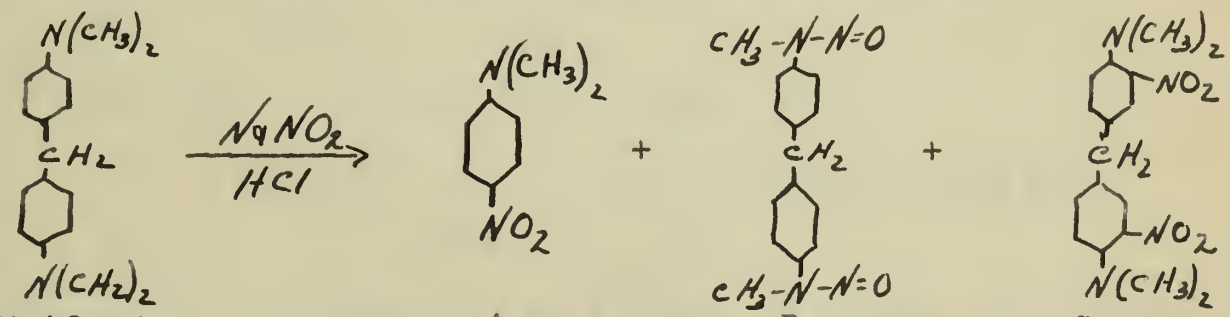
Chem 135 Seminar Report Leffler, M. T.

5/8/'35

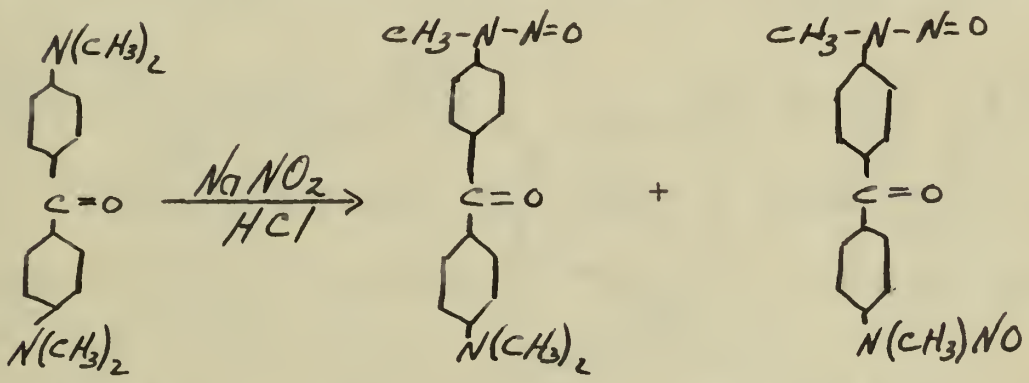
Subject: Action of Nitrous Acid on Aromatic Tertiary Amines.

Reference: Donald and Reade, J. Chem. Soc., (1935) 53.

Summary: Michler's ketone and Michler's hydride do not follow the general rule that nitrous acid does not react with para-substituted aromatic tertiary amines. Instead they give the following products:




Michler's Hydride — A: Cleavage + Nitration — B: Nitroso-Amine — C: Nuclear Nitration




Michler's Ketone — D: Mononitroso-amine — E: Dinitroso-amine

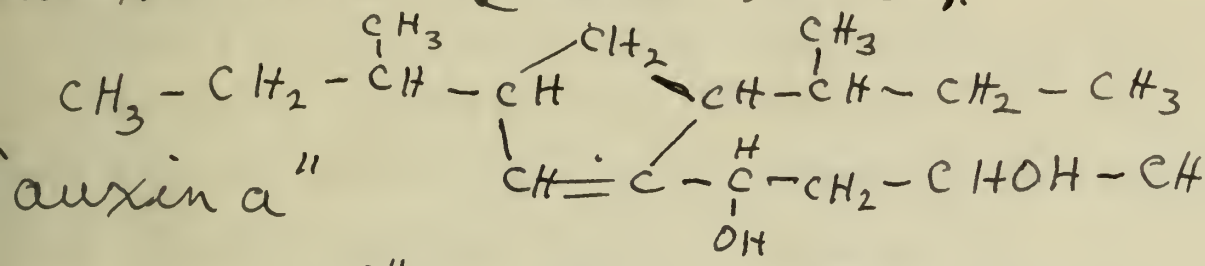
These reactions may be so controlled by regulating the acidity of the solution as to yield a maximum amount of any one of the products and a minimum of the others. A is favored by low acidity, B by medium, and C by high (9 N HCl); D by low, and E by high. The nitroso-amines are probably intermediates in the formation of the nitro compounds, since (sodium nitrate + HCl) alone will not produce them.

# Plant Hormones.

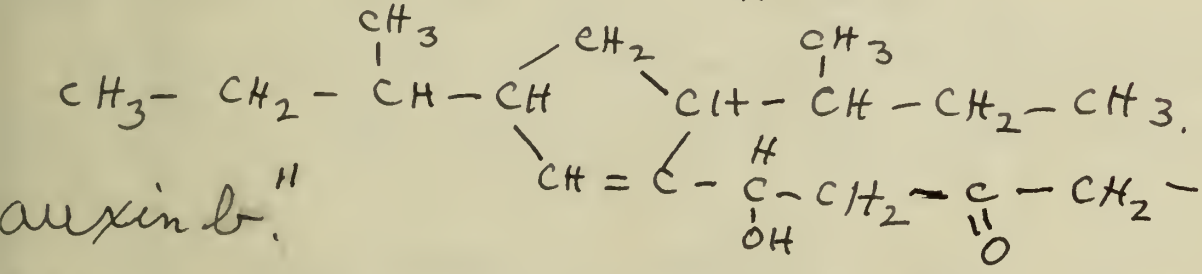
Fritz Kögl (Utrecht)

Ber. 68A. 16-28 1935.

Two plant vitamins have been found and their structures shown to be,



"auxin a"

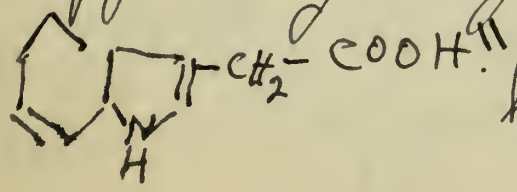


"auxin b."

These compounds were isolated from many sources eg. malt, grass, animal urine, human urine and many other plant sources. They are optically active.

The entire investigation used only about 800 – 900 milligrams of pure substance. The human hormones and vitamins were found to be inactive.

Kögl has also discovered what he considers a pseudo hormone. Active for growth but appearing only in human urine.



"hetero-auxin"

# THE REACTION OF ISOCYANIC ACID ESTERS WITH ORGANIC ACIDS

I. The theory and application of the reaction for the preparation of acid anhydrides. von C Naegli and H Fryabyi Helv. Chim. Acta. 17 931 (1934)

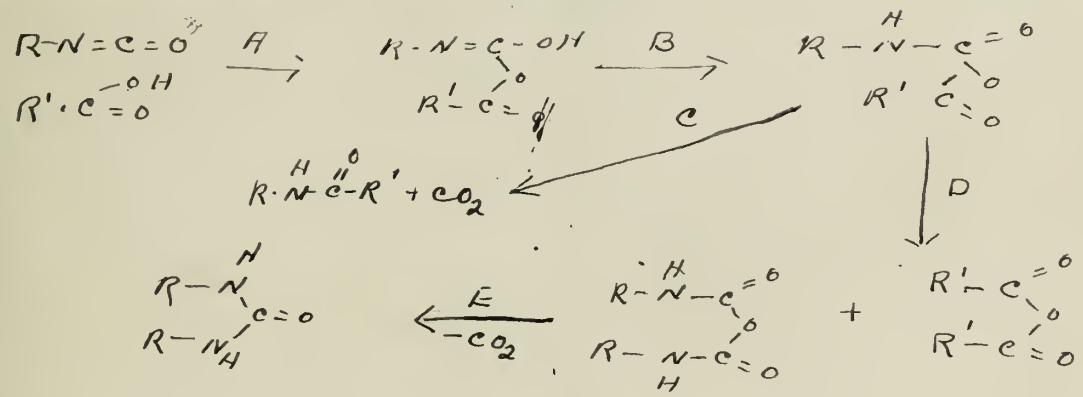
Zürich, Chemisches Institute of the University. Works: 1. 7 papers on Modified Curtius Degradation. 2. Indicators

Naegli reported in an earlier paper, Helv. 12, 206 (1929), that aliphatic isocyanates treated with aliphatic acids in a boiling benzene solution gave acylated amines, while, if the isocyanate was areomatic, diphenyl, ureas were obtained along with the pure acid anhydride.

The arylisocyanate does not act as a true dehydrating agent on the acid, as $ZnCl_2$, $P_2O_5$, etc., but reacts with the acid to form an intermediate product.

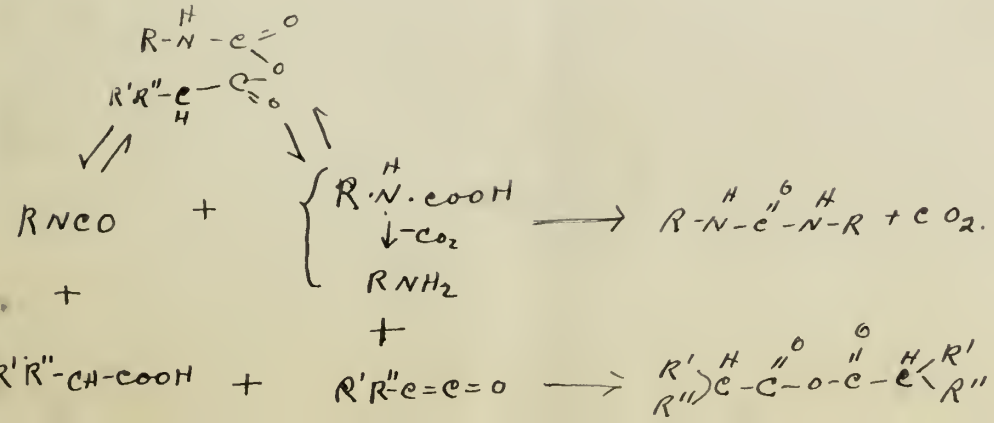
There are two mechanisms possible.

1.




The reaction is in the direction of C in the case of aliphatic isocyanates and in the direction of D and E when the isocyanate is areomatic. Naegli presents several analogies such as ketenes and acids to give anhydrides, etc.

2.



These two mechanisms explain several reactions which until now had no explanation or else a false one. Some of these reactions are: 1) reaction of isocyanates and formanalide to give isonitriles and substituted ureas, 2) reaction of isonitriles on acids to give acid anhydrides and formanalide, 3) rearrangement of vinyl alcohol esters to the anhydrides and aldehydes. To establish in which direction the reaction actually proceeds, the mixed anhydride must be isolated and decomposed in the absence of excess acid or phenylisocyanate.

The action of phenylisocyanate on acids proceeds at low temperatures and is valuable for obtaining heat-sensitive anhydrides. The 3,5-dinitrophenylisocyanates increase the yields of the acid anhydrides.

I.

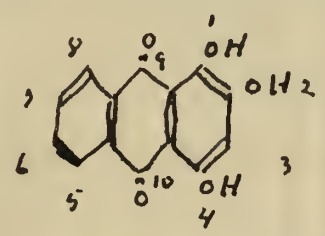
H. G. Kolloff

Structure of Boletol

Synthesis of Boletol and Isoboletol

F. Kögl and W. B. Deizs Ann. 515 10,23 (1934)

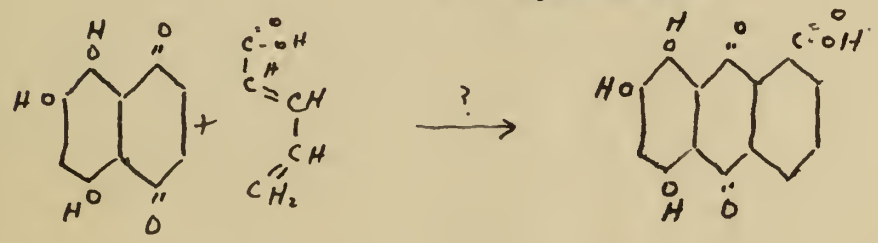
Material from certain fungi which turns blue on exposure to air. Analyzed as $C_{15}H_8O_7$ gives triacetate $C_{21}H_{14}O_{10}$ with acetic anhydride. With zinc and acetic anhydride gives colorless pentacetate $C_{25}H_{20}O_{12}$. When treated with $CH_2N_2$ and then zinc and acetic anhydride a trimethyl leuco diacetate is obtained. When subjected to zinc dust distillation anthracene was obtained. On decarboxylation with soda lime the compound yielded purpurin. Hemi-mellitic acid resulted from oxidation of the original compound by hydrogen peroxide. Structure in view of reactions is



with COOH either in the 5 or 8 position.

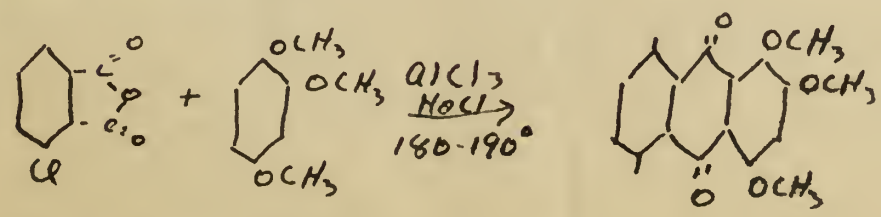
II. Synthesis

I.



Reaction did not go.

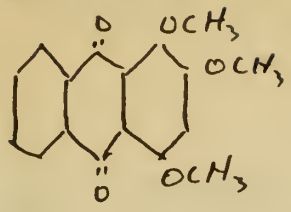
II.



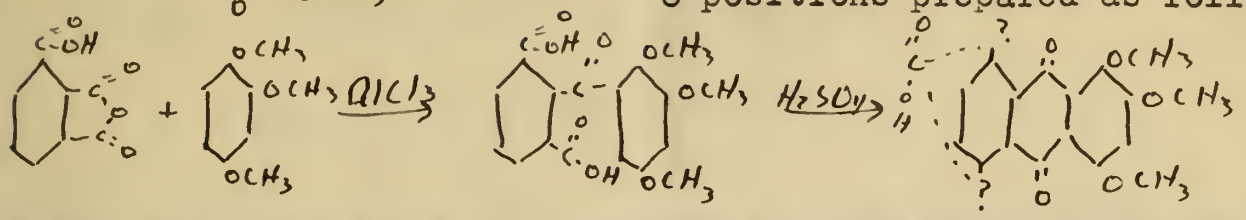
Mixture with Cl in 5 and 8 positions. Did not separate and go ~~through cyanide~~

through cyanide.

III.

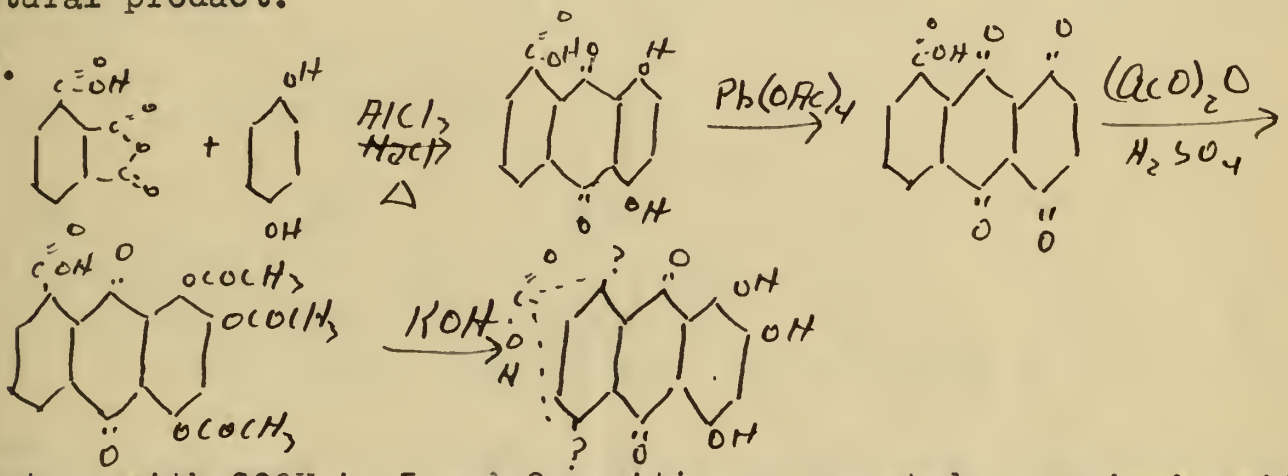


Mixture with carboxyl group in 5 and 8 positions prepared as follows:



Mixture separated and one of products when treated with zinc and acetic anhydride was identical with corresponding derivative of natural product.

IV.



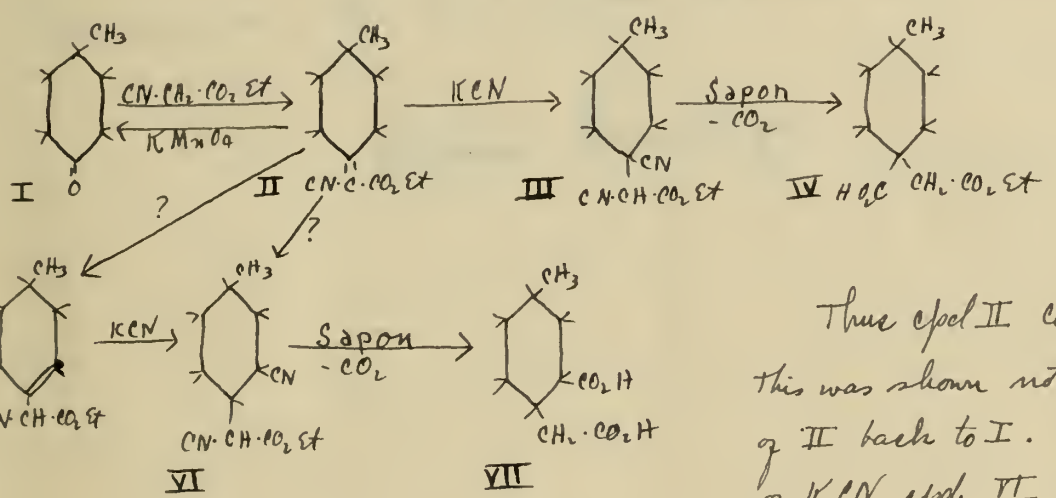
Mixture with COOH in 5 and 8 positions separated, one checks with natural product.

# The Stereoisomerism of 4-methyl cyclo hepane, 1 acetic acid 1 carbopylic acid.

Stefan Goldschmidt & Gräfinger

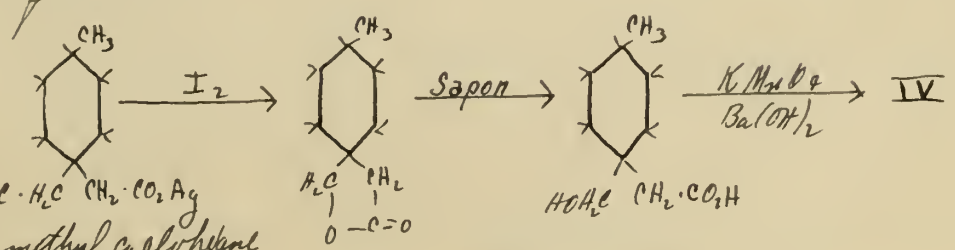
Ber 68, 279 (1935)

Goldschmidt, in checking over the work of Khuda [J. Ind. Chem Soc. 8, 277 (1931)] the isolation of 4 stereoisomers of 4 methyl cyclohepane, 1 acetic acid, 1 carbopylic acid found that during the course of the reaction that there was the possibility present, that the 4 isomers were at least in part structure isomers.




Thus cpd II could rearrange into cpd V. this was shown not to take place by oxidation of II back to I. Also during the addition of KCN cpd. VI could be formed, and finally the acid VII would be isolated and not IV.

Goldschmidt synthesized IV by another method & attempted to isolate the acids A, B, C & D of Khuda.




Silver salt of 4 methyl cyclohepane 1,1 diacetic acid.

Goldschmidt could not isolate acids B & D but obtained acids A & C pure. He found that the melting point of a mixture of:

1 mol A + 1 mol C corresponds to the M.P. of Khuda's acid D

4 mols A + 1 mol C " " " M.P. " " " B

Seminar

Feb. 6, 1935.

Conversion of Carboxylic Acids into Their Next Higher Homologs.

W. O. Peters

## Conversion of Carboxylic Acids into their next higher homologs.

F. Arndt and B. Eistert, Ber. 68, 200 (1935).
Univ. of Breslau — main Lab. of I. G.

The methods available for conversion of a carboxylic acid into the next higher homolog are sometimes rather long, involving numerous steps, and also when certain groups such as the nitro or keto group are present in the molecule such a method can not be used.

The authors have developed a method whereby the acid containing one more carbon atom can be synthesized. This method involves only three steps, is quick, and produces the desired product in good yields. It can be represented as follows:

$$R\text{-}\overset{O}{\overset{\|}{C}}\text{-}OH + SOCl_2 \longrightarrow R\overset{O}{\overset{\|}{C}}\text{-}Cl + {}^{2}CH_2N_2 \longrightarrow R\overset{O}{\overset{\|}{C}}\text{-}CHN_2 + CH_3Cl + N_2$$

$$R\overset{O}{\overset{\|}{C}}\text{-}CHN_2 \xrightarrow{HOH + Cat.} RCH_2COOH$$

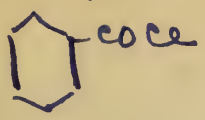
$$R\overset{O}{\overset{\|}{C}}\text{-}CHN_2 \xrightarrow{ROH + Cat} RCH_2COOR$$

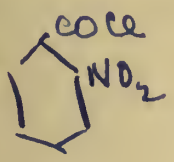
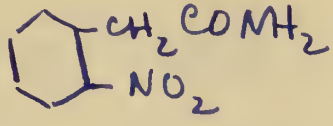
$$R\overset{O}{\overset{\|}{C}}\text{-}CHN_2 \xrightarrow{NH_3 + Cat} RCH_2\overset{O}{\overset{\|}{C}}\text{-}NH_2$$

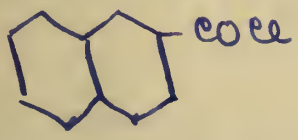
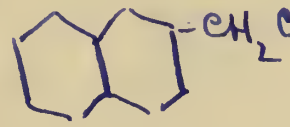
The catalyst can be one of the following: Cu, Pt, $Ag_2O$, or Colloidal Ag.

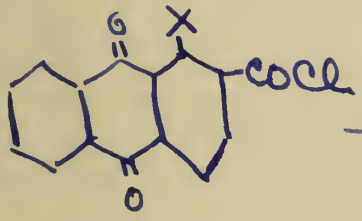
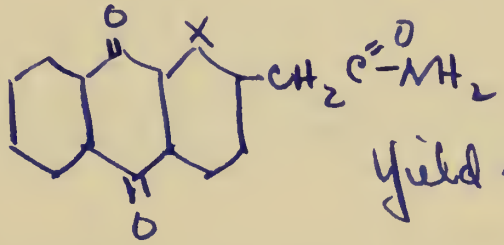
The authors state that the reaction goes the smoothest when the diazo-methyl ketone is rearranged in the presence of ammonia to give the amide which can be easily converted to the acid.

ome of the Cpds prepared are as follows:

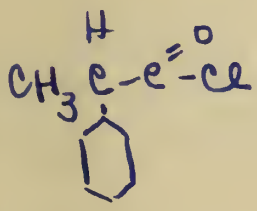
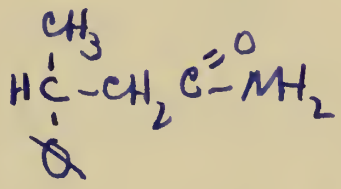
1)  → Isolated as the Amide 71% yield

2)  →  60%

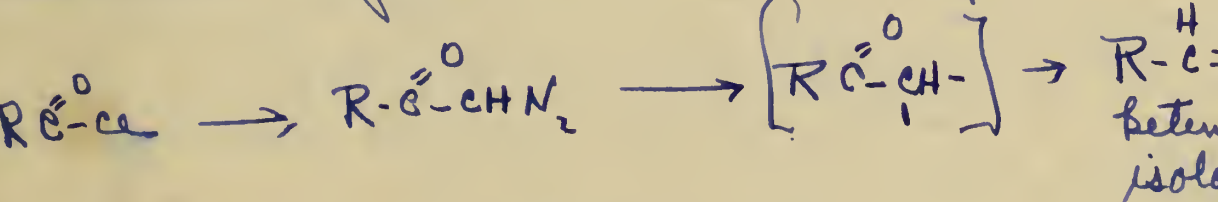
3)  →  90%

4)  →  Yield not stated.

X = H
X = Cl
X = $NO_2$

5)  →  No yield stated.

Mechanism Proposed is similar to one for Curtius Rearrangement



Ketene actually isolated in certain cases.

Ketene + Water → Acid
Ketene + Ammonia → Amide
Ketene + Alcohol → Ester

W.O. Teters —

The Preparation of Ketols by Means of Mixed Organo Magnesium Compounds

Colonge, J. comptes rendus 194 929 (1932)
Grignard, V. and Colonge, J. comptes rendus 196 1414(1933)
Colonge, J. bull soc chim (5) 1 1101-1114 (1934)

The aldol condensation has long been known but similar reactions with ketones have not been widely applied until recently.

$$RCH_2COCH_2R' \longrightarrow \begin{matrix} RCH_2 \\ R'CH_2 \end{matrix} COH-\underset{R}{C}H\cdot COCH_2R'$$

The first known example was that of acetone(R=H) in the presence of a strong alkali. Later it was applied to methyl ethyl ketone which gave a small yield of the ketol on long standing over alkali. Grignard and Fluchaire succeeded in isolating the ketols from a whole series of methyl ketones by use of MgORX as a condensing agent Finally Courtot an Cuperoff, still working with methyl ketones succeeded in getting them to condense with themselves by the use of aluminum chloride in the presence of alkylated aromatic amines $ArNR_1R_2$. The yields in these reactions were poor.

In the present work the Grignard reagent prepared by treating a primary or secondary amine with an alkyl magnesium halide is used as the condensing reagent, the reaction being thought to take place as follows:

$$RCOR' + XMgNR_1R_2 \rightarrow \begin{matrix} RCOMgX \\ R' \quad NR_1R_2 \end{matrix} \xrightarrow{RCOR'} \begin{matrix} RCO\cdot MgX \\ R' \quad R'''CH_2C{=}O \end{matrix} R' + R_1R_2N\text{-}H$$

This mechanism is supported by the fact that the best yields are obtained by the use of one mol of $RR_2MgX$ for every two mols of the ketone. Good yields are obtained if one of the R's in the amine is aromatic, but primary amines work just as well as secondary. Methyl aniline or aniline is usually used.

This reaction can be applied to other than methyl ketones, which is an important advance over the older methods. Higher ketones such as diethyl ketone and butyrone give only slightly smaller yield than the methyl ketones. Cyclic ketones can also be made to condense. In general all aliphatic ketones undergo this reaction if there exists on the carbon atoms immediately adjacent to the carbonyl a total of at least three atoms of hydrogen. Ketones such as benzophenone and fluorenone which by the above rule could not condense with themselves will nevertheless add the Grignard reagent as above and may then be allowed to react with other ketones to form mixed ketols.

The value of this work lies in the fact that it opens the way to the preparation of a whole series of compounds hitherto unobtainable by simple condensation methods.

M. Bowman

Zur Kenntnis der Perkinschen Synthese By Eugen Müller, Gawlick and Kreutzman.

II. Ann. 515 97 (1935)

I. Ann. 491 251 (1931)

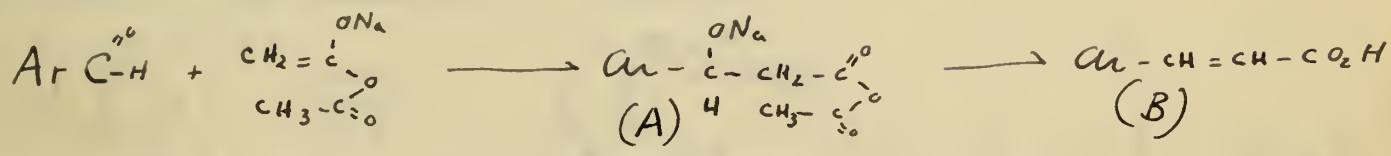
Review of Perkins Reaction. Kalnin, Helv. Chim. Act. 11 977 (1928)

Field (Müeller) Danzig

Azobenzenes

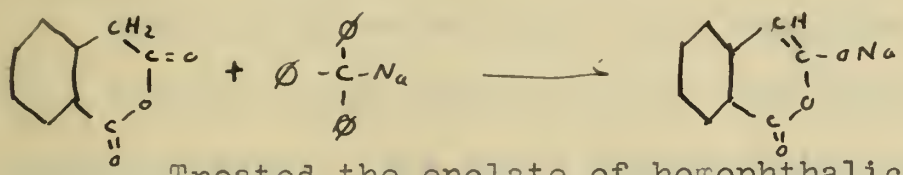
Sterols

Müller considers the Perkins Reaction a special case of the aldol condensation.

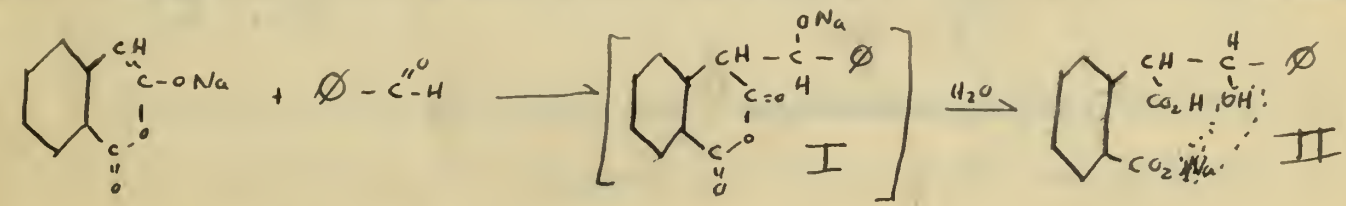


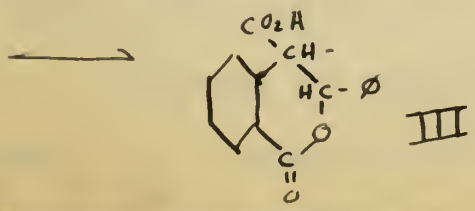
Proof of this mechanism would be indicated by the isolation of compounds analagous to (A) and (B).

Prepared the pure enolates, in almost quantitative yields, using triphenylmethyl sodium as the enolizing agent. Prepared the pure enolate of homophthalic anhydride



Treated the enolate of homophthalic anhdride with benzaldehyde, using no condensing agent. Did not isolate the anhydride(I), which is analagous to (A), but did isolate the hydroxy acid (II). More often the lactone (III) of the acid was obtained, in 85% yields.



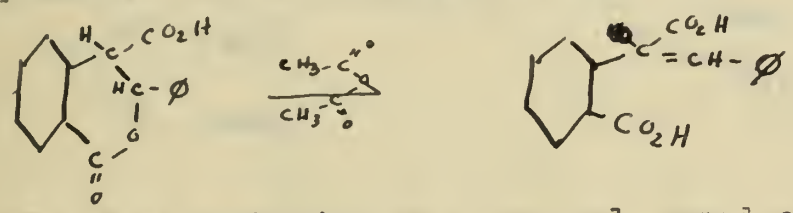


Proof of III

1. CH analysis $C_{16}H_{12}O_4$
2. Molecular weight determination
3. Neutral equivalent- for one carboxyl
4. Treatment with diazomethane, and determination of Zeisel number showed one $OCH_3$
5. Compound III not identical with benzal homophthalic ~~anhydride~~ acid (IV)

On treatment of III with acetic anhydride obtained benzalhomophthalic ~~anhydride~~ acid (IV) which is analagous to (B).

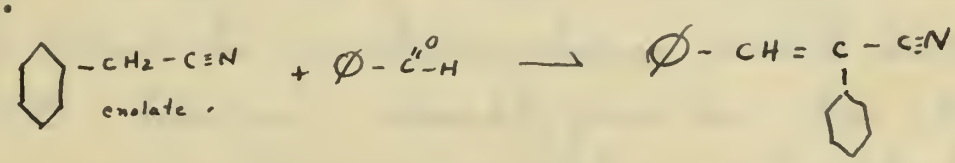
Thus compounds analagous to both (A) and (B) are indicated, and proof of the mechanism is possible.



To show mechanism was general, used o-nitrobenzaldehyde, o-methoxy benzaldehyde, and p-dimethylaminobenzaldehyde. Obtained yields of lactones analagous to (III) of 83%, 55% and 17% respectively.

Reaction of benzaldehyde with enolates of succinic anhydride, ethyl acetate, ethyl phenylacetate, and benzyl cyanide, without condensing agent, gave small yields of the expected $\alpha$-$b$ unsaturated compound.

Example.



Reaction of benzaldehyde with ~~enolates~~ enolates of compounds containing one hydrogen on $\alpha$-C atom did not proceed, as is the case in the aldol condensation.

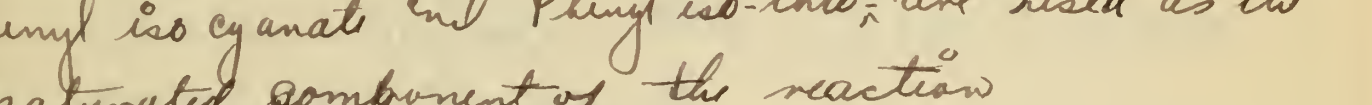
Contrary to expectations, the sodium salt of malonic ester would not condense with benzaldehyde.

Extension of the Michael's Reaction Ghosh & Guha

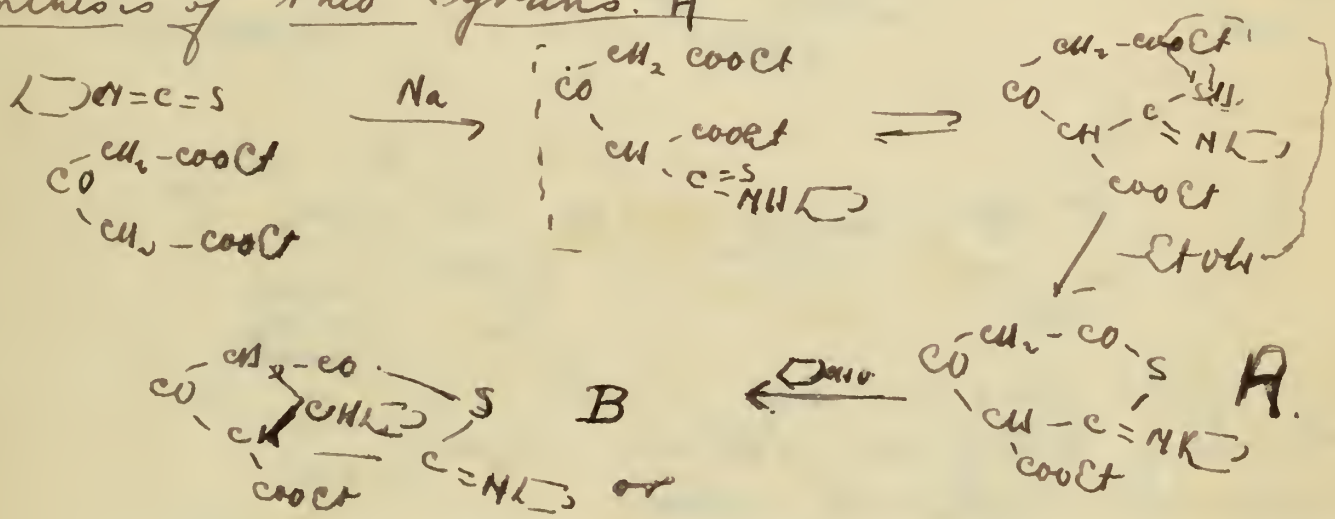
J. Ind. Chem. Soc. XI, 353, (1934)

Ethyl carbamate is substituted for the active methylene cpds in the condensation.

Phenyl iso cyanate and Phenyl iso-thio cyanate are used as the unsaturated component of the reaction



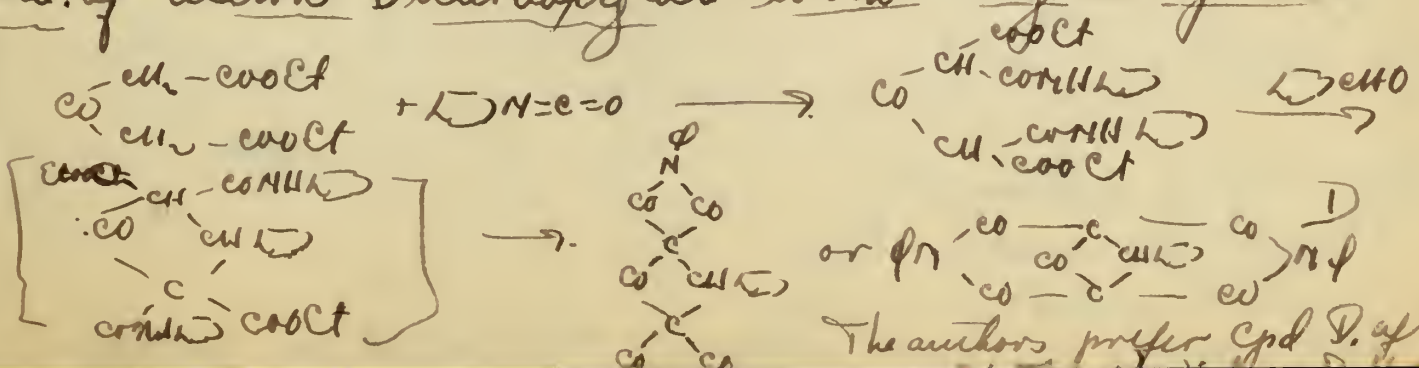
Synthesis of Thio Pyrans. A



Cpd B is preferred by the authors as Cpd A gives a di-Sodium deriv. while the cpd. resulting from it gives no Na derivative. Cpd B thus enolization would form double bond on C atom involved in the bridge and hence be in discordance with Bredt's Rule.

Cpd C however should give a Na derivative

cond. of acetone Dicarboxylate with Phenyl iso cyanate



The authors prefer Cpd D. after

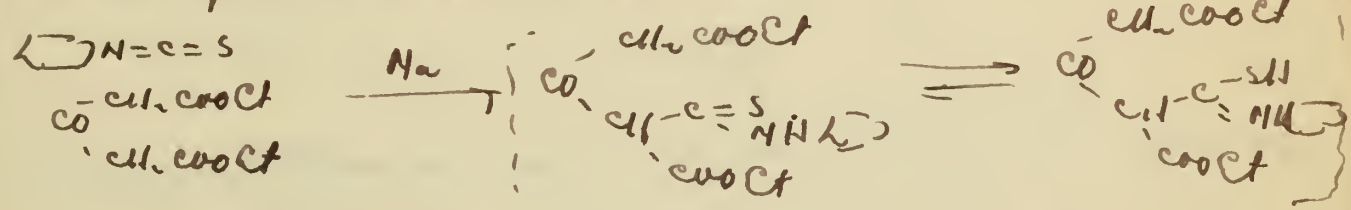
Extension of the Michaels' Reaction  Ghosh & Guha.
J. Ind. Chem. Soc. XI, 353, (1934).

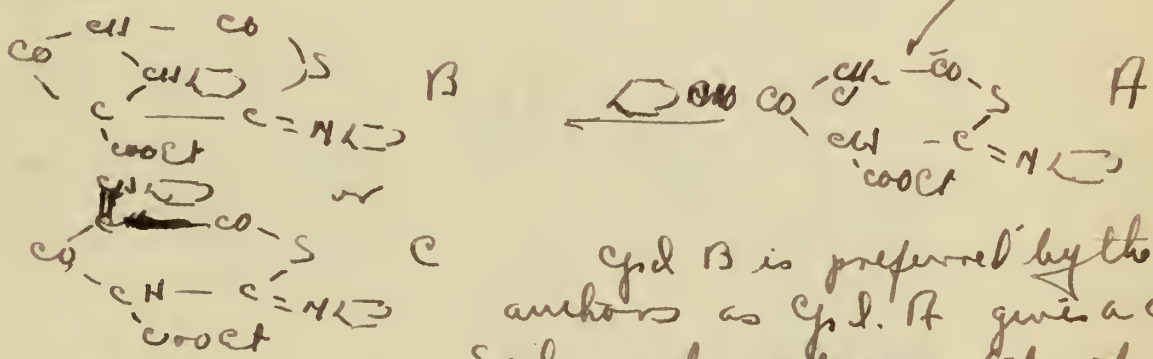
Ethyl carbamate is substituted for the active methylene cpds in the Michaels condensation.

Phenyl isocyanate and phenyl isothiocyanate are used as the unsaturated component of the reaction.



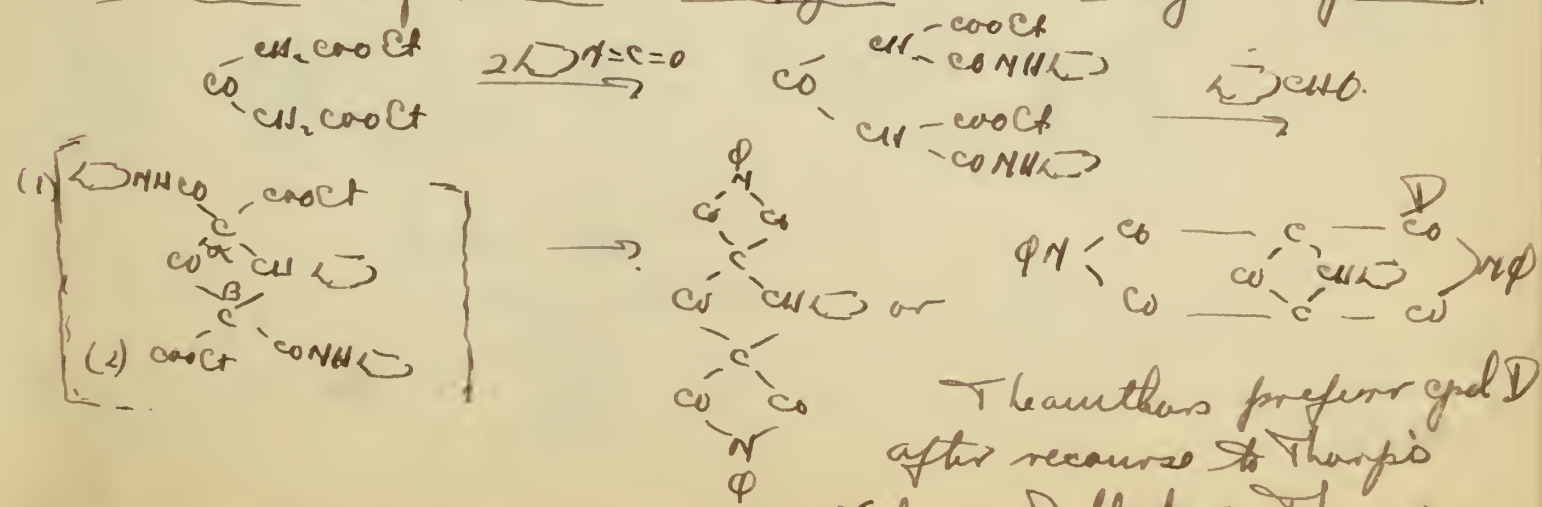
Synthesis of Thio Pyrans A.





Cpd B is preferred by the authors as Cpd. A gives a di-Sodium derivative, while the cpd resulting from its condensation with benzaldehyde gives no Na derivative. Cpd B thus enolization would form a double bond on C atom involved in the bridge, and hence be in discordance with Bredt's Rule. Cpd. C, however should give a Na derivative.

Condensation of Acetone Dicarboxylate with Phenyl isocyanate.



The authors prefer cpd D after recourse to Thorpe's Valency Deflection Theory. decrease in angles α & β result in widening of angle above

# Seminar Report

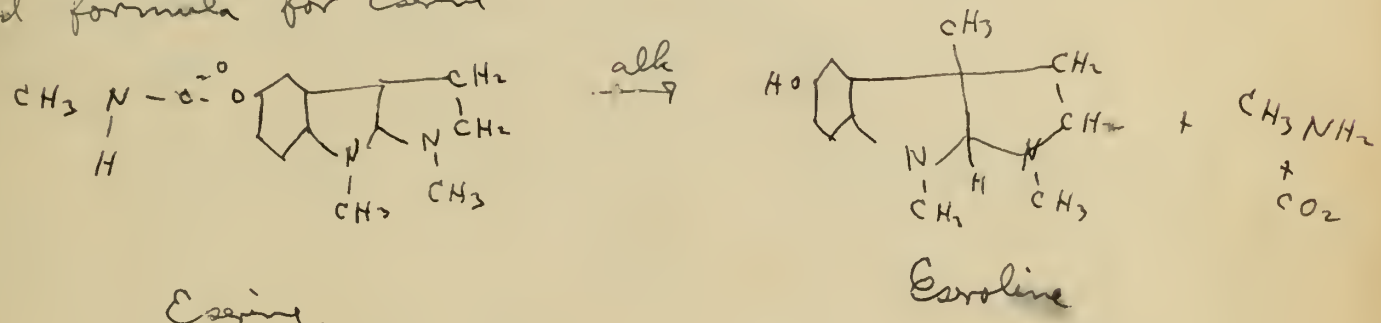
## Synthetic Studies on Eserine (physostigmine)

A) Ann 500 42 (1932) Hoshino and Kotake
" 516 76 (1935)
" " 81 (1935)

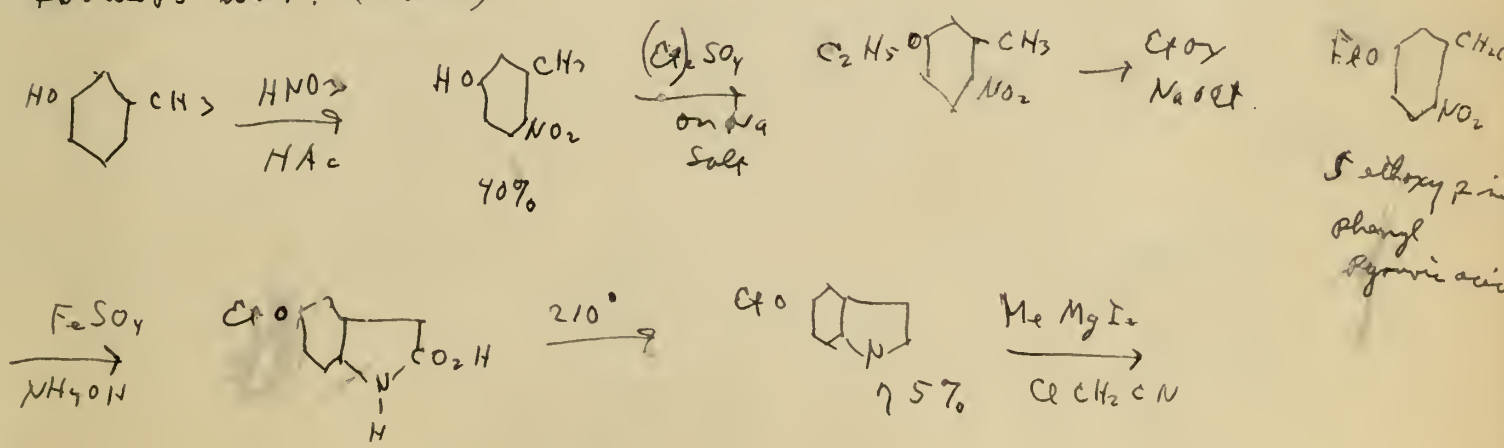
B) J. A. C. S, 56, 1796, (1934) Julian and Pikl
" 57 539 (1935) " "
" " 563 " " "
" " 755 " " "

from the organic chemical division of the Technical University of Tokyo - Ookayama.

① Proposed formula for Eserine




② Hoshino's work. (Refs A.)



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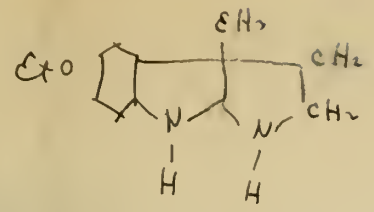
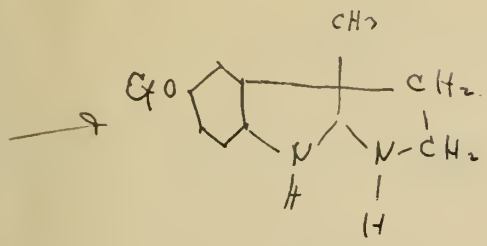


resolved using d tartaric acid and Brom camphor sulfonic acid

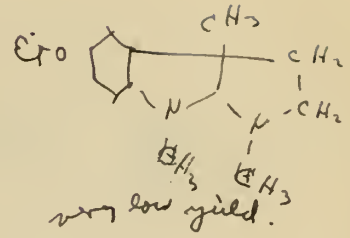


l form

+ d form

HI + Me

~~hydl~~ ~~eserolines~~

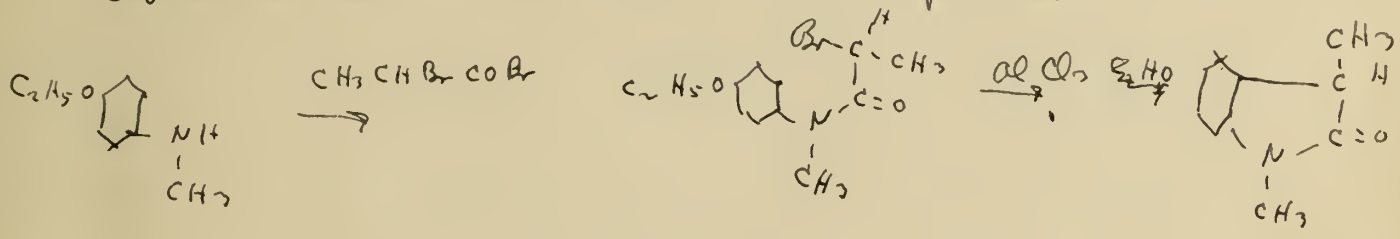


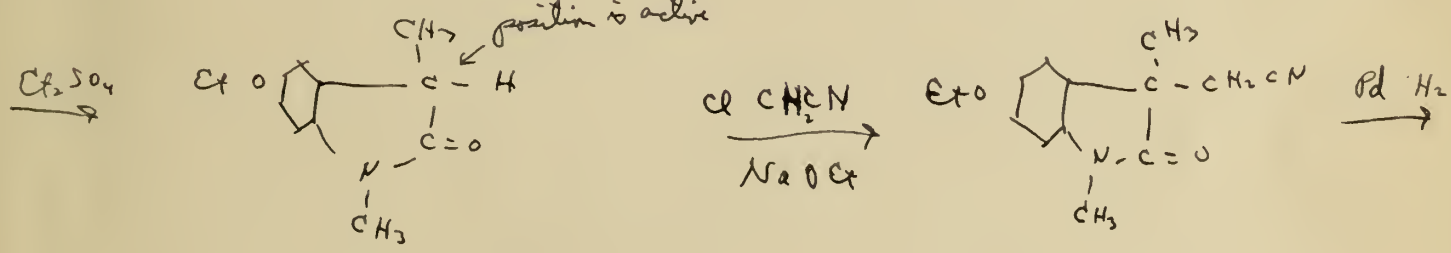
very low yield.

↓ hydl.

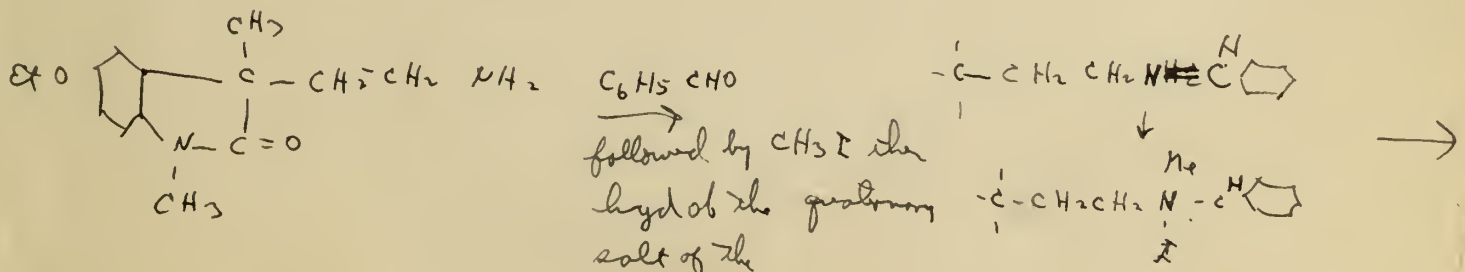
Eserolines l form identical with that from natural sources also all derivatives identical.

(3) Julian has substantiated the Japanese authors (Ref B) showed oxindoles to be reactive in the 3 position.

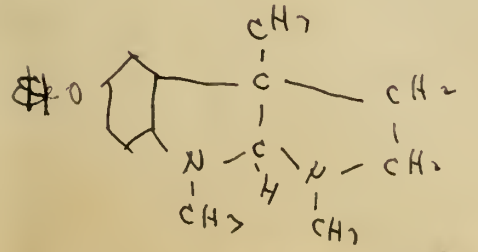






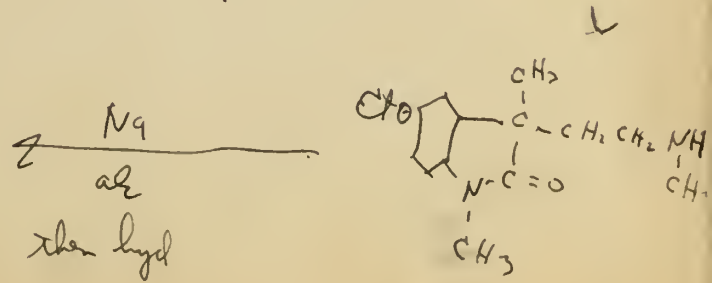


followed by $CH_3I$ then hydl of the quaternary salt of the



85%

dl eserolines



Na
alc
then hydl

d l esseroline $\xrightarrow[\text{resolution}]{\text{d tartaric}}$ l esseroline identical with that of the Japanese authors and with the natural product.

l esseroline + $CH_3CNO$ methyl isocyanate → l eserine also identical with natural product.

A better method of resolution was to resolve the diamine before ring closure.

# The Influence of Acid, Ester + Nitrile Groups on Intramolecular Transformations of the Allyl Type I, II, III

Rambaud Bull. Soc. Chim 1531 1206, 1318, 1342 (49)

The author has studied the affects of acid ester and nitrile groups on a molecule of the following type $CH_2=CH-\underset{X}{CH}-R$ where $R = COOH$, $COOR$, or $CN$ and $X = Cl, Br, OH$ + $OCOCH_3$. His starting material is vinyl α hydroxyacetonitrile which is prepared as follows

$$CH_2=CH-CHO + KCN + CH_3COOH \rightarrow CH_2=CH-\underset{OH}{CH}-CN + CH_3COOK$$

70-77% yield

The acid + ester group are produced by hydrolysis and esterification of the cyanohydrin respectively. The hydroxyl group is then replaced by Cl, Br + $OCOCH_3$ and these derivatives treated with various reagents to see whether or not a rearrangement takes place. The author classifies the types of reactions into three groups.

(A) Normal reactions - ones in which the X group has merely been replaced by another as Y.

(B) Anionotropic reactions - ones in which the X group has been replaced by Y with a shift to the γ position from the α and a corresponding shift of the double bond

(C) Prototropic reactions - ones in which the X group is not replaced, but instead a hydrogen atom shifts from the α to γ position with a corresponding shift of the double bond.

The author arrives at three general conclusions from his work.

