I. CYCLIZATION OF 1,5-HEXADIENES

II. INACTIVITY OF BROMINE IN BROMACETAL

A Thesis

by

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CLAIM TO ORIGINAL RESEARCH

I

Four 1,5-hexadienes, namely hexadiene-1,5 (diallyl), 2,5-dimethyl-hexadiene-1,5 (dimethallyl), 1,1,5-trimethyl-hexadiene-1,5 (geraniolene) and 1,1,6,6-tetramethyl-hexadiene-1,5 (2,7-dimethyl-octadiene-2,6) were treated with various acids in different concentrations in order to determine the conditions necessary for the formation of cyclic products and study the mechanism of polymerization by acid catalysis. The study of polymerization through intramolecular reactions constituted a novel method of attacking this problem.

As a result of this investigation the theories of acid catalysis polymerization advanced by various workers were criticized and a new theory proposed.

During the course of investigation the experimental conditions favourable for the formation of 1,1,5,5-tetramethyl-pyrane were observed and hitherto unreported constants of this compound determined. A report found in the literature of the formation of 1,1,6,6-tetramethyl-hexamethylene oxide from 2,7-dimethyl-octandiol-2,7 was disproven. It was found that 2,6-dimethyl-heptanol-6 when treated with acids dehydrated without the formation of cyclic compounds.

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The activity of the bromine atom in bromacetaldehyde dimethyl acetal was investigated. It was found to be surprisingly unreactive. This property was attributed to the presence of two alkoxy groups on the adjacent carbon atom.

It was found that bromacetal would not form the grignard compound, nor would it react with lithium to give the lithium alkyl, or react with zinc to form the corresponding zinc alkyl bromide.

Furthermore, it would not react with methyl magnesium chloride, or with lithium propyl and lithium butyl.

Reports that bromacetaldehyde dimethyl acetal is a powerful lachrymator were found to be erroneous, this property being found to be due to the presence of small amounts of bromacetaldehyde impurities.

ACKNOWLEDGMENT

The writer takes this opportunity of expressing his sincere appreciation to

Dr. Philip G. Stevens

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The study of naturally occurring cyclic compounds is one of the most fascinating chapters in Organic Chemistry. The occurrence of a very large number and many types of cyclic compounds in nature, and their seemingly simple relationship with many straight chain compounds has excited the curiosity of many workers. The logical possibility of a common source of simple units for the synthesis of many large and complex compounds has led to all sorts of speculations.

We must however admit that we know virtually nothing about the vital synthesis of even the simplest types of compounds. The plant, let alone the animal, is a very complex type of mechanism. The processes taking place within the plant are so many, and perhaps the energy transfers so different from the types met with in the laboratory, that it is difficult to draw definite conclusions from certain experiments.

Thus, because a certain plant on being fed with glucose increases say, its sterol content, it does not mean that the plant took the sugar molecules and so rearranged them, that sterols were formed. Nor does it tell us just how those sterols were formed, because during that period the plant was carrying out a thousand and one other processes which were in all probability closely tied up with the formation of the sterols.

Although the problem is extremely complicated, we try to make certain observations and draw certain conclusions as regards the origin and biogenesis of plant constituents.

Study of plant physiology and the abundant occurrence of carbohydrates suggest, that by absorbing carbon dioxide and water, and giving off oxygen in a fairly definite ratio, the plant synthesizes carbohydrates.

It was first suggested by von Baeyer in 1864 that formaldehyde was the very first product of photosynthesis. This, upon aldol condensation yields hexoses and other more complex carbohydrates. It is to be noted that the reaction

$$6\ CO_2 + 6\ H_2O + 677.2\ cal. \longrightarrow C_6H_{12}O_6 + 6\ O_2$$

requires 677.2 calories of energy. This energy is supplied by the sun and the transfer carried out through the medium of chlorophyll. In view of the preponderance of hexoses, it is to be assumed that the plant has the capacity to arrest aldol condensation at certain stages.

Baly (1-4) and co-workers successfully synthesized hexoses by exposing a solution of carbon dioxide in water, in a quartz vessel, to the light of a mercury vapour lamp. They observed that light of short wave length ($200\mu\mu$) induced the formation of formaldehyde while the longer wave length ($290\mu\mu$) brought about aldol condensation. Additional proof of the

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1.- E.C.C. Baly et al., J.C.S.T. 119, 1025, (1921).
2.- E.C.C. Baly et al., Ind. Eng. Chem., 16, 1016, (1924).
3.- E.C.C. Baly et al., Proc.Roy.Soc. London, A-116, 197 (1927).
4.- E.C.C. Baly et al., Science, 68, 364, (1928).

Note.- See Bibliography for more detailed references.

theory of formaldehyde formation as the first step in photosynthesis is provided by the fact that the plant Elodea canadensis (5) will absorb formaldehyde in the dark with the production of starch. Hence, the aldol condensation is apparently independent of photosynthesis. Pollaci (6) reports detection of formaldehyde in the water condensed on the walls of a glass container when fresh leaves are illuminated and a rapid vacuum applied to the system.

If the formation of sugars is the first step in the building up of plants, then it is logical to assume that all plant ingredients are the result of transformation of sugars. Or else, one might assume that formaldehyde undergoes various stages of aldol condensation yielding a great variety of substances. These might then combine through various reactions and give many new types of compounds. Aside from the regular types of sugars, there are a number of rare sugars which are probably derived from other sugars, since it is difficult to see how they could form directly from formaldehyde. Thus, d-isorhamnose may be derived from the reduction of d-glucose, alpha-d-fucose from the reduction of alpha-d-galactose and alpha-l-rhamnose from the reduction of alpha-l-mannose.

Another peculiar sugar hamamelose has been isolated from hamamelitannin (7) by means of the action of the enzyme tannase. This sugar cannot be derived from a normal hexose,

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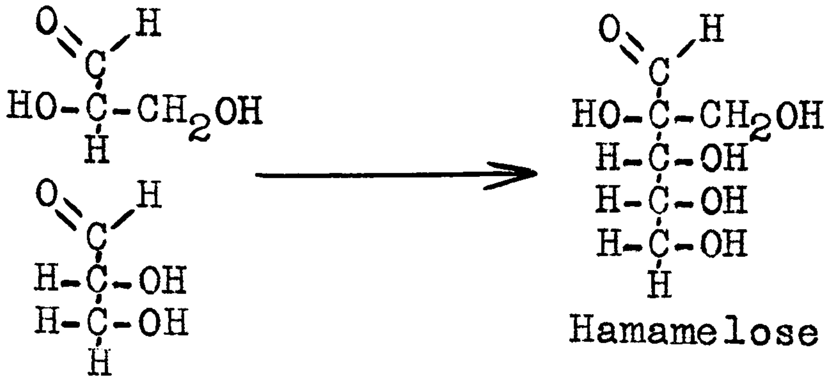
5.- Sabalitchka and Theidling, Biochem.Zeit. 172, 45, (1926).
176, 210, (1926).

6.- G.Pollaci, Bull.Soc.ital.biol.sper., 12, 692, (1937).

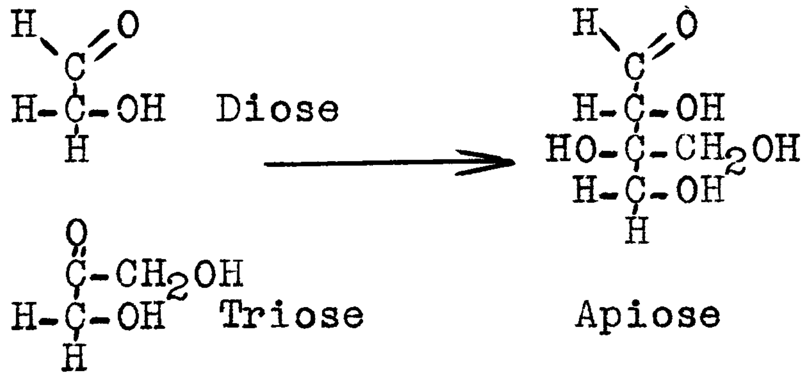
7.- Freudenberg, Ann., 440, 45, (1924), Schmidt, Ann., 486,250 (1929).

but is probably the result of aldol condensation of two molecules of glyceric aldehyde.



2 mols. Glyceric Aldehyde

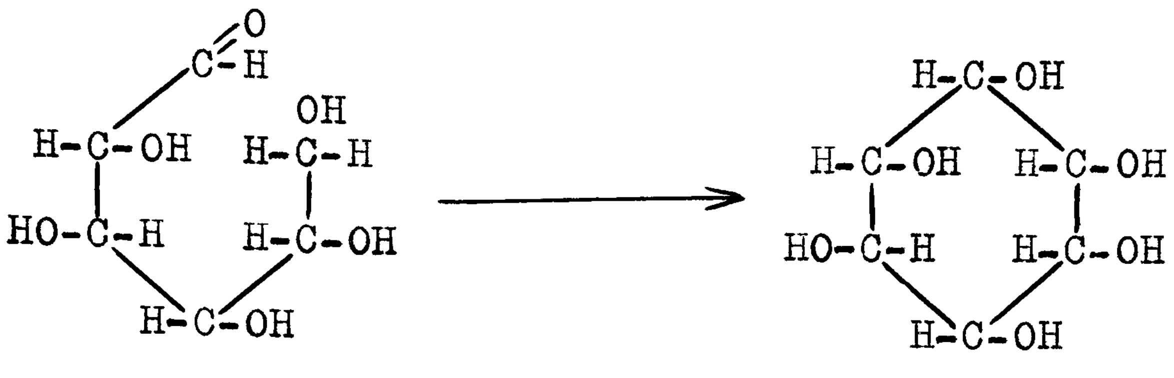
Another curious sugar, apiose(8) has been isolated by the hydrolysis of the glucoside apiin. It again cannot be a derivative of simple sugars. It may however be formed by the aldol condensation of a diose and the triose, dihydroxy acetone.



The occurrence of these sugars strengthens the theory that the formation of sugars is the result of aldol condensation of a simple unit formaldehyde.

A very interesting cyclic sugar namely, inositol, has been found in several plants. It is isomeric with the simple hexoses and may have resulted from the cyclization of aldohexoses.

8.- Schmidt, Ann. 483, 115, (1930).

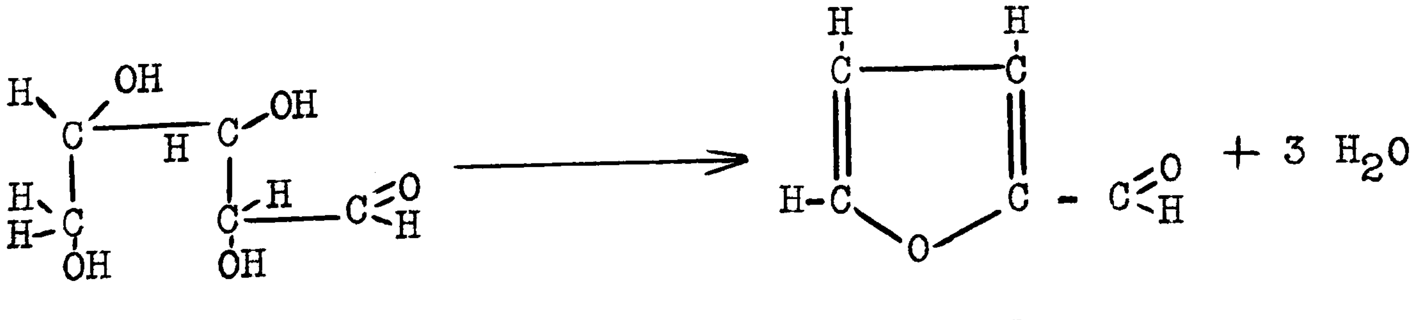


Proof that inositol is synthesized in the animal body under certain conditions has been advanced by Needham(9). An attempt to prepare inositol in vitro from d-glucose-6-phosphoric acid has been unsuccessful(10).

Besides these interesting sugars, there are, occurring in plants, various substituted sugars. Thus 2-aminoglucose occurs combined in chitin, 2-amino galactose in chondrus, etc.

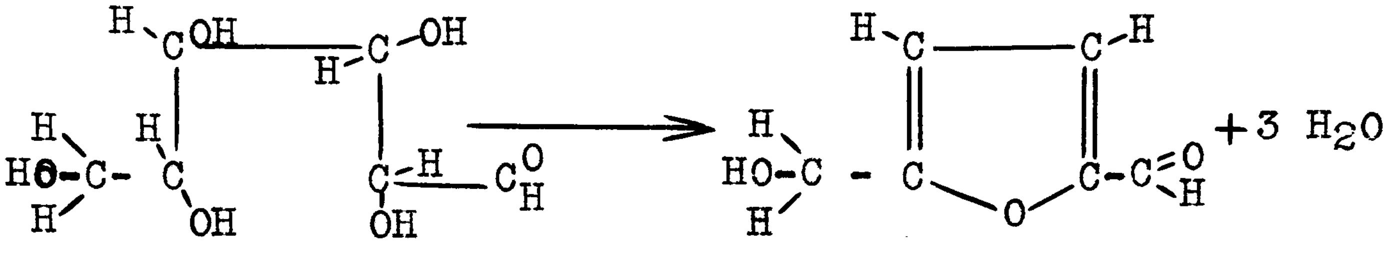
A study of the chemistry of sugars illustrates the flexibility of the hexose molecule. It is capable of many kinds of transformations in the laboratory, and probably of a greater number in the plant.

One characteristic reaction of pentoses is the formation of furfural upon boiling with 12% hydrochloric acid.



9.- J. Needham, Biochem.J. 18, 891, (1934).
10.- F. Micheel and H. Ruhkopf. Ber. 70B, 850 (1937).

Under similar conditions the hexoses yield substituted furfurals, hydroxy methyl furfural being commonly prepared from hexoses(11).



Glucose Hydroxy methyl furfural

It appears that in the plant, sugars are transformed into fats. Since fats have a higher energy content, this causes an accumulation of a more concentrated form of energy.

There is a great deal of evidence supporting the theory that fats are directly derived from carbohydrates. It is common practice for the farmer to fatten his hogs with corn and his horses with barley, both very rich sources of carbohydrates. Similar examples are found in the vegetable kingdom. Thus certain moulds(13) and yeasts(14) have been grown successfully in media containing glucose only, and the resulting plant has been found to contain fat.

It is significant that fatty acids occurring in nature have an even number of carbon atoms. It is true that there are a number of branched chain acids of low molecular weight, but these probably have their origin in proteins(12). It is a well

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11.- I.J. Rinkes, Org. Syntheses. XIV. 62 (1934).
12.- Ehrlich, Ber. 40, 2547, (1904).
13.- Prill, Wenck and Peterson, Biochem.J. 29, 21, (1935).
14.- Smedley-MacLean and Haffert, Biochem.J. 18, 1273, (1924).

known fact that in the vegetable kingdom the C_{18} fats are in an overwhelming majority. Most of these are unsaturated. However, in the palm oils lauric acid (C_{12}) predominates. There is also a C_{22} Erucic acid in rape and ravison oils. Besides these, there are a number of rare hydroxylated and keto acids.

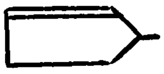
The predominance of C_{18} fats suggest that they might be formed from three hexose molecules. Similarly the comparatively rare C_{12} and C_{24} fats might be derived from two and four molecules of hexose respectively. The remainder fatty acids might conceivably be derived from these three through beta oxidation.

It is difficult to decide the source of unsaturated hydroxy or keto-acids. It has been shown that in flax seeds there is first a maximum fat content before an increase in the unsaturated fatty acid content(15) takes place. Saturated fatty acids may readily be dehydrogenated through widely occurring dehydrogenases(16). This is the reason why the position of the double bonds has no real value in determining the point of original chain condensation. As each type of animal has a fat content whose unsaturation is practically constant for each species, it is reasonable to expect that each species dehydrogenates to its own requirement. As a general rule the colder the habitat, the more unsaturated are the fats present in the body.

15.- Eyre, Biochem.J. 25, 1902, (1931).
16.- Harrison, Erg. Enzymforsch. 4, 297, (1935).

In the plants, generally speaking there is an accumulation of carbohydrates before ripening and germination, while in germination there is a decrease in the carbohydrate content and an increase in the fat content.

There is a second theory as to the origin of fats which postulates the building up of fatty acids from units smaller than the sugars. Acetaldehyde might serve as the building unit but as yet we have no proof supporting this idea. However, certain bacteria will grow in a calcium lactate medium producing various acids up to C_{10}. In other words, fats can be synthesized from the precursor of acetaldehyde. Ethyl alcohol(17) and salts of acetic acids(18) are the only other carbon compounds which lead to the formation of fats when acted on by certain yeasts.

The occurrence of cyclic fatty acids is of great interest. These acids having a cyclopentenic ring occur in a number of plants. It is curious that the side chain shows such regularity in its variation. Cole and Cardoso recently studied the constituents of chaulmoogra oil (Hydnocarpus wightiana). This oil contains cyclopentenic acids of the general formula $-(CH_2)_n$ - COOH. The following acids of this series have definitely been identified(19), chaulmoogric($n = 12$), hydnocarpic($n = 10$), alepric($n = 8$), aleprylic ($n = 6$), aleprestic($n = 4$), aleprolic($n = 0$). No acid has been

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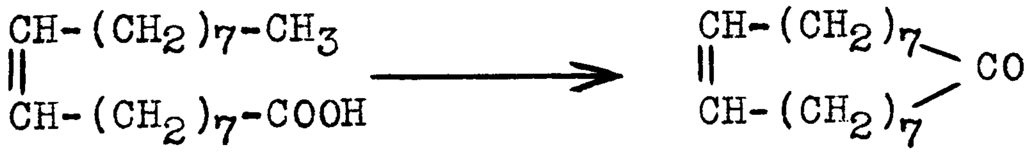
17.- Halden, Biochem.Abs. 225, 249, (1934).
18.- Smedley-MacLean and Hoffert, Biochem.J. 17, 720, (1923).
19.- H.I. Cole and H.T. Cardoso, J.Am.Chem.Soc. 2349, (1939).

found having n= 2. Gorlic acid, also found in this oil,has a double bond in the side chain otherwise being similar to chaulmoogric acid.

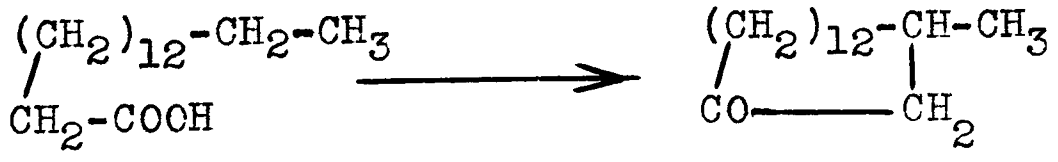
It is possible through beta oxidation and oxidation with cleavage of double bonds in unsaturated acids, to arrive at any acid which occurs in waxes. The formation of omega oxidized acids may be explained in this manner. An unusual acid, namely juniperic acid (15 hydroxy pentadecanoic acid) occurs in the resins of certain pine trees. It also occurs as a lactone in the oil of angelica(20).

It has often been suggested that civettone, muscone and similar compounds may be directly derived from fatty acids, though it is difficult to see how such a reaction could take place(21).



Oleic Acid

Civetone



Palmitic Acid

Muscone

Several attractive theories have been advanced to explain the formation of more complex substances. It is not our purpose to make a review of all these theories. Such a review has already been made by K. Bernhauer, in Grundzuge der Chemie und Biochemie der Zuckerarten, (Berlin, 1933).

20.- Kerschbaum, Ber., 60B., 902, (1927).
21.- L.Ruzicka, Helv.Chim.Acta. 9, 7, 236, (1926),and 9,1008,(1928).

It might however be worth while to mention a few of these theories in a cursory manner.

Stewart(22) has developed the polyketide theory which lends itself to a plausible genesis of some plant pigments. A polyketide may form in the following manner.

$CH_2OH\text{-}CH(OH)\text{-}CH(OH)\text{-}CH(OH)CH(OH)\text{-}CHO$

removal of three molecules of water leads to the following

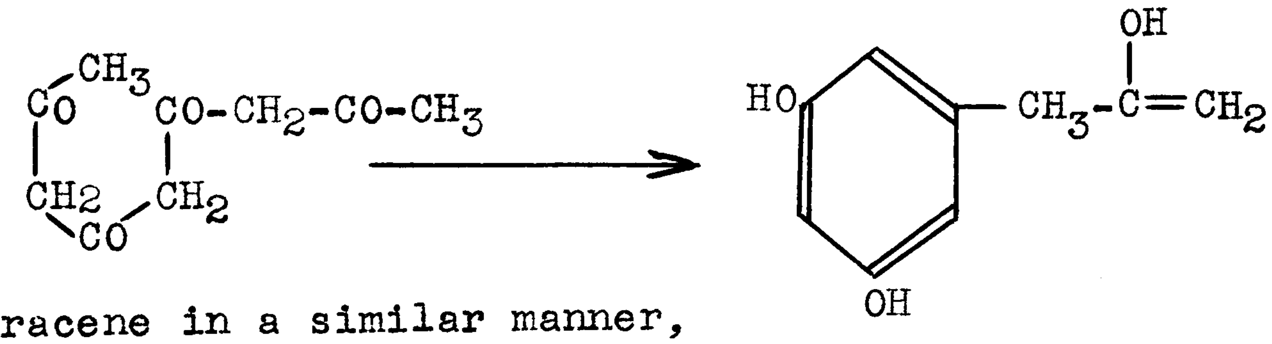
$CH_2{=}C(OH){-}CH{=}C(OH){-}CH{=}CO$

which is the enolic form of

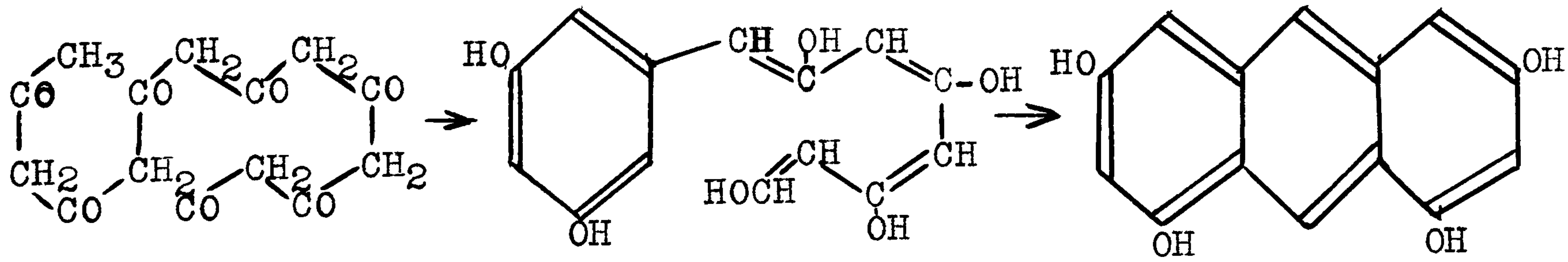
$CH_3{-}CO{-}CH_2{-}CO{-}CH{=}CO$

Polyketides lead very easily to the formation of benzene derivatives which are widely found in nature.

for example,

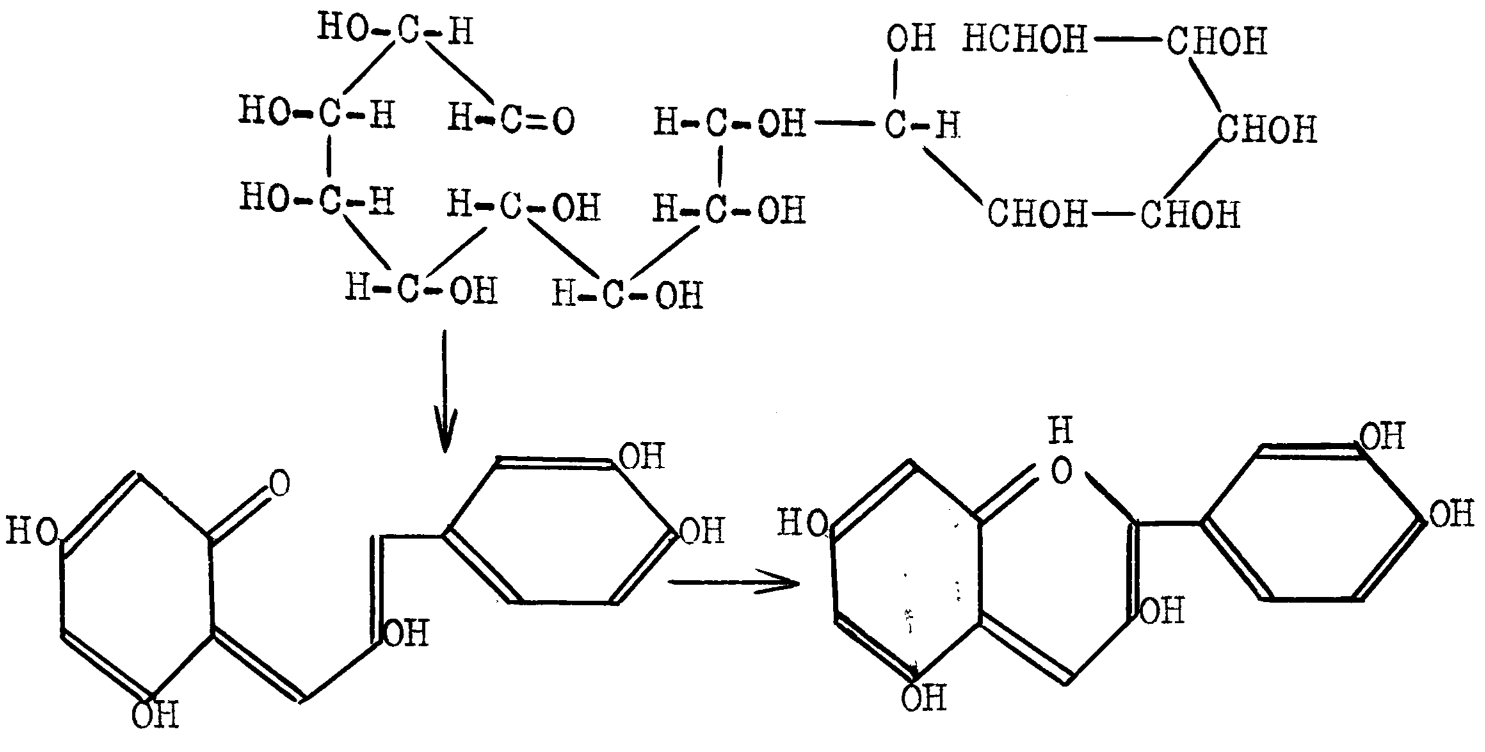


or anthracene in a similar manner,



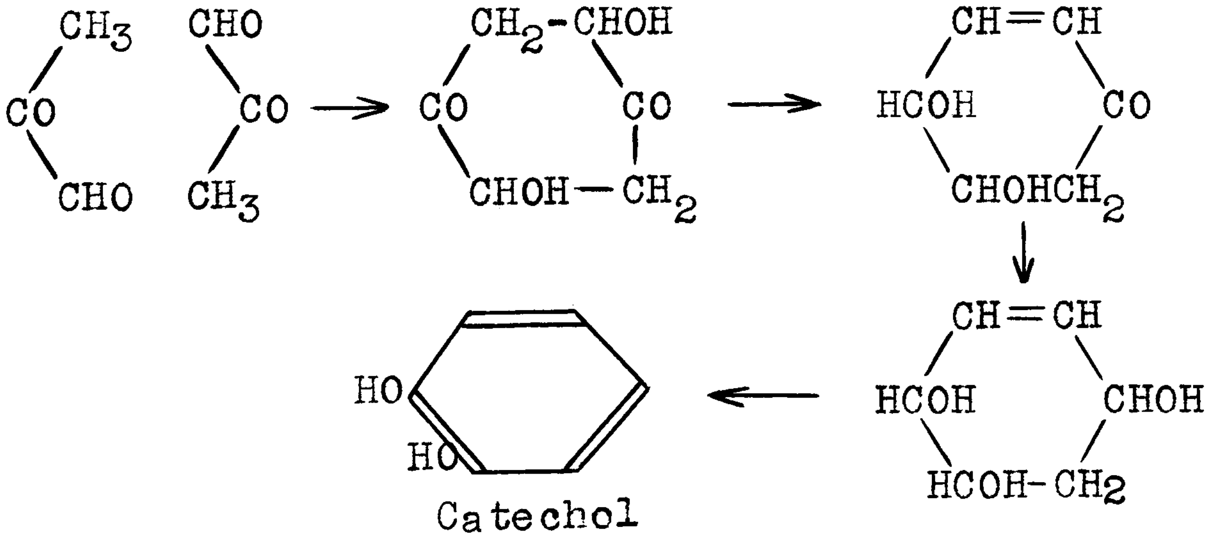
For the synthesis of plant pigments for example, cyanidin, it is necessary to have a carbohydrate of the structure $CH_2(OH)(CH.OH)_{13}.CHO$. The synthesis may thus be represented in the following manner.

22.- Stewart, Recent Adv. in Org. Chem. Vol.II, page 283. (1931).



Stewart's polyketide theory applies equally well to the formation of protein products, depsides, etc. However, since we are mainly interested in compounds of terpenoid nature and the polyketide theory does not lend itself to this problem, we shall not discuss it any further.

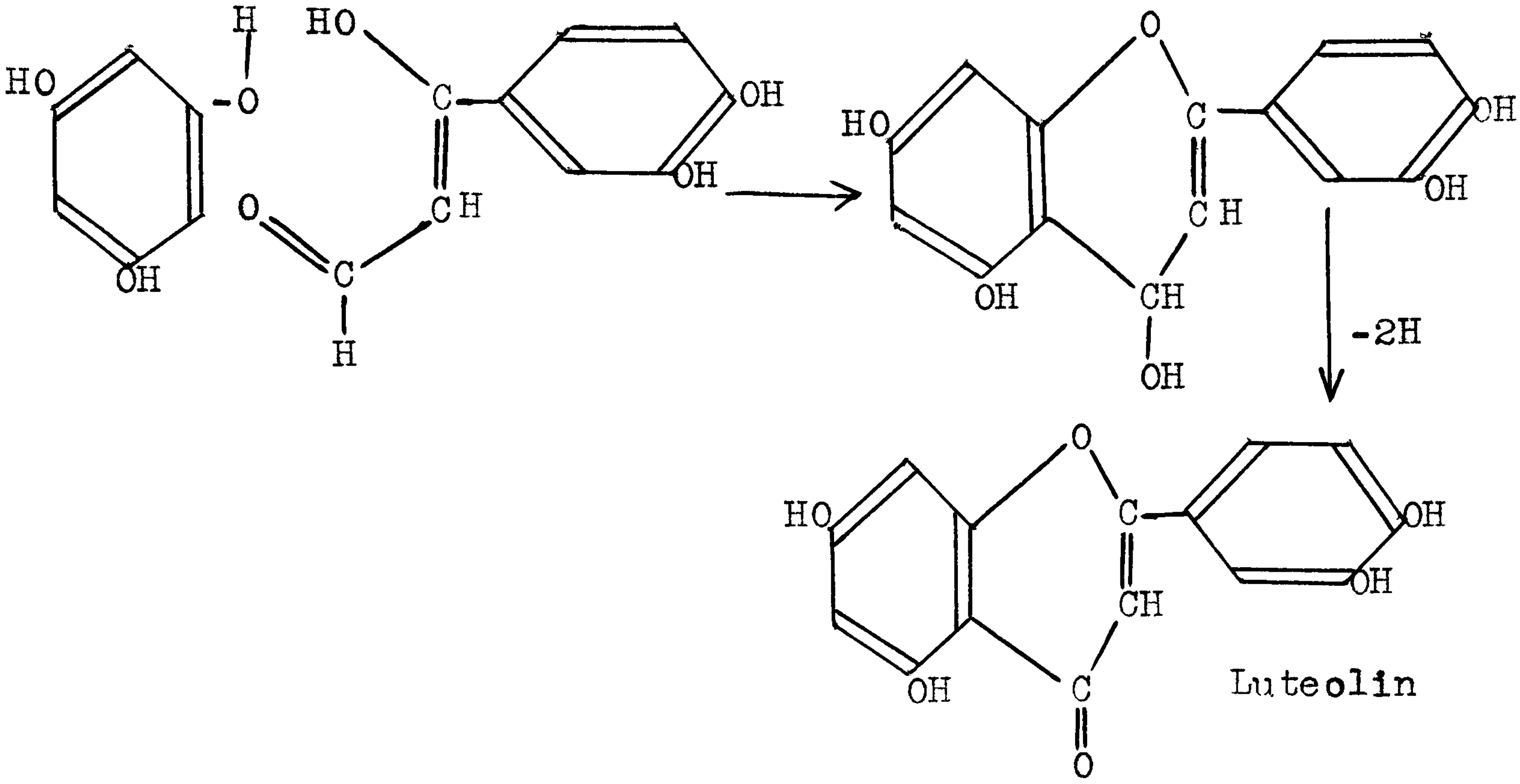
Hibbert(22) regards methyl glyoxal as being the building unit of lignin substances. He offers the following mechanism for the formation of catechol from methyl glyoxal.



This type of mechanism may be extended to a great variety of naturally occurring substances.

22.- Private Communication.

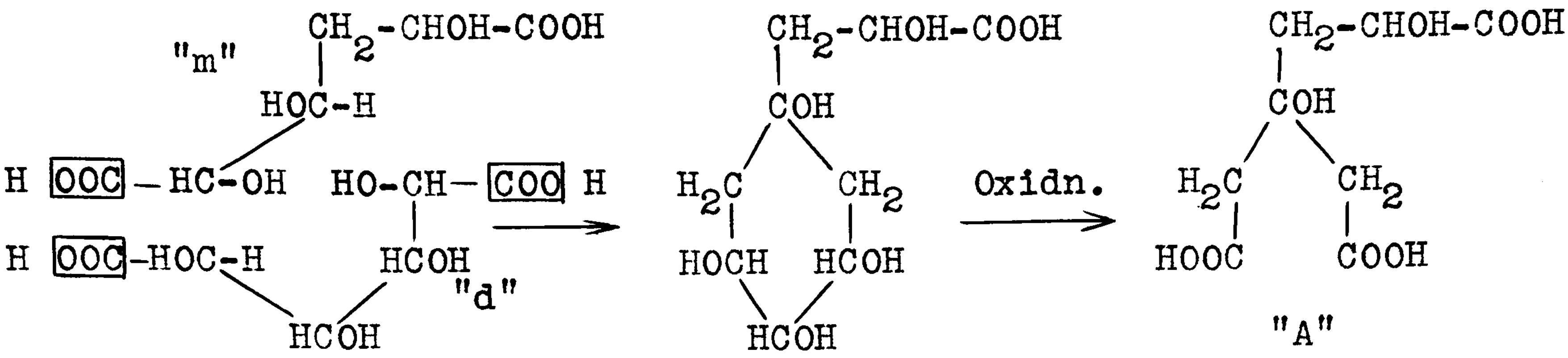
Hibbert also proposes a new scheme for the possible formation of plant pigments. He indicates the existence of C_6-C_3 (-C-C-C) systems in plant products and postulates the following mechanism for the formation of the flavone luteolin.



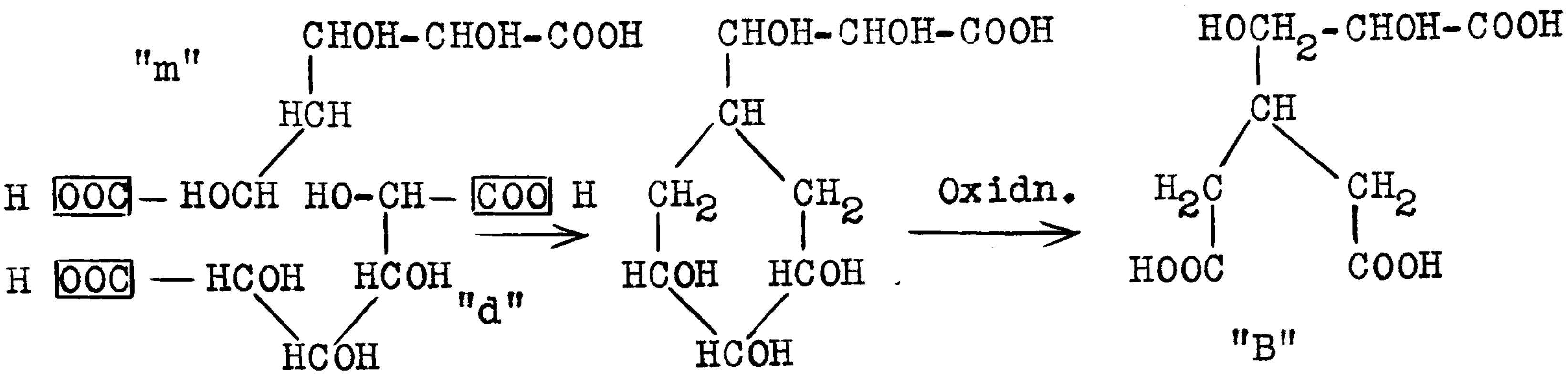
Luteolin

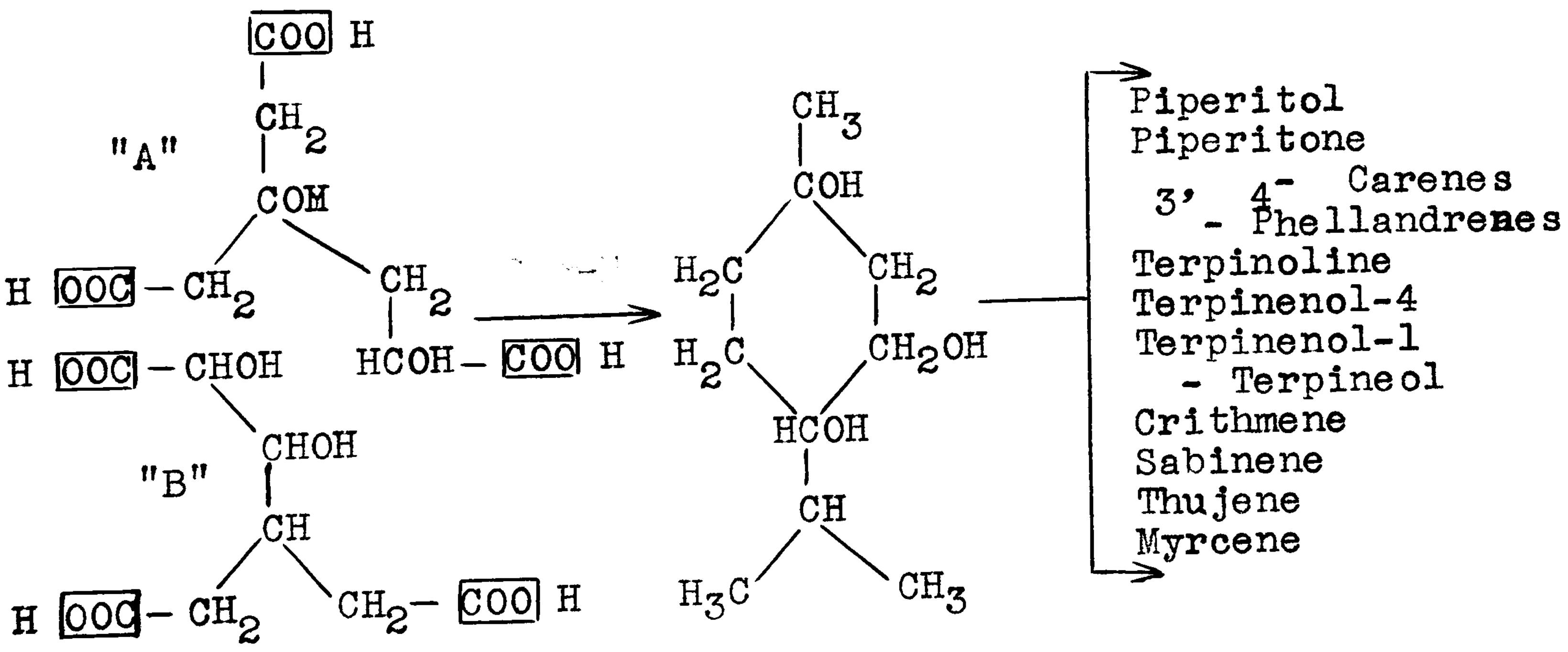
A rather extensive phytochemical study relating to terpenoids has been made by Hall(23). Hall uses a combination of hexose and metasaccharonic acid as the building block of all the terpenes and terpenoid materials such as carotenoids, abietic acid, etc., for the sake of convenience, we will take only one type of combination in order to illustrate the ideas expressed by Hall.

23.- J.A. Hall, Chem.Rev.. 305-345, (1937).



We also may have the following combination:





"m" - metasaccharonic acid.

"d" - Dicarboxylic sugar.

By taking the other three combinations of A and B, Hall has shown that these may yield all the possible terpenes. It is all a matter of hydration and dehydration at proper places.

Read(24) has taken geraniol as the precursor of terpenes, and Hall(25) has developed the idea to completion. However, there is nothing said about the formation of geraniol in the plant.

There is the generally well known and widely used fact that terpenoids and carotenoids are built up of isoprene units. The polymerization taking place in several ways, such as direct linear head-to-tail union resulting in either acyclic or cyclic hydrocarbons, and generally yielding the terpenes. This type of union with concurrent hydrogenation results in phytol type of compounds. If however, head-to-tail polymerization is accompanied by dehydrogenation in 1:4 position we get a conjugated continuous system of carotenoids. It is well known however that the head-to-tail polymerization stops at a certain stage and carotenoids consist of two such similar units joined together. The center of the molecule is of course a tail-to-tail joint.

The mere fact that practically all the constituents of essential oils and many other compounds are built up of complete isoprene unit has led to the so called "isoprene rule".

24.- Read, J. Chem.Rev., 7, 1-50, (1930).
25.- J.H.Hall, Chem.Rev., 479, (1933).

The application of this rule has been of immense value in the study of many terpene compounds, especially those of sesquiterpene and polyterpene series.

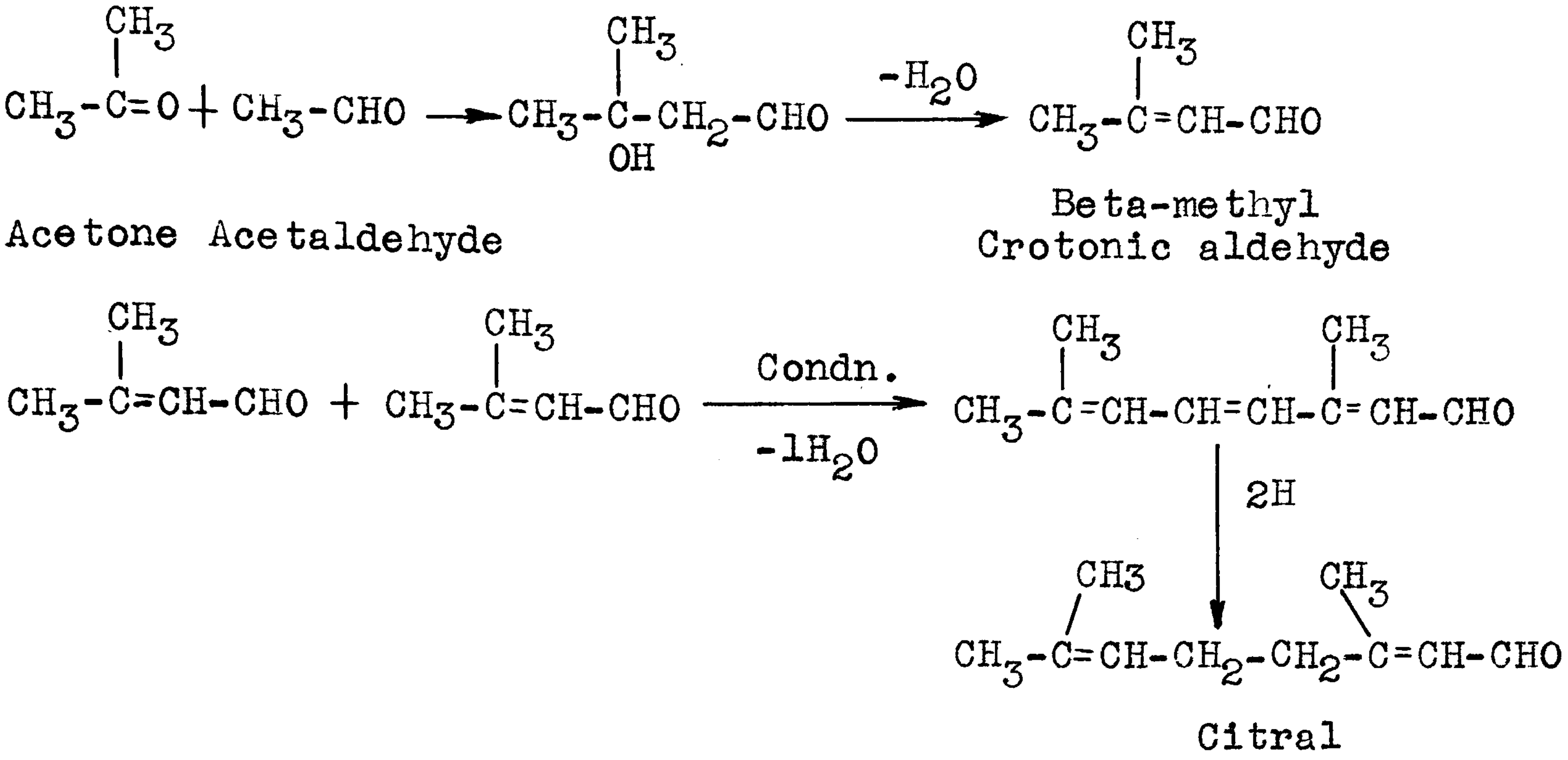
It is noteworthy that Jauregg(26), on treating isoprene with acetic acid containing a little sulphuric acid, obtained various condensation products, among which, he identified geraniol, cyclogeraniol, linalool, alpha-terpineol, 1.4- and 1.8- cineol, a monocyclic sesquiterpene, a hydrocarbon containing three double bonds, etc.

