THE SYNTHESIS OF SOME ENYNE EPOXY COMPOUNDS

by

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I. INTRODUCTION

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The availability of a proved method of obtaining biologically active synthetic vitamin A products makes it desirable to investigate the effect of various substituents on the β-ionone ring. For example, one could leave all methyl groups out of the ring or introduce one methyl group <u>ortho</u> to the side chain or even use a phenyl ring instead of the cyclohexene ring. In order to effect these changes several new key intermediates were synthesized. Their synthesis and elucidation of structure constitutes the subject of this thesis.

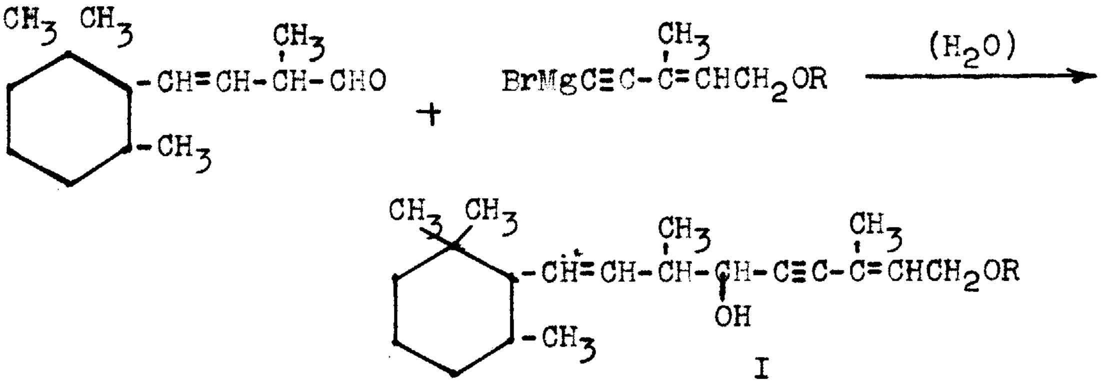
II. DISCUSSION

II. DISCUSSION

Recently Milas and co-workers[1] described three synthetic methods of preparing vitamin A derivatives which possessed biological activity similar to that of vitamin A. This work has since been repeated by workers[2a,b] in other laboratories; therefore, of the several synthetic approaches to this vitamin which have been published, it represents the only detailed description of work that has been substantiated by reproduction.

These new methods which proved to be means of obtaining biologically active substances make feasible an attempt to synthesize similar compounds differing slightly in structure. A series of such related compounds will make it possible to determine the contribution of various functional groups to the activity displayed. Too, if a significant amount of activity is demonstrated by any of these new compounds, there will be at hand a method of synthesizing desirable biologically active vitamin A substances from more available materials than the β-ionone employed by Milas.

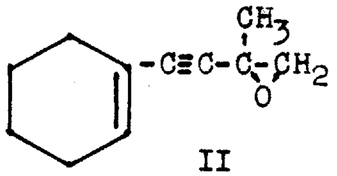
In one of the methods described by Milas, the carbon skeleton of the vitamin is formed by the condensation of a Grignard reagent with an aldehyde as represented below:



I

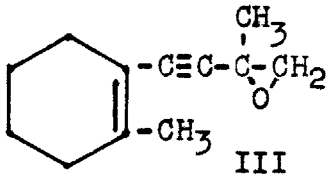
Since an aldehyde group can be formed from an epoxy group at the end of a chain by rearrangement[3,4], it was hoped that a number of compounds similar to I, each containing an identical terminal epoxy group but differing in the structure of the ring would furnish intermediates useful in the synthesis of a series of products which might prove biologically active.

Accordingly, the following four compounds were selected as models for study, and their preparation and proof of structure are the objects of the research described in this thesis. The triple bond, which is not present in vitamin A, is admitted as an integral part of the structure of each intermediate, since it makes possible a marked convenience in the synthesis and also eliminates one potential source of cis-trans isomerism; it can be selectively hydrogenated[4] at a later stage in the synthesis of the homolog.