I. The introduction of an acid, ester or nitrile group tends to prevent any rearrangement, $\alpha \rightarrow \gamma$; altho rearrangement takes place it is not as readily as in the corresponding hydrocarbon

II The introduction of an acid, ester, or nitrile group prevents any of the reverse rearrangement $\gamma \rightarrow \alpha$

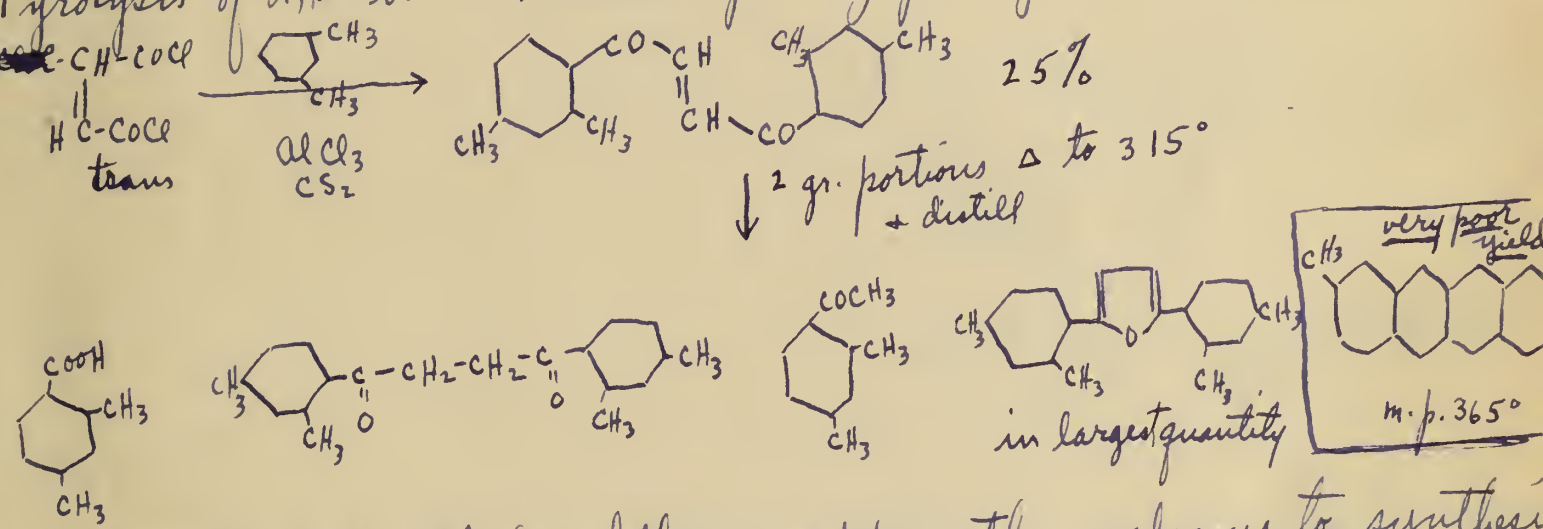
III The introduction of an acid, ester or nitrile group promotes the shift of a hydrogen atom rather than a negative group as OH, Cl, $OCOCH_3$ etc. especially in basic solutions.

ward A. Coulson

Homologues of Naphthacene I. 2,6-dimethylnapthacene. J.C.S. (1934), 1402
" " " II. 2-methyl- and 2,7-dimethylnaphthacene. J.C.S. (1935), 77

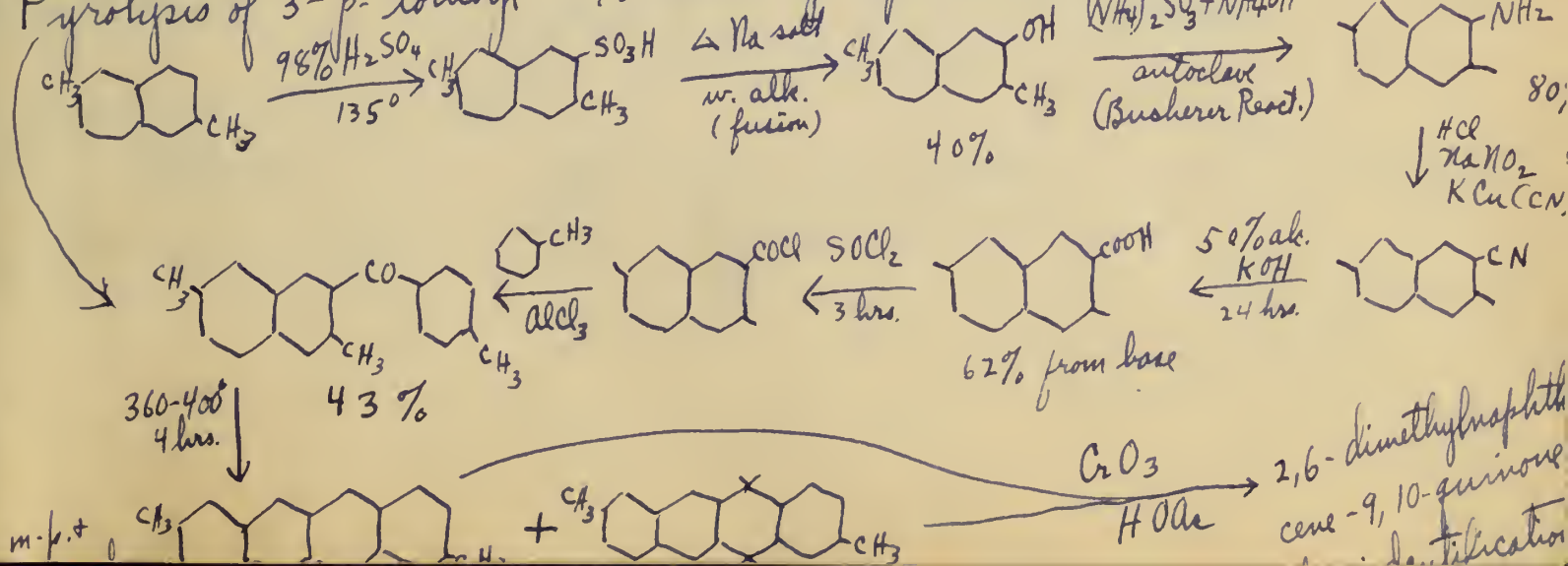
lson isolated from coal tar (a) golden-orange hydrocarbon, which he concluded consisted one or more napthacene homologues. No homologues of naphthacene ve previously been synthesized so he started out with the synthesis 2,6-dimethylnaphthacene, which he felt quite certain was the main stituent of his colored material. He accomplished the synthesis by three ethods:

(1) Pyrolysis of α,β-bis-2,4-dimethylbenzoylethylene

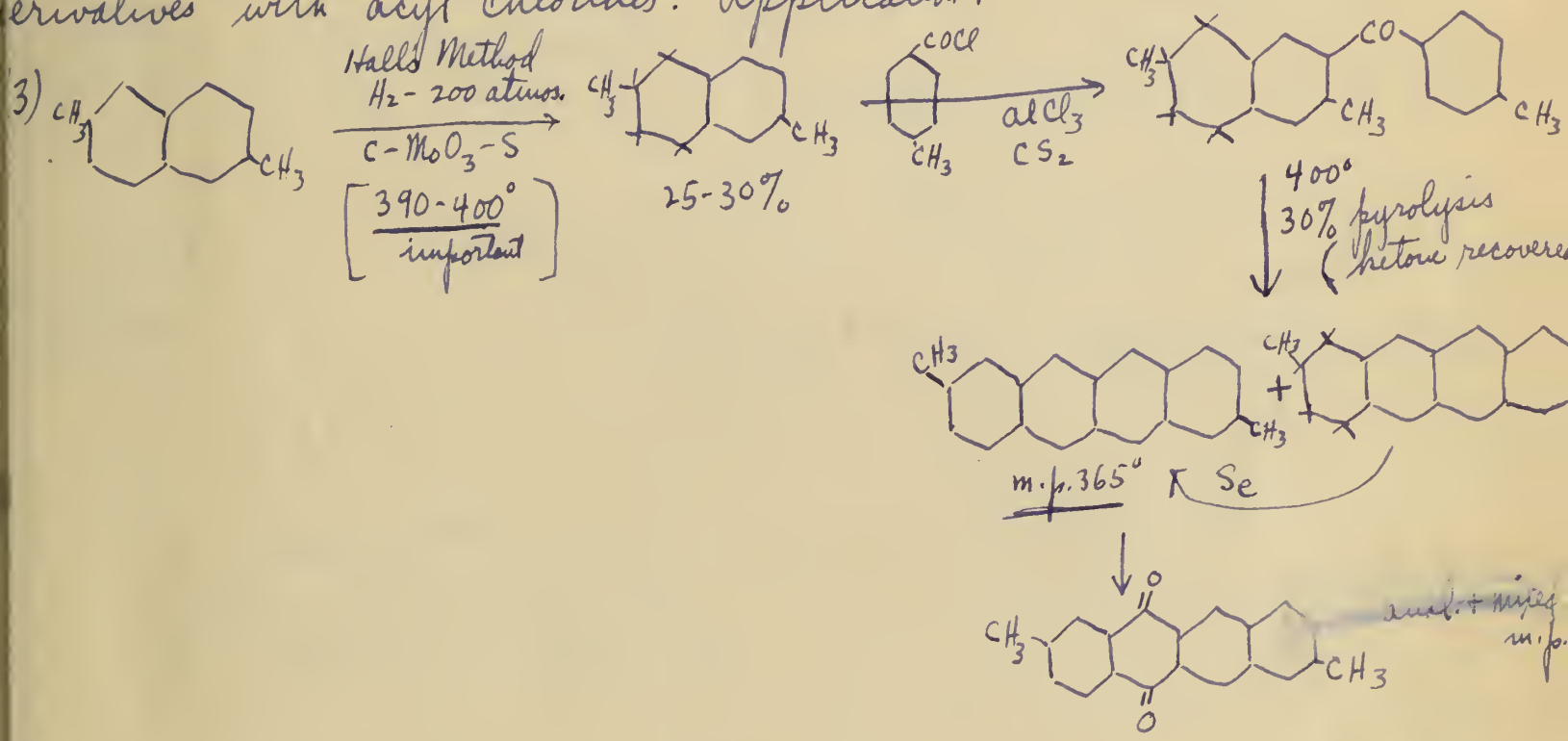



Formation of 2,6-dimethylnaphthacene apparently analogous to synthesis of anthracene by Elb's Reaction.

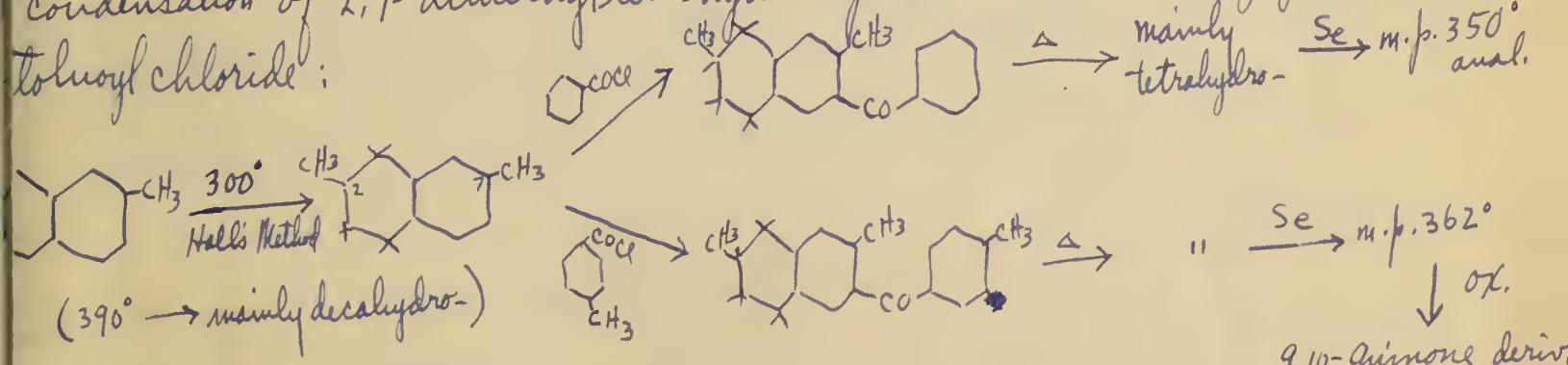
2) Pyrolysis of 3-p-toluoyl-2,6-dimethylnaphthalene



In attempting to prepare 2,7-dimethylnaphthacene by a si
densation of 3,6-dimethyl-2-naphthoyl chloride, there was obta
ly ill-defined and resinous products. The problem was solved by
eparation and use in the Friedel-Crafts' condensation of the tetra-
ydro derivatives of 2,6- and 2,7-dimethylnaphthalenes. These tetra-
ydro derivatives reacted as smoothly and quantitatively as benzene
erivatives with acyl chlorides. Application:

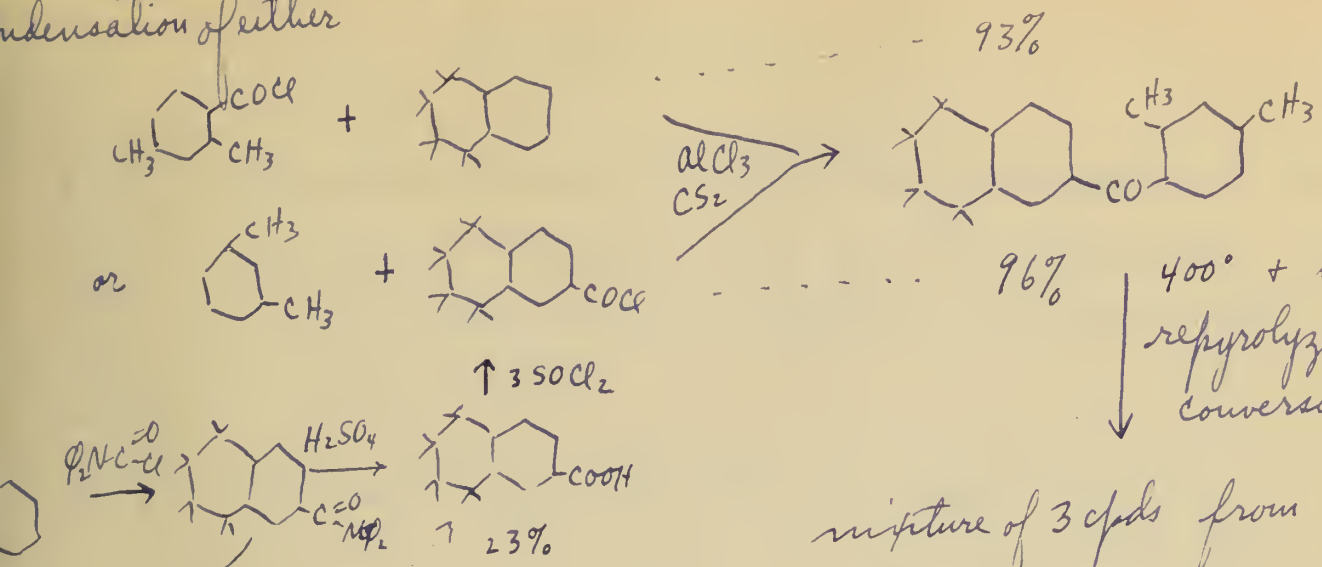



thesis of 2-methyl- and 2,7-dimethylnaphthacenes were prepared simile
condensation of 2,7-dimethyl-tetrahydronaphthalene with benzoyl chloride and with
toluoyl chloride:



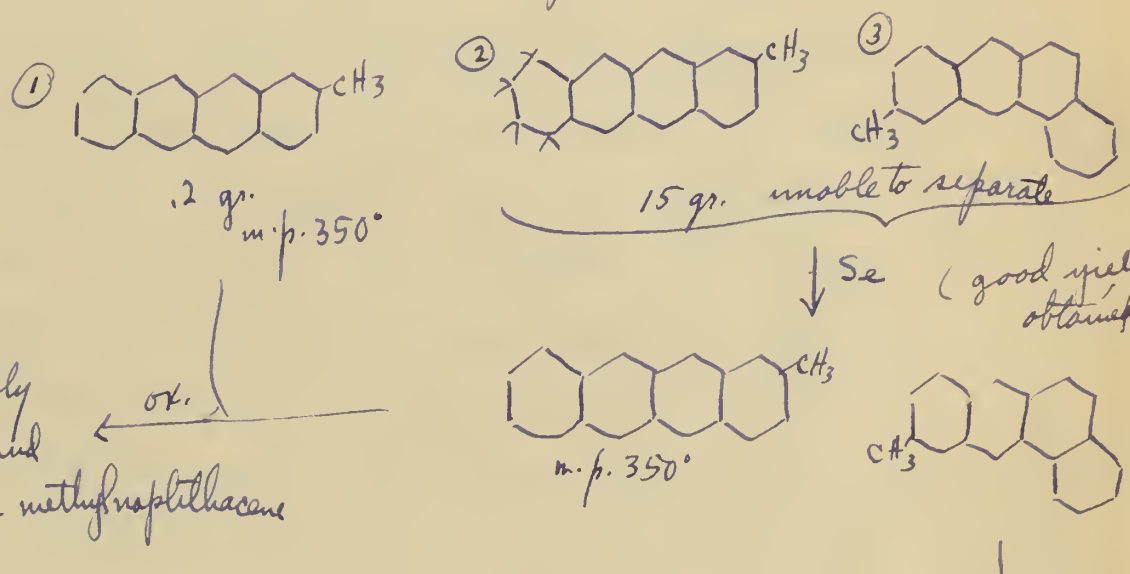
## cond Synthesis for 2-methylnaphthacene

ndensation of either




400° + unchanged keton repyrolyzed till 30% conversion was obtained

mixture of 3 cpds from 50 g. of ketone




roof for this ndensation

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ral methods have been presented for the synthesis of naphthacene homologues, cpds not previously synthesized.

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tension of the Friedel Crafts condensation of tetrahydro derivatives of aphthalene (or substituted naphthalenes) with acyl chlorides should prove valuable in the synthesis of certain, more important compounds than the naphthacene homologues.

E. K. Skoog

Seminar Abstract

Reciprocal Transpositions of Phenylacetylcarbinol and Benzoylmethylcarbinol- a New Type of Tautomerism.
A. E. Favorsky and T. I. Tewnikowa, Bull. Soc. Chim. (5), 2, 253-73, (1935).

Neuberg and Ohle, and Auwers and Mauss found that $C_6H_5COCHOHCH_3$ + $C_6H_5CHOHCOCH_3$ gave the same products with semicarbazide, thiosemicarbazide, and phenyl isocyanate. The authors found that with benzoyl chloride both gave mixtures of benzoates and with $CH_3MgI$ both gave a mixture of glycols. With $C_6H_5MgI$ the first gave a mixture of glycols while the second gave $C_6H_5-\underset{OH}{\overset{H}{C}}-\underset{OH}{\overset{H}{C}}-C_6H_5$. Thus the two carbinols are chemical individualities which do not rearrange by themselves. There takes place a new type of tautomerism in their reactions, like keto-enolic; this is keto-anolic or keto-carbinolic. There takes place a migration of two atoms of hydrogen.

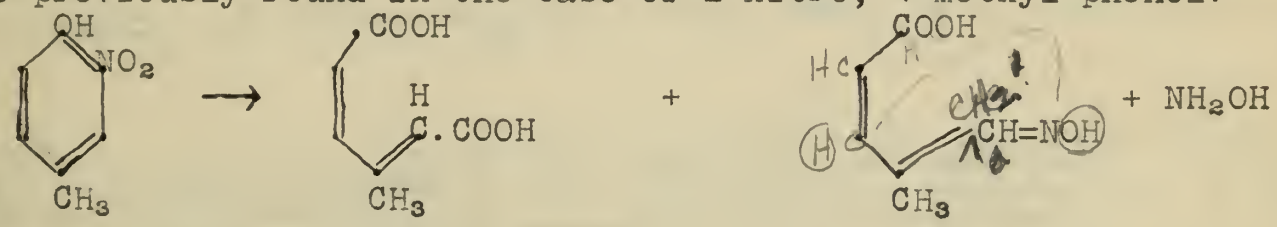
# ORGANIC SEMINAR

## Ring Cleavage of o-nitro Phenols by $H_2SO_4$. I

by O. Neunhoeffer and H. Kölbel
Chem. Inst. Univ. Greifswald

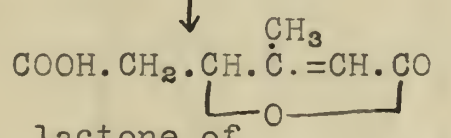
Reference: Ber. 68 620 (1935)

The reaction of concentrated or fuming sulfuric acid with the para substituted, o-nitrophenols (1) 2,4-dimethyl 6-nitrophenol, (2) 2,4-dibromo 6-nitrophenol and (3) 1-nitro-2-naphthol, results in ring cleavage with the formation of (A) the lactones of the substituted muconic acids, (B) the substituted mucomonohydroxamic acids, (C) the pyrroline derivatives resulting from (B) by loss of $H_2O$ or (D) a mixture of (A)-(B). These products are analogous to those previously found in the case of 2-nitro, 4-methyl phenol.



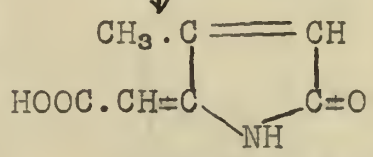

2-nitro 4-methyl phenol

β-methyl muconic acid




lactone of β-methyl muconic acid

β-methyl muco-monohydroxamic acid lactone




pyrroline derivative.

In the case of the 2,4-dibromo 6-nitrophenol, the lactone formed had a bright red color, for which the author gave the possible explanation of tautomerism to a hydroxyfurane form.

The mechanism of the reaction was studied, but not determined. Experimental results indicated that an intermediate $H_2SO_4$ derivative was formed, which on hydrolysis produced the products which were observed.

Meredith Sparks

Chem 135 b. April 24, 1935.

The addition of Sulfur Dioxide to Olefines.

by Staudinger and Ritzenthaler, Ber., 68B, 455 (1935)

Staudinger ~~is~~ located at the U. of Freiburg and is noted mainly for his work on polymerization.

The results of Staudinger's work may be recorded as follows:

| Olefine | Without Catalyst | | with − catalyst | | with + catalyst | | n | mol. wt. |
|---|---|---|---|---|---|---|---|---|
| | Monomer | Polymer | Monomer | Polymer | Monomer | Polymer | | |
| Ethylene | | | | | | 100% | | |
| Propylene 13 cc | | 13 g. | | | | 100% | 3700 | 390,000 |
| Butadiene 15 cc | 10 g. | 13 g | 30% | | | 60% | 1300 | 106,000 |
| Isoprene 15 cc | 2.7 g. | 17 g. | 16 g. | 3 g. | 0 g. | 12% | 1000 | 135,000 |
| Dimethyl Butadiene 25 cc | 21 g. | 8.8 g. | 27 g. | 0 g | | 21% | 840 | 120,000 |

The following conclusions can also be observed:

1. Dimethyl Butadiene > Isoprene > Butadiene in % yield monomer
   " < " < " in % " polymer
2. An increase in the number of moles of $SO_2$ per mole of olefine causes an increase in the percentage yield of monomer and a decrease in % yield of polymer.
3. The larger the amount of anticatalyst used causes an increase in the % yield of butadiene monomer.

Reported by

J. C. Eck

# The Synthesis of Jasmone

J. R. Little
May 1, 1935

W. Treff and H. Werner: Ber. 68, 640 (1935).
" " " Ber. 66, 1521 (1933).

Ruzicka and Pfeiffer: Helv. 16, 1208 (1933)
Staudinger and Ruzicka: Helv. I, 212, 236, 245 (1924).

Trieff located at Chem. Lab. of Heine & Co., Leipzig and Gröba.
Werner located at Univ. of Hamburg. Work mostly with Schmalfus.

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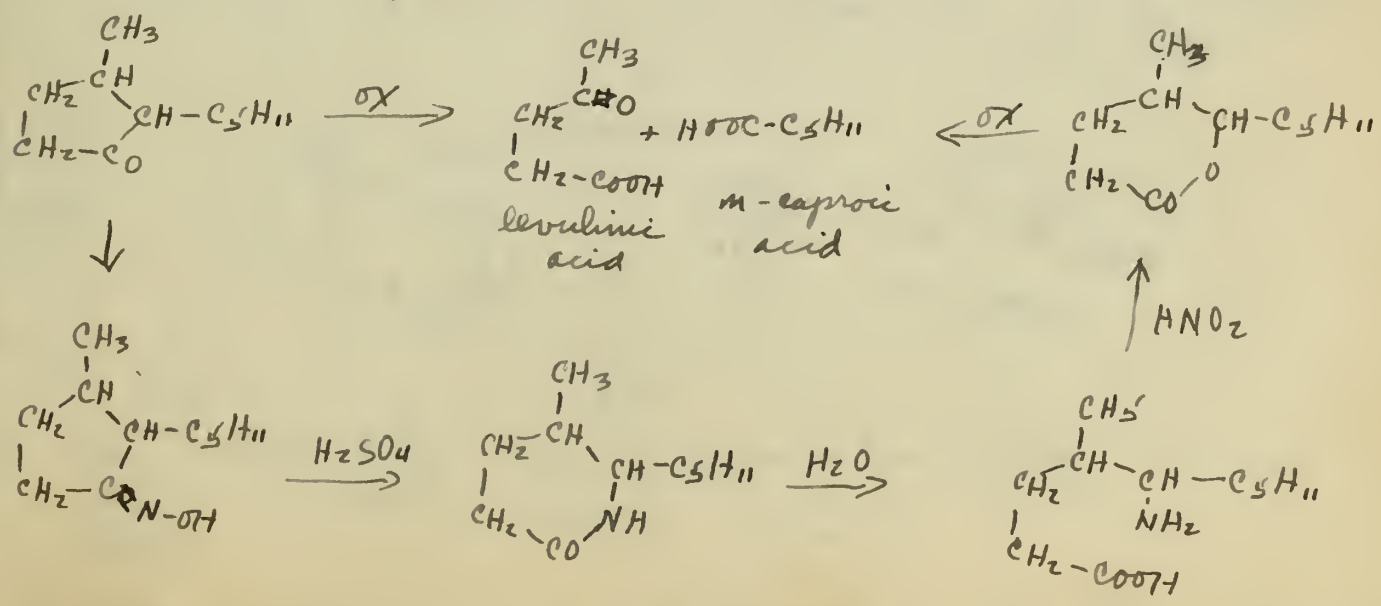
Jasmone discovered in 1899 by Hesse and composition determined as $C_{11}H_{16}O$.

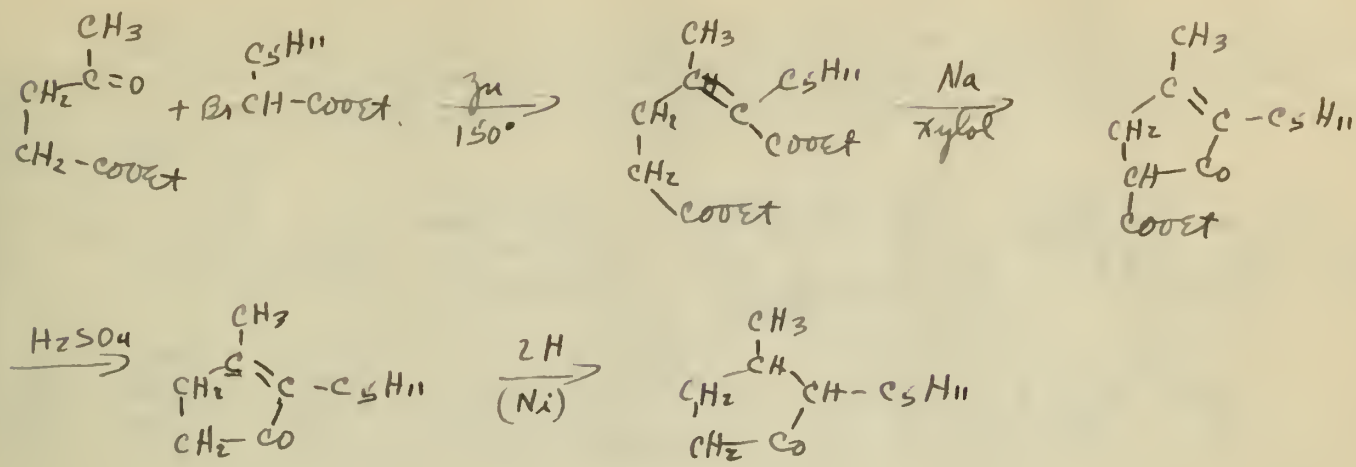
Jasmone has same carbon skeleton as pyrethrolone which was determined by Staudinger and Ruzicka in 1924.

Pyrethrolone $C_{11}H_{16}O_2$ (a keto alcohol) $\xrightarrow[\text{(Skita)}]{4H}$ Tetrahydropyrethrolone $C_{11}H_{20}O_2$ (also a ketone alcohol) $\xrightarrow[\text{Skita}]{2H}$ Tetrahydropyrethrone $C_{11}H_{16}O$ (a ketone)

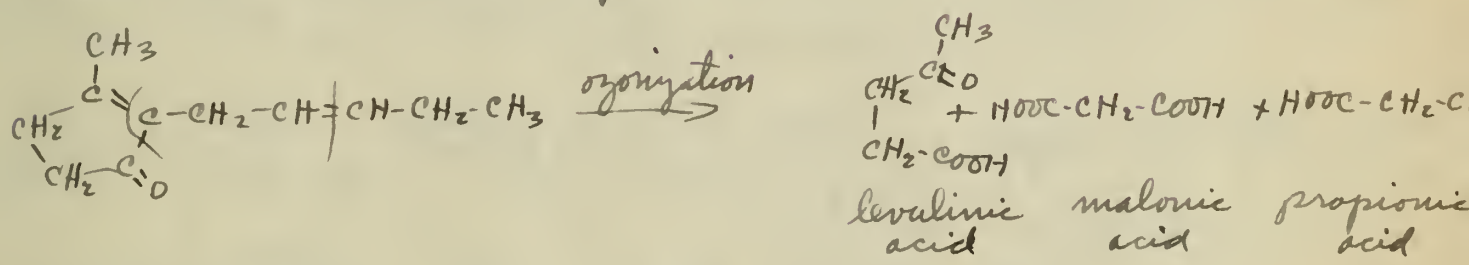
Tetrahydropyrethrone later found identical with tetrahydrojasmone. Structure shown by:



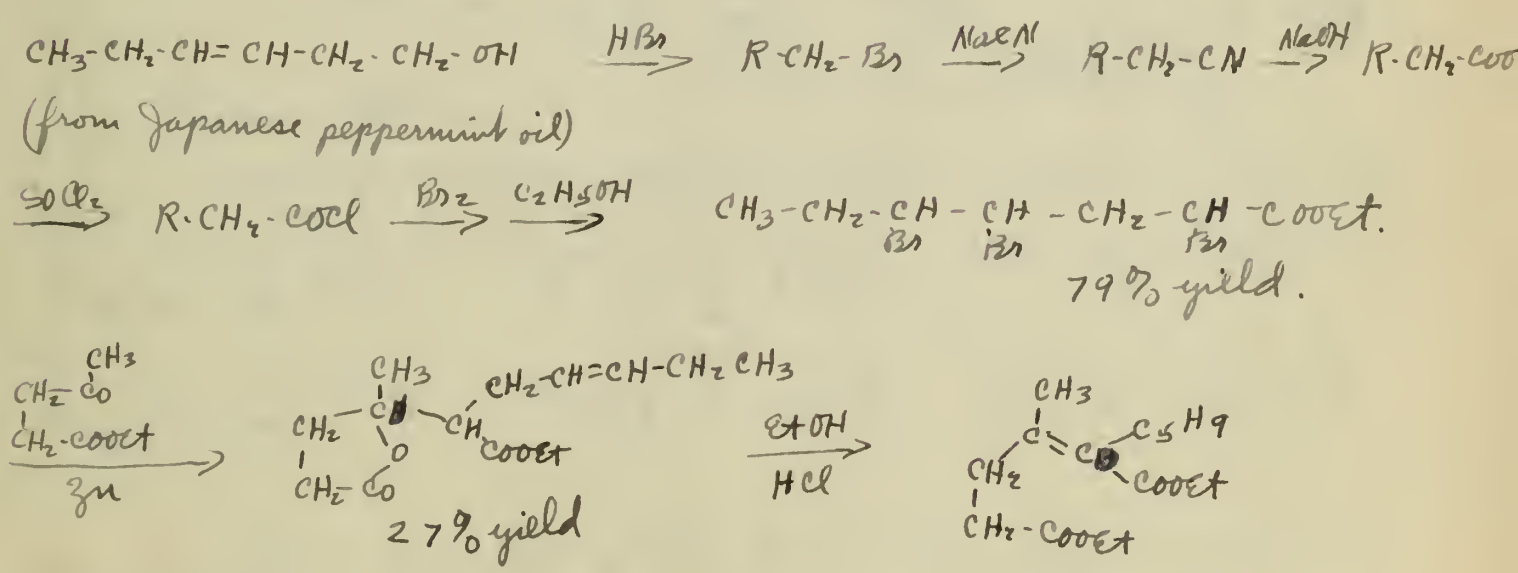
Tetrahydropyrethrone synthesized as further proof of structure.




Tetrahydrojasmone found to be identical with tetrahydropyrethrone
Double bonds located by:




Synthesis of Jasmone by Treff and Werner.




Synthetic product found to be identical with natural product.

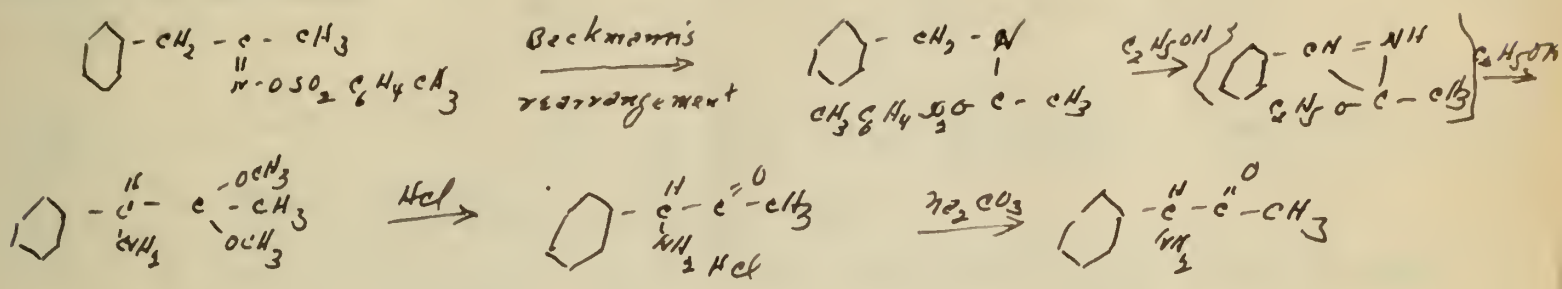
# A NEW METHOD FOR MAKING α AMINO KETONES

BY

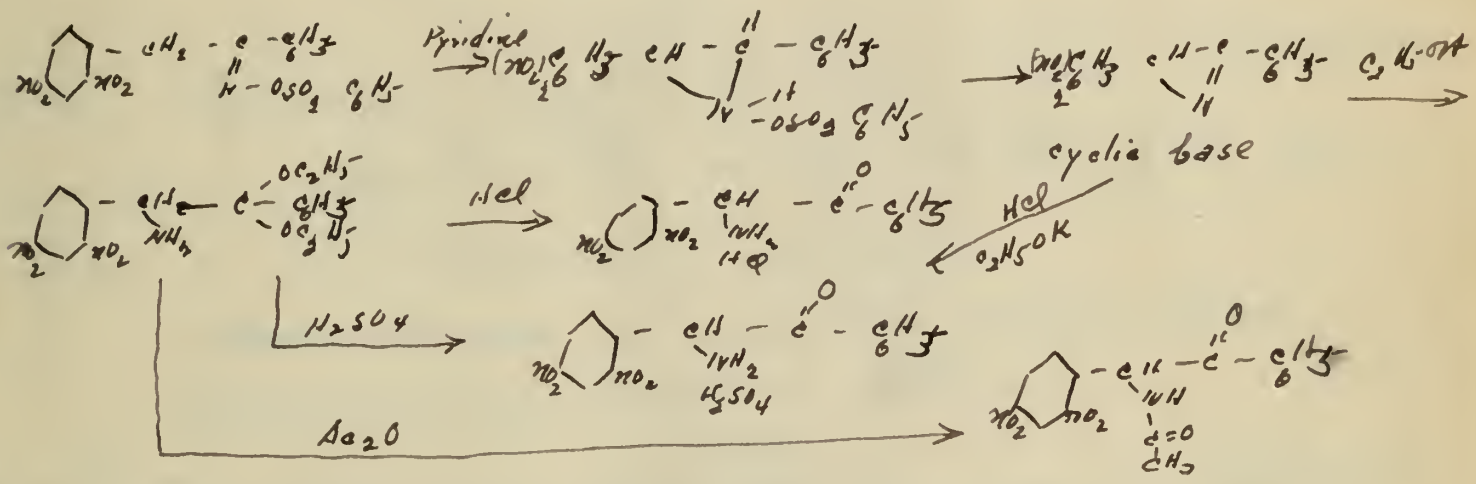
P. W. NEBER and GINGANG HUH

Ann, 515, p. 283 1935. Hmd. J Fuhrzer

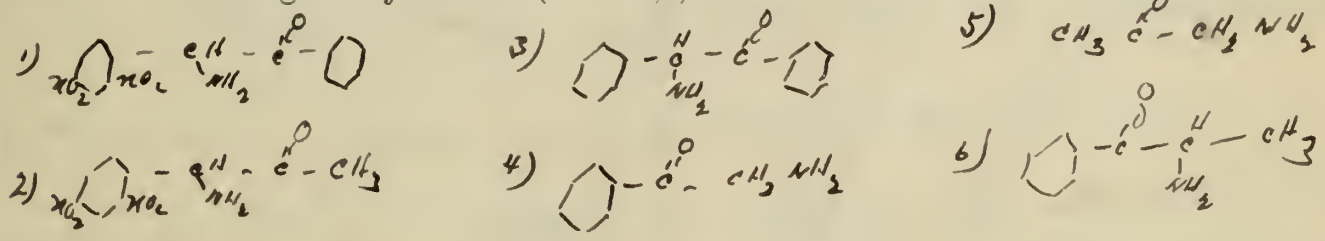
Neber obtained an acetal by treating benzyl-methyl-ketoxime p-toluolsulfoester with potassium ethoxide and acetic acid. The acetal on hydrolysis gave an α amino ketone. The first mechanism indicated by the author is as follows:




In a later research, the author obtained a cyclic base from 2,4 dinitro, benzyl methyl ketoxime. When the cyclic base was treated with potassium ethoxide and hydrochloric acid, it yielded an α amino ketone salt. It proved that the first proposed mechanism was wrong.




A series of α amino ketones have been prepared by means of this reaction with good yields (65-75%).



This reaction can be used as a general method for making α amino ketone provided that

1) The starting ketoxime is derived from a ketone which contains this grouping (-CH₂-C(=O)).

2) The ketones must be transfered to the p-toluolsulfoester in the first step, otherwise they do not undergo the desired reactions, as shown by the authors working with esters of another nature.

Reported by Hsing. Chi I

Relations between Acidity and Tautomerism, Part II and III

The Imid Group, Hydroxamic, Sulfinic, and Sulfhydroxamic Acids;
The Nitro Group and the Nitronic Esters.

Report by W. C. Ashley

Fritz Arndt and J. D. Rose, II, Ann., 510, 62 (1934); III, J. C. S., 1 (1935).

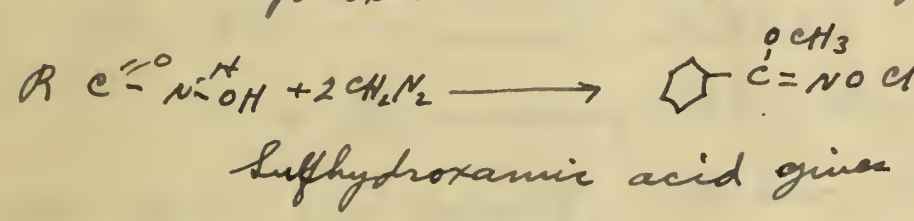
Published since 1911 (Uni. of Kiel, Uni. of Breslau, Oxford Uni now).

a. Various sulfur compounds.
b. Cyclic azoxy compounds; aliphatic azo compounds.
c. Triazines and triazoles.
d. Dipyrylenes and dipyrylium salts, fulvene.
e. Syntheses with diazomethane.

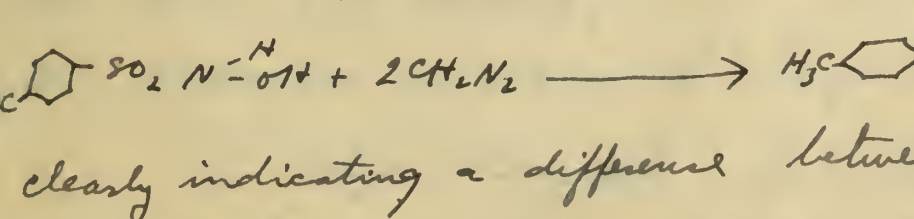
Part II: Saccharin reacts with $CH_2N_2$ to give an N-methyl and a O-methyl derivative or only N-methyl if the Apt. is added to the diazomethane solution.

Phthalimid does not react with diazomethane.

Hydroxamic acid reacts as follows:

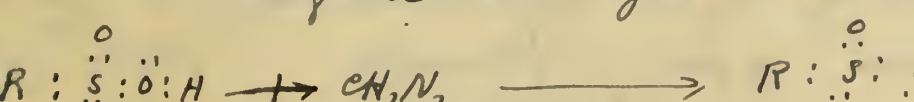


Sulfhydroxamic acid gives an N-methyl deriv.



clearly indicating a difference between the structure of $=SO_2$ and $=C$

Sulfinic acid gives no sulfone but all sulfinic ester



III. Nitro-Group and Nitronic Esters: In acidity promoting action the nitro-group is about equivalent to two sulfones or three carbethoxy groups, i.e., the cpds. are soluble in aqueous alkali.

A. Mode of action; questions involved:

1. Only empirical acidity or transformation into more acidic form

Evidence is as follows:

a. Carbonyl is purely acidifying - no enoligation.

b. Hantzsch obtain the nitronic acid, unstable.

c. Nitro-ketones enolize and it is the carbonyl that is involved rather than the nitro-group.

2. Constitution of acidic form:

a. Old form of Hantzsch, $RCH \underset{O}{=} N-OH$, cyclic.

b. Present structure of " , $RCH::N\begin{smallmatrix}:O:\\:O:H\end{smallmatrix}$, does not explain active nitro compounds.

B. Nitro-compounds studied:

1. p-Bromophenylnitromethane, forms a nitronic ester with $CH_2N_2$ very rapidly in the aci-, slowly in normal-form. Ester decomposes by heating (80°) to p-bromobenzaloxime and HCHO.

2. Ethyl nitroacetate and methyl nitromalonate which do not enolize appreciably react vigorously to form nitronic esters with $CH_2N_2$. Apparently a case of indirect methylation or addition to the $:N::O$ ~~group~~ double bond in the nitro group.

3. p-Toluenesulfonylnitromethane: reacts with $CH_2N_2$ to form only nitronic ester.

4. ω-Nitroacetophenone; $C_6H_5-C(OCH_3)=CHNO_2$ and $C_6H_5-C(=O)-CH=N-OCH_3$ formed

bject: The use of per-acetic acid as an oxidizing agent for organic compounds.

J. Böeseken and co-workers.

est article: Oxidation of some phenols by per-acetic acid. A passage from the aromatic to the aliphatic series.
J. Böeseken and C.F. Metz, Rec. trav. chim. 54, 345 (1935).
(Org. Chem. Lab. of the Haute Ecole Technique, Delft, Holland)

iew article: Böeseken, Chem. Weekblad, 31, 166-70 (1934).

A. Preparation of per-acetic acid.
According to the method of Frey, Ber. 45, 1845 (1912).

$$(CH_3CO)_2O + 2H_2O \xrightarrow{\text{conc. } H_2SO_4} 2\,CH_3CO_3H + H_2O$$

$\downarrow$ distill reduced-press.

3. Action of per-acetic acid on;

1. Double bonds:

$CH_3-CH=CH-COOH$ (crotonic acid) $+ CH_3CO_3H \xrightarrow{HOAc}$ no action.

$C_6H_5-CH=CH-COOH$ (cinnamic acid) $+ CH_3CO_3H \xrightarrow{''}$ hardly ~~no~~ action.

$CH_3-CH=CH-CH=CH-COOH$ (sorbic acid) $+$ '' $\longrightarrow$ $CH_3-\overset{OH}{CH}-\overset{O\,C=O\,CH_3}{CH}-CH=CH-COOH$ (only one of double bonds attack

$CH_2=CH-CH_2-CH_2-COOH$ $+$ '' $\longrightarrow$ $\overset{CH_3-C=O\,O}{CH_2}-\overset{OH}{CH}-CH_2CH_2-C\overset{=O}{-O}H$

$\downarrow$ spontaneously

lactone

The authors were unable to generalize as to the effect of the carbonyl or carboxyl upon the character of the $>C=C<$, except that

when the C=O group was next to the >C=C< the double bond was indifferent to the oxidizing action of per-acetic acid. (1)



$$\underset{\text{2 butene}}{CH_3-CH=CH-CH_3} + CH_3CO_3H \xrightarrow{CHCl_3} CH_3-\overset{OH}{\overset{|}{C}H}-\overset{OH}{\overset{|}{C}H}-CH_3 \quad (40\% \text{ yield})$$

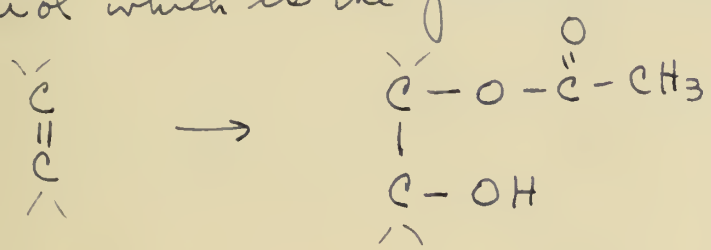
$$C_6H_5-CH=CH-CH_3 + CH_3CO_3H \longrightarrow C_6H_5-\overset{OH}{\overset{|}{C}H}-\overset{OH}{\overset{|}{C}H}-CH_3 \quad (\text{rapid})$$

$$C_6H_5-CH_2CH=CH_2 + CH_3CO_3H \longrightarrow C_6H_5-CH_2-\overset{OH}{\overset{|}{C}H}-\overset{OH}{\overset{|}{C}H_2} \quad (\text{slow})$$

The two latter reactions show that if the double bond is conjugated with a benzene nucleus, oxidation takes place rapidly – if the benzene nucleus is farther removed, oxidation is slower. (2.)

In general oxidation depends upon:
1. The number of H atoms attached to the unsaturated C atoms
2. The character of the other groups.

Mechanism:
The first step in the oxidation process is probably the addition of the reagent to the double bond, yielding the mono-acetate of a diol which is the product isolated in most cases.



In in few cases (Me 9,12 linoleate) the oxido derivative was isolated. (=C-O-C=) The isolation of this product was more frequent in the case of per-benzoic acid (2).

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J. Böeseken, Rec. trav. chim. 45, 838 (1926).
J. Böeseken & Maas Geesteranus, Rec. trav. chim. 51, 551 (1932).
J. Böeseken & Elsen, Rec. trav. chim. 48, 363 (1929).
[illegible] 838 (1928)

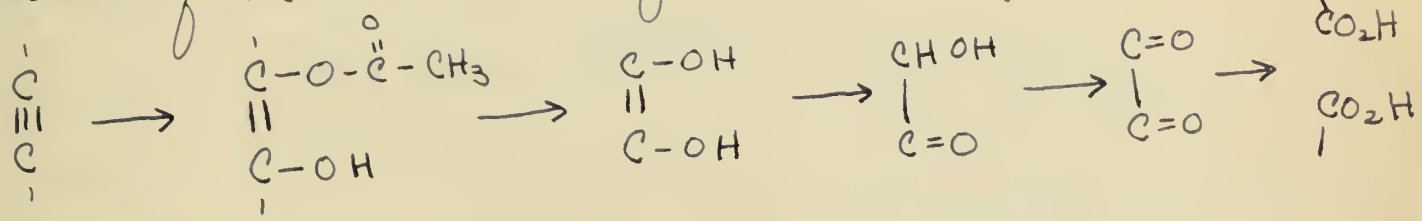
2. Triple-bonds:

$$C_6H_5-C\equiv CH + CH_3CO_3H \longrightarrow \text{no action}$$

$$H-C\equiv C-H + CH_3CO_3H \longrightarrow \text{no action}$$

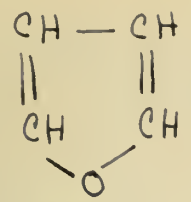
$$\underset{\text{(stearolic acid)}}{C_8H_{17}C\equiv C(CH_2)_7COOH} + CH_3CO_3H \xrightarrow[\text{yield: 60\%}]{\text{slow}} \underset{\text{(pelargonic acid)}}{C_8H_{17}COOH} + \underset{\text{(azelaic acid)}}{HOOC(CH_2)_7COOH}$$

Peracetic acid reacts very slowly with triple bonds. The course of the reaction is postulated as follows: (1)

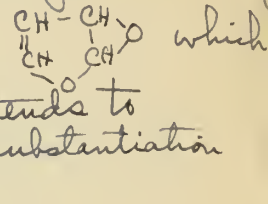


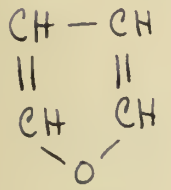
(1) Böeseken and Slooff, Rec. trav. chim. 49, 95-9 (1930).

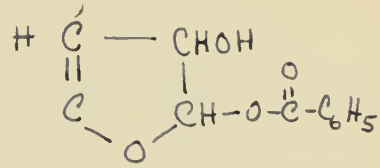
## 3. Furan and furan derivatives: (1).



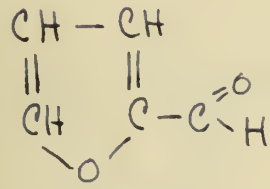
(furan) + $CH_3CO_3H$ $\xrightarrow{HOAc}$ only resin formation

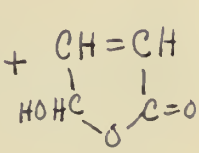
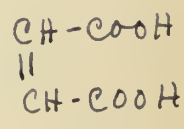
Note: The authors explain this behavior by postulating the initial formation of an oxide ie  which in the presence of the acid (HOAc) tends to polymerize. This might find substantiation in the following reaction.

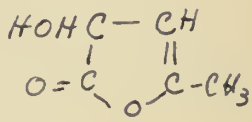


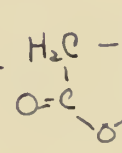
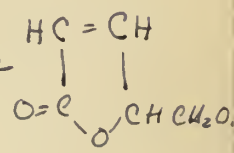
(furan) + $C_6H_5CO_3H$ $\xrightarrow{CHCl_3}$ 

2-monobenzoate of 2,3 dihydroxy-2,3 dihydro-furan.



(furfural) + $CH_3CO_3H$ (10%) $\xrightarrow{HOAc}$ HCOOH 96% +  40% (aldehydomaleic acid) +  7%

2-methylfurane + $CH_3CO_3H$ $\xrightarrow{HOAc}$ 90% resin + 

~~furf~~ furyl-2-methanol + " $\longrightarrow$ 80% resin +  + 

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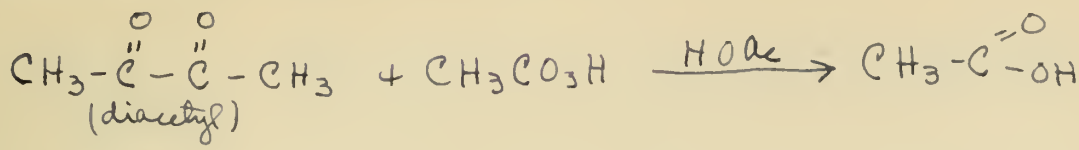
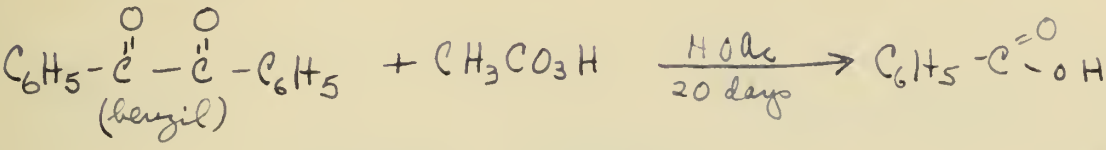
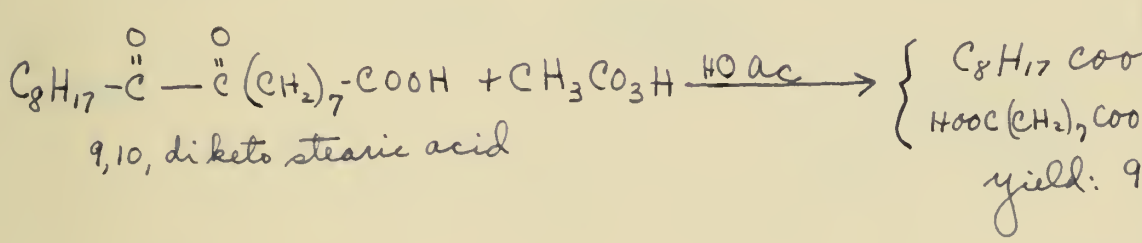
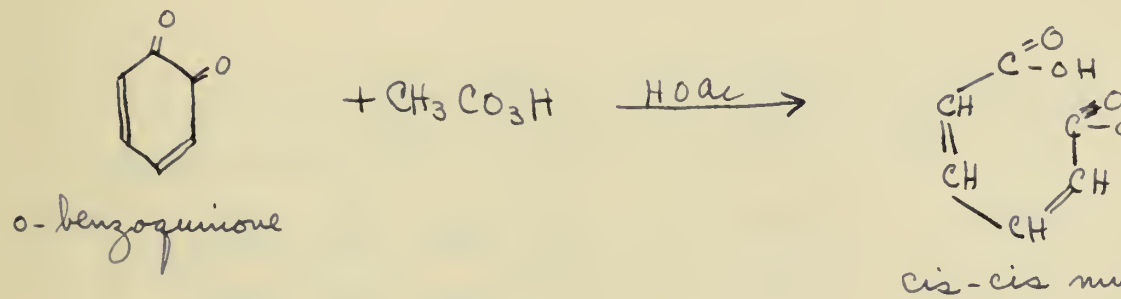
(1) Böeseken, Vermij, Bunge, Meeuwen, Rec. trav. chim. 50, 1023 (1931).

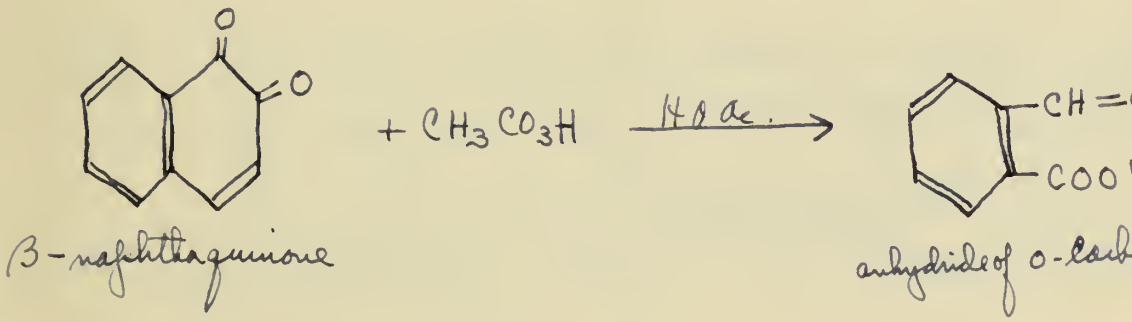
4. <u>1,2 di-ketones</u> : (1)

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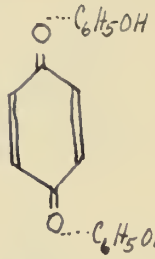
) Böeseken and Slooff, Rec. trav. chim. 49, 91 (1930).

## 5. Phenols and substituted phenols:

$+ CH_3CO_3H \longrightarrow$ not attacked

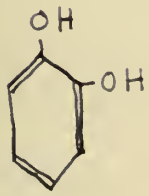
$+ CH_3CO_3H \xrightarrow[\text{10 days}]{HOAc}$ CH=CH-COOH / CH=CH-COOH (cis-cis muconic acid (yield: 35-40%)) +  + some reduced substances (glyoxylic acid, maleic acid) (small amts.)

phenoquinone (yield: 40%)

In order to explain the formation of these two products, the authors postulate the following course of the reaction: (1.)

1. If the C-atom ortho to the -OH is attacked $\longrightarrow$ o-quinone $\longrightarrow$ muconic acid
2. If the C-atom para to the -OH is attacked $\longrightarrow$ p-quinone $\xrightarrow{2\,\emptyset\text{-}OH}$ phenoquinone

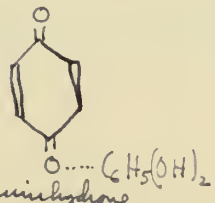
Note: The above reaction constitutes a good synthesis for muconic acid. The authors have also found that the cis-cis muconic acid, when allowed to come in contact with free $Br_2$ or $I_2$ changes over quantitatively to the stable trans trans isomer (2.)



(catechol)

$+ CH_3CO_3H \longrightarrow$ muconic acid (20%) $+ CO_2 +$ fumaric acid (small amt).

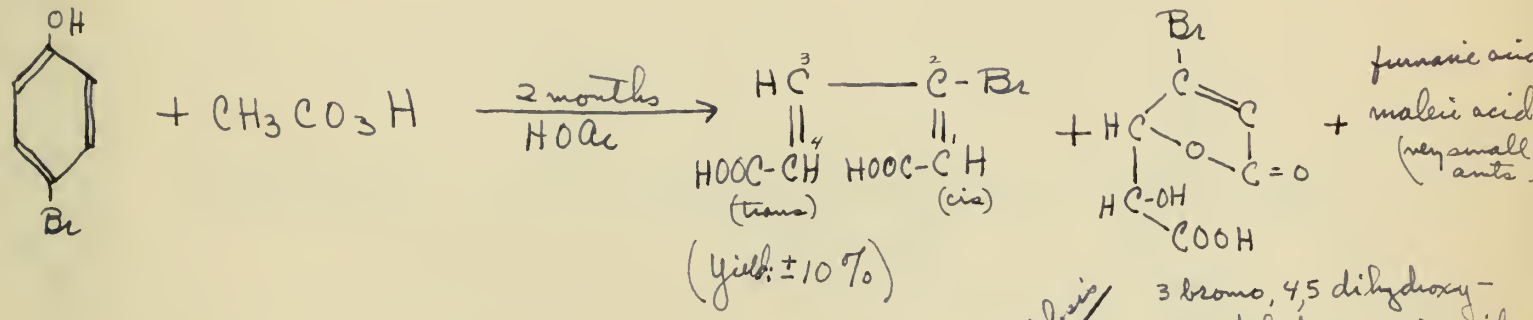
hydroquinone

$+ CH_3CO_3H \longrightarrow$  + fumaric acid (small amt)

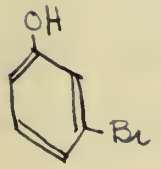
quinhydrone (yield. 75-80%)

(1.) Böeseken, Proc. Acad. Sci. Amsterdam 35, 750-5 (1932); C.A. 27, 1333 (1933).

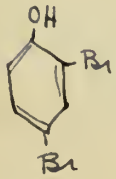
In consideration of the course of the reaction in the case of phenol, the authors reasoned that by substituting the p-pos. the oxidation in the direction of p-quinone would be prevented, thereby forming exclusively and with increased yields β-substituted muconic acids. It was found however that the oxidation proceeded more slowly and that the yields were poorer, accompanied by by products (lactones and hydroxy-lactones of β-subst. muconic acids).



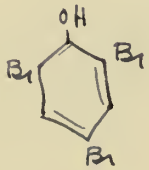

Note: During this oxidation a little tri-bromo phenol is formed, which owes its existence to the formation of some free $Br_2$. As was stated before this catalyst is able to stable the muconic acids. Since the β-bromo muconic acid isolated was stable the authors assign 1,2 double bond the cis config. (Br-repels COOH) and assign the 3,4 double bond the trans config. (1)




+ $CH_3CO_3H$ ⟶ 3 bromo muconic acid (very poor yield)

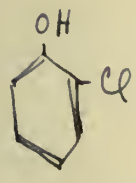



and



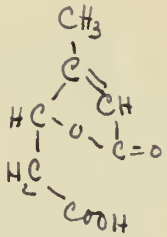
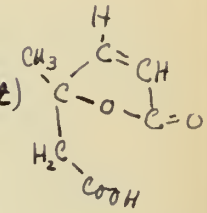

were not attacked by $CH_3CO_3H$.

$+ CH_3CO_3H \xrightarrow{\text{2 months}}$ { β-chloro muconic acid; β-chloro dihydroxy dihydro-muconic acid lactone } compounds analogous to p-cresol



$+ CH_3CO_3H \xrightarrow{\text{3 months}}$ α chloro-muconic acid (very poor yield) + HOOC-CH=CH-CH=C(Cl)-C(=O)-H (aldehydo-acid)

p-cresol

$+ CH_3CO_3H \longrightarrow$ 3-methyl-muconic acid +  (or) 

yield: 3 to 5%
one time 20%

Note: The authors state that a cyclanization similar to the above occurs in the case of o-carboxy-cinnamic acid when heated above its melting point.

## Summary:

Per-acetic acid is a useful oxidizing agent for organic compounds.

1.) Double bonds are converted to the mono-acetate of a diol
2.) Triple bonds are cleaved, yielding acids
3.) 1, 2 diketones are cleaved, yielding acids
4.) Furans derivatives lead to a variety of products.
5.) In phenols and substituted phenols, oxidation occurs on the C-atoms ortho or (and) para to the phenolic hydroxyl in most cases, yielding the corresponding muconic acids.
6.) A good synthesis for muconic acid is found in the reaction between phenol and per-acetic acid.

Abstract of Sem. Report March 1935 B Fri

# The Occurrence of Free Radicals in Chem. Reaction

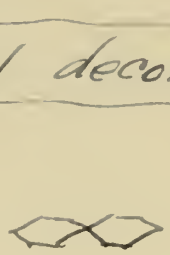
Heinrich Wieland & Others München

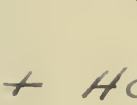
Ann 514 - 145 (1934)

**Other work** Bile Acids, Strychnos Alkaloids, Oxidation processes Toad poisons.

**Purpose** To study free radicals by thermal decomp. of azo compds

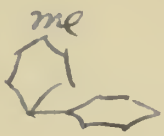
**Reactions** | **Deductions**

$\phi n{=}n{-}c\phi_3 \xrightarrow[C_6H_6]{70^\circ\ in} N_2 + \phi_3c{-}o{-}o{-}c\phi_3 +$ 

" $\xrightarrow[\text{solvent in vac}]{\text{no}} N_2 + 5\%\ \text{of}\ C\phi_4 + HC\phi_3 + C_6H_6$ & no 

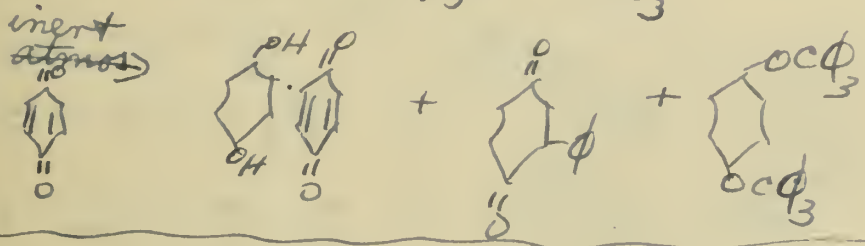
a) extra H must come from reac. mixture

b) phenyl radical does not unit with another $C_6H_5^-$

" $\xrightarrow[\text{me}]{\Delta\ in}$ $N_2 +$ & 

shows part played by solvent.

" 10 gm. $\xrightarrow[55^\circ]{CCl_4} N_2 + .65g.\ C_6H_5Cl + \phi_3c{-}cCl_3$ " " "

" 

H in quinhydrone comes from reactn mixture.