Recently Favorskii(27) treated $CH_3\text{-}C(CH_3)(OH)\text{-}CH{=}CH_2$ with 20 percent sulphuric acid at room temperature and obtained linalool, geraniol, terpin hydrate and other products.

Mechanisms differing from isoprene condensation and yet involving an active isoprene skeleton have been proposed by many workers.

MacLean(28) suggested that citral arises from the condensation of two molecules of acetone and two of acetaldehyde. This theory has been elaborated by Singleton(29) and also by Kremers(30). It has naturally been pointed out that citral, by various reactions, may lead to practically all types of terpene compounds. However, the condensation of acetone and acetaldehyde must take place in the following manner in order to lead to the formation of citral.

26.- T.W.Jauregg, Ann. 496, 52, (1932).
27.- A.E.Favorski, J.Gen.Chem. (USSR), 8, 879, (1938).
28.- MacLean, J.Chem.Soc. 99. 1621, (1911).
29.- F. Singleton, J.Chem.Soc. 989, (1931).
30.- Kremers, J.Biol.Chem. 50, 31, (1922).



$$CH_3-\overset{CH_3}{\overset{|}{C}}=O + CH_3-CHO \longrightarrow CH_3-\underset{OH}{\overset{CH_3}{\overset{|}{C}}}-CH_2-CHO \xrightarrow{-H_2O} CH_3-\overset{CH_3}{\overset{|}{C}}=CH-CHO$$

Acetone Acetaldehyde

Beta-methyl
Crotonic aldehyde

$$CH_3-\overset{CH_3}{\overset{|}{C}}=CH-CHO + CH_3-\overset{CH_3}{\overset{|}{C}}=CH-CHO \xrightarrow[-1H_2O]{Condn.} CH_3-\overset{CH_3}{\overset{|}{C}}=CH-CH=CH-\overset{CH_3}{\overset{|}{C}}=CH-CHO$$

$$\Big\downarrow 2H$$

$$CH_3-\overset{CH3}{\overset{/}{C}}=CH-CH_2-CH_2-\overset{CH_3}{\overset{\backslash}{C}}=CH-CHO$$

Citral

This type of condensation between acetone and acetaldehyde has not been successfully carried out in vitro, the product of condensation always being $Me-CHOH-CH_2-COMe$.

This difficulty has been shelved by assuming beta methyl crotonaldehyde as being the progenitor of terpenoid compounds. Von Euler in his book Grundlage und Ergebnisse der Pflanzenchemie, Vol. 3, p. 319, (1909)(31), put forward the idea of beta methyl crotonaldehyde as being the common building unit of terpenes. Karrer(32) extended this idea in his studies of carotenoids.

Many attempts to synthesize carotenoids using beta methyl crotonaldehyde have not met with great success. However, Fischer and Lowenberg(33) succeeded in carrying out an aldol condensation between two molecules of this aldehyde and obtained the corresponding aldol, and by dehydration, the triene, $(Me)_2C=CH-CH=CH-C(Me)=CH-CHO$.

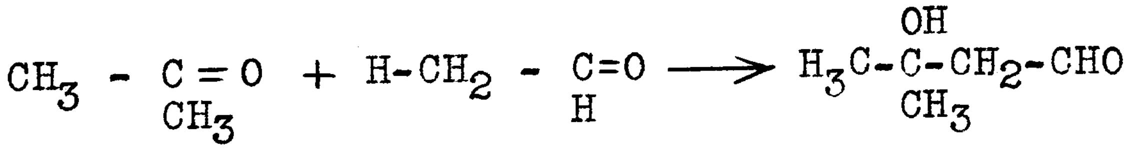
31.- Through J.A. Hall, Chem.Rev. 306, (1937).
32.- P. Karrer, Helv.Chim.Acta. 19, E33, (1936).
33.- F.G.Fischer and K.Lowenberg, Ann. 494, 263, (1932).

Fuson and Christ(34) have indicated the possibility of condensing beta cyclocitral with two molecules of dimethyl acrolein, according to the principle of vinology, and obtaining vitamin A by reduction of the resulting aldehyde. However, attempts to condense citral with 2,6-dimethyl-8-octatrienal have failed(35).

Kuhn(36) has claimed the synthesis of vitamin A by condensing ionylidene acetaldehyde with dimethyl acrolein and reducing the resulting aldehyde. Karrer(37) questions Kuhn's results by failing to repeat this synthesis.

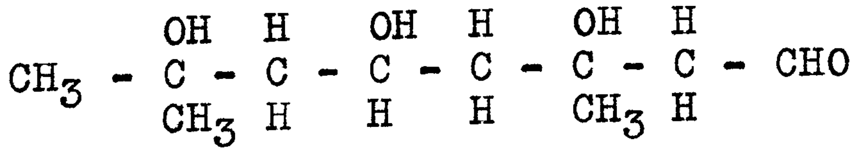
Heilbron(38) and co-workers have lately succeeded in condensing citral with dimethylcrotonaldehyde by using sodamide.

Rogers and Gisvold(39) present a plausible theory somewhat similar to the one advanced by Karrer. They cite the occurrence of branched chain sugars such as apiose and hamamelose, as evidence of the possibility of the type of condensation occurring in plants which apparently cannot be carried out in the laboratory. Thus,



$$CH_3-\underset{CH_3}{C}=O + H-CH_2-\underset{H}{C}=O \longrightarrow H_3C-\overset{OH}{\underset{CH_3}{C}}-CH_2-CHO$$

Head-to-tail condensation of two of these units give,



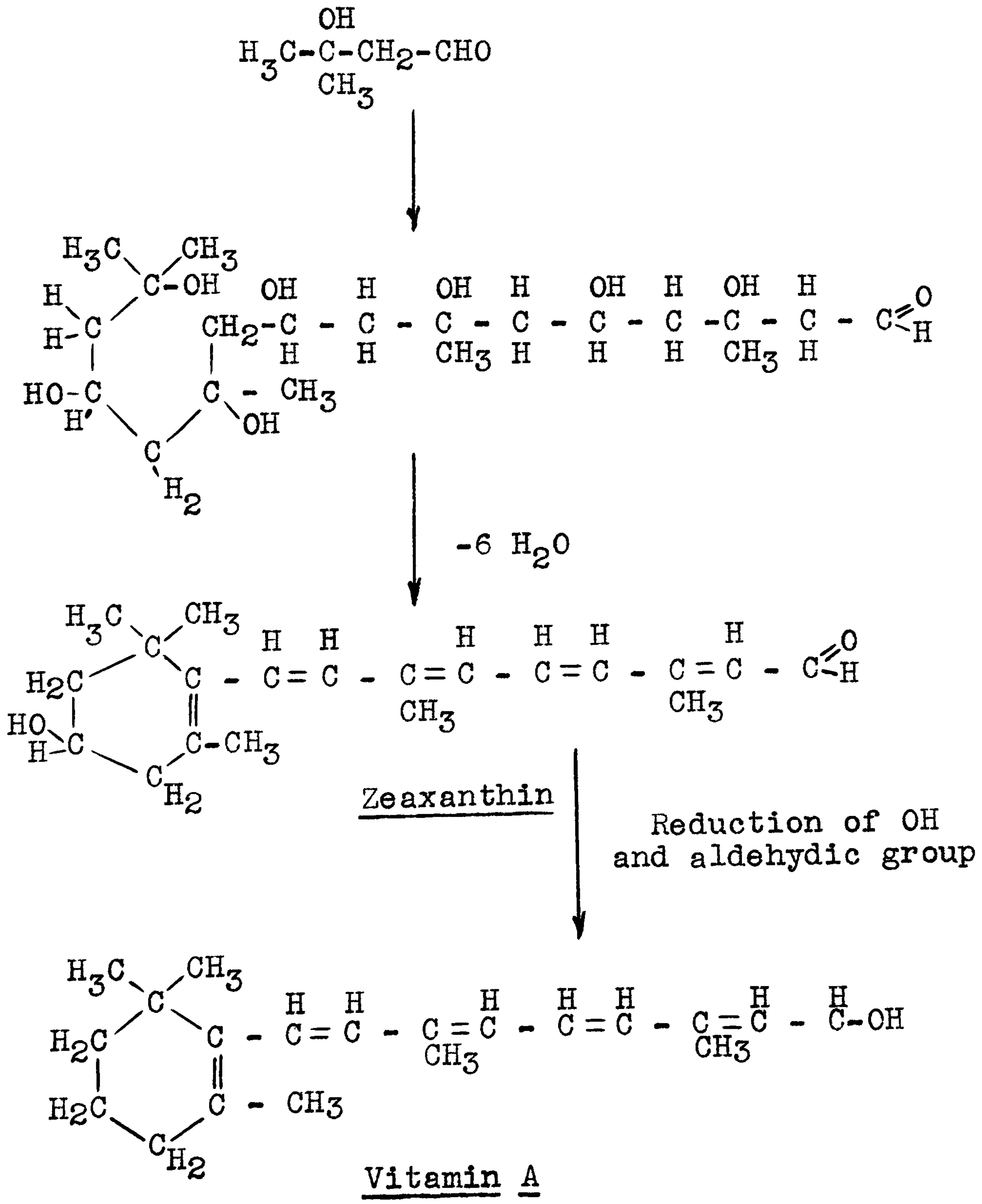
$$CH_3-\overset{OH}{\underset{CH_3}{C}}-\overset{H}{\underset{H}{C}}-\overset{OH}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-\overset{OH}{\underset{CH_3}{C}}-\overset{H}{\underset{H}{C}}-CHO$$

34.- R.C.Fuson and R.E.Christ, Science, 84, 294, (1936).
35.- Bernhauer and co-workers, Ann. 525, 43, (1936).
36.- Kuhn and Morris, Ber., 70B. 853, (1937).
37.- Karrer and A.Ruegger, Helv.Chim.Acta. 23, 284, (1940).
38.- Heilbron, et al., J.Soc.Chem. 1549 - 1963, (1939).
39.- C.H.Rogers and O.Gisvold, The Chemistry of Plant Constituents (1939).

from which through dehydration cyclization, hydrogenation etc., one can build up any type of terpene or carotenoid molecule.

It is noted that in the carotenoid pigments which are cyclized at the ends, there occurs no double bond between the 4 and 5 carbon atoms. However, the 4 carbon atom may contain a hydroxyl or a ketonic group.

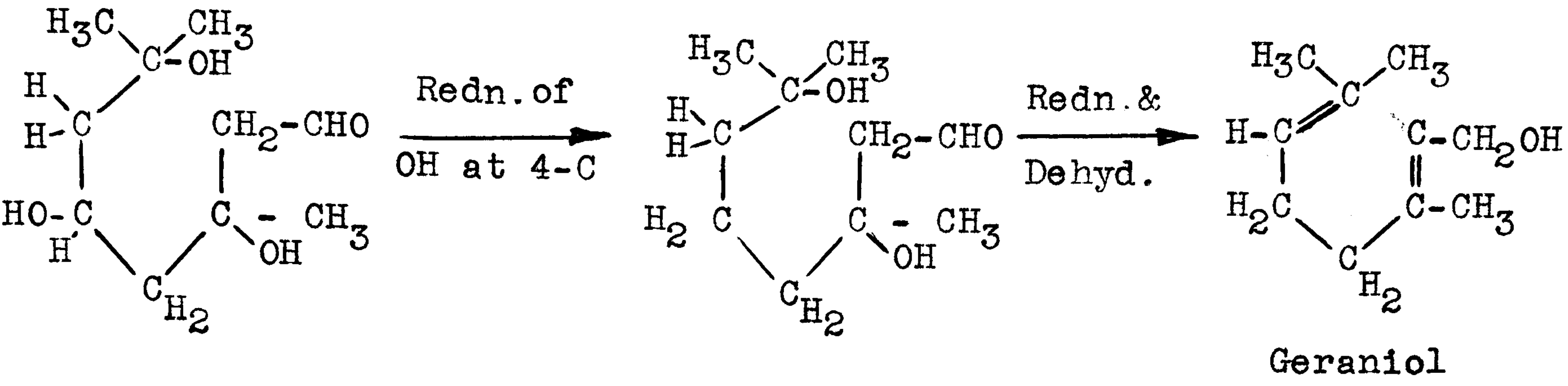
For the sake of clarity it is worth while to illustrate the formation of carotenoids and terpenoids from the



Zeaxanthin

Vitamin A

Formation of Terpenes may also take place in the following manner:



Geraniol

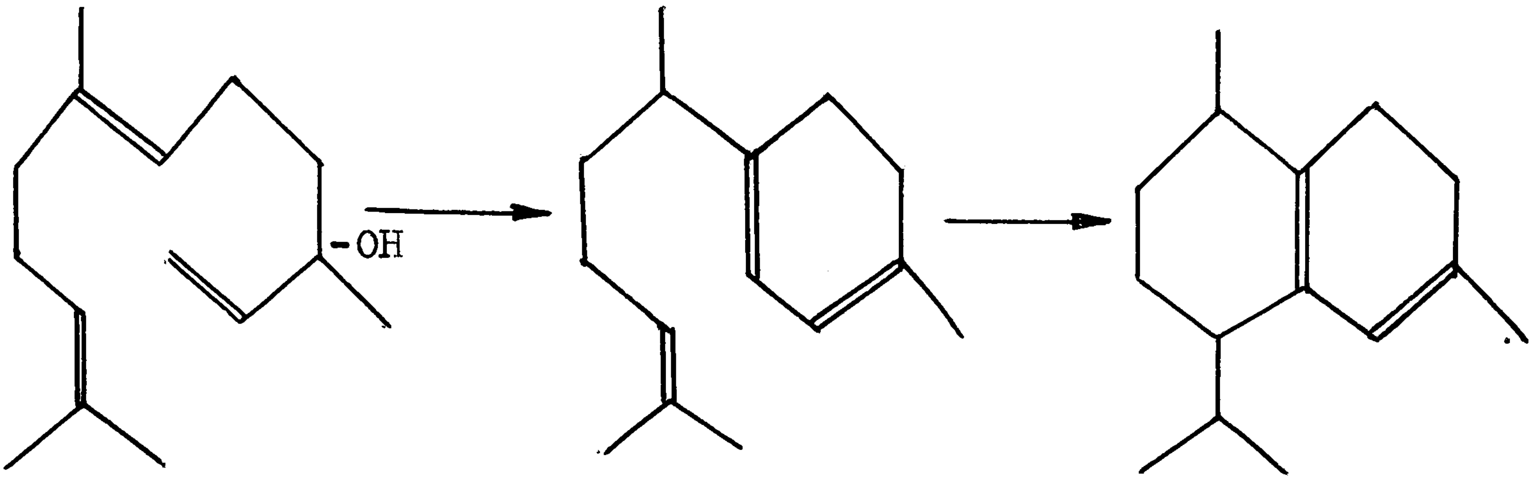
Volatile oils consist of acyclic and cyclic terpenes. The ease with which acyclic terpenes undergo cyclization to yield cyclic terpenes similar to the ones found in nature suggests that they may be the progenitors of cyclic compounds. These cyclizations may be carried out through the addition and splitting out of water. Such hydration and dehydration in the terpene series are commonly accepted as occurring in nature and there is considerable laboratory experimental evidence to support it.

Having discussed the possible biogenic origin of simpler classes of compounds, carotenoid in nature, it becomes necessary to say a few words of the more complex terpenoids.

A class of terpenoids known as sesquiterpenes have been studied extensively in the last two decades. Again the isoprene rule is obeyed, and cyclizations may be carried out through the action of acids on acyclic compounds. Thus, farnesol yields farnesene which, under the influence of formic acid, gives the monocyclic sesquiterpene alcohol bisobolol(40). When nerolidol is boiled for some hours with formic acid it yields a dicyclic hydrocarbon isocadinene. The last reaction is rather

40.- Ruzicka, Capato, Helv.Chim.Acta. 8, 259, (1925).

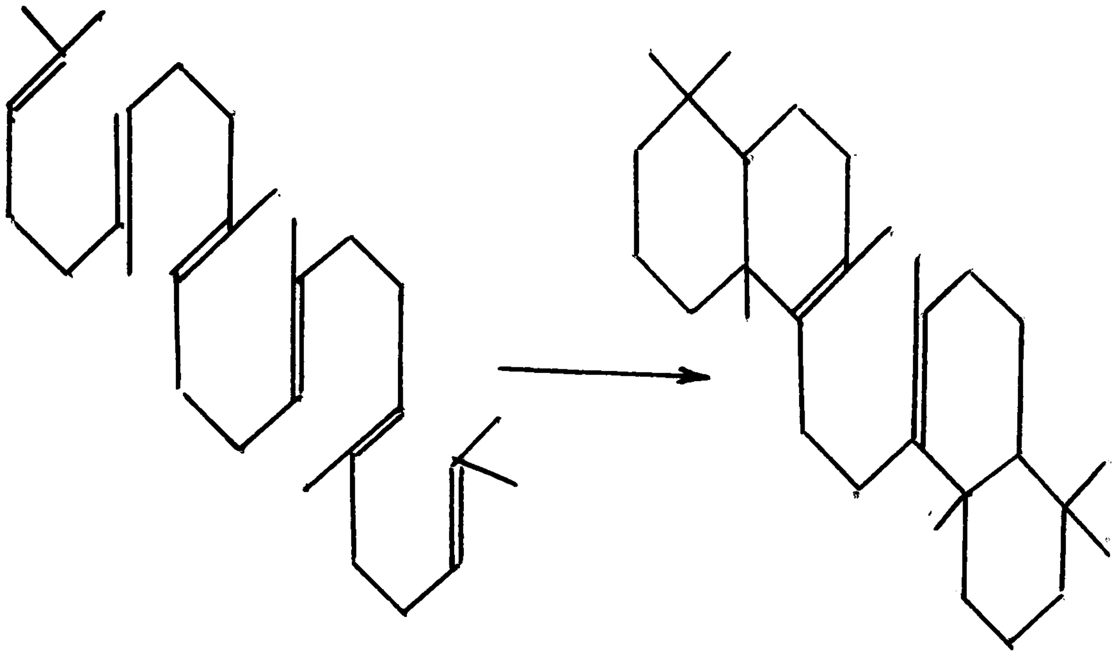
difficult to see from the hydration dehydration viewpoint.



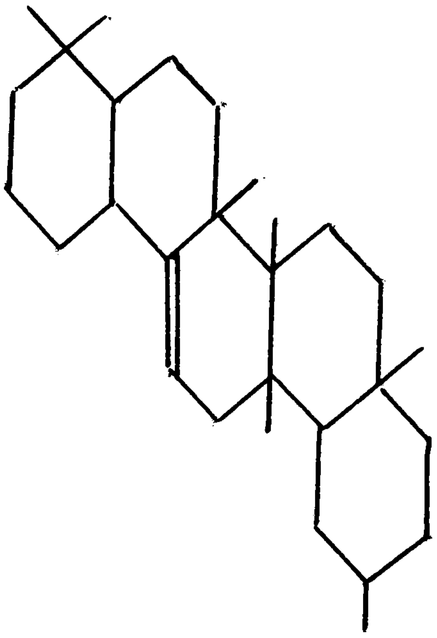
The triterpenes are also of great importance. There is the well known class of triterpenoid saponins which have a pentacyclic structure. Occurrence of pentacyclic non-sapogenin triterpenes have been reported, oleanic acid being a well known example. Oleanic acid is associated with the cuticle waxes of various fruits such as apples, grapes, pears, cherries, etc., while sapogenin triterpenoids are found in different parts of the plant, usually in combination with acids, sugars, etc.

A very interesting acyclic triterpenoid which has been extensively studied and synthesized is squalene(41). It occurs in shark liver oils. It is significant that Heilbron(42) on boiling it with formic acid for several days obtained the tetracyclo compound but could not force the formation of the fifth ring.

41.- Karrer & Helfenstein, Helv.Chim.Acta. 14, 78, (1931).
42.- I.Heilbron et al., J.Chem.Soc., 1630, (1926).



Squalene Tetracyclosqualene



Oleanic Acid

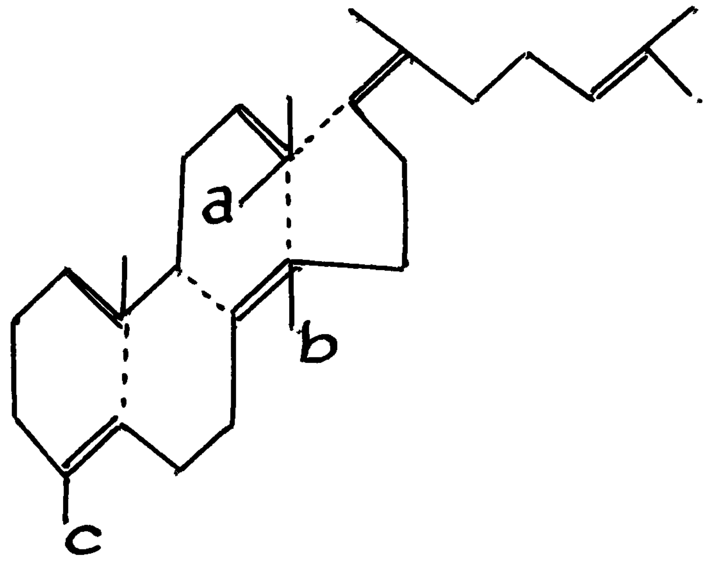
The possible relationship between triterpene squalene and sterols has been put forward by many workers. Heilbron(43) reports that experiments carried out by H.J. Channon of University College, London, showed that when rats were administered squalene, the cholesterol content of the liver of rats more than doubled.

Andre and Canal(44) have shown that the cholesterol and squalene content in young and old sharks appears to bear a reciprocal relationship. In young fish the cholesterol predominates while in the old ones the opposite holds true.

Karrer has suggested a possible relationship between squalene and cholesterol(45).

43.- Heilbron et al., J.Chem.Soc., 130, 1630, (1926).
44.- Andre and Canal, Compt. Rend. 181, 612, (1925).
45.- Karrer, Helv.Chim.Acta. 14, 78, (1931).

Robinson(46) has drawn attention to the fact that cholesterol skeleton is contained intact and without rearrangement in squalene. In the following diagram



it seems that there should be no difficulty in elimination of carbons a and b. The elimination of carbon c seems strange but it may be lost through a beta-ketonic acid type elimination of carbon dioxide.

Vanghelovici(47) made a similar suggestion and added the following sequence for the synthesis of cholesterol in the animal organism. Carbohydrates → saturated fatty acids → unsaturated fatty acids → poly-isoprenic carotenoids → cholesterol.

Bryant(48) criticizes the theory of Robinson(46) on the following grounds: (a) that cyclization must begin near the middle of the squalene to avoid the formation of large rings, (b) the carbon atom common to rings C and D of sterol is involved in two ring closures, (c) there is no

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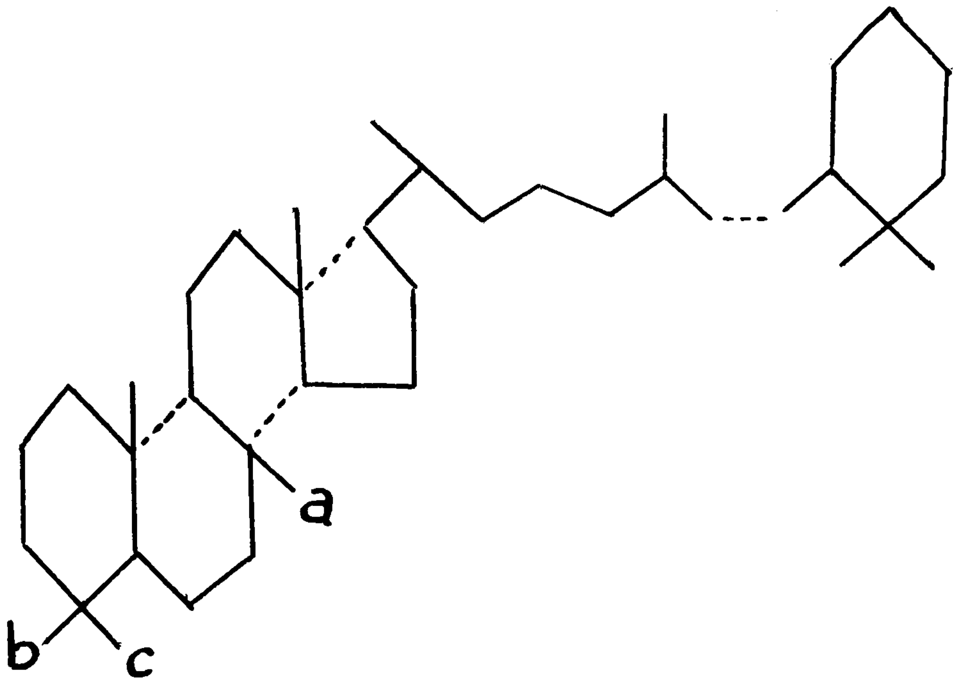
46.- R. Robinson, J.Soc.Chem.Ind., 53, 1062, (1934).
47.- M. Vanghelovici, J.Soc.Chem.Ind., 998, (1934).
48.- W.M.D.Bryan, J.Soc.Chem.Ind., 907, (1935)

structural peculiarity of the carbon chain forming ring D which would favour the formation of a five membered ring, instead of a six membered ring involving the carbon atom "a".

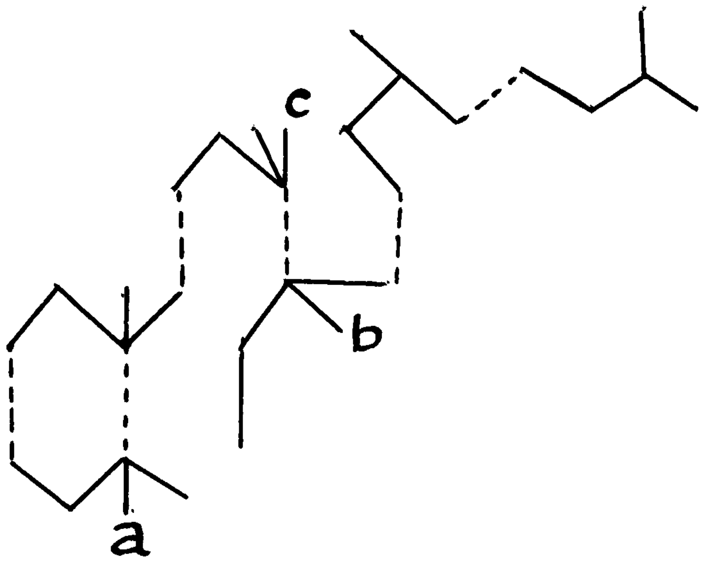


None of these objections are serious since we can eliminate all three by selecting alpha or beta carotene instead of squalene as the starting point. The formation of a five membered ring is due to the presence of four unbranched carbon atoms formed by the symmetrical union of two partially cyclized phytyl chains in carotene. The aliphatic side chain is the result of cutting off a terpene molecule from the other end of carotene. The disposal alone of the carbon atoms of gem grouping should be easily carried out(49), and the other two b and c as suggested by Robinson.

Spring(50) criticizes all of the previous views on the ground that many steroid compounds possess a different

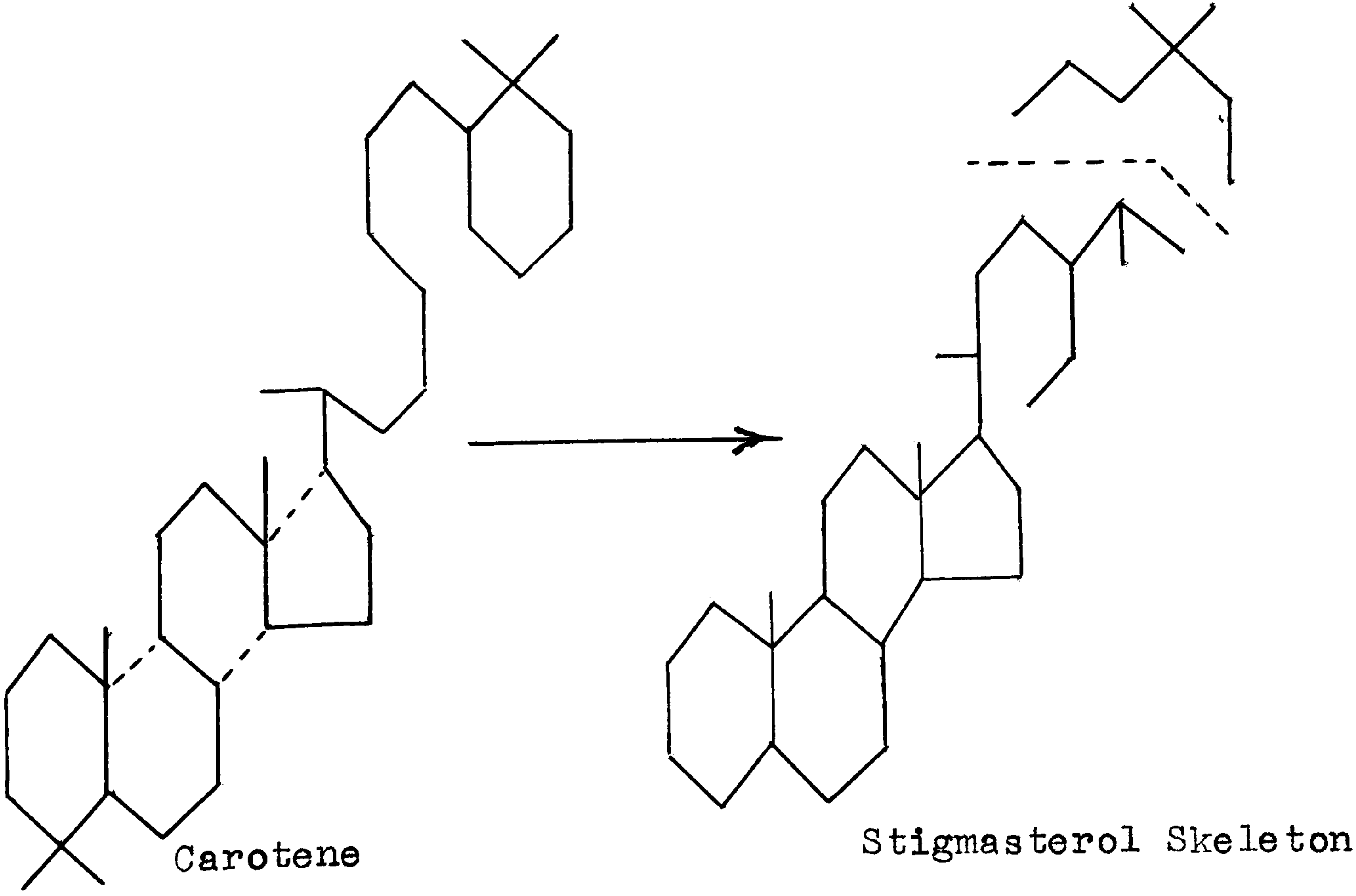
49.- Ruzicka, Helv.Chim.Acta., 16, 169, (1933).
50.- F.S.Spring, J.Soc.Chem.Ind., 972, (1935).

side chain from the sterols. He proposes the following scheme to show the terpenoid nature of sterols:



by condensation, cyclization and accompanying disposal of carbon atoms a, b, c, we get the typical cholestane, coprostane and stigmasterol structures.

In reply to Spring's(50) criticism, Robinson(51) points out the possibility of a biological variation in scission of the end carbon atoms in carotenes to produce the required side chain structure.



51.- W.M.D.Bryant, J.Soc.Chem.Ind., 1082, (1935).

Many of the above theories put forward to explain the possible biogenesis of plant constituents are admittedly attractive, however, we must keep in mind the fact that they are based almost wholly on theoretical grounds and as such have no great scientific value.

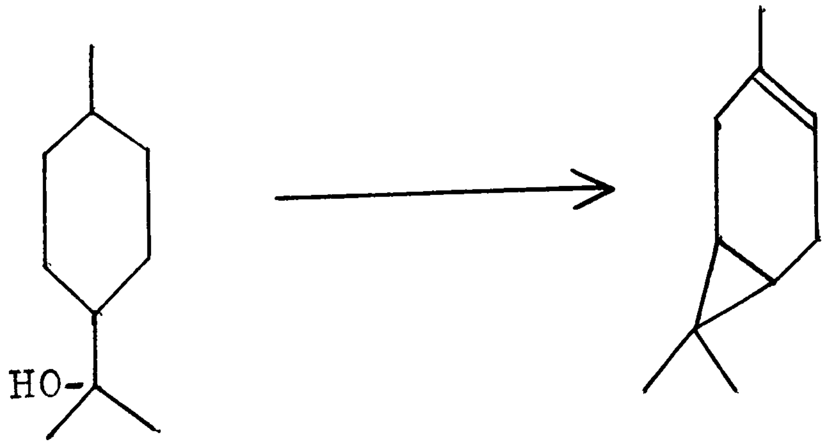
One might perhaps gain some knowledge concerning the ease of biogenic synthesis of plant constituents by reviewing the frequency of occurrence of carbocyclic compounds of various sizes.

This has been done in the following section.

Frequency of Occurrence of Size of Carbocyclic Compounds in Nature

When reviewing naturally occurring carbocyclic compounds, one is amazed at the preponderance of six membered compounds. It appears that next in line for the frequency of occurrence are the cyclopentanic compounds followed by cycloheptanes, cyclobutanes and cyclopropanes. This order suggests that ease of formation and ring strain have something to do with the frequency of occurrence of these compounds.

Beginning with cyclopropane type compounds we find that these occur only in a few cases. In the terpenoid series there are a class of compounds known as caranes, thujanes and sabinanes. They occur as the unsaturated hydrocarbon, or the alcohol, ketone, etc. It is probable that their formation is due to the usual type of elimination of water, for example:



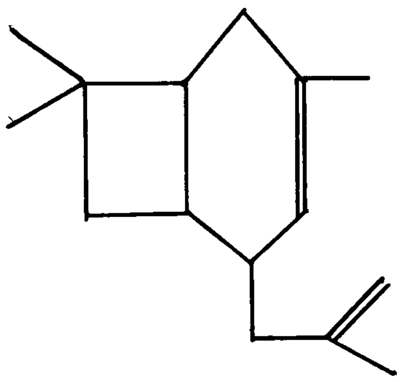
α-Terpineol

Carene

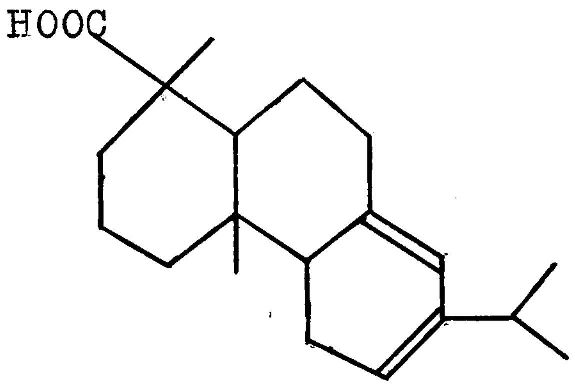
Perhaps one should not attach too much importance to these as being cyclopropane type compounds since they are linked to a six membered ring through two carbon atoms.

The only other type of cyclopropane compounds are the chrysanthemic acids occurring as esters of pyrethrolone in pyrethrins. Close examination of their structure reveals a rather curious fact. Both the mono- and dicarboxylic acids are apparently terpenoid in nature but the isoprene units are combined in a very unusual manner.

It must be recalled that all the known terpenoid and carotenoid compounds are a head-to-tail chain up to C_{20}. Caryophyllene and abietic acid also a few others are known exceptions to the continuous head-to-tail rule.

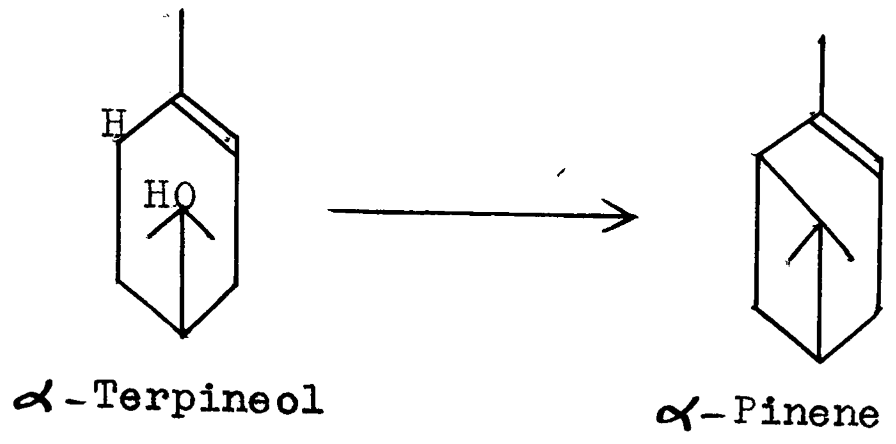


Caryophyllene



Abietic Acid

The occurrence of cyclobutane compounds is also comparatively rare. An important class of terpenes namely the pinenes contain a cyclobutane ring which have three carbon atoms in common with the six membered ring. As in the case of thujane or carane type compounds this may not have great significance due to the bicyclic nature of the compound. Formation of this class of compounds could again possibly take place through simple dehydration. Caryophyllene may also be included in cyclobutane class of compounds.

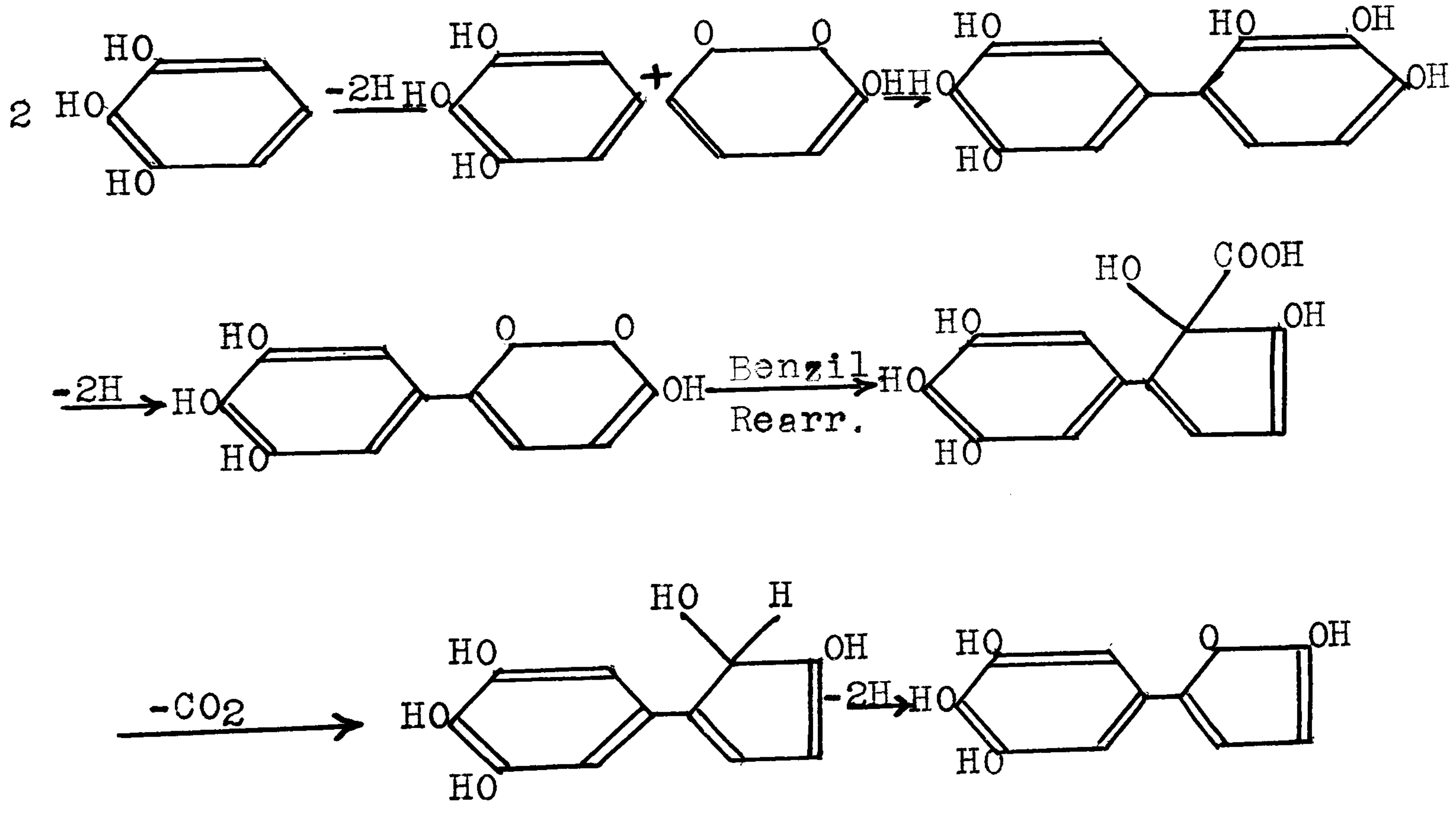


Two isomeric acids, namely truxillic and truxinic acids, (diphenyl-cyclobutane-dicarboxylic acids) occur together with alkaloids in coca leaf. It is quite possible that these are formed from cinnamic acids through the action of light. This type of synthesis has already been carried out in vitro. One must also remember the stabilizing influence of phenyl groupings on the ring structure.

The five membered rings are somewhat greater in number. In the terpene series the camphanes, fenchanes, etc., may be looked upon as consisting of two adjacent five membered rings with three common carbon atoms. However, actually we have a case very much similar to the previous two cases, the formation of five membered ring being due to bridge formation in a six membered compound. Again its formation may be due to the elimination of water from another compound.

We have already mentioned the chaulmoogric acid series, which have a non-terpenoid structure. Nothing is known of their origin. Jasmone, the odourous principle of jasmine flowers is a cyclopentanone. In spite of its occurrence with terpenoid compounds, it does not obey the isoprene rule. Pyrethrolone occurring in pyrethrine insecticides is somewhat similar to jasmone in its structure, being a substituted cyclopentanone. Purpurogallin is another cyclopentanone derivative. The occurrence in plants of these three somewhat similar cyclopentanone derivatives suggests a similar if not a common derivation.