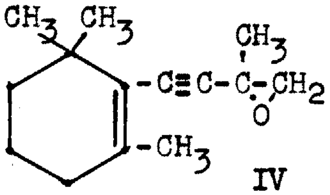
II

1-(Cyclohexene-1'-yl)-3-methyl-3-epoxybutyne-1



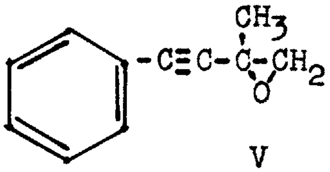
III

1-(2'-Methylcyclohexen-1'-yl)-3-methyl-3-epoxybutyne-1



IV

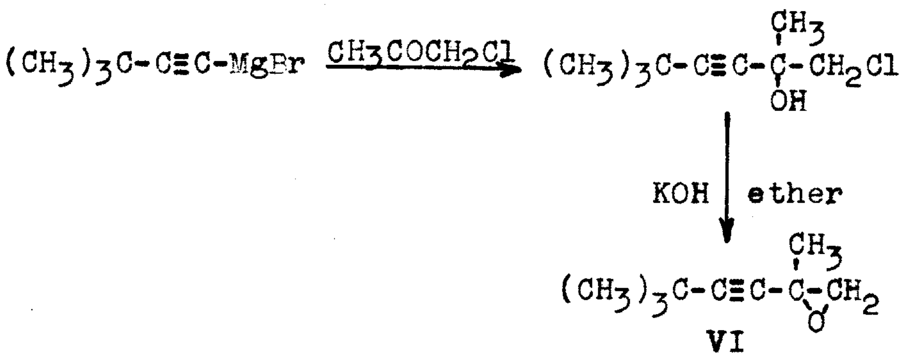
1-(2',6',6'-Trimethylcyclohexen-1'-yl)-3-methyl-3-epoxybutyne-1



V

3-Methyl-3-phenyl-3-epoxybutyne-1

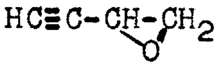
Only four compounds in which a triple bond is located <u>alpha</u> to an epoxy group have been described in the literature. Favorsky and Tikhomolov[3] synthesized 1,1,1,4-tetramethyl-4-epoxypentyne-2 (VI) by the following sequence of reactions:



$$(CH_3)_3C-C\equiv C-MgBr \xrightarrow{CH_3COCH_2Cl} (CH_3)_3C-C\equiv C-\overset{CH_3}{\underset{OH}{C}}-CH_2Cl \xrightarrow[\text{KOH}]{\text{ether}} (CH_3)_3C-C\equiv C-\overset{CH_3}{C}\underset{O}{\diagdown\!\diagup}CH_2$$

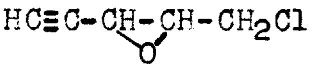
VI

Lespieau has synthesized 3-epoxybutyne-1(VII)[5] and 5-chloro-3-epoxypentyne-1 (VIII)[6], and Herschstein[7] has prepared 3-methyl-3-epoxybutyne-1 (IX) by similar reactions.



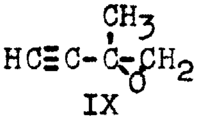
$HC\equiv C-\underbrace{CH-CH_2}_{O}$

VII



$HC\equiv C-\underbrace{CH-CH}_{O}-CH_2Cl$

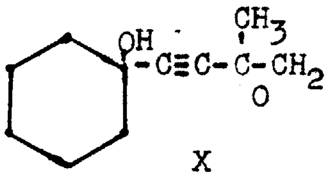
VIII



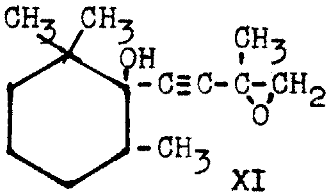
$HC\equiv C-\underbrace{\overset{CH_3}{C}-CH_2}_{O}$

IX

In this laboratory 1-(cyclohexan-1'-ol-yl)-3-methyl-3-epoxybutyne-1 (V) and 1-(2',6',6'-trimethylcyclohexan-1'-ol-yl)-3-epoxybutyne-1 (XI) have been prepared, also by similar methods.



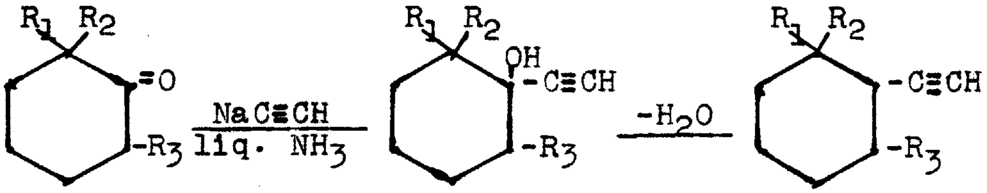
X



XI

No compounds in which a conjugated enyne system and an epoxy group are present have been described in the chemical literature.