$\phi{-}c{=}o{-}n{=}n{-}c\phi_3 \xrightarrow[\Delta]{CCl_4} \phi c{=}o{-}Cl$ in good yield

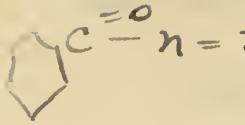
dem. reactivity of $\phi c{=}o$ radical

" $\xrightarrow[Br_2\ in]{\Delta dl} N_2 + \phi c{=}o{-}Br$, but no $\phi c{=}o{-}c{=}o{-}\phi$ & no $\phi c{=}o{-}o{-}o{-}c{=}o{-}\phi$

$c{=}o{-}n{=}n{-}c\phi_3 \xrightarrow[\text{in } N_2\text{ atmos}]{\Delta} 72\%$ y. of $c{=}o{-}c\phi_3 + N_2$

40-75°

shows mech. of pyrolysis is different from that for reaction #2 (only 5% $C\phi_4$ in



$\xrightarrow[\text{in cyclohexane or with no solvent in vac.}]{\Delta}$ no $\phi\overset{=O}{C}H$ & no $\phi C^{=O}{}_{C}{}^{=O}\phi$

(here $\phi CHO$ should be found just as $C_6H_6$ is found in reactn #2)

∴ Wieland states mech. of pyrolys. of acyl azo compds involves a rearr. within the molecule & then a decomp. with evol. of $N_2$

Further the bond is much more

$\phi C^{=O}\!\cdot\!\cdot\!\cdot

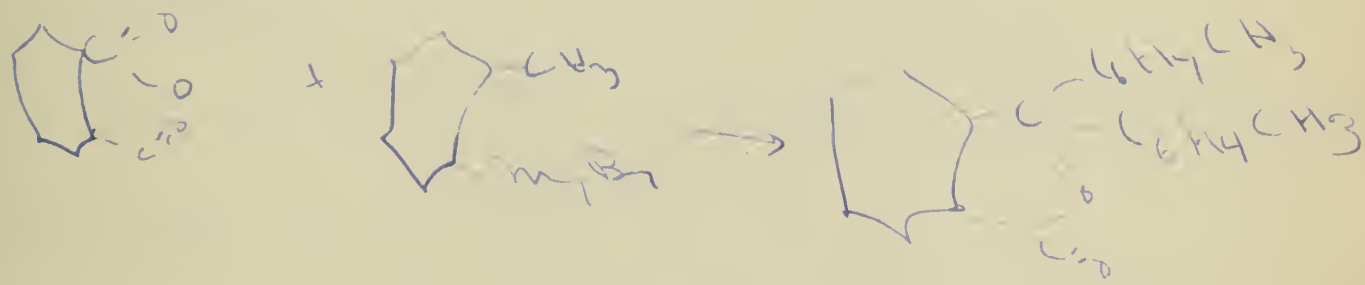
Triphenylmethanes whose benzene nuclei are connected to one another

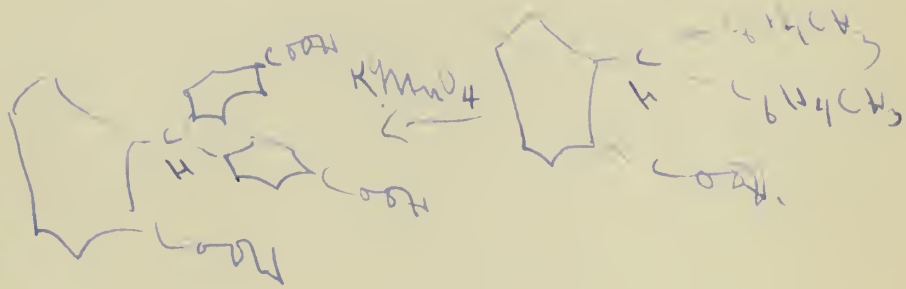
R Weiss Vinylbenzene

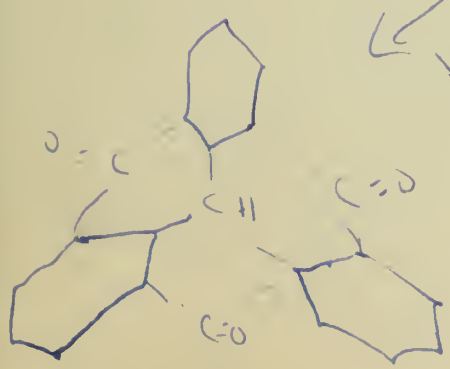
Monat 65 (1934) 1-34

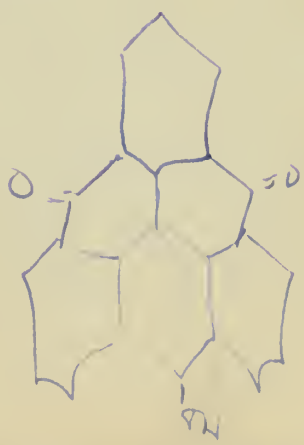
Preparation

General method









This proved by derivative

Some series of compounds prepared from succinyl chloride and p-xylene by the Friedel-Crafts reaction, & their ring closure by the above methods.

The compounds obtained were high melting amorphous solids which could not be easily obtained in a crystalline form due to their insolubility in all solvents.

Dr Skinner does not believe the proof of structure is sufficient.

SUMMARY OF SEMINAR REPORT

by

Fred Condo

(April 24, 1935)

Topic: The Structure of Hydroxy-Azo Compounds

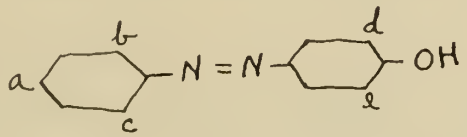
References: Richard Kuhn and Fritz Bär, Ann., 516,143 (1935)
(Heidelberg -- Carotenes, flavines, and conjugated double bonds.)

Lauer and Miller, J. Am. Chem. Soc., 57,525 (1935).
(U. of Minnesota -- $\alpha,\beta$, Unsaturated ethers and Miscellaneous.)

The fact that there are two general methods for the preparation of hydroxy-azo compounds, (a) the coupling of diazo compounds with phenols and (b) the reaction of substituted hydrazines with quinones, serves to immediately emphasize the question of the structure of these compounds. Reaction (a) would normally be expected to lead to an azo compound, while (b) should yield a hydrazone, but the same product is obtained in both cases.

The subject has an extensive bibliography including the names of many investigators. In recent years the great champion of the hydroxy-azo form has been von Auwers (working at Marburg), while the equally ardent defender of the quinone-hydrazone form has been Burawoy (until recently at Leipzig, now at the U. of London).

Lauer and Miller sought to test for the hydrazone form by use of the Diels and Alder reaction, adding cyclopentadiene to the quinone portion of the molecule. They found that cyclopentadiene would add to ~~the~~ benzoquinone-2,4-dintrophenylhydrazone (2,4-dinitrobenzeneazophenol). The structure of the product was proven by adding cyclopentadiene to benzoquinone and reacting this product with 2,4-dinitrophenylhydrazine. The bis-hydrazone was formed, however, and in order to complete the structure proof, it was necessary to react the addition product of benzoquinone-2,4-dinitrophenylhydrazone with 2,4-dinitrophenylhydrazine. The results with other hydroxyazo-compounds were as indicated in the following table:




Added Cyclopentadiene

| | a | b | c | d | e |
|---|---|---|---|---|---|
| 1. | $NO_2$ | $NO_2$ | | $CH_3$ | |
| 2. | $NO_2$ | $NO_2$ | | Br | |
| 3. | $NO_2$ | $NO_2$ | | | |

Did Not Add Cyclopentadiene

| | | | | | |
|---|---|---|---|---|---|
| 1. | $NO_2$ | $NO_2$ | | Br | Br |
| 2. | | $NO_2$ | | | |
| 3. | Br | $NO_2$ | | | |
| 4. | $NO_2$ | | | | |
| 5. | COOH | $NO_2$ | | | |
| 6. | $NO_2$ | Br | Br | | |
| 7. | | COOH | | | |
| 8. | $SO_3H$ | | | | |
| 9. | | | | COOH | |
| 10. | OH | | | | |
| 11. | O-Ethers, acetates, and benzoates | | | | |

Kuhn and Bär attacked the same problem but with quite a different tool. They studied the absorption spectra. They worked first with phenyl-azo-α-naphthol and were able to show that the equilibrium between the azo and the hydrazone forms of this compound is dependent almost entirely upon the solvent. The method depended upon a comparison of the spectra in different solvents with the spectra of the O- and N- methyl ethers. In pyridine the spectrum indicated only the azo form, while in glacial acetic acid and in nitrobenzene only the hydrazone form was indicated. In benzene there seemed to be about equal amounts of the two forms, and in alcohol, while the azo form seemed predominant, there was distinct evidence of the hydrazone form also.

Investigation of the isomeric ortho compounds, α-phenylazo-β-naphthol and β-phenylazo-α-naphthol, indicated that these compounds exist only in the hydrazone form (confirming work of Burawoy), regardless of the solvent. It was impossible to prepare the O- ether of the β-naphthol and very difficult in the case of the α-naphthol.

Investigation of o-, m-, and p-hydroxy-azobenzene revealed that the structure of these compounds was also independent of solvent. But in this case all three of the compounds existed in the azo form only. (This is a direct contradiction of recent work by Burawoy in the case of the ortho compound.)

Attempts to isolate the two desmotropes of phenyl-azo-α-naphthol failed.

It was concluded from these two papers that in the hydroxy-azo- compounds there is an equilibrium between a hydroxy-azo form and a quinone-hydrazone form. The proportion of these two forms present at equilibrium varies very widely and is usually dependent upon the substituents (structure of the molecule) but may depend almost entirely upon the solvent.

J. T. Thurston

Seminar Feb 13, 1935.

53

Concerning 1,1,2,2 Tetraphenylcyclopropane
G. Wittig and B. Obermann
Ber 67 2053 (1934).

This is the sixth paper of a series on ring closures, radical formation and valence tautomerism of unsaturated systems. In previous papers the senior author (Wittig) studied the tetraphenyl ortho xylylenes. It was prepared from dimethyl phthalate by treating with lithium phenyl. The resulting glycol was methylated and the methyl ether cleaved with sodium potassium alloy forming the dipotassium derivative. When this was treated with tetramethylethylene bromide it formed 9,9',10 triphenyl dihydro anthracene. In another paper he studied the formation of 9,10 tetraphenyl dihydrophenanthren from diphenic ester as indicated in the above procedure.

In this particular paper 1,1,2,2-tetraphenylcyclopropane was prepared from 1,1 diphenyl-2-bromo ethyl alcohol, which was made by treating malonic ester with phenylmagnesium bromide. The keto-carbinol was then converted to the glycol by means of lithium phenyl. This was then

methylated with methyl alcohol having a trace of hydrogen chloride. This dimethyl ~~e~~ether on cleavage with sodium ~~and~~ potassium alloy yielded the 1,1,2,2-tetraphenylcyclopropane on treatment with tetramethylethylene bromide. The substituted cyclopropane is unusually stable toward boiling acetic acid and a boiling solution of bromine in carbon tetrachloride.

The 1,1,4,4,tetraphenyl-1,4-dipotassium butane yielded only unsymmetrical diphenylethylene on treatment with tetramethylethylene bromide. The 1,1,5,5 tetraphenyl-1,5 dipotassium pentane, prepared from dimethyl glutarate and lithium phenyl as previously described, formed a polymeric hydrocarbon which on treatment with sodium and potassium alloy followed by decomposition with alcohol yielded the substituted pentane.

From this work it is concluded that the substituted cyclopropane, formed from intermolecular saturation, does not have a weakened valence bond between the substituted carbon atoms. In the case of the butane and pentane derivatives the molecules lose two potassium atoms forming unsymmetrical diphenylethylene and a polymeric hydrocarbon respectively.

Report by L.E.Schniepp.
February 6,1935.



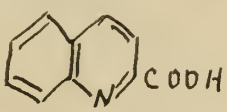
QUINOLINE DICYANIDE: A CONTRIBUTION TO THE STEREOCHEMISTRY OF TRIVALENT NITROGEN.

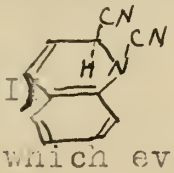
References:
O.Mumm and H.Ludwig,Ann. 514,34-60(1934).
O.Mumm and Herrendorfer,Ber. 47,758(1914).
O.Mumm and Bruhn,Ber. 68,176-83(1935).

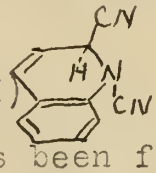
Location of the authors:
Chemical Institute of the University of Kiel,Germany.

Quinoline when treated with BrCN and anhydrous HCN in dry benzene solution at 0°,yields a dicyanide,$C_9H_7N(CN)_2$,which melts at 100°. Treatment of this compound with a basic nitrogen compound,such as ammonia or methylamine,converts it to an isomer melting at 130°. Reactions and properties indicate that these are stereoisomers;i.e., cis and trans forms.

Both isomeric dicyanides yield quinaldinic acid (I) on hydrolysis. Therefore formulas (II) and (III) are proposed for these isomers.

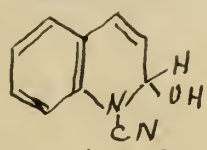
(I) 

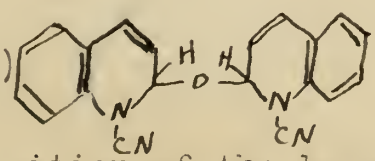

(II) 

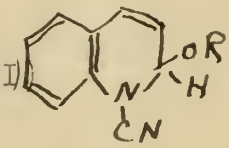

(III) 


This is the first case in which evidence has been found favoring the existence of stereoisomers where a trivalent nitrogen is involved.

Quinoline and BrCN only,in dry benzene,reacts to yield N-cyano-α-hyroxy-dihydroquinoline (IV) and the bimolecular compound (V). This is probably due to the action of a trace of moisture on the BrCN addition product. Neither the hydroxy nor the alkoxy compounds(VI) show any tendency to isomerise.

(IV) 


(V) 


(VI) 


Substituents in the o-position of the benzene ring or the α-position of the pyridine ring block the formation of dicyanides and only γ-cyanoquinolines are obtained from compounds whose rings are so substituted.

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I Semester 1935-36


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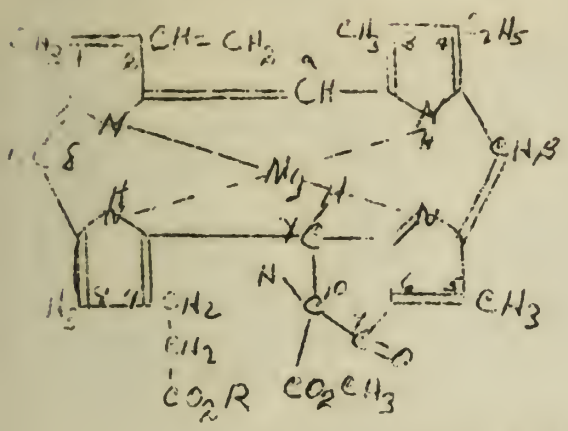
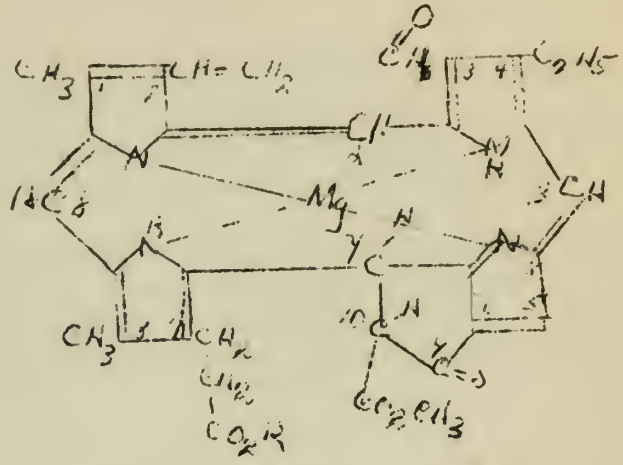
# Further Contributions on the Structure of Chlorophyll

H. Fischer and co-workers at the Technical High School at Munich. Ann. 513, 107 (1934); 516, 61 (1935); 519, 1, 58 (1935); Dietz, J. Chem. Ed., 12, 208 (1935); Armstrong, Chem and Ind., 52, 809 (1935).

Introduction: Fischer's latest proposed formulae for chlorophyll-a and -b are:



Chlorophyll (a)
I



Chlorophyll (b)
II

$$R = CH_3\underset{\displaystyle CH_3}{\underset{|}{CH}}-CH_2CH_2CH_2\underset{\displaystyle CH_3}{\underset{|}{CH}}CH_2CH_2CH_2\underset{\displaystyle CH_3}{\underset{|}{CH}}CH_2CH_2CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}=CHCH_2OH$$

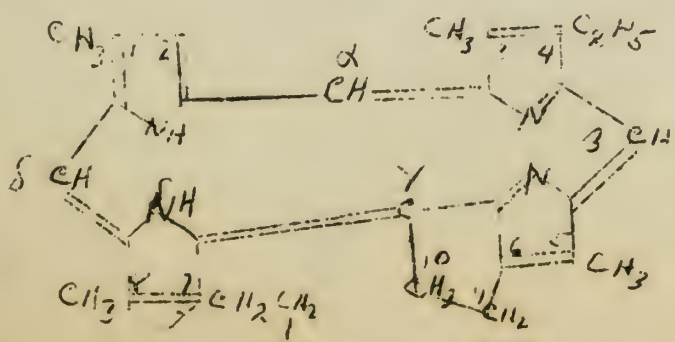
These papers are concerned with

I Proof of the presence of the vinyl group at the 2-position in chlorophyll-a.

II Proof of the presence of the formyl group at the 3-position in chlorophyll-b.

III The asymmetry of the gamma-carbon atom.

I After the magnesium atom and the phytyl radical are removed, the vinyl group is converted to an acetyl group by the action of hydrogen iodide in glacial acetic acid. This acetyl group, together with the carbomethoxy group on carbon atom 10 and the oxygen atom on carbon atom 9, is replaced by hydrogen upon treatment with hydrogen bromide in glacial acetic acid at 190° in a bomb. The new substance is 2-desethyldesoxophylloerythrine (III). This compound was synthesized,



III

20 Jan 36 J. Roger Adams

and the synthetic product shown to be identical with the one from chlorophyll-a.

II In a similar way 3-desmethyldesoxophylloerythrine was prepared and shown to be identical with the product obtained from chlorophyll-b by causing it to undergo the same reactions, save for that with hydrogen iodide, that chlorophyll-a was submitted to.

III Optical activity of chlorophyll derivatives was supposed to be due entirely to the asymmetry of carbon atom 10. Replacement of the carbomethoxy group with hydrogen yields a product still optically active. Asymmetry of the gamma-carbon atom is therefore postulated.

Reported by Dr. S. H. Babcock, Jr.
September 18, 1935

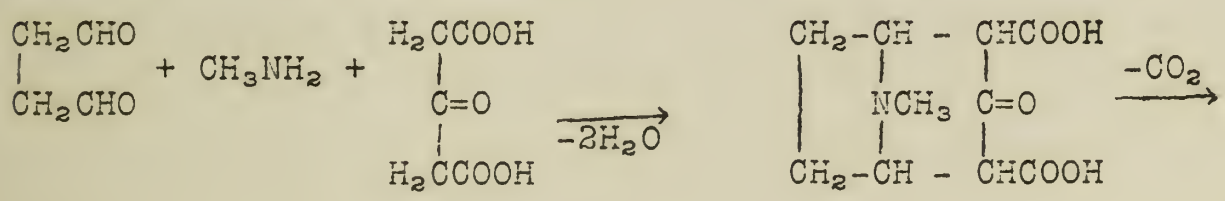
Synthesis of Tropinon, Pseudopelletierin, Sobelanin, and related alkaloids under physiological conditions.

Clemens Schöpf and Gerhard Lehmann
Ann. 518, 1 (1918).

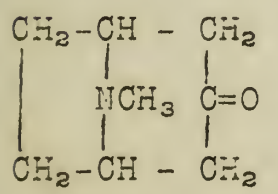
The authors report syntheses of tropanone and a number of other closely related alkaloids or intermediates. The starting materials and conditions in most cases are such as could exist in plant cells where these compounds are synthesized naturally. The point is stressed that natural products such as alkaloids, glucosides, etc. are probably synthesized in plants without the aid of catalysts such as enzymes and that attempts should be made to prepare such compounds in vitro under mild conditions. This investigation was suggested by a previous observation of the authors concerning the condensation of $\alpha$ amino benzaldehyde with $\beta$ keto acids. If this reaction is carried out at pH 13 the product is an $\alpha$ substituted quinoline $\beta$ carboxyllic acid, but if the pH is from 5 to 9 the reaction goes smoothly, with good yields, to form $\alpha$ substituted quinolines. Here as in later attempts to synthesize alkaloids better yields are obtained nearer neutrality than in strongly acidic or alkaline solutions. Since the starting materials need no special purification, the reactions are easily run and the yields good, these methods may be suitable for synthesis of quantities of these products.

Tropanone (II) was prepared by allowing a mixture of succindialdehyde, methylamine, and acetone dicarboxyllic acid to stand together at warm temperature for 3 days. Yields obtained from reaction mixtures having different pH are tabulated below and it will be noticed that yields are greater near the point of neutrality than at the extremes of pH.

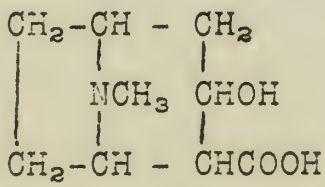
| pH of reaction mixture | 3.0 | 5.0 | 7.0 | 9.0 | 11.0 | 13.0 |
|---|---|---|---|---|---|---|
| Percent of theoretical yield | 68 | 83 | 78 | 61 | 64 | 5 |



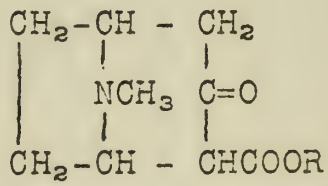
I



II



IV



V (R=H); VI (R=$CH_3$)

The authors disagree with the theory of Robinson that ecgonine (IV) is formed in the plant cell by elimination of one carboxyl group from tropanone dicarboxyllic acid (I). They suggest that cocaine may be formed by condensation succindialdehyde, methyl amine, and the mono methyl ester of acetone dicarboxyllic acid to form tropanone monocarboxyllic acid methyl ester (VI) (which they prove by experiment) and a subsequent reduction of the carbonyl group

followed by benzoylation.

Several other alkaloids and intermediates were also prepared. Glutaraldehyde, methyl amine and acetone dicarboxyllic acid condense under proper conditions (with elimination of $H_2O$ and $CO_2$) giving good yields of pseudopelletierin. If acetone is substituted for acetone dicarboxyllic acid no reaction takes place. Sobelanin was prepared by condensation of glutaraldehyde, methyl amine, and benzoyl acetic acid. Two alkaloids not occuring naturally, N-methyl $\alpha, \alpha'$ diphenacyl pyrrolidin and N-methyl $\alpha\alpha'$ diacetonyl pyrrolidin, were prepared.

Reported by A. E. Knauf
September 18, 1935

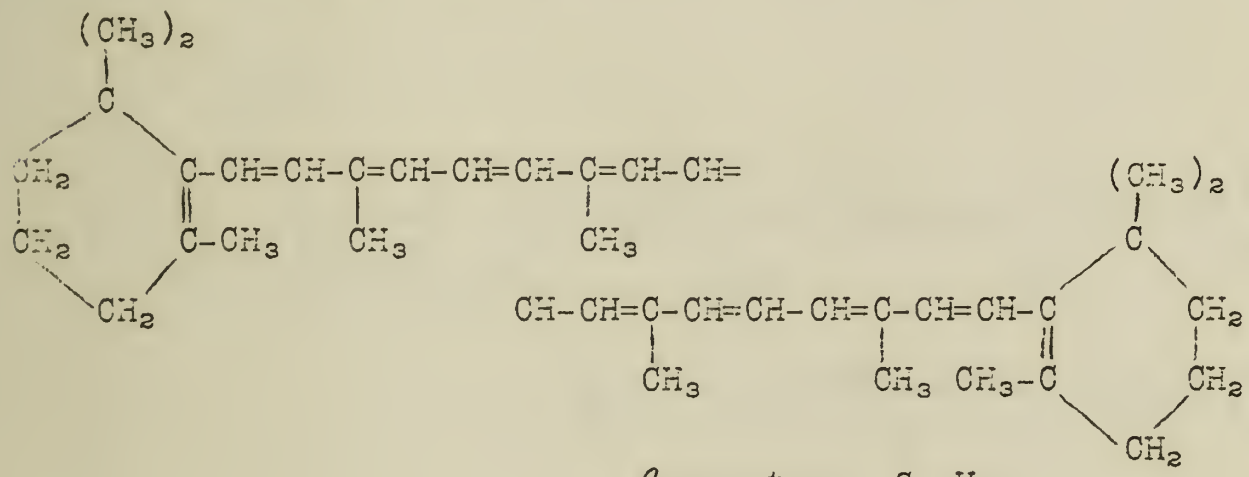
# The Stepwise Degradation and the Constitution of β-Carotene

von Richard Kuhn and Hans Brockmann
Ann. 516, 95-143 (1935)

Place: Kaiser Wilhelm-Institute for Chem., Heidelberg
Previous Work: 1. Carotenes, carotenoids, anthocyanins, chlorophylls and flavins

2. Structure of Hydroxy-azo-compounds

Only limiting proof has been obtained for the constitution of the pigments of the carotene-series with the exception of lycopin. The following work confirms the structure assigned by Karren (Helv., 13, 1084 (1930)) to β-carotene, who, by strong oxidation obtained geronic acid from β-carotene (16 percent of the theory for the two ionon rings).

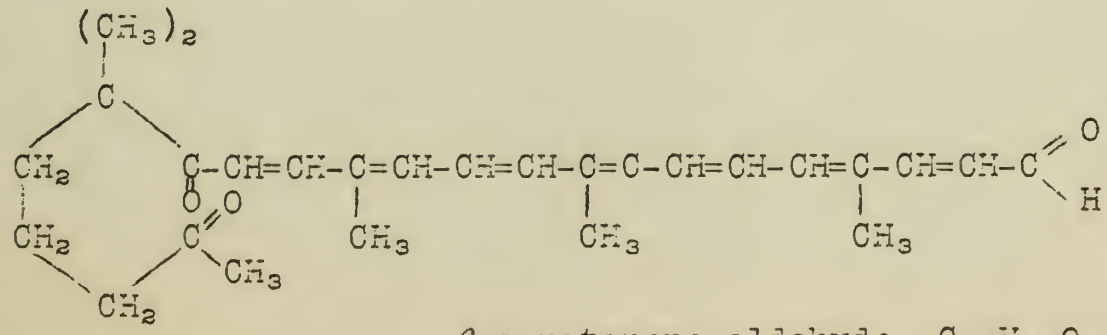


β-carotene $C_{40}H_{56}$

In an earlier work Kuhn, (Ber., 67B, 885-888 (1934)), oxidized β-carotene with chromic acid and obtained an aldehyde which he converted to the amide via the oxime and nitrile. This amide was dehydro-azafrenone amide. No experimental work was given.

This work is a continuation of the first and definitely establishes the structure of β-carotene.

β-carotene was oxidized by the alternate use of chromic acid and a mixture of chromic acid and lead tetraacetate to β-carotene-aldehyde.



β-carotenone aldehyde $C_{27}H_{36}O_3$

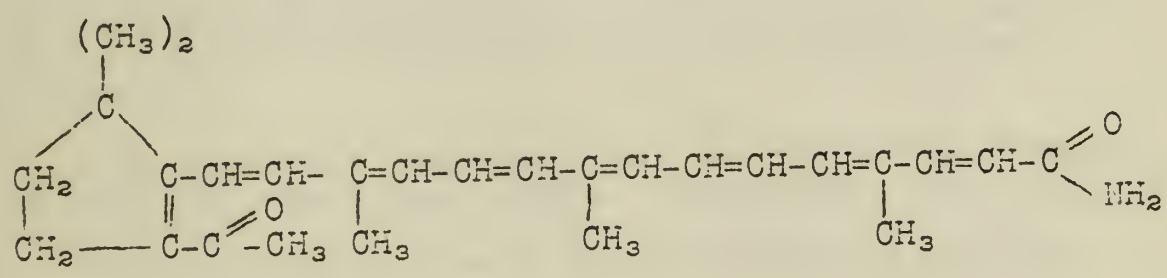
6

Five intermediate oxidation products were isolated and they appear in the reaction in this order; β-Hydroxy-carotin $C_{40}H_{58}O_2$, semi-β-carotenone $C_{40}H_{56}O_2$, β-Hydroxy-semi-carotenone $C_4H_{58}O_4$ and β-carotenone $C_{40}H_{56}O_4$.

β-carotenone-aldehyde was converted through the oxime and nitrile to anhydro-azafrenoneamide $C_{27}H_{37}O_3N$. Azafrene was then used as starting material for the synthesis of anhydro-azafrenoneamide showing clearly the relation between β-carotene and azafrene.

Azafrene was degraded stepwise to 3,8-dimethyl decapentane-1,10-dicarboxylic acid.

Kuhn establishes the position of the methyl groups by thermal decomposition of azafrene which gives m-tolyic acid and m-xylene.



Anhydro-azafrenoneamide $C_{27}H_{35}O_2N$

Reported by R. F. Miller
September 25, 1935

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# The Constitution of Alkannin

Randnitz et al., Ber. 68, 1479 (1935)
" 67, 1955 (1933)
" 65B, 159 (1932)
" 64, 1835 (1931)

From the laboratory of the German University at Prague.

In 1930 Randnitz showed by color reactions and spectra that alkannin did not compare with known anthraquinone derivatives and products, even though it did give anthracene derivatives on zinc dust hydrogenation.

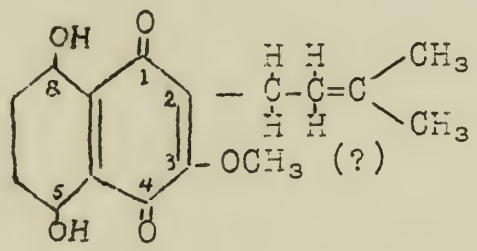
It did compare with a 5,8-tetrahydro-1,4-dihydroxy naphtha quinone derivative. He concluded that it belonged to the naphthalene C skeleton. It contained two hydroxyl groups and two quinone O atoms. It could be by reduction acetylated to a tetra acetyl-levo-alkannin.

By catalytic hydrogenation two ethylenic linkages in the side chain were shown. His analysis was $C_{16}H_{14}O_4$.

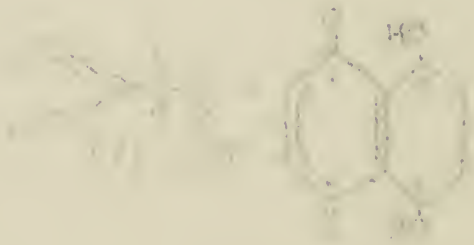
He repeated his work and confirmed it in 1931.

In 1932 he showed that a compound $C_{17}H_{18}O_5$ (alkannin plus one MeO group picked up from the methyl alcohol used in purification) took up 7 mols of H with Pt.

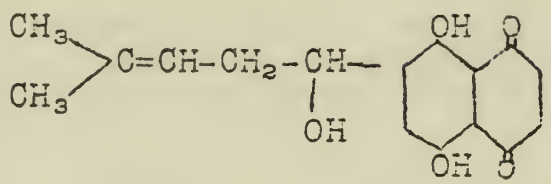
It yielded with ozone 0.7 mol of acetone and by reduction with Zn and NaOAc in boiling $Ac_2O$ a tetra-acetyl dihydro alkannin. The product he concluded to be,




In 1935 Randnitz obtained the dyestuff in pure form without the methylation and his analysis was $C_{16}H_{16}O_5$. He made the methyl ether and coupled it with 2,3-dimethyl butadiene and showed that the side chain was on the hydroquinone and not on the quinone nucleus; also, that the $CH_3O$ group was on the side chain and not on the nucleus as previously supposed.



Diazomethane also added on the nucleus confirming the positions so the new formula for alkannin is as follows:



Brand (Ber. 68, 1488) obtained angelic acid from the red oil which later gave the crystaline product so that alkannin is the ester of angelic acid.

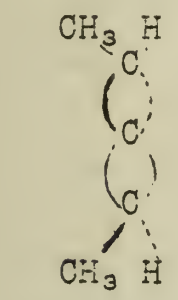
Reported by R. C. Cary
October 2, 1935

University of Illinois
Library-Chemistry

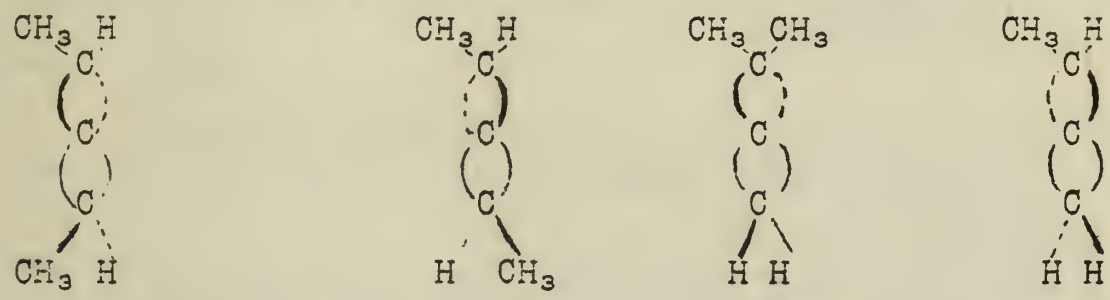
# RESOLUTION OF ALLENIC COMPOUNDS

By E. P. Kohler, J. T. Walker
and H. Tishler. J. Amer. Chem. Soc.
57, 1743-45 (1935), Harvard University

In the simplest cumulative double bond compound



H, it is necessary only to replace one hydrogen at each end to obtain non-superposable mirror images using the tetrahedral model of the carbon atom as proposed by van't Hoff in 1877.



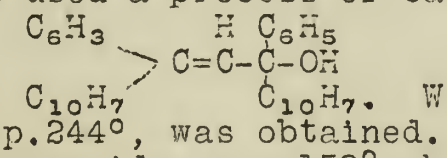
d,l forms of sym. dimethyl allene

Non-resolvable unsymmetrical dimethyl allene.

For 50 years, efforts to confirm the optically active character of properly substituted allenes as predicted by van't Hoff have met with failure.

Recently Ziegler and Sauermilch have prepared a number of allenes by dehydration of unsaturated tertiary alcohols. Using Ziegler's general method for preparing allenes, Mills and Maitland claim to have succeeded in verifying van't Hoff's prediction of enantiomorphism in unsymmetrically substituted allenes.

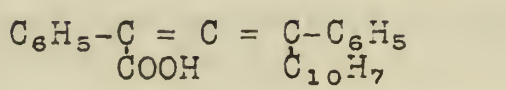
Mills used a process of catalytic asymmetric degradation on



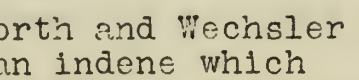
. With no catalyst an inactive allene, m.p.244°, was obtained. With d-camphor sulfonic acid, an isomeride, m.p.159°, having a rotation of $\alpha_{546}$l + 437 was produced. With l-camphor sulfonic acid the rotation was -438. The two antipodes were readily obtained pure but when mixed and crystallized from solution the racemic form, m.p.244°, was recovered. The active forms lose their activity slowly at 160°C.

Some time prior to the publication of Mill, the announcement of the preparation of the first authentic allenic acid was made from the Illinois laboratories and it was predicted that certain types of allenic acids would prove to be easily synthesized.

Kohler, who has worked in this field for many years, decided that the compound

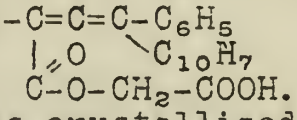


prepared and characterized by Lapworth and Wechsler in 1910 was really an allene and not an indene which Lapworth and Wechsler thought it might be. The synthesis involved treatment of diphenyl naphthyl butyrolactone with $PCl_5$. HCl was evolved and upon treatment with pyridine and $C_2H_5OH$ the ester



was formed.

This was converted to the acid chloride which on reaction with glycollic acid gave



The brucine salt of this derivative was crystallized from methyl alcohol. On treatment with HCl, the pure acid, m.p.145° was precipitated. The rotation was +29.5. A mixture of the d and l forms, m.p.145°, gives on crystallization the racemic acid, m.p.195°, which is identical with that obtained by hydrolysis of the ethyl ester. The structure of these was proved by oxidation to phenyl naphthyl ketone and phenyl glyoxylic acid.

Reported by W. J. Sparks
October 2, 1935

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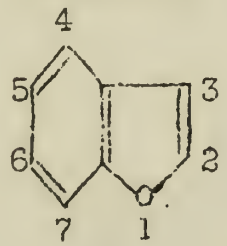
# SYNTHESIS OF COUMARONE-2-CARBOXYLIC ACID AND HYDROXYCOUMARONES

By: T. Reichstein, R. Oppenaur, A. Grusser, R. Hirt, L. Rhyner and G. Glatthaar. Helv. Chim. Acta. 18, 816 (1935).

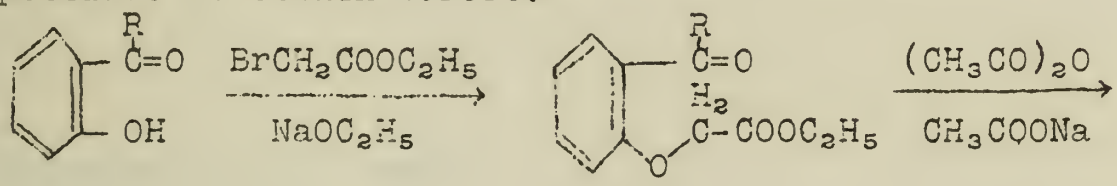
Place: Organic Chemistry Laboratory of the Eidg. Techn. High School, Zurich.

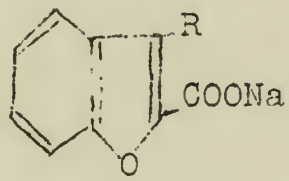
Previous work: Methylfurans, 2-Isopropylfuran, Isotubaic acid.

Coumarone

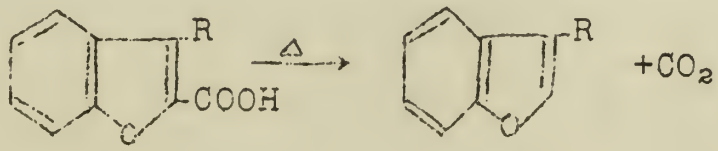



Reichstein and co-workers have shown that a slight modification of Rossing's (Ber. 17, 3000 (1884)) synthesis has proved successful in the preparation of many of the substituted coumarones which have been impossible to obtain before.




Removal of the carboxyl group is accomplished by treating the acid with copper-bronze powder in a boiling solution of quinoline.

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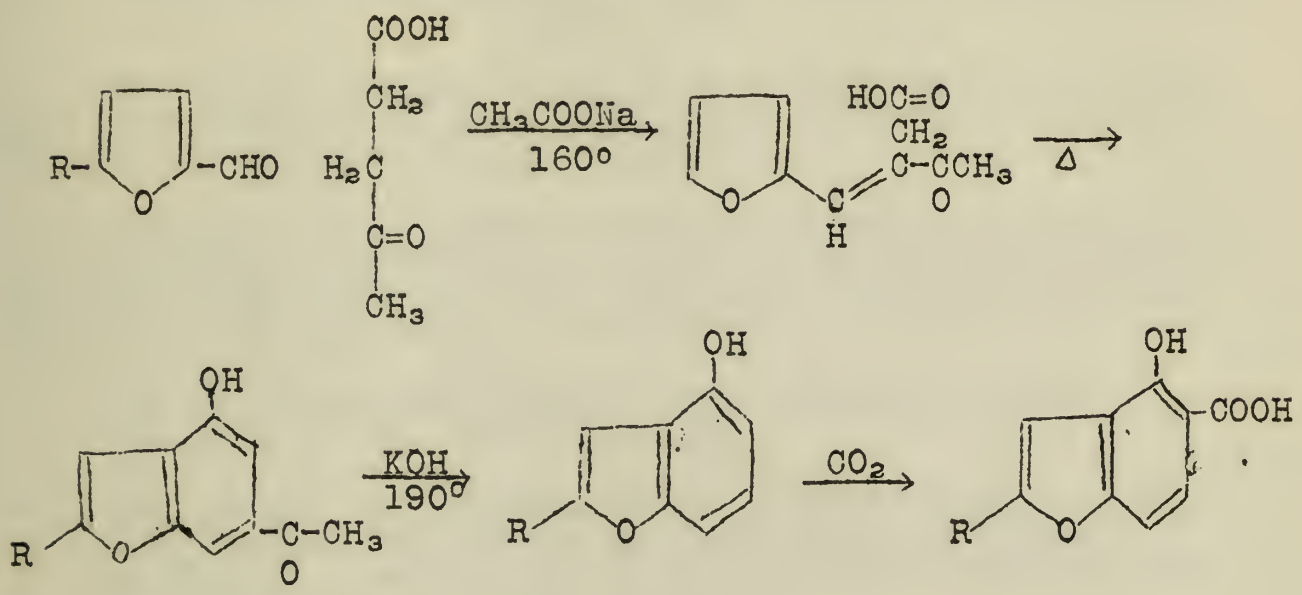
The various substituted coumarones that were made by this method were prepared by replacing the salicylaldehyde by the following compounds, o-vanillin, pyrogallol, 2-hydroxy-3, 4-dimethoxybenzaldehyde, resorcyl-aldehyde-4-benzyl ether, phloroglucinaldehyde-2-methyl-4-benzyl

ether and 2,4-dihydroxyisobutyrophenone.

An alternate method has had a limited application.




Reported by L. R. Drake
October 9, 1935

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$BF_3$ forms molecular complexes with certain types of organic compounds. A considerable number of these complexes have been isolated and characterized [1,2,3,4], and they are in general monomolecular addition compounds of $BF_3$ and the organic compound.
e.g. $CH_3OH \cdot BF_3$, $CH_3CO_2H \cdot BF_3$, $(C_2H_5)_2O \cdot BF_3$, $(CH_3CO)_2O \cdot BF_3$, $C_6H_5NH_2 \cdot BF_3$

The $BF_3$ is thought to be held to the organic molecule by a coordinate-covalent linkage with the O or N atom as "donor" and the B atom as "acceptor".

Although these complexes have been known for some time, their practical importance has been recognized only within the last 5-10 years and they have been utilized with some success in various organic reactions.

(1) Alcohols and glycols with acetylene in the presence of $BF_3$ yield acetals[5].

(2) Acids and alcohols react in the presence of $BF_3$ to give fair yields of the corresponding esters[6]. Similarly, acetates may be formed from acetamide and alcohols in the presence of $BF_3$[7].

(3) Alkyl aryl ethers are rearranged by $BF_3$ to phenols, alkyl phenols, and alkyl phenyl ethers[8].

(4) Propylene may be condensed with phenols in the presence of $BF_3$ to yield isopropyl aryl ethers, isopropyl phenols, and the isopropyl ethers of these isopropyl phenols[9].

(5) Propylene may be condensed with acids in the presence of $BF_3$ to yield isopropyl esters[10], and in the case of hydroxybenzoic acids, these are rearranged to give isopropyl hydroxybenzoic acids and their esters[11].

(6) Ethers are cleaved by acid chlorides and acid anhydrides in the presence of $BF_3$ to yield esters[12].

(7) $BF_3$ may be substituted for $AlCl_3$ in reactions e.g. the synthesis of ketones and $\beta$-diketones[13].

(8) Phenols are alkylated by alcohols to the corresponding ethers with $BF_3$[14].

(9) Propylene and other olefins condense with aromatic hydrocarbons to give the alkyl hydrocarbons in the presence of $BF_3$[15].

(10) Certain alifatic hydrocarbons, both open-chain and cyclic, have been condensed with ethylene in the presence of $BF_3$ to yield higher hydrocarbons[16].

1. Nieuwland, et al, J. Am. Chem. Soc. 53, 3909 (1931)
2. Meerwein, et al, Chem. Abstracts 26, 1871; J. prakt. Chem. 141, 123 (1934)
3. Morgan and Taylor, Chem and Ind. 50, 869 (1931); J. Chem. Soc. 1932, 1497.
4. O'Leary and Wenzke, J. Am. Chem. Soc. 55, 2117 (1933)
5. Nieuwland, et al, J. Am. Chem. Soc. 52, 1018 (1930) Proc. Indiana Acad. Sci. 40, 203 (1931)
6. ibid., 54, 2017 (1932)
7. ibid., 55, 5052 (1933)
8. ibid., 54, 2019 (1932); 55, 3402 (1933)
9. ibid., 54, 3694 (1932)
10. ibid., 56, 2689 (1934)
11. ibid., 56, 2054 (1934); 57, 1549 (1935)
12. ibid., 55, 2857 (1933) Meerwein, et al, J. prakt. Chem. 134, 51 (1932)
13. Meerwein, et al, Ber. 66B, 411 (1931); J. prakt. Chem. 141, 149 (1934)
14. Nieuwland, et al, J. Am. Chem. Soc. 57, 709 (1935)
15. ibid., 57, 1547 (1935)
16. Ipatieff, et al, J. Am. Chem. Soc. 57, 1616, 1722 (1935)

Reported by M. F. Roy
October 9, 1935

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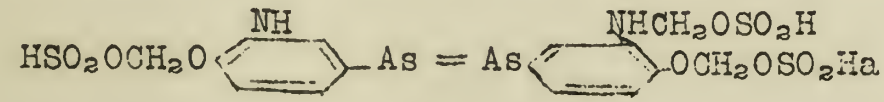
# CONSTITUTION OF SULPHARSPHENAMINE

By: Dyke and King, J. Chem. Soc., 1933, 1003; J. Chem. Soc., 1934, 805.

Place: National Institute for Medical Research.

The structure of sulpharsphenamine had been given by the authors to be the sodium salt of 3,3'-diamino-4,4'-dihydroxy-arsenobenzene-O,O',N-trimethylene sulfite.




This formulation was built on the following experimental considerations:

1. Proof of presence of three methylene sulfite groups as a part of the molecular structure.
2. Only one of the three groups was oxidized to sulfate by alkaline iodine.
3. Authors had shown that mono-N-methylene sulfites of anilines gave a quantitative yield of sulfate by the same treatment.

Mainly from these facts, the authors concluded that of the three groups the one capable of undergoing oxidation by the alkaline iodine conditions was an amine derivative while the other two were on the phenolic hydroxyls. The main objections to the formula were the difference in reaction indicated by the O- and N-methylene sulfite groups toward alkaline iodine, and the fact that no methylene sulfites of phenolic hydroxyls had been prepared.

In the present work the authors submit evidence toward a new formula.

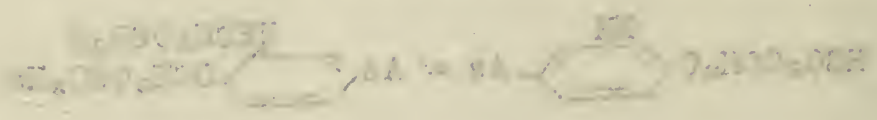
1. Formation of a tetramethylene sulfite derivative of salvarsan from which less than one mol of sulfate be precipitated by the iodine method. This showed that an O-union of the group was not necessary for prevention of oxidation.
2. Preparation of o-aminophenol derivative with an excess of sodium bisulfite and formaldehyde to yield a dimethylene sulfite which formed a trisodium salt, and in which only a portion of the sulfite could be oxidized to sulfate by iodine.
3. In reaction of anilines with performed sodium formaldehyde sulfite, a mono-N-methylene sulfite was formed, which gave a quantitative precipitation of sulfate by iodine.
4. Erratic results in sulfate quantities on oxidation and difference in mono-N- and N,N-dimethylene sulfite toward oxidation by the same reagent indicated an intermediate sulfur form. Authors have considered a dithionate formation.

## CONSTITUTION OF [illegible]

By: [illegible] and [illegible], [illegible]
[illegible], [illegible], [illegible], [illegible]

Project: National Institute [illegible] Medical Research.

The structure of [illegible] was given by the authors as the [illegible] of 2,2'-dimethoxy,3'-[illegible]-[illegible]-5,6'-[illegible]-[illegible] [illegible].

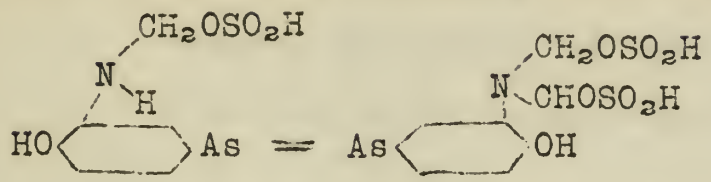


The [illegible] was built on the following [illegible] considerations:

1. Proof of presence of [illegible] [illegible] as a part of the [illegible] structure.
2. Only one of the [illegible] [illegible] [illegible] for [illegible] [illegible].
3. Authors [illegible] that [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible].

Mainly from these facts, the authors [illegible] part of the [illegible] [illegible] the one possible of [illegible] [illegible] by the [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible]

From these results the authors present the new formula




for sulpharsphenamine, and suggest a series of new compounds of interest.

Reported by L. L. Alexander
October 16, 1935

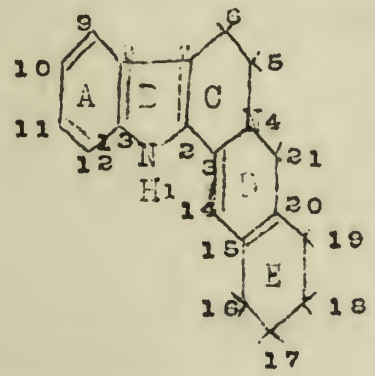
# ON THE CONSTITUTION OF YOHIMBINE

By: Caesar Scholz.
Helv. Chim. Acta., 18, 923 (1935).

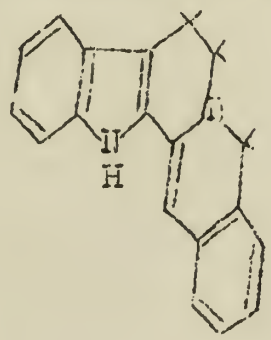
Place: University of Edinburgh.

Previous work: Alkaloids (Harman).

Yohimbine ($C_{21}H_{26}O_3N_2$) yields upon selenium dehydrogenation yobyrine, tetrahydroyobyrine and ketoyobyrine. The present paper is concerned with the structure of the degradation products.



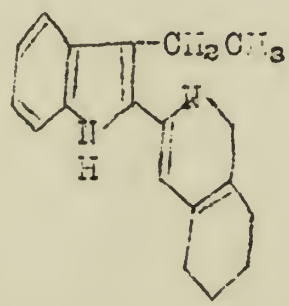
Tetrahydroyobyrine
$C_{19}H_{20}N_2$



Yobyrine
$C_{19}H_{16}N_2$

The above formulae were those accepted for these compounds before the present work.

Tetrahydroyobyrine yields upon ozonization a compound $C_{19}H_{20}O_2N_2$. The same compound is obtained on treatment with chromic acid. Hydrolysis of this compound yields o-aminopropiophenone and Bz-tetrahydroisoquinoline-3-monocarboxylic acid. Oxidation leads to berberonic acid. In view of the above, tetrahydroyobyrine is



Yobyrine gives no clear-cut ozonization product, but oxidation leads to oxy-yobyrine $C_{19}H_{14}ON_2$.

On purely circumstantial evidence, the secondary hydroxyl group present in yohimbine is placed in the 14 position, and

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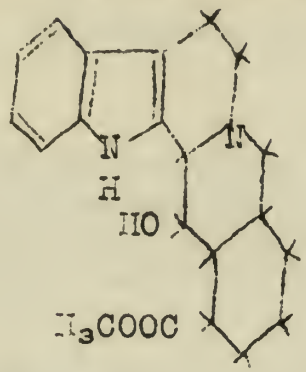
the structural formula is believed by Scholz to be




Reported by H. G. Kolloff
October 16, 1935

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Michel Lesbre
Bull. Soc. Chim.,(5) 2, 1189 (1935)
Lab. of Gen. Chem., Sorbonne.
Kozeschkow, K. A., Ber., 66, 1661, (1933)

The A and B subdivisions of the fourth group in the periodic table differ widely in their tendency to form organic compounds. Those under silicon form organic compounds more or less comparable, in their formation and properties, to carbon compounds.

The following series of compounds are arranged in order of decreasing stability:

$$SnR_4 \longrightarrow R_3SnH \longrightarrow R_2SnH_2 \longrightarrow RSnH_3$$

$$RCH_3 \longrightarrow R_2CH_2 \longrightarrow R_3CH \longrightarrow R_4C$$

The Sn-H bond is much less stable than the C-H bond. Sn-Sn bonds are rare.

A nomenclature, analogous to that of carbon compounds, is suggested:

| | | | |
|---|---|---|---|
| $Sn_nH_{2n+2}$ | $RSnOOH$ | $R_3SnOH$ | $R_2SnO$ |
| Stannanes | Stannonic acids | Stannols | Stannones |

The methods of producing stannonic acids and stannones are analogous to those for the production of aliphatic acids and ketones.

The reactions of $SnO_2KH$ with $CH_3I$ and of $HCl_2K$ with $CH_3I$ show a fundamental difference in the structure of stannites and formates. The potassium atom must be attached directly to the tin atom.

The reaction of $KSnO_2$ with halogen derivatives has been made general for the production of stannonic acids.

Reactions of stannonic acids and derivatives:

$$RSnO_2H + 3HX \longrightarrow RSnX_3 + 2H_2O$$

$$RSnX_3 + 2HX \longrightarrow RSnX_5H_2$$

$$RSnX_5H_2 + 2NH_3 \longrightarrow RSnX_5(NH_4)_2$$

Reactions of stannones:

$$R_2SnO + 2HCl \longrightarrow R_2SnCl_2 + H_2O$$

$$2R_2SnO \xrightarrow{\Delta} R_4Sn + SnO_2$$

20

Formation and reactions of stannols:

$$R_3SnX + HOH \longrightarrow R_3SnOH + HX$$

$$3RI + 3SnO_2KH + 4KOH \longrightarrow R_3SnOH + 2SnO_3K_2 + 3KI + 3H_2O$$

$$R_3SnOH \longrightarrow [R_3Sn]^+ + OH^-$$

$$2(C_6H_5)_3SnOH \xrightarrow[400^\circ]{H_2O} (C_6H_5)_4Sn + (C_6H_5)_2SnO + H_2O$$

The order of decreasing acidity and solubility is:

$$RSn(OH)_3 \longrightarrow R_2Sn(OH)_2 \longrightarrow R_3SnOH$$

Reported by L. L. Ryden
October 23, 1935.

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LIBRARY-CHEMISTRY

# ACYL HYPOHALITES

Bockmüller and Hoffmann
Ann. 519, 165 (1935)
Chem. Inst. of University of Würtzburg

The authors report that chlorination of allyl chloride in glacial acetic acid solution gave the expected 1,2,3-trichloropropane plus a 30 per cent yield of a lower boiling compound which proved to be the following dichloropropyl acetate:

$$CH_3\overset{O}{\overset{\|}{C}}-O-CH_2CHCl-CH_2Cl$$

They postulate that there is a reaction between acetic acid and chlorine to produce acetyl hypochlorite,

$$CH_3\overset{O}{\overset{\|}{C}}-OH + Cl_2 \rightleftharpoons CH_3\overset{O}{\overset{\|}{C}}-OCl + HCl$$

and that in this reaction the equilibrium is shifted far to the left. The acetyl hypochlorite then adds to the allyl chloride in the same manner as hypochlorous acid.

$$CH_2{=}CHCH_2Cl + HOCl \longrightarrow HOCH_2CHClCH_2Cl$$

$$CH_2{=}CHCH_2Cl + CH_3COOCl \longrightarrow CH_3COOCH_2CHClCH_2Cl$$

The formation of acyl hypohalites is analogous to the hydrolysis and alcoholysis of halogens,

$$HOH + X_2 \longrightarrow HOX + HX$$

$$ROH + X_2 \longrightarrow ROX + HX$$

Methyl and ethyl hypochlorite were first prepared and isolated by Sandmeyer in 1885. They readily add to >C=C< systems with the formation of halogenated ethers.

$$\overset{|}{C}{=}\overset{|}{C} + CH_3OCl \longrightarrow CH_3O\overset{|}{C}-\overset{|}{C}Cl$$

The authors have found that acyl hypohalites are best prepared by the action of halogen on the silver salt of the acid;

$$RCOOAg + X_2 \longrightarrow RCOOX + AgX$$

An extensive study of the reactions of acyl hypohalites was carried out under the following heads:

1. Oxidizing Power, $RCOOX + HX \longrightarrow RCOOH + X_2$
2. Spontaneous decomposition, $RCOOX \longrightarrow RX + CO_2$
3. Reaction with water, $RCOOX + HOH \longrightarrow RCOOH + HOX$
4. Hologenation, $RCOOX + RH \longrightarrow RX + RCOOH$
5. Addition to C-C double bonds, $\overset{|}{C}{=}\overset{|}{C} + RCOOX \longrightarrow RCOO\overset{|}{C}-\overset{|}{C}X$

Reported by J. H. Brown
October 23, 1935

# The Peroxide Mechanism of Kolbe's Hydrocarbon Synthesis

## Applied to Monoethyl Adipate

Fichter and Buess, Helv. 18, 445 (1935)

Place: University of Basel, Switzerland.

Previous work: Primarily electro-organic, with special regard to mechanism of Kolbe's hydrocarbon synthesis.

Fichter and his co-workers have been trying to establish the peroxide mechanism of Kolbe's hydrocarbon synthesis since 1918. Briefly, their method of attack has been:

a. Synthesis of numerous peroxides,
b. Thermal decomposition of these peroxides,
c. Comparison of decomposition products with electrolytic products.

The net reaction and Fichter's mechanism follow:

$$2\ RCOO^- \xrightarrow{\text{electrolysis}} R\text{-}R + 2\ CO_2$$

$$\downarrow$$

$$(RC{=}O)_2O \xrightarrow{1/2\ O_2} \begin{matrix} RCOO \\ | \\ RCOO \end{matrix} \xrightarrow{H_2O} \begin{matrix} RCOOH \\ + \\ RCOOOH \end{matrix} \longrightarrow ROH \longrightarrow R'CH{=}CH_2$$

The present paper deals with the above mechanism applied to monoethyl adipate as typical of Fichter's work.

He thermally decomposed monoethyl adipyl peroxide in a steel bomb. From the decomposition product he secured a neutral oil, which was fractionally distilled as follows:

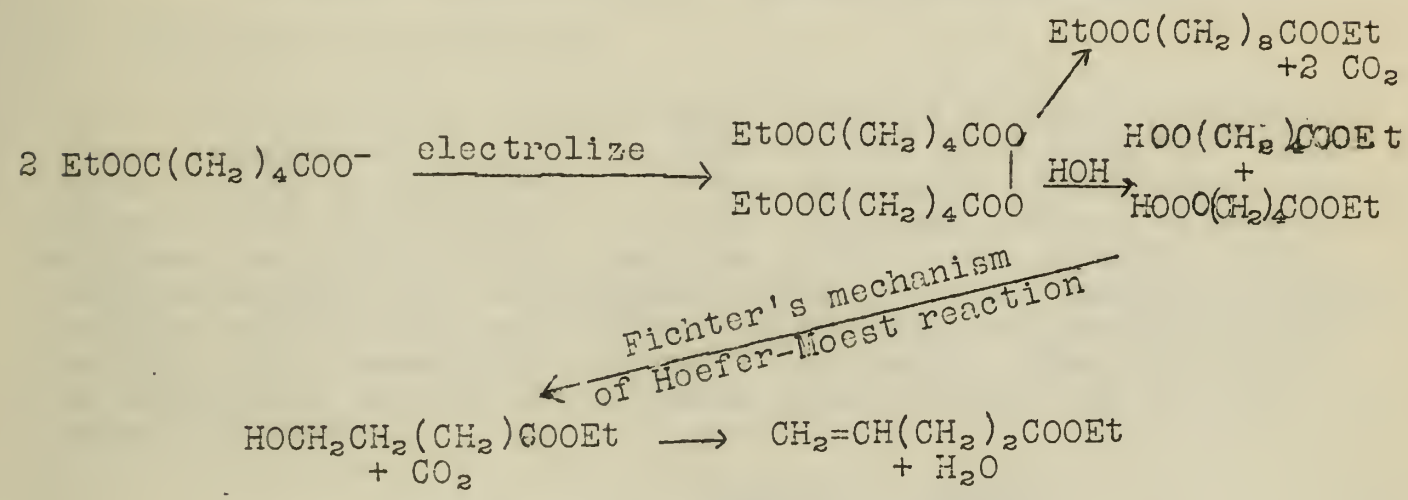
Fraction I (2.5 g.) was found to be a mixture of ethyl n-valerate and ethyl ester of allyl acetic acid.
Fraction II (3.1 g.) was found to be diethyl adipate.
Fraction III (3.0 g.) was found to be diethyl sebacate.
Fraction IV (1.7 g.) was found to be essentially diethyl sebacate.
Fraction V (4.2 g.) was found to be essentially diethyl sebacate.