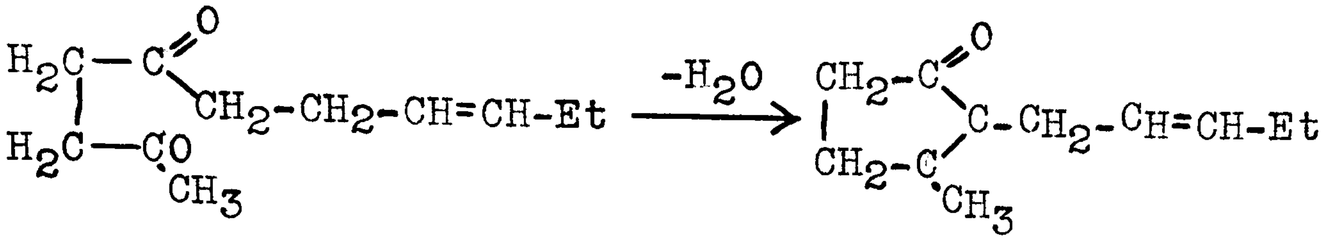
It has been suggested(52&53) that purpurogallin is probably formed in plants from pyrogallol by the following series of enzymic reactions:



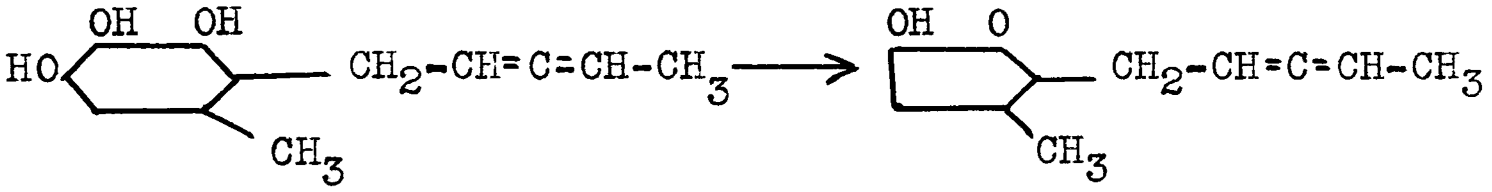
Purpurogallin

It is quite possible that jasmone is produced in the plant from a 1,4-diketone in which the methylene group in position 5 brings about the condensation(54).

52.- Willstatter and Heiss, Ann. 433, 17.
53.- Willstatter and Haber, Ber. 64, 2844.
54.- M.T.Bogert, Organic Chemistry (Gilman), 1215, (1938).



This view is opposed by the fact that pyrethrolone, possessing very much the same structure is obviously not derived from a 1,4-diketone, unless one assumes dehydration and hydrogenation followed by hydroxylation in the ring system. A mechanism similar to the one postulated in connection with the formation of purpurogallin would be more suitable for this case.



Another class of naturally occurring cyclopentanic compounds are found in petroleum. Both simple cyclopentanes and naphtenic acids consisting partly of alkylated fatty acids are found in petroleum. The derivation of these compounds is open to speculation, but may possibly result from the rearrangement of cyclohexanes(55).

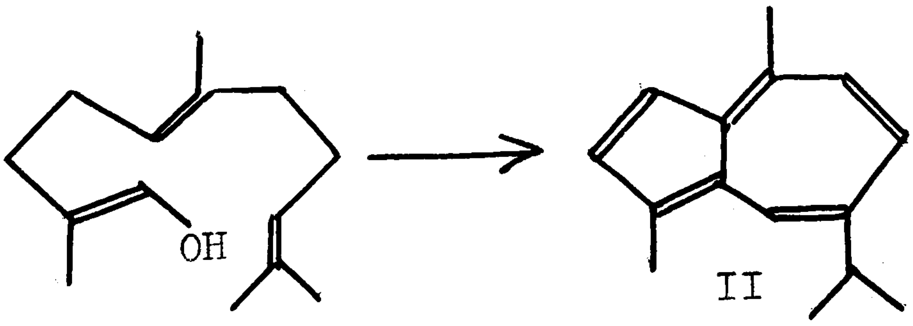
A class of substances found in many essential oils is known as azulenes. The presence of these substances is detected by the formation of a blue-violet colour on the slow addition of bromine to a chloroform or acetic acid solution of the essential oil(56). These azulenes have

55.- Nenitzescu, Ber. 66, 1099.
56.- R.T.Baker and H.G.Smith, "A Research on the Eucalyptus." Sydney, p.417, (1920).

been found to possess the formula $C_{15}H_{18}$, but their chemical structure has not yet been definitely elucidated. Hydrogenation and refractivity studies have shown that they contain a dicyclic system with five double bonds, one of which resists reduction through hydrogenation. Various decomposition and dehydrogenation studies have indicated the presence of a five and seven membered rings.

It is not definitely known whether azulenes occur as such in plants or are formed during extraction of volatile oils(57). However, many different ones have been isolated from various oils.

Pfau and co-workers(58) have been active in this field and have already synthesized several compounds resembling the natural products in their physical properties. The parent hydrocarbon has an intense blue colour indistinguishable from S-guaiazulene found in geranium oil. Further studies(59) on the decomposition of guaiazulene and also the synthesis of 1,4-dimethylbutylazulene indicate that guaiazulene has the probable structure II. Note its terpene structure and its close relationship to farnesol.



II

57.- K.Graham, J.Am.Pharm.Ass. 22, 819, (1933).
58.- A.S.Pfau and P.Plattner, Helv.Chim.Acta., 19, 858, (1936)
ibid. 20, 469, (1937).
59.- P.Plattner and L.Lemay, Helv.Chim.Acta., 23, 897. (1940).

The occurrence of a five membered ring in the sterol type of molecules has already been mentioned. This point is connected with the problem investigated and will be elaborated later on.

We have mentioned the preponderance of cyclohexane type compounds. Cyclohexane itself occurs in Caucasian petroleum, and many other oils, such as oil from coal tar, shale tar, rosin oil, etc. Various classes of terpenes may be considered as substituted cyclohexenes. Resins, sterols, bile acids, etc. consist of six membered polycyclic compounds.

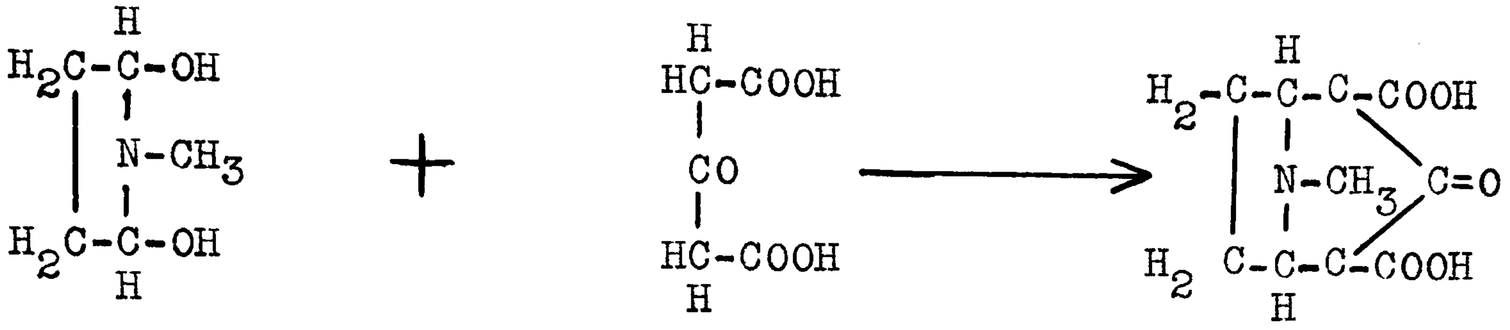
Seven membered rings are comparatively rare. They occur in the cocaine and tropane group of alkaloids. Robinson carried out a simple and brilliant synthesis on tropanone by reacting succinaldehyde, ammonia and acetone. Upon this experimental data he postulated the following mechanism for the formation of these alkaloids in plants(60). Condensation of succinaldehyde methylamine and acetone dicarboxylic acid may undergo the following series of reactions involving decarboxylation, reduction and esterification.

$$\begin{array}{l} H_2C-CHO \\ \quad | \\ H_2C-CHO \end{array} \quad \begin{array}{l} H \\ H \end{array}\!\!>N-CH_3 \longrightarrow \begin{array}{l} \qquad\quad H \\ H_2C-C-OH \\ \quad | \quad N-CH_3 \\ H_2C-C-OH \\ \qquad\quad H \end{array}$$

Succindialdehyde

Carbinol Amine

60.- Robinson, J.Chem.Soc., 876, (1917).



Carbinol Amine

Acetone Dicarboxylic Acid

Tropanone by Decarboxylation

Pomegranate bark contains an alkaloid, pseudopelletierine which is an eight membered cyclic compound with a nitrogen bridge. Other alkaloids allied to pseudopelletierine such as granatanine also contain an eight membered ring.

Higher cyclic compounds occurring in nature are extremely rare. They are isolated examples and we know very little about their origin. Muscone and civettone have already been mentioned and need not be repeated here. We have also mentioned the occurrence of lactone of 15-hydroxy pentadecanoic acid in angelica oil.

Aside from these, it is curious that none other cyclic large membered compounds have yet been found in nature.

THEORETICAL PART

Nature of the Problem

It was mentioned previously that we know virtually nothing about the vital synthesis of plant products. It is true that a large number of naturally occurring substances have been synthesized in the laboratory, but many of the reactions involved in these syntheses are carried out under conditions which are far too vigorous to be actually occurring in the plant cells. Thus, we cannot imagine the plant carrying out reactions at much over 100°C., yet such temperature ranges are very commonly employed in the laboratory. Nor can we suppose that the plant has an acid medium equivalent to a strength of 50 per cent sulphuric or 85 per cent phosphoric acid, commonly employed in many cyclization reactions of aliphatic terpenes.

However, we must keep in mind the fact that reactions both in the plant and in the laboratory must necessarily obey the same laws. Consequently, both the plant and the laboratory methods may achieve the same results through different routes.

A great deal of work has been done in the study of many terpenes. It is significant that in the cyclization of aliphatic terpenes in practically all cases the cyclic compounds obtained in the laboratory are identical with the ones found in nature. It is also significant that both the aliphatic and acyclic terpenes occur side by side in the plant indicating a common origin and interrelationship. The practical studies of Charabot(61) and his co-workers over a period of many years indicate that the plant first synthesizes aliphatic terpene alcohols, and the formation of cyclic compounds takes place at a later stage.

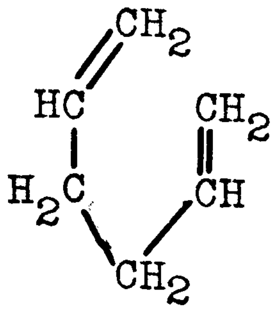
In view of these facts the author has considered the following argument. If certain sets of experiments yield cyclic terpene compounds from aliphatic terpenes, both of which occur in nature, then these same sets of experiments may be applied to the study of cyclization of compounds which are similar though not identical in structure with terpenes.

It was thought that this type of study might serve as a new approach to the problem of the possible biogenesis of some plant constituents. It is obviously of prime importance to know the type of skeleton which is necessary for the formation of four, five or six membered and other cyclic compounds.

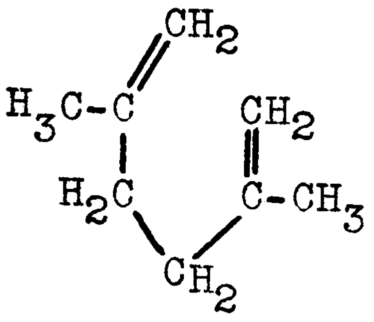
Aside from terpenes, very little work has been done in the study of cyclization of diolefins or compounds which yield diolefins under the experimental conditions.

The following four compounds were chosen for the study of this problem.

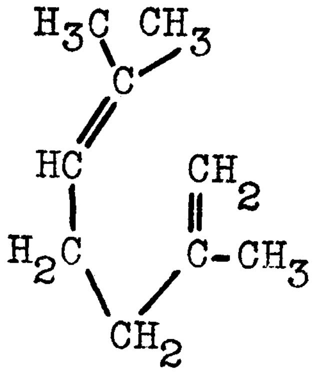
61.- E.T.Charabot, La Parfum Chez la Plante, Paris, 1908.



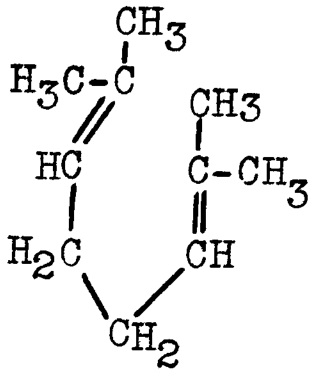
Hexadiene-1,5.
(diallyl)



2,5-dimethyl-hexadiene-1,5.
(dimethallyl)



2,6-dimethyl-heptadiene-2,6.
(geraniolene)



2,7-dimethyl-octadiene-2,6.

It will be noticed that although these compounds are simple types, they serve well for the study of cyclization experiments.

Diallyl was chosen to test various theories of cyclization put forward. It would also serve as a basis of comparison for determination of the influence of methyl groups.

Dimethallyl was chosen because it is a typical terpenoid compound like geraniolene, having one less carbon atom between the isopropylene groups. The behaviour of this compound would naturally throw some light upon the nature and mechanism of cyclization.

Geraniolene is the typical terpene compound and considerable work has already been done upon its cyclization. It should be noted that the terminal carbon atom is missing, but this has no influence in so far as cyclization is concerned.

Dimethyl octadiene is actually a terpene compound consisting of two isoprene units with tail-to-tail union instead of the usual type of head-to-tail as found in all the C_{10} terpenes. This type of union is not unusual amongst many naturally occurring substances. All carotenoids have this type of union in the middle of the molecules, we might also mention the presence of this system in the middle of triterpene molecules and also in the five membered ring of all the sterol type of compounds. It was hoped that the behaviour of this compound would throw light upon the possible biogenesis of the five membered rings in the sterols and the six membered ring in the middle of pentacyclic triterpene molecules.

One might bring forward the criticism that the naturally occurring cyclic compound may have been derived from continuous conjugated compounds and hence the behaviour of dienes might not present a fair basis of comparison. That this is not the case in so far as cyclization is concerned is revealed upon reading the following sections of this Thesis, where the behaviour of both dienes and trienes is discussed.

The type of reaction employed throughout the course of investigation was cyclization in acid media of various strengths. Particular attention was paid to the type and concentration used by various workers in their studies of cyclization of terpene compounds.

Although even saturated aliphatic compounds may be cyclized by subjecting them to various catalysts such as Boron Trifluoride, activated Alumina, Floridin, etc., at temperatures of 300-600°C, the conditions involved are so drastic that they probably involve such mechanisms as free radical formation, etc. As mentioned previously, we have employed acid catalysis for the simple reason that this type of treatment of aliphatic terpenes results in the formation of cyclic compounds which are exactly the same ones found in the plant itself.

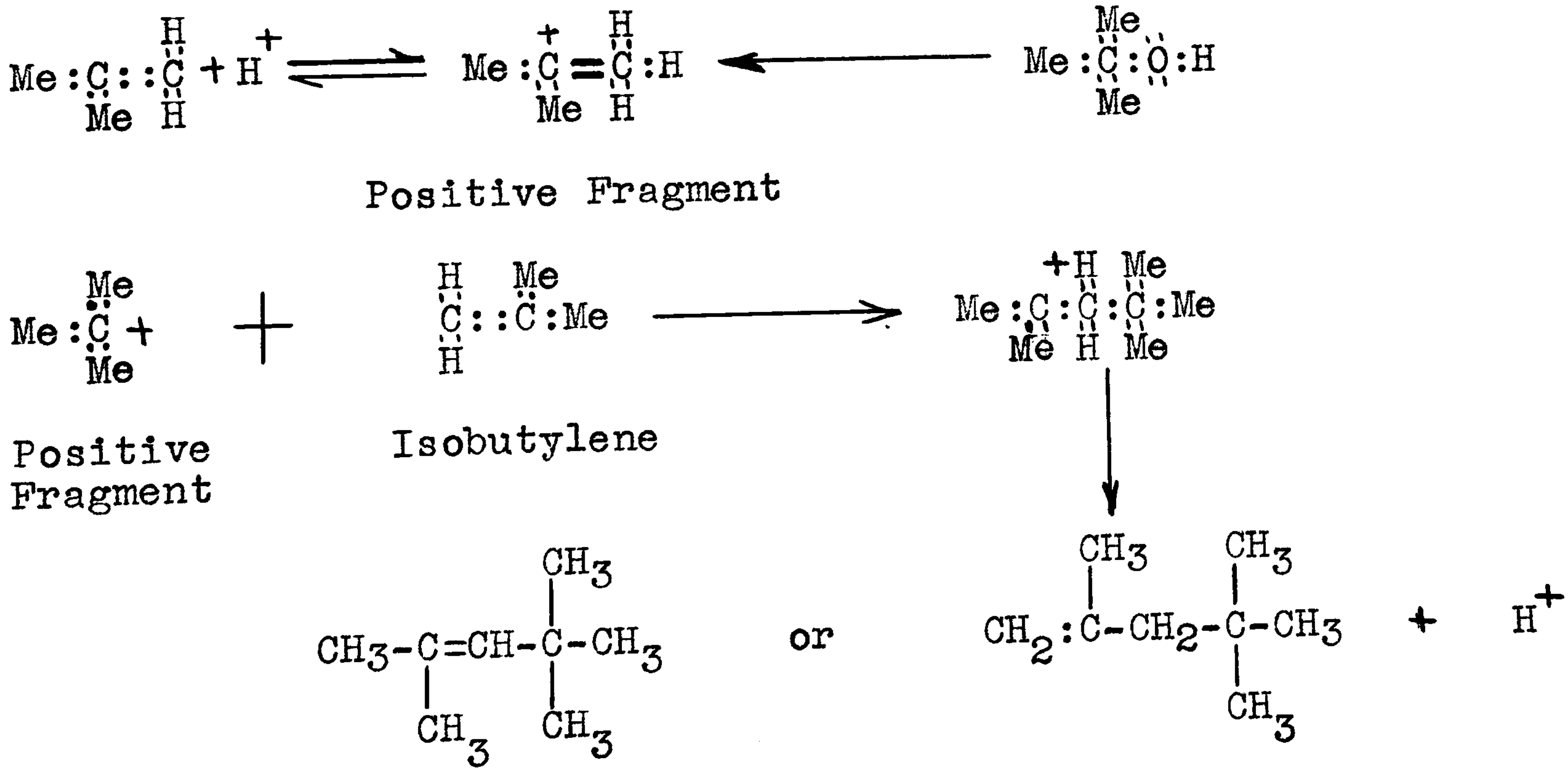
A close examination of such cyclization reveals the fact that it is essentially an intramolecular polymerization brought about by acid catalysis. Thus, cyclization of dimethallyl may be looked upon as being polymerization between two methallyl molecules. Similarly, cyclization of dimethyl-octadiene is essentially intramolecular polymerization of two molecules of iso-amylenes.

Various mechanisms have been suggested for this type of polymerization. A few of these are enumerated below. As early as 1877 Berthelot(62) suggested that in the polymerization of propylene with phosphoric acid, a molecule of the ester is formed which reacts with another molecule of olefin giving a dimer.

Whitmore(63) has put forward a widely publicized theory of acid catalysis polymerization. According to

62.- Berthelot, Die Chemische Synthese, Leipzig, 1877.
63.- Whitmore,F.C., Ind.Eng.Chem., 26, 94, (1924).

Whitmore's idea the first step involves the addition of a hydrogen ion (a proton) to the double bond. By this process one carbon is left with only six electrons, which may be satisfied in three different ways, (a) union with a negative ion having a complete octet of electrons. (b) Reversal of the process by the loss of the same or a different proton to give the same or a new olefin. (c) Rearrangement of the carbon skeleton followed by the loss of a proton to give a new olefin. (d) Polymerization i.e. addition of a positive organic fragment which can undergo further changes, such as (1) addition of an olefinic molecule or (2) loss of a proton to give a larger olefin to which a positive fragment may add. These ideas are embodied in the following illustration, involving the behaviour of isobutylene under acid catalysis:

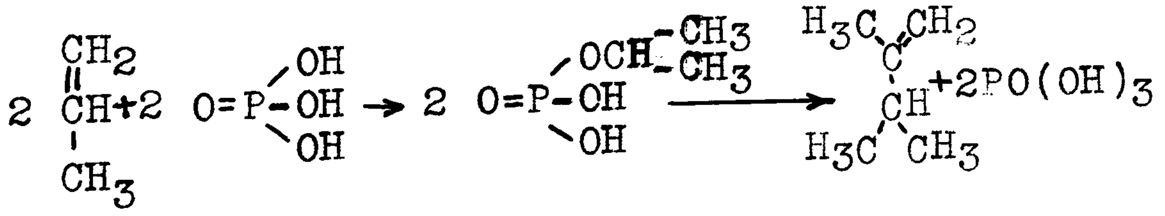


This process may continue to give more complex polymers.

The mechanism of Whitmore has been criticized by several workers. Kline and Drake(64) treated isoamylene with 75 per cent sulphuric acid and obtained 3,4,5,5-tetramethyl-2-hexene and 3,5,5-trimethyl-2-heptene. Whitmore's mechanism does not explain the formation of these products without assuming complicated rearrangement. Instead, they propose the formation of an activated molecule which behaves as a positive and negative fragment and adds to the double bond in the usual manner.

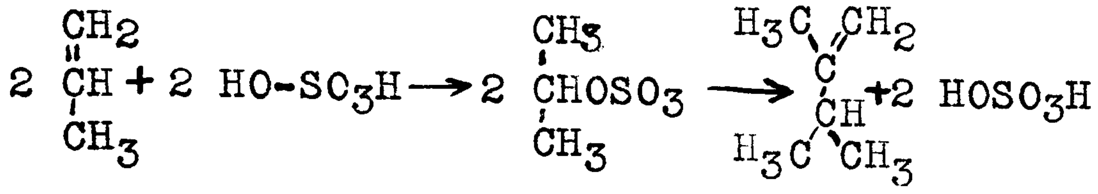
Whitmore's mechanism has also been criticized by others, the criticism being based upon experimental results(65).

Concrete proof of the mechanism of acid polymerization has recently been offered by Ipatieff and co-workers. In one of their studies(66) of polymerization of isopropene with phosphoric acid they succeeded in isolating the isopropene ester of phosphoric acid thereby indicating that polymerization proceeds through acid ester formation.



64.- Kline G.M. and N.L.Drake, Bur.Stan.J.Res. 13, 705, (1934).
65.- O.Schmitz-Dumont, K.Hamann, A.Diebold, Ber. 11B, 205, (1938).
66.- V.N.Ipatieff, B.B.Carson, Ind. Eng.Chem. 1069, (1935).

In another study(67) of polymerization with sulphuric acid they obtained esters of sulphuric acid, and proposed a similar mechanism.



$$2\ \overset{CH_2}{\underset{CH_3}{\overset{\parallel}{CH}}} + 2\ HO\text{-}SO_3H \longrightarrow 2\ \overset{CH_3}{\underset{CH_3}{CHOSO_3}} \longrightarrow \overset{H_3C\ \ CH_2}{C}\underset{H_3C\ \ CH_3}{CH} + 2\ HOSO_3H$$

It was hoped that in the study of the cyclization of the four dienes chosen, further light would be thrown upon the polymerization mechanism.

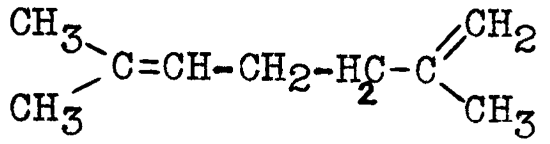
As to how far we have succeeded in our efforts to study cyclization of these dienes and propose a possible biosynthesis of some naturally occurring cyclic products such as the five membered ring in sterols, the middle six membered ring in triterpenes, etc., and also how our results effect the polymerization mechanisms proposed by various workers will be unfolded in the following sections of this Thesis.

67.- V.N.Ipatieff, H.Pines, B.S Friedman, J.Am.Chem.Soc. 1825, (1939).

Cyclization of Aliphatic Terpene Compounds

This section covers the field of terpenes. The field is extremely large and ramified, and yet one can see a definite trend of behaviour in practically all cases of cyclization reactions. In the following pages of this section we shall endeavour to choose typical cases rather than attempt to make a more or less complete bibliographical survey.

GERANIOLENE.-

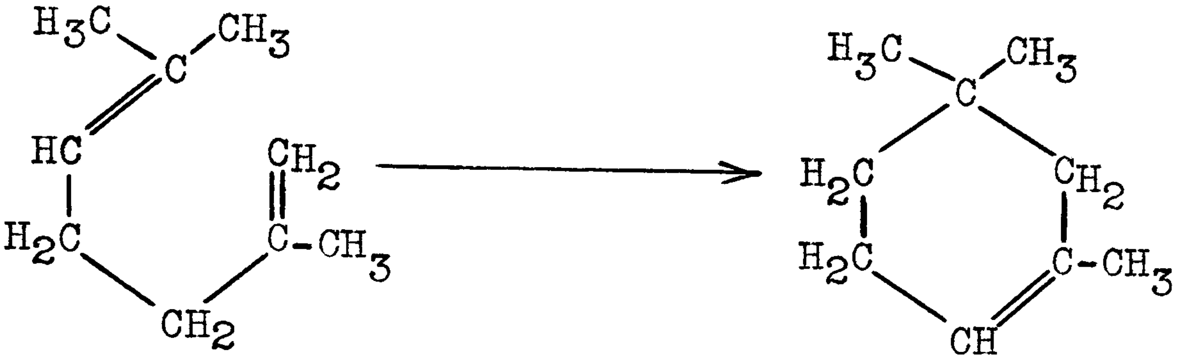


$$(CH_3)_2C=CH-CH_2-H_2C-C(=CH_2)-CH_3$$

This compound was first prepared by Tiemann and Semmler(68) by distillation of geranic acid at atmospheric pressure with the loss of carbon dioxide. (b.p. 142-3°C., d^{20} 0.757 n_D 1.4368). Grignard (69) prepared it by the action of methyl magnesium iodide on methyl heptenone, with subsequent dehydration of the tertiary alcohol. The hydrocarbon prepared by Harries and Weil(70) by the elimination of hydrogen bromide from 2,6-dimethyl2,6-dibromoheptane, had the constants(b.p. 140-142°C., d^{22} 0.7626, n_D^{22} 1.4436). Auwers and co-workers(71) prepared geraniolene by different methods and made a study of the constants of the hydrocarbon. They reached the conclusion that in no case was the substance homogeneous, as the double bond could be in alpha or beta position at both ends of the molecule, thus giving rise to four possible isomers.

68.- Tiemann and Semmler, Ber. 26, 2724, (1893).
69.- V.Grignard, These de Doctorat, 81, (1901).
70.- Harries and Weil, Ber., 37, 846, (1904).
71.- Auwers and Eisenlohr, J.Pr.Chem. 1910, II. 82, 76.
Auwers and Moosbruger, Ann. 387, 183, (1912).

Tiemann(68) observed that when geraniolene was warmed with 60 per cent sulphuric acid it isomerized to a cyclic hydrocarbon. This hydrocarbon was shown to be a mixture but mainly alpha-cyclogeraniolene(72). This conclusion was supported by Wallach and Franke(73) who prepared the nitrosate and nitrosochloride of alpha-geraniolene.

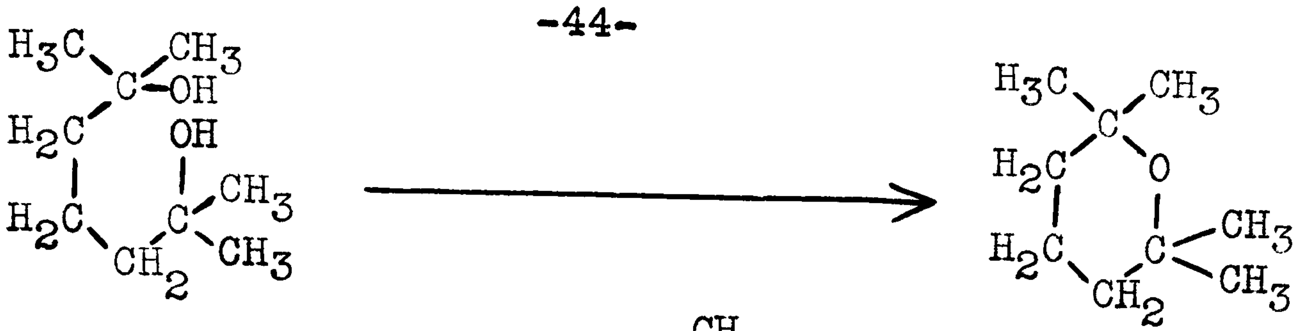


Harries and Weil(70) obtained cyclogeraniolenes by the dehydration of 2,6-dimethyl-2-heptene-ol-6.

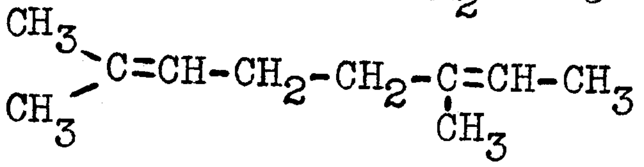
Cyclogeraniolenes have the constants b.p. 138-9°C., d^{20} 0.8072, n_D 1.4473.

Rupe and Schlochoff(74) shook 2,6-dimethyl-2-heptenol-6 with 20 per cent sulphuric acid and obtained 2,6-dimethyl heptan-2,6-diol. On warming with dilute sulphuric acid it gave the cyclic oxide, b.p. 744, 142-142.5°C. Bruylants(75) treated diethyl glutarate with methyl magnesium bromide and obtained the same diol m.p. 76-77°C. It crystallized from water with 1 molecule of water of hydration (m.p. 60-71°C). On warming with dilute sulphuric acid it gave the cyclic oxide 2,2,5,5-tetramethyl pyrane.

72.- Tiemann, Ber., 33, 3711, (1900).
73.- Wallach and Franke, Ann., 324, 114, (1902).
74.- Rupe and Schlochoff, Ber., 38, 1500.
75.- Bruylants, Rec.Trav.Chim., Zents. II, 797, (1909).



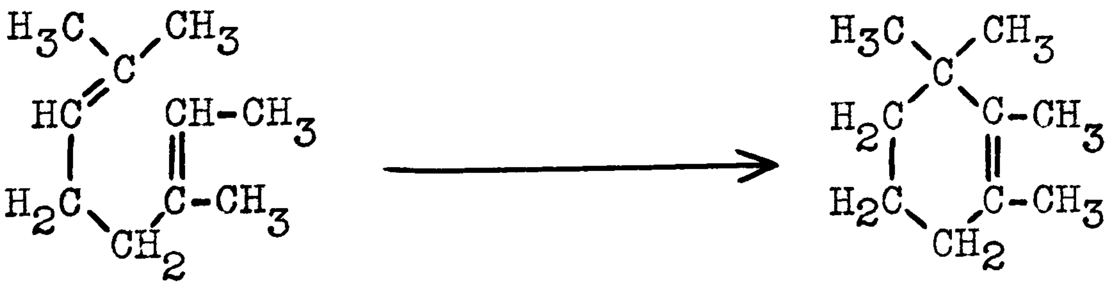
DIHYDROMYRCENE.-



$$\begin{matrix}CH_3 \\ CH_3\end{matrix}\!>C=CH-CH_2-CH_2-\underset{CH_3}{C}=CH-CH_3$$

This compound is 2,6-dimethyl-2,6-octadiene, thus being a higher homolog of geraniolene. It has been prepared by a great many workers. Semmler(76) prepared it by the reduction of myrcene with sodium and alcohol. It has also been prepared by the reduction of ocimene in a similar manner(77) and also by treatment of geraniol or linalool with sodamide in alcoholic solution(78). Dihydromyrcene from the reduction of myrcene has the following constants, b.p. 166-168°C., b.p.$_{17}$ 62-63°C., d^{15} 0.7802, n^{20}_D 1.4507 (78).

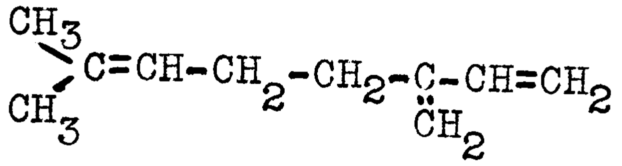
Semmler(79) obtained cyclodihydromyrcene by treatment of dihydromyrcene with a solution of sulphuric acid in acetic acid. (b.p. 169-72°C., d 0.828, n_D 1.462). Tiffeneau(80) heated synthetically prepared ethyl methylgeranate with sulphuric acid and obtained the cyclic acid which, upon distillation lost carbon dioxide and yielded cyclodihydromyrcene. (b.p. 168-70°C., d^{14} 0.8325, n^{14}_D 1.460.)



76.- Semmler, Ber., 34, 3126, (1901).
77.- Enklaar, Rec.Trav.Chim. 26, 157, (1907).
78.- Chablay, Ann.Chim., ix, 8, 193, (1917).
79.- Semmler, Ber., 27, 2520,1901,(1894), 34, 3126, (1901).
80.- Tiffeneau, Compt.rend., 146, 1153, (1908).

Semmler(81) cyclized linaloolene and obtained cyclolinaloolene. This should be identical with cyclodihydromyrcene but had somewhat different physical constants, viz. b.p. 165-7°C. d^{17} 0.8112, n_D 1.4602.

<u>MYRCENE</u>.-

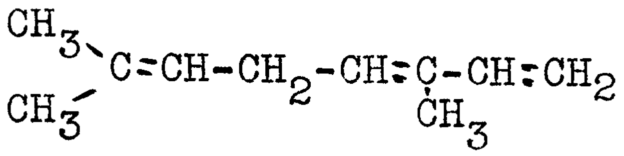


$$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C{=}CH{-}CH_2{-}CH_2{-}\underset{CH_2}{\overset{\|}{C}}{-}CH{=}CH_2$$

Myrcene is a naturally occurring hydrocarbon. (2-methyl-6-methylene-2,7-octadiene) b.p. 166-168°C., d^{15} 0.8013, n_D^{19} 1.4700 (77). Although it has not been synthesized, it has been prepared by passing linalool over activated copper at 130-140°C.(82). The presence of conjugated linkage has been proven both by reduction of myrcene with sodium and by Diels-Alder(83) synthesis with maleic anhydride.

It was shown by Harries(84) that when myrcene was heated in a sealed tube at 300°C., it gave a high boiling oil b.p.$_{12-16}$ 160-200°C., which was named dimyrcene; also a viscid gum polymyrcene. He prepared a nitrosite of dimyrcene. Dimyrcene was further investigated by Semmler and Jonas(85) who showed it to be a complex mixture which contained alpha-camphorene, which has been found to occur in blue camphor oil. It may be characterized as the trihydrochloride.

81.- Semmler, Ber., 27, 2521, (1894).
82.- Enklaar, Chem.Weekblad., 9, 68, (1912).
83.- Diels, Alder, Ann. 470, 65, (1929).
84.- Harries, Ber., 35, 3259, (1902).
85.- Semmler and Jonas, Ber. 46, 1567, (1913), see also Ruzicka and Stoll, Helv.Chim.Acta., 7, 272,(1924).



$$\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>C{=}CH{-}CH_2{-}CH{=}\underset{CH_3}{C}{-}CH{=}CH_2$$

OCIMENE.- Ocimene is an isomer of myrcene, occurring in several oils. It was first reported by van Romburgh(86) but our knowledge of its chemistry is due mainly to Enklaar(87). He reported ocimene (2,6-dimethyl-2,5,7-octatriene) as having the following constants, b.p.$_{30}$ 81°C., d^{15} 0.8031, n^{18}_{D} 1.4857. Ocimene rapidly oxidizes in air into a resin.

Ocimene may be reduced with sodium in alcohol yielding dihydroocimene, which has been shown to be identical with dihydromyrcene.

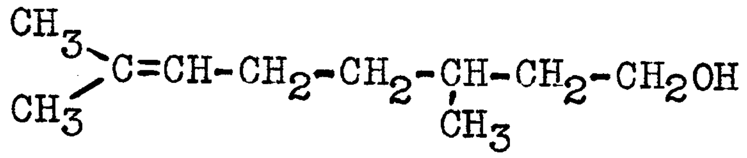
Enklaar(88) reports that during the oxidation of alloöcimene (an stereoisomer of ocimene?) he obtained a product, probably an allo-ocimene oxide, (b.p.$_{13}$ 105°C., d^{20} 0.909) which had no aldehydic or ketonic function.

In another study Enklaar(89) heated ocimene with sulphuric acid and obtained an oil (b.p.$_{19}$ 200°C.) in 90 per cent yields.

86.- van Romburgh, Proc.K.Acad.Wet.Amst., 3, 454, (1900).
87.- Rec.trav.chim., 26, 157, (1907), 27, 422, (1908), 36, 215, (1916), 45, 337, (1926).
88.- Enklaar, Chem.Weekblad, 21, 101-2, (1924).
89.- Enklaar, Rec.trav.chim., 26, 169.

Having considered the hydrocarbons, it now becomes necessary to review the behaviour of alcohols, since these under the influence of acids dehydrate, readily giving reactions similar to hydrocarbons.

CITRONELLOL.-



$$\begin{matrix}CH_3 \\ CH_3\end{matrix}\!\!>C=CH-CH_2-CH_2-\underset{CH_3}{CH}-CH_2-CH_2OH$$

This compound has been extensively investigated. It is needless to go into its history, isolation, purification, identification, etc., as this is not directly related to our problem. Suffice to say that like all other terpenoid compounds, it probably has never been prepared in a state of purity, although the following constants may be taken as being that of a relatively pure sample. b.p.$_{12}$ 114-115°C., d^{22} 0.856-0.862, n^{22}_{D} 1.4561.

Besides being isolated from numerous natural sources, citronellol has been synthesized by the reduction of ethyl geranate with sodium in alcohol(90). It has also been prepared by the reduction of citronellal(91), by partial hydrogenation of geraniol(92) and also reduction of geraniol in alcohol with sodium(93).

Tiemann and Schmidt(91) treated citronellol with

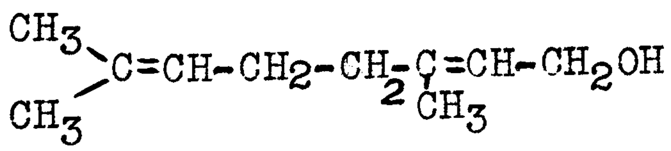
90.- Bouveault and co-workers, Ber., 31, 818, (1898).
91.- Tiemann and Schmidt, Ber., 29, 903, (1896).
92.- Paal,G.P., 298193, and 346949.
93.- Hesse,G.P. 256716.

strong sulphuric acid and got mainly polymers along with a small amount of cyclocitronellol(?), dilute sulphuric gave octan-diol.

When citronellol is shaken with 30 per cent sulphuric acid it yields the corresponding octan-diol. The diol when treated with 5 per cent sulphuric dehydrates giving the original alcohol(94).

Several higher homologs of citronellol have been prepared but these are of little importance. Rupe(95) and co-workers prepared 2,6-dimethyl-octan-diol-2,8 by the action of methyl magnesium iodide on citronellal, and treatment of the alcohol with 10 per cent sulphuric acid to yield the diol. The diol (b.p.$_{19}$ 153-156°C.), on boiling with dilute sulphuric acid gave menthocitronellol(96).

<u>GERANIOL</u>.-



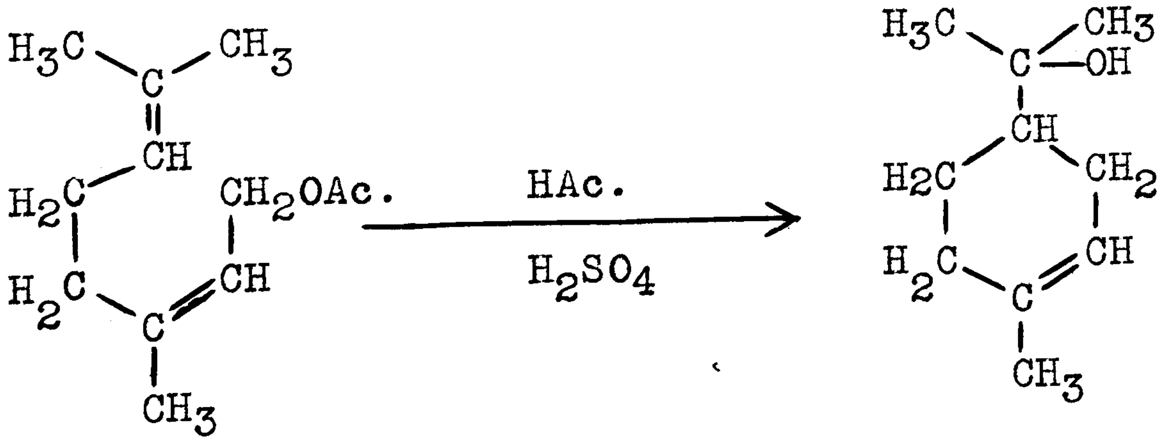
$$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>C{=}CH{-}CH_2{-}CH_2{-}\underset{CH_3}{C}{=}CH{-}CH_2OH$$

Geraniol is another aliphatic terpene alcohol, having one more

94.- Barbier and Locquin, Compt.rend.. 157, 1117.
95.- Rupe, Pfeiffer and Splittgerber, Ber., 40, 2816.
96.- Wallach, Ann. 296, 130.

double bond than citronellol and occurring very widely in various essential oils. It has been subjected to critical studies by many workers. It is beyond the scope of this Thesis to make a review of its occurrence, properties, etc. When purified through its calcium chloride addition compound, geraniol has the following constants, b.p. 229-230°C., b.p.$_{12}$ 114-115°C., d_{15} 0.883, n^{20}_{D} 1.4766.

Geraniol is very much more easily cyclized than citronellol. When it is shaken with 5 per cent sulphuric acid, the main product is terpin hydrate, which is produced from alpha-terpineol the primary product of the reaction(97). Acetic acid or acetic anhydride alone will not convert geraniol to alpha-terpineol, but in the presence of one or two per cent sulphuric acid will convert geranyl acetate to alpha-terpineol(98). The geometrical isomer of geraniol, namely nerol, cyclizes with even greater ease and rapidity, indicating that it is the trans isomer, while geraniol is the cis isomer.



97.- Tiemann and Semmler, Ber., 28, 2137, (1895).
98.- Bertram and Gildmeister, J.pr.Chem., ii, 49, 194, (1894).

When geraniol is treated with phosphoric acid(99), or gaseous hydrogen chloride(100) it is converted to dipentene. Digestion with formic acid yields a mixture of dipentene and terpinene(101) along with geranyl and terpinyl formate. Phosphorous pentoxide also converts geraniol to dipentene(99).

When heated with activated carbon at 220°C., geraniol is converted to myrcene and dipentene(102). Even Japanese acid clay cyclizes geraniol to terpineol(103).

Many higher homologs of geraniol have been prepared but these need not be discussed here.

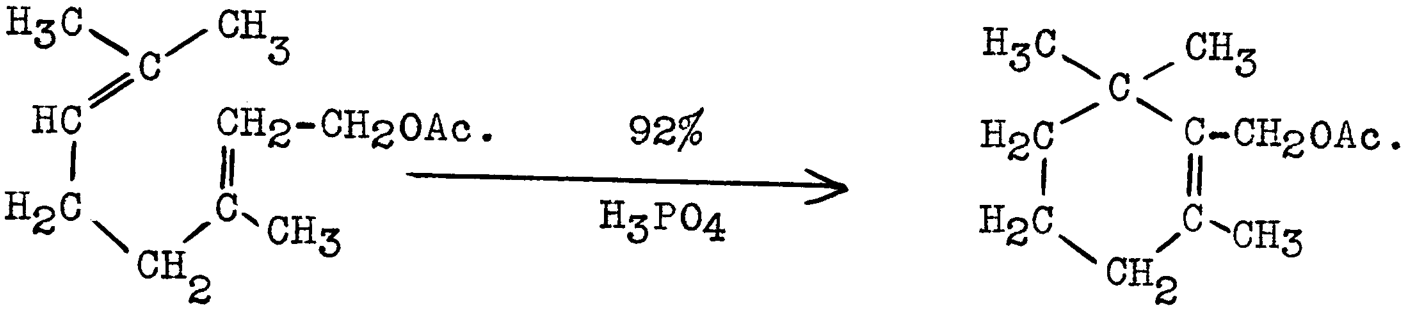
Geraniol will undergo another very characteristic type of cyclization, differing fundamentally from the above types. These cyclic products are known as cyclogeraniols.