In the cases of the cyclohexenyne compounds, the following sequence of reactions, with the exception of compound (IV), led to the formation of the desired epoxy compounds:

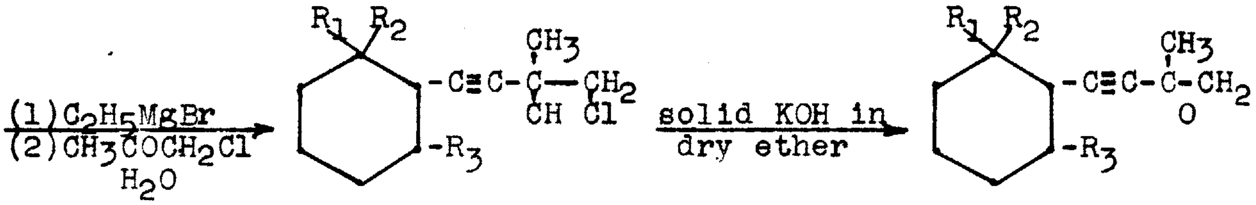


XII. $R_1=R_2=R_3=H$ XIII. $R_1=R_2=R_3=H$ XIV. $R_1=R_2=R_3=H$

XVI. $R_1=R_2=H$ XVII. $R_1=R_2=H$ XVIII. $R_1=R_2=H$

$R_3=CH_3$ $R_3=CH_3$ $R_3=CH_3$

XX. $R_1=R_2=R_3=CH_3$ XXI. $R_1=R_2=R_3=CH_3$ XXII. $R_1=R_2=R_3=CH_3$



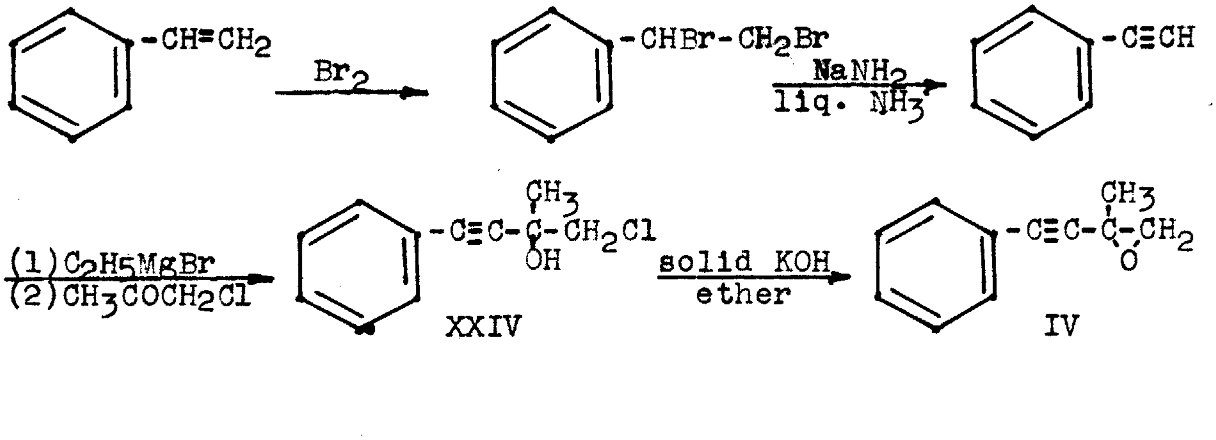
XV. $R_1=R_2=R_3=H$ II. $R_1=R_2=R_3=H$

XIX. $R_1=R_2=H$ III. $R_1=R_2=H$

$R_3=CH_3$ $R_3=CH_3$

XXIII. $R_1=R_2=R_3=CH_3$ IV. $R_1=R_2=R_3=CH_3$

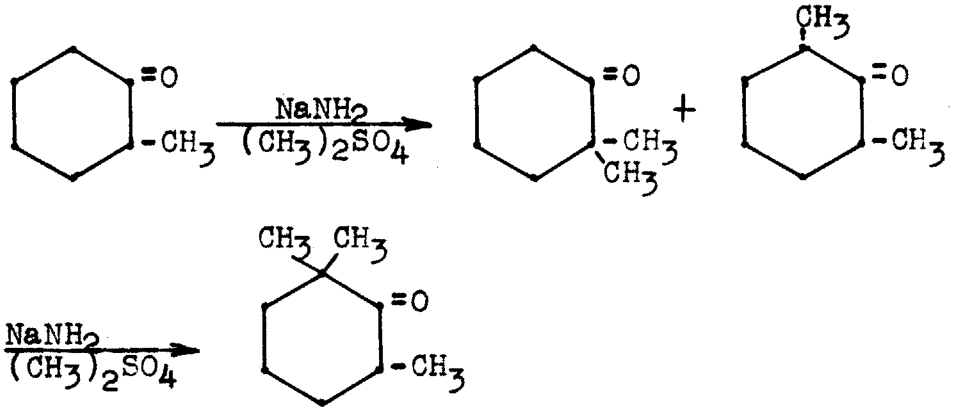
Phenylacetylene, the starting material in the synthesis of the epoxy compound containing a phenyl ring, was prepared from chemicals available in the laboratory because of the savings in time and cost. The starting material was styrene.