Note that the main product of thermal decomposition of the peroxide was diethyl sebacate (11 g. total), just as it is the main product in the electrolysis of potassium, ethyl adipate. In addition one secures the same unsaturated ester by thermal decomposition as by electrolysis.

Under carefully controlled conditions (high C.D., well cooled anode, proper electrolyte, etc.) the presence of peracid

(7.22 mg.) and peroxide (13.95 mg.) in the electrolyte was established by titrating the iodine released from KI with $Na_2S_2O_3$.

According to Fichter hydrolysis of the peroxide yields the peracid, which, by loss of $CO_2$, accounts for the Hoefer-Moest reaction, and the resulting "alcohol" upom dehydration forms the unsaturated ester, thus:




In view of the establishment of the peroxide and peracid in the electrolyte, and the parallelism of products from thermal decomposition and electrolysis, Fichter concludes that peroxide and peracid must be intermediates to successfully account for all the products of the Kolbe hydrocarbon synthesis.

Reported by Rene Oehler
October 30, 1935.

# MECHANISM OF NITRATION

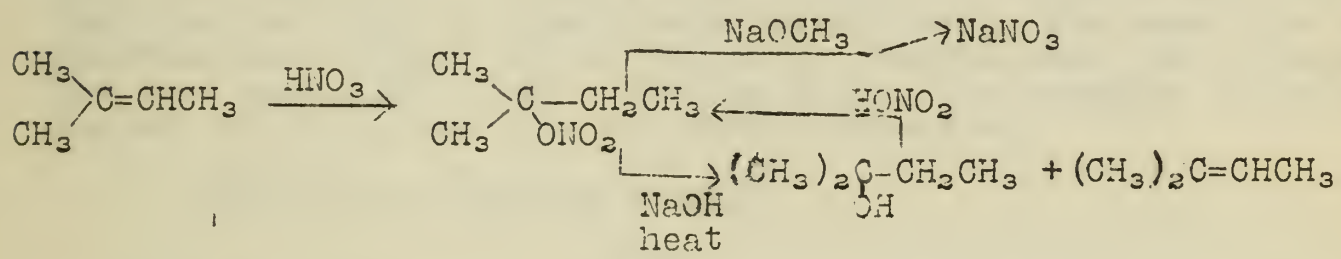
By: A. Michael and G. H. Carlson.
J. Am. Chem. Soc., 57, 1268 (1935)

Place: Harvard University.

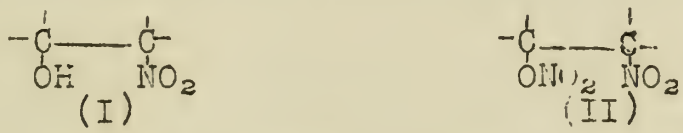
Previous work: Relationship between structure and chemical and physical properties. Acetoacetic ester condensation. Michael condensation.

## I. Nitration of Alkylenes:

Contrary to the generally accepted nitration mechanism first proposed by Wieland in 1930, nitric acid (98.6 per cent) does not add to alkylenes to yield saturated nitrohydrines or nitro-nitric acid esters. Neither ethylene nor $\alpha,\alpha$-diphenylethylene react with cold, absolute nitric acid; however, trimethylethylene and isobutylene, being of a more additive nature, combine with nitric acid (absolute or 98.6 per cent) at -20° to form the corresponding nitric acid esters, the structures of which were proved as indicated below in the case of trimethylethylene:

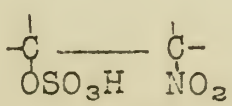



The earlier work of Wieland mentioned above indicated that concentrated nitric acid functioned as HO + $NO_2$ when adding to alkylenes to form first a nitrohydrine (I) which was then converted by more nitric acid into a nitro-nitric acid ester (II).



(I) (II)

The authors point out that the active nitrating agent used by Wieland was not nitric acid but more probably the mixed anhydride $HOSO_2ONO_2$ (formed by the sulfuric acid present), which added to the ethylenic bond to produce a nitro-sulfuric ester (III), and



(III)

which in turn could easily undergo substitution by the more negative nitric ester radical to yield the type (II).

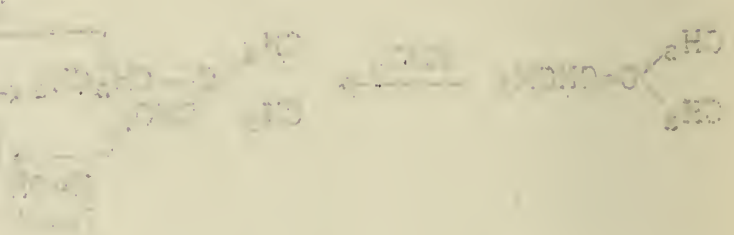
Bur. A. Thomas and E. E. Taylor,
J. Am. Chem. Soc., 71, 1038 (1949)

Tulane University

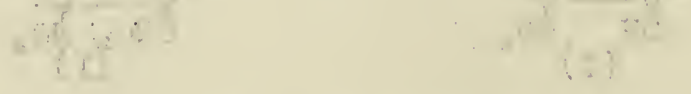
Dienyl ethers. Methylenedi methoxy (propoxy) and phenoxy and alkyl-1 or -2-dienyl ethers. Benzene-diazonium coupling. Diene condensation.

I. Dienyl of diphenyl

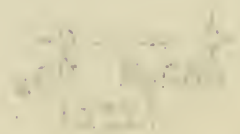
Contrary to the generally accepted dienyl mechanism first proposed by Michael in 1931, acetic acid (98.0 per cent) does not lead to dienyl ethers by yield and rate of dienyl ether formation. Rather, only the cis-dienyl ether, methylenedimethoxy-diphenyl, is formed. Methyl ether of cis-dienyl ether, methylenedimethoxy-diphenyl, is formed in a more rapid reaction, possible only with acetic acid (possibly 98.0 per cent) at 50° to form the corresponding dienyl ether. The structure of which has been established by the case of bromination.



The reaction mechanism of Michael as above indicated that corresponding dienyl ether (I) with water which was found to be dienyl ether, methylene (I) which was then converted by some unknown acid into a dienyl ether (II).



The authors point out that the acetic acid reaction appears to be by Michael's dienyl ether with the same reagent, the mixed ether, methyl $CH_3OCH_2$ (formed by the phenol acid product), which model on the dienyl ether and to produce a diphenylmethyl ether (III).



which in turn could readily undergo substitution by the nucleophilic dienyl ether, which reacts to yield the type (IV).

Nitric acid (98.6 per cent) does not attack $\alpha,\alpha$ - diphenylethylene at room temperature, but as soon as the reaction mixture is warmed to the point of evolution of nitrous fumes, $\alpha,\alpha$-diphenyl-$\beta$-nitroethyl alcohol is obtained. In fact, all nitration reactions which are <u>not</u> carried out in the cold involve the action of nitrogen tri- and tetroxide. This could account for the formation of the previously mentioned nitrohydrines, thus:

$$R_2C{=}C- \xrightarrow{N_2O_3} R_2\underset{NO}{C}-\underset{NO_2}{C}- \xrightarrow{\text{Moisture}} R_2\underset{OH}{C}-\underset{NO_2}{C}-$$

Nitric acid itself does not yield such products, but functions in a normal way to add H + $NO_3$ to alkylenes.

II. Aromatic Nitration:

In support of the HO + $NO_2$ addition theory for the nitration of benzene, Reddelein and Wieland stated that phenanthrene when treated with nitric acid (absolute) gave the ether of 8-hydroxy-9-nitrophenanthrene. The present authors claim the formation of this compound to be another case of the action of the oxides of nitrogen on a double bond linkage, in view of the fact that they obtained a phenanthrene nitric acid ester when the same reaction was carried out in the cold. Furthermore, it is pointed out that according to the addition theory for aromatic nitration, benzene should yield tri- not mononitrobenzene.

Michael and Carlson propose,

$$C_6H_6 + HONO_2 \longrightarrow C_6H_5 - N\begin{matrix}OH\\O\\OH\end{matrix} \longrightarrow C_6H_5 - NO_2 + H_2O$$

for the mechanism of aromatic nitration, in which the first step proceeds by the common aldolization reaction.

Reported by Marlin T. Leffler
October 30, 1935.

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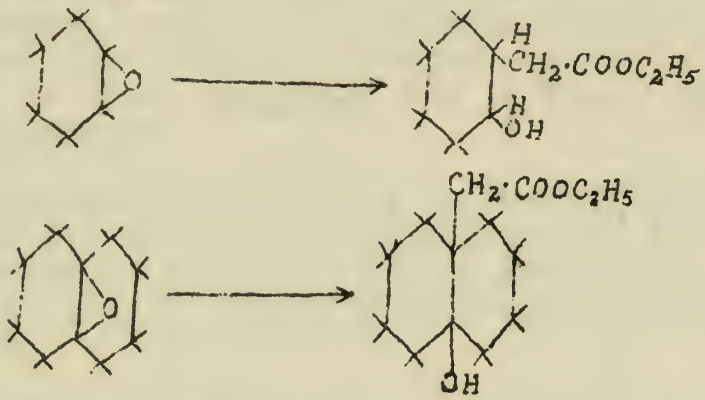
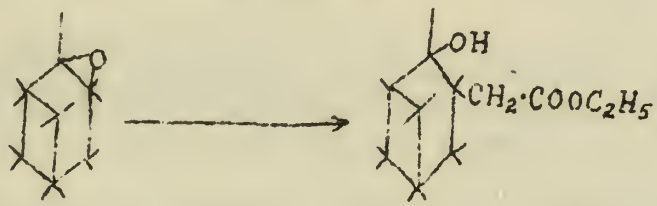
# Isomerism of α-Pinene Oxide with Reformatsky's Reaction.

B. Arbusow
Ber., 68, (8), 1430-1438 (1935)
Butlerow Institute of Kasan, U.S.S.R.

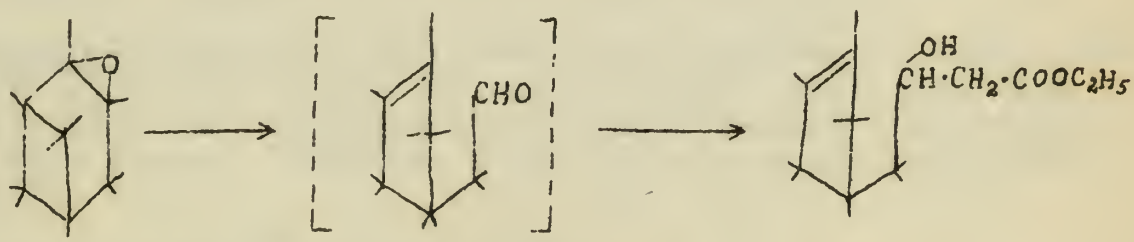
The action of ethyl bromoacetate and zinc on cyclohexene oxide and on 9,10-octalin oxide has been shown to yield the following products:




From these facts the normal product of the reaction of ethyl bromoacetate and zinc on α-pinene oxide would be expected to be the saturated ester:



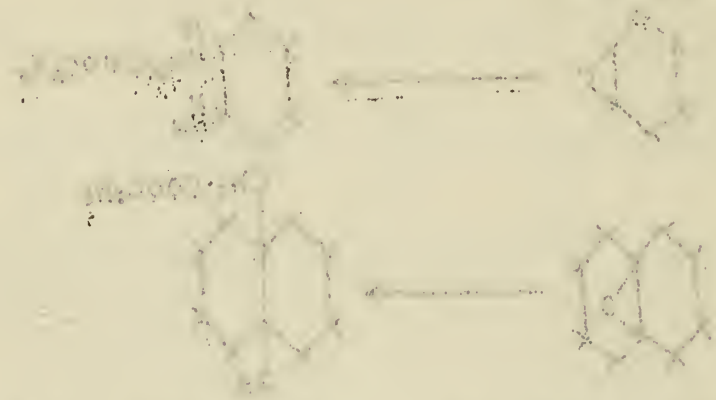

However, there was actually obtained an unsaturated ester, $C_{14}H_{24}O_3$, which is identical with that produced by the direct action of the reagents on α-campholenaldehyde. It is shown that α-pinene oxide may be rearranged to α-campholenaldehyde by the action of small amounts of zinc bromide. Evidently, therefore, the reaction is not directly on the α-pinene oxide but on the product produced by the isomerization with traces of zinc bromide present.



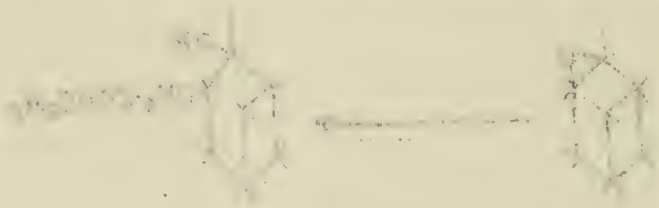

α-Pinene oxide  α-Campholenaldehyde  $C_{14}H_{24}O_3$

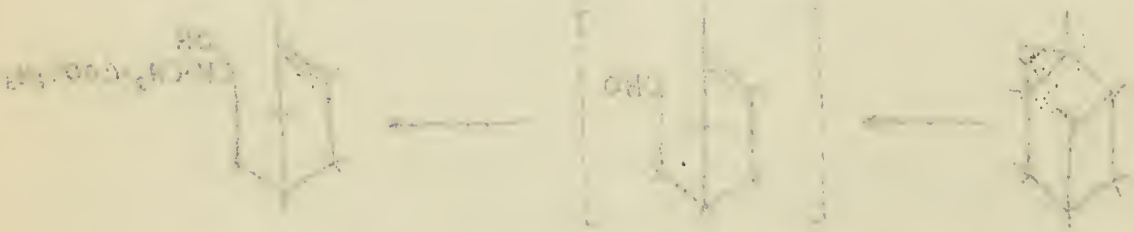
Mechanisms are offered for the rearrangement of α-pinene oxide to α-campholenaldehyde and the production of α-campholenaldehyde is verified by oxidation to α-campholenic acid by silver oxide and thence to dihydroxy-α-campholenic acid by potassium permanganate.

Reported by George B. Brown
November 6, 1935





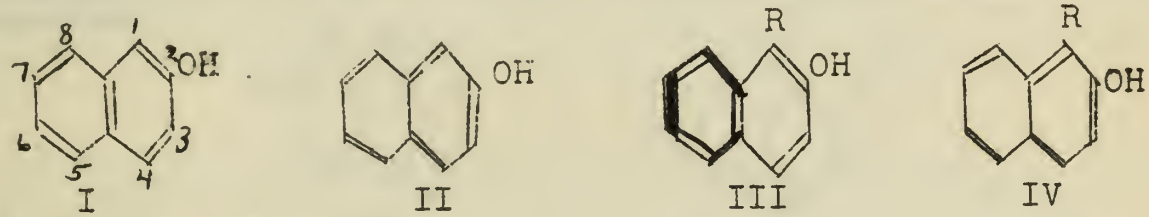




L. F. Fieser and W. C. Lothrop
Harvard University
J. Am. Chem. Soc., 57, 1459, (1935)

It has long been known that the anomalous reactions of the naphthalene nucleus are unexplainable on the assumption of two condensed aromatic rings with oscillating bonds. This review indicates that the bonds of naphthalene differ from those of benzene only in their mobility and in their reactivity or degree of unsaturation.

Early attention was called to the difference in the behavior of the (1) and the (3) positions of β-naphthol and β-naphthyl amine, i.e., the "ortho" positions. These differences are most easily understandable by a fixed condition of the bonds.




1. Nuclear Substitution

a. Coupling reaction.-All mechanisms require a double bond between the hydroxyl and the entering position. Diazonium salts couple at (1), indicating formula I rather than II.

1-Alkyl-2-naphthol will not couple. Since IV should couple, III is evidently the correct representation of β-naphthol.

b. Allyl ether rearrangement.-This involves a 1,3 shift, and requires a double bond. β-Naphthol allyl ethers easily rearrange to 1-allyl-2-naphthols. The allyl group never rearranges to the (3) position.

Furthermore, if position (1) is filled, rearrangement will not occur. Formulae I and III are indicated.

c. Skraup's reaction.-This reaction requires a double bond in order to proceed. β-Naphthylamine always closes the ring in position (1). If this position is substituted, the reaction will not take place. Formulae I and III are again preferable to II and IV.

2. Reaction of the functional group.

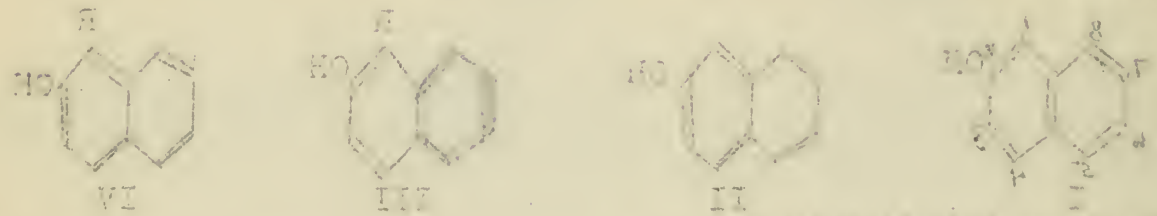
a. Etherification.-Henry's mechanism indicates that the general reaction of esterification requires addition to a double bond followed by a splitting out of water. The replacement of the H by an R group on the double bond involved should retard the reaction. Treatment with methyl alcohol and dry hydrogen chloride resulted in the following reactions:-

| | | |
|---|---|---|
| β-naphthol | ⟶ ether | easily |
| 1-methyl-2-naphthol | ⟶ ether | difficultly |
| 3-methyl-2-naphthol | ⟶ ether | very easily |

L. F. Fieser and W. C. Lothrop
Journal Organic Chemistry
2, No. Chem. Soc., 57, 1935, (1944)

It has long been known that the aromatic reactivity of the naphthalene nucleus are unexplainable on the assumption of a conjugated aromatic ring with localizing bonds. This review indicates that the bonds of naphthalene either have lower or because only in their mobility were in study reactivity or degree of substitution.

Early attention was called to the difference in the behavior of the (1) and the (2) positions of β-naphthol and β-naphthyl amine, i.e., the "ortho" positions. These differences are most easily understandable by a fixed condition of the bonds.



IV III II I

1. Naphthol Substitution

a. Coupling reaction.-All mechanisms require a double bond between the hydroxyl and the ortho position. Diazonium salts couple at (1), indicating formula I rather than II.

1-Alkyl-2-naphthol will not couple. Since IV should couple, III is evidently the correct representation of β-naphthol.

b. Alkyl ether rearrangement.-This involves a 1,3 shift and requires a double bond. β-Naphthol alkyl ethers easily rearrange to 1-alkyl-2-naphthols. The alkyl group never rearranges to the (3) position.

Furthermore, if position (1) is filled, rearrangement will not occur. Formulas I and III are indicated.

c. Bromine reaction.-This reaction requires a double bond in order to proceed. β-Naphthols always direct the ring in position (1). If this position is substituted, the reaction will not take place. Formulas I and III are again preferable to II and IV.

2. Reaction of the Naphthyl group.

a. Isomerization.-Naphthyl carbinols undergo that to remove a mol. H. by acetylation reactions addition to a double bond followed by a splitting out of water. The rearrangement of the H by an R group on the double bond involved should reduce the reaction. Treatment with methyl alcohol and dry hydrogen chloride results in the following reactions:-

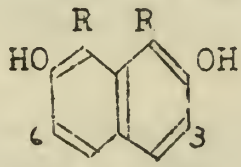
β-naphthol ---- ether ---- resin
1-methyl-β-naphthol ---- ether ---- diffusivity

The two latter reactions indicate that the effect is not ortho steric hindrance, but is rather steric hindrance of the double bond between positions (1) and (2).

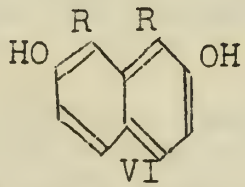
3. Halogenation.-Evidence of the immobility of the double bond.
Treatment of 1-chloro-2-naphthol with bromine results in the formation of a 1-bromo-1-chloro-2-keto derivative with a quininoid structure, rather than the 1,3-dihalogen compound which would be expected if a shift of double bonds could take place.

4. Failure to form 2,3 quinones.-1,2-Dihydroxy-naphthalene forms an ortho quinone, whereas the 2,3 isomer does not. The formation of a quinone from a dihydroxy compound requires a double bond between the hydroxyls.

5. Establishment of the points of unsaturation in the rest of the molecule.




V




VI

Because of the position of the double bonds, V should be incapable of substitution at positions (3) and (6). VI should be substituted at (3).
Actually, the substituted dihydroxy-naphthalenes do not couple with diazonium compounds, nor do their allyl ethers rearrange. This indicates the symetrical formula, V, as the correct one.

6. Ease of reduction of one ring, and the activity of the $\alpha$-position.-The valence claim made on the double bond between the two rings makes one ring less aromatic and more unsaturated, or aliphatic than the other. This would make naphthalene somewhat analagous to a 1,4 conjugated system with both ends connected to the same ring. It should show the reactions of $C_6H_5-CH=CH-CH=CH-C_6H_5$. The 1,4 conjugated positions of this compound correspond to the (1) and (4), or $\alpha$-positions of naphthalene, and account for the ease of reduction, and the reactivity of the $\alpha$-position to halogenation, nitration, and other reactions.

Fries suggests that the tendency for both rings to remain aromatic suppresses oscillation of the bonds.

Reported by Harry H. Weinstock, Jr.
November 9, 1935

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The two latter compounds indicate that the effect is not simply steric hindrance, but is rather a simple interaction of the bulkier ring substituents (2) and (3).

3. Substituents which lower the reactivity of the chromene ring.

The chromenes (4) and (5) have been prepared in the same manner as the quinolinyl analogues, except that the 1-chloroisoquinoline which would have been required for the preparation of (5) could not be obtained.

4. Stability of 2-(2,3,4,5,6-pentachlorophenyl)-1,1-dimethylchromenylium perchlorate (6). The 2,3,4,5,6-pentachlorophenyl group prevents the formation of a quinone from (6). The corresponding 2-phenyl derivative (7) is quite unstable and rapidly decomposes to a dark tar.

5. Effect of the nature of the substituent on the rate of hydrolysis.

Because of the stability of the 2-phenyl compound, it would be impossible to investigate its reactivity (7) as (6). It could be substituted as (8).

Although the substituted 2-phenylchromenylium ion (8) is not stable, which indicates more strongly than (6) the effect of steric interaction, this indicates the conjugated formula, (9), is the major one.

6. Effect of the substituent on the stability of the chromenylium ion.

[illegible]

Thanks are extended for fellowships from Sun Oil Company to [illegible]

Supported by Army [illegible], [illegible].
November 6, 1[illegible]

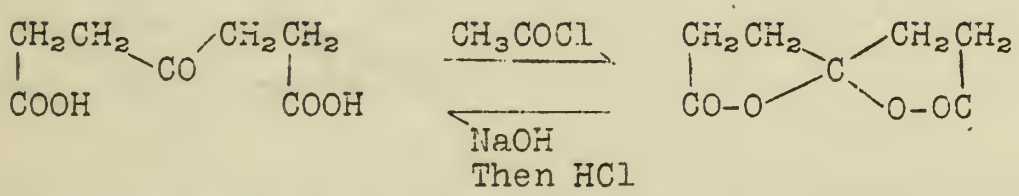
H. Sutter and N. Wijkmann
Ann., 519, 97 (1935)
Chem. Laboratorium der Bayer, Akademie der Wissenschaften, Munich

Previous work:- Sutter - Oxidase, peroxidase
Wijkmann, Compounds formed by molds.

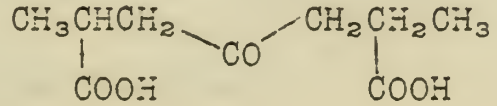
Two substances which can be isolated from mold cultures, $C_{18}H_{20}O_7$ and $C_{12}H_{20}O_6$, are known as glauconic acid I and II, or glauconic acid and glaucanic acid. Glauconic acid on heating undergoes degradation, $C_{18}H_{20}O_7 \longrightarrow C_{11}H_8O_6 + C_7H_{12}O$. $C_7H_{12}O$ has been shown to be $\alpha,\beta$-diethyl acrolein. The other fragment whose constitution is under investigation, is called glauconin.

Glauconin, on treatment with HCl in a sealed tube, yields an acid mixture and a small amount of a neutral substance, $C_9H_{12}O_4$, m.p., 144°. $C_9H_{12}O_4$ reacts with 2 moles of NaOH. When this is neutralized with HCl a dicarboxylic acid is obtained which, on treatment with $CH_3COCl$ regenerates $C_9H_{12}O_4$. The acid mixture, after treatment with $CH_3COCl$, may be fractionally crystallized into three compounds, all with formula $C_9H_{12}O_4$, but m.p. 116°, 126°, 144°. Last is identical with 144° above. 126° and 144° with NaOH and then HCl yield the same dicarboxylic acid, m.p. 140°; 116° yields dicarboxylic acid, m.p. 127°.

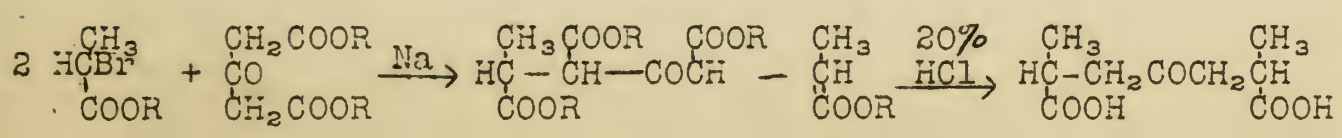
Hydrochelidonic acid, studied by Volhard, has similar reactions.




Its absorption spectra and that of 140° are similar. 140° has 2 $CH_2$ groups more than hydrochelidonic, and since on $HNO_3$ oxidation, pyrotartaric acid is formed, there must be two methyl groups substituted on the hydrochelidonic residue. Absorption spectra studies favor:-




It was synthesized according to the following scheme:-



# On the Constitution of Glycerinic Acid

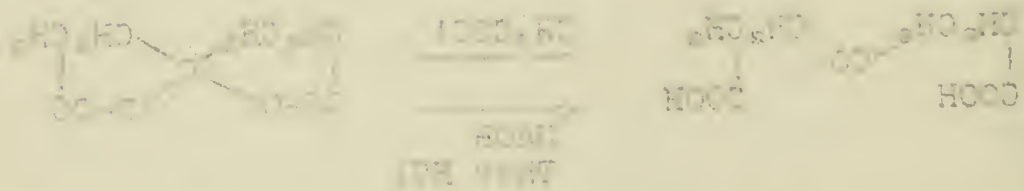
K. Auwers und O. Willemsen
Annal. 419, 97 (1920)
Ebenso. Isomerieverhältnisse der Oxyder. Zeitschrift
für Elektrochemie, 26, 1920

Previous work:- Lutz[1] - Crimmes, Reynolds[2]
Dijkstra, Chemische Ferment by malic.

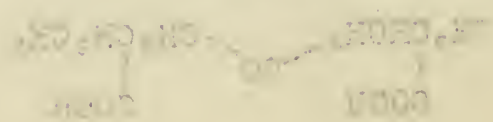
Two substances which can be isolated from malic mixtures, $C_{12}H_{20}O_7$ and $C_{12}H_{20}O_8$, are thought to glycerinic acid I and II or glycerinic acid and glycerinic acid. Glycerinic acid on heating undergoes dehydration, $C_3H_6O_4 \longrightarrow C_3H_4O_3 + H_2O$. $C_6H_{12}O$ has been shown to be glycerinic acid. The other fragment whose constitution is under investigation, is called glycerin.

Glycerin, on treatment with HCl in a sealed tube, yields an acid mixture and a small amount of a neutral substance, $C_6H_{12}O_4$, m.p., 144°. $C_6H_{12}O_4$ reacts with 2 moles of NaOH. When this is neutralized with HCl a crystalline acid is obtained which, on treatment with $CH_3COCl$ regenerates $C_6H_{12}O_4$. The acid mixture, after treatment with $CH_3COCl$, may be fractionally crystallized into three components, all with formula $C_6H_{12}O_4$, but m.p. 112°, 125°, 135°. Lactic is identical with 144° above. 125° and 144° with NaOH and then HCl yield the same dioxybutyric acid, m.p. 120°; 112° yields dioxybutyric acid, m.p. 127°.

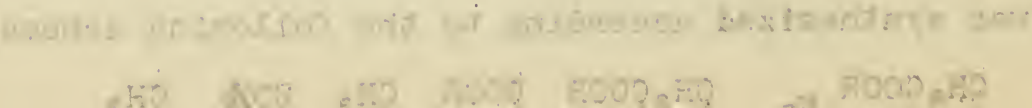
Hydroxybutyric acid, studied by Volhard, has similar reactions.



Its constitution depends the test of 120° was similar. 120° has $CH_3$ groups when hydrogenolysis, not when on $CH_2$ oxidation, corresponding only in terms. There must be the methyl carbon substituents on the hydroxyl-bearing carbon. Absorption spectra studies prove:-

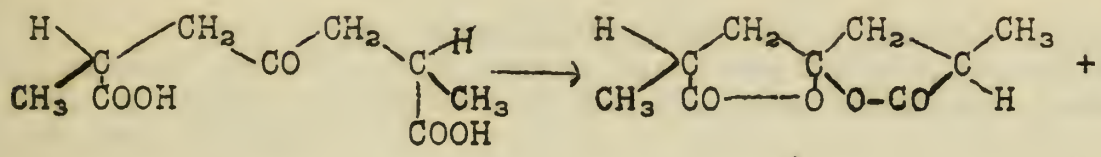


It was synthesized according to the following scheme:-

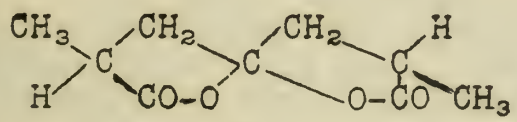


One meso and two active acids are possible, and correspondingly six lactones. 127° is the meso acid; 140° is the racemic.

Meso

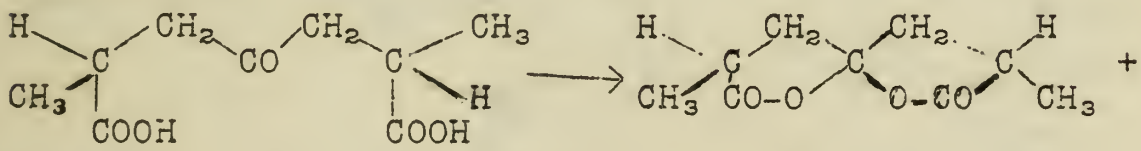


A

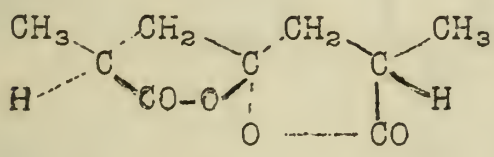


B

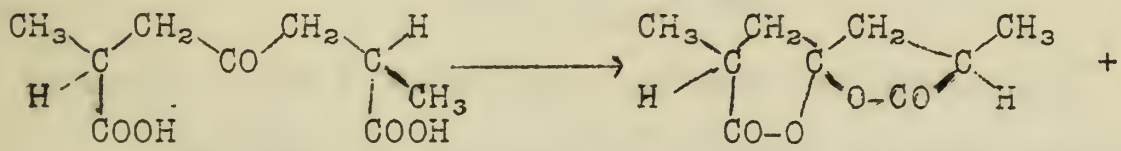
Racemic



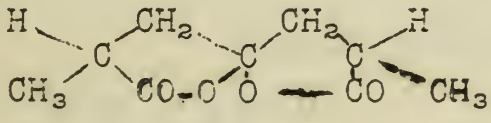
C



D



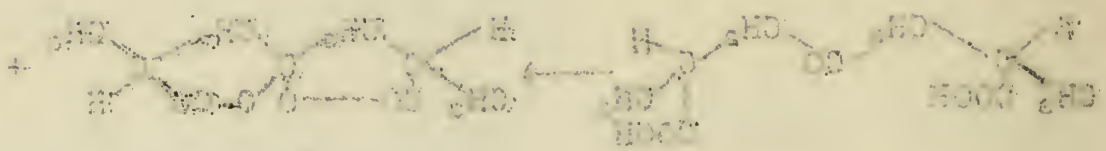
E



F

The three racemate lactones, AB, CD, and EF were prepared and identified with those isolated from glauconin by mixed melting point determinations. No formulae are as yet proposed for glauconin or glauconic acid.

Reported by Lillian H. Meyer
November 13, 1935.



A

B

C

D

E

F

The three primary lactones, A, B, and C were prepared and identified with known lactones from chemists in which decided motor activities. Mr. Cornelius was so put prepared the gluconic or glucuronic acids.

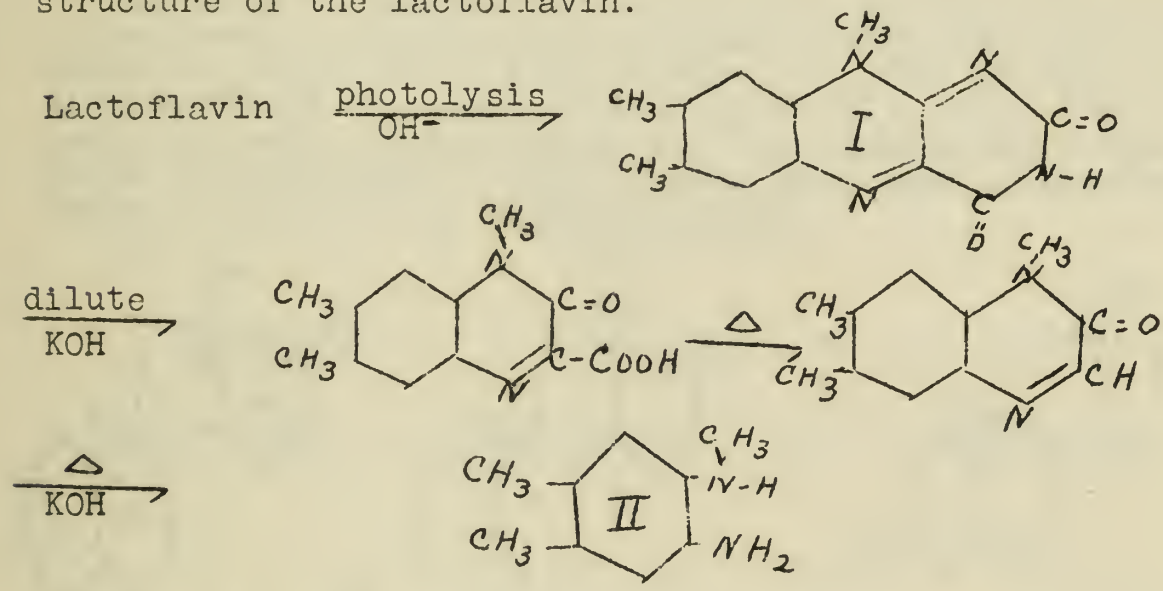
Respectfully, Mr. William E. Dunlap
November 17, 1953.

# Synthesis of Lactoflavin (Vitamin $B_2$)

Richard Kuhn and others
Kaiser-Wilhelm Institute, Heidelberg
Ber., 68, 1768 (1935)

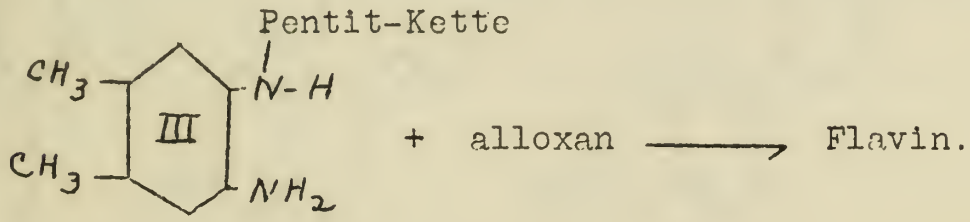
Since 1926, when Goldberger discovered vitamin $B_2$, an enormous amount of research has been undertaken to determine the chemical constitution and the physiological characteristics of the vitamin.

In 1933, the work on chemical structure was given a great impetus by the isolation of pure vitamin $B_2$. The degradation of this pure vitamin gave an insight into the actual structure of the lactoflavin.




Products I and II have been confirmed by synthesis.

In 1934, by condensing III with alloxan both Kuhn and Karrer obtained vitamin-like substances.




The only part of the structure remaining to be established was the configuration of the sugar side-chain (Pentit-Kette). This part was accomplished by the synthesis of 6,7-dimethyl riboflavin which is identical with the natural vitamin in physical, chemical, and physiological properties.

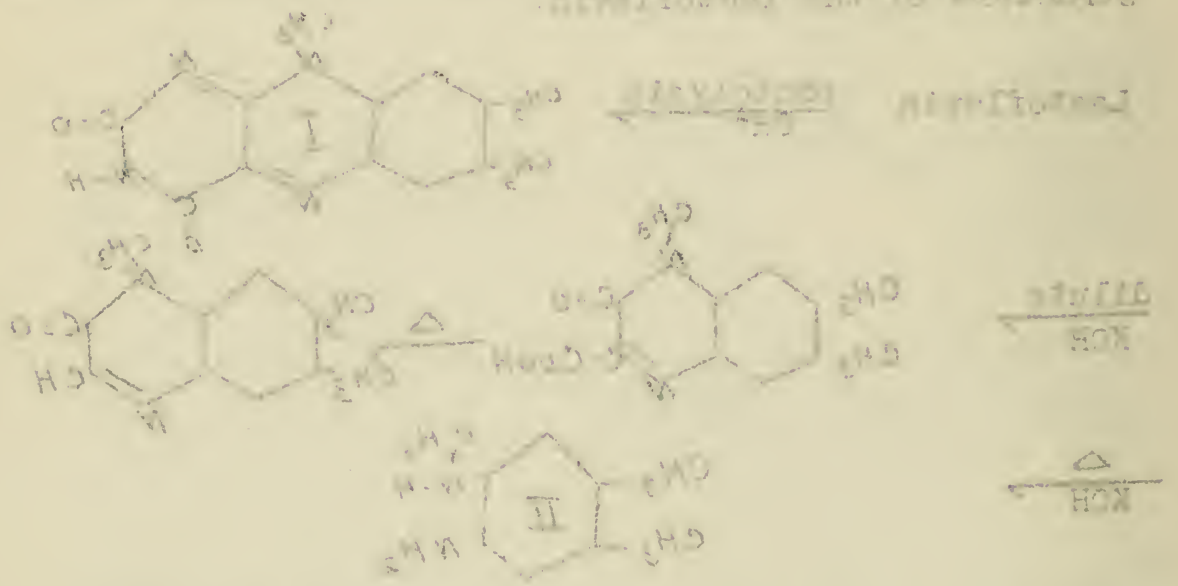
Reported by J. C. Cowan
November 13, 1935

## Synthesis of Lactoflavin (Vitamin $B_2$)

Richard Kuhn and others
Kaiser-Wilhelm Institute, Heidelberg
Ber., 68, 1728 (1935)

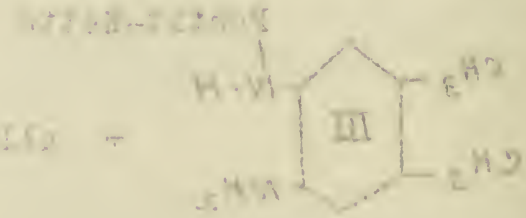
Since 1930, when Goldberger discovered vitamin $B_2$, an enormous amount of research has been devoted to determining the chemical constitution and the physiological characteristics of the vitamin.

In 1932, the work on crystalline adsorbates was given a great impetus by the isolation of pure crystalline $B_2$. The degradation of this pure vitamin gave an insight into the actual structure of the lactoflavin.




Products I and II were both identical to synthetic.

In 1934, by condensing III with ribose, both Kuhn and Karrer obtained vitamin-like substances.



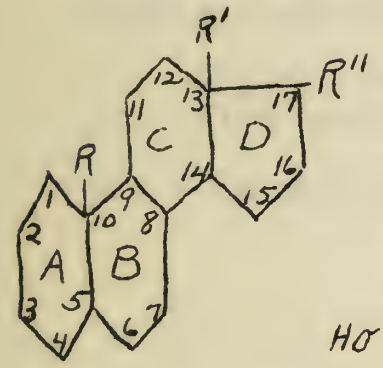

The only part of the structure remaining to be established was the configuration of the ribose. Vitamin $B_2$ was then synthesized. The last was synthesized by the condensation of 3,4-dimethyl-vitamin $B_2$ with the natural vitamin in aqueous, neutral, or alkaline properties.

On the Artificial Preparation of the Testicular Hormone, Testosterone.

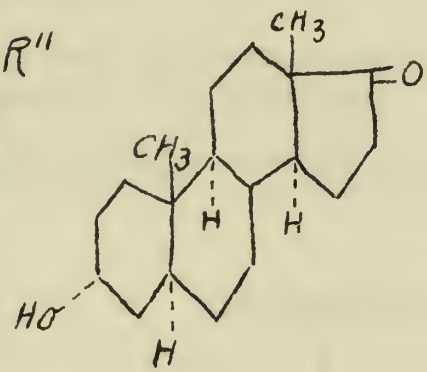
(Androstene-3-one-17-ol)

L. Ruzicka and A. Wettstein
Helv., 18, 1264 (1935)
Zurich, Organisches Chemisches Laboratorium der Eidg. Technisches Hochschule and Basel, Wissenschaftliche Laboratorien der Gesellschaft fur Chemische Industrie, Pharmazeutische Abteilung

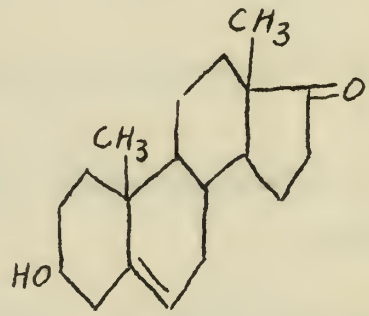
In 1934 L. Ruzicka and assistants oxidized the four stereoisomeric dihydrocholesterols to the corresponding four forms of 3-hydroxy-17-keto-cholane.[1,2] One of these isomers, 3-epi-hydroxy-etio-allo-cholanone-17 (II), they found to be identical with the purified male sex hormone extracted from urine by Butenandt.[3] This hormone was named androsterone. Chromic acid was the oxidizing agent.



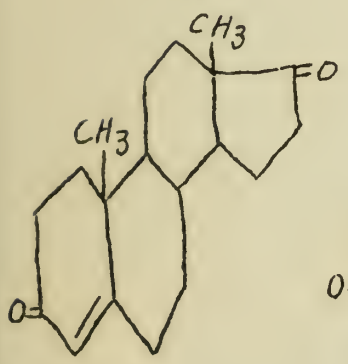

I



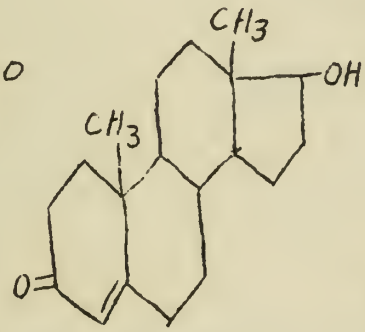

II



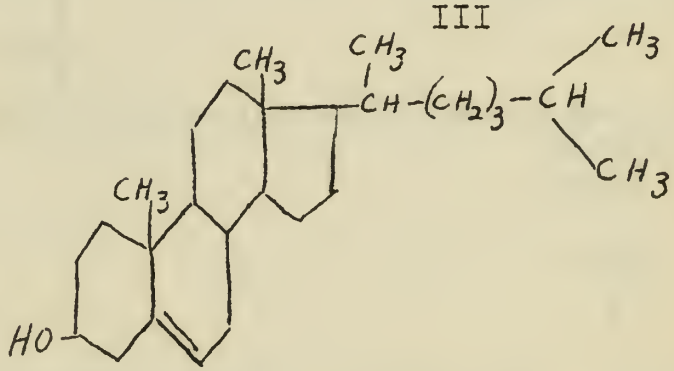

III




IV




V




VI (Cholesterol)

I is the type formula of the cholane group with the numbering system.

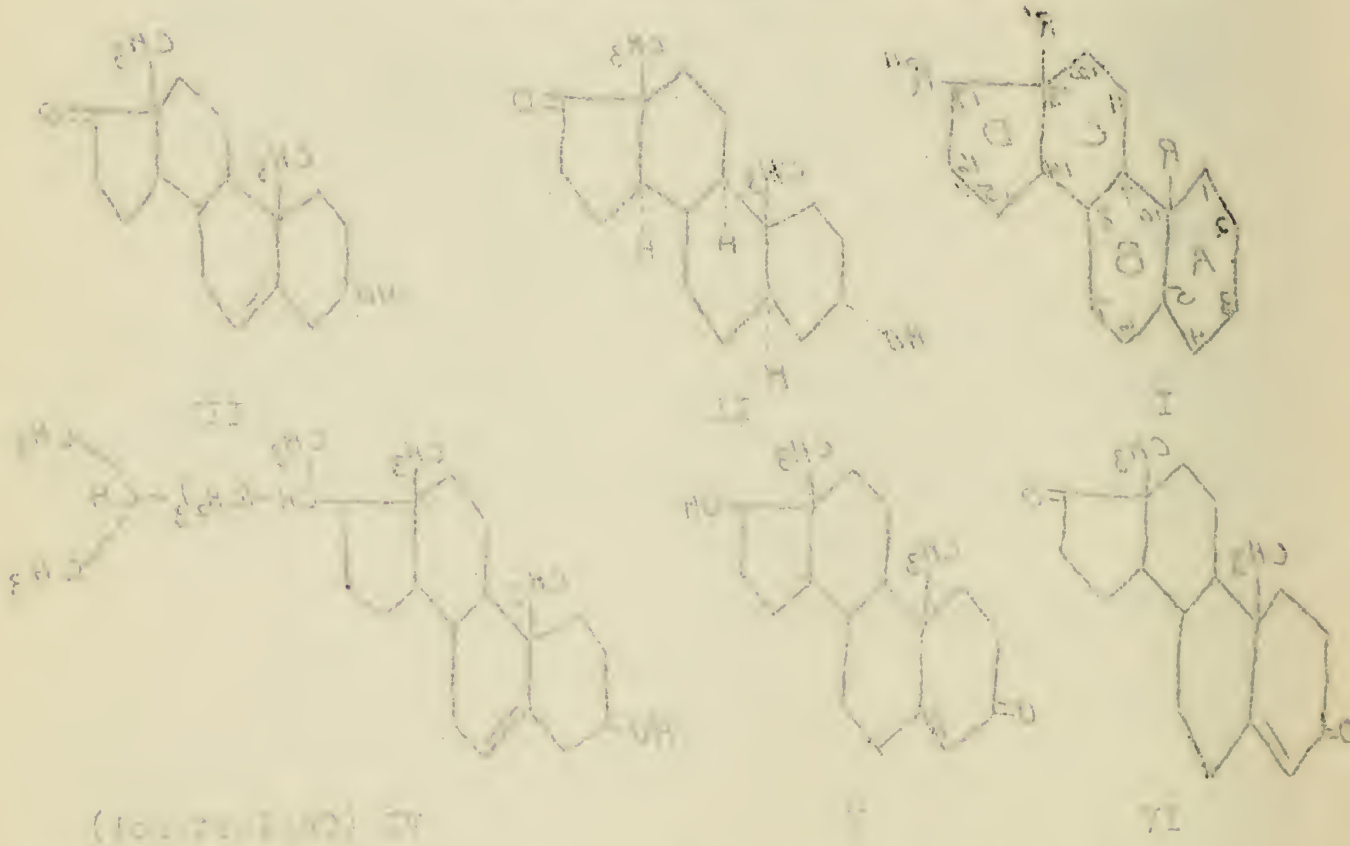
In July 1935 Ruzicka and A. Wettstein reported the oxidation of cholesterol to trans-dehydro-androsteron (III), protecting the hydroxyl group and double bond from oxidation

On the Artificial Preparation of the Testicular Hormone, Testosterone.

(Androstane-3-one-17-ol)

L. Ruzicka and A. Wettstein
Helv. 19, 1264 (1936).
Ibid. Organisches Chemisches Laboratorium der ETH. Technische Hochschule zu Zürich, Wissenschaftliche Informationen für Qualitätsarbeit für Chemische Industrie. Dreizehnte Ausgabe, Abteilung

In 1934 L. Ruzicka and Wettstein obtained the same androsterone dihydrotestosterone prior to the corresponding form of 3-hydroxy-17-keto-androstane.[1,2] One of the isomers 3-epi-hydroxy-androstane-17-androstanolone (II), they found to be identical with the product obtained by the hydrogenation of androsterone by Butenandt.[3] This hormone was prepared from androsterone. Chromic acid was the oxidation agent.



I

II

III

IV

V (androsterone)

I is the male hormone. It is an active agent with the androgenic action.

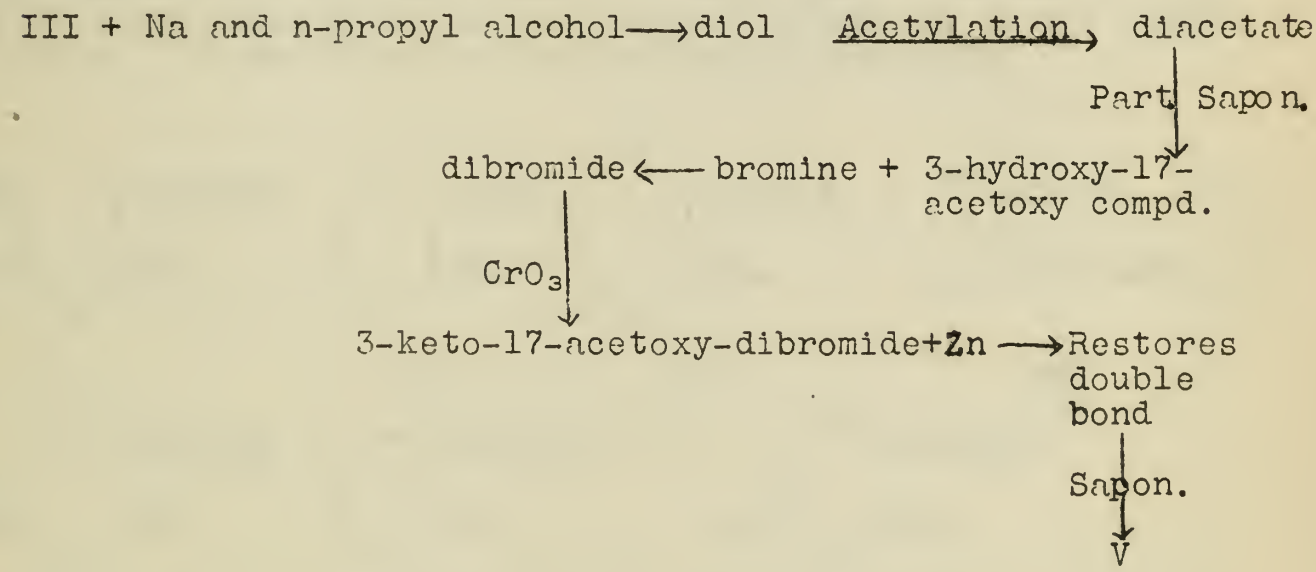
In July 1937 Ruzicka and A. Wettstein discovered the oxidation of androsterone to androstane-dione-androsterone (III), producing the androgenic group. It results from oxidation

by acetylation and addition of bromine.[4] III was found to be physiologically active by the capon comb growth test and was identified as the unsaturated hydroxy-ketone, $C_{19}H_{28}O$, isolated by Butenandt and Dannenbaum from urine.[5]

III was oxidized further to androstene-dione (IV), which was a little less active in the capon comb growth test than was androsterone itself.

From the observation that a sample of testicular extract concentrate was much more active in rat tests than was a sample of urine extract concentrate of equal activity in the capon comb growth test, Ruzicka reasoned that testicular extracts must contain a hormone more active in the rat test than either androsterone or trans-dehydro-androsterone, which were the only active compounds extracted from urine. Furthermore, the hormone activity of the testicular extracts could be destroyed by treatment with alkali which is not the case with urine extracts, since androsterone and trans-dehydro-androsterone are alkali stable. Ruzicka postulated that this alkali unstable hormone must be an $\alpha,\beta$-unsaturated ketone identical with IV or with 3-keto-17-hydroxy-androstene (V).

Ruzicka and Wettstein succeeded in preparing V by the following series of reactions:




V was identified by means of m.p., mixed m.p., absorption band, m.p. of derivatives, and hormone activity as testosterone found by various workers in testicular extracts.

1. Helv., 17, 1389, (1934)
2. Helv., 17, 1395, (1934)
3. Naturwissenschaften, 21, 54, (1933)
4. Helv., 18, 986, (1935)
5. Z. Phys. Chem., 229, 192, (1934)

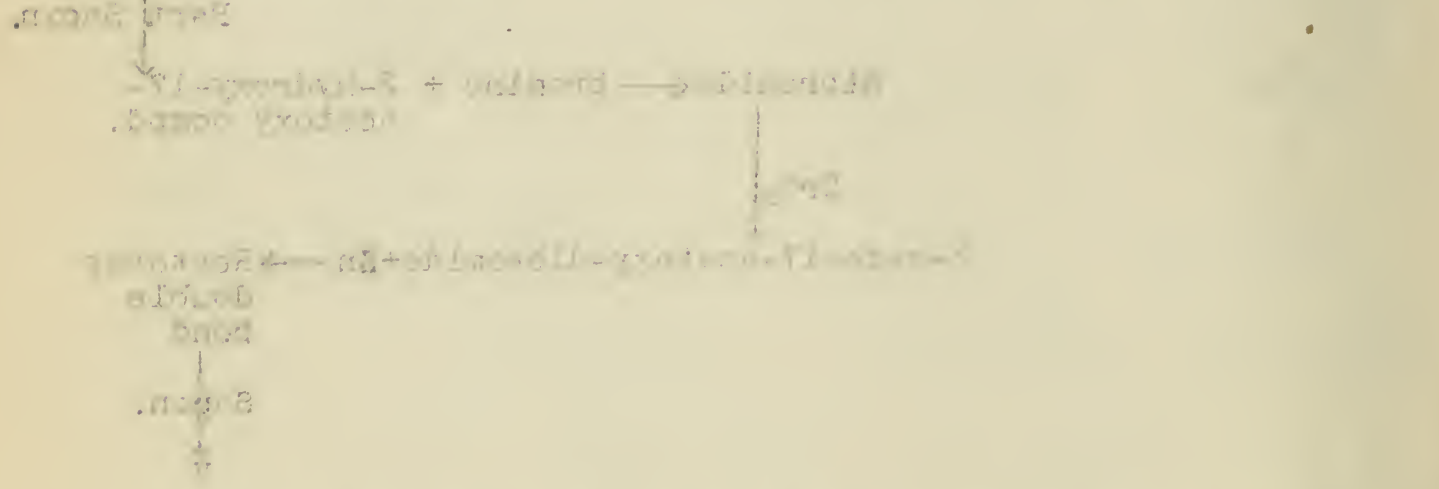
Reported by G. A. Nesty
November 20, 1935

by acetylation and addition of bromine.* III was found to be physiologically active by the capon comb growth test and was identified as the unsaturated hydroxy-ketone, $C_{18}H_{30}O$, isolated by Butenandt and Dannenberg from urine.[5]

III was oxidized further to androstane-dione (IV), which was a little less active in the capon comb growth test than was androsterone itself.

From the observation that a sample of testicular extract somewhat more than twice as active in rat tests than was a sample of urine extract corresponds to of equal activity in the capon comb growth test, Ruzicka concluded that testicular extracts must contain a hormone more active in the rat test than either androsterone or trans-dehydro-androsterone, which were the only active hormones extracted from urine. Furthermore, the hormone activity of the testicular extracts could be destroyed by treatment with alkali which is not the case with urine extracts, since androsterone and trans-dehydro-androsterone are alkali stable. Ruzicka postulated that this alkali unstable hormone must be an α,β-unsaturated ketone identical with IV or with 3-keto-17-hydroxy-androstane (V).

Ruzicka and Wettstein succeeded in preparing V by the following series of reactions:




* See literature on group of $C_{19}$, mixed $C_{19}$, Adrenocortical Hor., of Zimmermann, and Reichstein relativity to Kendall from Ruzicka's review in Vestnik extracts.

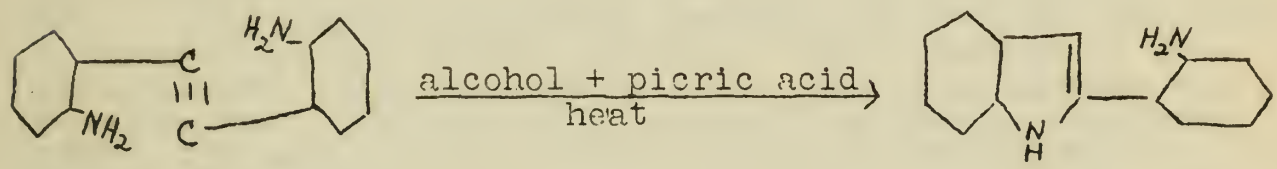
1. Ruz., Helv. Chim. (1934)
2. Wett., Ibid. (1934)
3. Ruzicka-Wettstein, Helv. (1937)
4. Butz., Ber. (1934)
5. Z. Phys. Chem. 229, 99. (1934)

Discovered by G. A. Hardy
November 20, 1935

Rearrangement respectively of o-aminated Tolans and Stilbenes into Derivatives of Indol and Indolin. Also Concerning the Aminated Double Stilbenes.

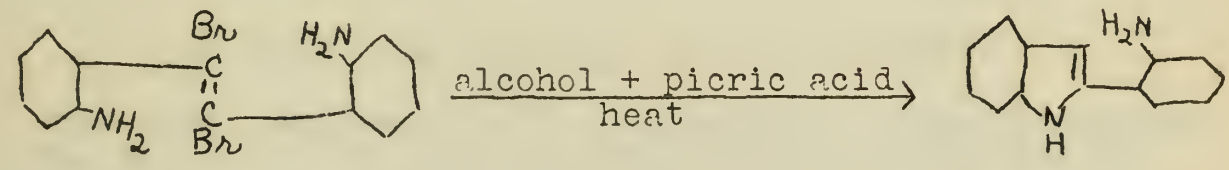
Ruggli and Schmidt, Helv., 18, 1215-1229(1935)
University of Basel

Previously Ruggli had observed that o,o'-diamino-tolan rearranged into 2-(o-aminophenyl)-indol when heated with alcoholic picric acid solution.