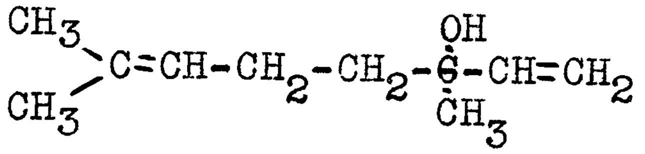
Cyclogeraniols cannot be prepared directly from geraniol since dehydration precedes cyclization resulting in various cyclic hydrocarbons. If however the hydroxy group is protected(104) then it is possible to obtain cyclogeraniols through the action of strong sulphuric and phosphoric acids. The resulting cyclogeraniol is practically always a mixture of the alpha and beta isomers (b.p.$_{12}$ 95-100°C., d^{20} 0.935-0.955, n_D 1.48).

99.- Eckart, Ber., 24, 4205, (1891).
100.- Monnet and Barbier, Compt.rend., 117, 1094, (1893).
101.- Bertram and Gildmeister, J.pr.chme., 49,194,(1894), 53,236,(1896).
102.- S. Kimura, J.Chem.Soc. Japan, 53, 497-503, (1932).
103.- T.Kuwata, J.Soc.Chem.Ind.Japan, 36, 583, (1933).
104.- G.p. 138141.

The proportion of isomers depends upon the acid cyclizing agent used, sulphuric acid yielding mostly the beta isomer while phosphoric yields mainly the alpha isomer.

Recently(105) geranyl acetate has been cyclized with 85 per cent phosphoric acid at -5°C., with formation of some terpin hydrate. With 92 per cent phosphoric acid only pure cyclogeranyl acetate is formed.



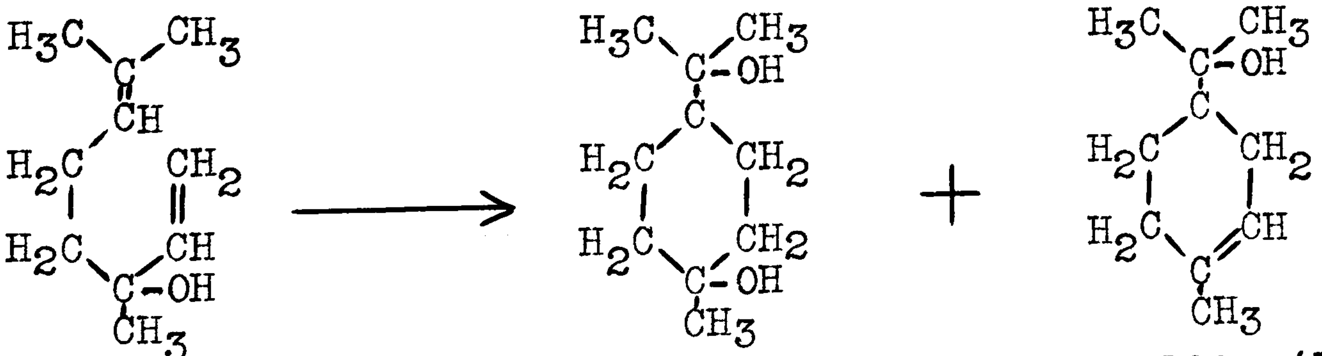
LINALOOL.- 
$(CH_3)_2C{=}CH{-}CH_2{-}CH_2{-}\overset{OH}{\underset{CH_3}{C}}{-}CH{=}CH_2$
Of all the aliphatic terpene alcohols, linalool has received more attention than perhaps all the other straight chain terpene alcohols put together. Like citronellol and geraniol it has been subjected to intense studies by a great number of workers. Unfortunately linalool is a tertiary alcohol and does not yield easily obtainable crystalline derivatives. Consequently its constants as reported by various workers always show some variation. The following may be taken as average values, b.p. 198-199°C., d^{15} 0.870, n_D^{20} 1.4668.

105.- V.Z.Isagulyants and G.A.Serebrennikov, J.Gen.Chem. (U.S.S.R.) 9, 917-23, (1939) CA 34, 370.

Linalool has been synthesized by Ruzicka and Fornasir(106) by the classic method of condensing methyl heptenone with sodium acetylide and reducing the resulting dehydrolinalool with sodium in moist ethereal solution.

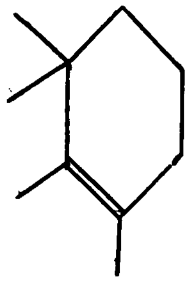
Linalool has the characteristic property of isomerizing to geraniol with great ease. The reverse may also be accomplished under certain conditions.

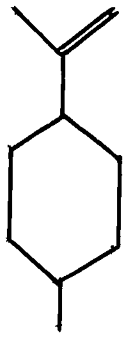
When linalool is shaken with dilute sulphuric acid the products obtained are, geraniol, nerol, d-(or l)-alpha-terpineol, and terpin hydrate(107). Somewhat similar products are obtained when linalool is acted on by cold formic acid(108). At room temperature linalool reacts vigorously with formic acid yielding dipentene and terpinene(109). Unlike geraniol, linalool is acted on by acetic anhydride alone yielding geraniol, nerol, d-(or l)-alpha-terpineol and terpin hydrate(110). The formation of an active terpineol has aroused a great deal of interest and controversy.



106.- Ruzicka and Fornasir, Helv.chim.acta. 2, 182, (1919).
107.- Tiemann and Schmidt, Ber., 28, 2137, (1895).
108.- Stephan, J.pr.chem., 58, 116, (1898).
109.- Bertram and Walbaum, J.pr.chem., 45, 601, (1892).
110.- Various workers.

The action of strong sulphuric acid on linalool gives a hydrocarbon (b.p. 165-7°C., d^{17} 0.8112, n_{12} 1.4602) which according to Semmler(111) is possibly represented by I, and may also contain some of the hydrocarbon represented by II. Chapman(112) has obtained a hydrocarbon of somewhat similar constants (b.p. 170-175°C., d 0.815, n_D 1.459), by the action of sodium on squalene.


I


II

Kimura(113) passed linalool over activated carbon at 200°C., and obtained myrcene, dipentene and alpha-camphorene. Somewhat similar results were obtained by passing linalool over alumina (Al_2O_3) at 310°C.(114).

Vinogradova(115) passed linalool over alumina (Al_2O_3) at 160-205°C. for 40 hours and obtained the following, 30 per cent dipentene, trace of myrcene, 2 per cent camphor, 0.8 per cent borneol, 22 per cent camphorene, 15 per cent resin and 8.5 per cent water.

It has been reported(116) that linalool upon being

111.- Semmler, Ber./ 27, 2521, (1894).
112.- Chapman, J.Chem.Soc., 113, 465, (1918).
113.- S.Kimura, Bull.Chem.Soc.Japan, 10, 330-40, (1935).
114.- N.A.Rosanov and Belikov. J.Russ.Phys.Chem.Soc., 61, 2303, (1929).
115.- I.V.Vinogradova, Ber., 64B, 1991, (1931).
116.- K.Ono and S.Hirayama, J.Chem.Soc.Japan, 58, 238, (1937).

treated with phosphoric acid at 0°C., yields terpinene and sesquiterpene $C_{15}H_{24}$.

Matuura(117) treated linalool with 30 per cent sulphuric acid at 100°C. for one hour and obtained the following. Hydrocarbons 44 per cent, of which 35 per cent was aliphatic and 65 per cent p-menthene. The presence of myrcene, dipentene, alpha-terpinene, terpinolene and p-cymene was confirmed. The product contained 12 per cent alcohols which was chiefly terpineol. There was also 22 per cent of 1,4-cineole with a small amount of 1,8-cineole.

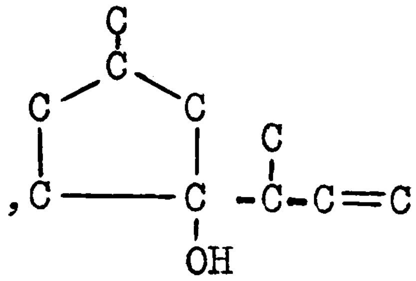
Ikeda and co-workers(118) heated linalool in an atmosphere of nitrogen at 250°C., under a pressure of 250 atmospheres, for several hours. The product was a crystalline solid m.p. 94, b.p. 209°C. It had the composition $C_{10}H_{18}O$, had one double bond and was a tertiary alcohol, called plinol. Dehydration gave plinolene. Oxidation of another liquor from plinol gave isoplinol m.p. 41 b.p. 203°C.

In a later communication(119) it is reported that both plinolene and isoplinolene condense with maleic anhydride but not with α-naphthoquinone.

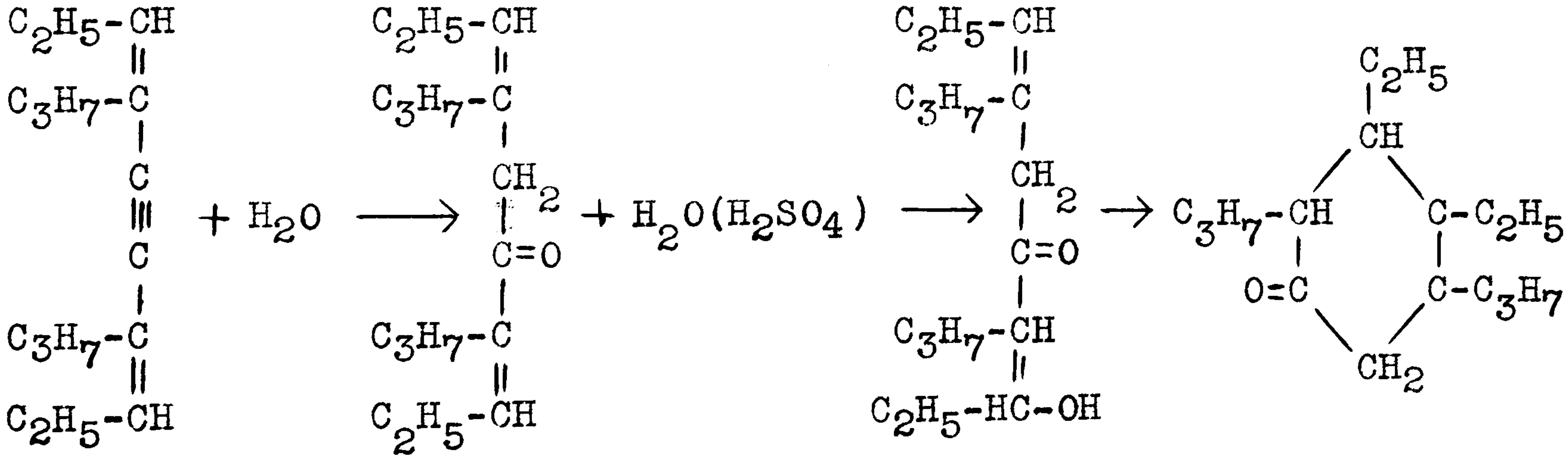
Isoplinol, probably obtained by a transformation of plinol is represented by the following formula. It is

117.- T.Matuura, J.Sci.Hirosima Univ. 8A, 303, (1938).
118.- T.Ikeda, K.Hakatsuki, J.Chem.Soc.Japan, 57, 425, (1936).
119.- T.Ikeda, S.Takada, J.Chem.Soc.Japan, 58, 71, (1937).

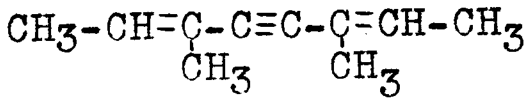
difficult to see how this compound is formed from linalool.

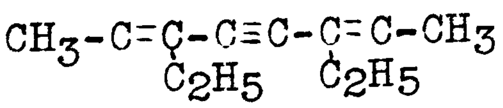


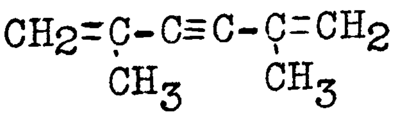
A rather interesting series of experiments have been carried out by Marvel and Blomquist(120), and Marvel and Mitchell(121). They prepared divinylacetylene which upon treatment with sulphuric acid yielded not only the olefinic ketone(122) but also a cyclic product, which was identified as a substituted cyclohexenone. The reactions may be conveniently represented as follows:



Similar results were obtained with $CH_3\text{-}CH\text{=}\underset{CH_3}{C}\text{-}C\equiv C\text{-}\underset{CH_3}{C}\text{=}CH\text{-}CH_3$ and $CH_3\text{-}C\text{=}\underset{C_2H_5}{C}\text{-}C\equiv C\text{-}\underset{C_2H_5}{C}\text{=}C\text{-}CH_3$. It is significant that under similar conditions $CH_2\text{=}\underset{CH_3}{C}\text{-}C\equiv C\text{-}\underset{CH_3}{C}\text{=}CH_2$ would not undergo cyclization.



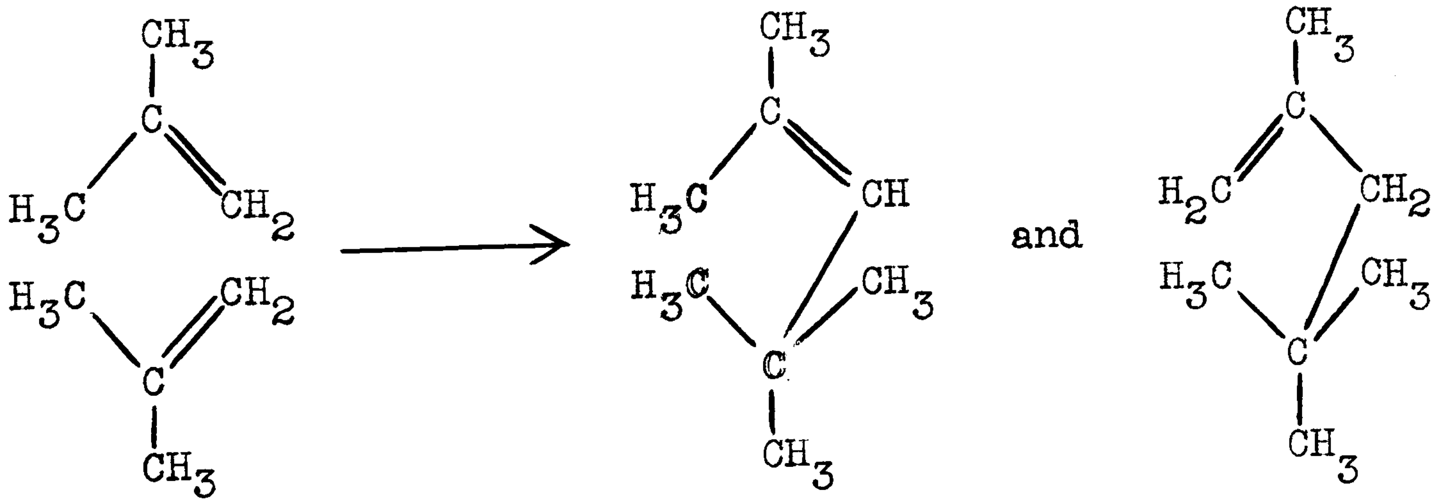




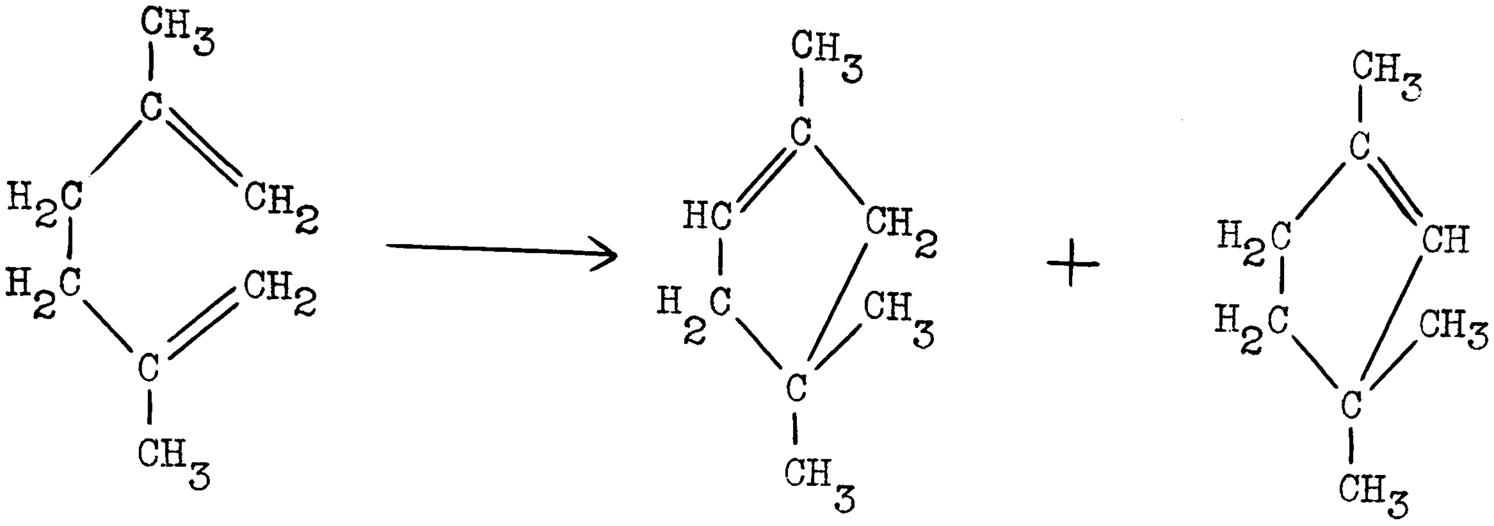
120.- C.S.Marvel and A.T.Blomquist, J.Am.Chem.Soc. 1655.(1933).
121.- C.S.Marvel and D.T.Mitchell, J.Am.Chem.Soc., 4276, (1933).
122.- V.Grignard and Tcheoufaki, Compt.rend., 188, 527, (1929).

Polymerization of Isobutylene

The polymerization of isobutylene is closely related to the problem investigated by the author, since it contains the essential grouping $CH_3-C(CH_3)=CH_2$. It will be noticed that this grouping is present in dimethallyl. geraniolene and 2,7-dimethyl-octadiene-2,6. Hence, isobutylene may be looked upon as being the half molecule of these compounds. The reaction between two molecules of isobutylene would be expected to be similar to that of the reaction between the two ends of the dienes under investigation. Thus, if two molecules of isobutylene yield two pentenes, namely 2,4,4-trimethyl-1-pentene and 2,4,4-trimethyl-2-pentene,



then, dimethallyl might be expected to undergo a similar reaction under acid catalysis giving, two cyclopentenes namely 2,4,4-trimethyl-1-cyclopentene and 2,4,4-trimethyl-2-cyclopentene.



This reasoning might be extended to geraniolene, and 2,7-dimethyl-octadiene-2,6.

Polymerization of isobutylene and related compounds has engaged the attention of early workers. It has received a tremendous impetus in recent years owing to the fact that there are unlimited quantities of such compounds evolved during the production of cracked gasoline. Various processes have been devised and numerous patents issued for the conversion of isobutylene to gasoline of high octane rating.

Butlerow(123) was one of the earliest workers in this field. He found that on passing isobutylene into 50 per cent sulphuric acid he obtained mainly tertiary butyl alcohol. Warming the acid solution to 100°C. gave diisobutylene.

123.- Butlerow, Ann. 180, 246, (1875), 189, 48, (1877).

A much more concentrated solution of five parts of sulphuric and one part of water yielded triisobutylene(124).

In one of his earlier high pressure technique(125) experiments, Ipatieff(125) heated isobutylene under high pressure and obtained different polymers.

More recently isobutylene has been subjected to the action of $AlCl_3$ at 100-150°C.(126). It was found that liquid paraffins and higher naphtenic hydrocarbons were obtained. The unsaturated compounds formed only a small portion of the oil obtained. There were organic aluminium compounds formed of the general formula $(AlCl_3C_4H_x)_x$ which decomposed on the addition of water with liberation of heat. The author is of the opinion that the bulk of the polymerization product is of cyclic unsaturated nature.

It has been found(127) that high voltage silent discharge will polymerize isobutylene with the production of a wide range of compounds, indicating the complete breakdown of the molecule and formation of various rearrangement products.

Active floridin has been found to yield polymeric products some of which were of higher polymers than the tetramer(128).

124.- Butlerow, J.Russ.Phys.Chem.Soc. 11, 198, Zentr. 12, 1482.
125.- V.N.Ipatieff, J.Russ.Phys.Chem.Soc. Ber., 44, 2984.
126.- A Szayna, Przemyls Chem., 12, 637-47, (1928).
127.- D.N.Pryanishnikow, Ber., 61B, 1358-63, (1928).
128.- R.vanWinkle, J.Am.Pharm.Assoc. 17, 544, (1928).

When isobutylene was passed over alumina (Al_2O_3) at a mean temperature of 40°C., various straight chain polymeric products were obtained(129). (two dimeric fractions, b.p.$_{765}$ 101-102°C., d^{20}_{4} 0.7167, and 0.7179, n^{20}_{D} 1.4100, 1.4103, trimer fraction, b.p.$_{20}$ 71-2°C., d^{20}_{4} 0.7584, n^{20}_{D} 1.4306, tetramer fraction, b.p.$_{4}$ 101-102°C., d^{20}_{4} 0.7935, n^{20}_{D} 1.4492).

It was reported by Nametkin(130) that on treating isobutylene with concentrated sulphuric acid at room temperature, there resulted polymeric products which were saturated and also some which were unsaturated. The process was called hydropolymerization.

McAllister(131) upon treatment of isobutylene and normal butylene with sulphuric acid obtained 75 per cent diisobutylene and 25 per cent trimers. There was also formed some 2,2,4-trimethyl pentane.

Several studies of extreme importance, were carried out by Ipatieff and co-workers on the mechanism of acid catalysis.

In one of the studies, polymerization was carried out with phosphoric acid and intermediate products in the form of esters of phosphoric acid isolated(132). It was found that the product consisted entirely of olefins, being soluble in 96 per cent sulphuric acid in the cold.

129.- H.I.Waterman, J.J.Lindertse, A.J.deKok. Rec.trav.chim. 53, 1151, (1938).

130.- S.S.Nametkin, L.N.Abakumovskaya, J Gen.Chem.(USSR). 6, 1166, (1936).

131.- S.H.McAllister, Oil Gas J., 26, 139, 142,

132.- V.N.Ipatieff, B.B.Corson, Ind.Eng.Chem. 1069, (1935).

In another study(133) of polymerization with proper concentration of sulphuric acid olefins were obtained through the intermediate formation of sulphonates. If however, concentrated 96 per cent sulphuric acid was used, various side reactions took place involving cyclization, hydrogenation, etc.

It has been found(134) that propene by itself will yield practically 100 per cent sulphonates with sulphuric acid. However, in conjunction with isobutylene cross polymerization proceeds with the production of isoheptenes and isooctenes. There was also some 2,3-dimethyl pentene formed probably from 2,3-dimethyl pentenes and/or 2,3-trimethyl butene.

The constitution of diisobutylene has been subject to considerable study.

Prileshajew(135) employing Butlerow's method for its preparation, considered it to be equal parts of 2,2,4-trimethyl pentene-3 and 2,2,4-trimethyl-pentene-4.

Kline and Drake(136) treated methyl isopropyl carbinol with 75 per cent sulphuric acid and obtained two dimers, 3,4,5,-tetramethyl-2-hexene (b.p.$_{210}$ 110-80°C., n_D^{25} 1.4340) and 3,5,5-trimethyl-2-heptene (b.p.$_{210}$ 116-8°C., n_D^{25} 1.4375). The structure of these compounds was established through ozonolysis.

133.- V.N.Ipatieff and H.Pines, J.Org.Chem., 1, 464, (1936).
134.- V.N.Ipatieff,H.Pines,B.S.Friedman,J.Am.Chem.Soc.1825,(1939).
135.- Prilesjew, Zentr. II, 2032, (1907), 39, 769.
136.- G.M.Kline and N.L.Drake, Bur.Stand.J.Res. 13,705,(1934).

Whitmore and Wrenn(137) polymerized 2500 gms. of commercial tertiary butyl alcohol with 3300 cc. of water and 2700 cc. of sulphuric acid. They obtained 1500 cc of diisobutylene (b.p.$_{738}$ 100-5°C.) 500 cc. of triisobutylene and higher polymers. By means of an efficient laboratory column with an adiabatic total condensation variable take-off they were able to separate two isomers of diisobutylene, 2,4,4-trimethyl-1-pentene and 2,4,4-trimethyl-2-pentene.

When isobutylene was polymerized by Butlerow's method (five parts sulphuric and one part water) it gave only 1 per cent of dimer, 90 per cent trimer, 9 per cent of higher products. When the polymerization was carried out over activated floridin the following results were obtained, 17 per cent dimer (b.p. 101-2°C.), 50 per cent trimer (b.p. 174-5°C.), 17 per cent tetramer (b.p.$_7$ 105-7°C.), 5 per cent pentamer (b.p.$_7$ 147-9°C.), 1 per cent hexamer and 0.5 per cent heptamer(138).

Isobutyl alcohol heated with ferric chloride at 200°C. yields diisobutenyl(139), (b.p.$_{756}$ 102-5°C., d^{15} 0.715). Diisobutylene obtained by Kondakow(140) had the following constants b.p. 101-101.7°C., d^{21}_{21} 0.7158. When isobutylene alcohol is heated with phosphorous trichloride in pyridine it yields diisobutylene and triisobutylene(141).

137.- F.C.Whitmore and S.N.Wrenn, J.Am.Chem.Soc., 53,3136,(1931).
138.- S.V.Lebedev, G.G.Koblyanski, Ber. 63B, 103, (1930).
139.- Oddo, G. 31, I, 326.
140.- Kondakow, J.Russ.Phys.Chem.Soc., 28,789,J.pr.Chem.2,54,447.
141.- Milobedzki, Sachnowski, Zentr. I, 911, (1918).

The formation of phosphites $(C_4H_9O)_3P$ was postulated.

A number of similar other experiments have been reported both with isobutylene and isoamylene. They need not be discussed here since the above examples suffice to illustrate the polymerization reactions of isobutylene.

Reactions of Diallyl and Related Compounds

Diallyl has been extensively studied by various workers. It is beyond the scope of this work to make a complete report of these investigations. However, a survey dealing with the behaviour of diallyl and related compounds towards reagents which cause isomerization or formation of cyclic compounds has been made, and will be briefly discussed in this section.

Favorski(142) found that when diallyl is heated at 170°C. with alcoholic potassium hydroxide, it yields isomeric products indicating wandering of the double bond.

Similar behaviour of diallyl under conditions which usually cause cyclization of terpene type compounds has been reported by a number of Russian workers. Thus, Lebedev(143) heated diallyl to 250°C., and obtained a polymer having $b.p._{20}$ 97-98°C., and also a rubber like residue.

142.- Favorski, J.Pr. 44, 216.
143.- Lebedev, J.Russ.Phys.Chem.Soc. 45, 1372, Zents. 1914, I. 1411.

In another report, Lebedev(144) passed diallyl over floridin at 225°C., and obtained dipropenyl. This type of isomerization has also been obtained by passing diallyl over palladium at 200°C.(145). A similar result has been obtained by Levina(146) by passing diallyl over alumina at 300-360°C. It is significant that in all these reactions no claim of the formation of cyclic products has ever been made.

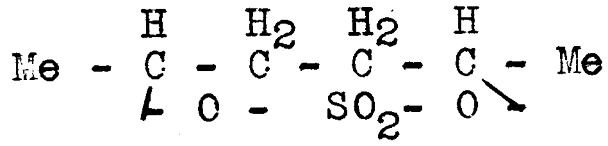
Considerable work has been done on the behaviour of diallyl towards acid catalysts. Jekyll(147) treated an equal volume of diallyl and benzin (b.p. 55-60°C.), with concentrated sulphuric acid and obtained 1,4-dimethyl tetrahydrofurane (b.p. 93°C.) and polymers of diallyl.

Behal(148) obtained a compound of the formula $C_6H_{12}O_4S$ on mixing diallyl with concentrated sulphuric acid at 0°C. This compound was very soluble in alkali solutions and easily yielded the oxide of diallyl.

Cortese(149) has carried out rather extensive studies on diallyl. He prepared diallyl by Lespiau's(150) method and determined the constants of the pure product with great care. He reports the following results: b.p._{760} 59.57 ± 0.05, m.p. -140.9 ± 0.1 d_4^{25} 0.6863, n_D^{25} 1.4012 ± 0.0002.

144.- S.V.Lebedev and Y.M.Slobodin, J.Gen.Chem.(USSR) 4,23-30, (1934), C.A. 28, 5399.
145.-R.Y.Levina, J.Gen.Chem.(USSR) 6,1092-5 (1936) C.A.31,1002.
146.-R.Y.Levina, J.Gen.Chem.(USSR) 7,1587-93,(1936) C.A.31,8516.
147.-Jekyll, Z. 1871, 36.
148.-Behal, Ann.Chim. 7, 17, 265.
149.-F.Cortese, J.Am.Chem.Soc., 51, 2266-9, (1929).
150.-Lespieau, Ann.Chim. 8, 27, 149.

In another study(151) he treated diallyl with five times its volume of concentrated hydrochloric acid for 120 hours. He obtained 80 per cent chlorination products, 57 per cent being the dichlor and 23 per cent monochlor compound. The remainder consisted of diallyl oxide with traces of condensation products.

Cortese(152) studied the action of sulphuric acid on diallyl. He reports that there are two esters of sulphuric acid formed, both crystalline, one being the cyclic mono-ester  $$\begin{array}{l} \mathrm{Me - \overset{H}{C} - \overset{H_2}{C} - \overset{H_2}{C} - \overset{H}{C} - Me} \\ \quad\ \ \llcorner\ \mathrm{O - SO_2 - O} \searrow \end{array}$$ and the other the di-ester of hexandiol. $(CH_2CHMeOSO_3H)_2$.

The glycol itself was found to be easily attacked by acids yielding the oxide. Diallyl was found to be particularly resistant to dilute acids, the minimum concentration of sulphuric acid required for the ester formation being 65 per cent.

It must be realized that both hexene-1-ol-5 and hexandiol-2,5 are compounds which behave like diallyl in acid media. Dehydration of these compounds yields diallyl, while hydration of diallyl may give either the alcohol or the glycol.

Prevost(153) has carried out catalytic dehydra-

151.- F.Cortese, J.Am.Chem.Soc., 52, 1519-21, (1930).
152.- F.Cortese, Ber., 62B, 504-9, (1929).
153.- C.Prevost, Compt.rend. 208, 1589, (1939).

tion of hexenols over alumina at 360°C. In the case of hexen-1-ol-2 he obtained 70 per cent dehydration products of which 2 per cent was hexadiene-1,4, 15 per cent hexadiene-1,3, and 83 per cent hexadiene-2,4. Hexene-2-ol-3 gave 95 per cent dehydration products of which 2 per cent was 1,4-hexadiene, 12 per cent hexadiene-1,3 and 86 per cent hexadiene-2,4. The percentages were determined by careful fractionation. Dehydration over sodium bisulphate at 170°C., yielded somewhat similar results.

It has been reported by Duden and Lemme(154) that treatment of hexandiol-2,5 with dilute sulphuric acid yields 1,4-dimethyl tetrahydrofurane.

Having considered hexadiene and related products, it becomes necessary to say a few words about the compounds having an extra double bond, namely hexatriene-1,3,5, hexadienols and hexendiols.

Perkin(155) reports that treatment of the hexatriene with concentrated sulphuric acid results in the formation of a solid polymeric mass.

Enklaar(156) treated 3-methyl-heptadiene-2,6-ol-4 with acetic acid containing 2 per cent sulphuric acid and obtained a brownish oil of unknown composition. Heating with sodium produced a rubber like mass.

154.- Duden and Lemme, Ber., 35, 1335.
155.- Perkin, J.Chem.Soc., 91, 814
156.- C.S.Enklaar, R. 36, 226. (1916)

It has recently been reported(157) that dehydration of 1,5-hexadiene-3-ol with phthalic anhydride gives hexatriene and possibly some cyclohexadiene.

Tiffeneau and Weill(158) heated divinyl glycol at 100-200°C., with 50 per cent sulphuric acid and obtained principally MeCH=C(Et)-CHO and also some Et_2CH-CH_2OH. Thus migration of the vinyl radical and displacement of the double bond had taken place.

Zalkind and Nogaideli(159) brominated a mixture of stereoisomeric butendiols in a solution of chloroform and obtained a mixture of 3,4-dibromo-hexan-2,5-diol, and 2,5-dimethyl-3,4-dibromo-tetrahydrofurane. When vacuum distilled the latter cleaved, yielding 2,5-dimethyl-3-bromo-dihydrofurane.

A number of other interesting trienes have been prepared, but since these were not studied from the point of view of acid catalysis, they will not be discussed in this Thesis.

It is noteworthy that in no case has diallyl yielded a carbocyclic compound upon treatment with acids.

157.- L.W.Butz, E.W.Butz, A.M.Geddes, J.Org.Chem. 5, 17(1940).
158.- M.Tiffeneau and P.Weill, Compt.rend. 204, 590-2, (1937).
159.- Y.S.Zalkind and A.I.Nogaideli, J.Gen.Chem.(USSR), 8 1816-22, (1938).

Reactions of Diisobutenyl and Related Compounds

Diisobutenyl was first prepared by Przibytek(160) who obtained it by heating isobutenyl chloride with sodium at 100°C. for a period of two to three months. He reported that diisobutenyl (b.p. 113-4°C) on heating with alcoholic potassium hydroxide at 180°C. isomerizes to diisocrotyl.

Krestinski(161) prepared a number of 2,5-dimethylhexadienes. In one case he obtained 2,5-dimethyl-2-hexene-ol-4 by the interaction of the grignard of methallyl bromide with isobutyl aldehyde. When the carbinol was dehydrated by passing it over Alumina (Al_2O_3) at incipient redness, the resulting product was chiefly the isomeric hexadiene diisocrotyl, (b.p. 132-8°C., dibromide m.p. 65°C.).

When studying the chemistry of diisobutenyl it becomes necessary to also consider the properties of diisocrotyl, since the latter is an isomeric form of the former. Furthermore, under certain conditions diisobutenyl isomerizes to the more stable diisocrotyl form and it becomes necessary to distinguish between the two when considering the reaction products of these compounds.

Faworski(162) heated diisobutenyl with alcoholic potassium hydroxide at 180°C. and obtained diisocrotyl (m.p. 7°C., b.p.768.8 134-5°C.).

160.- Przibytek, Ber., 20, 3240, (1887).
161.- W.Krestinski, Ber., 55B., 2754-74, (1922).
162.- Faworski, J.pr. 2, 44, 228, (1891).

Lebedev and Slobodin(163) obtained diisocrotyl in 70 per cent yield by passing diisobutenyl over floridin at 205-210°C. The isomerization was accompanied by polymerization of the conjugated diene.

Levina(164) reports that when diisobutylene is passed over Alumina (Al_2O_3) at 220-225°C., it is isomerized to diisocrotyl.

When the cyclic oxide of diisocrotyl is ruptured the product is the more stable diisocrotyl, rather than diisobutenyl. Pogorzelski(165) heated 1-1,4,4-tetramethyl-tetrahydrofurane with five times its volume of one per cent aqueous hydrochloric acid at 180-190°C., and obtained diisocrotyl (m.p. 6°C. b.p. 132-4°C.).

Lebedev(166) heated diisocrotyl to 290°C., and obtained a polymeric compound $C_{16}H_{28}$. (b.p.$_{24}$ 130-132°C., d^{20}_{4} 0.8491 n^{20}_{D} 1.47751). This compound was thought to be 1,1,2,2,4,4-hexamethyl-3-(beta,beta-dimethyl-vinyl)-cyclohexene-5. However, Lebedev gives no direct proof of the structure of this compound.

Lebedev(166) heated diisocrotyl for ninety days at 150°C. and obtained practically no polymerization.

We mentioned above that one must consider the

163.- S.V.Lebedev and Y.M.Slobodin, J.Gen.Chem.(USSR) 4, 23-30, (1934). C.A. 28, 5399, (1934).

164.- R.Y.Levina, J.Gen.Chem.(USSR) 7, 1587-93,(1937).C.A.

165.- S.Pogorzelski,J.Russ.Phys.Chem.Soc.30,977,(1899), Zentr. I, 773, (1899).

166.- S.Lebedev, J.Russ.Phys.Chem.Soc.45,1322,Zentr.I,1407,(1914).

chemistry of diisocrotyl when studying the properties of diisobutenyl. This holds equally true for the tertiary alcohol and tertiary glycol of diisobutenyl.

Henry(167) obtained the glycol by the action of methyl magnesium bromide on levulinic ethyl ester. He found that dry distillation yielded the hexenol (b.p. 165°C.). Fuming hydrochloric acid replaced the hydroxyl groups of the glycol with chlorine. Dilute hydrochloric, and sulphuric, or heating with glacial acetic acid yielded 1,1,4,4-tetrahydro-tetramethylfurane.

A new method of preparing these glycols was first reported by Zalkind(168). He first prepared 2,5-dimethyl-3-hexine-2,5-diol and then hydrogenated with platinum black to the saturated glycol. A similar method was reported by Dupont(169). ($b.p._{18}$ 111°C.).

Zalkind and Markaryan(170) prepared the higher acetylenic homolog, namely 3,6-dimethyl-4-octine-3,6-diol and then hydrogenated it to the saturated octandiol, d_4^{19} 0.9255, n_D^{96} 1.45523, which upon distillation under reduced pressure, or warming with dilute aqueous sulphuric acid yielded mainly the unsaturated alcohol with a little of the oxide. The octene diol (d_4^0 0.9216, $n_D^{19.6}$ 1.45593) under similar conditions also gave the oxide (dihydrofurane) b 156-8°C., $d_4^{13.5}$ 0.848, $n_D^{13.5}$ 1.43508.

167.-Henry,Compt.rend., 143, 496.
168.-Y.S.Zalkind,J.Russ.Phys.Chem.Soc., 45, 1883.Zentr.I,1813(1914).
169.-Dupont, A.ch. 8, 30, 526.
170.-Zalkind and Markaryan,J.Russ.Phys.Chem.Soc. 48,548,(1916), Zentr. I, 1486, 1923.

Similarly, Zalkind and Bystryakow(171) prepared another higher homolog namely, 3.6-diethyl-4-octene-3,6-diol (m.p. 66-67.5°C.) by hydrogenating the corresponding octine-diol. It again yields the dihydrofurane compound on warming with dilute sulphuric acid.

Pace(172) prepared 2,5-dimethyl-2,5-hexandiol, 2,5-diethyl-2,5-hexandiol and 2,5-dipropyl-2,5-hexandiol by the action of the proper alkyl grignard on acetonyl acetone. He succeeded in forming the furane compound in each case by heating the glycol with acetic acid for two hours at 120-150°C. in presence of sulphuric acid, or better still, in presence of zinc chloride. He discovered that oxide formation also takes place when the glycols are kept over sulphuric acid in vacuo. The oxide from the methyl diol had a b.p. of 119.5°C., from ethyl diol 165°C., and from propyl diol 186°C. The yields were of the order of 70-75 per cent.

Bennett and Wain(173) prepared rather interesting furane type of compounds which contained the benzene ring. They obtained o-xylylene-glycol (m.p. 166°C.) by the action of methyl magnesium iodide on methyl phthalate. This glycol when shaken with 60 per cent sulphuric acid at 50-60°C. for one hour yielded 1,1,4,4-tetramethyl phthalane, (m.p. 71-72). In another experiment methyl phenyl succinate yielded 3-phenyl-2,5-dimethyl-hexan-2,5-diol (m.p. 61-62°C.) when reacted with

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71.-Zalkind and I.Bystryakow,J.Russ.Phys.Chem.Soc. 47,680, (1915), Zentr. I. 921, 1916.

72.-E.Pace, Univ.Pisa Atti.acad. 6, 7, 757, (1928).

73.-G.M.Bennett and R.L.Wain, J.Chem.Soc. 1108-20, (1936).

methyl magnesium iodide. This upon treatment with 70 per cent sulphuric acid for two hours yielded 3-phenyl-2,2,5,5-tetramethyl-tetrahydrofurane.

The question of cyclizing the dienes and related compounds is intimately connected with cyclizing of trienes. It is therefore necessary to review the chemistry of trienes and compounds of similar structure related to 2,5-dimethyl-hexadiene-2,5. The pioneering work in this field has been done by Dupont and especially by Zalkind.

Dupont(174) has prepared 2,5-dimethyl-hexadiene-1,5-in-3, (b.p. 123-4°C., d^{15} 0.7898 n_D 1.4859) (diisopropenyl-acetylene) by two methods. First, by heating 2,5-dibrom-2,5-dimethyl-hexine-3 with potassium hydroxide and second, by dehydrating the corresponding glycol 2,5-dimethyl-hexine-3-diol-2,5, with dilute sulphuric acid. Dupont succeeded in obtaining 2,5-dimethyl-hexen-1-ine-3-ol-5 (b.p. 159-60°C., d^{15} 0.8772, n_D 1.4687), by heating the glycol with dilute sulphuric acid in an atmosphere of carbon dioxide and also by passing the glycol vapour over alumina (Al_2O_3) at 330°C.

Of extreme importance in the study of cyclization is the compound 2,5-dimethyl-hexatriene-1,3,5, or its glycol. Zalkind(175) prepared 2,5-dimethyl-hexene-3-diol-2,5 (m.p. 76.5-77°C.) by hydrogenating the corresponding hexine compound with platinum and palladium catalyst. He also obtained

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174.- Dupont, Compt.rend. 152, 1991.

175.- Zalkind, J.Russ.Phys.Chem.Soc., 48, 1830, Ber. 56, 189, (1923).

a second or beta form the geometrical isomer of the alpha form which had a lower melting point of 69-69.5°C. On heating with potassium bisulphate at 140-160°C. or by warming it with 15 per cent sulphuric acid or with a small amount of iodine, he obtained the corresponding oxide 1,1,4,4-tetramethyl-dihydrofurane. (b.p.$_{755}$ 102-102.5°C., $d_4^{17.5}$ 0.8093, $n_D^{17.5}$ 1.40926).

Zalkind and Markaryan(176) prepared a higher homolog namely, 3,6-dimethyl-octen-4-diol-3,6 ($d_4^{19.6}$ 0.9216, $n_D^{19.6}$ 1.44593) by hydrogenating the corresponding octine compound. Distillation under reduced pressure or warming with dilute sulphuric acid yielded the corresponding oxide 1,1,-dimethyl-4,4-diethyl-dihydrofurane, possessing a camphoraceous odour.

Recently Zalkind and Saboiev(177) studied the action of hydrobromic acid on the beta form of 2,5-dimethyl-hexen-diol-2,5. They found that the product was mostly an unstable liquid dibromide which resinified in a few days. However, by distilling it under reduced pressure they obtained a small amount of 2,2,5,5-tetramethyl-3-bromo-tetrahydrofurane (b.p.$_{14}$ 115-20°C.). The reaction product also contained some of the dihydrofurane, which absorbed two atoms of bromine.

176.- Zalkind and Markaryan, J.Russ.Phys.Chem.Soc., 48, 540, Zentr. I. 1486, (1923).

177.- Y.Zalkind and S.Saboiev, Ber. 62B, 2169-76, (1929).

Bourguet and Rambaud(178) made extensive studies on the dehydration of the isomers of 2,3-dimethyl-hexen-3-diol-2,5. They claim that the alpha isomer (m.p. 74-76°C.) dehydrates with greater difficulty and may be resolved into a second (m.p. 70.7-71°C.) and third or gamma (m.p. 101°C.) isomer. The latter fails to give the oxide upon dehydration but instead yields 2,5-dimethyl-hexatriene-1,3,5 (b.p. 124-6°C., d^{15} 0.778 n_D^{15} 1.483) and 2,5-dimethyl-5-hydroxy-hexadiene-1,3. (b.p. 145-6°C.). They consider the second form as being the cis form and the third the trans form. These authors made a study of the catalytic influence of hydrogen ions on the rates of dehydration and found that dehydration is dependent on the hydrogen ion concentration(179). In another study they made a quantitative study of the internal dehydration of the three glycols and denoted cis and trans configurations to the various isomers(180).