XXIV IV

The cyclohexanone used was a commercial grade which was fractionated before use; o-methylcyclohexanone was prepared by the oxidation of o-methylcyclohexanol by sodium dichromate and sulfuric acid.

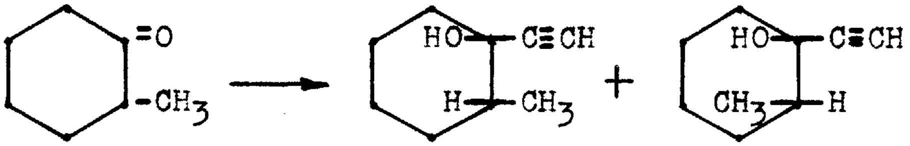
The 2,6,6-trimethylcyclohexanone was obtained by two successive methylations of o-methylcyclohexanone; sodamide was used as the enolizing agent and dimethyl sulfate as the methylating agent, each reaction being carried out in an inert solvent. The introduction of a second methyl group leads to the formation of a mixture of the α,α and α,α' isomers, in which the former has been shown to predominate by a ratio of 85 to 15.[10] Both of these isomers form the same compound when another methyl group is introduced.



The possibility of carrying out a methylation directly in the liquid ammonia solution in which the sodamide was formed, thus eliminating the need of replacing this solvent with ether or benzene, was investigated. When *o*-methylcyclohexanone was methylated in this manner, the dimethylcyclohexanone was obtained in substantially lower yield than in the case where ether was used as the solvent.

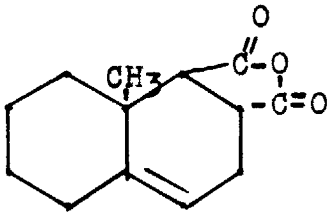
These three ketones were converted to the corresponding acetylenic cyclohexanols by the extension of a procedure described for the acetylenization of simple ketones[11].

The formation of the tertiary alcohol from *o*-methylcyclohexanone introduces a second asymmetric carbon atom, and leads to the anticipation of two pairs of enantiomorphs. Indeed, the 2-methyl-1-ethynylcyclohexanol-1 separates into a solid and a liquid phase, approximately equal in weight, when cooled at 0° for sixteen hours. This fact was overlooked by earlier investigators of this cyclohexanol[12,13].

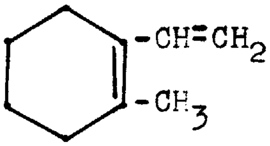


XVI XVIIA XVIIB

Cook and Lawrence[12] obtained only the liquid form of this ethynylcyclohexanol. By partially hydrogenating the triple bond, dehydrating the resulting ethylenic cyclohexanol, and subjecting the diene which was obtained to a Diels-Alder reaction with maleic anhydride, these workers obtained 9-methyl-$\Delta^{4,10}$-octahydronaphthalene-1,2-dicarboxylic anhydride (XXV). This compound could be formed only if the double bond formed by dehydration



XXV

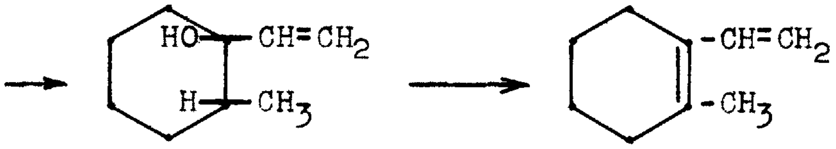


XXVI

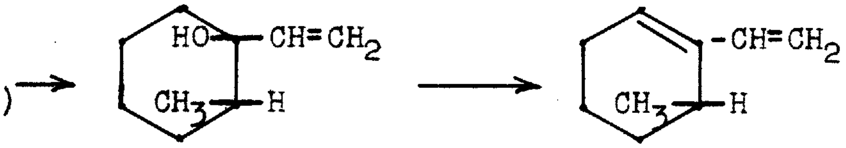
was located between the carbon atoms bearing the methyl group and the ethylenic group (XXVI). Meggy and Robinson[14] lent support to this interpretation by synthesizing XXV from the diene XXVI which they prepared by a method different from that of Cook and Lawrence.