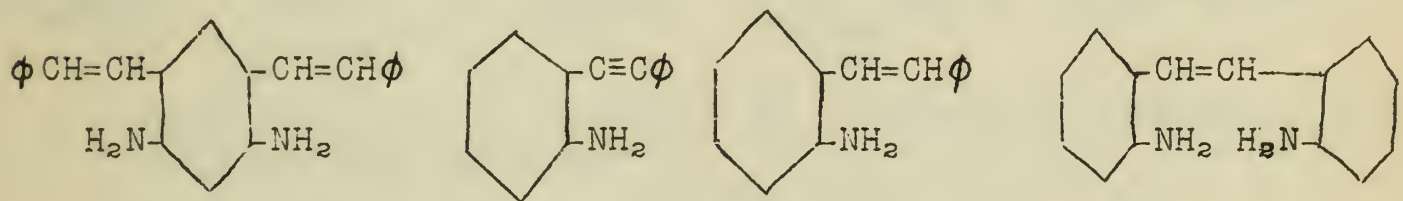



I II

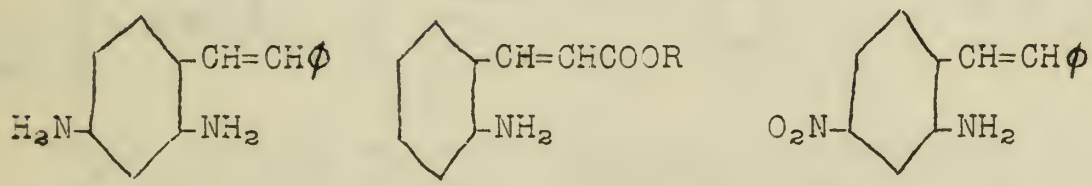
and



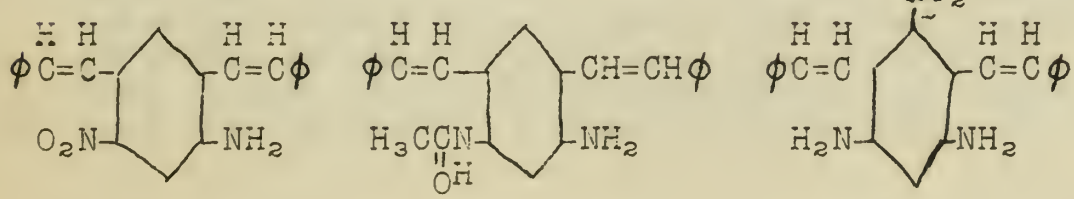

The purpose of this work was to investigate the use of this mild ring-closing medium for further syntheses in the indole series. It was tried on the following compounds:



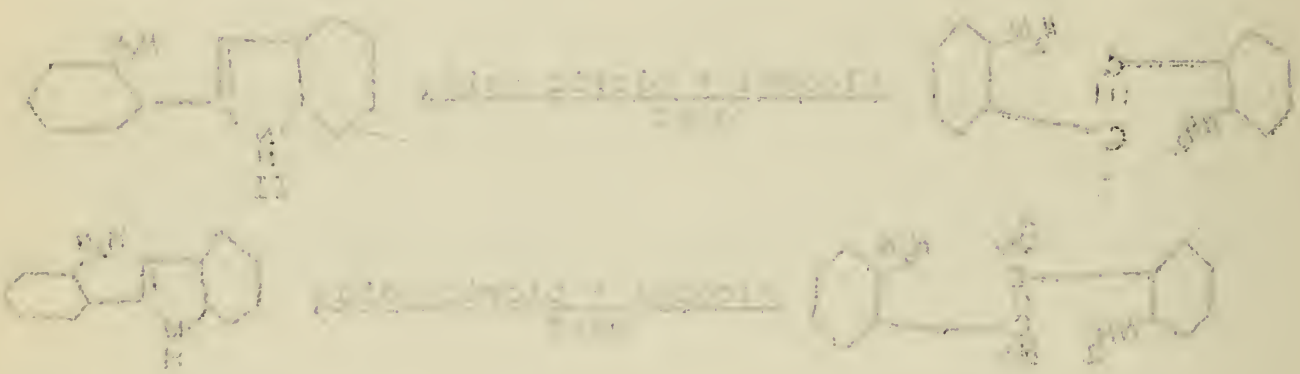
V XIII XIV XV



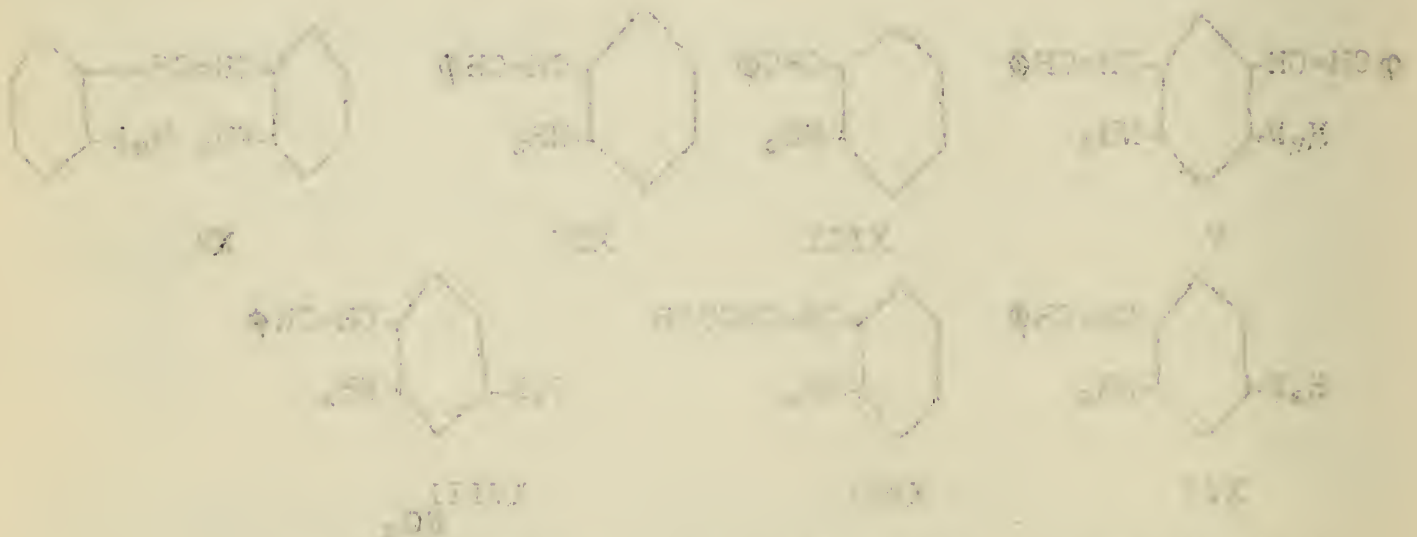
XVI XVII XVIII

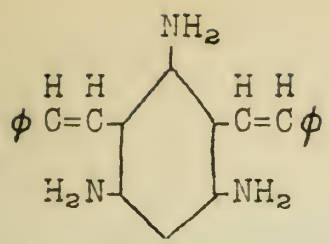


XIX XX XXI

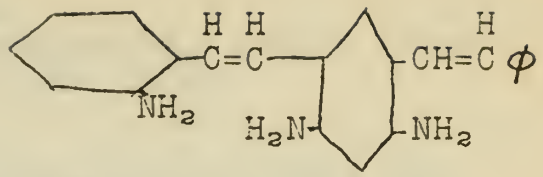


The synthesis of this ring system by a modification of the use of this ring-closing method by Dodge appears in the Dodge thesis. It is taken on the following compounds:





XXII

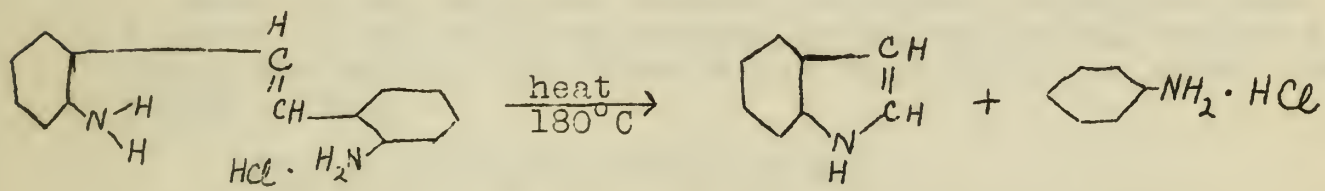


XXIII

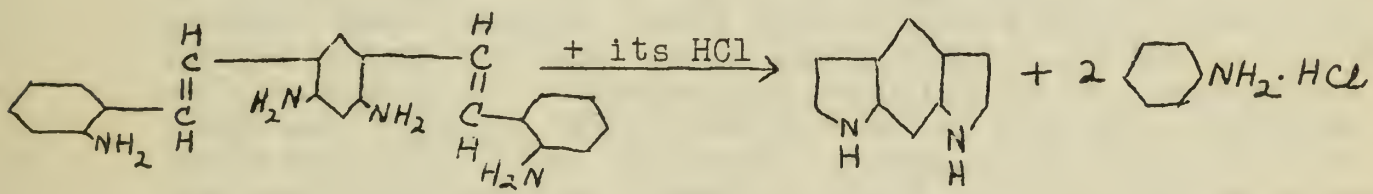
A rearrangement was obtained only with the compounds V and XVI. 1,3-distyrl-4,6-diamino benzene (V) gave the expected 1-phenyl-5-styryl-6-amino indolin. The structure of this indolin derivative was established. The same indolin derivative was obtained in the case of 2,4-diamino-stilbene (XVI). No explanation for its formation was offered.

## Concerning the Aminated Double Stilbenes

The indol synthesis of J. Thiele and O. Dimroth depends on the fact that dry o,o'-diamino-stilbene mixed with an equivalent amount of its dry dihydrochloride with heating decomposes as follows:



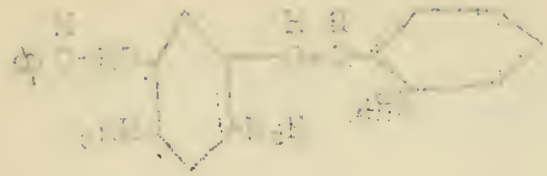

Using this type of synthesis the authors had intended to try the following synthesis:



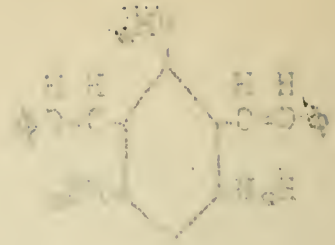

This starting material could not be prepared. The synthesis of the double stilbene was tried starting with 1,3-distyryl-4,6-diamino benzene. In this case two molecules of benzene must split out instead of two molecules of aniline. A new amine was formed but not the desired double stilbene. The structure of the new amine was not established. This type of ring closure was tried on several similar compounds, but in no case was the desired double stilbene obtained.

Reported by J. M. Cross
November 20, 1935.

UNIVERSITY OF ILLINOIS
LIBRARY-CHEMISTRY



XVIII



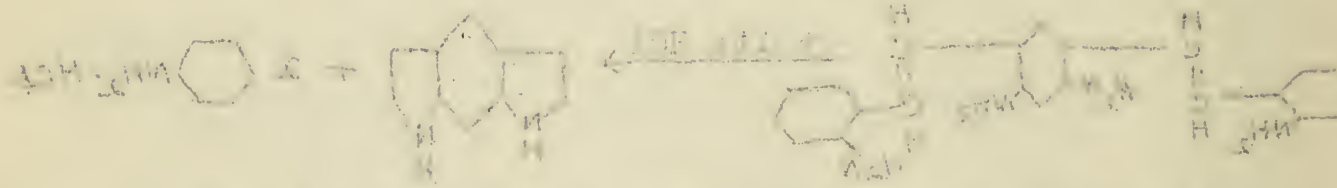
XVIX

A quantity of each was obtained only from the compounds V and XVI. 6,7-Dihydro-4,9-dimethyl benzene (V) was the product of 1-ethyl-2-vinyl-3-methyl indole. The structure of this indole derivative was established. The case indole derivative was obtained in the case of 1,4-butadiene-addition (XVI). No explanation for the formation was offered.

## Considering the Activated Double Addition

The final experiments of J. Thiele and J. Dimroth appear on the first sight very p,p'-dialkyl-stilbene-diline with an equivalent amount of its dry alkylhydrohalide with heating occurrence as follows.

Using this type of synthesis the authors had intended to try the following synthesis:



This starting material could not be prepared. The synthesis of the double addition was total starting with 1,5-dialkyl-1,5-triazo pentane. In this case two molecules of benzene must split out instead of two molecules of aniline. A new method was tried but not the desired double addition. The formation of the new ring was not established. This type of ring closure was tried on several similar compounds, but in no case was the desired double addition obtained.

Imported by J. H. Orrs
November 20, 1955.

# The Reaction of Hydroxymethylene Ketones with Grignard Reagents

Robert E. Meyer
Anstalt für Anorganische Chemie, Basel
Helv., 18, 461-473 (1935)

In a search for a method of synthesizing citral and similar naturally-occurring $\alpha, \beta$-unsaturated aldehydes, the author investigated the following possibility:

$$R\text{-}CO\text{-}CH_2R' + HCOOEt \xrightarrow{NaOEt} R\text{-}CO\text{-}CR'{=}CHOH \xrightarrow{R''MgX}$$

$$R\text{-}CR''(OH)\text{-}CR'{=}CHOH \longrightarrow R\text{-}CR''(OH)\text{-}CHR'\text{-}CHO$$

$$\xrightarrow{-H_2O} R\text{-}CR''{=}CR'\text{-}CHO$$

The possibility of 1,4-addition of the Grignard to the hydroxymethylene ketone was also considered, in which case such a series of reactions would not lead to the desired products, but an $\alpha, \beta$-unsaturated ketone.

$$R\text{-}CO\text{-}CR'{=}CHOH \xrightarrow{R''MgX} R\text{-}C(OH){=}CR'\text{-}CHR''OH \longrightarrow$$

$$R\text{-}CO\text{-}CHR'\text{-}CHR''OH \xrightarrow{-H_2O} R\text{-}CO\text{-}CR'{=}CHR''$$

Most of the work was carried out with 2-methyl-hepten-2-one-6 as the starting ketone and $CH_3MgI$ as the Grignard, since the desired reactions would then lead to a known compound, citral.

$$(CH_3)_2C{=}CH\text{-}CH_2CH_2\text{-}C(CH_3){=}CH\text{-}CHO$$

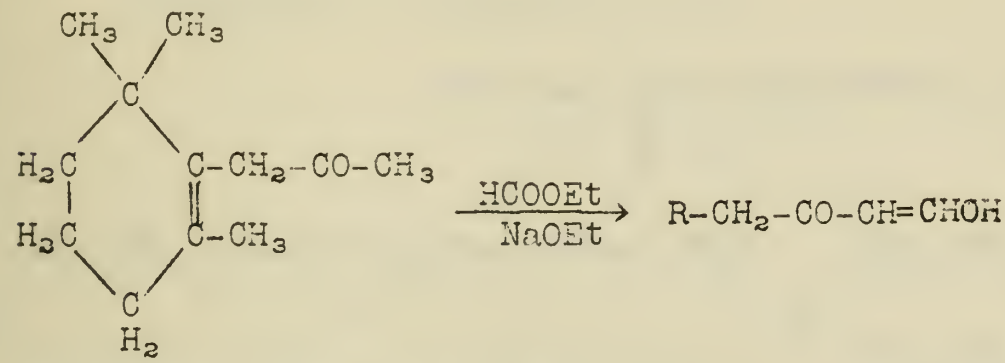
The author was unable to obtain the hydroxycarbonyl compound in a pure form or any crystalline derivative. The crude product gave aldehyde tests with Schiff's and Tollen's reagents and on heating formed acetaldehyde and the original methyl heptenone. Dehydration resulted in an unsaturated compound, $C_{10}H_{16}O$, which was not citral but gave aldehyde tests with the above reagents. Permanganate oxidation of the partially reduced compound, $C_{10}H_{18}O$, obtained by starting with methyl heptanone, gave methyl caproic acid. This indicated $(CH_3)_2C{=}CH\text{-}CH_2\text{-}CH_2\text{-}CO\text{-}CH{=}CH\text{-}CH_3$ as the formula of $C_{10}H_{16}O$.

In an attempt to account for the formation of acetaldehyde and methyl heptenone, a study was made of the hydrolytic cleavage of double bonds which are conjugated with carbonyls. These cleavage products were formed from the hydroxycarbonyl compound both on heating and on treatment with 10 per cent $K_2CO_3$ solution. It was found that the $\alpha, \beta$-unsaturated ketone also formed these products on alkaline hydrolysis.

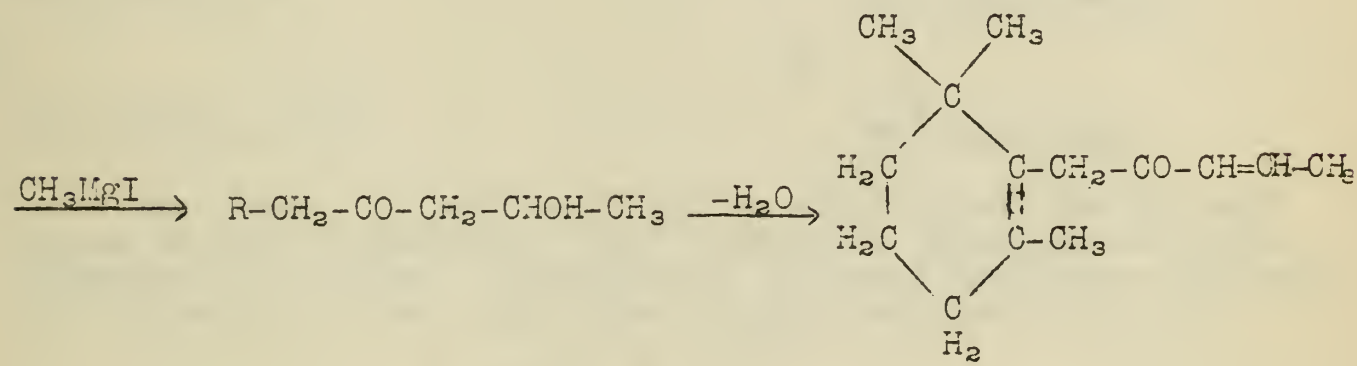
The final proof of 1,4-addition of the Grignard was the fact that alkaline hydrolysis of the hydroxycarbonyl compound

formed by the action of $C_2H_5MgBr$ on hydroxymethylene methyl heptanone resulted in the formation of methyl heptanone with no trace of a higher ketone.

The synthesis of $\alpha$, $\beta$-unsaturated aldehydes was thus shown to be impossible by the method investigated. This method was nevertheless found useful in the synthesis of an isomer of irone:




Cyclogeranyl-methyl-ketone




2',6',6'-trimethylcyclohexene-1-yl-1-pentene-3-one-2

Reported by P. S. Pinkney
November 25, 1935.

UNIVERSITY OF ILLINOIS
LIBRARY-URBANA

formed by the action of $C_6H_5ONa$ on hydroxymethylene-methyl heptanone resulted in the formation of methyl heptenone with the loss of a hydroxy group.

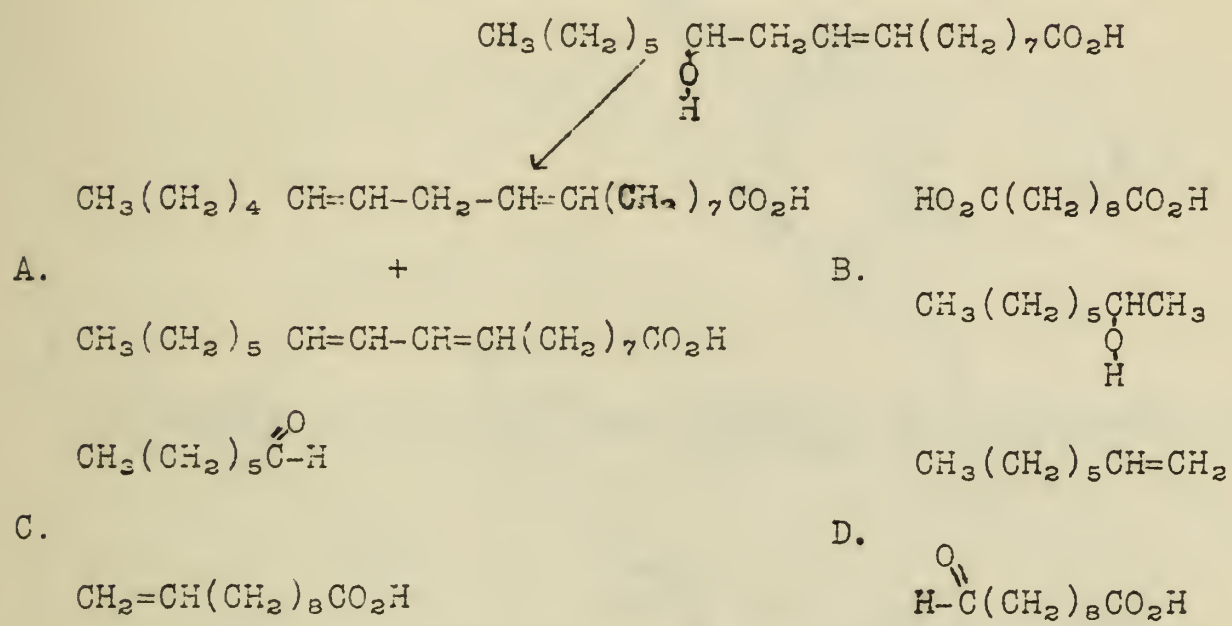
The synthesis of 4, 5-dimethyl-2-cyclohexenone was then shown to be impossible by the method investigated. This defect was corrected from benzal in the synthesis of 4-methyl-2-cyclopentenyl-ethyl-ketone.

# Existence of a $\beta$-Epoxy Tautomerism in the Degradation Reactions of Certain Organic Compounds

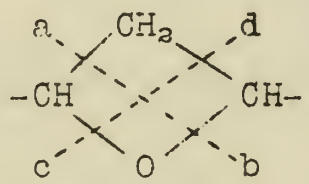
A. Barbot
Bull. Soc. Chim., 2, 895 (1935)
Bull. Soc. Chim., 2, 1438 (1935)

Institut de Chimie de Paris

Reactions of ricinoleic acid:




The theory is proposed that by addition of the hydroxyl group to the neighboring $\diagdown C{=}C \diagup$ linkage a trimethylene oxide structure is formed. Reactions B, C, and D are then explained by a fission of the ring either along the line ab or cd.




Evidence is offered for the plausibility of the assumption that this ring is formed.

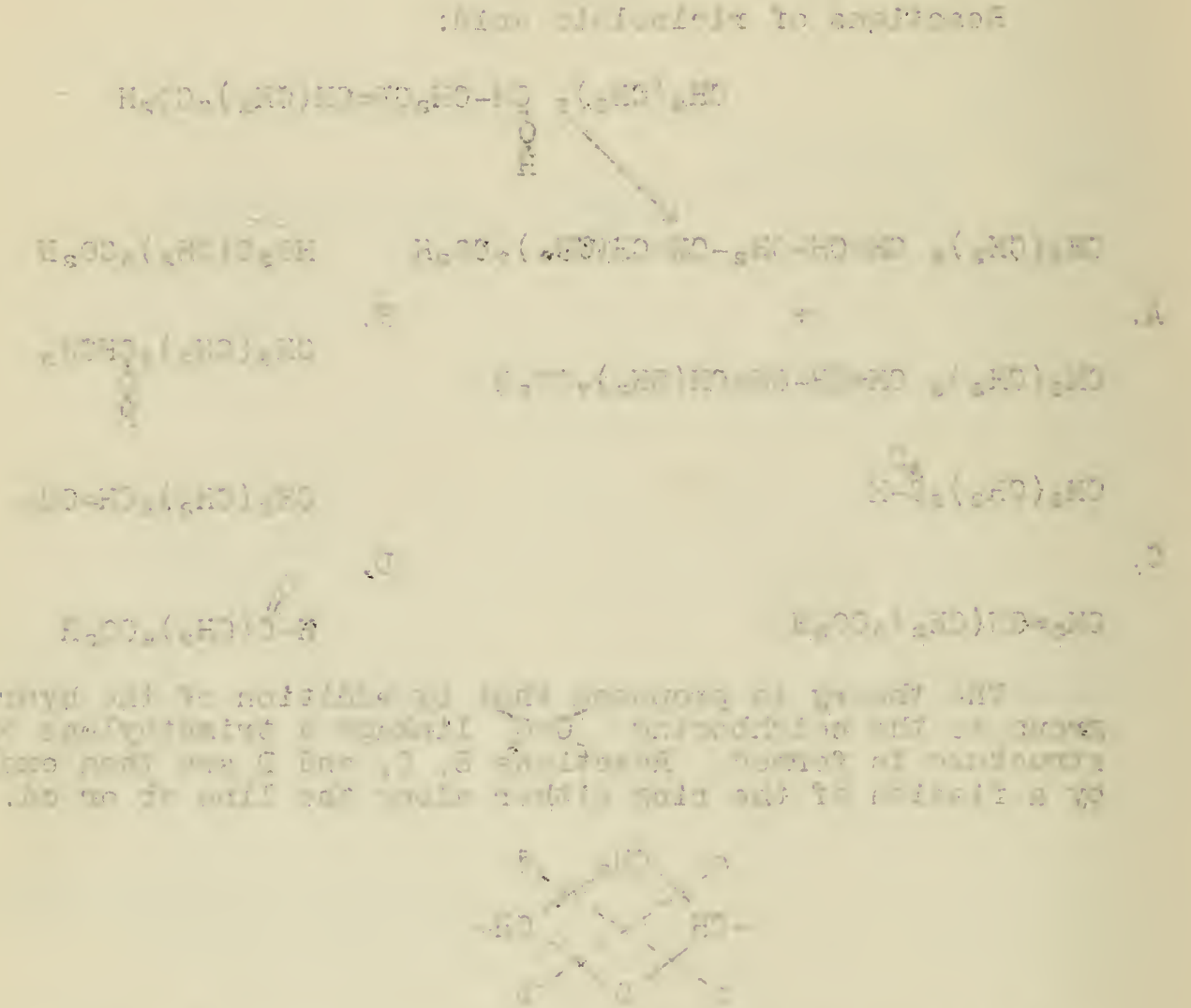
A similar mechanism will explain a large number of other degradations, the requisite functional groups being a hydroxyl group, alcoholic, enolic, or acidic, and an unsaturated linkage between the gamma and delta atoms.

Reactions of a β-Keto Dialkylamide in the Decomposition Sequence of Dialkyl Phosphite Enolates

J. Sorbet
Bull. Soc. Chim., 2, 396 (1969)
Bull. Soc. Chim., 10, 3458 (1970)

Institut de Chimie de Paris

Reactions of primary amide:



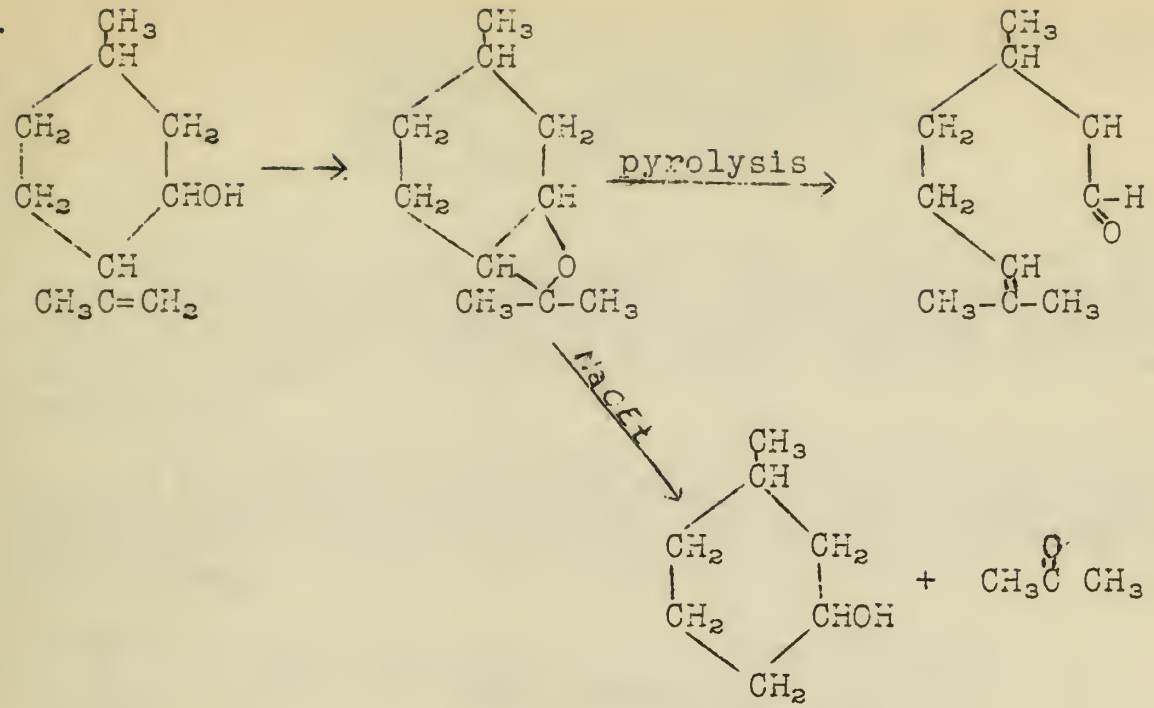
The theory is proposed that the addition of the dynamical enone in the α-hydroxyl. Cyclo. Indicate a tritetrahydra ketal formation in former. Reactions B, C, and D are then explained by a fission of the bond (after enlarge the line ab or ac).



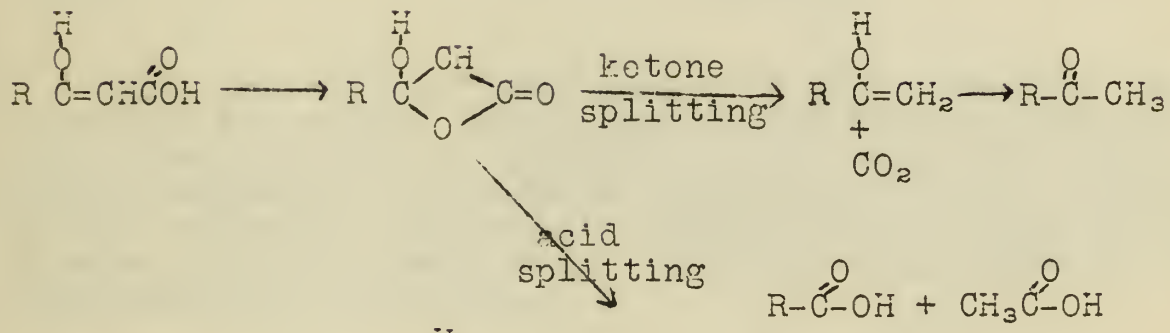
Evidence is offered for the generality of the reaction that this rule is based.

A similar mechanism will explain a large number of other transformations. The inductive structural effects being a hydroxyl group, alkoxyl, amino, or acetic, and on substituent (ish-ion or screen the group, and data items).

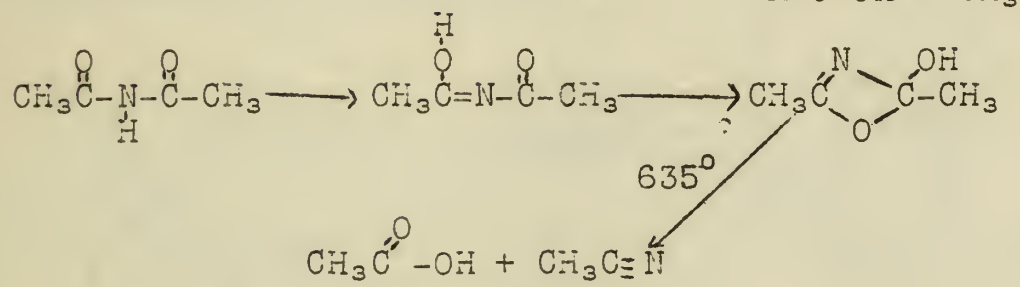
1.



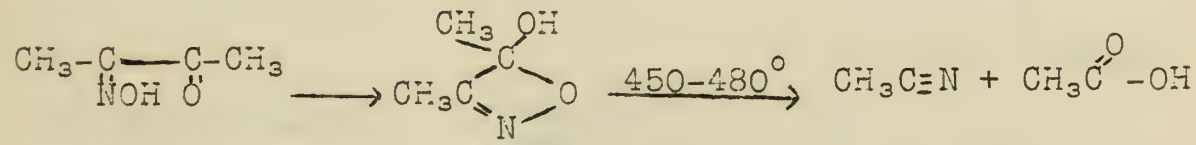

2.



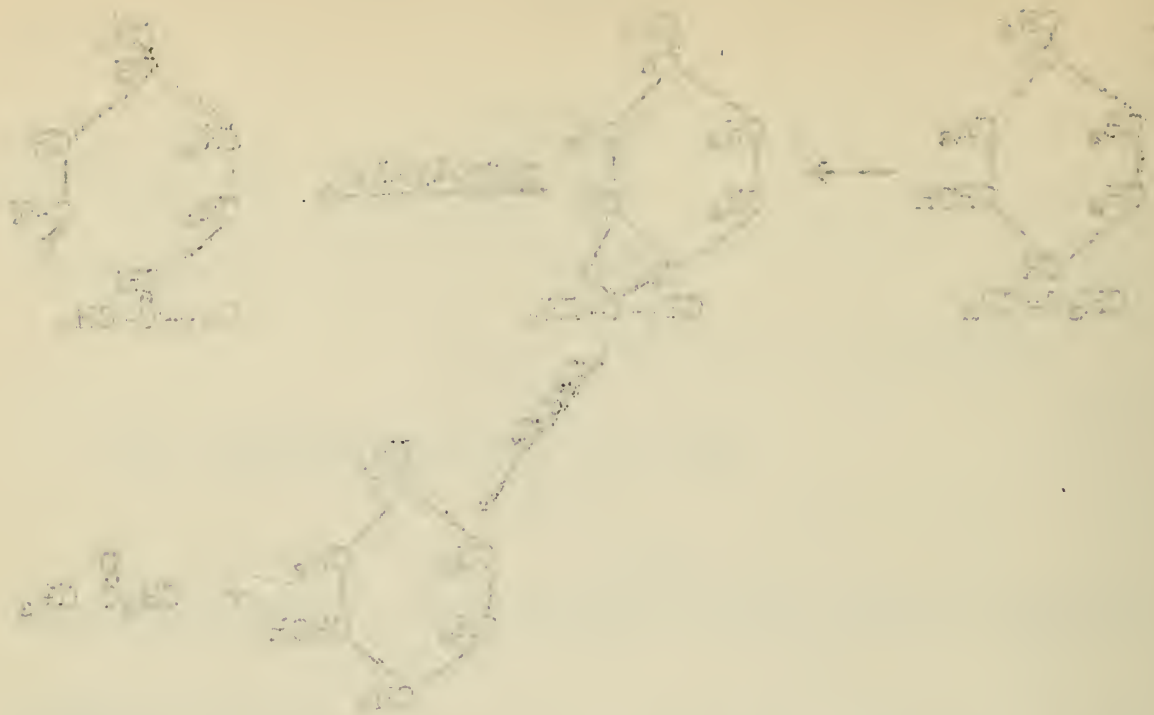

3.

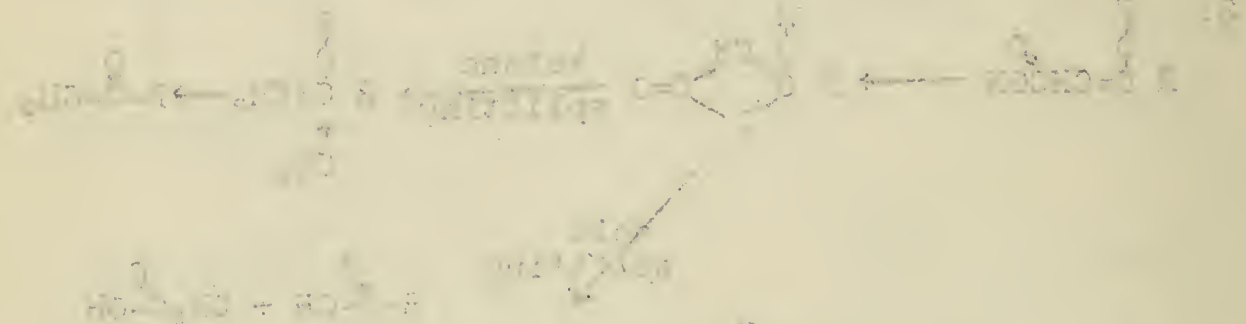



4.




Reported by William Fessler
November 27, 1935.



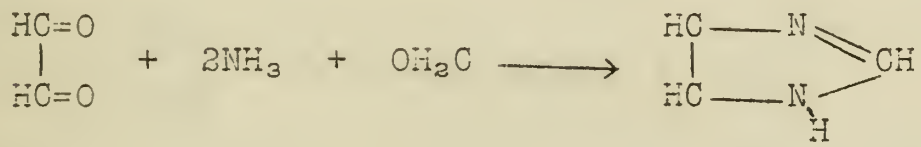


Reproduced by Western Reserve University
Microfilm 1964.

Weidenhagen and Herrmann.
Biochem. Abteil. d. Instituts für Zucker - Industrie, Laudwirtschfte.
Abteil. d. Universität Berlin.
Ber., 68, 1953 (1935)

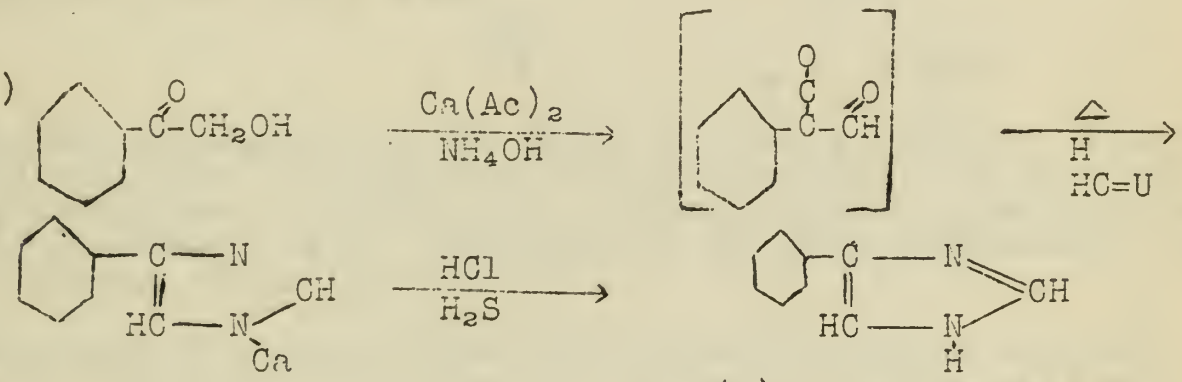
For a long time biochemists have attempted to synthesize imidazoles in large quantities. During the past fifty years several synthetic methods have been developed, but none of them is a simple and smooth reaction. The yield in every case is low.

A new synthesis of imidazoles was worked out by the authors based on the previous work of Radziszewski who synthesized imidazol from glyoxal, ammonia and formaldehyde as follows:



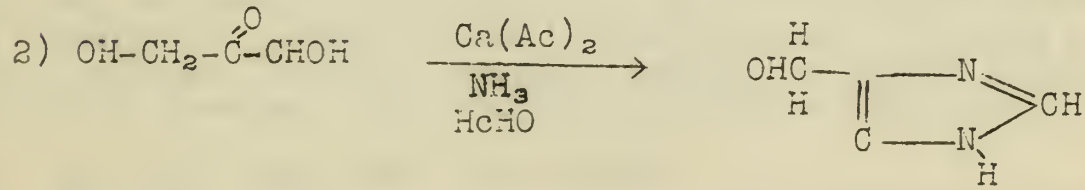
The limitation of this method is that diketones are difficult to obtain. The authors found that 1,2-oxyketone or 1,2-oxyaldehyde, in the presence of ammoniacal cupric acetate solution, is oxidized immediately to the 1,2-diketone. In the presence of aromatic or aliphatic aldehyde, the ring closure proceeds immediately. The following examples will illustrate the reactions.--

1)



4(5)-phenylimidazol.

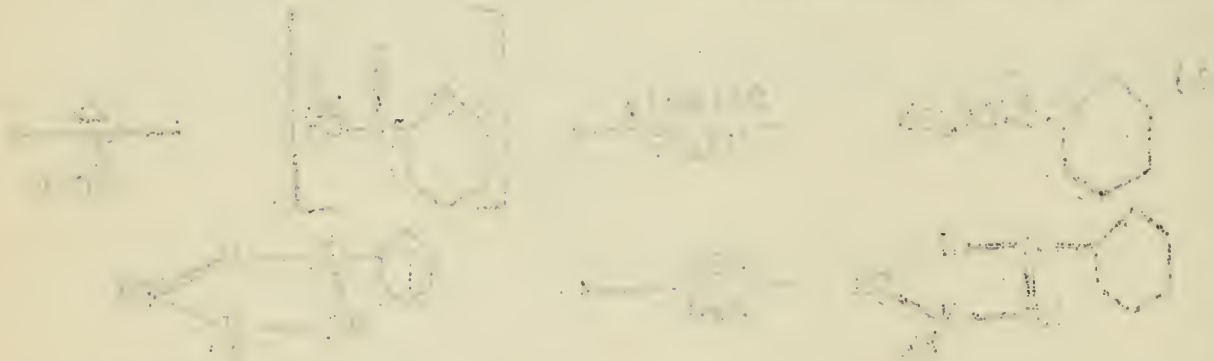
2)



4(5)-oxy-methylimidazole

Fifteen substituted imidazols were prepared. Most of the reactions are smooth and some of the yields are as high as ninety per cent.

Reported by Chi I. Hsing
December 4, 1935



# The Mechanism of the Reactions between Diacylperoxides and other Organic Substances. Their Thermal Decomposition.

P. H. Hermans, Rec. trav. chim., 54, 760 (1935)
Breda Laborat. der Hollandische Kunstzyde Industrie.
Previous work: Acylperoxides.

A new scheme to explain the various reactions of diacylperoxides is formulated by the author, replacing an older one advanced in 1926.

Diacylperoxides can react in any of the following ways:

A. $\begin{matrix} RCOO \\ | \\ RCOO \end{matrix} \longrightarrow R\text{-}R + 2CO_2$

B. $\begin{matrix} \phi COO \\ | \\ RCOO \end{matrix} \longrightarrow RC_6H_4COOH + CO_2$

C. $\begin{matrix} RCOO \\ | \\ RCOO \end{matrix} \longrightarrow RCOOR + CO_2$

D. $\begin{matrix} RCOO \\ | \\ RCOO \end{matrix} + R'H \rightarrow \begin{matrix} R'COO \\ RCOO \end{matrix} \longrightarrow$ A, B or C. $+ RH$ ; $\begin{matrix} RCOO \\ RCOO \end{matrix} + R\text{-}R'$ ; $\begin{matrix} RCOO \\ HCOO \end{matrix} \longrightarrow$ A, B or C.

Thermal decomposition can cause reaction A, B or C. Aliphatic peroxides react preferentially according to A when thermally decomposed. Aromatic and aromatic-aliphatic peroxides can react according to A or, depending on the particular nature of the R groups, according to B or C.

Reactions of acylperoxides with other substances follow D. There is a possibility of two new peroxides being formed which, in turn, can react according to A, B or C. The term R'H in D is not limited to a hydrocarbon. Reactions were studied where R'H was an alcohol, a base, an alkyl halide, a cyclic saturated hydrocarbon, benzene, substituted benzenes and an aliphatic acid.

Ber., 58, 287, 476, 765, 770 (1925)
Ber., 59, 664 (1926)
J. Am. Chem. Soc., 27, 161 (1905)
Rec. trav. chim., 46, 72 (1927)
Rec. trav. chim., 48, 933 (1929)
Rec. trav. chim., 49, 102 (1930)
Ann., 513, 105 (1934)

Reported by W. E. Ross
December 4, 1935

# The Structure of Oestrin, Equilin and Equilenin

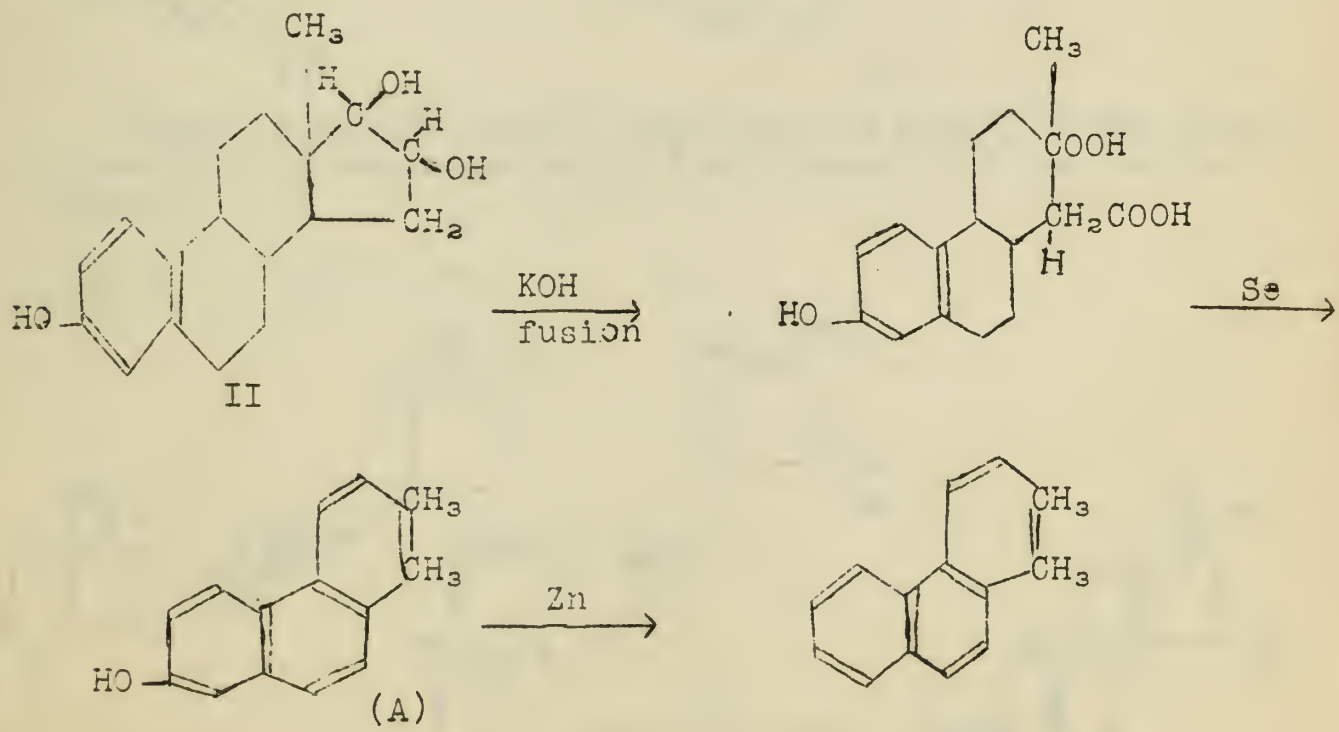
A. Cohen, J. W. Cook, C. L. Hewett
Research Institute of The Cancer Hospital (Free), London
J. Chem. Soc., 1935, 445

Previous work:
Cook and Hewett - polycyclic aromatic hydrocarbons, carcinogenic substances, substances related to sterols and bile acids.
Cohen - synthesis of substances related to sterols and bile acids.

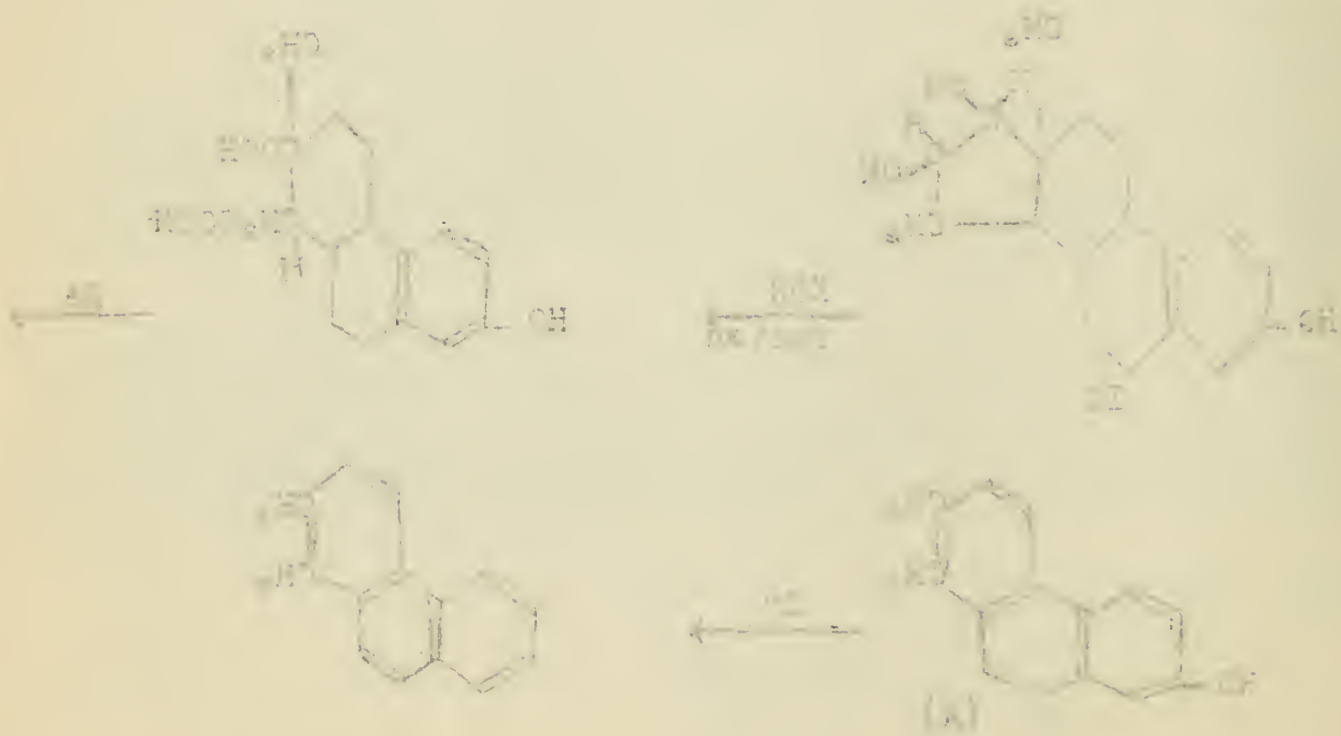
Oestrone (I) and oestriol (II) were first isolated from gravid urine of the human by Doisy,[1] Butenandt[2] and Marrian.[3] A number of other sources are now known.

Oestrone (also called theelin and follicular hormone), $C_{18}H_{22}O_2$, is weakly acidic, has one phenolic group, adds six atoms of hydrogen, melts at 250° and is dextro-rotatory. Clemmensen reduction produces desoxotheelin, $C_{18}H_{24}O$.

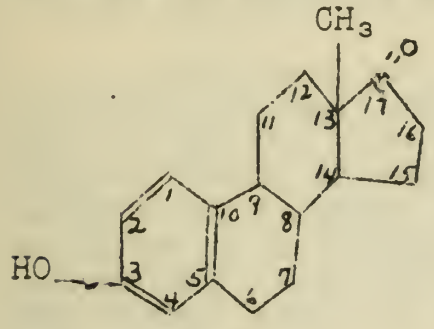
Oestriol (also called theelol and trihydroxyoestrin), $C_{18}H_{24}O_3$, has three hydroxyl groups, one of which is acidic. It has phenolic properties, adds three molecules of hydrogen, is dextro-rotatory and melts at 273°. Oestriol distilled over $KHSO_4$ produces oestrone. Early investigation showed that oestriol fused with KOH gave a dibasic acid, which, by selenium dehydrogenation followed by reduction with zinc dust, gave 1,2-dimethylphenanthrene.[4] The reactions are interpreted as indicated:



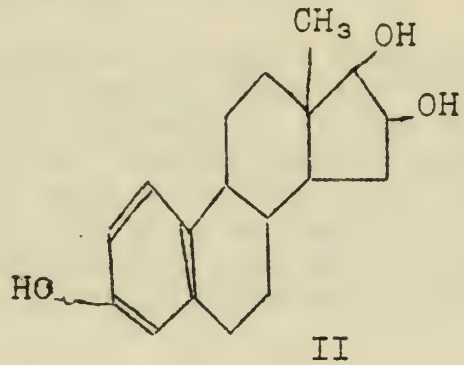

The final product is identical to 1,2-dimethylphenanthrene synthesized from naphthalene and partially synthesized from aetiobilianic acid (a degradation product of cholanic acid). 7-Hydroxy-1,2-dimethylphenanthrene synthesized by Haworth[5] was identical to the substance (A) above.



From these facts and others the following structures have been assigned to oestrone (I) and oestriol (II), the positions of the methyl group, the keto group and the two non-phenolic hydroxyls alone remained to be definitely proved by the present work of Cohen, Cook and Hewett:

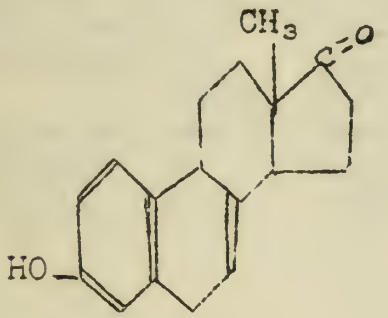



I

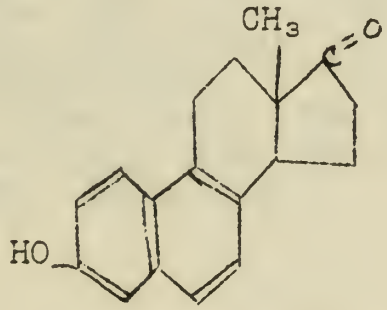



II

Equilin, $C_{18}H_{20}O_2$, and equilenin, $C_{18}H_{18}O_2$, were first obtained from the urine of mares by Girard.[6] The structure assigned to equilin is (III),[7] and to equilenin (IV):

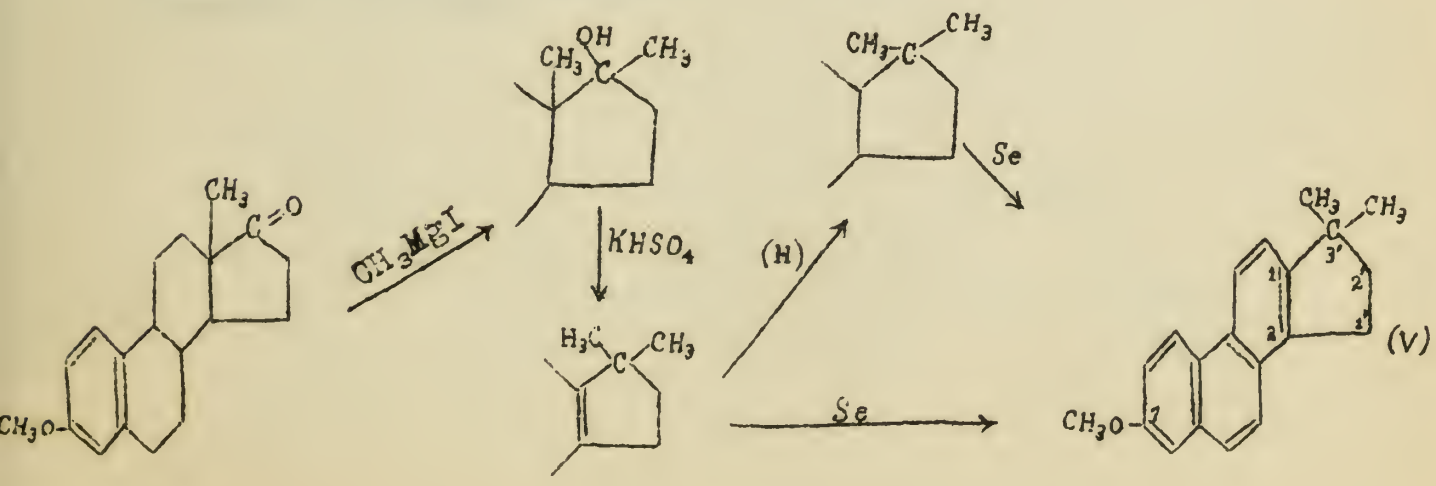



III




IV

Cohen, Cook and Hewett completed the proof of the structures I-IV by reactions which they showed to occur as indicated:




V.

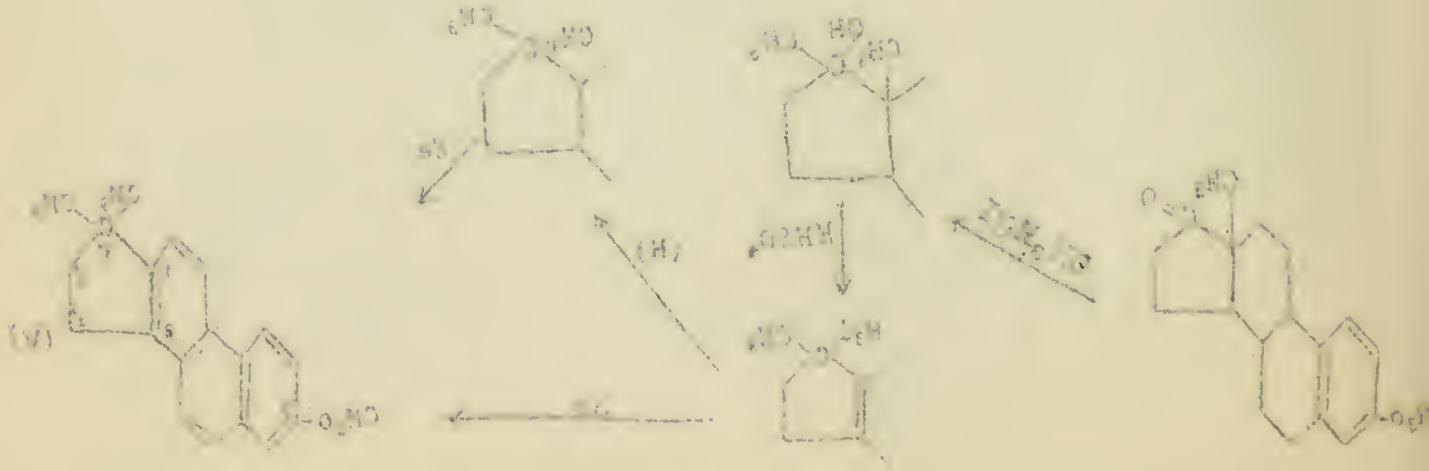
From these facts and other the following alternatives have been assigned to neotoxin (I) and equilenin (II), the positions of the methyl-groups, the keto group and the hydroxyl hydroxyl alone remained to be definitely proved by the usual work of Cohen, Cook and Hewett:

II I

Equilin, Cohen, and equilenin, Cohen, were then obtained from the urine of mares by Marrian. The structure assigned to equilin is (III), and to equilenin (IV):

IV III

Cohen, Cook and Hewett completed the proof of the structures I-IV by reactions which they showed to occur in Diketo:



The methyl ether of each of I, III and IV was used as starting material, each substance giving the same final product. The investigators expected the product to be either the 1', 2' or 3'-methyl derivative of 7-methoxy-1,2-cyclopentenophenanthrene. Each of these substances are synthesized, but did not correspond to their end-product. V was synthesized and found to be identical to the product of their series of reactions.

The reactions are considered to give indisputable evidence of position 13 for the methyl group in the hormones and 17 for the keto group. The migration of the methyl group occurs during dehydration and not during dehydrogenation. The authors have shown, however,[7] that when the keto group or oestrone or equilenin was reduced to a methylene group and the methyl ether of the product dehydrogenated by selenium, the methyl group at position 13 is eliminated instead of migrating.

1. Doisy, et al, J. Biol. Chem., 86, 499 (1930); 91, 641 (1931).
2. Butenandt, Z. physiol. Chem., 191, 127 (1930); 199, 243 (1933).
3. Marrian, Biol. Chem. J., 24, 435 (1930); 26, 27 (1932).
4. Chem. Ind., 52, 268 (1933).
5. Haworth and Sheldrick, J. Chem. Soc., 1934, 864.
6. Girard, et al, Compt. rend., 194, 909; 194, 1020 (1932).
7. Cohen, et al, J. Chem. Soc., 1934, 653.

Reported by Allene Jeanes
December 11, 1935.

The methyl ether of each of I, III and IV was used as starting material, each substance yielding the same final product. The investigators expected the product to be either the 1', 2' or 3'-methyl derivative of 5-hydroxy-1,1-cyclopentanedimethyleneacridine. Each of these substances was synthesized, but did not correspond to their co-product. It was synthesized and found to be identical to the product of their series of reactions.

The results are considered to give indisputable evidence of position 1? for the methyl group in the hormones and IV for the rich group. The alternation of the methyl group occurs during hydrogenation and not during hydrogenolysis. The authors have shown, however, that when the both group or oestrone or equilenin was reduced to a methylene group and the methyl ether of the product hydrogenolysed by solution, the methyl group at position 13 is eliminated instead of migrating.

1. Dodds, et al, J. Biol. Chem., 96, 465 (1932); 91, 641 (1931);
2. Butenandt, E. Physiol. Chem., 191, 127 (1929); 189, 243 (1930).
3. Marrian, Biol. Chem. J., 24, 1255 (1930); 26, 27 (1932).
4. Chem. Ind., 52, 805 (1933);
5. Haworth and Sheldrick, J. Chem. Soc., 1934, 864.
6. Ziegler, et al, Chem. Ind., 194, 976; 194, 1020 (1933);
7. Cohen, et al, J. Chem. Soc., 1934, 887;

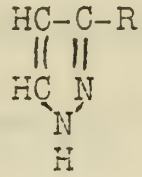
Reported by Eileen Jones
December 31, 1935.

# Wietere Beobactungln Über Alkylierung und Acylierung von Pyrazolen.

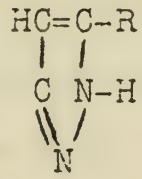
v. Auwer und Breyhan
Jour. für Prakt. Chemie (2), 143, 259, (1935)

This paper is the latest of a series by v. Auwers and co-workers dealing with the substitution of pyrazoles and the problem of isomers formed from such substitution. Acylation and alkylation results are presented.