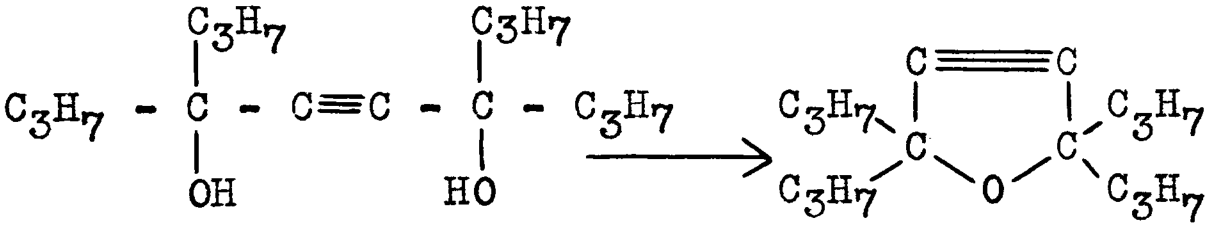
Zalkind and Bukovets(181) repeated the experiments of Bourguet and Rambaud as well as their own original experiments and reinstated the original conclusion of Zalkind as to the presence of only two isomeric forms and in contradiction to the claims of Bourget and Rambaud.

Considerable work has been done on the cyclization of the acetylenic compound 2,5-dimethyl-hexadiene-1,5-ine-3 and its higher homologs. Dupont prepared 3,6-dimethyl-octin-

178.-M.Bourguet and R.Rambaud, Bull.Soc.Chim. 47,173-94,(1930).
179.-Bourguet and Rambaud, Compt.rend., 187, 663-6, (1928).
180.-Bourguet and Rambaud, Compt.rend, 187, 383-4, (1928).
181.-Y.Zalkind and S.V.Bukovets,J.Gen.Chem.(USSR) 7, 2419-22, 1937. (CA. 32, 2086).

4-diol-3,6, and also 2,5-diethyl-hexine-3-diol-2,5. The latter upon treatment with mercuric sulphate or acetate yielded the very unusual compound 3-oxo-1,4-methyl-1,4-ethyl-tetrahydrofurane.

Dupont(182) carried out very similar experiments and obtained identical results. Furthermore he prepared 3,6-dimethyl octadiene-2,6-ine-4 by warming the corresponding glycol with 20 per cent sulphuric acid. On heating 1,1,4,4-tetraisopropyl-butine-2-diol-1,4, with mercuric sulphate he obtained the very unusual oxide 1,1,4,4-tetraisopropyl-dehydrofurane.



A similar result was obtained from 1,4-propenyl-butine-2-diol-1,4. The existence of such compounds is not possible on stereochemical grounds, and in all probability, Dupont was dealing with a different kind of molecule.

Marvel and Blomquist(183) repeated Dupont's(182) experiment, using 1,1,4,4-tetraisopropyl-butine-2-diol-1,4. They succeeded in obtaining the oxo-tetrahydrofurane compound, but in no case could a dehydrofurane compound be prepared. They also reduced the acetylenic glycol to the ethylenic glycol, but all attempts to dehydrate the glycol to the

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182.- Dupont, A.ch. 8, 30, 495, (1913).
183.- C.S.Marvel and A.T.Blomquist J.Am.Chem.Soc., 1655, (1933).

corresponding hextriene failed, the resulting compound being the dihydrofurane.

Johnson and Johnson(184) refluxed cis-2,5-dimethyl-3-hexene-2-diol with 15 per cent sulphuric acid for two hours and obtained the oxide, (b.p.$_{747}$ 100-2°C., n_D^{25} 1.4078). The transisomer under similar conditions gave hexatriene.

It is significant that in all these reports as well as in many numerous others not mentioned in this section, there has been no claim made for the formation of carbocyclic compounds upon treatment of diisobutenyl or related compounds with acids.

Reactions of 2,7-Dimethyl-Octadiene-2,6 and Related Compounds

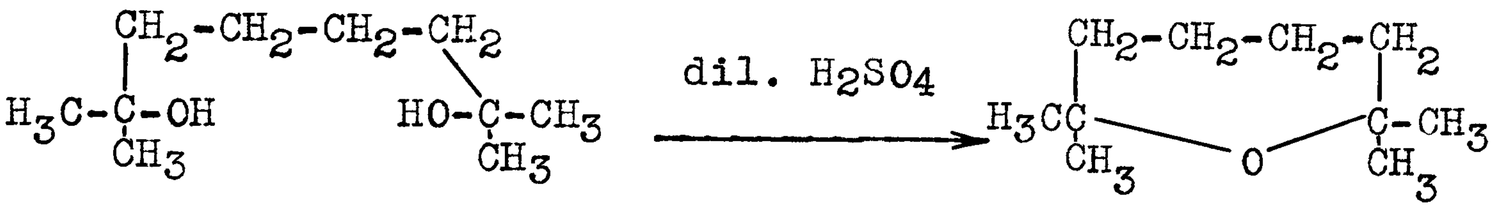
This substance and its tertiary glycol have been reported in the literature several times. It is needless to mention cases where merely preparation of these compounds have been carried out. We will confine ourselves solely to investigations involving the influence of acid catalysts upon these compounds.

Bouvet(185) prepared a whole range of 2,7-octandiols by the action of various alkyl grignards on diethyl adipate. This method was first employed by Zelinski(186) in preparing 2,7-dimethyl-octandiol-2,7. Bouvet converted the diol to the dichloride by the action of hydrochloric acid and then

184.J.R.Johnson and O.H.Johnson, J.Am.Chem.Soc., 2615, (1940).
185.- M.M.Bouvet, Bull.Soc.Chim., 4, 17, 205, (1915).
186.- Zelinsky, J.Russ.Phys.Chem., 38, 931, (1906).

obtained the diene by heating it in pyridine at 100°C., in the presence of alkali. The octadiene thus obtained had the following constants, b.p. 163.5-64.5°C. It absorbed four bromine atoms in chloroform solution. When the glycol was recrystallized from water it had a melting point of 59°C., and contained two molecules of water hydration. Upon being dried over sulphuric acid it lost its water of hydration and yielded the pure glycol m.p. 92°C. Bouvet investigated the action of acetic acid and acetic acid plus hydrochloric acid on 1,1,6,6-tetraphenyl-hexandiol-1, 6 and obtained simple dehydration in both cases.

Michiels(187) prepared the diol and claimed to have obtained the hexamethylene oxide by treating it with dilute sulphuric acid.



In the words of Michiels' original paper "when adipic glycol is treated with dilute sulphuric acid and warmed, it rapidly transforms into tetramethyl-hexamethylene oxide. The latter is a liquid with a fruity odour and boils at 156-7°C., at 756 mm. pressure". We shall refer to Michiels' work in our Discussion section.

Petrov and Sanin(188) prepared a large number of 2,7-diols and their dehydration products. The 2,7-dimethyl-octadiene-2,6 obtained had the following constants, b.p. 161-3°C., d_{20}^{20} 0.8005, n_D^{20} 1.4501. In no case do they mention

187.-Michiels, Bull.Soc.Belg., 27, 25, (1912).
188.-A.D.Petrov & P.S.Sanin, J.Gen.Chem.(USSR),9, 2129-37, (1939), C.A. 34, 4054.

the formation of the oxide or any cyclic compounds.

It is needless to mention the necessity of considering the chemistry of the trienes of this series. Although 2,7-dimethyl-octatriene-2,4,6 as well as its glycol (octendiol) and octadienol have been prepared, no work has been done concerning the influence of acid catalysts on these compounds. Consequently no mention will be made of these compounds.

Cyclization of Various Other Dienes

The study of cyclization of many other dienes and alkenols has attracted the attention of great many workers due to its importance to the synthesis and study of naturally occurring cyclic compounds.

The object of this research has not yet been fully attained. However, considerable progress has been made. We have already discussed many cases of cyclizations in the Historical section. The typical cyclizations of terpene compounds are well known, however no attempt has been made to determine the structural relationships necessary to bring about cyclodehydration till very recently.

R.P. Linstead and co-workers(189) have carried out rather extensive studies in this series. They found that of

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189.- R.P.Linstead, J.Chem.Soc., 470, (1936).

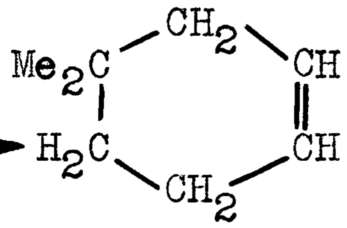
the following four substances only the last one underwent the typical type of cyclodehydration.

I $CMe_2(OH)-CH_2-CH_2-CH=CH_2$

II $CMe_2(OH)-CH_2-CH=CH-CH_2Me$

III $CMe_2(OH)-CH_2-CH_2-CH=CHMe$

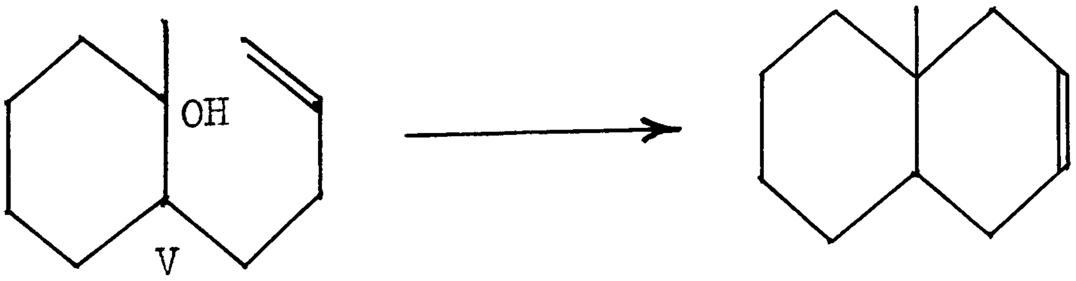
IV $CMe_2(OH)-CH_2-CH_2-CH_2-CH=CH_2 \longrightarrow$



Treatment of the alcohols I, II, III with phosphoric acid yielded the corresponding open chain dienes and their polymers. No cyclization either to the five membered or six membered compounds could be detected. Cyclization of 1-me-heptene-6-ol-2 (IV) took place with ease on treatment with phosphoric acid.

Consideration of these results led Linstead and co-workers to the study of cyclizations of this class of compounds attached to a ring system.

Treatment of 1-me-2-butenyl-3-cyclohexanol (V) with phosphoric acid led to cyclodehydration with the formation of methyloctalin. The reaction required higher temperatures that the simple diene.

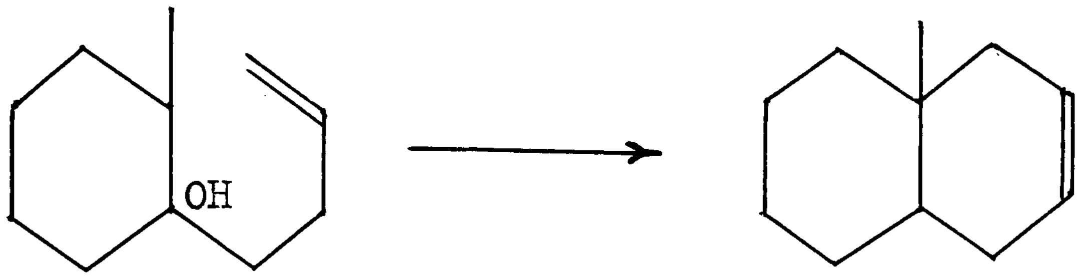


V

In another communication Linstead(190) and co-

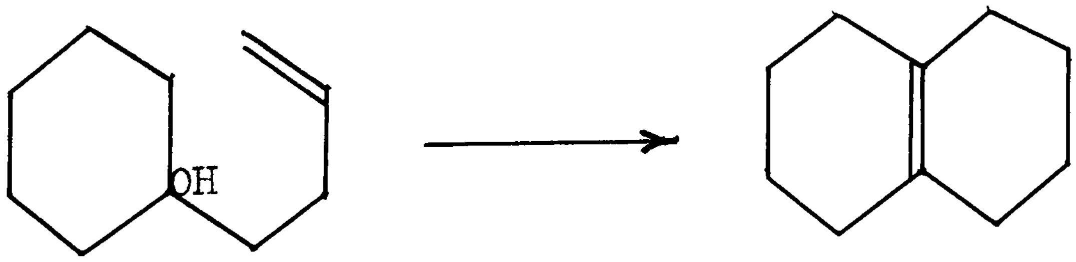
190.- Linstead, J.Chem.Soc., 476, (1936).

workers report the similar cyclization of 2-Me-1-butenyl-3-cyclohexanol. It was necessary to boil the alcohol at 150°C. for one hour in order to convert the dienes formed through simple dehydration but without cyclization, into the cyclic product. The product obtained was essentially cis-9-methyloctalin.



Due to the intermediate formation of the diene, the authors assume that cyclization takes place through the diene rather than the alcohol or its ester, though the latter possibility is not excluded.

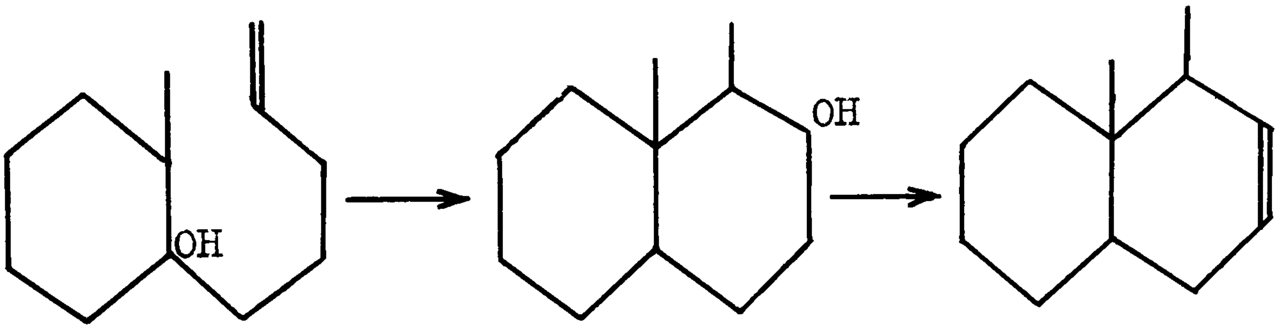
Linstead and co-workers(191) have extended their investigations to compounds of the same type but without the angular methyl group. They found that 1-butenyl-4-cyclohexanol gave only one diene without the migration of the double bond and this upon treatment with phosphoric acid and its oxide gave octalin-9,10. Similar results were obtained directly from the alcohol.



191.- Linstead and co-workers, J.Chem.Soc. 1136, (1937).

When this 1-butenyl cyclohexanol was treated with acetic anhydride containing a little sulphuric acid, it yielded cis-beta-decalyl acetate.

In a recent study Linstead and Elliott(192) carried out a cyclization experiment using 2-Me-pentenyl-4-hexanol. The structure of the products was not fully established, but using acetic and sulphuric acid mixture they obtained 1,9-dimethyl decalol which was dehydrated to 1,9-dimethyl-2-octalin. The possibility of the presence of spiro type of compound was not excluded.

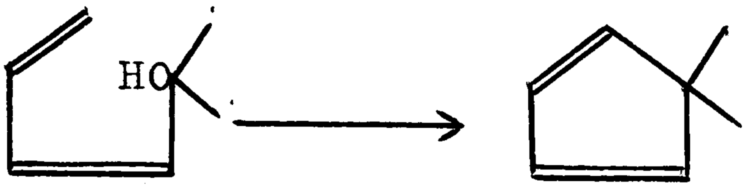


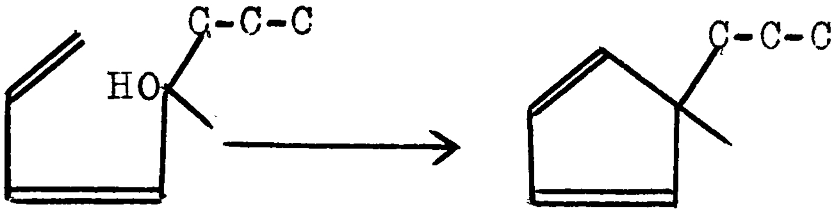
The general conclusion from these experiments is that only six membered rings are obtained. The absence of any indication of the presence of any five membered rings is significant.

However, there is one recent report which claims the formation of cyclopentane ring. S. Zonis(193) hydrogenated 5-Me-1-hexen-3-yn-5-ol (b.p.$_{35}$ 76-7^{o}C.) and also 5-Me-1-octin-3-yn-5-ol (b.p.$_{5}$ 65-6^{o}C.) to 5-Me-1,3-hexadiene-5-ol (b.p.$_{12}$ 50-1^{o}C., d^{20}_{4} 0.858, n^{20}_{D} 1.4566) and 5-Me-1,3-octadiene-5-ol (b.p.$_{12}$ 78-80^{o}C., $d^{18.5}_{4}$ 0.8611

192.- Linstead and Elliott, J.Chem.Soc., 660, (1938).
193.- S.Zonis, J.Gen.Chem.(USSR) 9, 2191, (1939).

$n^{18.5}$ 1.8597). On heating with 3-4 volumes of 25 per cent sulphuric acid on a water bath for 10-20 hours, both were dehydrated to give 1,1-dimethyl-2,4-cyclopentadiene b.p. 108-11°C., d^{20}_{4} 7838, n^{20}_{D} 1.46 and 1-Me-1-propyl-2,4-cyclopentadiene b.p. 78-80°C., $d^{16.5}_{4}$ 0.7999 $n^{16.5}_{D}$ 1.4745 respectively. Exhaustive hydrogenation yielded the corresponding dialkyl cyclopentanes. (No constants given).

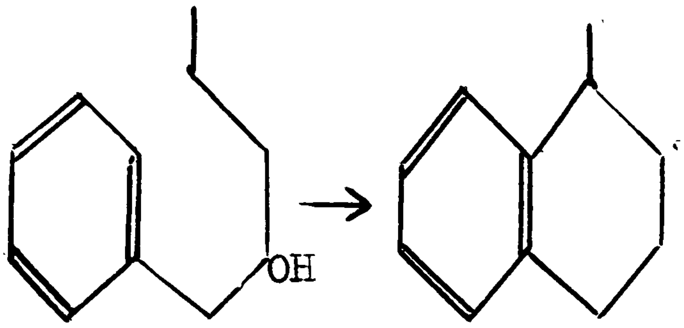


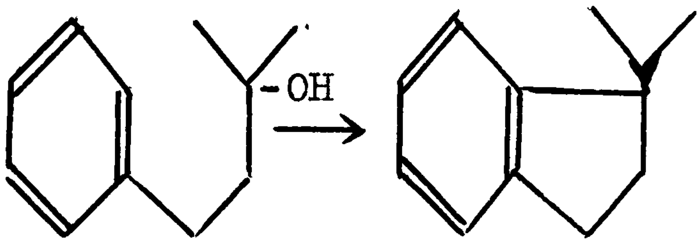


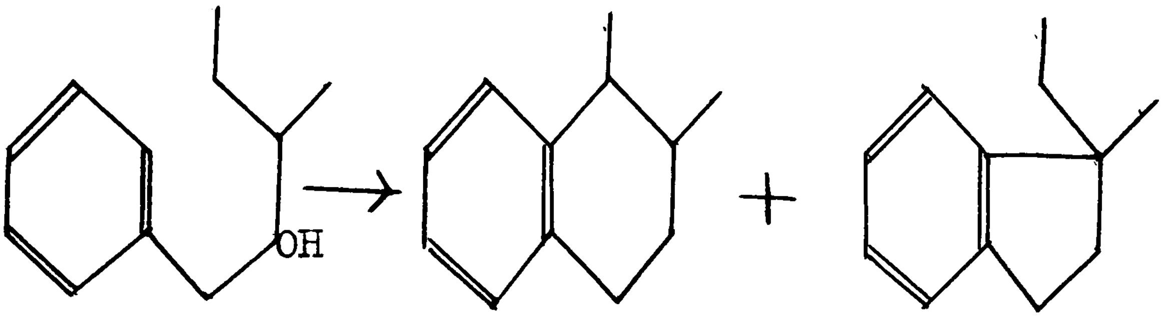
Cyclization attempts have also been carried out involving a double bond and an aromatic nucleus. Extensive studies have been carried out in this field by M. T. Bogert (194) and co-workers. It is needless to enumerate all the experiments carried out by these workers. The results however, may be generalized as follows. Benzene derivatives with an unbranched side chain of five to seven atoms, containing a double bond or hydroxyl group will give a tetralin on treatment with sulphuric acid except when the hydroxyl group or double bond adjoins the phenyl group, in which case polymerization occurs. Larger rings than six-membered are

194.- M.T.Bogert and co-workers, J.Am.Chem.Soc., 151, (1935).

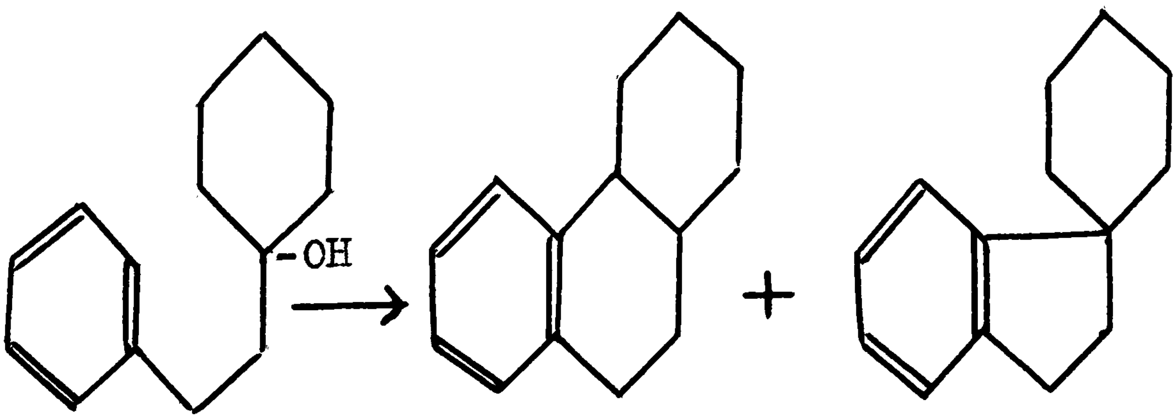
not formed. When the side chain carried a methyl group on C_3 (phenyl group on C_1) derivatives of both indane and tetralin are formed.





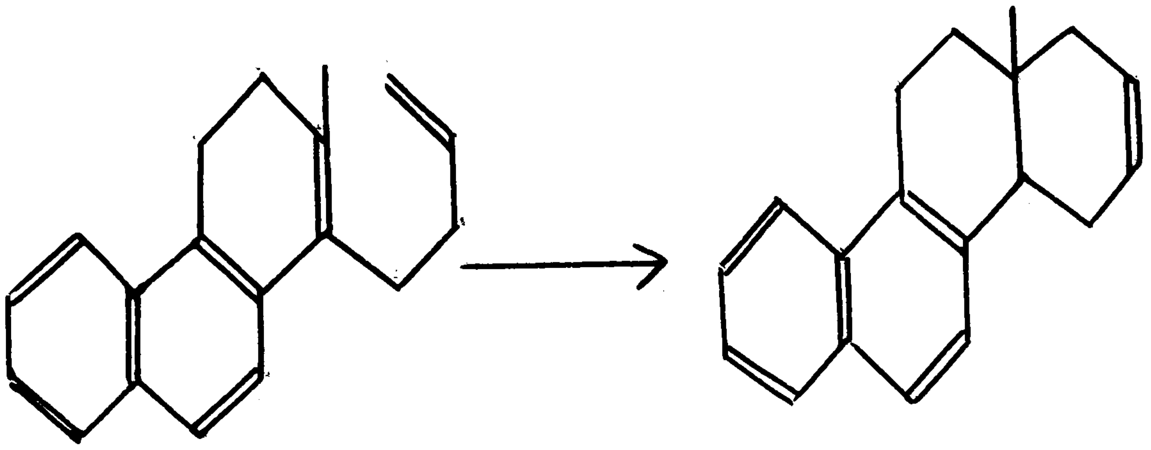


Many similar cases have been reported in the literature dealing with the formation of five and six membered rings, and involving more complex compounds. Thus 1-beta-phenyl ethyl cyclohexanol has yielded the olefin by mild dehydration but conc. sulphuric acid yielded as.-octahydrophenanthrene(195). This product on fractionation actually yielded two different compounds one of which proved to be the spiran(196). The whole reaction is analogous to the formation of a mixture of indane and tetralin as reported in the previous paragraph.



195.- Bogert, Science, 77, 289, (1933).
196.- Bogert, J.Org.Chem. 288, (1936).

A cyclization involving the principles reported previously but involving a more complex compound was first reported by Cook and co-workers(197) and repeated by Linstead and co-workers(198). It deals with the cyclization of 2-me-1-butenyl-4-dihydrophenanthrene to a hydrochrysene derivative of similar skeleton. This was accomplished successfully.



197.- Cook and co-workers, J.Chem.Soc., 1633, (1935).
198.- Linstead and co-workers, J.Chem.Soc., 729, (1940).

DISCUSSION OF EXPERIMENTS AND RESULTS

Experimental Procedures.

In the next section is given an account of the experimental procedures and the results obtained from these procedures. It is felt that at this point it would be desirable to say a few words as to why these procedures were adopted and to make criticisms of the advantages and disadvantages of the methods employed.

It will be noticed that apart from the preparation of the diene compounds, practically all the remaining procedures consist essentially of treating the dienes or the corresponding glycols with various concentrations of acids, especially formic and phosphoric acids, the resulting products then washed free of acids, dried and fractionated to determine their constituents.

We have mentioned elsewhere in this Thesis that since this type of acid treatment of geraniolene and numerous other terpene compounds results invariably in the formation of cyclic compounds which occur in nature, the procedure serves as a basis of comparison for the behaviour of other types of dienes when the latter are treated in the same manner. Furthermore, the results from such experiments would tend to prove or disprove the possibility of such reactions taking place in the plant. It would also serve as a basis of speculations as to the possible biogenesis of some related plant constituents.

It is a well known fact that in terpene compounds the experimental conditions determine largely the cyclic end products formed. Consequently we have carried out a great number of experiments with each diene, with the hope of finding out the optimum conditions.

It must be remembered that dienes, such as the ones employed, when subjected to the influence of acids not only may cyclize, but also may undergo isomerization and polymerization. In the case of isomerization which is invariably present, a wandering of the double bond takes place with the production of a number of compounds which have close physical constants. Very often the cyclic compounds formed may have their constants well within the limits of the various constants of the isomeric products. Consequently the determination of the presence of small amounts of cyclic products becomes a problem of great difficulty.

In all our experiments we have employed a modified Podbielniak distilling column which has been found to have an efficiency of 12-15 plates under actual operating conditions. Such a column, easily operated and capable of fractionating liquids as little as 5 cc. with the loss of less than 1 cc. of liquid, has been found of great assistance in the course of these investigations. By means of a special receiver, collections of a large number of small fractions have been made and each fraction examined for the existence of cyclic products.

Normal cyclic products such as the ones obtained in the terpene series have considerably lower boiling points than aliphatic dienes. They also have a considerably higher density. Hence, if in a particular case, say 20 per cent cyclization took place, and the liquid was fractionated into 10 fractions, the first fractions should show considerable variations in their physical constants from the last fractions.

It is obvious that the real criterion of the formation of cyclic compounds is the existence of one double bond instead of two. Determination of unsaturation is commonly made by either hydrogenation or halogen absorption. Due to the lack of suitable apparatus and the difficulties involved, little use was made of hydrogenation procedures. In the case of halogenations, it is a well known fact that iodine number determinations by Wij's or Hanus' method are useless for these types of compounds. As a matter of fact, there is no exact method for the determination of unsaturation of this class of compounds by halogen absorption.

However, it was found, that by determining the amount of bromine absorbed in a dilute carbon tetrachloride solution, (till decolouration of bromine no longer took place), fairly uniform results could be obtained, which showed a maximum variation of 10 per cent with many known compounds. Thus in a series of experiments with known compounds the following results were obtained. 0.1325 gms. of pure dimethyloctadiene in 10 cc. of carbon tetrachloride absorbed 4.2 cc. of bromine solution containing 1.000 gm. of bromine in 10 cc. of carbon tetrachloride. This indicated the presence of 1.98 double bonds. In a similar manner 0.1365 gms. of cyclogeraniolene absorbed 2.3 cc. of bromine solution indicating the presence of 1.0 double bonds; 0.3383 gms. of 2,6-dimethyl heptene absorbed 6.1 gms. of bromine solution indicating the presence of 1.05 double bonds, and 0.3037 gms. of tetrahydrolinaloolene absorbed 5.4 cc. of bromine solution indicating the presence of 1.1 double bonds. The bromination experiments were carried out at 0°C. by adding the bromine solution slowly in order to prevent the occurrence of excessive substitution reactions. This method was found to be as accurate as various methods reported in the literature and possessed the further advantage of being a direct, simple and rapid process.

Experimental Results.

The results obtained with all the dienes investigated showed a uniformity of behaviour for each case, in spite of the difference in concentration and type of acid employed, and also variations in experimental conditions present. This may be explained by assuming that one type of mechanism is involved when these dienes are treated with acids.

Of the many types of mechanisms of polymerization proposed, that of Whitmore(137) and Ipatieff(132) are the most outstanding. In view of experimental results obtained the writer

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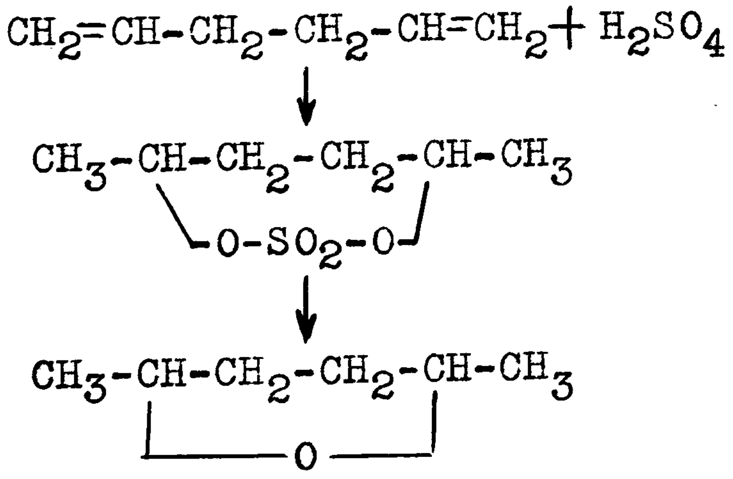
132.- V.N.Ipatieff, Ind.Eng.Chem., 1069. (1935).
137.- F.C.Whitmore, J.Am.Chem.Soc., 53, 3136. (1931).

prefers the mechanism proposed by Ipatieff. However there are cases, such as the formation of dicyclic sesquiterpenes from farnesol which cannot be explained by Ipatieff's mechanism.

Cyclization Experiments with Diallyl.

In all cases the end products were either unchanged diallyl or the formation of 1,4-dimethyl tetrahydrofurane. It must be recalled that Cortese reports that the minimum concentration of sulphuric acid which will attack diallyl is 65 per cent. In other words, diallyl is very resistant to the action of dilute acids. The formation of sulphuric acid esters has been reported both by Cortese(152) and other investigators.

Considering the results obtained by Cortese and the author, the following mechanism is proposed for the formation of the oxide,



$$CH_2{=}CH{-}CH_2{-}CH_2{-}CH{=}CH_2 + H_2SO_4 \downarrow CH_3{-}CH{-}CH_2{-}CH_2{-}CH{-}CH_3 \ (O{-}SO_2{-}O) \downarrow CH_3{-}CH{-}CH_2{-}CH_2{-}CH{-}CH_3 \ (O)$$

Strong acids cause rupture of the oxide ring with the formation of isomers and higher polymeric substances.

It is significant that there is no case reported in the literature where treatment of diallyl with acids caused

152.- F.Cortese, J.Am.Chem.Soc., 51, 2266, (1929).

the formation of carbocyclic compounds. In the many experiments carried out by the author, employing different acids of various concentrations, the results indicated the absence of the formation of any carbocyclic compounds.

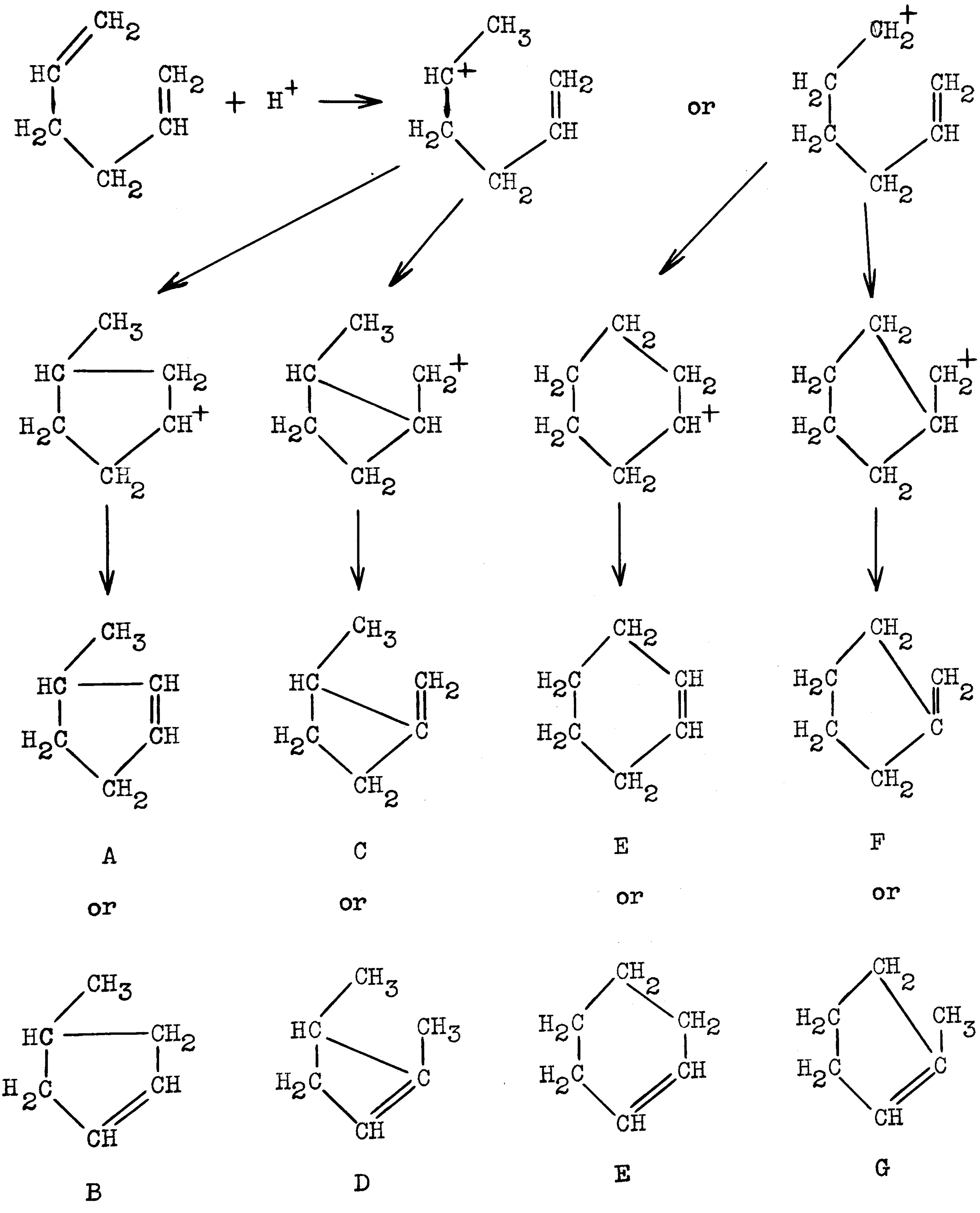
According to Whitmore's(137) polymerization theory treatment of Diallyl with acids would result in the formation of five and six membered cyclic compounds as shown in the following scheme: (Please see next page).

It will be noticed that it is possible to obtain eight cyclic products. However, if one assumes that the proton hydrogen adds according to Markownikow's rule, then this number is reduced to four, namely A,B,C,D, and in all probability to two, A and B, if we assume that the positive carbon atom also obeys Markownikow's rule.

Whitmore's theory becomes unacceptable since experimental results indicate the absence of the formation of any carbocyclic compounds. Nor does Whitmore's theory explain the formation of 1,4-dimethyl tetrahydrofurane.

It is concluded, that in the case of diallyl, addition of acid molecule, takes place to the double bond and this is then hydrolyzed to give the furane compound or polymers of diallyl.

137.- F.C.Whitmore, J.Am.Chem.Soc., 53, 3136, (1931).

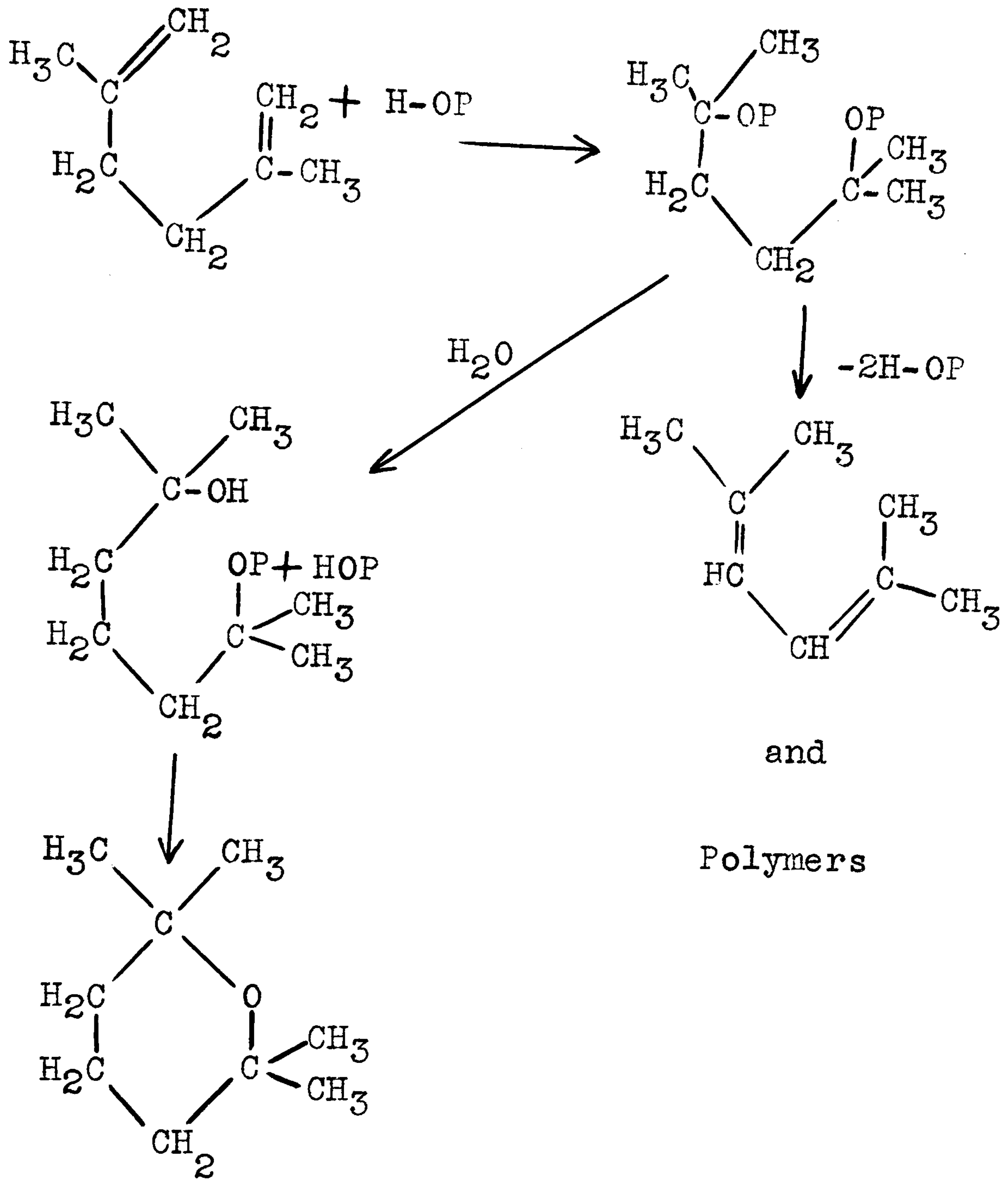

+ H⁺
or
A
C
E
F
or
or
or
or
B
D
E
G

Cyclization Experiments with Diisobutenyl.

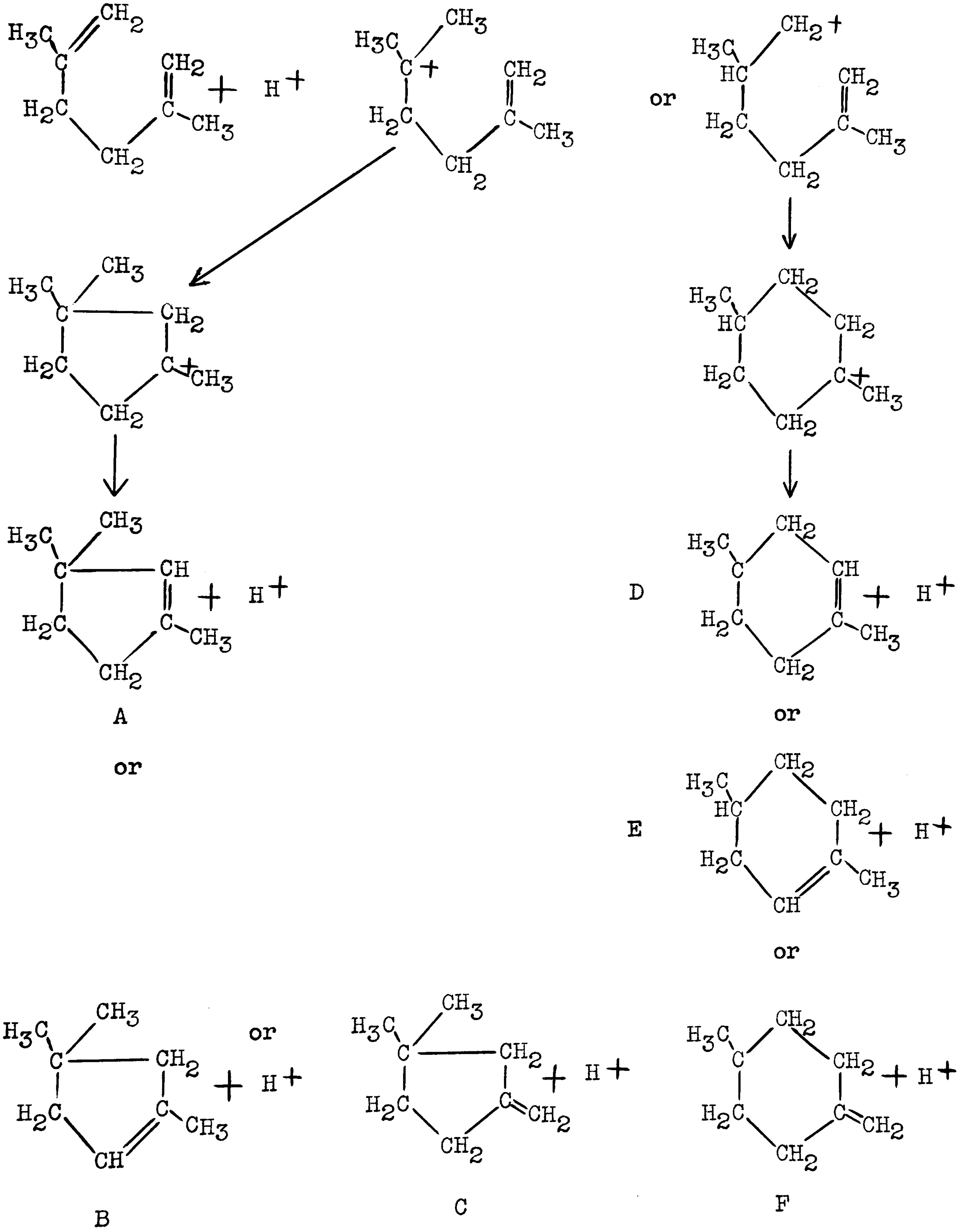
This compound is very suitable for the study of the mechanism of cyclization. Numerous experiments were carried out to study the influence of various acids in different concentrations. All of the results indicated a uniform mechanism and behaviour toward acids.

Treatment with 85 per cent phosphoric acid gave an addition product which slowly decomposed giving mainly diisocrotyl. If however hydrolysis of the phosphate was brought about by addition of ice-water to the reaction product, then the usual type of reaction took place with the formation of 1,1,4,4-tetramethyl tetrahydrofurane. The presence of phosphates was proven by the fact that a mixture of diisobutenyl and phosphoric acid, when subjected to vacuum distillation did not yield any distillable products. However, attempts to isolate phosphates failed, presumably due to the ease of hydrolysis of the acid addition compounds. Further evidence that the acid catalyst adds to the double bonds was provided by the isolation of formates when diisobutenyl was treated with 98-100 per cent formic acid.

In all the experiments carried out, the only cyclic product was the furane compound. Other products obtained were diisocrotyl, an isomer of diisobutenyl, and polymeric products. These results might be predicted through the following scheme; where H-OP represents $\mathrm{H\text{-}OSO_3H}$, or $\mathrm{H\text{-}OP}\overset{\mathrm{OH}}{\underset{\mathrm{O}}{\lessgtr}}\mathrm{\text{-}OH}$ or $\mathrm{H\text{-}O\text{-}}\overset{\mathrm{O}}{\mathrm{C}}\mathrm{\text{-}H}$ (i.e.-sulphuric, phosphoric and formic acids).

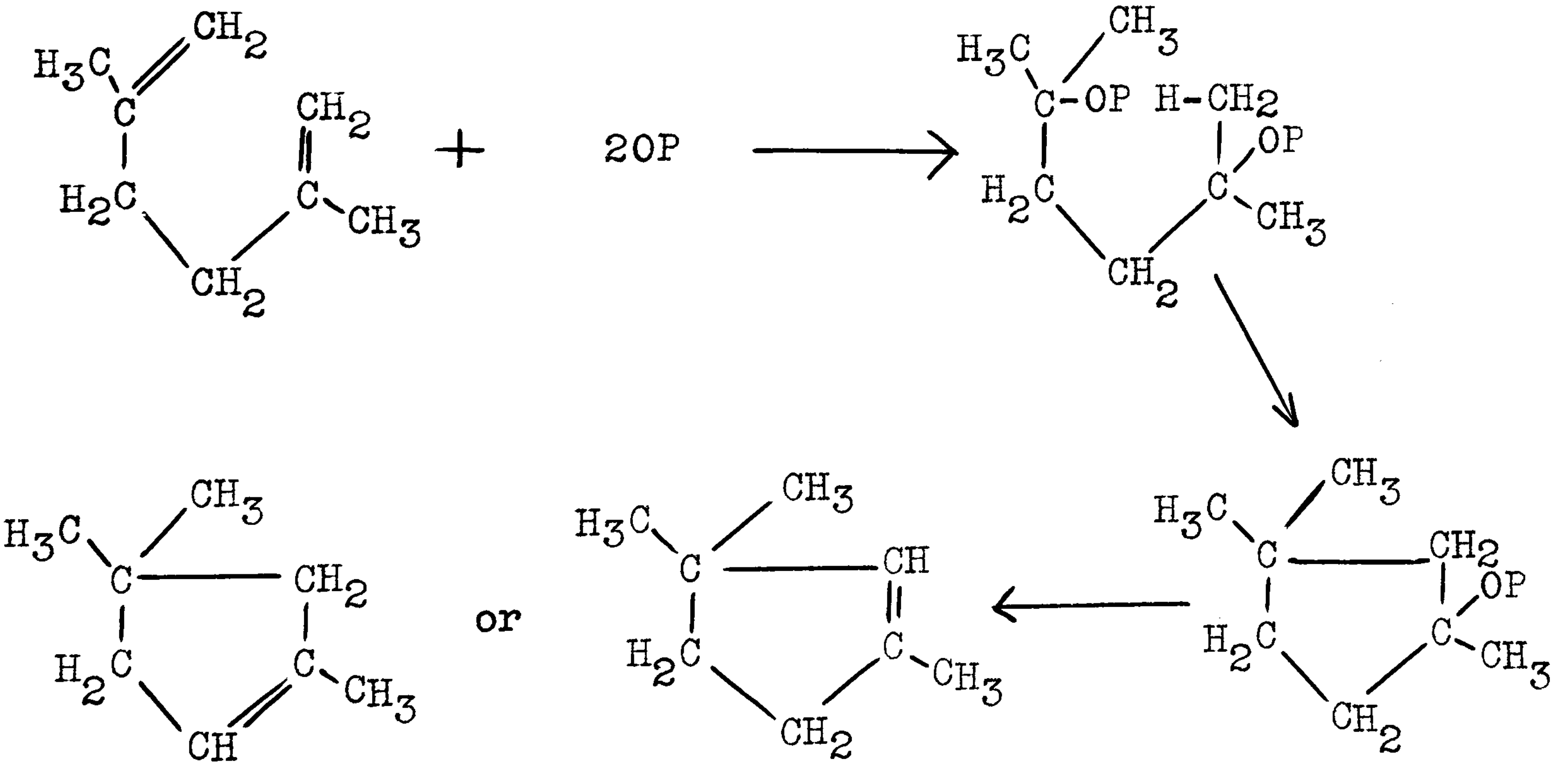


It is evident that these results, which agree with the results of many other workers, cannot be explained by Whitmore's proton polymerization theory. Whitmore's theory, which seems to have found wide acceptance, would yield several carbocyclic products, but no furane compound. Furthermore, the presence of an acid addition product definitely disproves not only Whitmore's theory but also many other theories involving the positive carbonium atom. For the sake of clarity, the following scheme is presented, which represents the products expected from Whitmore's theory:



We have mentioned the fact that Ipatieff(132) and co-workers have actually isolated phosphates and sulphates in their studies of polymerization. However, their mechanism of polymerization involves a reaction between one molecule of olefin and one of phosphate or sulphate. Our studies with diolefin, which is in reality an intramolecular polymerization, indicate that polymerization between two molecules of olefins involves a reaction between two phosphates or two sulphates, rather than between a phosphate and an olefin. The absence of any $R_2HC-O-CHR_2$ and $R_3C-O-CR_3$ may be explained on the basis of instability of these compounds.

According to the writer's theory, there is the possibility of the formation of a cyclopentene compound in the following manner,



the absence of such a compound may be due to steric factors, or due to the fact that less energy is required to isomerize to the diisocrotyl than revert to the original compound or form a cyclic compound. Even when the oxide is ruptured by strong acids the product is exclusively diisocrotyl or its polymerization products. Once diisocrotyl is formed, there is no possibility of formation of cyclopentenic products and the only types of reactions expected are polymerization or formation of cyclic products through the diene reaction.

In spite of claims made(199) that diisocrotyl type compounds are incapable of polymerization, it was proved definitely that such is not the case, and diisocrotyl yields dimers and trimers. The constitution of these compounds was not investigated.

It must be admitted that the existence of very small amounts of cyclopentenic and cyclohexenic compounds presents great difficulties. However, in view of the many experiments performed with the introduction of various factors it is reasonable to expect that there would have been variations in the yields if such compounds were formed, resulting in their detection. It is felt that the methods employed would have enabled the writer to detect any carbocyclic compounds present in the order of 5 per cent.

199.- G.S. Whitby, Can. J. Res., 280, (1932).

During the course of investigations it was noticed that dimeric products obtained exhibited a peculiar phenomenon. When certain fractions of these products were dissolved in chloroform and a few drops of bromine solution added, a brilliant permanent bluish colour developed. The same phenomenon was observed with dimers of dimethyl octadiene. It is interesting to note that such a phenomenon has been observed only in the case of azulenes which contain a series of continuous conjugation.

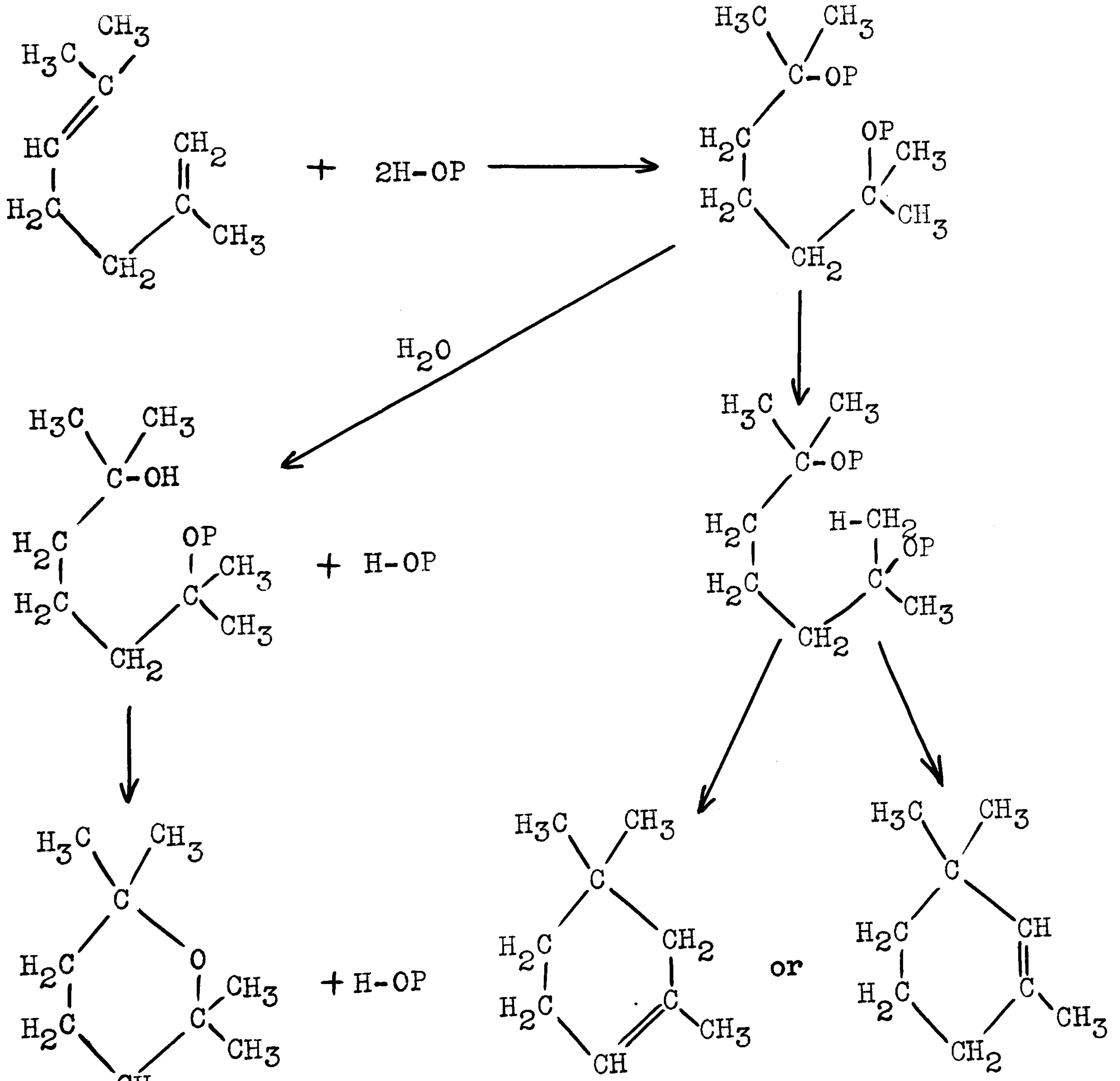
Cyclization Experiments with Geraniolene.

The problem of cyclization of geraniolene and many other terpene compounds has been extensively investigated by various workers. It was decided to repeat the work partly as a test for the efficiency of our methods and partly to investigate the formation of the little studied pyrane compound of geraniolene.

It was found that cyclogeraniolene formed with great ease in all cases. This indicated that if there were cyclic products formed in the other dienes investigated. such compounds were sufficiently stable to withstand the acid treatment and their isolation by the methods employed would have been comparatively simple.

The formation of the oxide compound was of direct interest since it supported the polymerization theory presented by the writer. It was significant that the oxide compound formed when the acid-geraniolene compound was diluted with ice-water (hydrolysis) immediately after solution of geraniolene into the acid solution had taken place. Otherwise if the acid-geraniolene mixture was allowed to stand, separation of cyclogeraniolene took place. In other words, the acid addition product is not stable, but nevertheless it is present as the first step in the reaction. It is also significant that the stability of the geraniolene-acid addition product is much less than that of diisobutenyl, indicating that steric factors come into play in these reactions. Proof that the first step in cyclization reactions involves the addition of two acid molecules to the diolefin is supplied by the high yields of oxide obtained under suitable experimental conditions.

The following scheme represents the products which might be expected according to the writer's polymerization theory:

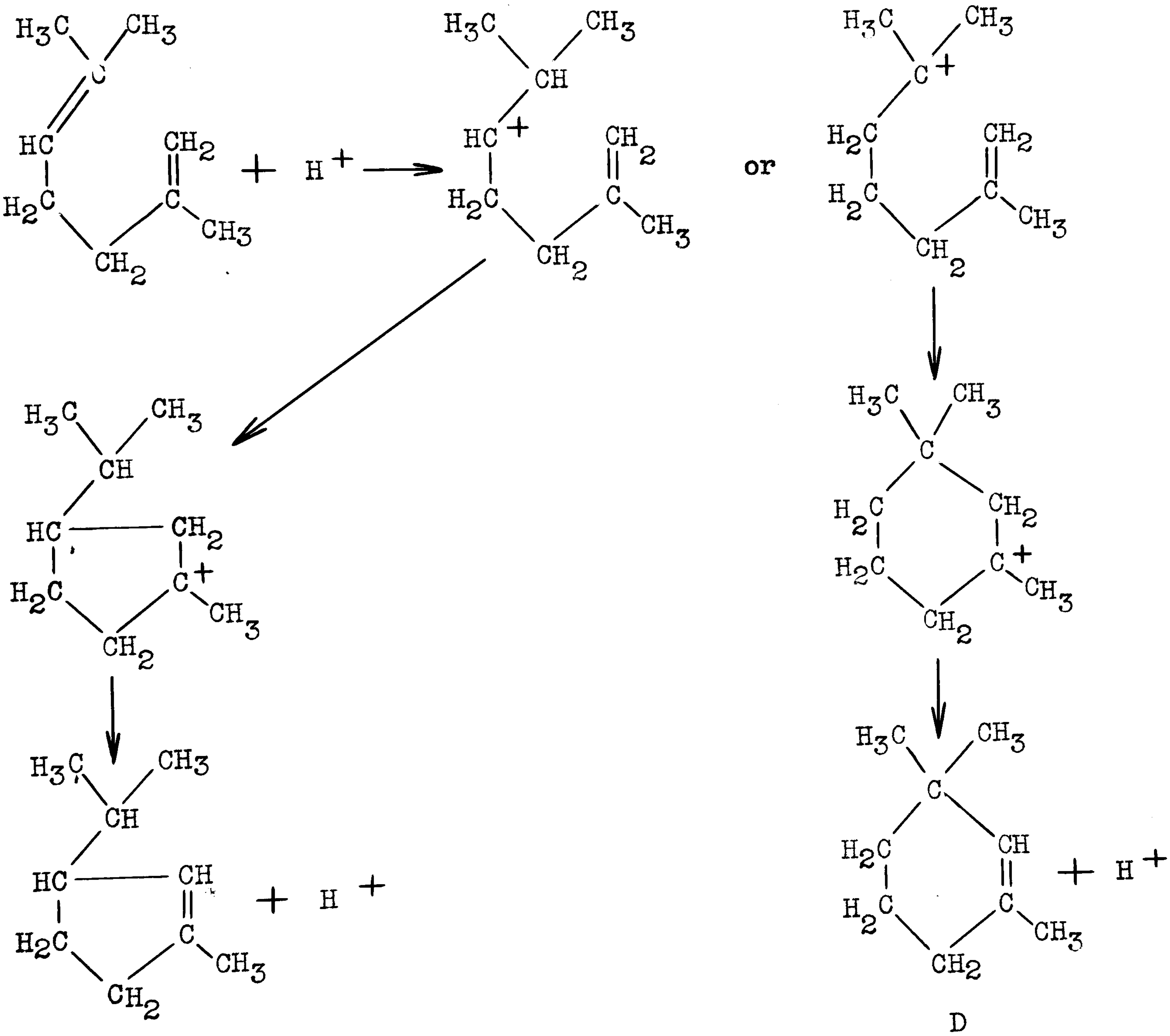


1,1,5,5-tetramethyl pyrane

alpha-cyclogeraniolene

beta-cyclogeraniolene

All of the above products were obtained with ease, and fit in very nicely into author's polymerization theory. On the other hand, neither Ipatieff's nor Whitmore's theory can explain the formation of the pyrane compound. The presence of alpha and beta isomers is not explained by Ipatieff's theory except through isomerization. The application of Whitmore's theory will yield the following products:

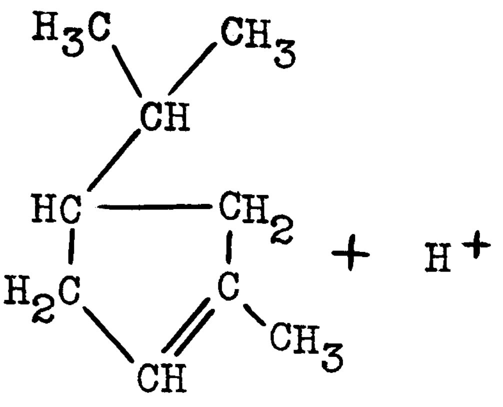


A

or

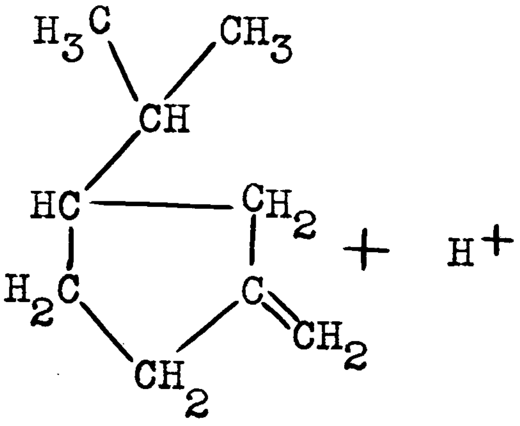
D

or

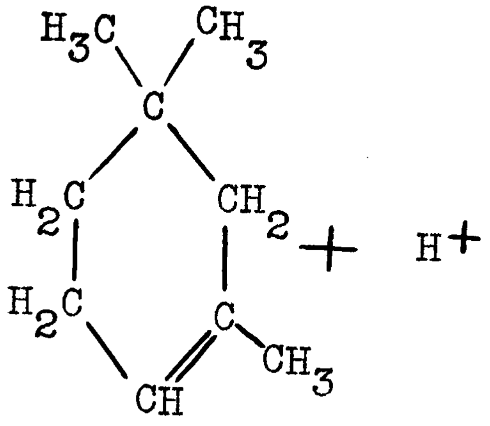


B

or

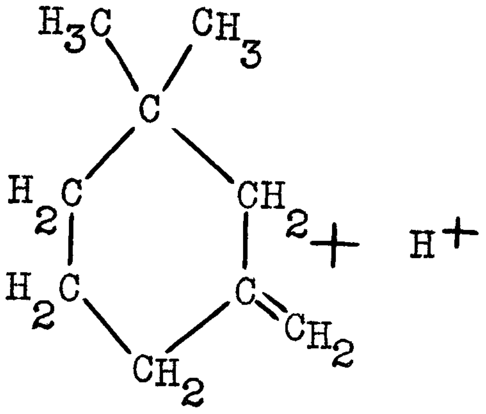


C



E

or



F

Of course, it is quite possible that addition of proton takes place according to Markonikow's rule, in which case only the cyclohexenic compounds are formed. However, even if such were the case, the other objections enumerated above still make Whitmore's theory untenable.

In the study of cyclization of terpene compounds. one is impressed by the number of investigators who advocate a hydration dehydration theory for the formation of cyclic compounds. Numerous such cases are cited in Simonsen's well known book "The Terpenes". The idea involves simple splitting off of H-OH to give the cyclic compound. That this is not the case (except in rare cases where an active hydrogen is involved) was proven by the failure to cyclize tetrahydrolinalool and 2,6-dimethyl-heptan-ol-6. Matsuura(200) also failed to cyclize tetrahydrolinalool by treatment with sulphuric acid. No attempt to cyclize the heptanol has been reported previously, and our failure to cyclize it is presented as additional evidence against the simple hydration dehydration theory.

Attempts to Cyclize 2,7-dimethyl-Octadiene-2,6.

The work with this compound proved to be rather difficult and somewhat confusing. Numerous experiments were conducted using different acids and involving variations in the concentration of acids and time of treatment.

It was found that in all cases compounds were produced which absorbed from 3.5 to 4.5 atoms of bromine.

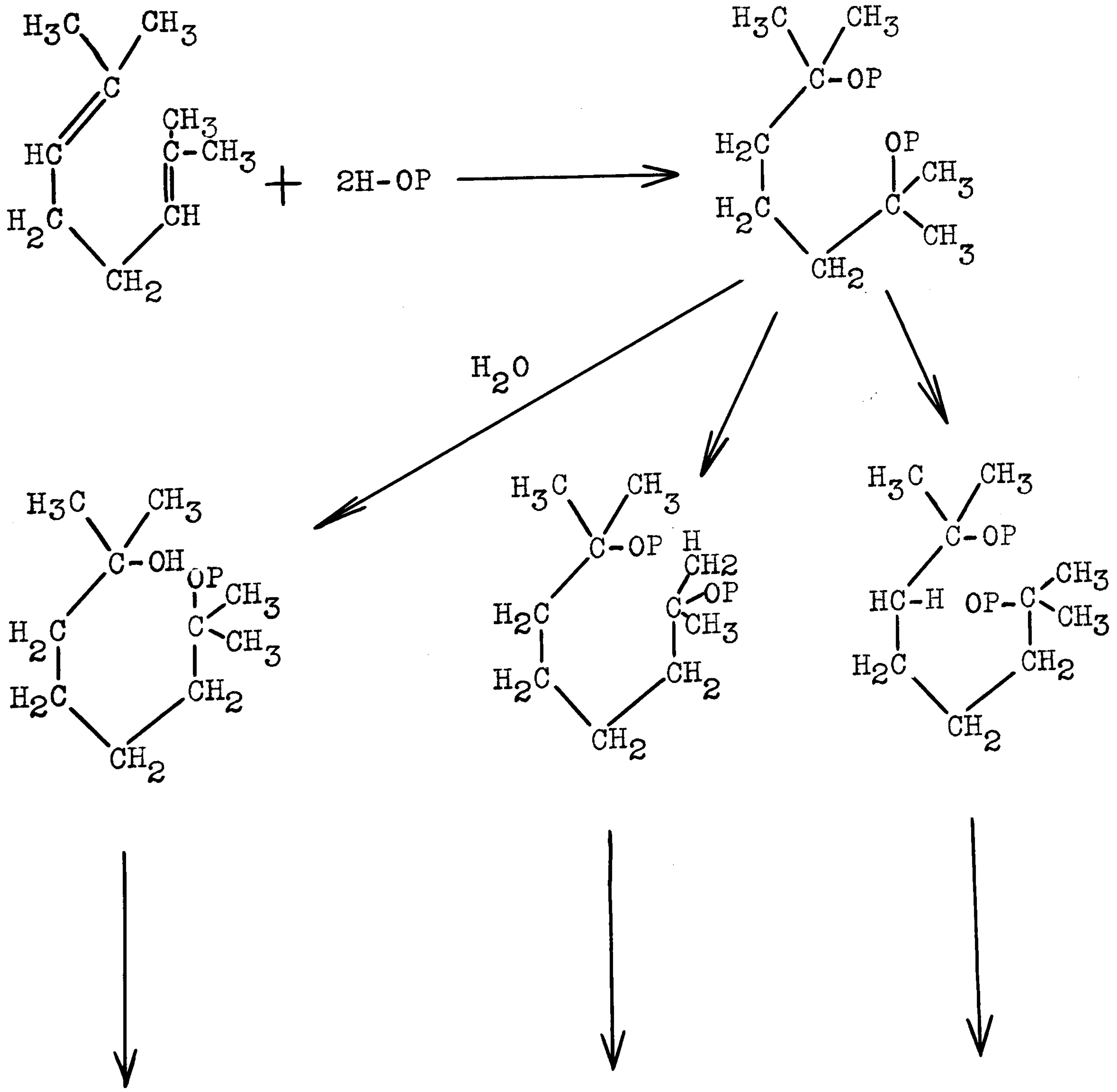
200.- T. Matsuura, J.Sci.Hirosima Univ., 8A, 121, (1938).

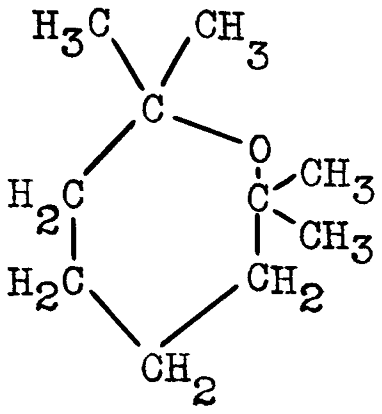
Such variations might be explained by assuming that different isomers of octadiene behave abnormally towards absorption of bromine. This is not unusual for this type of compounds. Considerable variations in boiling point, density and refractive index of the products obtained indicated the presence of isomeric products.

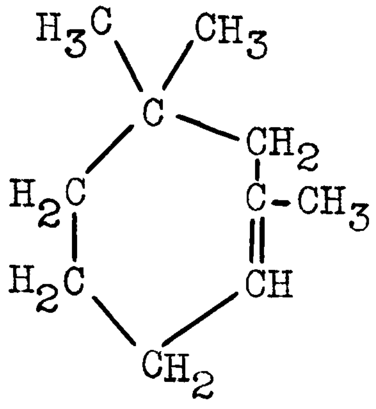
There were other factors present which made the issue even more confusing. Thus, in most cases the product had too high a density to be a non-cyclic product and yet it absorbed about four atoms of bromine. Attempts to hydrogenate it fully and thus obtain a uniform saturated compound namely 2,7-dimethyl-octane, were unsuccessful because in all cases the compound absorbed only about one molecule of hydrogen and all efforts to force the absorption of the second molecule of hydrogen failed. Bromination experiments with the hydrogenated product indicated the presence of unsaturated products. Absorption of 0.5-0.75 molecules of bromine took place with the hydrogenated product. It is possible that cyclic products were present. It must however be recalled that hydrogenation of olefins is extremely difficult.

Another factor added to the already existing confusion. It is well known that hydrogenation of straight chain diolefins to olefins and then to aliphatic compounds causes a definite lowering of boiling points, densities and refractive indices. On the other hand with cyclic compounds there is a rise in boiling point and lowering of densities and refractive indices. The change in the latter two constants is of a smaller degree. Hydrogenation of the products obtained by acid treatment of 2,7-dimethyl-octandiol-2,7 produced compounds whose boiling point increased, indicating that they were cyclic in nature. Furthermore the hydrogenated products had too high densities to be non-cyclic in nature.

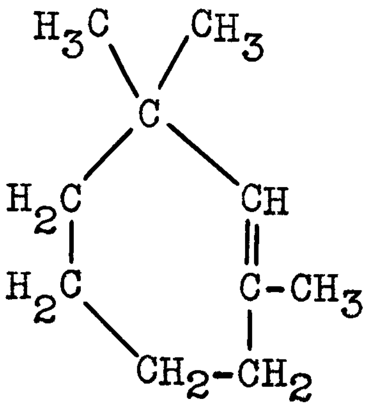
The writer feels that some cyclic products were formed and according to the writer's polymerization theory, these were probably cyclopentenic or cycloheptenic in nature. The formation of these cyclic compounds may be shown by the following scheme:

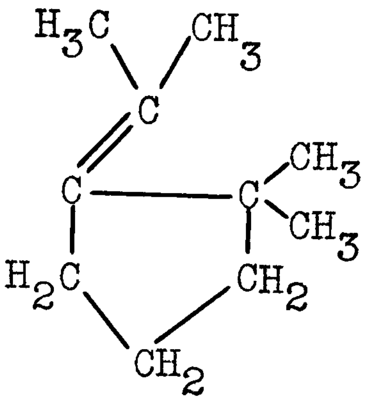




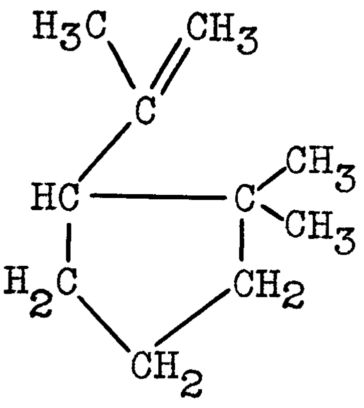


or





or

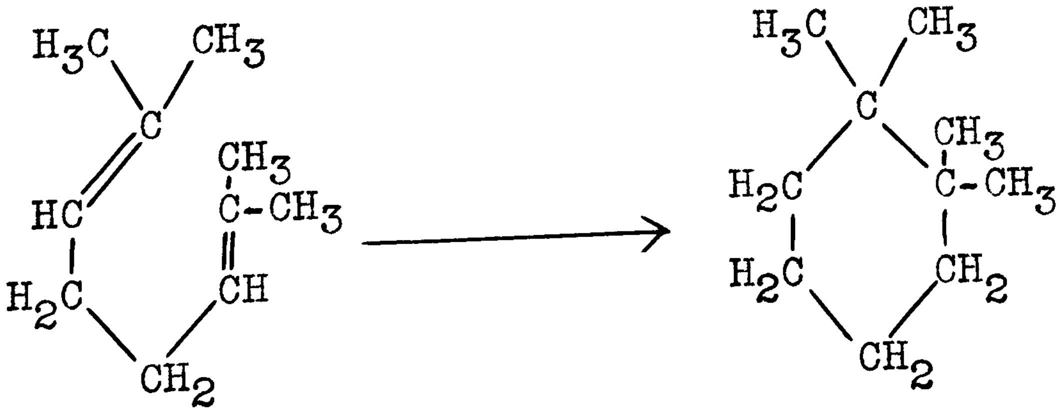


All attempts to obtain the hexamethylene oxide failed and although Michiels(187) reports the formation of this compound by the treatment of the glycol with dilute sulphuric acid he does not present sufficient proof except the boiling point of his product. In view of the fact that his experiment was repeated several times with variations and other attempts to prepare the oxide always yielded unsaturated compounds of the boiling range reported by Michiels for his oxide, it must be concluded that Michiels had an unsaturated compound and not the oxide. It is also recalled that the oxide of geraniolene was much less stable than the oxide of diisobutylene and on this basis it might be concluded that the seven membered oxide of the octandiol would be very unstable and extremely difficult to isolate. The oxide would have a boiling point about 8 C^{o}. higher than Michiels' compound.

187.- Michiels, Bull.Soc.,Belg., 27, 25, (1912).

The polymerization scheme presented above indicated the possibility of the formation of five and seven membered rings. Proof of the existence of a five membered ring would indicate that the five membered ring in the sterols is possibly formed from straight chain compounds. This would support the view that this class of compounds is formed in nature from straight chain compounds. The existence of seven membered rings is unlikely since they are formed with much greater difficulty.

It will be recalled that triterpene compounds have a middle six membered ring which has two angular methyl groups. The chief evidence of pentacyclic structure of these compounds is the formation of 1,8-dimethyl-picene by dehydrogenation of triterpenes. The writer does not consider this sufficient evidence for the existence of such a middle ring. It is highly probable that pentacyclic triterpenes are derived from straight chain triterpenes in which case it is difficult to see how the middle ring with two angular methyl groups could have formed. It will be noticed that the dimethyl octandiol investigated involves the same type of skeleton. The formation of a ring similar to the middle ring present in the triterpenes would involve cyclization analogous to the following scheme:



In view of the fact that no such product was obtained and also considering that such a cyclization is contrary to any type of polymerization theory including the one presented by the author, it is concluded that either such a ring is non-existent in the triterpenes or else if present it is not derived from straight chain triterpene molecule. Heilbron(42) obtained a tetracyclic compound from squalene but could not force the formation of a fifth ring. This is entirely in agreement with the theories advanced by the writer.

During the course of these investigations it was noticed that treatment of dimethyl-octandiol with cold concentrated sulphuric acid gave a saturated compound which separated out from the acid solution. This is the result of so called hydro-polymerization reported by various workers. When the acid was diluted an oil was obtained which gave a permanent purple blue colour when dissolved in chloroform and a few drops of bromine added. This is rather curious since the only class of compounds which exhibit this phenomenon are the azulenes which contain a chain of continuous conjugation. Could it be that the production of saturated compounds is the result of further unsaturation of dimeric products?

There is little doubt that the investigation of the results obtained from dimethyl-octandiol constituted the most important phase of the research. The determination of the presence of any cyclic products and their constitution was considered

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42.- I.Heilbron et al, J.Chem.Soc., 1630, (1926).

to be the main goal of the research conducted.

The writer regrets that further investigation had to be discontinued at this stage in the interest of War Research.

In conclusion, we might say that as a result of our work and also the result of other workers, diallyl and dimethallyl do not yield carbocyclic products upon treatment with acids. Geraniolene type compounds invariably yield typical cycloterpene compounds. The results of cyclization experiments with 2,7-dimethyl-octadiene-2,6 indicate that some cyclic-products are formed.

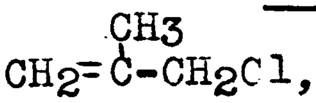
There is one single report of ring formation which is contrary to all expectations. Zonis reports that 2-methyl-hexadiene-3,5-ol-2 and 2-propyl-hexadiene-3,5-ol-2 yield cyclopentadiene compounds upon treatment with sulphuric acid(193). In view of the fact that Linstead(189) obtained no cyclic products from 2-methyl-hexene-5-ol-2 and also the abnormal constants presented by Zonis, the writer is of the opinion that in all probability Zonis did not have a cyclic compound.

193.- S.Zonis, J.Gen.Chem. (USSR) 9, 2191, (1939).
189.- R.P.Linstead, J.Chem.Soc., 470, (1936).

EXPERIMENTAL PART

I. Experiments with 2,5-Dimethyl, Hexadiene-1,5.

Preparation of 2,5-dimethyl, Hexadiene-1,5.

Methallyl Chloride.- Commercial methallyl chloride,  $CH_2=\overset{CH_3}{C}-CH_2Cl$, obtained from Shell Development Company, was of a light brownish colour with a strongly pungent odour. It was distilled at atmospheric pressure and the fraction boiling at 73-74°C. was taken as pure methallyl chloride.

Coupling of methallyl chloride through the Grignard Reaction.- The usual type of the Grignard reaction apparatus was set up including a Herschberg type of efficient stirrer with a mercury seal. A three litre three neck flask was washed with absolute ether and a few small crystals of iodine placed in it. Magnesium turnings weighing 24.5 gms (1 mole) were placed over the iodine crystals and the flask connected to the rest of the apparatus. The small quantity of dry ether left in the flask was slowly evaporated so that the air contained in the apparatus was driven out by the ether vapour. A calcium chloride tube placed at the end of the condenser prevented the admission of any moist air into the apparatus. The iodine crystals were gradually heated with a small flame till iodine vapours appeared in the free space in the flask. Heating was stopped at this point and the iodine vapours allowed to condense and form a coating on the magnesium turnings. The flask was allowed to cool and sufficient dry ether added to cover the magnesium turnings. The stirrer was started and a mixture of 181 gms. of methallyl chloride and 181 gms. of dry ether added slowly so that a constant rate of ether refluxing took place. After the addition of this mixture the whole mass now containing considerable chalky solid material, was allowed to stand for two days. The grignard was then decomposed with water containing sufficient hydrochloric acid to take care of the magnesium salt formed. The ether layer containing the hexadiene was withdrawn and the ether distilled off. The crude hexadiene was redistilled and yielded 69 gms. of pure hexadiene (65 per cent yield of the theory).

The physical constants of 2,5-dimethyl, hexadiene-1,5 were determined and the following values obtained, b.p.$_{760}$ 113-114°C., n_D^{25} 1.4264 D_4^{25} 0.7417, 2,5-dimethyl, hexadiene-1,5 is a water white liquid with a slightly pungent odour.

The preparation of the above hexadiene was carried out several times in order to obtain the requisite amount of material for experimental purposes. The yields were of about the same order in all cases.

Efforts to cyclize 2,5-dimethyl, hexadiene-1,5.

With sulphuric acid.- The hexadiene (20 gms.) was added to 150 gms. of cold concentrated sulphuric acid. It was necessary to keep the mixture on ice in order to prevent excessive rise of temperature. At no time was the temperature allowed to rise above 30°C. After 15 minutes, the whole mixture, now of reddish-brown colour, was dumped into 500 cc. of ice water. A milky solution formed, indicating the formation of sulphates and/or sulphonates and a thick oil separated out.

The oil was drawn off and the aqueous portion extracted twice with ether. The ether was evaporated off and the oil obtained combined with the main fraction. About 19 gms. of crude oily mixture was thus obtained.

The oil was distilled at 20 mm. Hg. pressure. About 6 gms. of oil distilled over, up to 122°C. The remainder would not distil even when the bath temperature was raised over 200°C. It was obvious that the product consisted of polymers of hexadiene. The distilled oil had a refractive index of 1.4760 at 25°C.

With Phosphoric Acid.-

1.- The hexadiene (20 gms.) was slowly added to 150 gms. of 85 per cent phosphoric acid with vigorous agitation. No reaction took place and the hexadiene would not dissolve in the acid. The mixture was then slowly heated by means of a water bath. At 70°C. the hexadiene dissolved in the acid. The water bath was raised to 85-90°C. and held there for 25-30 minutes. The resulting viscous, light brown liquid was allowed to cool and dumped into 500 cc. of ice water. An oil separated which had a strong camphoraceous odour. with a slight irritating effect on the eyes and throat. The oil was drawn off. The aqueous solution was ether-extracted twice and the ether evaporated off. The resulting oil was combined with the main fraction.

The oil was distilled at atmospheric pressure. All of it distilled at 110-114°C. except for about 3 cc. of viscous brownish residue.

In another experiment 110 gms. of hexadiene was added to 550 cc. of 85 per cent phosphoric acid and the period of treatment extended to 45 minutes. Upon dilution of the oil-acid mixture an oil of similar odour separated out. Distillation yielded 90 gms. of the camphoraceous oil with a boiling range of 110-114°C. and 8 gms. of residue.

2.- Hexadiene (20 gms.) was added to 150 cc. of 85 per cent phosphoric acid and the reaction carried out in a water bath as above. The oil-acid mixture was cooled. It was odourless and there was no trace of the characteristic camphoraceous odour of the above oil. A small portion of it was added to water and immediately the camphoraceous odour became apparent. The oil-acid undiluted mixture was subjected to vacuum distillation at 20 mm. No oil could be distilled over except for a few drops of an unidentified unsaturated oil, even when the oil bath was raised to 200°C. After about 15 minutes the acid mixture was allowed to cool. Upon dilution no camphoraceous odour developed and there was no separation of any oil, instead a very stable milky solution resulted.

<u>Properties of the camphoraceous oil</u>.- The above camphoraceous products with a b.p. of 100-114°C. were redis-

tilled and the fraction boiling at 113-113.5°C. at atmospheric pressure was taken for further examination. It did not absorb any appreciable amount of bromine and decolourized permanganate only very slightly. About 53 gms. of this redistilled portion was taken and treated with cold 1 per cent permanganate solution till it would no longer decolourize it, upon shaking for several minutes.

The permanganate treated product had a boiling point of 113-113.5°C. at atmospheric pressure (760.5 mm. Hg.). Other physical constants were d_4^{25} 0.8051, n_D^{25} 1.4021.

These properties indicated that the product was 1,1,4,4-tetramethyl, tetrahydrofurane.

Carbon and hydrogen analysis

found C 74.8% H 12.9% O by difference 12.3%

calcd C 75.0% H 12.6% O by difference 12.4%.

Molecular refractive index $\frac{(n^2-1)}{(n^2\ 2)}\frac{M}{d} = \frac{(1.4021^2-1)\mathrm{x}128}{(1.4021^2\ 2)\mathrm{x}0.8051}$

$= 38.72$

Calculated $= 38.59$

<u>Properties of 1,1,4,4-tetrahydro-tetramethyl furane</u>.-

1.- Boiling with iodine for 2 hours did not break the oxide ring.

2.- When boiled with 50 per cent sulphuric acid for half an hour the ring is broken and unknown unsaturated compounds produced.

3.- Phosphorous pentoxide when added to the furane and allowed to stand at room temperature for several hours produced unknown unsaturated compounds.

4.- Boiling the furane with zinc chloride produced high boiling compounds with boiling points of over 150°C.

5.- Oxalic acid and the furane refluxed for three hours gave low boiling unsaturated hydrocarbons with a boiling range of 110-125°C.

6.- The furane is stable to alkali permanganate solution.

With Formic Acid.

The hexadiene (75 gms.) was added to 55 gms. of 98 per cent formic acid. The mixture was stirred for 45 minutes but the two liquids remained immiscible and no apparent reaction would take place. The flask containing the mixture was placed in a water bath and the temperature of the bath raised slowly. On warming the mixture gradually became clear and at 79°C. complete mutual solubility took place. The water bath was kept at 85-90°C. for 20 minutes. The mixture was allowed to cool and a separation of a layer of oil took place. The formic acid was diluted and the oil which separated drawn off. This oil was washed several times with water and finally with weak sodium carbonate solution in order to remove the last traces of acid. It was then dried over calcium chloride. The crude oil thus obtained weighed 74 gms.

In order to critically examine this oil as to the presence of any cyclic compounds, it was distilled into numerous small fractions in a modified Podbielniak column, having an efficiency of 12-15 plates under actual operating conditions. The constants of each fraction were determined in order to detect the possible presence of any cyclic compounds.

The oil was divided into two parts and distilled at atmospheric pressure.(x)

Lot 1.-

Fraction	Quantity cc.	Boiling Point °C.	Refractive Index 25°C.
1	1.8	up to 106	1.4271
2	4.9	106-108	1.4250
3	1.8	108-111	1.4261
4	5.3	111-111	1.4342
5	4.5	111-116	1.4343
6	1.0	116-124	1.4530
7	5.6	124-129	1.4584
8	0.9	129-143	1.4295
9	4.5	143-150	1.4286
10	8.5	166-167	1.4300
11	1.0	167-156	1.4265
12	0.1	156-154	1.4265
Residue	3.5		1.4620

Lot 2.-

1	1.0	106-110	1.4235
2	8.8	110-111	1.4260
3	7.5	111-113	1.4290
4	1.0	113-124	1.4475
5	5.0	124-126	1.4600
6	1.0	126-155	1.4338
Residue	30.0		1.4390

(x) In all the following distillation data, the constants will be given in this order, i.e. the first column indicating the fraction number, second column quantity of fraction in c.c., third column boiling point in °C., etc.

In order to obtain a sharper separation, the fractions 1, 2, 3, 4, 5, of Lot 1 and fractions 1, 2, 3, 4, of Lot 2, were combined and redistilled at atmospheric pressure.

Lot 3.-

1	0.3		1.4256
2	0.4		1.4210
3	0.6		1.4184
4	0.5		1.4220
5	3.1	110-113	1.4240
6	8.0	113	1.4240
7	2.2	113	1.4258
8	0.8	113	1.4260
9	6.1	113	1.4275
10	5.1	113-113.5	1.4290
11	1.6	113-110	1.4296
Residue	3.0		1.4510

Lot 4.- The fractions 4-11 inclusive of lot 3 were redistilled.

1	0.5	up to 110	1.4250
2	0.8	110-112	1.4170
3	1.9	112-113	1.4242
4	7.4	113	1.4260
5	6.2	113-113.5	1.4262
6	3.8	113.5	1.4261
7	2.0	113.5-114	1.4270
8	0.9	113	1.4270
Residue	4.0		1.4302

It is seen that the hexadiene treated with 98 per cent formic acid as described above has its low boiling fractions, namely Lot 1 fractions 1, 2, 3, 4, 5, and Lot 2 fractions 1, 2, 3, 4, of unchanged hexadiene. Out of a total of over 36 cc. only about 1.5 cc. of the low boiling fractions were unaccounted for and the refractive indices of these indicated that they could not be of a cyclohexene or cyclopentene structure.