A C-substituted pyrazole as

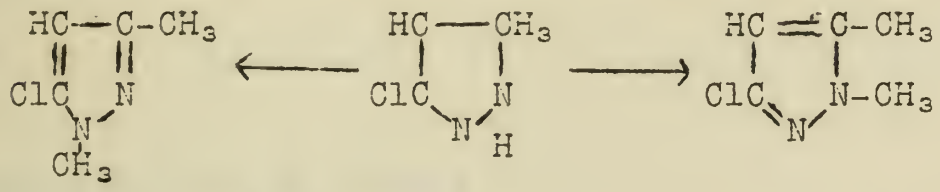


when further N-substituted may give rise to isomers. This is due to the possibility of the structure of the compound represented, isomerising into



There is probably a dynamic equilibrium between these formulas but when further substitution occurs isomers are formed.

Various alkylation and acylation reagents and conditions have been used but no generalizations have been made. For example:

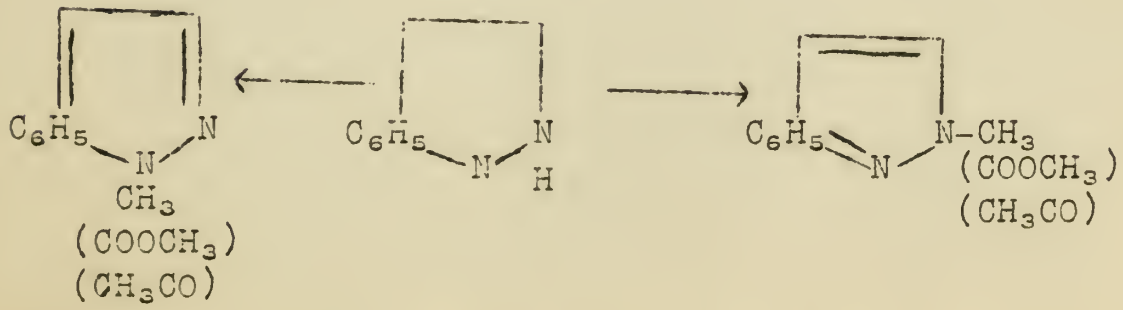


chief product ← $(CH_3)_2SO_4$ + alkali

100 per cent ← $CH_3Br$

chief product ← $CH_2N_2$

Na salt + $CH_3I$ → 100 %



$CH_3Br$ → chief product

100 per cent ← Na salt + $CH_3I$

$ClCOOCH_3$ → only.

only ← $CH_3COCl$

# Mixture Independent Ring Alkylations and Acylations via Pyridinium

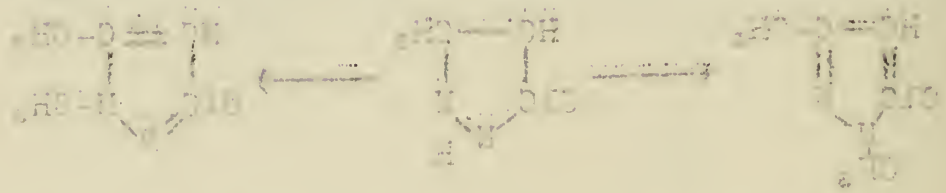
R. Alewin and Prosper
Univ. The Bronx, Thesis (M), 1967, 109, (Chem)

This paper is the result of a series of N. Alewin and Prosper working during the mid-1960s on pyridinium and the problem of bromide ions that gave substitution. Acylation and alkylation results are presented.

A 2-bromopyridine cyclohexyl ketone substituted was also also in the theory. This is due to the reactivity of the electrons of the compound rearrangement, investigating this

There is probably a dynamic equilibrium between these forms but when further substituent groups isomerize are formed.

Various rearrangement and cyclization reagents and conditions have been used but no generalizations have been made. For example:



Major product ⟶ $(CH_3)_2CO_4$ + alkyl

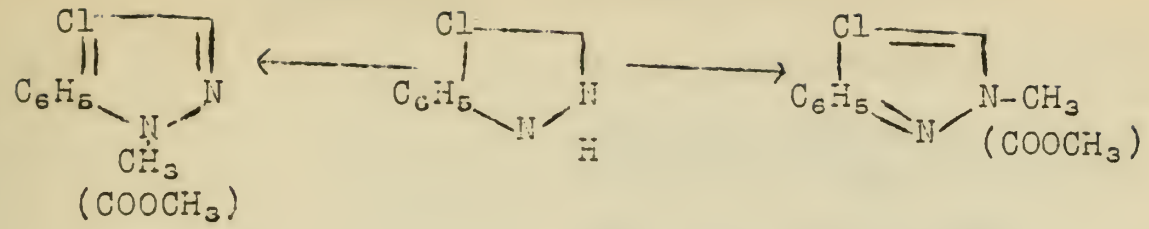
100 per cent ⟶ $CO_2Me$

major product ⟶ $CO_2Me$

M salt + $CH_3I$ ⟶ 100 %

$CO_2Me$ ⟶ major product

100 per cent ⟶ M salt + $CH_3I$




$CH_3Br$ ⟶ chief product.

$\left.\begin{matrix} NaOEt + CH_3I \\ NaOH + CH_3I_2SO_4 \end{matrix}\right\}$ ⟶ both products.

$CH_2N_2$ ⟶ no reaction

Na salt + $CH_3I$ ⟶ both products

$CLCOOCH_3$ ⟶ only

Reported by G. E. Ullyot
December 11, 1935

# The Synthesis of Carotinoid Chains by the Aldol Condensation of 3-methyl-buten-2-al-1.

F. G. Fischer and Coworkers.

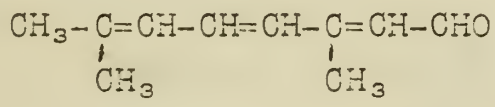
From the Chemical Laboratories
of the Freiberg University

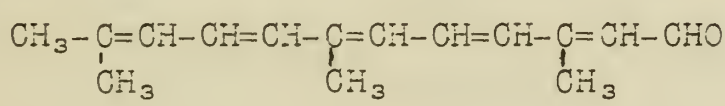
Ber., 68, 1726 (1935)
Ber., 64, 30 (1931)
Ann., 494, 263 (1932)

The synthesis of carotinoid chains, such as occur in Vitamin A, Carotin, Crocetin, and other naturally-occurring products, is now possible although none of these products has as yet been prepared.

Karrer, Ruzicka, and Gould and Thompson have synthesized hydrogenated carotinoid chains, while Kuhn and others have built up several series of conjugated unsaturated carbon chains.

Fischer has been able to condense β-methyl-crotonaldehyde with itself to give the following:





These have also been reduced to the corresponding alcohols.

Reported by Wm. E. Lundquist

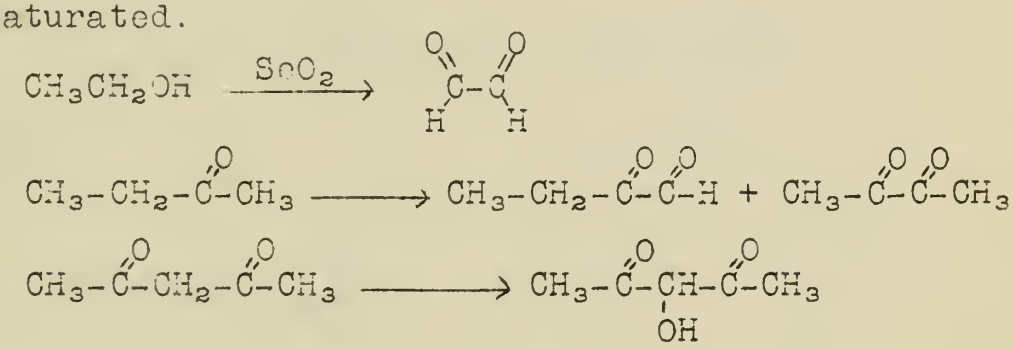
December 13, 1935.

Postowsky, J. J., Ber., 68B, 852-6 (1935)
Henze, M., Ber., 67B, 752-3 (1934)
Schwenk-Borqueordo, Ber., 65, 1601 (1932)
Urion, Edmond, Compt. Rend., 199, 363-5 (1934)
Truchet, M. M., Compt. Rend., 196, 706-9 (1933)
Dupont, G., Bull. Soc. Chem., 53, 599-603 (1933)
Riley, H. L., J. Chem. Soc., 1934, 844-8
Riley, H. L., J. Chem. Soc., 1935, 901-4
Riley, H. L., J. Chem. Soc., 1932, 2342-4

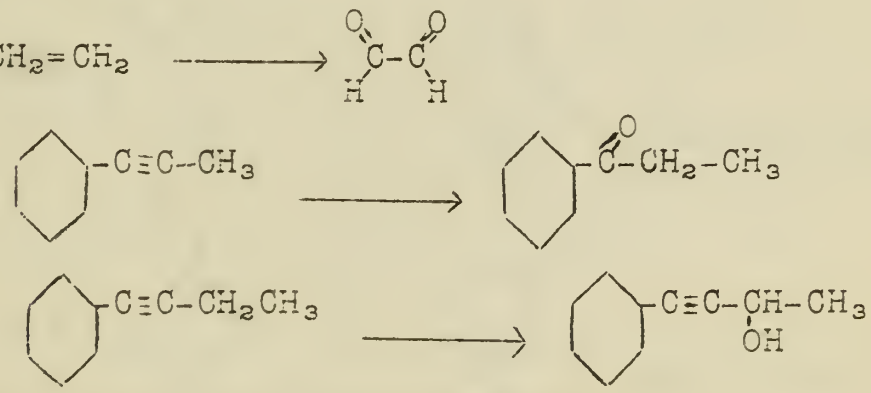
Selenium dioxide has become one of the best-known specific oxidizing agents available. In many cases by a single oxidizing reaction using selenium dioxide, it is possible to obtain in good yields compounds which are difficult to obtain by standard synthetic methods.

I. Aliphatic Series

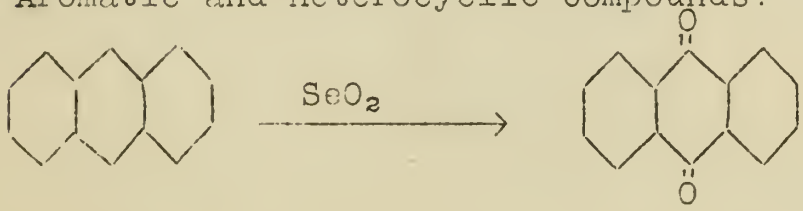
a) Saturated.



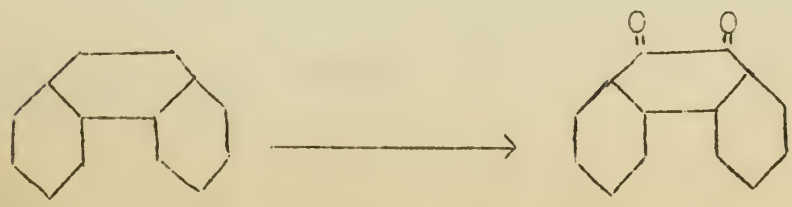
b) Unsaturated.



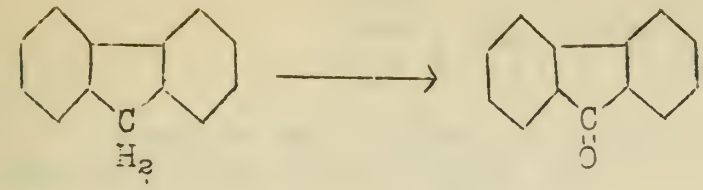
II. Aromatic and Heterocyclic Compounds.



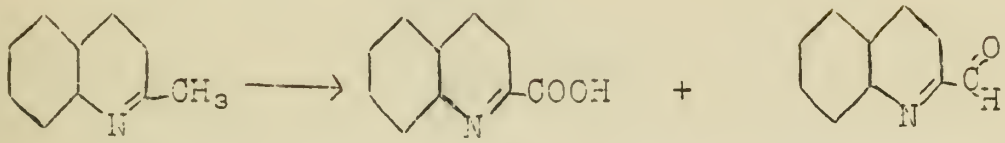
76 %



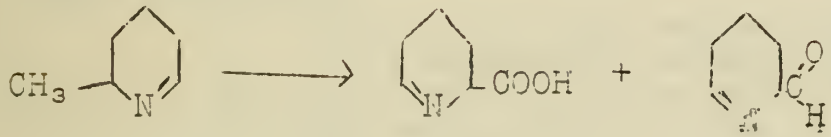
3 %



5 %



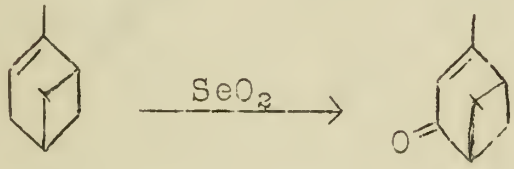
trace

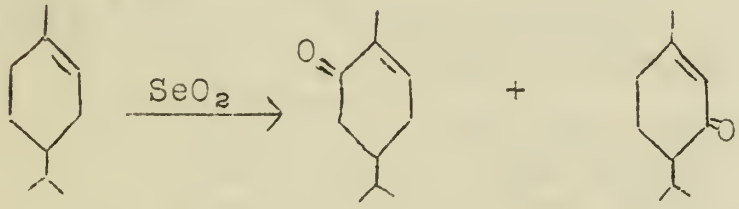


trace

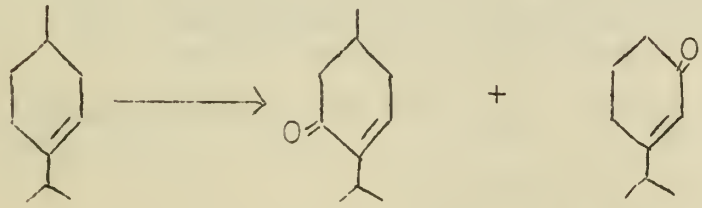
no reaction

III. Terpenes



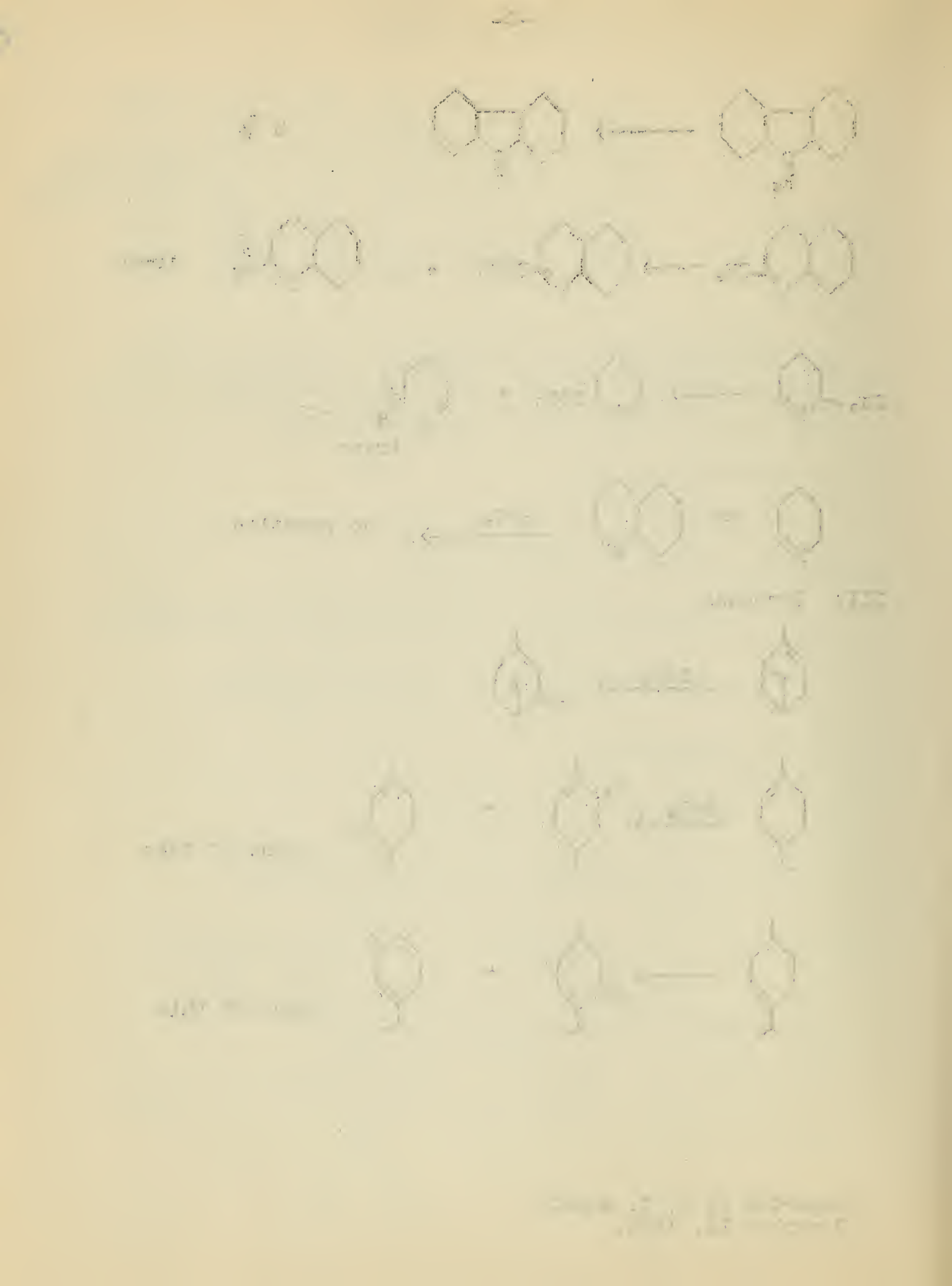


none of this



none of this

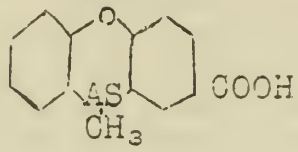
Reported by R. T. Arnold
December 13, 1935.



# Optically Active Arsines

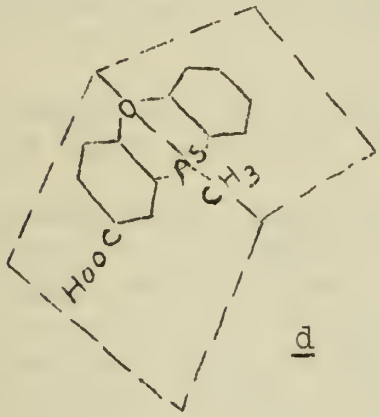
Kamai, Lesslie and Turner
Ber., 68, 1893 (1935)
J.C.S., 1170 (1934)

Lesslie and Turner succeeded in resolving 10-methylphenoxarsine-2-carboxylic acid.

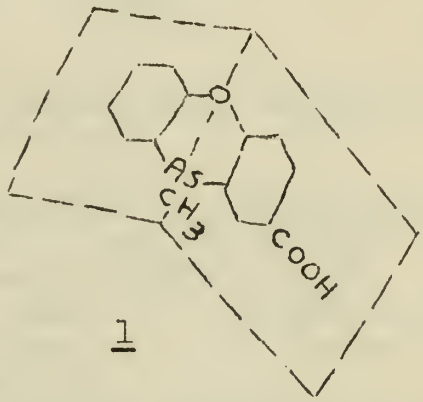



Two possible sources of optical activity in this compound were postulated.

1. The activity may be due entirely to the presence of an asymmetric arsenic atom.
2. The activity may be due to asymmetry of the molecule which results from a folded structure, as below.




d

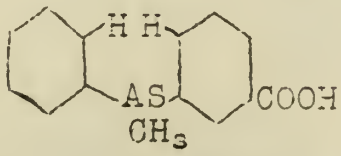



l

The folded structure is accepted as being the cause of the activity for the following reasons;

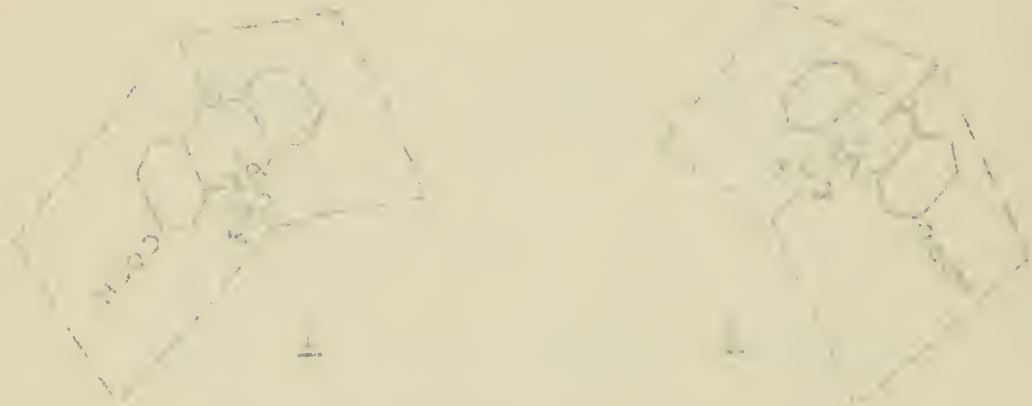
1. The atomic radii of arsenic and oxygen are widely different.
2. Calculations from the valence angles of the two atoms indicate that greater stability would result from a folded rather than a planar structure.
3. No known arsines have, as yet, been resolved.
4. Racemization, caused by addition of ethyl iodide, can be easily explained.

Kamai synthesized the o, m, and p isomers of the following compound.




Inability to resolve any of these compounds is given as further evidence in favor of the folded structure of 10-methylphenoxarsine-2-carboxylic acid.

Reported by R. E. Damschroder
January 8, 1936.

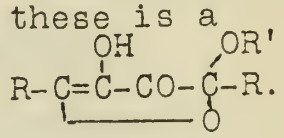
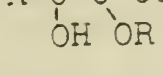


A. H. Blatt, J. Am. Chem. Soc., 57, 1103 (1935)
F. Micheel and W. Schulte, Ann., 519, 70 (1935)
P. Karrer and V. Segesser, Helv. Chim. Acta, 18, 873 (1935)
P. Karrer and C. Musante, Helv. Chim. Acta, 18, 1140 (1935)

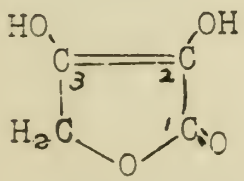
Karrer and V. Segesser have shown that the following formoins of the general formula, R-CO-CHOH-COCOR, exist in equilibrium of the benzoin-ene-dioltype. They have investigated this equilibrium quantitatively, by iodine titration, and give the following results:

| | M.P. | Per cent Ene-Diol Content | Per cent Carbonyl Content |
|---|---|---|---|
| Benzoylformoin | | 57 | 43 |
| p-p-Dimethoxybenzoylformoin | 151-2 | 40 | 60 |
| p-p-Dichlorbenzoylformoin | 190 | 100 | -- |
| p-p-Dibrombenzoylformoin | 196 | 95-100 | 5-0 |

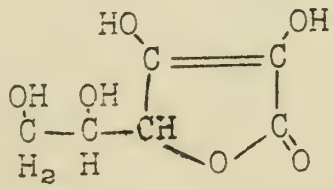
These compounds all reduce acetic acid-copper acetate solution, and are thus oxidized to the tetraketone.

Blatt has shown, through alkylation of benzoylformoin, two types of monomethyl derivatives. One of these is a glycosidic ether type of the general formula  . This is proven by convertibility, ease of formation, and blocking of the carbonyl group towards addition. The second type of derivative is the open-chain monomethyl ether of formula  . This derivative reacts with orthophenylenediamine to give a quinoxaline. It is obtained from the dimethyl derivative by removing the glycosidic alkyl group.

Micheel and Schulte compare the oxytetronic acid (I) and its alkylation derivatives to ascorbic acid (II) and its alkylation derivatives.



I.



II.

They are able to show that the $C_3$-atom is the one holding the strongly acidic hydroxyl group. This is accomplished by the ozonization of the two isomeric monoalkyl ethers, which are formed by entirely different methods.

Reported by William E. Holland
January 8, 1936.

1. R. Scott, J. Am. Chem. Soc., 67, 1549 (1945).
2. Linstead and R. Robinson, ibid., 67, 1414 (1945).
3. Barker and J. Grimshaw, Proc. Chem. Soc., 1957, 12.
4. Barker and J. Grimshaw, ibid., 1958, 1.

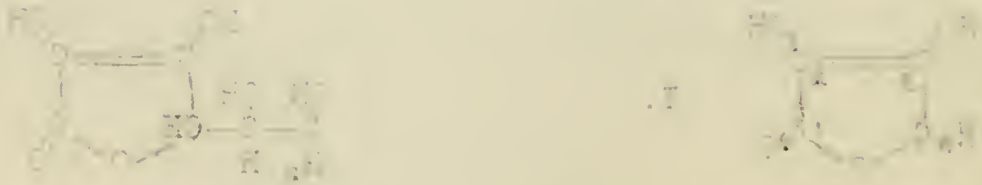

Barker and J. Grimshaw have shown that the facility of formation of the quinolyl ketones, in which, apart from quantities of the quinolinyl-ketones, they have invested, this antihistamine predominates, by 2-line titration, and give the yields obtained:

| | Yield, % | Mp, °C |
|---|---|---|
| 2-Quinolyl-2-pyridyl ketone | 70 | 85 |
| 2-Quinolyl-4-pyridyl ketone | 100 | 100 |
| 2-Quinolyl-3-pyridyl ketone | 100 | 95-100 |

These compounds all yield stable sulfuric acid solution, and are later soluble in the hydrochloric.

Grant and Jones, in their elucidation of benzylfurmedin, the types of secondary alcohols, and of these is a glycol/alcohol, the 2nd of the second compound. This is a case in point, which, as the 2-methyl-2-propanol, the 1-methyl-2-propanol, and 1-methyl-2-butanol. The sub-ject of activity is the compound monoethyl ether of 2-methyl-2-propanol. The derivative reacts with acetone to give a polycyclic, 1,3-dioxolane, from the methyl 1-methoxy-2-propanol by reacting the glycolate with acetone.

Dimmel and Shonle compare the carbinolamin and (I) and the alkylation derivative in methyl acid (II) and the alkylation derivative.



I.

II.

They are able to show that the 3-position is for one joining the primary cyclic dynamic group. This is accomplished by the derivatives of the two isomeric monoethyl ethers, which are formed by mildly differing methods.


Received by Editor E. Holland
January 2, 1962

Large Molecular Weight Compounds. 125-30

H. Staudinger, G. V. Schulz,
Ber., 68, 2313, (1935).

The report includes various types of molecular weight determinations used by Staudinger on high polymeric products.

The use and limitation of the following methods will be given:

1. Osmotic pressure method.
2. Viscosity method.
3. End group determination method.
4. Cryoscopic method.
5. Modification of above methods.

By use of a number of different methods in determining molecular weight of a polymer the limitations of a particular method were ascertained. Explanation for abnormal behavior was given in all these cases.

Reported by Rob't. Johnson

January 15, 1936.

Abstract of Master's Thesis, 1950.

Author: Stanislaw J. Ziemba.
Phm. D., Univ. Wisc., (1934).

The report includes various types of molecular weight determinations used by Staudinger on high polymeric products.

The use and limitation of the different methods will be given:

1. Osmotic pressure method.
2. Viscosity method.
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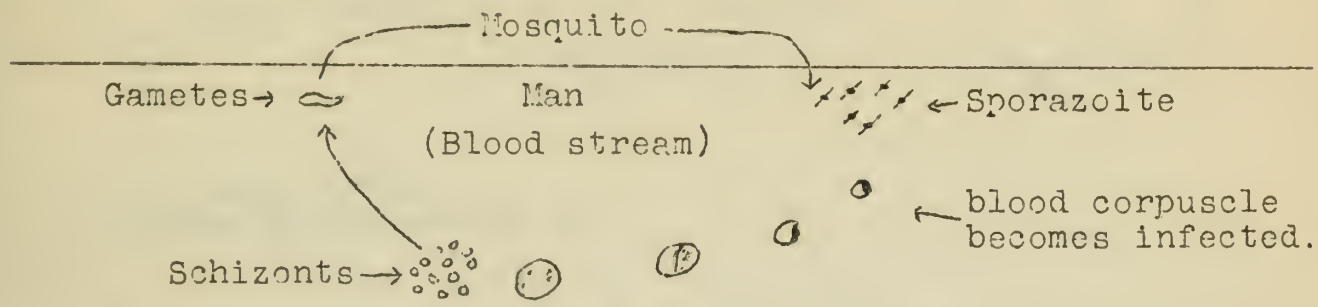
4. Cryoscopic method.
5. Limitations of above methods

By use of a number of different methods in determining molecular weight of a polymer the limitations of a particular method were demonstrated. Explanation for observed behavior was given in all these cases.

Reported by Dwight Johnson
January 17, 1950.

SYNTHETIC ANTIMALARIALS: Plasmochin and Atebrin

Malaria exists in three forms, malaria tertian, quartan, and tropical. The life cycle of the malaria germs, mosquito-man-mosquito, is of fundamental importance. (1)

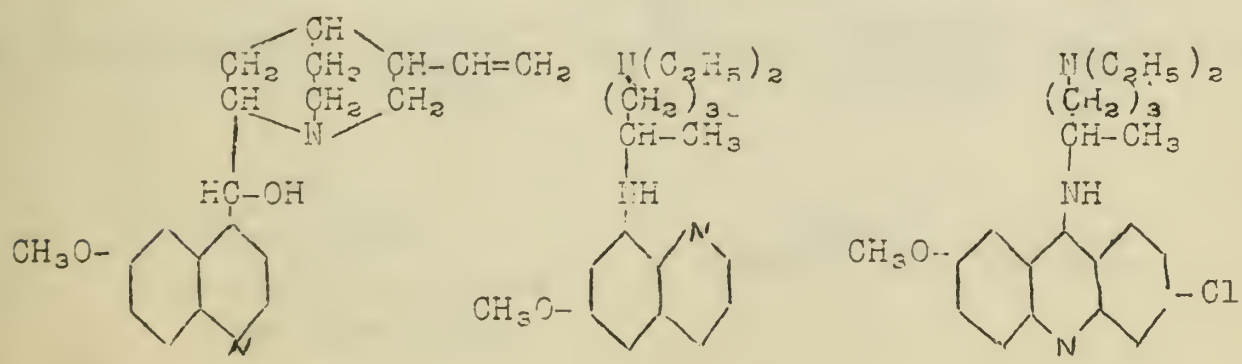



In this cycle arise the three forms of the malaria parasite--the sporozoites, the schizonts (asexual development forms) and the gametes (sexual forms).

By the bite of the anopheles mosquito (with malaria tropical infection) the sporozoites arrive in man's blood. These quickly penetrate into the red corpuscles and transform themselves into the schizonts. The schizonts increase by simple division and cause the symptoms of malaria. Besides the schizonts another form of the parasite is produced, namely the gametes. They have no influence on the disease in man, but are important because they are the only form which can live in the organism of the mosquito. Therefore, the gametes complete the link in the cycle of malaria infection.

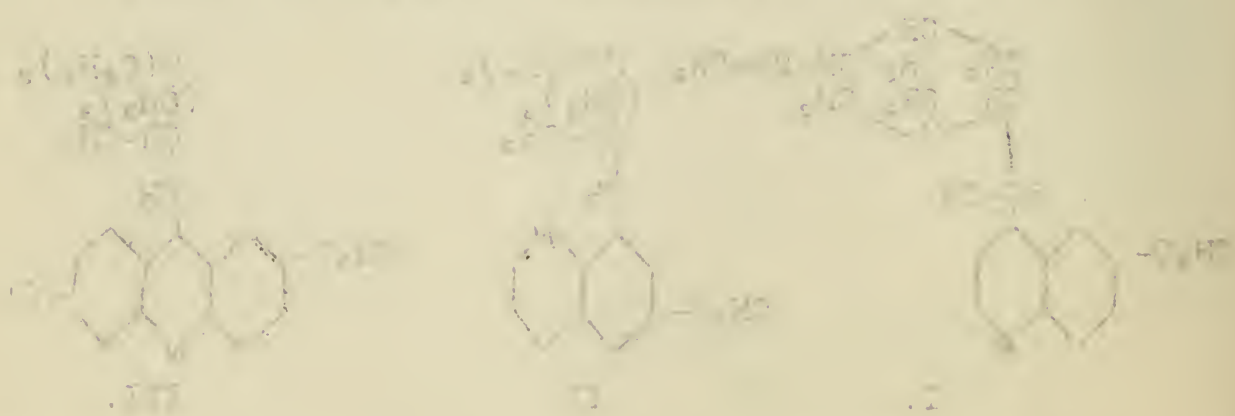
Quinine (I) was long the supreme remedy for malaria. It attacks the schizonts thereby destroying the symptoms of the disease, but it has no effect on the gametes or spread of the disease.

In 1926 Schulemann, Schönhöfer and Wingler (2) working for the I. G. Fabenindustrie (3) (4) discovered plasmochin (II) which has specific action on the gametes of tropical malaria. In 1930 Mauss and Mietzsch (5) working for the same company (6) (7) produced atebrin (III) which proved to be even more effective than quinine against the schizonts of tropical malaria.

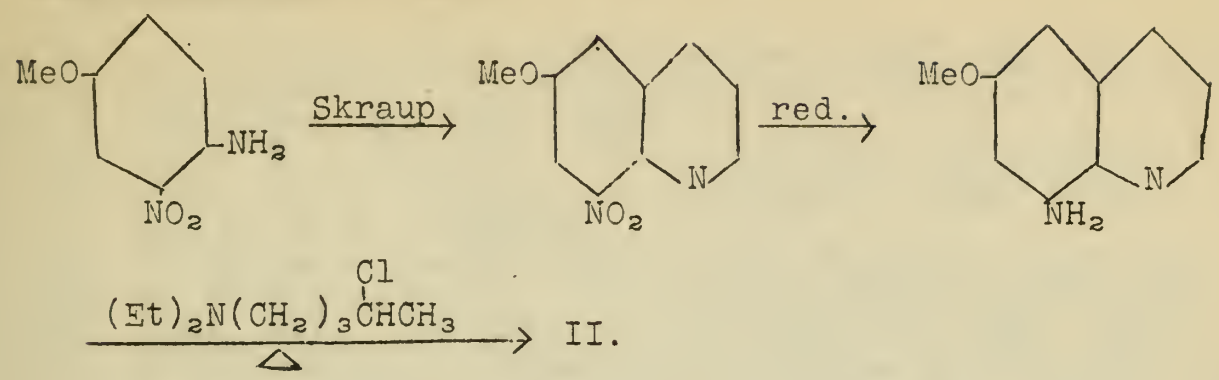



I. II. III.

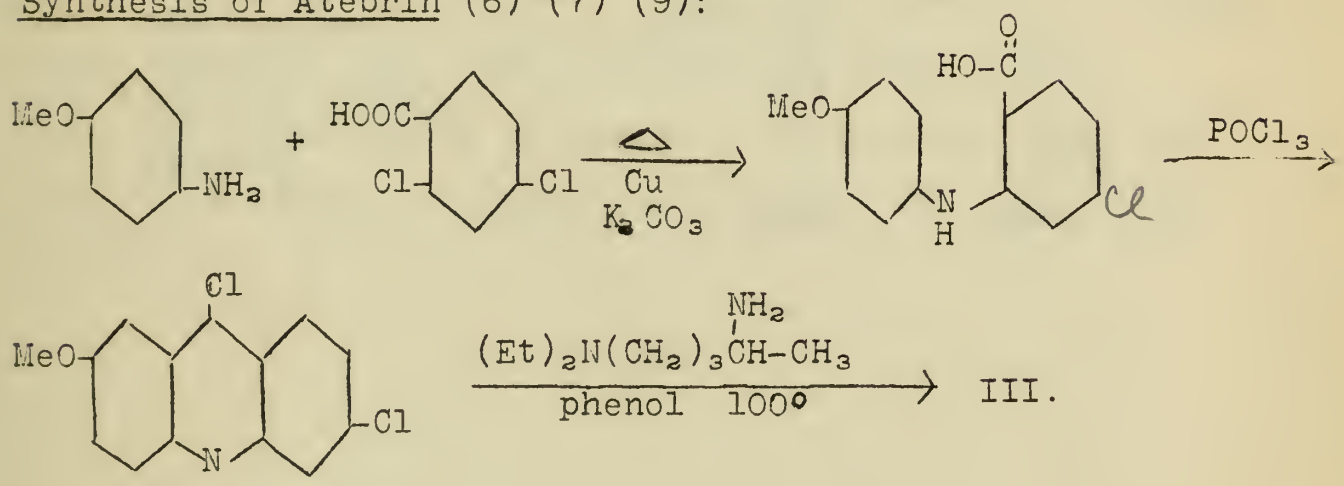
In the treatment of malaria plasmochin is combined with either quinine or atebrin thereby effecting a cure and at the same time the destruction of the infection cycle (8).



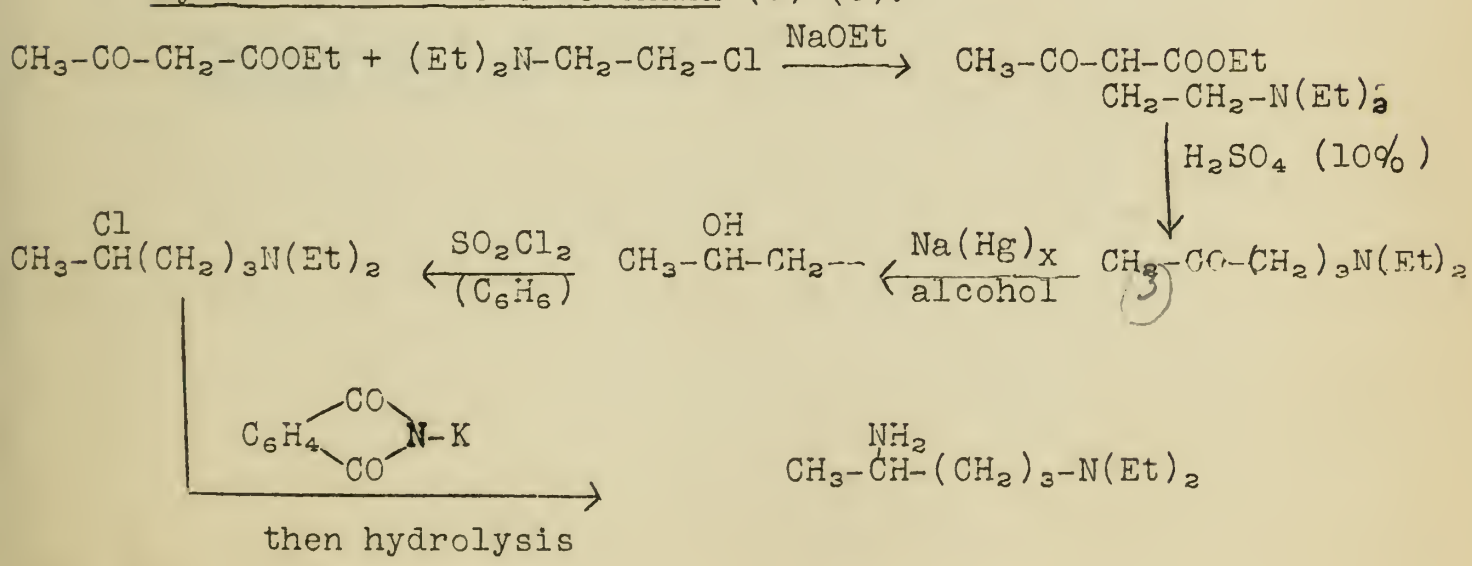
Synthesis of Plasmochin (3) (4) (9):




Synthesis of Atebrin (6) (7) (9):

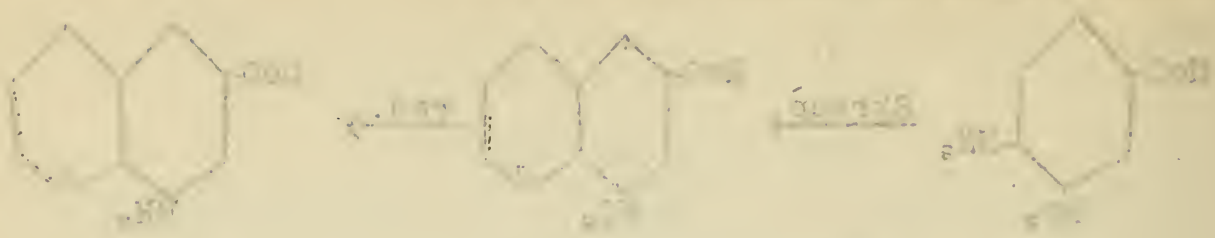



Synthesis of the side-chain (4) (9):



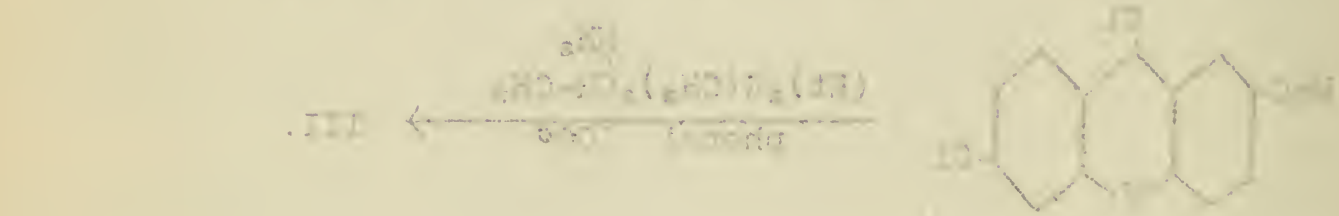

Other work in the field of synthetic antimalarials includes especially the work of the French chemist Fourneau (10) and the efforts of the British chemists, Barger and Robinson (11) and L. P. Walls (12).

Synthesis of Pleurotin (I) (A) (C):



Synthesis of Aureolin (B) (I) (II):

Synthesis of the aldehyde (II) (D):



Other work in the field of antibiotic antimetabolite studies especially the work of the French chemist Fourneau (16) and the efforts of the British chemists, Barger and Robinson (17) and H. R. Muir (18).

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2. W. Schulemann, F. Schönhöfer and A. Wingler, Klin. Woshschr., 11, 381 (1932).
3. D. R. P., 451,730, C. Z., 99 (I), 414 (1928).
4. Brit. Pat., 267,167, C. Z., 100 (I), 1965 (1929) cf. D. R. P., 486,079.
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11. G. Barger and R. Robinson, J. Chem. Soc., 1929 (III) 2947-68.
12. L. P. Walls, J. Chem. Soc., 1934, 104; 1935, 1405.


Reported by E. E. Gruber
January 15, 1936.

SEMINAR TOPICS

II Semester 1935-36


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# THIOCHROM FROM VITAMIN $B_1$


R. Kuhn et al, Inst. Chem. Heidelberg
1. Zeit. physiol. chem., 234, 196 (1935)
2. Ber., 68, 2375 (1935)

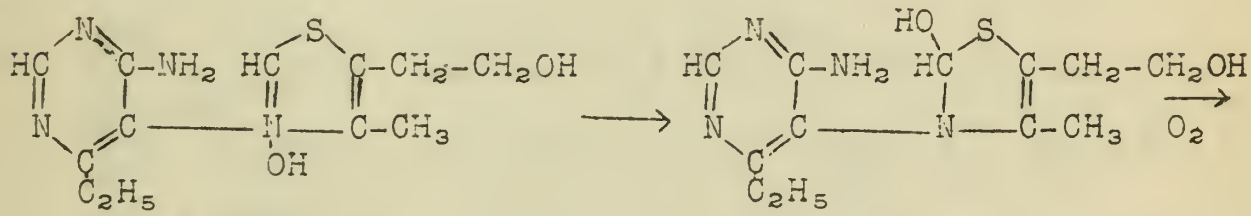
G. Barger, Medizin-chem. Inst. Univ. Edinburgh
3. Ber., 68, 2357 (1935)
4. Nature, 136, 259 (1935)

A. Windaus et al., Allg. Chem. Univ. Göttingen
5. Zeit. physiol. chem., 237, 98 (1935)

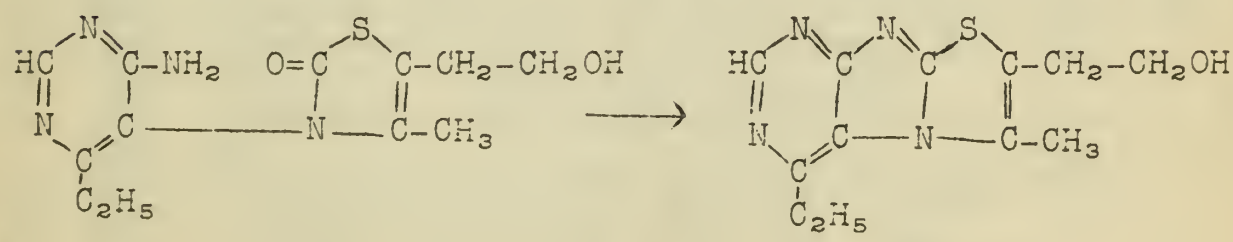

Kuhn[1] isolated a yellow dye from yeast, which in solution showed an intense blue fluorescence. He named this dye "Thiochrom" and found the formula to be $C_{12}H_{14}ON_4S$. The relation of this compound to Vitamin $B_1$ (also present in yeast) was studied because of the similiarities in their formulas and because of the fact that fluorescent substances had been observed during the oxidation of the vitamin. Thiochrom itself has no vitamin $B_1$ activity.

Barger[4] prepared Thiochrom from Vitamin $B_1$ in 33-40 per cent yields by oxidation with $K_3Fe(CN)_6$ in alkaline solution at 12-20°C.

Kuhn,[2] Barger,[3] and Windaus,[5] on the basis of further experiments, have each assigned the following structure to Thiochrom, and consider the following changes to take place during the oxidation.

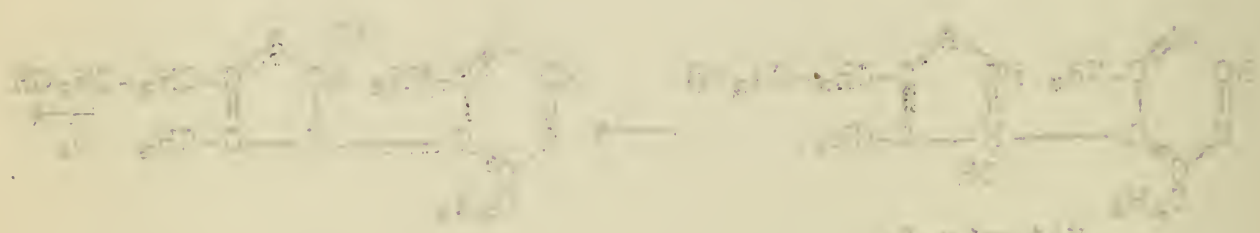


Vitamin $B_1$

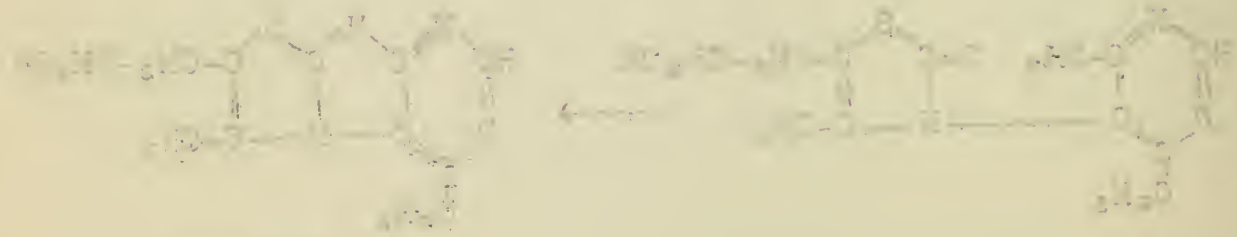


Thiochrom

Reported by Meredith Sparks
February 5, 1936



Vitamin $C_1$



Vitamin $C_2$

# Synthesis of Glutathione

Chas. Rob't. Harrington and Thomas H. Mead
Department of Pathological Chem., Univ. College Hosp.,
Medical School, London.

In 1921, Hopkins[1] isolated glutathione from yeast, and muscle and liver tissue, and gave evidence to show that the substance is a dipeptide containing glutamic acid and cystein. In 1923, Omastel, Tunnicliffe, and Stewart[2] obtained evidence which led them to believe that glutathione is γ-glutamylcystein. Later, in 1925, Stewart and Tunnicliffe[3] believed they had positive evidence for such a structure, by its supposed synthesis.

Hunter and Eagles (1927)[4], obtained a third amino acid from their glutathione preparations, thereby giving evidence for the incorrectness of the above structure. In 1930, Hopkins[5] reinvestigated the problem, and, by a better method for separation of the peptide, obtained crystalline glutathione. He then showed it to be a tripeptide of glutamic acid, cystein, and glycine. At about the same time, Kendall et al. reached the same conclusion by a different method for separation of the peptide.

Experimental evidence[2,5-11] established the structure of glutathione as γ-glutamylcysteylglycine. In 1935, Harrington and Meade confirmed this structure for glutathione by its synthesis[12-16].



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14. 1933 - Bergman and Zervas, Ber., 66, 1288.
15. 1931 - Lamb and Robson, Biochem J., 25, 1231.
16. 1935 - Melville, Biochem. J., 29, 179.

Reported by Leone A. Ruberg
February 5, 1936

## Summary of Discussion

Chas. Reif, Portland Cement Association
Department of Research and Tests, Duke College Park,
Indiana Report, Lorenz:

In 1927, Hunting[1] published a "Reinforced Concrete Power, and Sewage and Sewer Mains, and gave evidence to show that the overstress is a dynamic condition, usually with one operation. In 1927, Chatton, Functility, and Stewart obtained evidence which led them to believe that distortion is a distortionation. Later, in 1929, Stewart and Twelftree[2] believed they had positive evidence for such a structure, by its numerous epicenter.

Lorenz and Spring (1927)[3], obtained a value using pile from their distribution investigations, thereby giving evidence for the increasing of the above structure. In 1927, Hunting investigated the problem, and, by a better method for evaluation of the results, obtained negative evidence. He then showed it to be a triangular of circular arcs, circular and elliptic. At about the same time, Lorenz et al. produced the same conclusion by a different method for measuring the results.

### Dynamical Analysis

Dynamical analysis[14-16] established the structure of distortion as a X-distortionation-type. In 1929, Hunting and Lorenz confirmed this structure for giving values by the [illegible].

### References:


1. 1927 - Hunting, Alonzo, [illegible], 32, 29.
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3. 1927 - Lorenz and Spring, [illegible], [illegible], 27, 27.
4. 1930 - Hunting, [illegible], [illegible], 27, 27.
5. 1930 - Hunting, [illegible], [illegible], 27, 27.
6. 1930 - Lorenz, [illegible], [illegible], [illegible], 27, 27.
7. 1930 - Lorenz, [illegible], [illegible], [illegible], 27, 27.
8. 1930 - Lorenz, [illegible], [illegible], [illegible], 27, 27.
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11. 1930 - [illegible], [illegible], [illegible], [illegible], 27, 27.
12. 1930 - [illegible], [illegible], [illegible], 27, 27.
13. 1930 - [illegible] and [illegible], [illegible], 27, 27.
14. 1930 - [illegible] and [illegible], [illegible], 27, 27.
15. 1931 - [illegible] and [illegible], [illegible], 27, 27.
16. 1930 - [illegible], [illegible], [illegible], 27, 27.



Reported by Leon A. Hunter
February 9, 1930

# The Peroxide Effect in the Addition of Hydrogen Bromide to Unsaturated Compounds

Within the past three years Kharasch and coworkers (at the University of Chicago) have published the results of their systematic investigation of the various physical and chemical factors influencing the direction of addition of hydrogen bromide to a series of aliphatic compounds containing unsaturation involving a terminal carbon atom, e.g., allyl bromide,[1] vinyl bromide,[2] propylene,[3] 4,4-dimethylpentene-1,[4] vinyl chloride,[5] butene-1,[6] pentene-1,[7] allyl acetic acid,[8] and isobutylene,[9,10]. They have been able to make some very interesting generalizations, to which they have found no exceptions. These may be briefly summarized as follows:

1. The Peroxide Effect.--The presence or absence of peroxides in the reaction mixture is the sole factor determining the direction of the addition. In the absence of peroxides the addition is according to Markownikoff's rule (called "normal" addition), whereas even small amounts of peroxides cause terminal addition of the bromine atom (called "abnormal" or "peroxide-catalyzed" addition). In the presence of peroxides the two reactions are competitive, but the peroxide-catalyzed reaction is normally much the faster.

2. The Temperature Effect.--Increased temperature causes an increase in the velocity of both reactions. Their temperature coefficients may differ, however, that of the peroxide-catalyzed reaction usually being the higher.

3. The Solvent Effect.--The solvent has no direct effect on the direction of addition but may affect the stability of peroxides, resist the effect of oxygen, or affect the relative velocities of the two competing reactions.

4. The Light Effect.--Light of all wave lengths accelerates both reactions, but usually the peroxide-catalyzed reaction is accelerated much more than the normal one. This serves to amplify the effect of small amounts of peroxides.

5. The Effect of Metallic Salts.--Anhydrous ferric and aluminum halides have a tremendous accelerating effect upon the normal addition. Copper salts have a slight antioxidant and accelerating effect.

6. The Effect of Surface Catalysts.--Broken pyrex, glass wool, asbestos, and silica gel were without effect on either the direction or velocity of the reaction.

Different unsaturated compounds show considerable variation in their susceptibility to the peroxide effect and in the ease with which they form peroxides by oxidation. The vinyl halides were the most sensitive, whereas propylene, butene-1, and isobutylene were the least sensitive.

In 1935 Harris and Smith[11] showed that a terminal triple bond may be subject to exactly the same sort of peroxide effect by their investigation of the addition of HBr to $\Delta^{10}$-undecynoic acid. They also found a decided peroxide effect in the addition of HBr to undecenoic acid, but found that molecular oxygen was necessary, in addition to a peroxide, in order to produce terminal addition.

The only types of unsaturated compounds in which Kharasch has thus far been able to reverse the direction of addition of HBr, by the use of peroxides or antioxidants, are those in which the double bond is either adjacent to a carboxyl group (e.g. crotonic acid) or does not involve a terminal carbon atom (e.g. pentene-2).

References:


1. Kharasch and Mayo, J. Am. Chem. Soc., 55, 2468 (1933).
2. Kharasch, McNab, and Mayo, J. Am. Chem. Soc., 55, 2521 (1933).
3. Kharasch, McNab, and Mayo, J. Am. Chem. Soc., 55, 2531 (1933).
4. Kharasch, Hannum, and Gladstone, J. Am. Chem. Soc., 56, 244 (1934).
5. Kharasch and Hannum, J. Am. Chem. Soc., 56, 712 (1934).
6. Kharasch and Hinckley, J. Am. Chem. Soc., 56, 1212 (1934).
7. Kharasch, Hinckley, and Gladstone, J. Am. Chem. Soc., 56, 1642 (1934).
8. Kharasch and McNab, J. Soc. Chem. Ind., 54, 989 (1935).
9. Kharasch and Hinckley, J. Am. Chem. Soc., 56, 1243 (1934).
10. Kharasch and Potts, J. Am. Chem. Soc., 58, 57 (1935).
11. Harris and Smith, J. Chem. Soc., 1935, 1572.


Reported by F. E. Condo
February 12, 1936.

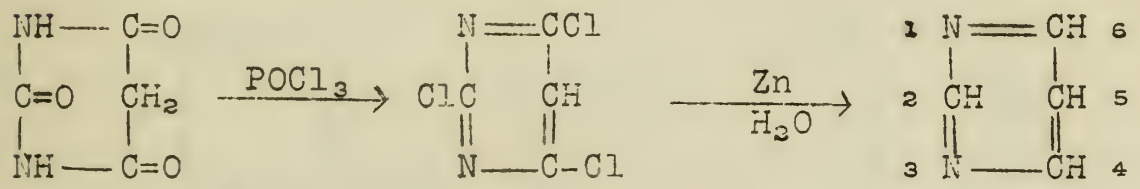
# PYRIMIDINES

References:

Caldwell and Ziegler, J. Am. Chem. Soc., 58, 78 (1936).
T. B. Johnson, J. Am. Chem. Soc., 57, 2252 (1935).
T. B. Johnson and D. Hahn, Chem. Rev., 13, 193 (1933).
Levene, Am. Chem. Soc. Monograph, No. 56, 35-74.

Pyrimidines have been of interest for a number of years due to their presence in animal and plant cells as a constituent of nucleic acids. Recently, the interest in this field has been renewed since the structure proposed for vitamin $B_1$ contains the pyrimidine ring.

Pyrimidine may be synthesized in the following manner:

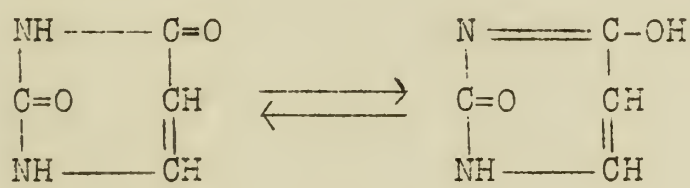



Barbituric Acid  Pyrimidine

## Properties

Pyrimidines are meta-diazines and are basic as would be expected from their structural relationship to pyridine. The introduction of oxygen into the nucleus, however, diminishes the basicity.

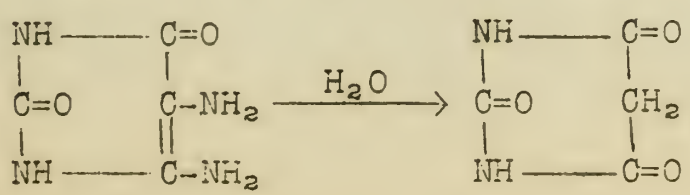
For example:



Uracil

Uracil is a weak acid while barbituric acid is sufficiently acidic to give a good neutral equivalent.

Many of the properties of the oxy- and amino-pyrimidines arise from their ability to tautomerize from the lactam and amine forms to the lactim and imine structures. The preparation of pyrimidine from barbituric acid is an example of the former. An example of the latter is the following:

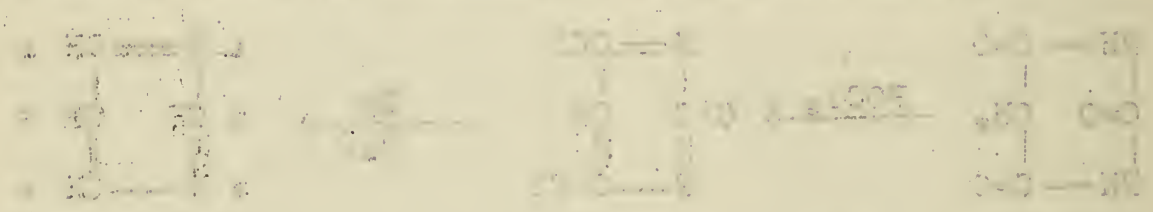


References:

[illegible]

Pyrimidine derivatives of biological importance [illegible] due to their presence in nucleic acid chemistry as well as [illegible] antibiotic action. Especially, the interest in this field has been stimulated since the discovery of [illegible] vitamin by combining the pyrimidine [illegible].

Pyrimidine may be considered as the following [illegible]



Barbituric Acid

Pyrimidine

## Barbituric Acid

Pyrimidine-2,4,6-trione, or barbituric acid, is well known as derived from Malonic diethyl ester and urea. The introduction of oxygen into the molecule [illegible] activated the hydrogen.