The residues consisting of 6-7 cc. in volume were too viscous and brownish for further examination. Considering the fact that the cyclic compounds have about the same boiling points but differ in refractive indices and densities, the above residues were in all probability polymerized products of the hexadiene, brought about by heating during the distillation. Thus about 45 per cent of the product consisted of unchanged hexadiene.

Lot 5.- The higher boiling fraction of Lot 1 and Lot 2 were combined except for fraction 10 of Lot 1 and distilled.

1	top layer	0.7	up to 90	1.4480
	bottom layer	0.3		1.3772
2		4.3	90-111	1.4285
3		2.0	111	1.4307
4		2.0	111-119	1.4361
5		0.6	119-126	1.4580
6	top layer	7.7	126-127.5	1.4700
	bottom layer	0.3		
7		1.4	127.5	1.4539

At this point fraction 10 of lot 1 was added to the distilling flask, a vigorous boiling took place and the distillate temperature went down,

8		4.0	111	1.4217
9	top layer	2.0	111	1.4370
	bottom layer	0.3		
10		4.8	111-166	1.4330
11		7.6	167-168	1.4330
12		5.0	168-172	1.4310
13		2.7	160-152	1.4250
Residue		4.5		1.4862

The fraction boiling near 111°C. had a strong formic acid odour and the lower layer consisted of formic acid. Apparently the formates were decomposing upon distillation.

Lot 6.- Redistilled fraction 5, 6, 7, of Lot 5.

1	1.3	up to	125	1.4430
2	0.5		125-130	1.4604
3	0.6		130-132	1.4707
4	3.5		132-133	1.4770
5	0.2		132	1.4778

At this point fraction 10, 11, 12, 13, 14, of Lot 5 were added to the distilling flask,

6 top layer	2.5	111	1.4450
bottom layer	1.0		1.3790
7	1.0	111-127	1.4525
8	2.8	127-166	1.4470
9	1.3	166-169	1.4345
10	5.4	169-172	1.4338
11	3.7	172	1.4338
12	0.8	172	1.4310
Residue			1.3755

Lot 7.- Redistilled fraction 9-13 inclusive of Lot 6.

1	2.1	up to	100	1.4320
2	0.7		100-111	1.4264
3	2.0		111-172	1.4330
4	4.6		172	1.4336
5	0.2		171	1.4304
Residue	2.5			1.4295

Here again we have no clue as to the presence of any cyclic compounds. We have the formate decomposing to the original hydrocarbon and formic acid. Apparently some tertiary alcohol is also formed.

Lot 8.- All the low boiling fractions were collected and redistilled. These included fractions 1, 2, 3, 4, 8, 9, of Lot 5. fractions 1, 2, 3, 6, 7, of Lot 6 and fractions 1, 2, of Lot 7.

1 top layer	1.7	up to 90	1.4350
bottom layer	1.5		1.3755
2	0.8	90-110	1.4225
3	1.5	110-113	1.4258
4	4.3	113-116	1.4307
5	2.4	116-120	1.4350
6	0.6	120-124	1.4475
7	2.1	124-130	1.4682
8	1.8	134-down	1.4380
Residue	3.2		1.4390

This concludes the examination of all the fractions of the product of treatment of hexadiene with 98 per cent formic acid. The fraction boiling at 113°C. exhibited all the physical properties of the original hexadiene. A pure sample of this fraction was saturated with bromine using carbon tetrachloride as a solvent. The carbon tetrachloride was allowed to evaporate and crude crystals were thus obtained. Recrystallization gave a m.p. of 96-98°C. A sample of the original pure hexadiene was treated similarly and the crystals obtained had a m.p. of 90-95°C. Recrystallization brought the m.p. to 94-97°C. A mixed m.p. was taken which gave a m.p. of 96-98°C.

The fractions 4 and 5 of lot 6 have an unusually high refractive index suggestive of conjugation. The density at $\underset{4}{24}$°C. was found to be 0.7586. It had a m.p. of 11.4°C. The physical constants indicate clearly that the compound was diisocrotyl.

Another substance which had formed upon the treatment of the hexadiene with formic acid was present in pure form in fraction 3 and 4 of lot 7. This was hydrolyzed and found to be the monoformate. Density for the formate at $\frac{21}{4}$ was 0.8829. Saturation indicated the presence of one double bond (actual bromine absorption was 90 per cent of theory).

A second experiment was carried out with formic acid. It appeared that in the former experiment the reaction was not allowed to go to completion since considerable amount of unchanged hexadiene was present in the reaction product.

Hexadiene (140 gms.) was added to 260 gms. of formic acid (98 per cent) and stirred vigorously. The flask containing the mixture was placed in a water bath and the temperature of the bath slowly raised to 85-90°C. and kept there for one hour. As before, when the bath temperature reached 70°C. the hexadiene dissolved in the acid. However, after about seven minutes an oil started separating out and in spite of vigorous stirring remained insoluble throughout the whole reaction. After half an hour the volume of the separated oil remained constant. After one hour the mixture was allowed to cool and the insoluble oil drawn off. On dilution of the acid an oil was separated out. Both oils were washed free of acids with dilute sodium carbonate solution and dried over calcium chloride. The formic acid insoluble portion weighed 75 gms. and the acid soluble portion 55 gms.

The formic acid insoluble oil was distilled.

Lot 1.-

1	2.5	up to 109	1.4230
2	7.0	109-112	1.4125
3	2.0	112	
	1.0	112-123	
	1.2	129-130	1.4341
4	8.0	130-131	1.4636
5	6.5	131-133	1.4680
6	7.0	132	1.4732
7	6.2	132-130	1.4760
8	1.5	130	1.4750

The residue consisted of a heavy yellowish oil and was distilled 2 mm. pressure.

Lot 2.-

1	2.5	57-65	1.4706
2	4.0	80	1.4724
3	8.0	80-83.5	1.4758
4	8.5	83-84.5	1.4800
5	6.3	84.5-86	1.4858
6	1.0	89-99	1.4820
7	1.0	99-131	1.4820
8	2.3	131-134	1.4860
9	0.6	134-143	1.4932
Residue	1.0		1.4990

It appears that in lot 1 the first three fractions are unchanged hexadiene while the rest is di-isocrotyl. In lot 2 a new type of high boiling compound is present.

Lot 3.- Fractions 2, 3, 4, 5, of lot 2 were redistilled at 2 mm. pressure.

1	1.4	72-77	1.4720
2	1.8	77-79	1.4762
3	6.5	79-81	1.4762
4	6.8	81-83	1.4790
5	1.3	83-84	1.4848
6	1.0	85-88	1.4870
Residue			1.4860

Lot 4.- Fractions 6, 7, 8, 9, of lot 2 were redistilled at 2 mm. pressure.

1	1.7	up to 107	1.4838
2	0.7	107-129	1.4843
3	0.8	129-135	1.4860
4	0.9	135-128	1.4890
5	0.1		1.4900
Residue	0.3		1.4960

It appears that both Lot 3 and lot 4 have at least two different substances.

Lot 5.- The formic acid soluble portion which weighed 55 gms. was distilled at atmospheric pressure.

1	2.9	up to 108	1.4095
2	1.5	108-109	1.4080
3	8.0	111-112	1.4065
4	8.0	111	1.4065
5	8.0	111-112	1.4060
6	8.5	112-128	1.4060
7	1.3	128-129	1.4067
8	6.7	129-130	1.4534
9	3.8	130-131	1.4600
10	7.6	131	1.4700
11	1.4	131-132	1.4700
Residue	10.0		1.4700

Lot 6.- Collected all the impure di-isocrotyl fractions and distilled them at atmospheric pressure.

1	2.5	112-113	1.4130
2	3.0	113-125	1.4210
3	4.2	125-130	1.4527
4	8.0	130-132	1.4667
5	8.3	132-133	1.4725
6	8.0	133-133.5	1.4762
7	5.0	133.5-134.5	1.4788
8	0.8	134 down	1.4763
9	2.8		1.4782

Fractions 5-9 were taken as pure di-isocrotyl for experimental purposes.

From the above cases it appears that the reaction had gone to completion as there was very little unchanged hexadiene and no formate. The low boiling fractions consisted of the furane identical with the main product of the phosphoric acid treatment of the hexadiene. The next higher boiling fraction was the isomer of hexadiene namely di-isocrotyl. Besides these, there were apparently four high boiling products, in all probability polymerization products of di-isocrotyl. These high boiling fractions were examined as to their physical constants.

Fraction 2 and 3 of lot 3, density $\frac{25}{4}$ 0.8414

Iodine number, Hanus method 270(i.e. 2.36 moles I_2 per $C_{16}H_{30}O$)

Wij's method 323 (i.e. 2.61 moles I_2 per $C_{16}H_{30}O$)

C and H analysis H 11.8% C 81.8%

Fraction 4 of lot 3, density $\frac{25}{4}$ 0.8416

Iodine number by Hanus method 278 (i.e. 2.41 moles I_2 per $C_{16}H_{30}O$)

Wij's method 298, i.e. 2.6 moles I_2 per $C_{16}H_{28}$

Fraction 5 of lot 3, density $\frac{25}{4}$ 0.8419

Iodine number by Hanus method 288 (i.e. 2.5 m. 2 per $C_{16}H_{30}O$)

Iodine number by Wij's method 288 (i.e. 2.5 moles I_2 per $C_{16}H_{30}O$)

C and H analysis H 12.71% C 86.54%

Fraction 1 and 2 of lot 4, density $\frac{25}{4}$ 0.8805

Iodine number by Hanus method 199 (i.e. 1.7 moles I_2 per $C_{16}H_{30}O$)

Iodine number by Wij's method 210 (i.e. 1.8 moles I_2 per $C_{16}H_{30}O$)

Fraction 4 and 5 of lot 4, density $\frac{25}{4}$ 0.8494

Iodine number by Hanus method 221 (i.e. 1.9 moles I_2 per $C_{16}H_{30}O$)

Iodine number by Wij's method 275 (i.e. 2.4 moles I_2 per $C_{16}H_{30}O$)

The source of the above high boiling fractions was obscure especially in view of the fact that di-isocrotyl has been reported as being incapable of polymerization(199).

Polymerization of Di-isocrotyl.- Redistilled di-isocrotyl (15 cc.) was added to 80 gms. of 98 per cent formic acid and stirred vigorously. The flask containing the mixture was placed in a water bath which was kept at 95°C. for one hour and 45 minutes. Some oil separated out which at the end of the reaction was drawn off. It measured 13 cc. Dilution of formic acid yielded only about 2 cc. of oil.

The 13 cc. of oil was fractionated at 2 mm. pressure.

Fraction	Temperature °C.	Quantity cc.	Refractive Index 25°C.	Density 25/4	Iodine No. Wij's Method
1	76	1.7	1.4706	0.8150	
2	76-76.5	1.7	1.4766	0.8450	277.5
3	77.5-78	1.2	1.4854		
4	82-82.5	1.8	1.4882	0.8442	274.0
Residue		1.5			

These values are somewhat similar to the values obtained in the previous experiment and it appears that di-isocrotyl contrary to generally held ideas is capable of undergoing polymerization.

An attempt was made to purify the high boiling fractions by redistillation.

Lot 7.- Redistillation of fractions 2 and 3 of lot 3 at 0.5 mm. pressure.

1	0.5	67	1.4700	
2	0.8	67-69	1.4684	
3	1.3	71-71.5	1.4704	430
4	0.7	73-76	1.4740	278
5			1.4816	
Residue			1.4882	

Lot 8.- Redistillation of fraction 5 lot 3 at 0.5 mm. pressure.

1	1.0	77	1.4785	
2	1.7	77	1.4821	
3	2.8	77	1.4824	d 0.8482 I_{no} 306
4	1.1	77-78	1.4878	
Residue	1.2		1.4895	

C and H analysis of fraction 2 plus three C 87.8% H 12.8%.

The polymers of di-isocrotyl are rather interesting. Unfortunately no idea of their nature could be gained from the above data. The fact that some of the fractions contain oxygen, supports the presence of furane type compounds.

<u>Further Experiments with Dimethallyl, Using Longer Periods of Time</u>.- Dimethallyl (25 gms.) was added to 75 cc. of 85 per cent phosphoric acid and the mixture stirred vigorously on the steam bath for 24 hours. At the end of this period, a very dark viscous oil was obtained which contained considerable semi-solid lumps. In view of the fact that the mixture consisted of high polymeric substances, no attempt was made to fractionate it.

In another experiment 50 cc. of dimethallyl was added to 150 cc. of 50 per cent sulphuric acid. The mixture was stirred vigorously for three hours. At the end of this period, the mixture was of a very dark reddish colour. The oil obtained was washed free of acids and dried with sodium carbonate. Distillation gave the following results.

1	1.0	up to 125	1.4416	Contains oxide as evidensed by odour and some diisocrotyl
2	0.9	125-132	1.4487	
3	0.8	132-140	1.4530	

Pressure lowered to 4 mm. Hg.

4	2.3	up to 80	1.4595	
5	1.5	80-90	1.4645	
6	3.0	90-102	1.4727	
7	6.8	102-106	1.4808	d^{18}_{4} 0.8311
8	2.8	106-108	1.4837	
9	1.8	108 down	1.4908	

Fraction 8 when diluted in chloroform gives a beautiful permanent purplish blue colour upon addition of a few drops of bromine solution. Bromine number as determined by the bromide-bromate method indicated the presence of 2.2 double bonds per two molecules of octadiene.

In view of the fact that 50 per cent sulphuric acid causes mostly polymerization it was decided to repeat the experiment using 25 per cent sulphuric acid. About 50 cc. of dimethallyl was added to 150 cc. of 50 per cent sulphuric acid and the mixture stirred vigorously on the steam cone for 24 hours. At the end of this period the insoluble oil was drawn off and washed free of acids, the dry oil was distilled at atmospheric pressure. The constants were taken at 18°C.

1	2.5	up to 112	1.4068	0.8122
2	4.0	112-115	1.4100	0.8042
3	4.5	115	1.4130	0.8042
4	4.6	115-115.2	1.4134	0.8044
5	4.1	115.2-116.2	1.4140	0.8015
6	4.0	116.2-117	1.4187	0.8005
7	4.4	117-119	1.4345	0.8003
8	4.4	119-122	1.4245	0.7991
9	3.0	122-131	1.4420	0.7975
10	0.8		1.4524	

All of the above fractions had a powerful odour of the oxide. Bromine number of each fraction was of the order of 0.1 indicating the presence of a little unsaturated product.

All the above fractions were combined and subjected to hydrogenation using platinum black catalyst. Reduction of the unsaturated compounds present took place with great ease. About one tenth mole of hydrogen was absorbed indicating the presence of about 5.5 gms. of dimethallyl.

In order to verify the absence of any carbocyclic compounds, the hydrogenated mixture was shaken with twice its volume of cold concentrated sulphuric acid. The mixture was allowed to stand overnight. The next day about 12 cc. of an oil had separated out. This was collected, washed free of acids and dried with potassium carbonate. Two thirds of the oil (about 7 cc.) was distilled and the following fractions collected.

1	0.3	up to 107	1.3950	d^{18}_{4} 0.6986
2	1.8	107-109	1.3942	
3	0.7	109-110	1.3935	

No other fractions could be collected, the remainder consisting of high boiling residues. It is apparent that the above fractions consist of 2,5-dimethyl, hexane, which has been reported to have the following constants b.p. 109.3°C., d^{20}_{4} 0.6969 and n^{20}_{D} 1.3930. The absence of any saturated cyclic products indicates that no cyclization had taken place upon treatment of dimethallyl with 50 per cent sulphuric acid.

II. Cyclization Experiments with 2,6, Dimethyl-Heptadiene-2,5.

Preparation of 2,6,dimethyl-heptene-5-ol-2.

Methyl heptenone (obtained from Fritszche Bros., Canada) was purified by distillation and the fraction boiling at 171-172°C. (769 mm. Hg.) taken as pure material. It had a refractive index of 1.4480 at 25°C.

The heptenol was prepared by the Grignard reaction of MeMgCl upon methyl heptenone. The MeMgCl was prepared in the usual manner using commerical MeCl gas from a cylinder. The reaction was initiated by the addition of several drops of methyl iodide and methyl chloride was passed into the magnesium ether mixture under 2-3 inches mercury pressure. It was found necessary to keep the ether cold in order to increase the solubility of MeCl in ether and thus increase the rate of the reaction. The reaction was considered completed when all the magnesium had dissolved. Naturally a considerable excess of MeCl was present, dissolved in the ether, but this was expelled by gentle refluxing of the ether.

Two moles of MeMgCl were thus prepared and 225 gms. of pure methyl heptenone added to the grignard at a constant rate so that a gentle refluxing of the ether took place. The reaction mixture was allowed to stand overnight and then decomposed with ammonium chloride solution. Finally hydrochloric acid was added to free all the heptenol and dissolve the magnesium salt.

The heptenol thus obtained was washed free of acids and dried over calcium chloride. It was distilled in a Claisen flask at 68 mm. pressure. Although practically all of it distilled at 112°C. apparently some dehydration took place as evidensed by the formation of a few droplets of water in the initial fractions and also by the regular variations in the constants.

Fraction	Volume in cc.	Refractive Index	Density
1	22	1.4445	0.8280
2	50	1.4470	0.8472
3	58	1.4489	0.8525
4	50	1.4488	0.8544
5	55	1.4494	0.8657
6	10	1.4495	

Since in the cyclization experiments the heptenol and heptadiene behave in similar manner, no attempt was made to prepare the heptadiene, instead, the heptenol was used in all the cyclization experiments.

Cyclization with 85 per cent Phosphoric Acid.- Ten cc. from each of the fractions 2, 3, 4, 5, were taken (making a total of 40 cc.) and added to 160 cc. of 85 per cent phosphoric acid. The flask containing the mixture was placed in a water bath and the temperature raised slowly. At about 70°C. solubility took place. The reaction was allowed to proceed for 15 minutes. An insoluble layer of oil separated out. The acid mixture was allowed to come to room temperature and the acid insoluble layer drawn off. It was measured and found to be 27 cc. in volume. The phosphoric acid was diluted and the oil which separated out measured 6 cc. in volume. It was noteworthy that the odour of the latter oil was camphoraceous.

The phosphoric acid insoluble oil was distilled at atmospheric pressure. Unfortunately during the distillation the flask came off and some of the liquid was lost.

1	3.5	137.5	1.4450	0.7975
2	6.7	137.5-138.5	1.4450	0.7975
3	4.0	138.5-down	1.4440	0.7973

at 15 mm. pressure

4	1.5	97	1.4497	0.8273
5	1.8	95	1.4627	0.8560
6	0.6		1.4725	

The first three fractions appeared to be one substance. They were combined and redistilled at atmospheric pressure.

1	1.0	up to 137	1.4420	
2	2.7	137-138	1.4431	
3	7.5	138	1.4423	0.7972
4	0.5	138 down	1.4430	

The fraction 3 was taken as the pure compound. The physical constants indicate clearly that it is cyclogeraniolene.

The nitrosite of cyclogeraniolene was prepared in the following manner. Two cc. of ethyl nitrate and 1 cc. of acetic acid were cooled in an ice water mixture and 2 cc. of cyclogeraniolene added. Then 1.5 cc. of nitric acid was added dropwise with constant stirring. Crystals were thus obtained which were recrystalized from alcohol. The melting point of the nitrosite was 101°C.

The oil obtained from the dilution of phosphoric acid appeared to be of a different nature. The amount obtained after drying was too small to warrant an examination. It had a camphoraceous odour, refractive index of 1.4480 and density of 0.8265 at 25°C.

The odour of this oil suggested that it might be the oxide. Several small scale experiments were run and it was noticed that when the phosphoric acid- heptenol mixture was diluted two or three minutes after solution a strong camphoraceous oil resulted. Again as in the previous experiments with hexadiene, a phosphate was forming which yielded the oxide on dilution.

Heptenol (25 cc.) was added to 100 cc. of 85 per cent phosphoric acid. The mixture was shaken to affect rapid solution and allowed to stand about three minutes after solution. It was then diluted. A strongly camphoraceous oil resulted. Upon distillation at atmospheric pressure a fraction was obtained which distilled at 140-145°C. This fraction absorbed very little bromine. It was treated with 2 per cent permanganate solution till it no longer caused any decolourization. The saturated product thus obtained was redistilled.

1	0.6	up to 142	1.4284	
2	5.5	142-142	1.4282	0.8379
3	1.6	142 down	1.4287	

The fraction 2 represents the pure oxide.

<u>Cyclization experiments using sulphuric acid</u>.-

Preliminary small scale experiments indicated that strong sulphuric acid caused resinification. Consequently a 70 per cent sulphuric acid was used.

Heptenol (25 cc.) was added to 100 cc. of 70 per cent sulphuric acid. Solution took place readily and after a few minutes an oil separated out. The mixture was shaken for two hours and then the insoluble oil was drawn off.

Distillation at atmospheric pressure gave the following results.

Fraction	Quantity cc.	Boiling Point °C.	Refractive Index 25°C.	Density
1	1.8	up to 137	1.4464	0.8037
2	2.4	137-140	1.4486	0.8077
3	1.2	140-142	1.4500	0.8156
4	1.4	at 16 mm. 82-92	1.4587	0.8535
5	1.3	at 16 mm. 92-106	1.4760	0.8709

6	1.3	at 8 mm.	up to 135	1.4842	0.8811
7	2.8	at 8 mm.	135-155	1.4884	0.8870

Bromination Data

Fraction	Wt. in gms.	Br. abs. in gms.	Unsaturation (double bonds)
1	0.1934	0.32	1.25
2	0.1284	0.20	1.20
3	0.1304	0.17	1.00
4	0.1334	0.10	0.58
5 plus 6	0.1202	0.062	0.40
7	0.1076	0.036	0.26
8	0.1620	0.072	0.44

It is thus seen that sulphuric acid gives mainly the cyclogeraniolene and also high boiling products.

Cyclization experiments with the saturated 2,6,dimethyl-heptanol-2.

Forty gms. of the heptenol was hydrogenated using platinum black catalyst. Hydrogenation took place readily and the resultant heptanol was found to be saturated to bromine and would not decolourize permanganate solution.

It was distilled at 50 mm. pressure and had a b.p. 97-98°C. n_d^{25} 1.4250, and d_4^{25} 0.8145.

Ten cc. of the saturated alcohol were added to 50 cc. of 98 per cent formic acid and allowed to stand at room temperature for 12 hours. An oil separated out which was drawn off, washed free of acids and distilled at atmospheric pressure. During distillation formic acid collected in the distillate fractions indicating as in many previous similar cases, that a formate had formed which was decomposing during distillation. Decomposition of the formate yielded the hydrocarbon 2,6, dimethyl-heptene-2 which had a b.p. 139°C. $n\frac{25}{4}$ 1.4200 and $d\frac{25}{4}$ 7.4478.

A similar experiment was carried out using the same quantities but employing 85 per cent phosphoric acid. In this case a very uniform product of the above hydrocarbon was obtained. Bromination indicated the presence of one double bond.

III. Cyclization Experiments with 2,7-Dimethyl-Octadiene-2,6.

Preparation of 2,7-dimethyl-octandiol-2,7.

This diol is most conveniently prepared by the action of MeMgCl of diethyl adipate.

The MeMgCl was prepared in the usual manner. Six and a half moles of magnesium turnings were placed in a 12 liter flask and the grignard prepared by passing into the ether a continuous stream of commercial MeCl till all the magnesium turnings were dissolved. The procedure employed was the same as the one described in the preparation of the heptenol. After all the magnesium turnings had dissolved 300 gms. (1½ moles) of redistilled diethyl adipate were added at such a rate that a constant refluxing of the ether took place.

The semi solid mass was allowed to stand several days and then decomposed with ammonium chloride solution. The magnesium salt was dissolved by the addition of hydrochloric acid.

A reddish coloured semi solid mass separated. The glycol was purified from the reddish oil by washing it repeatedly with cold ether. The glycol thus obtained weighed 125 gms. and consisted of the hydrated form with a m.p. of 59-60°C. The ether portion yielded a further 40 gms. of crude glycol. The reddish oil containing some glycol was kept for future investigation.

Cyclization experiments were carried out with the glycol, since in an acid medium there is constant hydration-dehydration taking place, thus making it immaterial whether one starts with the glycol or the diene.

<u>Treatment of the glycol with phosphoric acid 85 per cent</u>.

The glycol (25 gms. of the hydrated form) was placed in 150 cc. of 85 per cent phosphoric acid. It would not readily dissolve in the acid so a water bath was employed and the temperature raised to 65-75°C. Soon after solution had taken place an oily layer separated out which would not dissolve in the acid in spite of vigorous stirring. The insoluble layer was drawn off and washed free of acids. It measured about 13 cc. It was subjected to distillation at atmospheric pressure after being dried over calcium chloride.

			1.4408	
1	0.8	145-146	1.4436	0.7871
2	2.0	146-148	1.4463	0.7942
3	1.3	148-152	1.4504	0.8001
4	3.5	152-156	1.4517	0.8002
5	1.6	156 down	1.4606	0.8145
Residue	2.7			

Bromination Data

Fraction	Wt. in Gms.	Bromine Abs./ Gm.	Unsaturation c=c.
1	0.1260	0.31	2.13
2	0.1588	0.39	2.11
3	0.1578	0.41	2.23
4	0.1760	0.46	2.25
5	0.1378	0.36	2.25
Residue	0.1750	0.30	1.48

The phosphoric acid on dilution yielded no appreciable amount of oil.

Treatment of the glycol with 85 per cent formic and acetic anhydride.

The glycol (25 gms. Hydrated) was added to a mixture of 30 gms. of 85 per cent formic acid and 25 gms. of acetic anhydride. It dissolved readily and the solution was kept in a water bath at 75-85°C. for one hour. The acid mixture was then diluted and an oil separated out measuring about 10 cc. Upon ether extraction of the acid solution several gms. of a semi solid material was recovered. It consisted partly of the anhydrous glycol. The 10 cc. oil was washed free of acids and distilled.

1	0.3	up to	147	1.4474	
2	1.5	top layer	147-153	1.4460	0.7805
	0.2	lower layer			
3	1.4	top layer	153-159	1.4400	0.7908
	0.2	lower layer			
4	1.2		159-192	1.4428	0.8273
5	0.2		192-193	1.4451	

Bromination Data

2	0.1484	0.325	1.88
3	0.1410	0.30	1.84
4	0.1636	0.25	1.32
5	0.1688	0.225	1.15

The initial crude oil had a sweet linalool-geraniol odour. It appears that the mono formate and mono acetate were formed which partially decomposed upon distillation yielding the diene. This case is very much similar to the previous cases. It is rather curious that one hydroxyl group dehydrates while the other esterifies. The original oil had a density of 0.8504 and bromination indicated the presence of one double bond.

Obviously in the above experiments the reaction was not allowed to go to completion. A similar experiment was carried out using 25 gms. of hydrated glycol, 30 gms. of 85 per cent formic acid and 55 gms. of acetic anhydride and the mixture was allowed to boil under reflux for one hour. As in the previous case an insoluble oil soon separated out. Vigorous boiling caused intimate mixture of the oil with the acid.

The insoluble oil was drawn off, washed free of acids with dilute sodium carbonate solution and dried over calcium chloride. Distillation yielded the following results.

1	1	145	1.4440	0.7908
2	1.7	145-148	1.4444	0.7908
3	4.5	148-153	1.4497	0.7992
4	2.6	153-160	1.4458	0.7994
5	0.3	160-187	1.4506	
Residue	2.0		1.4690	

Bromination Data

1 plus 2	0.1676	0.375	1.93
3	0.1632	0.425	2.24
4	0.1740	0.475	2.35

Treatment of the glycol with acetic anhydride.

The hydrated glycol (22 gms.) was added to 110 gms. of acetic anhydride. Solution took place with great ease. A few minutes after solution a small portion of the mixture was diluted. A solid separated out which proved to be the anhydrous glycol. Hence the first step was the formation of anhydrous glycol. The main solution was allowed to stand three days and then diluted. An oil separated out which was washed acid free and dried over calcium chloride. It had a sweet linalool-geraniol odour. Distillation at 10 mm. yielded.

1	0.4	up to 102	1.4415	
2	1.9	102-112	1.4406	0.9210
3	3.5	112-117	1.4400	0.9271

This experiment was repeated using a larger quantity of materials. About 40 gms. of the hydrated glycol was added to 200 gms. of acetic anhydride and allowed to stand 48 hours. The acid was diluted and the separated oil washed free of acids and dried over calcium chloride. It was distilled at 11 mm. pressure.

1	0.7	104	1.4390	
2	5.0	104-105	1.4400	0.9233
3	2.0	105-109	1.4395	
4	6.5	109	1.4394	0.9265
5	1.8	109 down	1.4390	

Saponification indicated that the above fractions consisted of the mono acetate in the impure form. Both saponification and C and H analysis indicated about 86 per cent esterification.

Treatment of the glycol with aqueous 5 per cent sulphuric acid.

About 15 gms. of the glycol was added to 100 cc. of water containing 5 cc. of concentrated sulphuric acid. Although the glycol was insoluble in this mixture, vigorous boiling caused intimate mixture of the glycol with the acid. Boiling was continued for 1 hour and then the oil was drawn off and distilled at atmospheric pressure.

1	0.3	up to	151	1.4467	
2	0.4		151-153.5	1.4482	
3	1.5		153.5-157	1.4500	0.7814
4	1.7		157-160	1.4502	0.7804
5	1.2		160-192	1.4490	0.7973
6	1.2		192 down	1.4490	0.8384

Bromination Data

1 plus 2	0.1474	0.30	1.76
3	0.1844	0.39	1.82
4	0.1312	0.27	1.77
5	0.1342	0.21	1.35
6	0.1668	0.18	0.94

Thus dilute sulphuric acid caused partial and total dehydration.

Experiments with dimethyl octadiene.

It will be noted that all the above experiments were carried out using the glycol. It was thought advisable to repeat some of the experiments using the diene. The accumulated reddish oil from the grignard reaction in the preparation of the glycol was found to be partially dehydrated glycol. A distillation at atmospheric pressure yielded the pure 2,7-dimethyl-octadiene-2,6, b.p. 164°C. density at $\frac{25}{4}$ 0.7687 and refractive index 1.4436 at 25°C.

Ten cc. of the above hydrocarbon was added to 50 cc. of 98 per cent formic acid and boiled vigorously for one hour. The oil would not dissolve in the acid. At the end of one hour the oil was washed free of acid and dried over calcium chloride. Examination revealed that it had undergone practically no change.

Ten cc. of the hydrocarbon was added to a mixture of 10 cc. 85 per cent phosphoric and 90 cc. of acetic anhydride. Solution took place and mixture was allowed to stand at room temperature for one hour. The acid was then diluted, the separated oil washed free of acids and dried over calcium chloride. It was distilled at atmospheric pressure.

1	0.8	up to 153	1.4448	
2	1.0	153-157	1.4457	0.8005
3	0.5	157-158	1.4474	
4	0.8	158 down	1.4500	

Bromination Data

1	0.3790	0.89	2.02
2	0.3200	0.85	2.29
3	0.2700	0.67	2.15

In another experiment 15 cc. of anhydrous glycol was added to a mixture of 50 cc. of 85 per cent phosphoric acid and 350 cc. of 95 per cent ethyl alcohol. Previous experiments had indicated that in this proportion the above amount of the hydrocarbon was soluble. The use of a smaller amount of alcohol resulted in the separation of the hydrocarbon.

The above mixture was allowed to stand at room temperature for two weeks. At the end of two weeks the solution was diluted and about 5 cc. of acid free dried oil obtained. It was distilled at atmospheric pressure.

1	1.3	152-155	1.4463	0.8002
2	2.0	155-157	1.4487	0.8080
3	1.3	157 down	1.4497	0.8172

Bromination Data

1	0.2815	0.68	2.07
2	0.3081	0.715	2.01
3	0.3235	0.85	2.27

Further Experiments with 2,7-Octandiol-2,7-Dimethyl.

The glycol (25 gms.) was stirred vigorously over the steam bath for 36 hours with 75 cc. of 98-100 per cent formic acid. At the beginning of the reaction an oil separated out which gradually passed into solution. At the end of the above period the mixture was diluted, the oil washed free of acid and dried over sodium carbonate.

Distillation of the oil under 0.5 mm. of pressure gave the following results:

Fraction	Quantity cc.	B.p. °C.	Refr. Index 25°C.	Density 25°_{4}	Bromination (c=c Present)
1	1.9	up to 35	1.4503	0.8104	1.76
2	2.5	35	1.4520	0.8119	1.77
3	5.6	35-36	1.4530	0.8130	1.75
4	2.5	36-37	1.4557	0.8180	1.74
5	1.7	37-38	1.4608	0.8268	1.80

A similar experiment was carried out using 25 gms. of the anhydrous glycol and 75 cc. of 85 per cent phosphoric acid. The mixture was stirred on the steam cone for 24 hours.

At the end of this period the mixture was diluted with water and the oil thus obtained washed free of acid and dried over sodium carbonate. Only a small amount of oil was obtained and this was distilled at 0.5 mm. pressure.

1	3.0	36	1.4542	0.8169	1.70
2	0.8	37	1.4600	0.8278	1.72
3	0.6	37	1.4638		1.80

A third and very similar experiment was carried out using 25 per cent sulphuric acid. The oil obtained at the end of 24 hours was somewhat greater in quantity than in the case of phosphoric acid, but apparently a large portion had oxidized and was thus lost. The acid free dried oil was distilled at 0.5 mm. pressure.

1	2.8	up to 35	1.4487	0.8086	1.8
2	3.1	35-35.5	1.4503	0.8100	1.75
3	2.2	35.5-36	1.4543	0.8094	1.9

The above experiment was repeated using 50 per cent sulphuric acid. Distillation of the acid free dry oil at 0.5 mm. pressure gave the following fractions.

1	3.1	up to 35	1.4502	0.8100	1.8
2	3.4	35-35.5	1.4526	0.8143	1.85
3	2.8	35.5-36	1.4568	0.8211	1.75
4	2.9	36-36.5	1.4592	0.8249	1.75
5	0.5	36.5-37	1.4624		1.8

It was decided to carry out a larger batch experiment. About 65 gms. of anhydrous glycol was added to 100 cc. of 98-100 per cent formic acid and the mixture heated on the steam cone for 66 hours, with vigorous stirring. At the end of this period the mixture was diluted with water (although most of the product separated out as an insoluble layer) and the oil washed free of acids and dried over sodium carbonate. Distillation at atmospheric pressure yielded the following results. The constants were determined at 20°C.

1	5.2	up to 154.5	1.4492	0.8133	1.99
2	4.3	154.5-155	1.4498	0.8133	1.97
3	4.0	155-155.5	1.4500	0.8135	1.96
4	4.3	155.5-156	1.4506	0.8145	1.93
5	4.1	156-156.5	1.4515	0.8164	1.86

The bromine number of fraction 2 and 3 was checked by the potassium bromide-potassium bromate method. It was found that this method yielded unreliable results, apparently being largely influenced by experimental conditions. Thus fraction 2 gave a bromine number of 2.01, but fraction 3 gave 1.73.

One cc. of fraction 3 was added to 9 cc. of conc. sulphuric acid and the mixture shaken violently for about ten minutes. On standing an insoluble oil separated. This oil had a refractive index of 1.4500 and was practically saturated to bromine, The remainder of sulphuric acid solution upon dilution gave an oil which had a refractive index of 1.4849. Addition of a few drops of bromine in carbon tetrachloride or chloroform gave an intense bluish purple colour which persisted indefinitely. It will be recalled that a similar phenomenon was encountered with the dimeric product of dimethallyl. Since such a phenomenon is common for the highly unsaturated compounds azulenes, one might suspect the presence of highly unsaturated compounds in our product. The separation of saturated compounds from the sulphuric acid solution is due to the so called hydropolymerization reaction.

Fractions 1, 2, 3, 4, of the above were combined and hydrogenated with platinum black catalyst. From previous experiments it had been found that glacial acetic was the most suitable solvent for this compound. Absorption of one molecule of hydrogen took place within five minutes, but all efforts to force the absorption of a second molecule of hydrogen failed. Similar results had been obtained in previous experiments. The hydrogenation product was washed free of acid, dried with potassium carbonate and distilled at atmospheric pressure. The following results were obtained, the constants being determined at 19°C.

Fraction	Quantity	B.p. $^{\circ}$C.	Refr.Index	Density	Bromination (c=c Present)
1	0.3	up to 161	1.4360		
2	4.0	161-161.5	1.4431	0.8090	0.25 (Approx).
3	3.6	161.5-162	1.4431	0.8092	0.20 (Approx).
4	1.4	162 down	1.4430	0.8096	

The above results were similar to the results obtained on hydrogenation of about 12 gms. of dienes obtained in treatment of the glycol with various acids as outlined in this section. In this case the hydrogenation was carried out in ether in order to eliminate the possibility of transformation of the hydrocarbon through the influence of glacial acetic acid. Absorption of one molecule of hydrogen took place readily but all efforts to carry it to completion failed. The resulting oil was distilled at atmospheric pressure and its constants determined (at 18°C).

1	1.2	up to 161	1.4460	0.8094	0.67
2	5.0	161-162	1.4468	0.8100	0.60
3	3.3	162	1.4476	0.8106	0.50
4	1.1	162 down	1.4469	0.8024	0.70

It is difficult to explain the results of hydrogenation without assuming the presence of some cyclic products.

Treatment of Tetrahydrolinalool with Formic and Phosphoric Acids.

In view of the fact that linalool is a naturally occurring substance, it was decided to try cyclization experiments with tetrahydrolinalool, hoping that an insight might be obtained into the mechanism of the cyclization reaction.

Linalool was catalytically hydrogenated. It was treated with dilute permanganate solution to remove any unsaturated constituents and redistilled. It had the following constants,

Ten cc. of tetrahydrolinalool was added to 50 cc. of 98 per cent formic acid and allowed to stand at room temperature for 12 hours. At the end of this period the acid was diluted, the oil washed free of acid and dried over calcium chloride. It was distilled at atmospheric pressure.

1	1.5	up to 158	1.4276	0.7523
2	2.6	158-164	1.4277	0.7523
3	1.6	164-168	1.4274	0.7523
4	0.9	168 down	1.4273	

An analogous experiment was carried out using 85 per cent phosphoric acid instead of 98 per cent formic acid. The resulting oil was distilled at atmospheric pressure.

1	3.0	159	1.4276	0.7521
2	3.1	159	1.4278	0.7521
Residue	0.4		1.4314	

It is obvious that in this case dehydration proceeded more smoothly yielding a more uniform product.

IV Experiments with Diallyl.

Allyl Chloride.- Commercial allyl chloride, obtained from Shell Development Company, was of a brownish colour with a strong garlic like odour. It was distilled at atmospheric pressure and the fraction boiling at 44-44.5°C. was taken as pure allyl chloride.

Coupling of the Allyl Chloride through the Grignard Reaction.- The usual type of Grignard reaction as described in detail in the preparation of 2,5-dimethyl, hexadiene-1,5 was carried out, using ten moles of magnesium, twenty moles of allyl chloride and 4.5 litres of dry ether. No trouble was experienced in the operation of a 12 litre flask and after the completion of the reaction the semi-solid mass was allowed to stand for twenty hours.

About three litres of a mixture of ether, allyl chloride and diallyl was distilled off. The remaining solid mass was dissolved in water and the separated ether portion was dried and added to the main ether fraction. The combined ether mixture was carefully fractionated in a column having an efficiency of 8-12 plates. The pure fraction of diallyl, boiling at 59.3-59.9°C., was collected, and was found to weigh 490 gms. This constitutes a yield of 67 per cent of theory. About 400 cc. of a mixture of ether, chloride and diallyl was also obtained having a boiling range of 34.5 - 59.3°C.

The pure diallyl was found to have the following constants, $d\frac{25}{4}$ 0.6871 $n\frac{25}{d}$ 1.4020.

Efforts to Cyclize Diallyl.-

(a).- With Sulphuric Acid.

1.- Diallyl (25 cc.) was added to a mixture of 15 cc. of concentrated sulphuric acid and 135 cc. of ethyl alcohol. The mixture was allowed to reflux over the steam cone for six hours. At the end of this period the mixture (water white) was diluted with water and the oil separated (21cc.) was washed free of acid with dilute sodium carbonate solution and dried over calcium chloride. It was found to be unchanged diallyl distilling at 59-60°C. A residue of about 1 cc. of high boiling oil remaining in the flask was not investigated.

2.- Diallyl (50 cc.) was added to a mixture of 100 cc. of glacial acetic acid and 2 cc. of concentrated sulphuric acid. The mixture assumed a light brownish colour which increased with time. It was refluxed over the steam cone for thirty hours. At the end of this period it was of a dark brownish colour. The mixture was diluted with water, and the separated oil washed free of acids and dried over calcium chloride. It is worth mentioning that dilution of the mixture gave an emulsion which separated with difficulty. This is probably due to the presence of sulphates and/or sulphonates. Distillation of the oil yielded about 10 cc. of unchanged diallyl and a thick, dark viscous, high boiling oil which was not investigated.

3.- Diallyl (50 cc.) was added to a mixture of 50 cc. of acetic anhydride and 2.5 cc. of concentrated sulphuric acid. The mixture quickly became dark in colour and soon small droplets of reddish oil began separating out. The mixture was refluxed over the steam cone for one hour. At the end of this period the mixture was diluted with water and the separated oil washed free of acid and dried over calcium chloride. Distillation yielded 40 cc. of unchanged diallyl and 2-3 cc. of a viscous residual high boiling oil which was not investigated.

In all of the above experiments there was no odour of allyl oxide detectable.

(b).- <u>With Phosphoric Acid</u>.

1.- Diallyl (50 cc.) was added to 400 cc. of 85 per cent phosphoric acid and stirred vigorously for four hours, at 55-65°C. At the end of this period the insoluble diallyl had gone partly into solution, giving a reddish mixture. Dilution of the mixture with water gave an oil which was washed free of acids and dried over calcium chloride. Distillation of this oil gave about ten cc. of a fraction boiling at 91-92°C. This fraction had a characteristic suffocating minty odour and was saturated to bromine. It was obviously the oxide. The remaining oil consisted of brownish high boiling oil which was not investigated.

2.- Diallyl (25 cc.) was added to a mixture of 15 cc. of concentrated phosphoric acid and 135 cc. of alcohol. The mixture was refluxed over the steam cone for 6 hours. At intervals of 1 hour, samples were taken and diluted to detect the presence of any oxide by its odour. None was detected. At the end of six hours the mixture was diluted with water and the separated oil (19 cc.) was washed free of acids and dried over calcium chloride. Distillation of this oil yielded pure diallyl to the last drop.

3.- Diallyl (50 cc.) was added to a mixture of 100 cc. glacial acetic acid and 5 cc. of 85 per cent phosphoric acid. The resulting mixture was refluxed for 30 hours. At the end of this period the mixture was still water white. It was diluted with water and the resulting oil was washed free of acid and dried over calcium chloride. It distilled at 59-60°C. to the last drop, indicating unchanged diallyl.

4.- Diallyl (75 cc.) was added to 200 cc. of 90 per cent phosphoric acid and the mixture stirred vigorously for 4 hours. The flask was heated over the steam cone so that a constant gentle refluxing of diallyl took place. At the end of 4 hours the refluxing of diallyl stopped indicating that it had undergone some sort of transformation. The mixture was diluted with water and the separated oil washed free of acid and dried over calcium chloride. Distillation yielded about 20 cc. of the oxide b.p. 91-92°C. and a brownish viscous high boiling oil. The latter was not investigated.

(c).- Using Formic Acid 98 per cent.

1.- Diallyl (50 cc.) was added to a mixture of 50 cc. of 98 per cent formic acid and 50 cc. of acetic anhydride, and refluxed over the steam cone for 30 hours. At the end of this period the mixture was still water white. The mixture was diluted with water and the oil obtained washed free of acid and dried over calcium chloride. It distilled at 59-60°C. to the last drop, indicating unchanged diallyl.

2.- Diallyl (30 cc.) was added to 150 cc. of 98 per cent formic acid and shaken vigorously for $3\frac{1}{2}$ hours at room temperature. At the end of this period the mixture was still water white and there was an insoluble layer of oil which was drawn off and washed free of acid and dried over calcium chloride. It measured 26 cc. and distilled at 59-60°C. indicating unchanged diallyl. Dilution of the formic acid with water yielded 2-3 cc. of a viscous high boiling oil which was not investigated.

Constants of 1,4-dimethyl-tetrahydrofurane.

The impure fractions of diallyl oxide were combined and treated with 2 per cent cold permanganate solution till there was no further decolourization. The resulting oil was dried over calcium chloride and distilled carefully through a modified Podbielniak column. The fraction boiling at 91.3-91.9°C. was taken as pure oxide and its constants determined. d_{4}^{25} 0.8226 n_{d}^{25} 1.4023.

Note.- In all the above experiments where no stirring or shaking was employed, the mixture was of a homogeneous nature.

SUMMARY

Four 1,5-hexadienes, namely diallyl, dimethallyl, geraniolene and 2,7-dimethyl-octadiene-2,6 were treated with various acids in order to determine the conditions necessary for the formation of cyclic products and study the mechanism of polymerization by acid catalysis. The study of polymerization through intramolecular reactions constituted a novel method of attacking this problem.

Diallyl yielded no carbocyclic products. Comparatively weak acids gave 1,4-dimethyl-tetrahydrofurane, while stronger acids yielded high boiling polymeric products.

Dimethallyl gave 1,1,4,4-tetramethyl-tetrahydrofurane and diisocrotyl. It was shown that high boiling polymeric products obtained were the result of polymerization of diisocrotyl. In no case was the formation of carbocyclic products indicated, presumably due to the great ease of isomerization of dimethallyl to diisocrotyl.

Geraniolene yielded cyclogeraniolene in accordance with the reports of other workers. The experimental conditions favourable for the formation of 1,1,5,5-tetramethylpyrane were determined.

2,7-dimethyl-octadiene-2,6 yielded various isomeric products depending upon the acid employed and the time of treatment. The probable formation of carbocyclic products was indicated. The formation of 1,1,6,6-hexamethylene oxide from the glycol of this diene as reported in the literature was disproven.

The polymerization theories advanced by various workers were criticized and a new theory of acid catalysis polymerization advanced.

Both 2,6-dimethyl-heptanol-6 and tetrahydrolinalool dehydrate without yielding cyclic products when treated with various acids.

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TABLE OF CONTENTS

HISTORICAL INTRODUCTION

Several important naturally occurring classes of compounds, namely the terpenoids, the carotenoids, various resin acids, certain triterpene sapogenins, vitamin A and others, are made up entirely of complete isoprene units. It is also possible that sterol type of compounds including sex-hormones, bile acids, cholane type sapogenins are derived from a terpenoid or carotenoid type of substance(1), (2),(3),(4).

The biogenesis of these substances is obscure although many attempts have been made to bring forward a plausible theory explaining the formation of these products in the plant.

A rather extensive phytochemical study relating to terpenoids has been made by Hall(5). Hall uses a combination of hexose and metasaccharonic acid as the building block of all the terpenoids, carotenoids and related substances.

Read(6) has taken geraniol as the precursor of terpenes, and Hall(7) has developed the idea to completion. However, there is nothing said about the derivation of geraniol.

1.- R.Robinson, J.Soc.Chem.Ind., 53, 1062, (1934).
2.- M.Vanghelovici, J.Soc.Chem.Ind., 998, (1934).
3.- W.M.D.Bryant, J.Soc.Chem.Ind., 907, (1935).
4.- F.S.Spring, J.Soc.Chem.Ind., 972, (1935).
5.- J.A.Hall, Chem.Rev., 305-345, (1937).
6.- J.Read, Chem.Rev., 7, 1-50, (1930).
7.- J.A.Hall, Chem.Rev., 479, (1933).

The mere fact that practically all the constituents of essential oils and many other compounds are built up of complete isoprene unit has led to the so called "isoprene rule". The application of this rule has been of immense value in the study of many terpene compounds, especially those of sesquiterpene and polyterpene series.

It is noteworthy that Jauregg(8), on treating isoprene with acetic acid containing a little sulphuric acid, obtained various condensation products, among which he identified geraniol, cyclogeraniol, linalool, alpha-terpineol, 1.4- and 1.8-cineol, a monocyclic sesquiterpene, a hydrocarbon containing three double bonds, etc.

Recently Favorskii(9) treated $CH_3-C(CH_3)(OH)-CH=CH_2$ with 20 per cent sulphuric acid at room temperature and obtained linalool, geraniol, terpin hydrate and other products.

Mechanisms, differing from isoprene condensation and yet involving an active isoprene skeleton have been proposed by many workers.

Maclean(10) suggested that citral arises from the condensation of two molecules of acetone and two of acetaldehyde. This theory has been elaborated by Singleton(11) and also by Kremers(12). It has naturally been pointed out that citral by various reactions may lead to practically all types

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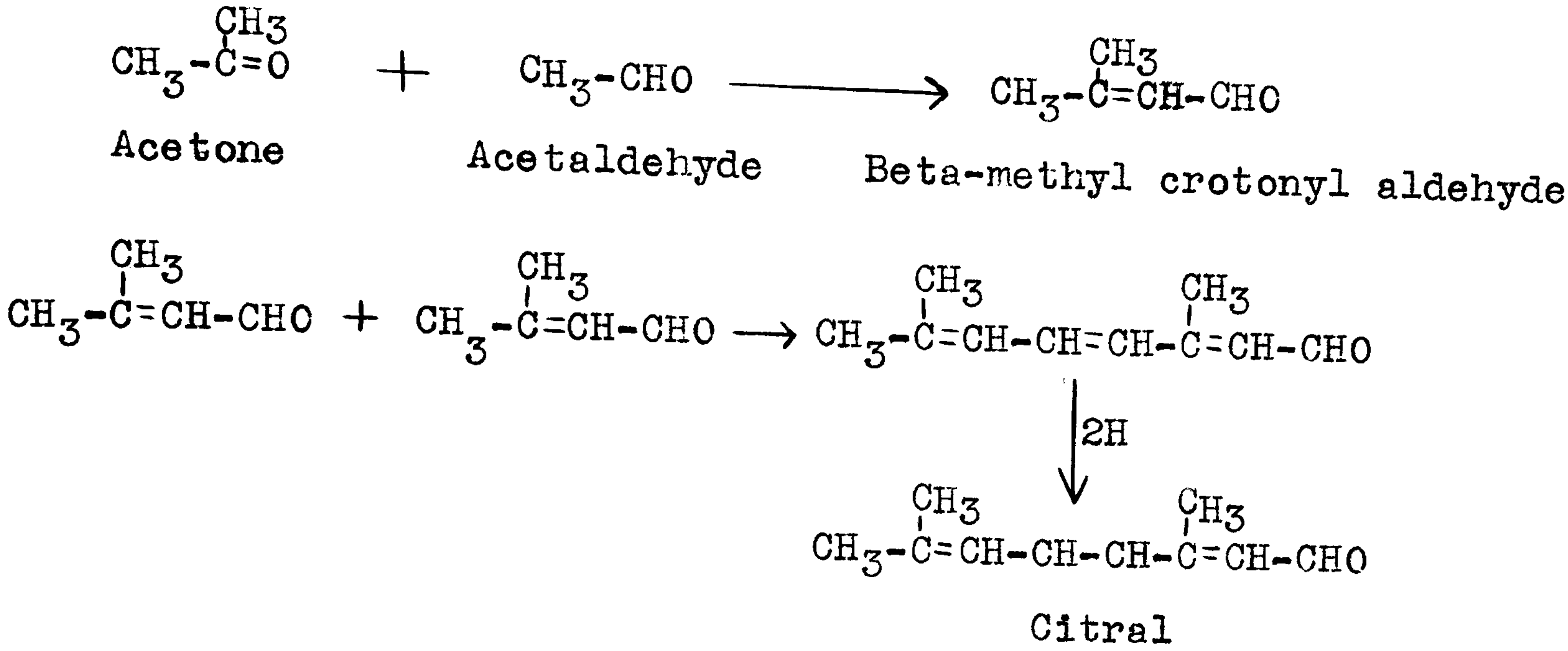
8.- T.W.Jauregg, Ann. 496, 52 (1932).
9.- A.E.Favorskii, J.Gen.Chem.(USSR), 8, 879, (1938).
10.- Maclean, J.Chem.Soc., 99, 1621, (1911).
11.- F.Singleton, J.Chem.Soc., 989, (1931).
12.- Kremers, J.Biol.Chem., 50, 31, (1922).

of terpene compounds. However, the condensation of acetone and acetaldehyde must take place in the following manner in order to lead to the formation of citral.



$$CH_3-\overset{CH_3}{\overset{|}{C}}=O + CH_3-CHO \longrightarrow CH_3-\overset{CH_3}{\overset{|}{C}}=CH-CHO$$

Acetone Acetaldehyde Beta-methyl crotonyl aldehyde

$$CH_3-\overset{CH_3}{\overset{|}{C}}=CH-CHO + CH_3-\overset{CH_3}{\overset{|}{C}}=CH-CHO \longrightarrow CH_3-\overset{CH_3}{\overset{|}{C}}=CH-CH=CH-\overset{CH_3}{\overset{|}{C}}=CH-CHO$$

$$\big\downarrow 2H$$

$$CH_3-\overset{CH_3}{\overset{|}{C}}=CH-CH-CH-\overset{CH_3}{\overset{|}{C}}=CH-CHO$$

Citral

This type of condensation between acetone and acetaldehyde has not been successfully carried out in vitro, the product of condensation always being $MeCHOHCH_2COMe$.

This difficulty has been shelved by assuming beta methyl crotonaldehyde as being the progenitor of terpenoid compounds. Von Euler in his book Grundlage und Ergebnisse der Pflanzenchemie, Vol. 3, p. 319, (1909)(13), put forward the idea of beta methyl crotonaldehyde as being the common building of terpenes. Karrer(14) extended this idea in his studies of carotenoids.

Many attempts to synthesize carotenoids using beta methyl crotonaldehyde have not met with great success. However, Fischer and Lowenberg(15) succeeded in carrying out

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13.- Through J.A.Hall, Chem.Rev. 306, (1937).
14.- P.Karrer, Helv.Chim.Acta. 19, E33, (1936).
15.- F.G.Fischer and K.Lowenberg, Ann. 494, 263, (1932).

an aldol condensation between two molecules of this aldehyde and obtained the corresponding aldol, and by dehydration the
CH_2-/
triene, $C(Me)_2{=}CH{-}CH{=}CHMe{=}CH{-}CHO$.

Fuson and Christ(16) have indicated the possibility of condensing beta cyclocitral with dimethyl acrolein according to the principle of vinology, and obtaining vitamin A by reduction of the resulting aldehyde. However, attempts to condense citral with 2,6-dimethyl-8-octatrienal have failed(17).

Kuhn(18) has claimed the synthesis of vitamin A by condensing ionylidene acetaldehyde with dimethyl acrolein and reducing the resulting aldehyde. Karrer(19) questions this synthesis by failing to repeat this synthesis.

Heilbron(20) and co-workers have lately succeeded in condensing citral with dimethylcrotonaldehyde by using sodamide.

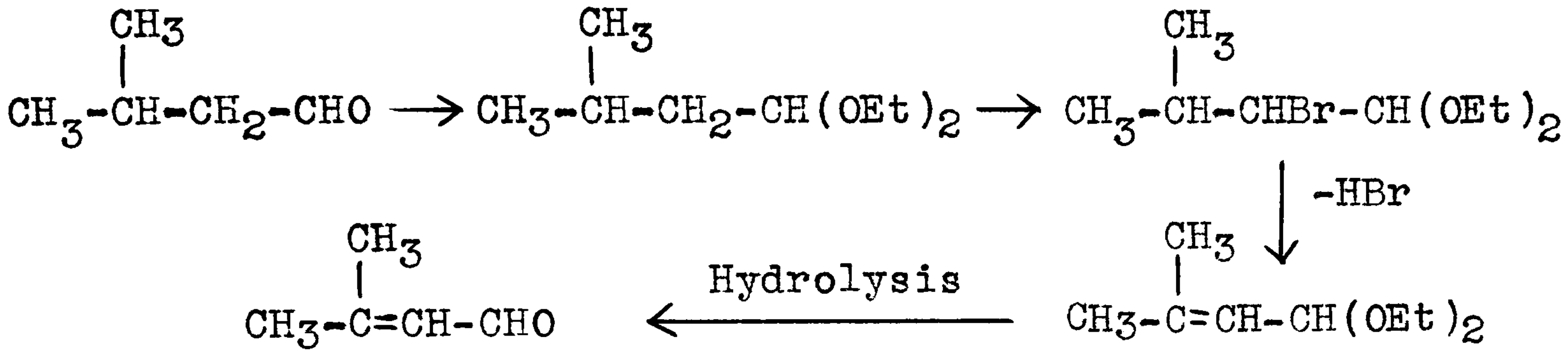
It is thus seen that the synthesis of these compounds depends upon the reactions of dimethylcrotonaldehyde.

Discussion of the Problem Under Consideration.

It is concluded from the discussion presented in the Historical Introduction that progress in the field of carotenoids depends largely upon the preparation and reactions of dimethylcrotonaldehyde.

16.-R.C.Fuson and R.E.Christ, Science, 84, 294, (1936).
17.-Bernhauer and co-workers, Ann. 525, 43, (1936).
18.-Kuhn and Morris, Ber., 70B. 853, (1937).
19.-P.Karrer and A.Ruegger, Helv.Chim.Acta, 23, 284, (1940).
20.-Heilbron et al., J.Soc.Chem., 1549-1963, (1939).

Preparation of this compound is rather difficult and the yields obtained very poor. Fischer(21) reports the most convenient method of preparation, involving the acetal formation of isovaleraldehyde, bromination of the acetal, elimination of hydrogen bromide, and finally the hydrolysis of the acetal to give the required dimethylcrotonaldehyde.

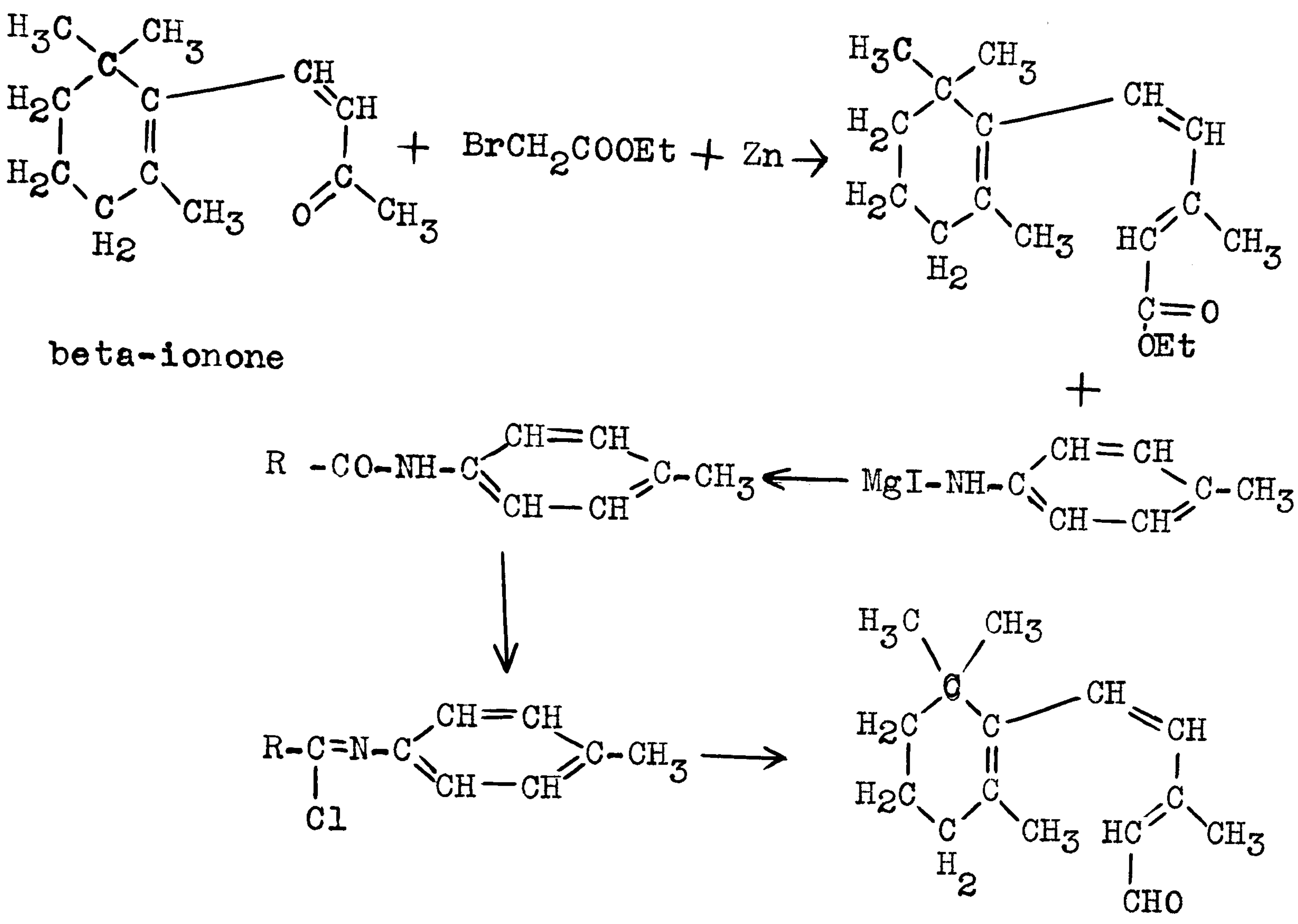


$$CH_3-\overset{CH_3}{\overset{|}{C}H}-CH_2-CHO \rightarrow CH_3-\overset{CH_3}{\overset{|}{C}H}-CH_2-CH(OEt)_2 \rightarrow CH_3-\overset{CH_3}{\overset{|}{C}H}-CHBr-CH(OEt)_2 \xrightarrow{-HBr} CH_3-\overset{CH_3}{\overset{|}{C}}=CH-CH(OEt)_2 \xrightarrow{\text{Hydrolysis}} CH_3-\overset{CH_3}{\overset{|}{C}}=CH-CHO$$

If a method could be found to bring about condensation between acetone and acetaldehyde to yield dimethylcrotonaldehyde, then the same reaction could be applied to the synthesis of many important compounds. It would then be possible to synthesize ionylidene acetaldehyde from ionone and acetaldehyde.

Numerous unsuccessful attempts have been made to prepare ionylidene acetaldehyde. Kuhn(22) carried out its synthesis through a very complex and difficult series of reactions. The synthesis depended upon a method discovered by von Braun(23), and involved the following steps:

21.- F.G.Fischer, L.Ertel, K.Lowenberg. Ber. 64, 30, (1931).
22.-R.Kuhn and C.Morris, Ber., 70B, 853, (1937).
23.-von Braun, W.Rudolf, Ber., 67, 269, 1735, (1934).

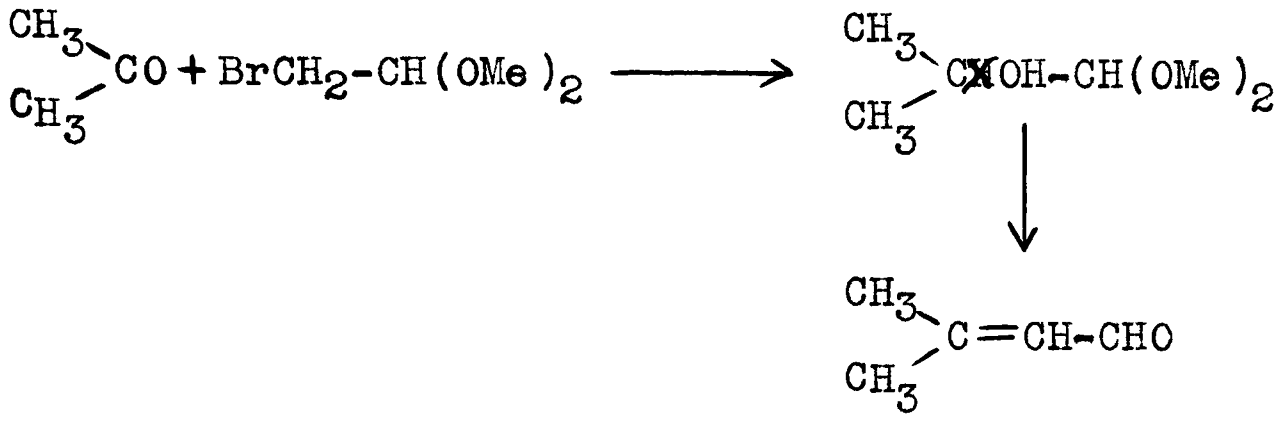


Kuhn claims an overall yield of 20 per cent but repetition of the first step by Giacolone(24) yielded only about one third the yield claimed by Kuhn. Since ionylidene acetaldehyde is considered as being the key substance to the synthesis of vitamin A, its preparation is of great theoretical and practical importance.

However, it has been found impossible to condense acetone and acetaldehyde in vitro and obtain dimethylcrotonaldehyde; the product of condensation always being $MeCHOH-CH_2-COMe$.

The subject of this investigation was the possibility of bringing about such a condensation by the interreaction of acetone with bromacetal. It was thought that such a reaction

24.- Giacolone, Gazz.Chim.Ital. 67, 464, (1937).



could be forced through one or more of the following methods. (a) Reformatzky type Zinc-alkyl reaction, (b) Grignard reaction of $MgBrCH_2-CH(OMe)_2$ with the ketone, and (c) condensation of the bromacetal with the ketone through the Lithium compound.

Failure to carry out this reaction, apparently due to the inactivity of the bromine atom in bromacetal will be unfolded in the following pages.

THEORETICAL PART

Preparation of Bromacetal.

Preparation of bromacetal has been reported by several workers. Hartung and Adkins(25) prepared it by adding bromine directly to acetal in the presence of calcium carbonate. Other methods of preparation have been reported by Stepanow(26) and Tschitschibabin(27).

A new and more convenient method of preparation of bromacetal has been reported by Filachione(28). This method depends on the addition of bromine to vinyl acetate in alcohol at temperatures below -40°C.

Reactions of Bromacetal.

Bromacetals or similar compounds have been subjected to studies only in a few cases.

Sabetay(29) prepared a large number of ether aldehydes by the following reaction:

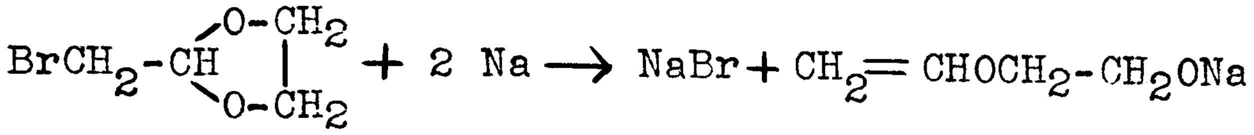
$$NaOR + BrCH_2\text{-}CH(OEt)_2 \rightarrow RO\text{-}CH_2\text{-}CH(OEt)_2$$

As early as 1878, Wislicenus(30) noted that bromacetaldehyde diethylacetal, when acted on by sodium would not couple, the reaction being exclusively as follows:

$$2\ Na + BrCH_2\text{-}CH(OEt)_2 \longrightarrow CH_2{=}\,CHOC_2H_5 + NaBr + C_2H_5OH$$

25.- Hartung and Adkins, J.Am.Chem.Soc., 49, 2517, (1927).
26.- Stepanow, Ber., 58, 1718, (1925).
27.- Tschitschibabin, Ber., 62, 1075, (1929).
28.- Filachione, J.Am.Chem.Soc., 1705, (1939).
29.- S.Sabetay, Compt.Rend., 196, 1508, (1933).
30.- Wislicenus, Ann., 192, 106, (1878).

Hill and co-workers(31) investigated the same reaction with cyclic acetals, and obtained similar results,



$$BrCH_2-CH\begin{matrix}/O-CH_2\\ |\\ \backslash O-CH_2\end{matrix} + 2\ Na \rightarrow NaBr + CH_2{=}CHOCH_2-CH_2ONa$$

Identical results were obtained with other cyclic acetals. In no case was there any evidence of a Wurtz reaction.

It has been found(32) that when bromacetal or chloracetal is boiled with alcoholic potassium hydroxide, the halogen atom is largely replaced by a hydroxyl ion. There is also the production of ethyl acetate and ethyl orthoacetate.

When iodoacetal is acted on by sodium ethylate in absolute alcohol, the result is 67.5 per cent of ethyl acetate and ethyl orthoacetate and 31 per cent $C_2H_5O-CH_2-CH(OEt)_2$.

When a less reactive medium is used, considerable ketene acetal is obtained, Thus,

$$BrCH_2-CH(OEt)_2 - tert.BuOK \longrightarrow 52\% \qquad CH_2{=}C(OEt)_2.$$

It has also been found(33) that dibromoacetal when treated with potassium ethylate did not give the desired product $(EtO)_2CH-CH(OEt)_2$, but instead gave bromoethoxyacetal and ethyl bromo-orthoacetate. Diiodoacetal and potassium tertiary butylate gave 82 per cent bromoketene,

$$I_2CH-CH(OEt)_2 + tert.BuOK \longrightarrow I-CH{=}C(OEt)_2$$

31.- Hill and co-workers, J.Am.Chem.Soc., 2718, (1928).
32.- J.M.McElvain, J.Am.Chem.Soc., 58, 529, (1936).
33.- J.M.McElvain, J.Am.Chem.Soc., 59, 2266, (1937).

Naftali(34) treated alpha-beta-dichloroacetals with alkali alcoholates and obtained the unsaturated compound,

$$CH_2Cl-CHCl-CH(OMe)_2 + MeONa \longrightarrow CH_2Cl-CH{=}C(OMe)_2$$

Similar results were obtained with higher homologs, although the rate of reaction was considerably slower.

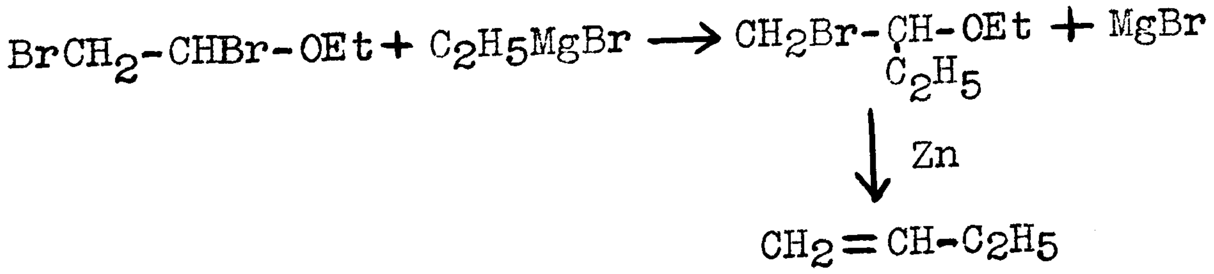
Reactions of Halo Ethers.

One might consider the bromacetal type of compounds as being somewhat similar to beta-bromo ethers.

Boord(35) studied the reactions of this class of compounds. He found that beta halogens in ethers were remarkable in their lack of reactivity towards some reagents. Thus when beta-ethoxy-isoheptyl bromide was treated with magnesium in dry ether, he obtained the olefin instead of the usual type of grignard reaction.

$$BrCH_2-RCH-OEt + Mg \xrightarrow{\text{Ether}} BrMgCH_2-RCH-OEt \rightarrow CH_2{=}RCH + EtOMgBr$$

In another study Boord(36) investigated the reactions of alpha-beta-halo ethers with grignard reagents; the results might be represented by the following reactions:



$$BrCH_2-CHBr-OEt + C_2H_5MgBr \rightarrow CH_2Br-\underset{C_2H_5}{CH}-OEt + MgBr$$

$$\downarrow Zn$$

$$CH_2{=}CH-C_2H_5$$

34.- N.Naftali, Bull.Soc.Chim., 4, 333, (1937).
35.- Boord, J.Am.Chem.Soo., 651.
36.- Boord, J.Am.Chem.Soc., 3396, (1930).

The reactions proceed smoothly, and serve admirably for the synthesis of alpha-olefins.

As early as 1904, Grignard(37) in his classic investigations of Grignard reactions, observed that an abnormal reaction took place in the following case:

$$BrCH_2\text{-}CH_2\text{-}O\text{-}C_6H_5 + Mg \longrightarrow C_6H_5\text{-}OH + H_2C{=}CH_2$$

Wohl and Berthold(38) treated the same compound with sodium and obtained analogous results.

In a more recent study Tallman(39) found that all compounds investigated of the type $R\text{-}O\text{-}CH_2\text{-}CH_2Br$ yield ethylene and alkoxy magnesium bromide, instead of the normal grignard reaction. Some coupling (Wurtz reaction) was also found to take place.

Naftali(34) found that $ClCH_2\text{-}ClCH\text{-}CO\text{-}CH_3$ gave resins when treated with sodium methylate. Higher homologs yielded unsaturated mono-methyl ethers.

It has been reported(40) that when beta bromo-ethers are treated with sodium acetylide, acetylenic ethers are formed.

$$R\text{-}O\text{-}CH_2\text{-}CH_2Br - NaC{\equiv}CH \longrightarrow R\text{-}O\text{-}CH_2\text{-}CH_2\text{-}C{\equiv}CH$$

When $C_6H_5\text{-}O\text{-}CH_2\text{-}CH_2Br$ is treated with sodium in liquid ammonia a small amount of coupling takes place(41).

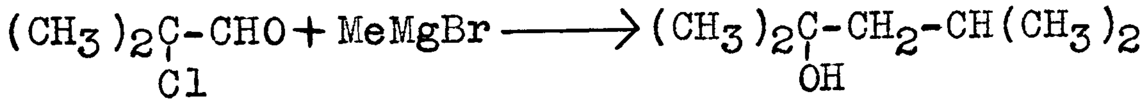
37.- V.Grignard, Compt.Rend., 38, 1048, (1904).
38.- Wohl and Berthold, Ber., 43, 2177, (1910).
39.- R.C.Tallman, J.Am.Chem.Soc., 56, 126, (1934).
40.- P.McCusker and J.W.Krueger, J.Am.Chem.Soc., 213, (1937).
41.- P.M.Dean and G.Berchet, J.Am.Chem.Soc., 52, 2823, (1930).

Gilman(42) cites examples of bromo-ethers which do not yield the grignard or lithium compounds under ordinary circumstances, but yield the lithium compound when acted on by a relatively active lithium alkyl such as normal butyl lithium. In a later study Gilman(43) makes a critical study of the various factors involved for the interconversion of lithium alkyls. Optimum experimental conditions are also discussed.

<u>Reactions of Alpha-halo Aldehydes.</u>

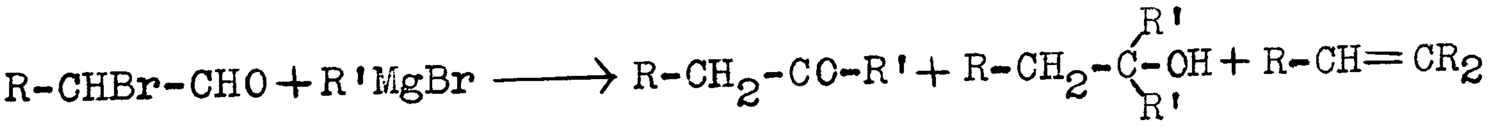
It would be interesting to note the behaviour of alpha-halogen in aldehydes.

Henry(44) treated alpha-chlor isobutyl aldehyde with methyl magnesium bromide, and obtained,



$$(CH_3)_2\underset{Cl}{C}-CHO + MeMgBr \longrightarrow (CH_3)_2\underset{OH}{C}-CH_2-CH(CH_3)_2$$

Kirmann(45) has carried out extensive investigations with various bromoaldehydes. He found that the halogen exhibits abnormal properties, thus



$$R-CHBr-CHO + R'MgBr \longrightarrow R-CH_2-CO-R' + R-CH_2-\overset{R'}{\underset{R'}{C}}-OH + R-CH=CR_2$$

All three products were obtained with alpha-bromo-heptaldehyde.

Zinc-methyl behaved somewhat similarly,

$$R-CHBr-CHO + MeZn \longrightarrow R-CH_2-CO-CH_3$$

42.- H.Gilman, J.Am.Chem.Soc., 348, (1940).
43.- H.Gilman, J.Am.Chem.Soc., 1842, (1940).
44.- L.Henry, Rec.Trav.Pays.Bas. 26, 416, (1907).
45.- Kirmann, Ann.Chim., 223-286, (1929).

The reactions of alpha-haloaldehydes towards magnesium acetylide have also been investigated(46). A stream of acetylene was passed into an ethereal solution of ethyl magnesium bromide. Addition of chloracetaldehyde to the mixture gave chlorhydrin $Cl-CH_2-CH(OH)-C\equiv CH$. Some trimolecular product, namely $Cl-CH_2-CH(OH)-C\equiv C(OH)CH-CH_2-Cl$ also resulted.

Chloracetal under similar circumstances yielded an analogous product, $Cl-CH_2-CH(OEt)-C\equiv C-(OEt)CH-CH_2-Cl$. It is significant that the halogen atom did not take part in the reaction.

46.- R.Lespieau, Bull.Soc.Chim., 43, 199, (1928).

EXPERIMENTAL PART

Preparation of Bromacetaldehyde Dimethyl Acetal.

Two methods were employed in the preparation of this compound. One method involved the bromination of acetal, and the other bromination of vinyl acetate.

Acetaldehyde dimethyl acetal was prepared by the interaction of acetaldehyde and methyl alcohol in the presence of calcium chloride(47). The acetal thus obtained was fractionated in a Whitmore column of 8-12 plates operating efficiency. The fraction boiling at 61-61.5°C., was collected as the pure acetal. The constants of this compound were, b.p.$_{756}$ 61-61.5°C., d_4^{25} 0.8554, n_D^{25} 1.3658.

Bromination of the acetal was carried out by the process of Hartung and Adkins(25). The method consisted of direct addition of Bromine to the acetal in presence of calcium carbonate. The crude bromacetal was distilled at atmospheric pressure and the fraction boiling at 143-5°C. collected. This was refractionated under reduced pressure and the fraction having b.p.$_{78}$ 80°C., collected as pure bromacetal. The other constants of this compound were d_4^{25} 1.4576, n_D^{25} 1.4467. A yield of about 30 per cent was obtained by this procedure.

A more convenient method giving somewhat higher yields was reported by Filachione(28). Vinyl acetate obtained from

47.- H.Gilman, Collective Syntheses, p. 1.

Shawinigan Chemicals Ltd. was fractionated and the fraction having a b.p. 73.4-73.8°C. collected as the pure material. It was brominated in methyl alcohol at a temperature of -60°C. Distillation of the reaction product gave a mixture of bromacetal and a compound with a density of 1.9 (dibromvinyl acetate?). The latter yielded bromacetal upon addition of methyl alcohol. The yield obtained was about 45 per cent, and could probably be raised by employing lower temperatures. The constants obtained after the bromacetal was treated with excess bisulphite solution to remove aldehydes, and then subjected to redistillation were as follows, n^{25}_{D} 1.4446, d^{25}_{4} 1.4338. Filachione reported the following constants, b.p.$_{18}$ 48-51°C., d^{20} 1.467, n^{20}_{D} 1.4475.

It is noteworthy that both Filachione and, Hartung and Adkins report that the bromacetal is a powerful lachrymator. The writer found this to be the case with impure samples of bromacetal, but on treatment of the acetal with bisulphite solution the lachrymatory property disappeared indicating that bromacetal itself is not a lachrymator but such property is due to the presence of bromacetaldehyde impurity. The pure bromacetal has a sharp and somewhat garlic like odour.

Attempts to Prepare the Zinc Compound of Bromacetal.

One of the well known reactions of Organic Chemistry is the Reformatzky reaction involving the condensation of ketones and alpha-bromo esters. The reaction depends upon the formation of zinc-bromo esters which add to ketones to give beta hydroxy esters. It was thought that this reaction might be applied to effect a condensation between bromacetal and ketones.

Bromoacetaldehyde dimethyl acetal (27 gms.) was added slowly to a mixture of 10.5 gms. of polished zinc foil, cut in small strips, and 125 gms. of dry benzene. No reaction would take place in spite of heating and adding small amounts of catalysts such as iodine, methyl iodide etc.

It has been reported by Newland and Daly that a more active reaction takes place if copper is added to the reaction mixture(48). The Reformatzky reaction would not take place with chloroacetic ester and Zinc, but the reaction proceeds smoothly if copper is present along with the Zinc. In view of these facts the procedure of Newland and Daly was tried in the hope of obtaining the Zinc compound of bromacetal. However, no reaction would take place. The thermodynamic conditions were tested by adding a few drops of chloroacetic ester to the reaction mixture. Immediately a reaction took place with darkening of the zinc foil, indicating that the thermodynamic conditions were favourable for the formation of zinc bromo compound. It was concluded that the bromine atom in bromacetal was not sufficiently active to give the zinc compound.

48.- Newland and Daly, J.Am.Chem.Soc., 1842, (1931).

Behaviour of Bromoacetaldehyde Dimethylacetal Towards Magnesium.

Attempts were made to prepare the grignard of bromacetal. The usual type of grignard apparatus was set up including a mercury seal efficient stirrer. About one tenth mole (2.5 gms.) of magnesium was used and the reaction started with a few drops of methyl iodide. Having made certain that the thermodynamic conditions were right as evidenced by the formation of MeMgI, the bromacetal was slowly added (one tenth mole). No apparent reaction took place. The mixture was gently heated to reflux for three hours. At the end of this period the ether solution was decanted off. The magnesium turnings weighed 2.5 gms. indicating that no grignard had formed. The ether solution was evaporated off and impure bromacetal recovered.

It has been reported(49) that a specially activated magnesium alloy consisting of about 12 per cent copper will form grignard reagent in cases where ordinary magnesium fails to react. In view of this report, the above experiment was repeated employing this specially activated magnesium alloy (from Eastman Kodak Co.). However, no reaction took place on adding bromacetal to the activated magnesium-ether solution. The thermodynamic conditions were tested and found to be favourable since every time a few drops of methyl iodide was added a vigorous reaction took place.

49.- H.Gilman, Rev.Trav.Chim., 47, 19, (1928).

Various other experiments were run with modifications, such as employment of different solvents, variations in the time and temperatures, etc. Both dry benzene and dibutyl ether were tried. In no case did a reaction take place and prolonged boiling at higher temperatures caused decomposition of the bromacetal.

Behaviour of Bromoacetaldehyde Dimethyl Acetal Towards Grignard Reagents.

Having failed to prepare the grignard of bromacetal, it was decided to investigate its behaviour towards grignard reagents.

In some of the previous experiments considerable methyl iodide were added to the reaction mixture. This was done to test periodically the thermodynamic conditions after the addition of bromacetal. In one case two grams of methyl iodide were added and the grignard MeMgI formed as evidenced by the spontaneous refluxing of the ether. At the end of the reaction the mixture was decomposed with ammonium chloride solution and the oil recovered was carefully distilled. No trace of acetaldehyde dimethyl acetal or propanal dimethyl acetal could be detected, showing the absence of any reaction between the grignard and bromacetal.

In another experiment one fifth of a mole of MeMgCl was prepared. The reaction was considered complete when all of the magnesium turnings had dissolved. At this stage 20 gms.

(one seventh mole) of bromacetal was slowly added. No apparent reaction took place. The mixture was heated to reflux for three hours and allowed to stand overnight. The next day the solution was hydrolyzed with ammonium chloride solution. The ether was carefully fractionated off. Distillation of the remaining oil showed no trace of acetaldehyde dimethyl acetal or propanal dimethyl acetal. Over 18 gms. of bromacetaldehyde dimethyl acetal were recovered.

Attempts to Prepare Lithium Alkyl of Bromacetal.

It appeared from the above experiments that magnesium was not sufficiently active to react with the bromine of bromacetal. We mentioned in the Historical Section that sodium yields ketene acetal with bromacetal. It is a well known fact that the alkali metals sodium and potassium are much more reactive than magnesium, but lithium occupies an intermediate position. Furthermore, lithium has been found to be very suitable where a 1:2 addition of an alkyl to a carbonyl radical is desired. In view of these facts it was decided to try the formation of the lithium compound of bromacetal.

Lithium (1.0 gm.) was cut in small pieces and added to 15 cc. of dry ether placed in a typical grignard apparatus. The mixture of lithium and ether was vigorously stirred and bromacetal added cropwise. The solution became slightly cloudy and the bright lithium particles became coated with a brownish layer. The mixture was stirred for two hours and allowed to stand overnight. However, there was no apparent reaction taking place and the lithium particles remained undissolved. The ether solution was filtered and the flame test applied to the clear ether solution. The absence of any violet colour characteristic of lithium, indicated that there was no trace of lithium alkyl formed. Of the ten grams of bromacetal added, over eight grams were recovered unchanged.

In other similar experiments variations of the above procedure were introduced, such as periodic addition of freshly cut lithium particles, addition of small amounts of normal butyl bromide which readily forms the butyl lithium and use of higher boiling solvents such as benzene and dibutyl ether. In no case was there an indication of the formation of the lithium compound of bromacetal.

Gilman(50) reports that he succeeded in preparing lithium compounds of bromoethers through metalation which otherwise would not form the lithium or magnesium compound in the normal manner. In view of this fact, it was decided to try the formation of lithium alkyl of bromacetal through a metalation reaction with normal propyl and normal butyl lithium.

Lithium propyl was prepared in the manner described by Gilman. About 6.5 gms. of normal propyl bromide were added to 0.7 gms. of lithium placed in dry ether. No difficulty was experienced and lithium propyl formed in a few minutes. A few

50.- Gilman, J.Am.Chem.Soc., 348, (1940).

drops of bromacetal were added and a slight reaction seemed to take place. However, further addition of 9 gms. of bromacetal gave no evidence of a reaction. The mixture was refluxed for two hours and allowed to stand overnight. Hydrolysis was carried out with ice water. The ether solution was carefully refluxed and care was taken to detect the presence of any acetal. No trace of acetal was detected and most of the bromacetal was recovered unchanged.

The above experiment was repeated with normal butyl bromide with identical results.

Experimental Results and Conclusions.

The experimental results indicate clearly that the bromine atom in bromacetaldehyde dimethyl acetal is extremely inactive, and will take part in reactions only under drastic conditions.

We mentioned in the Historical Introduction that the halogen atom is replaced by hydroxyl group on boiling with alcoholic alkali. It is also replaced by R-O- when boiled with sodium or potassium alcoholate. More drastic treatment such as with sodium, gives ketene acetal with the elimination of HX.

On the other hand, examination of the behaviour of alpha-haloaldehydes reveals that the halogen atom behaves abnormally and is quite sluggish towards many reagents. We also note the same abnormal behaviour in the halogen atom of haloethers.

Examination of the formula of bromacetaldehyde dimethyl acetal $BrCH_2-CH(OMe)_2$ might indicate that the compound is like a bromo ether with the bromine atom doubly inactivated by the presence of two methoxy groups. Such a phenomenon could not have been predicted either by reviewing the chemistry of alpha-haloaldehydes or by considering the abnormal behaviour of the halogen atom in halo ethers.

It is concluded that bromacetal not only fails to form zinc-bromacetal, lithium bromacetal and the grignard, magnesium acetal, but it will not react with such active compounds as methyl magnesium chloride or lithium propyl.

SUMMARY

The activity of the bromine atom in bromacetaldehyde dimethyl acetal was investigated. It was found to be surprisingly unreactive. This property was attributed to the presence of two alkoxy groups on the adjacent carbon atom.

It was found that bromacetal would not form the grignard compound, nor would it react with lithium to give the lithium alkyl, or react with zinc to form the corresponding zinc alkyl bromide.

Furthermore, it would not react with methyl magnesium chloride, or with lithium propyl and lithium butyl.

Reports that bromacetaldehyde dimethyl acetal is a powerful lachrymatorwere found to be erroneous, this property being found to be due to the presence of small amounts of bromacetaldehyde impurities.

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