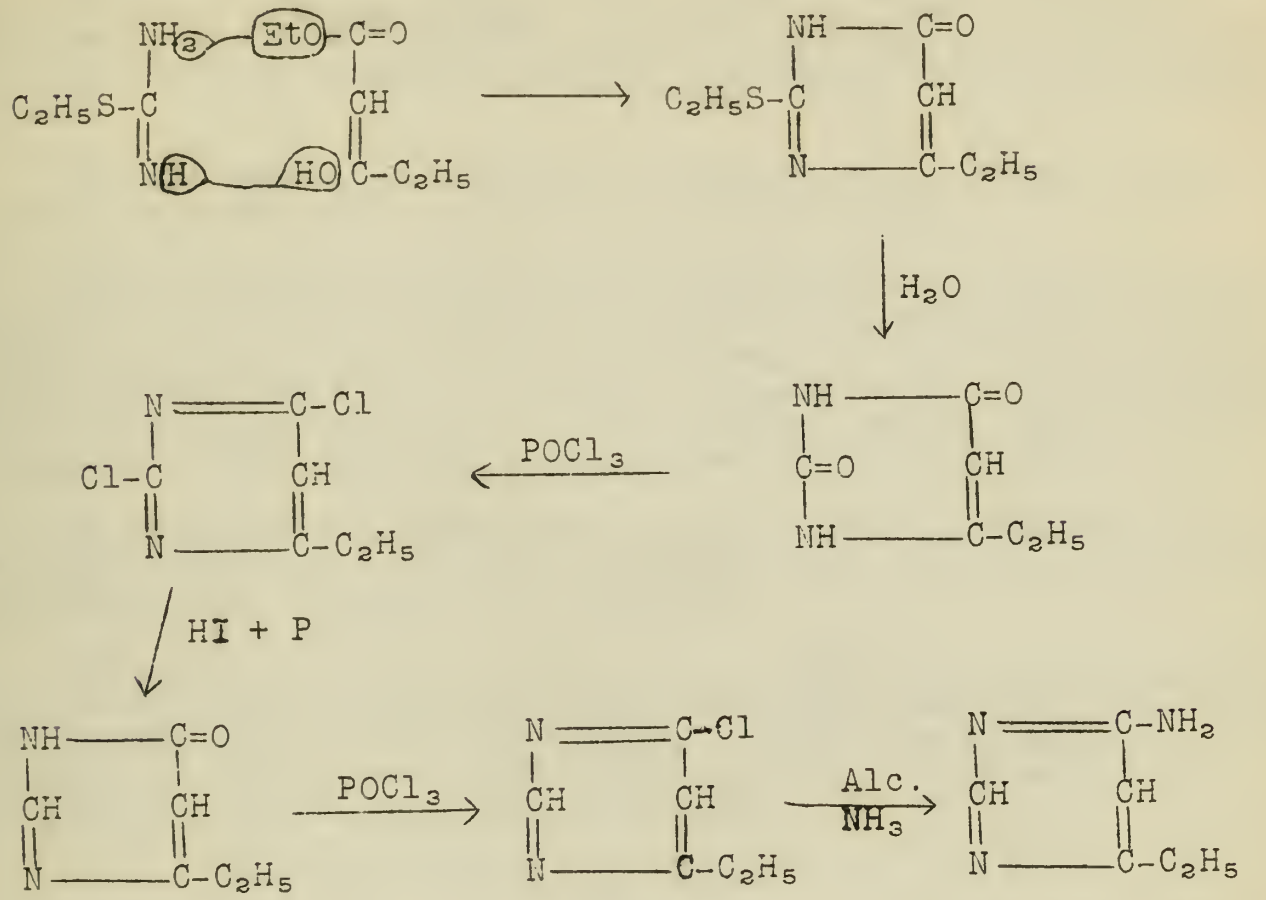
For example:

Uracil

Uracil is a weak acid with [illegible] and is [illegible] to give a good [illegible].

Many of the [illegible] of the [illegible] and [illegible] derivatives arise from their ability to [illegible] from the [illegible] and [illegible] forms to the [illegible] and [illegible] conditions. The [illegible] of [illegible] from [illegible] of the [illegible]. An example of this [illegible] is the [illegible]

The following, which represents a general method, is a synthesis for the pyrimidine likely present in Vitamin $B_1$.




4-ethyl-6-amino-
Pyrimidine

Reported by H. H. Hully
February 12, 1936.

Kögl and Boer, Rijks Univ., Utrecht
Rec. Trav. Chim., 54, 779 (1935)

Perezon is the orange-yellow coloring matter obtained from the roots of Perezia Adnata. The plant is found in Mexico. The material is of interest because of its physiological action. It has a strong purgative action, for which it is much used in Mexico.

Perezon was first isolated in 1885 by M. C. Wild, by an alcoholic extraction of the roots of the plant.

Analysis and molecular weight determinations show it to be $C_{15}H_{20}O_3$. Two of the oxygens belong to a quinone system and the third a phenolic hydroxyl. The presence of one double bond was shown by the addition of bromine. Treatment with aniline yielded an anilido compound which, on hydrolysis, yields oxy-perezon, $C_{15}H_{20}O_4$. This compound contains two phenolic groups.

On ozonization $\alpha,\beta$-diketo butyric acid is obtained. On warming oxy-perezon with concentrated $H_2SO_4$, water is split out and perezinon, $C_{15}H_{18}O_3$, is obtained.

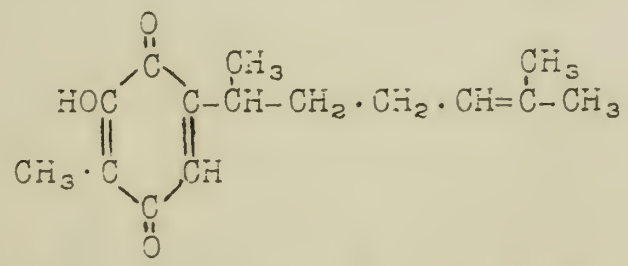
Oxidation of perezon with $H_2O_2$ in alkaline solution yields acetic acid and a higher boiling acid whose analysis and neutral equivalent showed it to be $C_9H_{16}O_2$. There are 91 possible isomers of this nonane acid. Kögl was able to show that the acid was identical with the following:

$$CH_3\cdot\underset{\underset{CH_3}{|}}{C}=CH\cdot CH_2\cdot CH_2\cdot\underset{\underset{CH_3}{|}}{CH}\cdot CO_2H$$

Proof of the positions of the side-chains on the quinone ring were shown by the following reactions:

Oxidation of tetramethoxy-leuko-dihydroxy-perezon yielded tetramethoxy-tere-phthalic acid.
Distillation with zinc dust of perezon gave an oil which on oxidation yielded tere-phthalic acid.

From the evidence which he had Kögl assigned the following structure to perezon:



Kögl states that this is the first natural product which has been found that contains a quinone of the sesquiterpene type.

Reported by R. C. Morris
February 19, 1936

# Synthesis of Diphenyl, 2,2'-Dipyridyl, 2,2'-Diquinolyl and Some of Their Homologs

Wibaut and coworkers: Rec. Trav. Chim., 54, 275 (1935)
" " " , 54, 804 (1935)
" " " , 54, 807 (1935)
" " " , 53, 584 (1934)
" " " , 53, 417 (1934)

Place: Laboratory for Organic Chemistry, University of Amsterdam.

Previous Work:

Diphenyl was prepared by heating benzene in a steel autoclave at 440° and 190 atmos. in the presence of nickel or iodine.

$$2C_6H_6 \longrightarrow C_{12}H_{10} + H_2$$

By the use of the same procedure 2,2'-dipyridyl, 2,2'-diquinolyl and 6,6'-dimethyl-2,2'-dipyridyl were synthesized. Some compounds of this type form highly colored complexes with ferrous salts. It was hoped to determine the conditions necessary for the formation of the complex in a molecule of this type. The 2,2'-linkage is necessary but not the sole factor.

2,2'-dipyridyl-3,3'-dicarboxylic acid was synthesized in order to attempt its resolution. Preliminary attempts failed but this work is being carried further.

The conditions for maximum yields for the dipyridyl were not as vigorous as those for diphenyl; consequently the pyridine nucleus must be more active than the benzene nucleus.

Reported by R. F. Miller
February 19, 1936

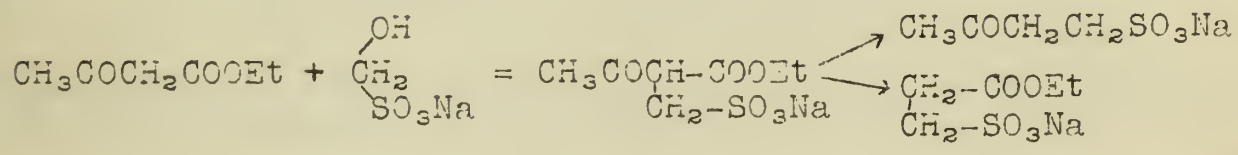
# The Constitution of the Sulfite Addition Compounds of Aldehydes and Ketones


1. Raschig and Prahl, Ludwigshafen a. Rh.
   Ber., 59, 859 (1926)
   " 59, 2025 (1926)
   " 61, 179 (1928)
   Ann., 448, 365 (1926)
2. Backer and Mulder, Groningue.
   Rec. Trav. Chim., 52, 454 (1933)
   " " " 53, 1120 (1934)
3. Lauer and Langkammerer,
   J. Am. Chem. Soc., 57, 2360 (1935)

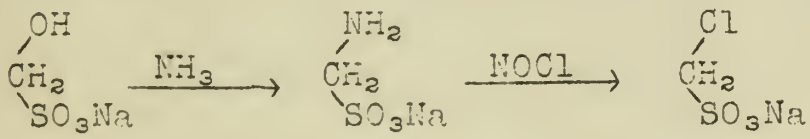

Early evidence on the structure of sulfite addition compounds consisted in the preparation of supposedly hydroxysulfonic acids which were not identical with the corresponding sulfite addition compounds.

Raschig and Prahl[1] in a series of investigations were able to show that previous workers had made the mistake of preparing, not the supposed hydroxysulfonic acids, but entirely different compounds. These were then compared with the sulfite addition compounds with the result that the sulfite additions were not found to be sulfonic acids.

In addition they have shown that formaldehyde sulfite adds to acetoacetic ester and subsequent cleavage always results in a sulfonic acid.



Further evidence in support of the sulfonic acid structure was brought out by Backer and Mulder,[2] who showed that treatment of the addition compound of formaldehyde and sulfite with $NH_3$ followed by NOCl resulted in a chlorosulfonic acid.



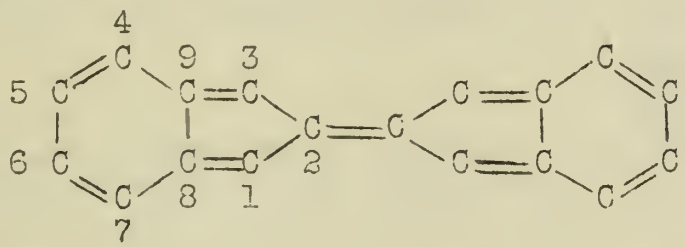
Lauer and Langkammerer,[3] with iodoform and the formaldehyde addition product as different starting materials, have built up sulfonic acids which they have shown to be identical, so establishing the identity of such addition as a hydroxysulfonic acid.

Reported by R. E. Damschroder
February 26, 1936.

In 1936, Moreau[1] discovered a red hydrocarbon, rubrene, by the action of heat on diphenylphenylethynylchloromethane:

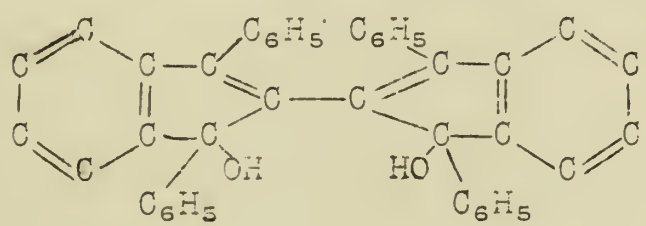
This orange-red hydrocarbon was slightly soluble in organic solvents, fluoresced, nitrated and sulfonated giving several isomers, and reacted with oxygen in the presence of light to give a dissociable dioxide. It had a characteristic absorption peak[2] at 4650, 4950 and 5300 A°. Vigorous oxidation gave a 50 per cent yield of o-dibenzoylbenzene, some benzoic and phthalic acids.

Various mechanisms[3] and structures have been offered for rubrene. Several methods of preparation have been offered and many substituted rubrenes have been made.[4] Willemart and Moreau[5] and coworkers, from the above information and the various reactions that it undergoes, have assumed that it is a dibenzobifulvene.



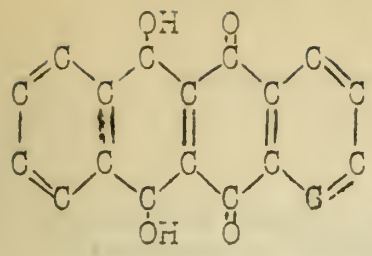
The continuous chain of conjugation as well as the o-quinoid structure contribute to its color.

Marvel and Eck[6] synthesized Bis-2,2'-(1,3-diphenylindol-3)

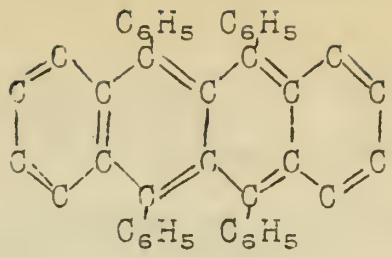


which should have been identical with dihydroxytetraphenylrubrene; however, the physical and chemical behavior of the compound did not agree with those of the dihydroxytetraphenylrubrene.

Recently, Dufraisse[7] synthesized 9,10,11,12-tetraphenylnaphthacene and has shown that this compound is identical with tetraphenylrubrene. The compound was prepared as follows:



1. $C_6H_5MgBr$
2. Dehydration
3. $C_6H_5MgBr$
4. Reduction

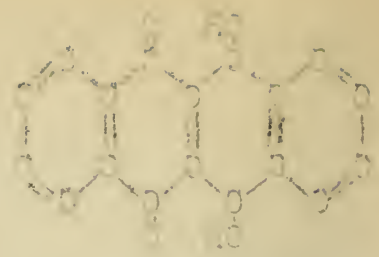


9,10-dihydroxynaphthacenequinone-11,12

Since this compound alters the structural formula of rubrene it must also alter the mechanism of formation and the explanation of its reactions.


1. Moreau and Dufraisse, Compt. Rend., 182, 1440 (1926)
   Bull. Soc. Chim., (4), 33, 934 (1923)
2. Dufraisse, Bull. Soc. Chim., 53, 739-849 (1933)
3. Willemart, Compt. Rend., 187, 385 (1928)
4. Dufraisse and others, Compt. Rend. 191, 619 (1930)
   192, 1389 (1931)
   194, 1664 (1932)
   195, 963 (1932)
5. Willemart, Compt. Rend., 187, 385 (1928)
6. Marvel and Eck, J. Am. Chem. Soc., 57, 1898 (1935)
7. Dufraisse and Velluz, Compt. Rend., 201, 394 (1935)


Reported by L. R. Drake
February 26, 1936.



9,10-Dihydroxyanthracene-1,4,5,8-tetrone

Since this compound is a strong acid, it reacts with bases to form salts. The mechanism of formation and the explanation of its reactions.


1. Morrow and Durkheimer, Chem. Rev., 22, 1-26 (1938)
2. Dufraisse, Bull. Soc. Chim., 37, 1-46 (1925)
3. Willstaedt, Chem. Abstr., 40, 4 (1946)
4. Dufraisse and Offerle, Compt. Rend., 210, 1-3 (1940)
5. Willstaedt, Compt. Rend., 1, 2, 2, (1939)
6. Harvel and Eck, J. Am. Ch. Soc., 57, 1-3 (1935)
7. Dufraisse and Velluz, Compt. Rend., 210, 1-3, 2, 3, 4 (1940)


Reference by E. E. Jones
February 20, 1950.

# ADDITION OF GRIGNARD REAGENTS TO β-KETO ALDEHYDES

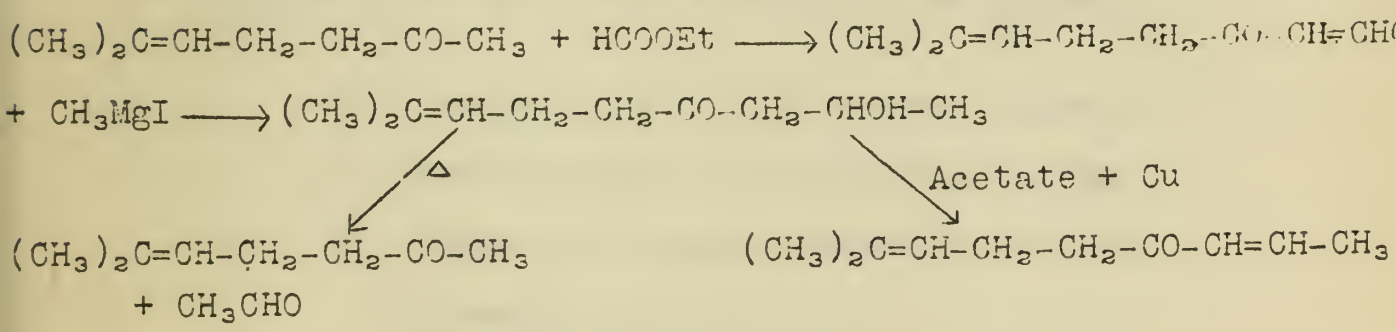
Meyer, R. E., Helv., 18, 101, 279, 282, 305, 461, 467, 470 (1935)
Basel, Institute for Inorganic Chemistry.

Previous work: Preservation and determination of citronellal; titrimetric determination of aldehydes and ketones.

The frequent 1,4 addition of the Grignard reagent to ordinary α,β-unsaturated ketones was studied by Kohler.

When Meyer reacted methylmagnesiumiodide with the oxymethylene derivative of 6-methyl-5-hepten-2-one, he obtained instead of the desired hydroxy aldehyde, which would give citral by dehydration, an oil which gave no crystalline phenylhydrazone or anil, positive tests with Tollen's and Schiff's reagents, and on dehydration by distillation gave besides the corresponding unsaturated compound, 60 per cent of 6-methyl-5-hepten-2-one and acetaldehyde. Careful dehydration by warming the acetate with powdered copper gave chiefly the corresponding compound.

To determine the structure of this product, the same reactions were carried out with 6-methylheptan-2-one and the product oxidized with permanganate, giving δ-methylcaproic acid. The reactions must then have been:




Both the positive aldehyde tests and the splitting of the product of the action of the Grignard reagent were ascribed to the β-hydroxyketone structure.

Although the absence of 1,2 addition prevents the formation of citral by this process, the 1,4 addition gives a fairly satisfactory way of augmenting a methyl ketone by an ethylidene group in compounds which do not readily undergo the Claisen-Schmidt reaction.

Reported by Frank C. McGrew
March 4, 1936.

# ADDITION OF BRANCHED FRAGMENTS TO β-KETO ALDEHYDES

Bauer, H. E., Helv. Ch. Acta, 46, 1, 1963, 2, 1963, 4, 1963, 46, 1, 1963.

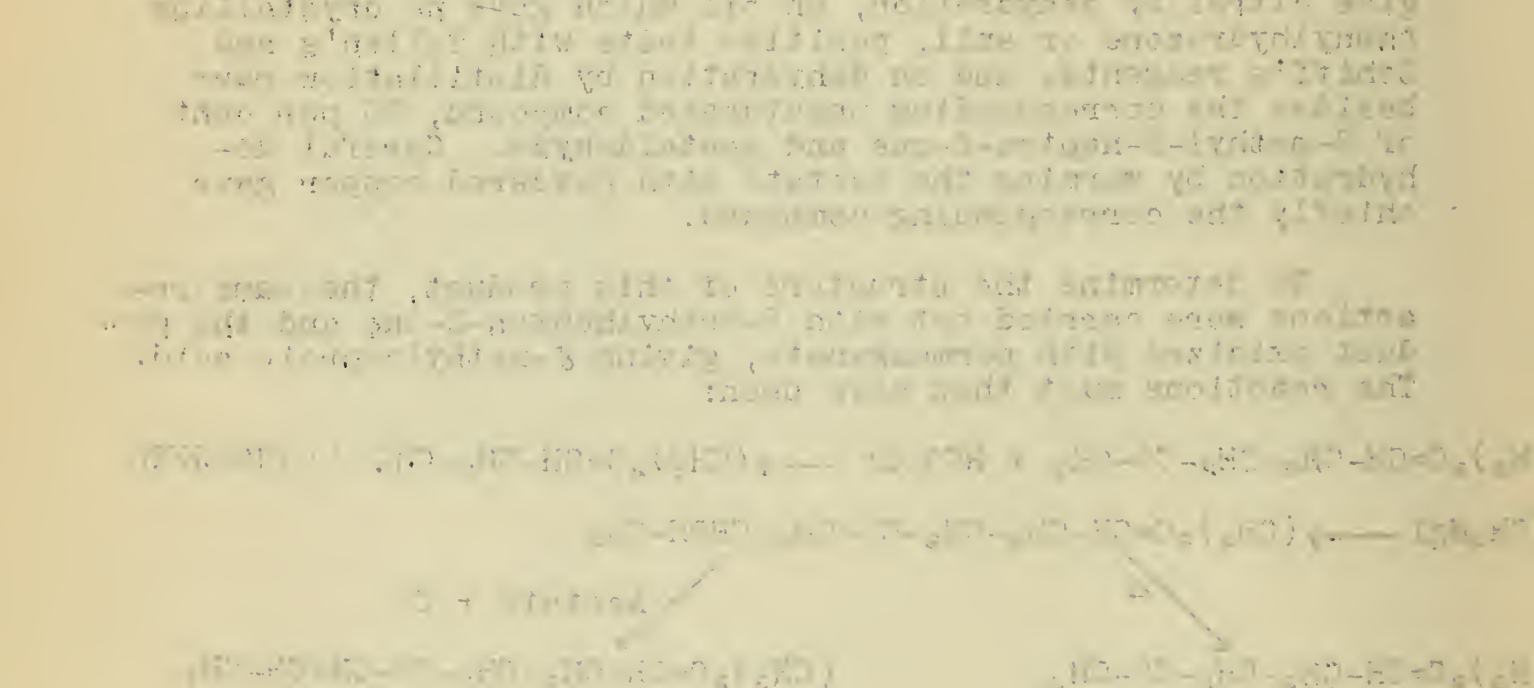
Bauer, Institute for Industrial Research.

Previous work: Preparation and fragmentation of alkoxyallenes; stereochemistry of alkoxyallenes and fragments.

The fragment $C_4H_9$ addition of the carbonyl compound to ethoxyallene β-hydroxyaldehyde was studied by Bauer.

Some hope remained regarding the work with the carbonyl-ene reactivity of 2-methyl-2-butene, by the behind interest of the history of the alkoxyl, which would give alkyl by hydrogenation, in all which case a carbonyl functionality or well, possible lists with [illegible] and [illegible] reactivity, and on dehydration by dialkylation, near basing the corresponding carbonyl compounds, in the case of β-methyl-butyl-2-one and methylbutyl. Clearly dehydration by writing the [illegible] with [illegible] compounds [illegible] the corresponding compounds.

To determine the structure of this product, the same reactions were repeated with [illegible] and the product obtained with [illegible], giving [illegible] with the reactions as [illegible] below:



Both the positive alkoxyl [illegible] and the addition of the product of the action of the [illegible] reactant were defined in the β-hydroxyaldehyde structure.

Since the [illegible] $C_4H_9$ addition prevents the formation of alkyl by [illegible], the addition [illegible] a [illegible] alkylation [illegible] by an alkylation group is necessary when [illegible] and [illegible] the [illegible] reaction.

Report by Frank T. Bauer
March 6, 1963.

Raman Spectra in Organic Chemistry

Kohlrausch and Pongratz, Monatsh, 64, 361 (1934)
Gredy, Ann. Chim., $11^{e}$, 4 (1935)
Gehman and Osterhof, J. Am. Chem. Soc., 58, 215, 1936.)

When monochromatic light (i.e., light of a single frequency) is passed through a compound or its solution, one observes not only the incident beam but also several other frequencies whose values are characteristic of the atomic bindings in the molecule. These studies are admirably adapted to the settlement of important organic questions of which the following are typical:

1. Determination of cis-trans isomers.
2. Determination of functional groups.
3. Types of linkages present; semi-polar normal covalent, etc.
4. Strength of atomic bindings.

Reported by R. T. Arnold

March 4, 1936.

## Future Studies in Organic Chemistry

Bullerwell and Thompson, Nature, 156, 344 (1945)
Grant, Ann. Chim., 12, 4 (1939)
Cohen and Cornwell, J. Am. Chem. Soc., 69, 1016, (1946).

When monochromatic light (i.e., light of a single frequency) is passed through a compound or its solution, one observes not only the incident beam but also several other frequencies which (also) are characteristic of the atomic grouping in the molecule. These studies are admirably adapted to the attainment of important organic questions of which the following are typical:

1. Determination of stereochemical isomers.
2. Determination of functional groups.
3. Types of linkages present: conjugated, normal, overlapped, etc.
4. Strength of certain linkages.

Reported by R. T. Lewis
March 5, 1953.

# THE RELATION BETWEEN ACIDITY AND TAUTOMERISM

F. Arndt and others,
Chemical Institute of
the University of Breslau.

Other Work: Use of diazomethane in synthesis.
Structure of Thiopyrones.

In 1932 F. Arndt and C. Martius studied the enotropic tendency (tendency to enolize) and the acidity of ketones carrying various substituents, and found these two qualities to be independent. The ability to confer acid properties by constituents is in the decreasing order:

$SO_3R$, $SO_2R$, $SO_2NR_2$, $CO_2R$, CHO, COR, whereas the enotropic tendency for the last three substituents is in the decreasing order: CHO, COR, $CO_2R$. These results were obtained by use of the ferric chloride color reaction, bromine titration, and reaction with diazomethane.

The reaction of diazomethane was extended to study the relation between acidity and tautomerism in amides, hydroxamic acids, sulfinic acids, and sulfohydroxamic acids,[2] and in 1935 nitro compounds were investigated.[3]

The acidifying effect of the CN group when substituted on ketones was found to be stronger than that of any C-containing simple substituents and follows the $SO_2R$ group in the list above.[4] It was found that the $>$CHCN group would be transformed into the enimide group if another group, such as CN, $CO_2R$, or $NO_2$, is present on the same carbon. The -C=C=NH group behaved toward $FeCl_3$, $Br_2$, and $CH_2N_2$ like the enol group.

1. Arndt and Martius, Ann., 499, 228 (1932).
2. Arndt and Scholz, Ann., 510, 62 (1934).
3. Arndt and Rose, J. Chem. Soc., 1-10 (1935).
4. Arndt, Scholz, and Frobel, Ann., 521, 95 (1935).

Reported by G. A. Nesty
March 11, 1936.

# THE REACTION BETWEEN ACIDITY AND BACTERICIDES

F. Arnold and Gerhard
Chemical Institute of
the University of Uppsala

Other Part: Use of Bioassays in Antibiotic Structure by Phenylpyrrole.

In 1957 F. Arnold and G. Gerhard studied the antibiotic tendency (bacteria to antibiotic) and the ability of bacteria carrying various substituents, and found that the activities to be independent. The ability to monitor acid (separation by constituents is in the decreasing order:

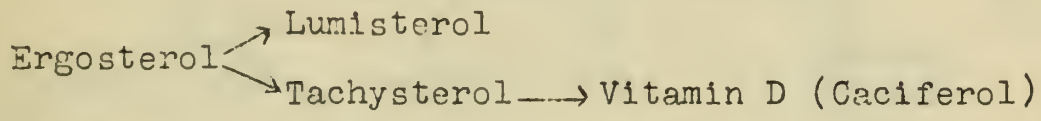
$SO_3H$, $SO_2H$, $SO_2NH_2$, $COOH$, $CHO$, $COR$, $CONH_2$, $CN$, $CONH_2$, $CONH_2$, $CONH_2

# On the Constitution of Vitamin $D_2$

A. Windaus and W. Theile
Ann., 521, 160 (1935)
University Laboratories, Göttingen

Previous work: On the sterols, recently on the irradiation of ergosterol.

The artificial irradiation of ergosterol leads to the following products:




Windaus has previously reported the isolation of Vitamin D from the irradiation products of ergosterol. This was described as Vitamin $D_1$, inasmuch as there were indications that a second antirachitic principle existed. Later it was found that $D_1$ was in reality the vitamin in combination with a physiologically inert isomer, lumisterol. Further purification resulted in the isolation of the vitamin, this being accomplished independently in the laboratories of Windaus and Askew. Askew used the term Calciferol for the vitamin, while Windaus designated it as Vitamin $D_2$.

The Vitamin $D_2$ obtained from the irradiation process is shown to have an empirical formula ($C_{28}H_{44}O$) identical with that of ergosterol. Thus it seems that the photochemical transformation must consist of a rearrangement of the double bonds or a steric transformation.

The vitamin is shown to possess four double bonds, in contrast to ergosterol which possesses only three, and hence it may contain only three rings.

Ozonization yields methyl iso-propyl aldehyde as does the ozonization of ergosterol. Hence the unsaturation in the side chain is between $C_{22}$ and $C_{23}$.

Maleic anhydride adds to the vitamin, which suggests the presence of a conjugated system. This addition is shown to take place between $C_6$ and $C_{18}$.

This vitamin-maleic acid addition product is reduced by the use of Pd and Hydrogen to the dihydro derivative in which the double bond between $C_{22}$ and $C_{23}$ is reduced.

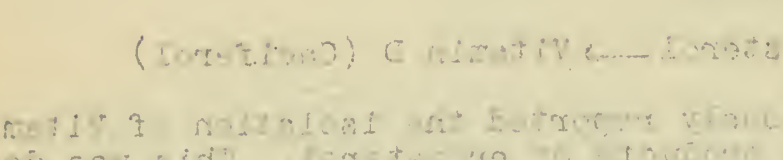
Ozonization of this derivative yields the ketone $C_{19}H_{34}O$ containing rings C and D.

# On the Constitution of Vitamin $D_3$

A. Windaus and W. Thiele
Ann., 521, 123 (1936)
University Laboratories, Göttingen

Previous work: On the steroids, especially on the irradiation of ergosterol.

The artificial irradiation of ergosterol leads to the following products:




Windaus has previously reported the isolation of Vitamin D from the irradiation products of ergosterol. This was described as Vitamin $D_1$. However, he later were indications that a second antirachitic principle existed. Later it was found that $D_1$ was in reality the vitamin in association with a physiologically inert isomer, lumisterol. Further purification resulted in the isolation of the vitamin, this being accomplished independently in the laboratories of Windaus and Askew. Below used the term Calciferol for the vitamin, while Windaus designated it as Vitamin $D_3$.

The Vitamin $D_3$ obtained from the Askew isolation process is shown to have an empirical formula ($C_{27}H_{44}O$) identical with that of ergosterol. Thus it seems that the chemical transformation must consist of a rearrangement of the double bonds or a steric transformation.

The vitamin is shown to possess four double bonds, in contrast to ergosterol which possesses only three, and hence it may contain only three rings.

Isomerization yields another isomer, lumisterol, which does not contain ergosterol. Hence the transformation in the rings chain is between $C_9$ and $C_{10}$.

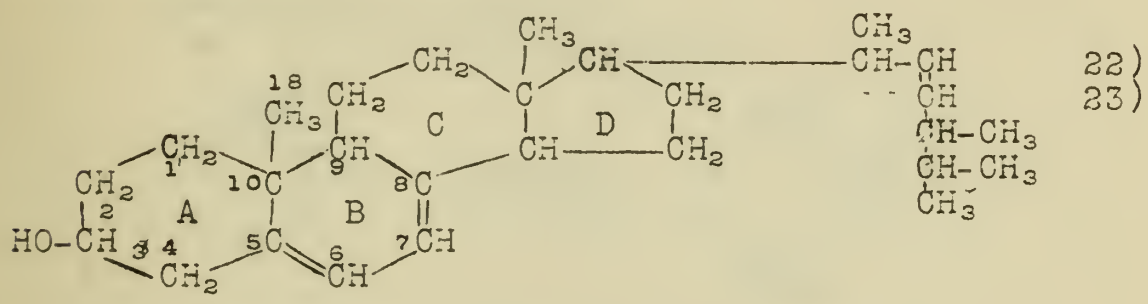
Nitric anhydride adds to the vitamin, which suggests the presence of a conjugated system. This addition is shown to take place between $C_5$ and $C_{10}$.

This vitamin-nitric acid addition product is reduced by the use of Zn and hydrogen to the dihydro isomeride, in which the double bond between $C_{10}$ and $C_{19}$ is reduced.

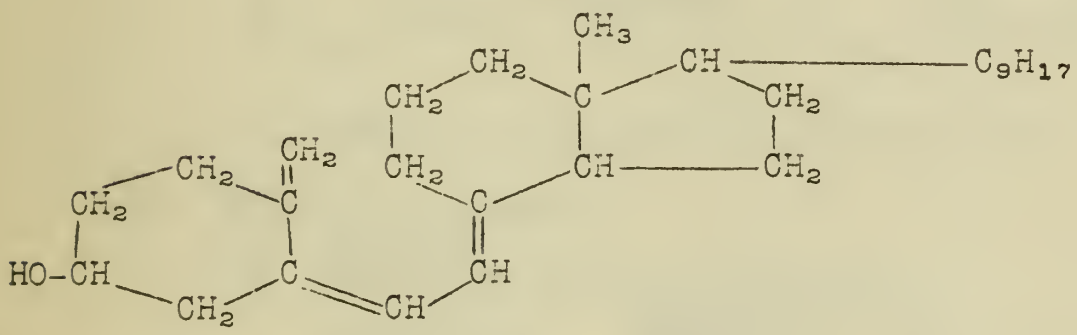
Oxidation of this isomeride yields two ketone fragments containing rings C and D.

Treatment of the vitamin-maleic acid addition product with Pd yields naphthoic acid and naphthalene. Treatment with Se yields 2,3-dimethyl naphthalene. Thus it is concluded that a carboxyl-containing naphthalene ring is present in this derivative.

From these facts Windaus postulates the accompanying structure for Vitaming $D_2$.



Ergosterol



Vitamin $D_2$ (Calciferol)

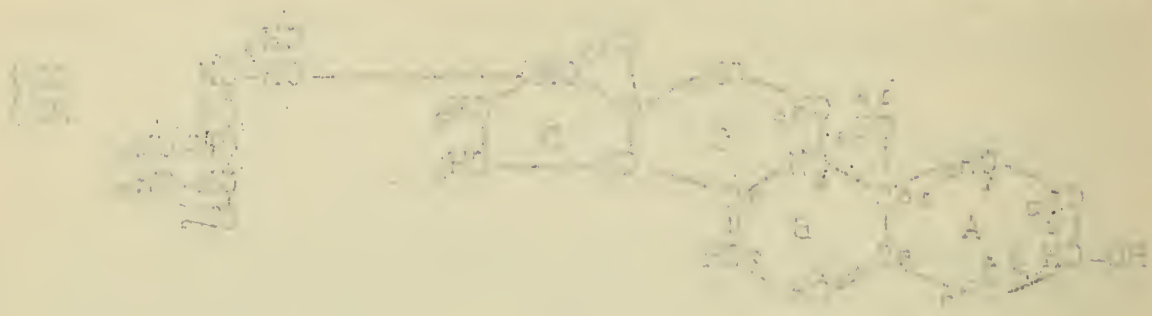
Bibliography:

Windaus, Ann., 489, 252 (1931)
ibid., Ann., 492, 226 (1932)
ibid., Ann., 499, 188 (1932)
ibid., Ann., 521, 160 (1935)
Lettre, Ann., 511, 285 (1934)
Heilbron, Jour. Soc. Chem. Ind., 54, 795 (1935)
Windaus, Angew. Chem., 48, 527 (1935).

Reported by George B. Brown
March 11, 1936.

Treatment of the 25(OH)-vit D with dehydration products yield 25 yields monohydroxy and dihydroxy. Treatment with Br yields 3,5-dihydroxy-monobromide. Thus it is concluded that a cyclopropyl-containing structure is also in present in this derivative.

Thus three first [illegible] conclusions for structure for vitamin $D_3$:



Scheme 1

Vitamin $D_3$ (cholecalciferol)

Bibliography:
[illegible] Ann. [illegible] (1961)
[illegible] Ann. [illegible] (1961)
[illegible] Ann. [illegible] (1960)
[illegible] Ann. [illegible] (1960)
[illegible] Ann. [illegible] (1960)
[illegible] Ann. [illegible] (1960)
[illegible] Chem. Ber. [illegible] (1960)
[illegible] Angew. Chem. [illegible] (1961).

Supported by Grants [illegible]
[illegible] [illegible].

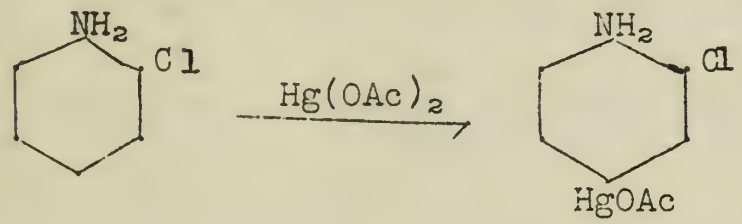
# REACTIONS OF MERCURIC ACETATE WITH ORGANIC COMPOUNDS

Matejka, K., Ber., 69, 274 (1936)
Carter, J. Biol. Chem., 112, 769 (1936)
Wright, J. Am. Chem. Soc., 57, 1993 (1935)
Abderhalden, Ber., 67, 530 (1934)
Nails and Patet, J. Ind. Chem. Soc., 9, 185 (1932)
and many others.

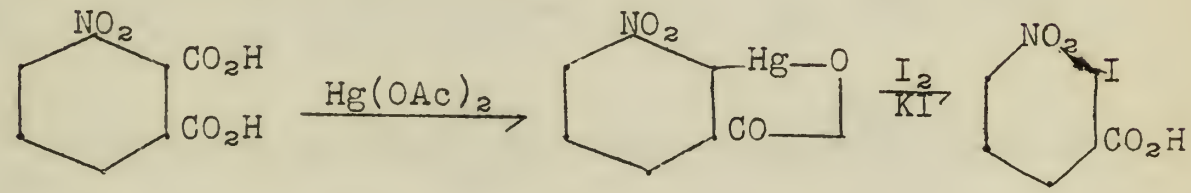
Previous work: Matejka -- none.

I. Substitution reactions

A. In an aromatic nucleus




B. Replacement reactions

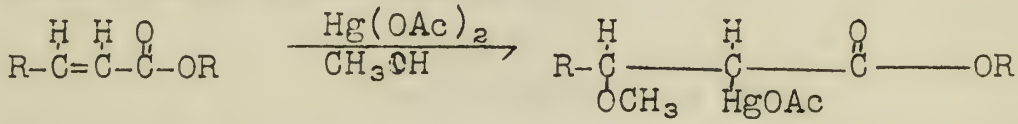



C. Effect of an active methylene group.

II. Addition reactions

A. Olefins

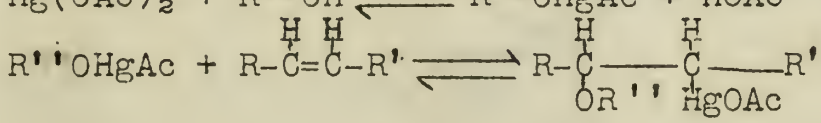
B. Unsaturated acids and esters

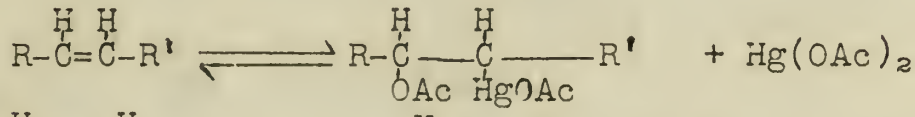


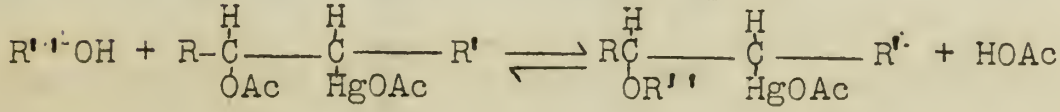

C. Unsaturated phenols, phenolic ethers and coumarins.

III. Mechanism of addition reaction

A. $Hg(OAc)_2 + R''OH \rightleftharpoons R''OHgAc + HOAc$



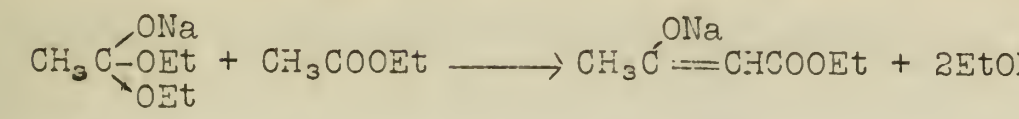

B. 

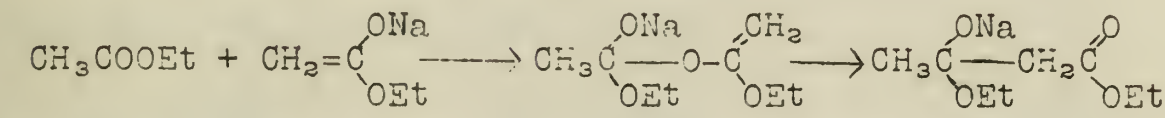

Reported by John Cowan
March 18, 1936

# THE MECHANISM OF THE ACETOACETICESTER CONDENSATION

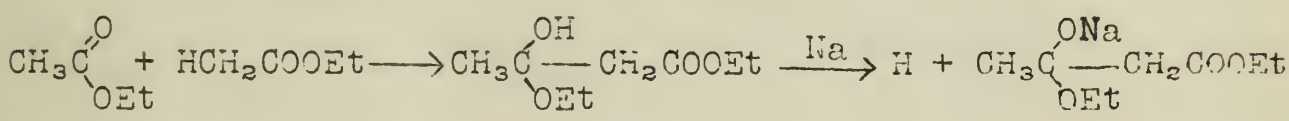
Claisen, Ber., 20, 652 (1887); Ann., 297, 92 (1897)



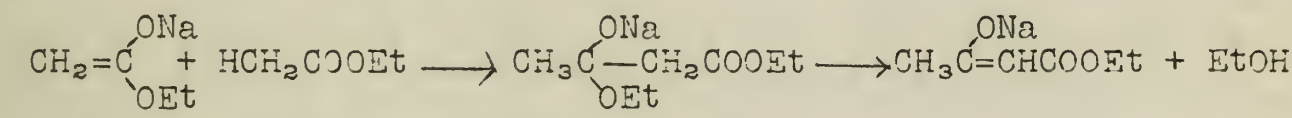
Claisen, Ber., 38, 709 (1905)



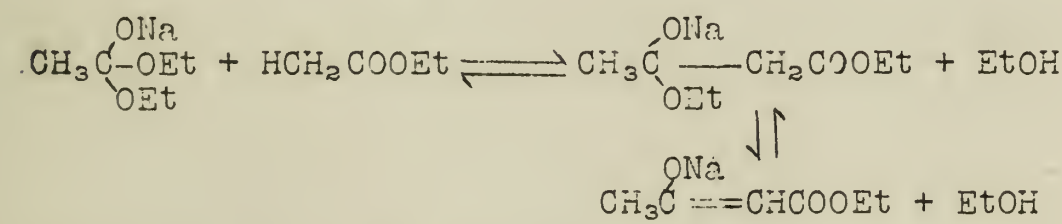
Michael, J. Prakt. Chem., (2) 37, 483 (1888)



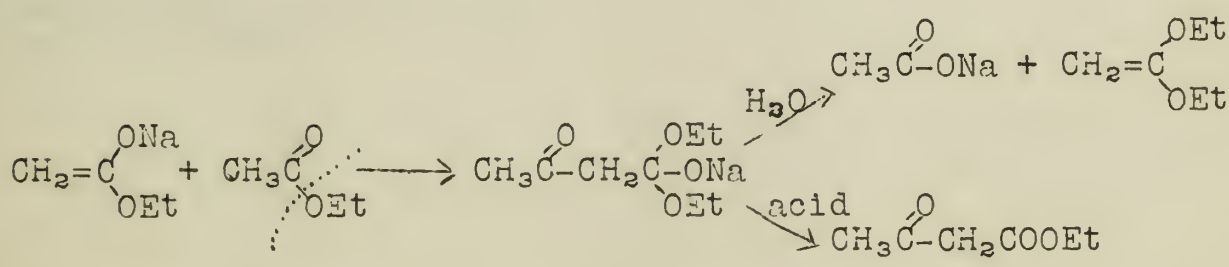
Nef, Ann., 298, 319 (1897); Michael, Ber., 38, 1922 (1905); Schroeter, Ber., 49, 2706 (1916)



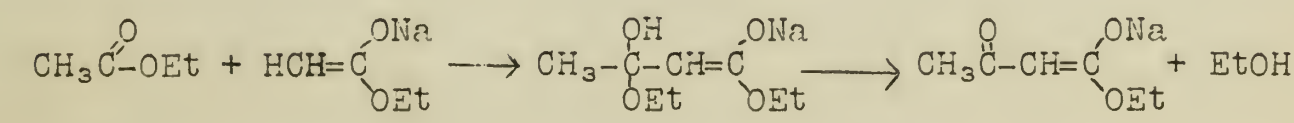
Dieckmann, Ber., 33, 2678 (1900)



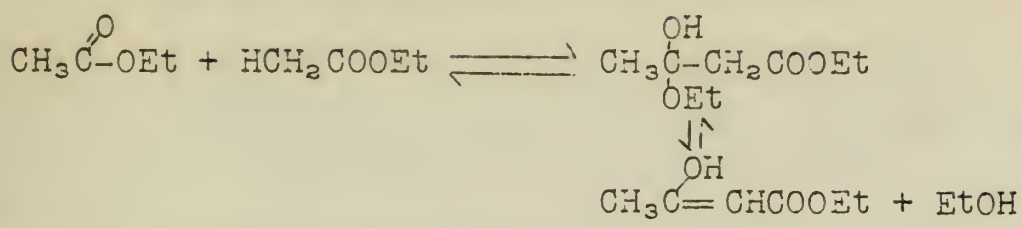
Scheibler, Ber., 55, 789 (1922); 59, 1022 (1926)



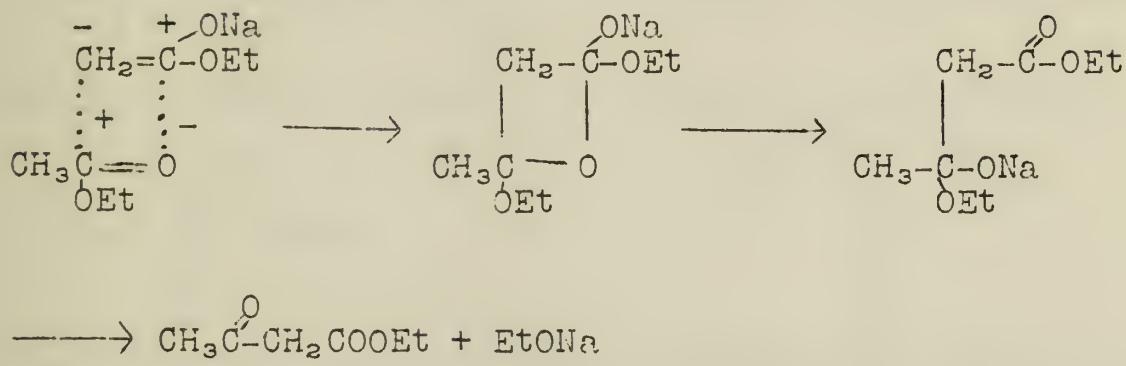
Chelintzev, Ber., 67B, 955-63 (1934)



McElvain, J. Am. Chem. Soc., 56, 1173 (1934)



Bodendorf, Ber., 67B, 1338 (1934)



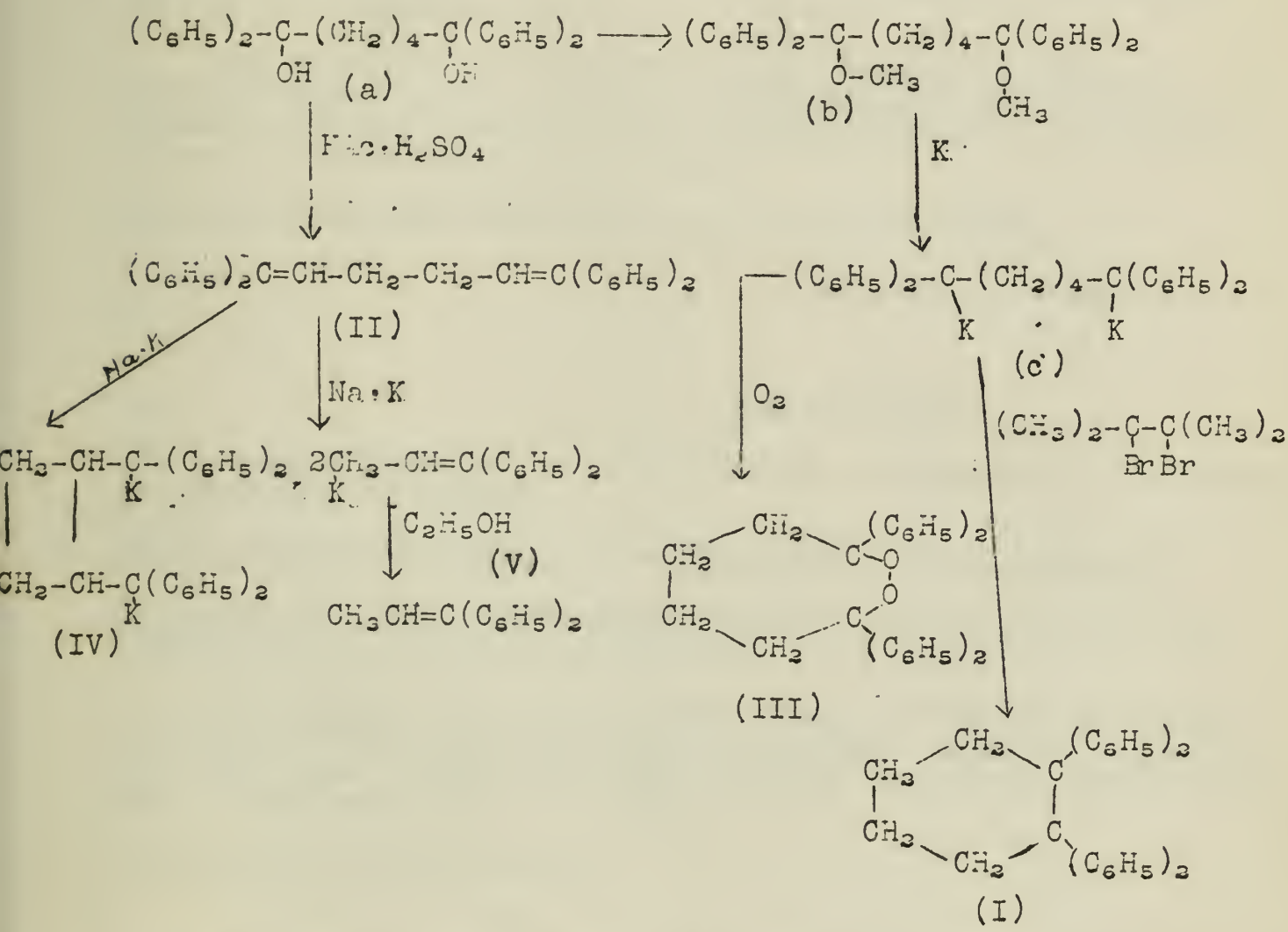
In the most recent work on the mechanism of this reaction, Adickes and Meister, Ber., 68, 2191 (1935), have obtained evidence indicating the mechanisms of Claisen and Scheibler to be incorrect. This work was done at the Chemical Institute of Tübingen University.

Reported by P. S. Pinkney
March 18, 1936

# Some Researches on the Effect of Tetra ($\beta,\beta$-Diphenylvinyl) Substitution on the Strength of the Ethane Band.

G. Wittig and Leo, Ber., 63, 943 (1930)
G. Wittig Ber., 64, 437 (1931)
G. Wittig and Obermann, Ber., 68, 2214 (1935)
Marbourg -- Chemical Institute

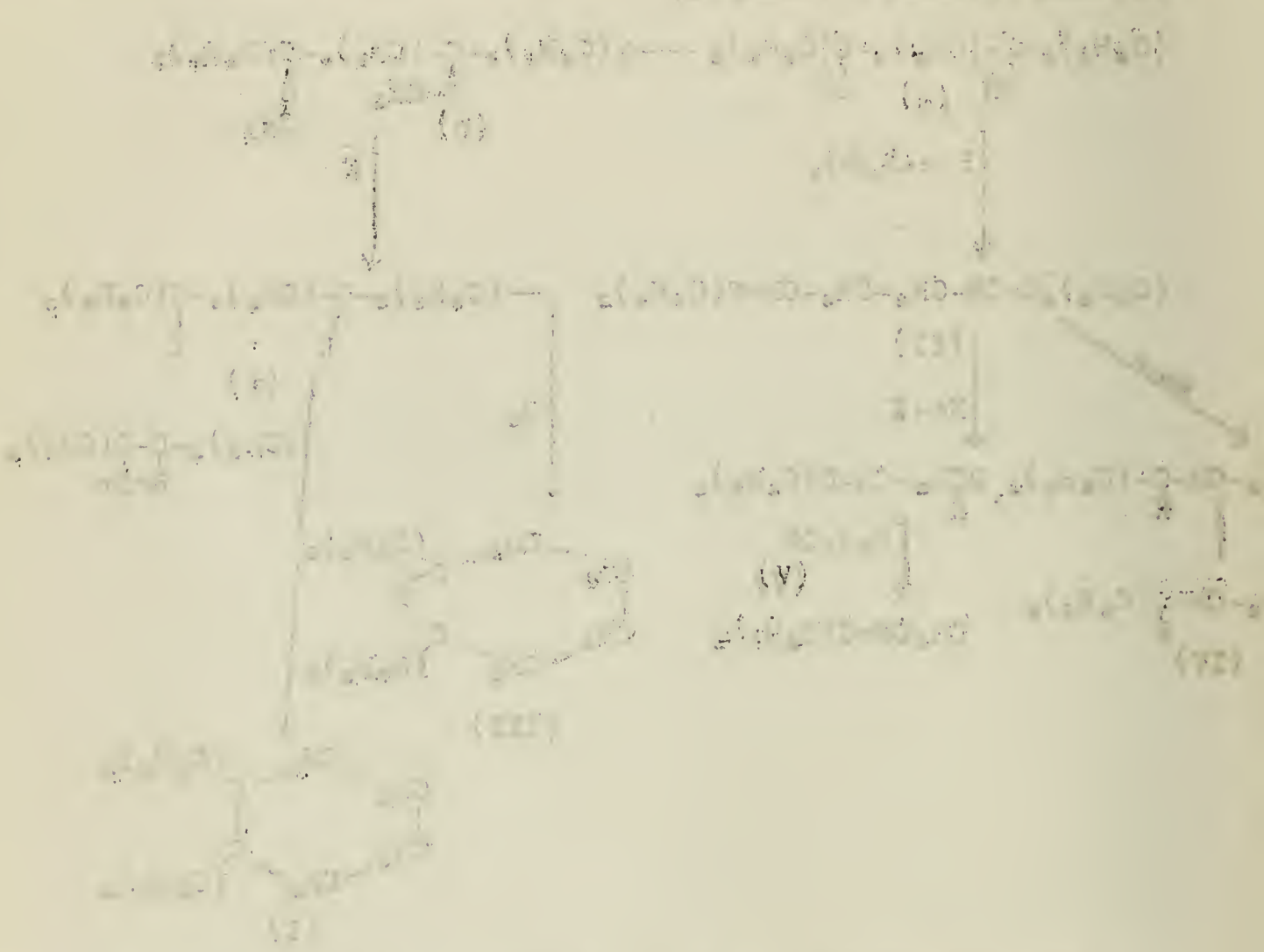
In an investigation on the effect of a ring structure on free radical formation Wittig et al attempted to prepare 1,1,2,2-tetraphenylcyclohexane by the following series of reactions:
(a) ⟶ (b) ⟶ (c) ⟶ (I)




The cyclohexane (I) was not obtained, instead a mixture of unknown composition resulted. However, a peroxide which analyzed for (III) could be obtained.

Treatment of the dipotassium compound (c) with alcohol formed 1,1,6,6-tetraphenylhexane.

It was thought that treatment of 1,1,6,6-tetraphenylhexadiene 1,5 (II) by Na · K alloy would give the cyclobutane (IV). Actually the K compound (V) was obtained and treatment with alcohol gave 1,1-diphenylpropene-1.



Further evidence of the splitting of the ethane band by an alkalie metal was obtained by the following series of reactions:

$$\underset{(IX)}{(C_6H_5)_2CH-CH_2-CH=C(C_6H_5)_2} \xrightarrow{Na\cdot K} (C_6H_5)_2CH-K + \underset{(XI)}{KCH_2-CH=C(C_6H_5)_2}$$

$$\downarrow CH_3OH$$

$$(C_6H_5)_2CH_2 + CH_3CH=C(C_6H_5)_2$$

Thus the ethane band is weakened by certain groups and the effect of such groups on this band is evidently transferred through the linkage -C=C-.

The weakness of the band is also observed in thermal decomposition. 1,1,6,6-Tetraphenylhexadiene-1,5 (II) can be vacuum distilled indecomposed, but distillation at atmospheric pressure causes disproportionation.

$$(C_6H_5)_2C=CH-CH_2-CH_2-CH=C(C_6H_5)_2 \xrightarrow{\Delta} (C_6H_5)_2C=CH-CH_3$$

50 per cent yield

+

$$[CH_2=C=C(C_6H_5)_2]$$

1,1,4,4-Tetraphenylbutene-1 is likewise decomposed on distilling at atmospheric pressure.

$$(C_6H_5)_2CH-CH_2-CH=C(C_6H_5)_2 \xrightarrow{\Delta} (C_6H_5)_2CH + [CH_2=C=C(C_6H_5)_2]$$

In contrast, 1,1,4,4-tetraphenylbutene 2 can be distilled indecomposed at atmospheric pressure.

This effect of a $\beta,\beta$-diphenyl group led Wittig to attempt to prepare tetra-($\beta,\beta$-diphenylvinyl)-ethane, with the expectation that such a compound might manifest some free radical tendency. This was done as follows:

$$(C_6H_5)_2C=CH-CH_2-CH=C(C_6H_5)_2$$

$$\downarrow Li \qquad (2)$$

$$(C_6H_5)_2C=CH-CH-CH=C(C_6H_5)_2$$

$$\downarrow Li \qquad (3a)$$

$$(CH_3)_2\underset{Br}{C}-\underset{Br}{C}(CH)_2$$

$$(C_6H_5)_2C=CH-CH-CH=C(C_6H_5)_2$$

$$|$$

$$(C_6H_5)_2C=CH-CH-CH=C(C_6H_5)_2$$

(4)

(4) is a colorless solid m.p. 169-175°. It dissolves in zylene to give a colorless solution. By heating the solution to boiling a yellow color develops; on cooling the color disappears. This can be repeated many times. However, on prolonged boiling the solution remains colored and the original material can not be recovered. This may be interpreted that (4) dissociates at high temperatures.

Reported by G. E. Ullyot
March 25, 1936.

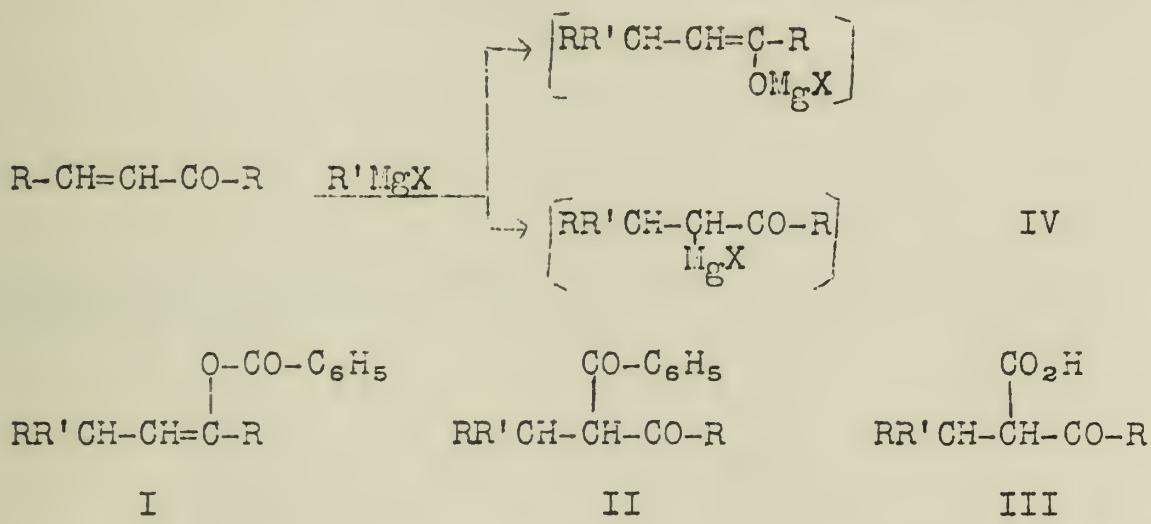
# The Structure of the Metallic Derivatives which are Formed by Adding Grignard Reagents to Unsaturated Ketones

Kohler and Tischler, J. Am. Chem. Soc., 54, 1594 (1932)
Kohler, Tischler and Potter, J. Am. Chem. Soc., 57, 2517 (1935).

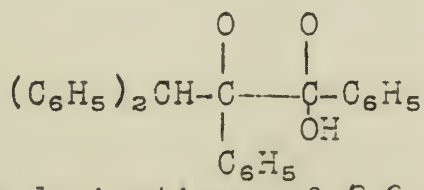
Harvard University

Kohler, in 1905, had suggested that the primary addition of a Grignard reagent to an $\alpha,\beta$-unsaturated ketone was 1,4 to the conjugated system. On treatment of the metallic addition compound with benzoyl chloride he obtained a substance which he thought to be the benzoate I, but which he subsequently found to be the $\beta$-diketone II.

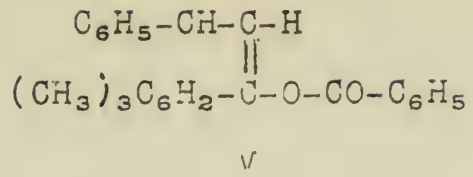
Because of the formation of the $\beta$-diketone on benzoylation, and because a $\beta$-keto acid III was formed when the metallic derivative was treated with carbon dioxide, Umnowa postulated the intermediate formation of a carbon-magnesium complex IV.




The first evidence that the addition was 1,4 was obtained when Kohler and Kischler treated an $\alpha,\beta$-unsaturated ketone which contained an aryl group in the $\alpha$ position with the Grignard reagent, and obtained, on hydrolysis of the addition compound, an enolic substance stable enough to form a peroxide.




The magnesium derivatives of $\beta,\beta$-diphenylpropionylmesitylene may be obtained by three methods. Treatment of a substance obtained by one of these methods with benzoyl chloride gives a different compound than is isolated when the magnesium derivative prepared by the other two methods is so treated. Ease of hydrolysis indicates that the two substances are the benzoates, V and its geometric isomer.



V

Isolation of these two isomers proves that the addition of the Grignard reagent to a conjugated system C=C-C=O gives rise to an -OMgX linkage.

The enol which is obtained on hydrolysis of the isomers has remarkable stability. It appears to be completely permanent in the solid form, and can be recrystallized without change. The unusual lack of mobility in this enol, doubtless is largely due to the mesityl group, for if the mesitylene nucleus is replaced by phenyl the mobility becomes normal.

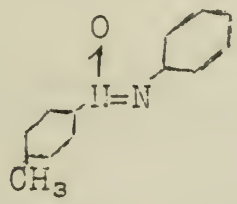
Reported by Harry H. Weinstock, Jr.
March 25, 1936.

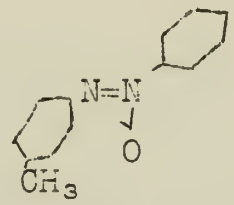
Bigelow, Chem. Rev., 9, 117 (1931)
Chu and Marvel, J. Am. Chem. Soc., 55, 2841 (1933)
Muller, Ann., 493, 166 (1932)
Muller, Ann., 495, 132 (1932)
Muller and Hory, Z. Physik. Chem., 162, 281 (1932)
Gerckens and Muller, Ann., 500, 296 (1933)
Muller and Illgen, Ann., 521, 72 (1935)

Location: Muller--Technische Hochschule Danzig-Langfuhr.

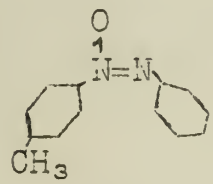
## I. Isomerism.

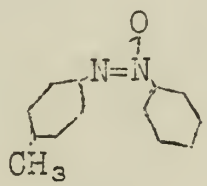
Structural isomerism permits an azoxybenzene of the type $ArN_2OAr'$ to exist in the two stable trans forms:





The cis isomers of some azoxybenzenes are also known giving the additional labile forms:





## II. Methods of preparation.

(a) Reduction of nitro compounds
(b) Oxidation of amines or azo compounds

(c) $Ar-\overset{O}{N}=O + H_2N-Ar \xrightarrow{Na} Ar-\overset{O}{N}=N-Ar$

(d) $Ar-N=O + H-\underset{\underset{H}{O}}{N}-Ar \longrightarrow Ar-\underset{O}{N}=N-Ar$

## III. Reactions.

(a) Oxidation and reduction
(b) Substitution (the tervalent nitrogen enhances the activity of the ring to which it is attached)
(c) Wallach's rearrangement.

Reported by William Fessler
April 1, 1936.

# The Synthesis of Phenanthrene and Hydrophenanthrene Derivatives

Louis F. Fieser and E. G. Hershberg, J. Am. Chem. Soc., 57, 1851, 2192 (1935).

Harvard University.

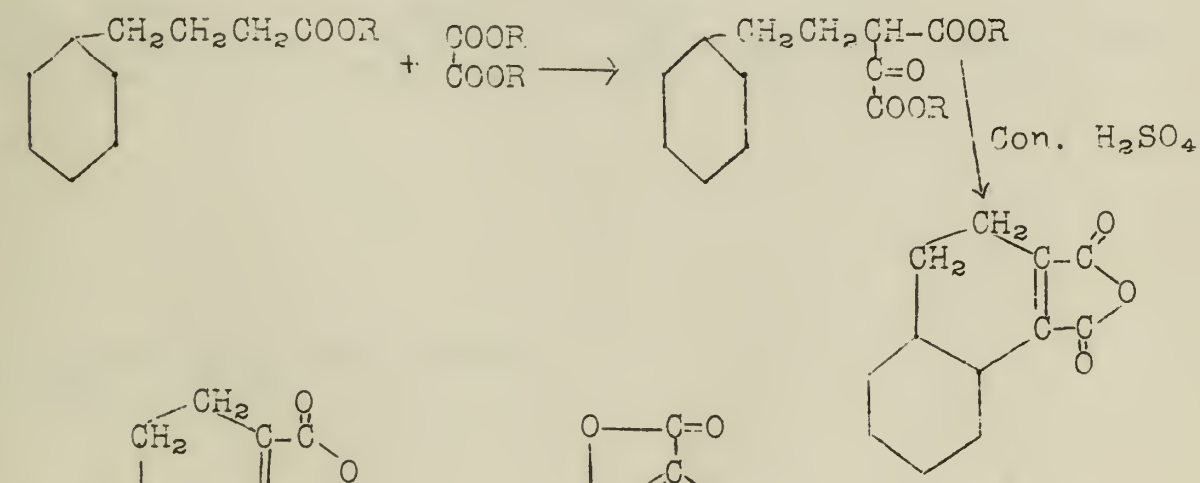
The most prominent synthetic routes to members of the phenanthrene series were developed to provide methods for the identification of degradation products of certain naturally occurring substances. Some of these synthetic methods are:

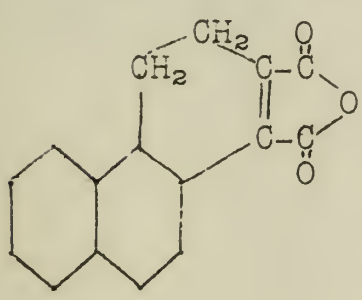
1. Pschorr's - developed for application to studies in the morphine series, it utilized o-nitrobenzaldehyde and phenyl acetic acid.[1]

2. Bardhan and Sengupta's - was first applied in studies on resin acids, it employed a cyclic beta-keto-ester and a substituted beta-phenyl ethyl bromide.[2]

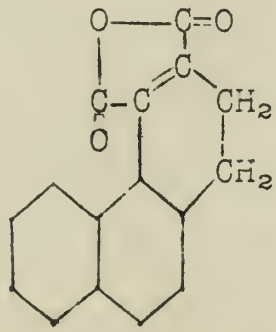
3. Cyclization of gamma-aryl butyric acids - used in studies on sterols and related substances.[3]

Fieser and Hershberg have used gamma-aryl butyric esters in the Bougault reaction as shown:



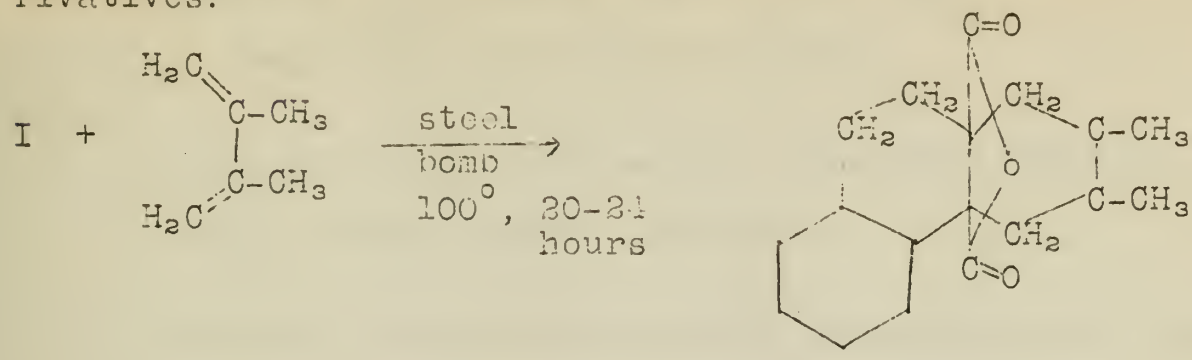

II.




III.

II and III have also been prepared.

These anhydrides are used in a new "Hydrocarbon Synthesis" for phenanthrene and hydrophenanthrene derivatives:




IV.

From IV there have been prepared the dibasic acid, the acid and the neutral esters, the reduced anhydride and the corresponding substituted aromatic hydrocarbon.

Further studies of the diene addition products and further applications of this new phenanthrene synthesis are in progress.

1. Pschorr, Ber., 29, 496 (1896).
2. Bardhan and Sengupta, J Chem. Soc., 1932, 2530, 2798.
3. Haworth, J. Chem. Soc., 1932, 1125.

Reported by Allene Jeanes
April 1, 1936.

# Oxidation of Olefinic Double Bonds with Perbenzoic and Peracetic Acids

From the work of Prilezhaev, Böeseken, Meerwein, Smit, Braun, Muskat, and others.

In 1909 Prilezhaev reported that perbenzoic acid would oxidize olefinic double bonds to give the cyclic oxide which in most cases could be hydrolized to the corresponding glycol. Since then much work has been done in this field so that it is now possible to use this acid and peracetic acid to quantitatively determine certain double bonds.

Ordinarily conjugated systems do not react normally, and $\alpha,\beta$-unsaturated carbonyls are especially inert to oxidation. However, the following observations have been made regarding isolated olefinic double bond oxidation:

1. The more highly alkylated the olefin, the greater will be the speed of oxidation.
2. With aryl compounds, the nearer the double bond to the aromatic nucleus, the greater will be the speed of oxidation.
3. With aliphatic compounds, RCOO and OH are added <u>trans</u> to the double bond.

Reported by Wm. E. Lundquist

April 8, 1936.

Oxidation of Sulfide Bonds with

Ferricyanic and Peracetic Acid

from the work of Inglesby, Eckstein, Horecker,

Smit, Brown, Hoefs, and others.

In 1956 Pulmanny reported that ferricyanic acid would oxidize sulfhydryl groups to give the cyclic cystine in most cases could be hydrolized to the corresponding cysteol. Since then such work has been done in this field so that it is now possible to use this acid and peracetic acid to quantitatively determine cystein disulfide bonds.

Continually conjugated systems do not react normally, and α,β-unsaturated carbonyls are especially inert to oxidation. However, the following conditions have been found favorable for isolated sulfhydryl groups:

1. The more highly ionized the sulfhydryl, the more will be the speed of oxidation.
2. With aryl compounds, the greater the resonance to the phenolic residue, the greater will be the speed of oxidation.
3. With aliphatic compounds, SO2 can be added trans to the sulfhydryl.

Been read by Wm. P. Lombardi

April 2, 1956.

# CIS-TRANS ISOMERISM IN SUBSTITUTED CYCLOPENTANOLS

G. Chiurdoglu, Bul. Soc. Chim. Belg., 44, 528 (1935)
G. Vavon, Bul. Soc. Chim. France, 49, 989 (1931)
W. Hückel, L. Annalen, 477, 154 (1930)

Some of the methods used in assigning structures to a pair of these geometric isomers are:

I. Methods of preparation.--Reduction with hydrogen and platinum in acid solution gives a preponderance of the cis isomer; while in neutral solution or with sodium and alcohol a preponderance of the trans isomer is formed in the reduction of substituted phenols, toluidides, cyclopentanones, etc.

II. Correlation of physical data on the two isomers.--Auwers' rule states that in a pair of cis-trans cyclanes the cis form has the greater density and index of refraction, and the smaller molecular refraction. This has been found generally true in cyclohexanes and cyclopentanes, but exceptions exist.

Stoermer found that in 19 cis-trans isomers containing the group $-CO_2CH_3$ the trans isomer had the higher boiling point in every case.

III. Chemical reactions of the two isomers.--In cyclopentanes containing an OH or $NH_2$ group, and a -COOH group, the formation of a lactone or lactan indicates a cis structure.

In a pair of substituted cyclopentanols the isomer dehydrating the most readily is the one where the OH is in a trans position with the H with which it is eliminated.

In a pair of substituted cyclopentanols the trans isomer will esterify faster than the cis, and the corresponding trans ester will saponify faster than the cis.

In the special case of cyclopentane-diols 1,2 the cis isomer gives a higher augmentation to the conductivity of boric acid solutions, reacts with acetone and HCl to form an acetal, and is split faster by lead acetate.

A new method of distinguishing the cis and trans isomers in dialkyl-1,2-cyclopentanols-1 has recently been developed by G. Chiurdoglu. Most of the above methods require the comparison of the two isomers before either can be assigned a structure. The new method permits the identification of one of these pentanols when its isomer is not available. He prepared dimethyl-1,2-methyl-1-propyl-2, methyl-1-ethyl-2, and diethyl-1,2-cyclopentanols-1 by the following reactions:

di Et. adipate $\xrightarrow{\text{Na + Toluene}}$ $\alpha$-carboxy-ethyl-cyclopentanone $\xrightarrow{\text{NaOEt.}}$

Na deriv. $\xrightarrow{\text{RI}}$ $\alpha$R,$\alpha$-carboxy-ethyl-cyclopentanone $\xrightarrow{\text{HCl}}$ $\alpha$R-cyclo-

pentanone $\xrightarrow{\text{RMgX then } H_2O}$ R' 1, R 2 cyclopentanol 1.

6. Chiurdoglu, Bull. Soc. Chim. Belges, 46, 592 (1937)
7. Ryan, Ind. Eng. Chem. Prod. Res. Ed. 2, 255 (1963)
8. Ryabov, Zh. Obshch. Khim. 10, 1 (1940)


Some of the studies used in evaluating structures to a given of these polymeric lubricants are:

I. Methods of synthesis.—Reduction with hydrogen gas solution gives a hydrocarbon of the oil lubricant; while in neutral solution or with sodium and alcohol a phenol derivative of the lubricant is formed in the reduction of substituted phenols, naphthols, cyclohexanones, etc.

II. Determination of physical data on the two lubricants.—Lowery's data states that in a pair of cis-trans isomers the cis form has the greater density and index of refraction, and the smaller molecular refraction. This has been found generally true in cyclohexanes and cyclopentanes, but exceptions exist.

Stoughton found that in 2C cis-trans isomers containing the group $-CO_2CH_3$ the trans isomer had the higher boiling point in every case.

III. Thermal reactions of the two lubricants.—In cyclopentanes containing an OH or NH group, and [illegible] group, the formation of a lactone or lactam indicates a cis structure.

In a pair of substituted cyclopentanols the lower boiling form most usually is the one where the OH is in a trans position with the H with which it is eliminated. In a pair of substituted cyclopentanols the trans lower will dehydrate faster than the cis, and the corresponding trans ester will saponify faster than the cis.

In the thermal cycle of cyclopentane-diols i.e. the cis lower gives a higher concentration in the equilibrated of liquid and solutions, treated with sulfuric and KCl to form an acetal, and by split fragment by lead acetate.

A new method of distinguishing the cis and trans isomers in dimethyl-1,3-cyclopentanediol has recently been described by G. Chiurdoglu. Each of the above methods requires the comparison of the two isomers before either is the standard or unknown. The new method permits the identification of any of these by remarks when the isomer is not specified. A separate dimethyl-1,3-methyl-1-propyl-3, methyl-1-ethyl-3, and dimethyl-1,3-cyclopentanol-1 by the following reactions:

(1) 2C. mixture $\xrightarrow{NaN_3 + Polyphosphoric\ acid}$ 2-methyl-2-cyclopentenone $\xrightarrow{Bromine}$

(2) 2A dorin. $\xrightarrow{Li}$ 2-methyl-2-cyclopentenone-ethyl-vinyl ketone $\xrightarrow{KOH}$ 1-methyl-2-cyclo-

$\xrightarrow{KOH\ then\ H_2O}$ 2-methyl-1,3-cyclopentanedione

These were separated by fractional distillation into the cis and trans isomers, with the exception of the diethyl-1,2-cyclopentanol-1, which could not be separated. Structures were assigned to these isomers by using physical data and the rule of transelimination of water. The rate of adsorption of hydrogen by these pentanols in the presence of platinum black was measured. Under comparable conditions all cis isomers react at the same rate, and all trans isomers at a faster but common rate. This enables one to definitely assign the trans structure to the diethyl cyclopentanol. In this reaction the product formed from either the cis or the trans cyclopentanol is identical, being about 80 per cent trans dialkyl-1,2-cyclopentane. The unreacted alcohol is unchanged in structure. The reaction does not go through the olefin. As in dehydration the rate of reaction is greatest when the tertiary OH and H are in a trans position with respect to each other.

Reported by K. Kearby
April 8, 1936.

These were separated by treating, distillation into the oil and tarry layers, with the exception of the diethyl-2,5-dihydroxyphenol-1, which could not be separated. Attempts were assigned to these layers by using physical data and the rate of transmembranation of water. The rate of absorption of hydrogen by these products in the presence of platinum black was measured. Under comparable conditions oil and layers were so the oil, water, and all tarry layers at a rather low pressure rate. This method was to definitely assign the tarry structure to the diethyl-2,5-dihydroxyl-1,4-benzene. In this reaction the most formed from either the oil or the tarry layers, respectively, is liquid, being about 80 per cent diethyl-2,5-dihydroxyl-1,4-benzene. The unreacted alcohol is recovered in structure. The reaction does not go through the olefin. As in dehydration the rate of reaction is greatest when the hydroxyl on and X are in a trans position with respect to each other.

Reported by A. Kurtz
April 4, 1926.

# The Reaction of Sodium with Aromatic Nitro and Nitroso Compounds

W. O. Lukaschewitsch, Ann., 521, 198 (1936)

Place: Forschungsinstitut für organische Zwischenprodukte und Farbstoffe, Moskau.

Previous work:

When 0.5 per cent sodium amalgam is allowed to react with aromatic nitro and nitroso compounds under an atmosphere of nitrogen, compounds containing sodium are formed.

In order to ascertain their structures these compounds were allowed to react with benzoyl chloride and with water.

The reaction of benzoyl chloride with the sodium derivatives of the nitro and nitroso compounds yielded $\alpha,\beta$-dibenzoyl aryl hydroxyl amines.

The action of water on the sodium derivatives gave rise to $\beta$-aryl hydroxyl amines.

The equations for the formation of the derivatives and their reactions are:

1. $RN{=}O{\atop\diagdown}O + 2Na \longrightarrow RN{\diagup}{ONa \atop ONa}$

2. $RNO + 2Na \longrightarrow RN{\diagup}{ONa \atop Na}$

3. $RN{\diagup}{ONa \atop ONa} + 2R'C{=}O{\atop\diagdown}Cl \longrightarrow RN{\diagup}{OCOR' \atop OCOR'} + 2NaCl$

$RN{\diagup}{OCOR' \atop OCOR'} \longrightarrow RNO + R'C{=}O{\atop\diagdown}O{\atop R'C{=}O}$

$RNO + RN{\diagup}{ONa \atop ONa} \longrightarrow RNO_2 + RN{\diagup}{ONa \atop Na}$

$RN{\diagup}{ONa \atop Na} + 2R'C{=}O{\atop\diagdown}Cl \longrightarrow RN{\diagup}{OCOR' \atop COR'} + 2NaCl$

4. $2RN{\diagup}{ONa \atop ONa} + 3H_2O \longrightarrow RNHOH + RNO_2 + 4NaOH$

5. $RN{\diagup}{ONa \atop Na} + 2H_2O \longrightarrow RNHOH + 2NaOH$

References:

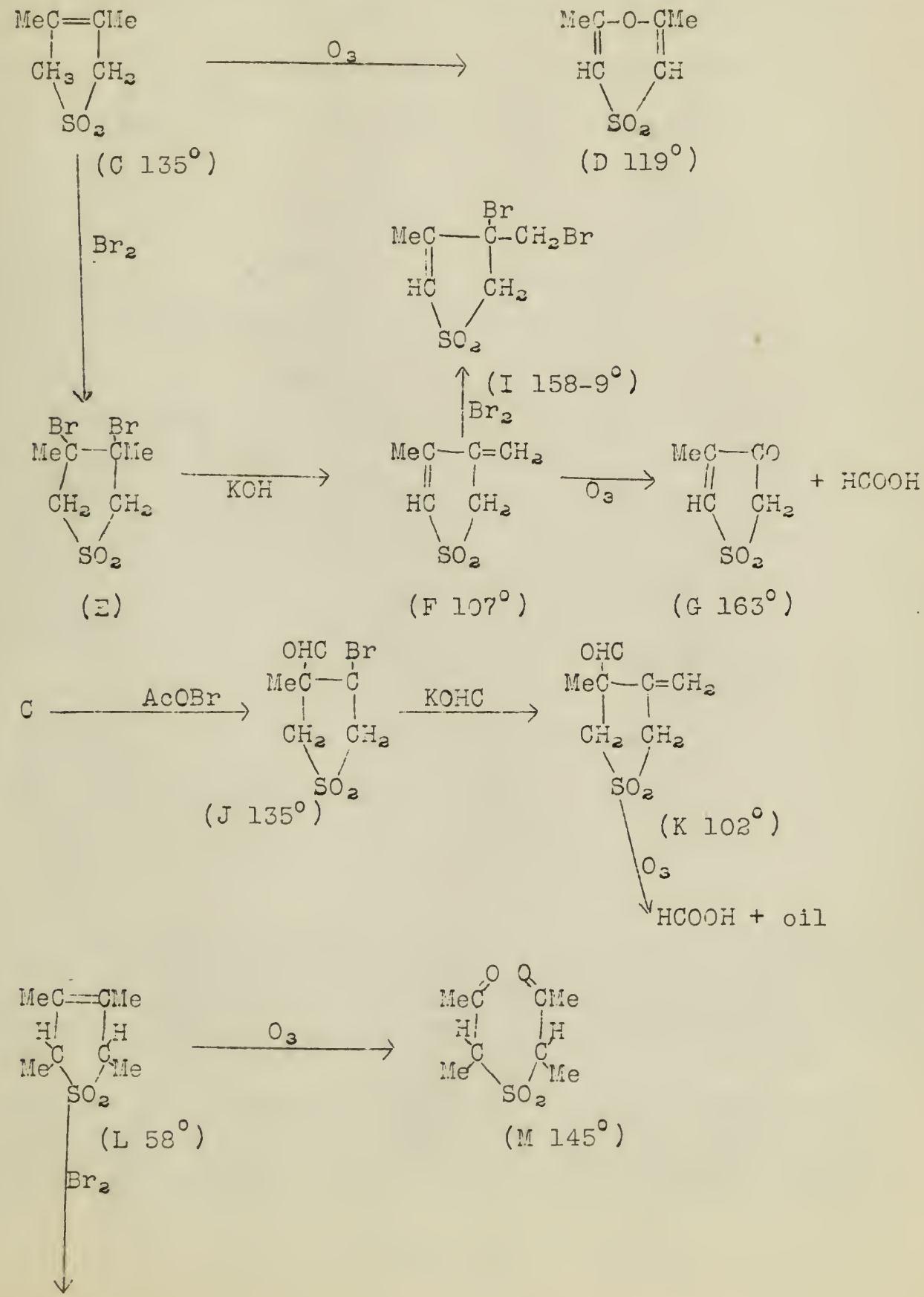
Ber., 5, 915 (1872)
Ber., 30, 1572 (1897)
Ber., 32, 2911 (1899)
Ber., 32, 2919 (1899)

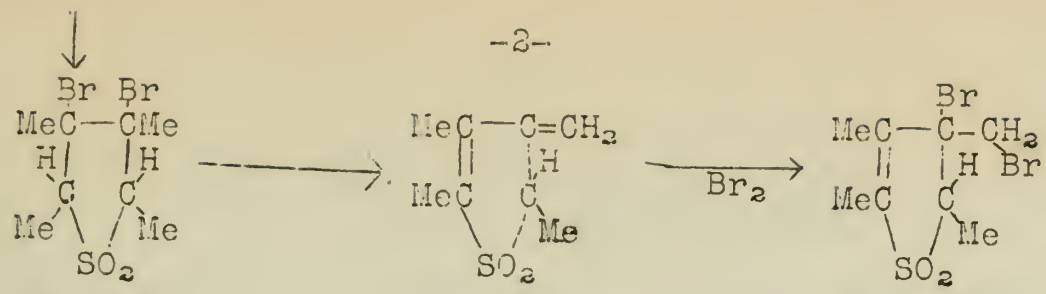
Reported by W. E. Ross
April 15, 1936.

# Structure of Cyclic Sulfone Derivatives of Butadienes

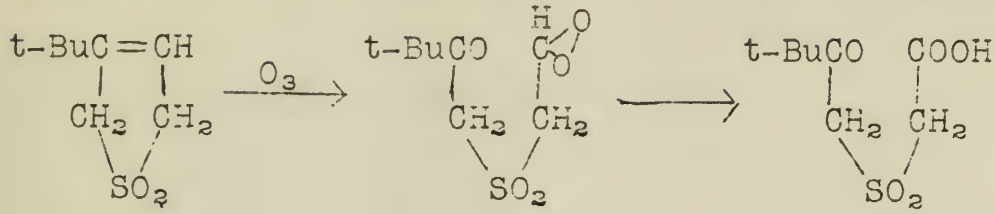
The addition of $SO_2$ to butadienes has been extended, and the structure of the resulting cyclic sulfones has been clarified by ozonizing them.

Structures for the following sulfones have been established:

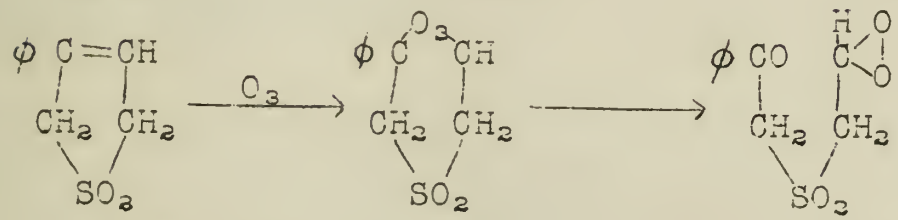




(N 137°) (O 93°) (P 125°)

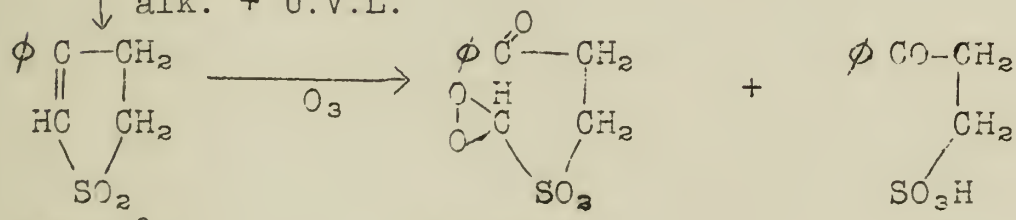


(Q 82°) (R 145°) (S 103°)

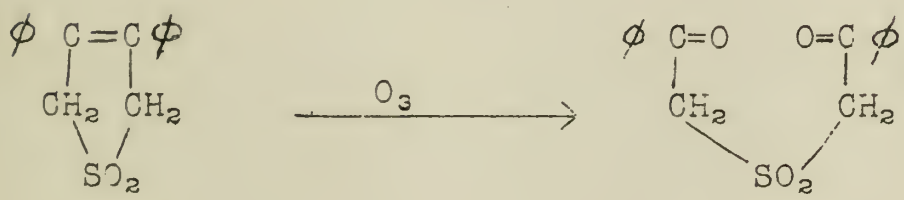


(T 132°) (U 99°) (V 139°)

alk. + U.V.L.



(W 166°) (X 118°) (small yield) 132 (principal product)



(Y 183°) (Z 124°)

Note that the sulfones of 2 tert.-butyl and of 2-phenyl-butadienes on ozonization form compounds which are isomeric with carboxylic acids, and may be termed isocarboxylic acids. These isocarboxylic acids in aqueous solution slowly isomerize to the ordinary acid according to law of monomolecular reactions.

Some of the butadienes isomerize in alkaline media when irradiated with ultra violet light. Ozonization studies indicate that this isomerization is not a <u>cis-trans</u> phenomenon, as Eigenberger supposed, but is due to a shift of the double bond.

Backer, Rec. Trav. Chim., 54, 170 (1935)
" " " " 53, 525 (1934)
" " " " 51, 295 (1932)

Eigenberger, J. Prakt. Chem., (2) 131, 289 (1931)
" " " " (2) 129, 312 (1931)
" " " " (2) 127, 309 (1930)

Staudinger, Ber., 68B, 455 (1935)

Reported by Rene Oehler
April 15, 1936.

# THE SYNTHESIS OF COMPOUNDS RELATED TO OESTRONE.

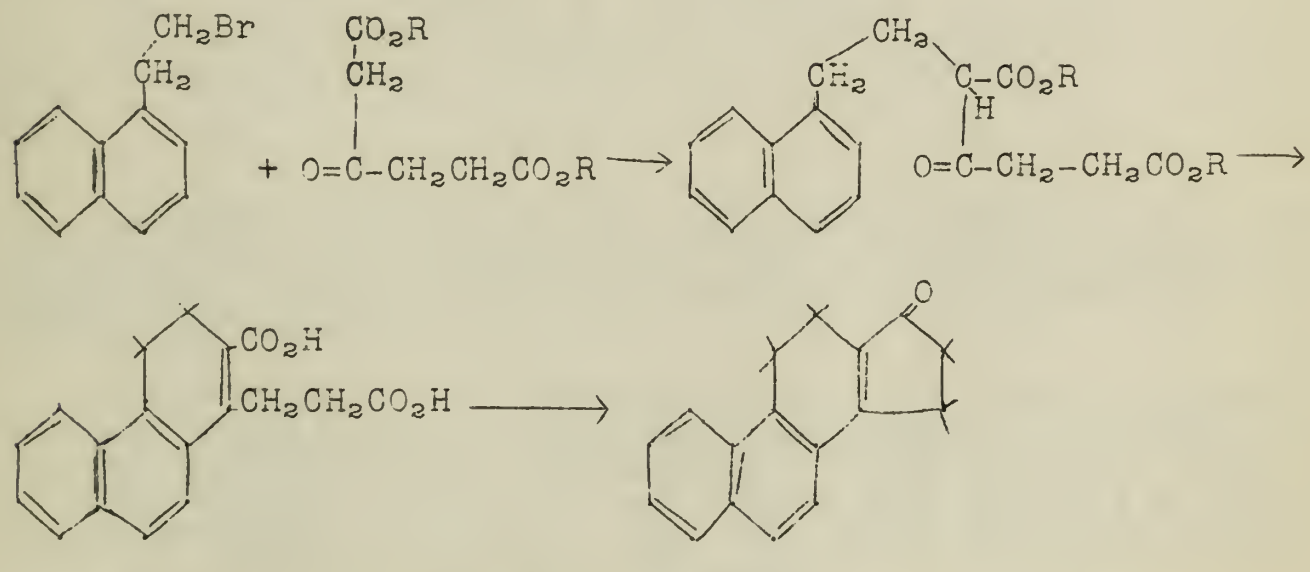
Hewett, J. Chem. Soc., 1936, 50.
Robinson and Walker, J. Chem. Soc., 1936, 192.
Cook and coworkers, Proc. Roy. Soc., 114B, 272 (1934).
Bardhan, Nature, 134, 317 (1934).

The synthesis of fused ring systems related to the hormones has been actively pursued since the structure of oestrone has been established, and the discovery that other fused systems are active oestrogenically. Cook and coworkers have tested several types of fused ring systems and find that oestrogenic activity is not limited to types containing the ring system of oestrone but that other types are also active.

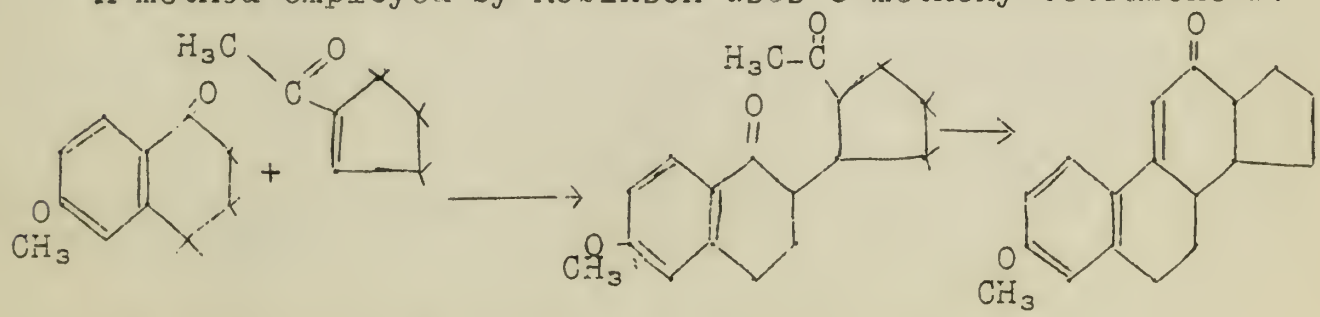
Examples of the last type are 1-keto-1,2,3,4-tetrahydrophenanthrene and 9,10-dialkyl-9,10-dihydroxy-1,2,5,6-dibenzanthracene.

Attempts to synthesize oestrone have so far been unsuccessful, but some of the compounds produced in these attempts possess oestrogenic activity and are quite closely related in structure to the natural hormone.

A method used by Bardhan for the preparation of this type of compound may be represented as follows.




A method employed by Robinson uses 6-methoxy-tetralone-1.




Other methods of preparation will be given.

H. G. Kolloff
April 23, 1936.

# SULFONATION OF NAPHTHALENE

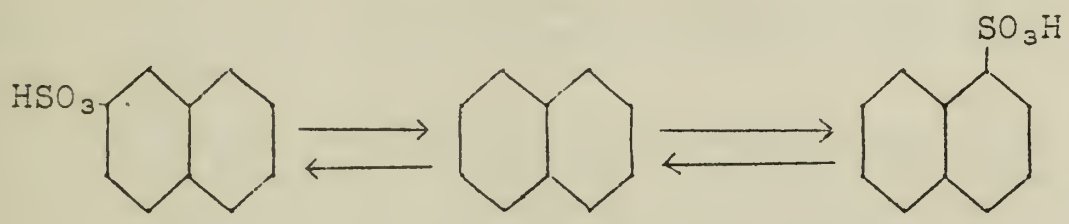
Lantz, Robert, Bull. Soc. Chim., (5) 2, 1913-32 (1935)
ibid (5) 2, 2092-2108 (1935)

Research Laboratory of the Dye and Chemical Products Association of St. Denis.

Previous Work: Naphthalene bisulfite compounds.
Naphthoquinone derivatives.
Sulfur dyes.

The transposition of the $\alpha$-naphthalene sulphonic acid I into the $\beta$-isomer may be explained on the basis of desulfonation and resulfonation in the $\beta$-position.

Lantz' work indicates the existence of an equilibrium:




III II I

At higher temperatures the rate of the reaction I $\longrightarrow$ II is accelerated while the reaction III $\longrightarrow$ II is relatively unaffected. This explains the formation of the $\beta$ acid at higher temperatures.

A procedure for the determination of the relative amounts of the $\alpha$ and $\beta$ acids in a mixture is presented. I is desulfonated and precipitated quantitatively as an insoluble polybromonaphthalene leaving III entirely in solution as a soluble polybromonaphthalenesulfonic acid. The insoluble product from I is then determined by $CrO_3$ oxidation.

Reported by L. L. Ryden
April 22, 1936.

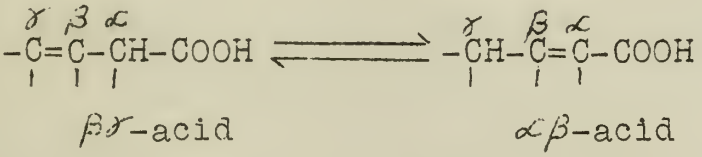
R. P. Linstead et al., Imperial College, London.

Work:

The authors have prepared a series of unsaturated acids and have studied the shift of the double bond and lactonisation under the influence of equilibrating agents such as, KOH, $H_2SO_4$ and heat alone.[1]

I. Stability of unsaturated acids toward equilibrating agents. A study of tautomeric change.

A. Comparative stability of isomeric $\alpha\beta$- and $\beta\gamma$-acids toward 25 per cent KOH at 100°C.[2] The general scheme for equilibria can be represented as follows:



$\beta\gamma$-acid $\alpha\beta$-acid

1. Butenoic acids without $\gamma$-substituents show no stability of the $\beta\gamma$-form even when substituted on the $\beta$-carbon atom.

2. Butenoic acids with one $\gamma$-substituent show a small but definite stability of the $\beta\gamma$-form, which is not appreciably affected by the nature of the substituent or the presence of an $\alpha$-substituent.

3. $\gamma$-substituted butenoic acids having a second alkyl group on the $\gamma$-carbon atom show a great stability of the $\beta\gamma$-form,[3] and a similar but weaker effect is produced if the second substituent is on the $\beta$-carbon atom. The maximum effect in the $\beta$-position is given by an ethyl group.

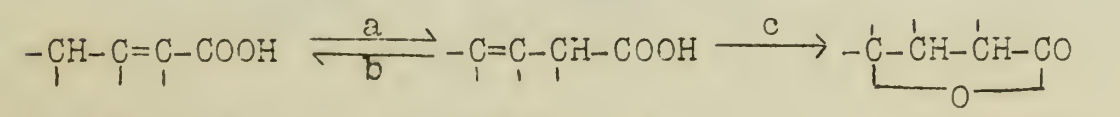
4. These principles are still valid if the substituting groups form part of a polymethylene ring.[3,4]

B. The $\gamma\delta$- and $\delta\epsilon$-unsaturated acids[5] show no tautomeric shift of the double bond when boiled with excess KOH, but are stable to this equilibrating agent.

II. Lactonisation and Tautomeric change. Equilibrating agent is $H_2SO_4$ (hot and cold--50 and 60 per cent) and sometimes heat alone.

A. In the $\alpha\beta$- and $\beta\gamma$-series of unsaturated acids.

All acid-lactone systems of this kind can be interpreted by the one general scheme:



$\alpha\beta$-acid $\beta\gamma$-acid $\gamma$-lactone

The variations between different systems can be attributed to differences in the ratio of the velocity of the tautomeric change (a and b) to that of ring closure (c). Four types of acids can be distinguished.[6]

1. Those in which both changes are slow but lactonisation is much faster than tautomeric change (acids with one $\gamma$-alkyl and no $\beta$-alkyl substituent.[6]

2. Those in which lactonisation is fast and tautomeric change is slow (acids with two $\gamma$-alkyl substituents).[6]

3. Those in which tautomeric change is faster than lactonisation (acids with one $\gamma$- and one $\beta$-substituent).[7]

4. Those in which tautomeric change is fast and irreversible in the direction $\beta\gamma \longrightarrow \alpha\beta$, no lactonisation being possible (acids without $\gamma$-substituents).[8]

B. In the $\gamma$-$\delta$ series of unsaturated acids.[9]

In this series the exclusive reaction is lactonisation and no tautomeric change occurs. The direction of lactonisation (i.e. $\gamma$-or $\delta$-lactone formation) depends upon the substituents about the double bond.

Lactonisation, in the case of $\gamma\delta$-acids having two $\delta$-alkyl groups, is reversible by heat alone. Probably this is the "purest" example of ring-chain tautomerism:

C. In the $\delta\epsilon$-series of unsaturated acids.[5]

Lactonisation was accompanied to an unusual extent by side reactions. Trustworthy experimental method for estimation of lactone content was not devised.

D. Some unsaturated acids have been studied in which the double bond is farther removed from the carboxyl. They are reported to yield $\gamma$-lactones by action of conc. $H_2SO_4$.[10]

Bibliography.

Linstead, R. P. et al., J. Chem. Soc.
(1) 1930, 1603; (2) 1928, 2343; (3) 1930, 2064; (4) 1935, 258; (5) 1934, 1995; (6) 1932, 115; (7) 1934, 599; (8) 1933, 577; (9) 1933, 580.
(10) Zhukov, A. A. and Shestakov, P. I., J. Russ. Phys. Chem. Soc., 40, 830 (1908), cf. C.A., 3, 1148 (1909).

Reported by E. E. Gruber
April 29, 1936.

## I

## Methods of Analysis

The difficulty involved in quantitatively determining the deuterium content of organic-d compounds has recently aroused considerable attention. Compounds of molecular weight above 150 and of low deuterium content cannot be effectively analyzed by the ordinary methods of analysis. The following new procedures have been developed:

Combustion of the organic compound followed by a density determination of the resulting water using,

a) The Zeiss interferometer method of density determination.[1]
b) The "submerged float" method.[2]
c) The "swimmer" method.[3]

The merits of each of these will be discussed.

## II

## Organic-d Compounds

Deuterium has supplied the physical chemist with an excellent means of studying reaction kinetics. Cleavage of the carbon-hydrogen bond by exchange reactions with deuterium have been studied. The following exchanges have been shown to occur:

$$CH_4 + 2D_2 \underset{Hg,\ \Delta}{\rightleftharpoons} CD_4 + 2H_2 \qquad [4]$$

$$CH_3\text{-}CH_3 + D_2 \xrightarrow[\substack{300^\circ \\ Ni}]{} 2\text{Methane-}d_x \qquad [5]$$

$$C_6H_6 + 6DCl \underset{AlCl_3}{\rightleftharpoons} C_6D_6 + 6HCl \qquad [6]$$

$$C_6H_6 + D_2O \underset{Ni,\ \Delta}{\rightleftharpoons} C_6D_6 + H_2O \qquad [7]$$

$$CH_2(COOH)_2 + D_2O \rightleftharpoons CD_2(COOD)_2 + H_2O \qquad [8]$$

Although the majority of organic deuterium studies have been mainly physical in nature, Schoenheimer and Rittenberg[9] have reported that deuterium is an ideal "indicator" in the study of intermediary metabolism. Since it is an isotope of hydrogen, the substitution of deuterium for hydrogen in foodstuffs has a distinct advantage over the introduction of such

groups as halogen, phenyls, etc.; in addition, it enables the transportation of food-stuffs in the body to be easily traced. Stearic 6-7-9-10-$d_4$ acid and coprostanone 4-5-$d_2$ have been synthesized and their physiological fate observed.

In an effort to study the questionable asymmetry of the type R'R''CHD, Erlenmeyer and Gärtner[10] prepared $\beta$-phenylpropionic $\alpha$-d,$\beta$-d acid by the deuterium iodide reduction of cinnamic acid. It was subsequently shown that this drastic reduction caused deuterium exchange to produce a product of the formula

$$C_6H_{2.18}\ D_{2.82}\ C_2H_{1.62}\ D_{2.38}\ COOH \quad .$$

On the assumption that part of the molecules would conform to the R'CHD-CHDR'' type, the strychnine salt was prepared and fractionally crystallized. No evidence of resolution was obtained.

References:

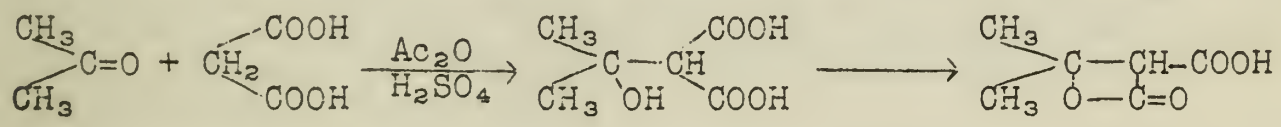
1. Crist, Murphy, and Urey, J. Am. Chem. Soc., 55, 5060 (1933)
2. Rittenberg and Schoenheimer, J. Biol. Chem., 111, 169 (1935)
3. Erlenmeyer and Gärtner, Helv. Chim. Acta, 19, 129 (1935)
4. Taylor and coworkers, J. Am. Chem. Soc., 57, 383, 592 (1935)
5. Taylor and coworkers, ibid., 57, 2735 (1935)
6. Kenner, Polanyi, and Szega, Nature, 135, 267 (1935)
7. Horiuti, Ogden, and Polanyi, Trans. Faraday Soc., 30, 663 (1934)
8. Halford, Anderson and Bates, Private communication.
9. Schoenheimer and Rittenberg, J. Biol. Chem., 111, 163, 183 (1935)
10. Erlenmeyer and Gärtner, Helv. Chim. Acta, 19, 145, 331 (1936)

Reported by Marlin T. Leffler
May 6, 1936.

# CARBON SYNTHESES WITH MALONIC ACID

Michael and Wiener, J. Am. Chem. Soc., 58, 680 (1936)
Michael and Ross, J. Am. Chem. Soc., 55, 3684 (1933)
Harvard University

A large literature exists on the use of malonic acid for the synthesis of $\alpha,\beta$-unsaturated acids by condensation with aldehydes. Acetone does not show an analogous reaction, however, Meldrum[1] observed that addition of a small amount of sulfuric acid brought about an aldolization, involving the carbonyl group of the ketone, followed by an intramolecular esterification of the formed $\beta$-hydroxy acid to $\beta,\beta$-dimethyl-$\beta$-propiolactonic acid, e.g.,




The Meldrum method was improved by Ott[2] in 1913 and since that time a number of $\beta$-lactonic acids have been prepared from ketones by use of the Meldrum-Ott method.

In 1933 Michael and Ross showed that aliphatic aldehydes may be substituted for ketones in the synthesis of $\beta$-lactonic acids. The most recent paper deals with the use of several aromatic aldehydes, e.g., benzoic, salicylic, acetylsalicyclic and cinnamic aldehydes. Benzaldehyde gives the expected $\beta$-lactonic acid but the others lead to different products.

The $\beta$-lactonic acids formed by the condensation of benzaldehyde with malonic and methyl malonic acids are of special interest since they are the first proved $\beta$-lactonic acids with only one substituent in the $\beta$-position.

The thermal and chemical properties of the $\beta$-lactonic acids have been further studied and it has been shown that all compounds of this type are cleaved by heat and by alkali through the first-formed $\beta$-hydroxy malonates by rupture at the $\alpha,\beta$-carbon linkage.

References:

1. Meldrum, J. Chem. Soc., 93, 598 (1908)
2. Ott, Ann., 401, 151 (1913)

Reported by J. H. Brown
May 6, 1936.

# Concerning Aldehyde Condensations by the Use of Secondary Amines.

(Knoevenagel reaction)

R. Kuhn, W. Bodstübner and C. Gundmann, Ber., 69, 98 (1936)
R. Kuhn and M. Hoffer, Ber., 63, 2164 (1930)
Blanchard, Klein and McDonald, J. Am. Chem. Soc., 53, 2809 (1931)
L. H. Smith and K. N. Welch, Jour. Chem. Soc., London, 1136 (1934)

The action of secondary amines (piperidine) on acetaldehyde or on a mixture of acetaldehyde and crotonaldehyde, previously represented the best way of obtaining polyene aldehydes. In order to obtain octatrienal, $H_3C(CH{=}CH)_3CHO$, free from its neighboring vinyl homologs, R. Kuhn and M. Hoffer tried the condensation of crotonaldehyde with itself.

$$H_3CCH{=}CHCHO + H_3CCH{=}CHCHO \xrightarrow{\text{Piperidine}} H_3C\left[CH{=}CH\right]_3CHO + H_2O$$

The condensation did not take place. If, however, the crotonaldehyde was exposed to sunlight then the addition of a small amount of piperidine caused the condensation to proceed as shown. The condensation goes equally well in the dark if crotonic acid, acetic acid or citric acid is added to the pure aldehyde. The active condensing agent, then, is the salt of the secondary amine instead of the amine itself as had previously been supposed.

From the foregoing facts the use of an amine salt is suggested for those condensations in which one of the reactants is not itself an acid. Such is the case of crotonaldehyde condensing with itself. The following unsaturated aldehydes and acid were prepared by the authors:

1. $$2CH_3CHO + CH_3CH{=}CHCHO \xrightarrow[\text{acetic acid}]{\text{piperidine}} H_3C(CH{=}CH)_4CHO + 2H_2O$$

2. $$(CH_3)_2C{=}CH{-}CH_2{-}CH_2C(CH_3){=}CHCHO + CH_3C(=O)H \xrightarrow[\text{acetic acid}]{\text{piperidine}}$$

$$(CH_3)_2C{=}CH{-}CH_2CH_2C(CH_3){=}CHCH{=}CHC(=O)H$$ 30 per cent yield

3. $$H_3C\left[CH{=}CH\right]_4CHO + CH_2(CO_2H)_2 \xrightarrow{\text{pyridine}} H_3C\left[CH{=}CH\right]_4CH{=}C(CO_2H)_2$$

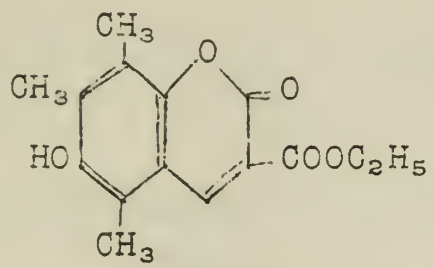
$$H_3C\left[CH{=}CH\right]_4CH{=}C(CO_2H)_2 \xrightarrow[\text{acetic anhydride}]{\text{acetic acid}} H_3C\left[CH{=}CH\right]_4{-}CH{=}CHCO_2H$$

Reported by J. M. Cross
May 13, 1936.

# THE REACTIONS BETWEEN QUINONES AND SODIUM ENOLATES

Smith and MacMullen, J. Am. Chem. Soc., 58, 680 (1936)
Smith and Denyes, J. Am. Chem. Soc., 58, 304 (1936)

In 1926 Smith showed that 3-carbethoxy-5,7,8,-trimethyl-6-hydroxy coumarin resulted when duroquinone reacted with sodium malonic ester.




One of the methyl groups had taken part in this reaction.

Von Peckman, Ikuta, Graebe and Levy, and others have reported various products previously from quinones and sodium enolates.

Pseudocumoquinone produces 5-hydroxy-2,4,6,7-tetramethyl coumarone and 5-hydroxy-4,6,7,-trimethyl isocoumaranone with sodium acetoacetic ester, and just the latter product with sodium malonic ester. No coumarin derivatives are formed.

## References

Smith and Dobrovolny, J. Am. Chem. Soc., 48, 1693 (1926)
Smith, J. Am. Chem. Soc., 56, 472 (1934)
Von Peckman, Ber., 21, 3005 (1888)
Ikuta, J. prakt. Chem., (2), 45, 65 (1892)
Graebe and Levy, Ann., 283, 251 (1894)

Reported by R. C. Cary
May 13, 1936

# HEATS OF HYDROGENATION OF OLEFINIC BONDS

G. B. Kistiakowsky et al., Harvard University

Previous work: Activated adsorption
Kinetics of reactions
1.) cis-trans isomerizations
2.) thermal decompositions

For most organic reactions, heats of reaction must be calculated from notably unreliable heats of combustion. The more accurate, but somewhat more difficult, direct calorimetric determination of heats of reaction has only occasionally been used.

Kistiakowsky and his coworkers plan to systematically develop this method, and at present are studying the heats of hydrogenation of olefinic compounds. To date, four papers have been published, and the data recorded is summarized in the following tables.

## Heats of Hydrogenation of Mono-olefins

| Compound | $\Delta H_{355^\circ}$ | Compound | $\Delta H_{355^\circ}$ |
|---|---|---|---|
| ethylene | -32,824 | isobutene | -28,389 |
| propylene | -30,115 | unsym-methylethylethylene | -28,491 |
| butene-1 | -30,341 | unsym-methylisopropylethylene | -27,997 |
| n-heptene-1 | -30,137 | pentenes-2 | -27,954 |
| cis-butene-2 | -28,570 | trimethylethylene | -26,920 |
| trans-butene-2 | -27,621 | tetramethylethylene | -26,663 |

## Heats of Hydrogenation of Dienes and Cyclic Olefins

| Compound | $\Delta H_{355^\circ}$ | Compound | $\Delta H_{355^\circ}$ |
|---|---|---|---|
| allene + $2H_2$ | -71,280 | cyclohexene + $H_2$ | -28,592 |
| 1,3-butadiene + $2H_2$ | -57,067 | 1,3-cyclohexadiene + $2H_2$ | -55,367 |
| 1,4-pentadiene + $2H_2$ | -60,790 | benzene + $3H_2$ | -49,802 |
| 1,5-hexadiene + $2H_2$ | -60,525 | cyclopentadiene + $2H_2$ | -50,865 |

$\Delta H$, the heat of reaction, may be defined as the heat absorbed in calories when one mol of reaction occurs at constant pressure. In the above tables $\Delta H$ is recorded at 355° K (83° C) at which temperature the reactions were carried out.

By combining certain of the above values the heats of reaction for several interesting reactions may be calculated.

| | |
|---|---|
| allene + $H_2 \longrightarrow$ propylene | $\Delta H_{355^\circ}$=-41,165 |
| 1,3-butadiene + $H_2 \longrightarrow$ n-butene-1 | =-26,720 |
| 1,4-pentadiene + $H_2 \longrightarrow$ n-pentene-1 | =-30,660 |
| 1,5-hexadiene + $H_2 \longrightarrow$ n-hexene-1 | =-30,400 |
| 1,3-cyclohexadiene + $H_2 \longrightarrow$ cyclohexene | =-26,700 |
| benzene + $H_2 \longrightarrow$ 1,3-cyclohexadiene | =+ 5,570 |

If an increase in $\Delta H$ may be interpreted as indicative of increased stability of the double bond, the following conclusions may be drawn.

1.) For simple olefins, substitution on the carbons carrying the double bond increases the stability of the bond.

2.) For dienes:
   (a) The allene type is the least stable.
   (b) The double bonds in a conjugated system are the most stable.
   (c) As the distance between the double bonds is further increased, the stability of the bonds approaches that of the simple olefin bond.

3.) In benzene, which may be considered a "continuously conjugated" system, an unusually stable type of unsaturation is present. It has been suggested that this condition be used as the criterion for aromaticity.

References

G. B. Kistiakowsky et al., J. Am. Chem. Soc., 57, 65 (1935)
Ibid., 57, 876 (1935)
Ibid., 58, 137 (1936)
Ibid., 58, 146 (1936)

Reported by M. F. Roy
May 20, 1936.

# DIOXANES

Boesekin and coworkers, Rec. trav. chim., 52, 1067 (1933)
" " " 50, 909 (1931)
" " " 54, 733 (1935)
J. Am. Chem. Soc., 55, 1284 (1933)
Baker, J. Chem. Soc., 1598 (1933)
Summerbell and coworkers, J. Am. Chem. Soc., 54, 3777 (1932)
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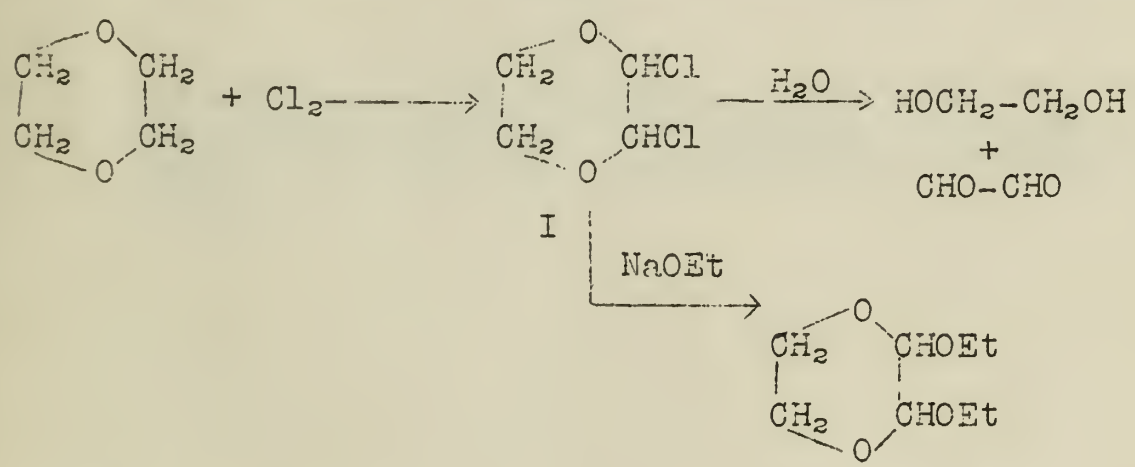
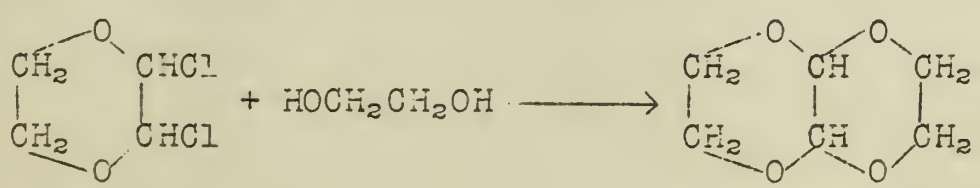
Dioxane was first prepared by several independent investigations in 1863. Although these initial works were followed by many others, the only results obtained were summarized in a characterization of the physical properties of the compound and in the observation that it was surprisingly resistant to most chemical reagents. It was observed that the compound formed many molecular compounds with several series of reagents.

Boesekin, in very recent years, observed that dioxane reacted with chlorine to produce a dichlorosubstituted dioxane which was shown by hydrolysis to be the 2,3-dichlorodioxane, (I). This hydrolytic reaction was an indication of the activity of the chloro substituents toward other reagents.




Subsequent work on the chemistry of dioxane has always involved this primary chlorination of dioxane, and can be divided into the following types:

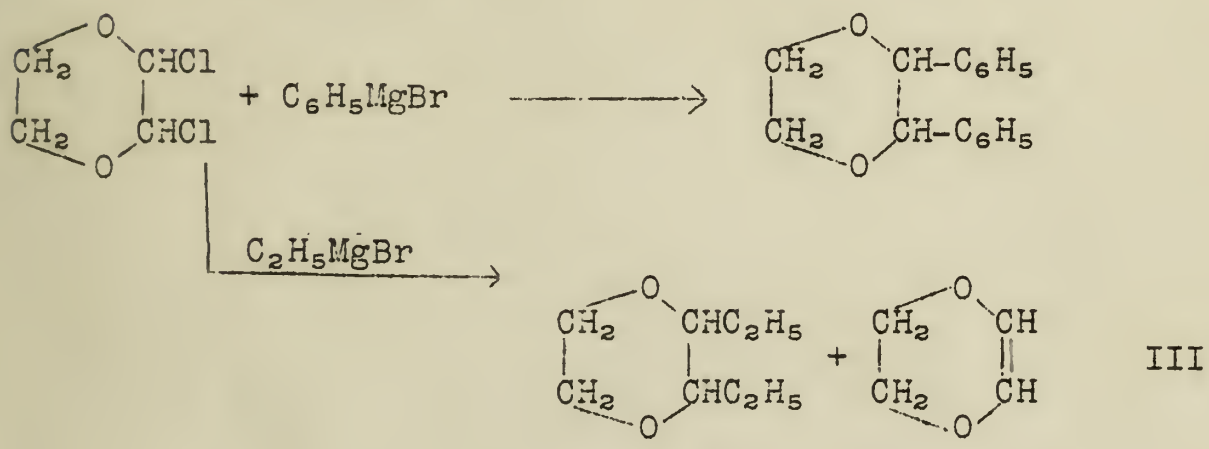
1. Formation of fused ring systems containing the dioxane nucleus. As an example naphtho-dioxane, (II) was formed by the action of ethylene glycol on 2,3-dichlorodioxane.




II

From this reaction two isomers were obtained. They were analogous to the cis-trans isomers of decalin.

2. Higher chlorinated dioxanes.--2,3-Dichlorodioxane and chlorine produced several isomeric tetrachlorodioxanes, the structures of which were determined by hydrolysis. The symmetrical tetrachlorodioxanes were quantitatively hydrolyzed to glyoxal.
3. Other disubstituted dioxanes and their reactions.--The activity of the chloro substituents of the 2,3-dichlorodioxane was further evidenced by the reaction with Grignard reagents.




III

The p-dioxene,(III) was shown to add chlorine, bromine and hydrogen bromide. The addition of hydrogen bromide served as a basis for the mechanism of chlorination of dioxane.

Reported by L. L. Alexander
May 20, 1936

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