On the other hand, Wang and Hu[15] isolated both solid and liquid forms of the ethynylcyclohexanol. By following the procedure outlined above with each form, they obtained two different octahydronaphthalene dicarboxylic anhydrides, which were identified by conversion to the corresponding naphthalene dicarboxylic anhydrides by dehydrogenation. From the evidence obtained in this manner, the Chinese workers deduced that two different dienes were produced when the two forms were partially hydrogenated and then dehydrated.

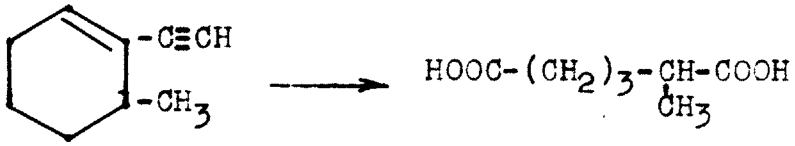
XVII A
(solid)



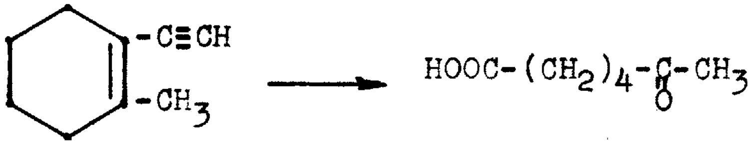
XVII B
(liquid)



With this evidence at hand, pure samples of the two enynes obtained by the dehydration of the two forms of the ethynyl cyclohexanol were ozonized. If two different enynes had been formed, two different acids would be obtained when the ozonides were treated with hydrogen peroxide.



$$\xrightarrow{} HOOC\text{-}(CH_2)_3\text{-}\underset{CH_3}{CH}\text{-}COOH$$



$$\xrightarrow{} HOOC\text{-}(CH_2)_4\text{-}\underset{O}{\overset{\|}{C}}\text{-}CH_3$$

Actually, the same ketonic derivatives were obtained in each case. The points of similarity between the two samples of enyne are summarized in Table I.

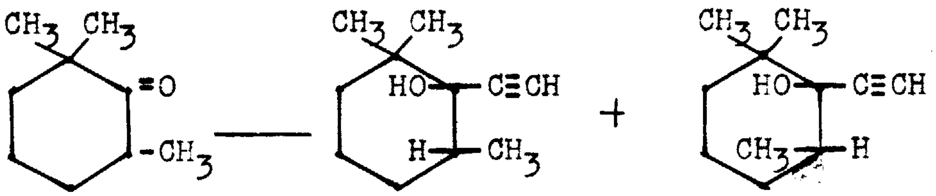
TABLE I

Comparison of Data of the Two Enynes

	Liquid form	Solid form
b.p. (20 mm.)	63-63.5°	63.5-64°
λ max.	2290	2290
ϵ mol.	10,000	11,450
m.p. of 2,4-dinitrophenylhydrazone of ozonization product	132.6-133.0°	132.6-133.1°
m.p. of 2,4-dinitrophenylhydrazone of synthetic keto acid	132.5°	
mixed m.p.	132.5-133.0°	132.6-133.1°
m.p. of semicarbazone	144.0-145.0°	145.0-146.0°
m.p. of semicarbazone fromliterature	144-145°	

Thus, under the conditions of dehydration used, evidently the same enyne is produced in each case. In view of the well-known tendency of organic compounds to dehydrate or dehydrohalogenate trans[16,17], it would appear logical that the double bond formed when compound XVII B was dehydrated would be located α to the methyl group, especially since the hydrogen atom is tertiary. The same enyne would form when compound XVII A was dehydrated if the hydroxyl group preferentially combined with the cis tertiary hydrogen atom rather than a secondary hydrogen atom *trans* to it. Moreover, as Cristol[18] has pointed out in a similar case, *trans* elimination would occur much more smoothly than a *cis* elimination involving identical atoms. This difference in the ease of dehydration was borne out in the present work.

Two pairs of enantiomorphs are also to be expected when 2,6,6-trimethylcyclohexanone is converted to an ethynyl cyclohexanol. In this case, however, no spontaneous separation of pairs of isomers was observed. Attempts to effect



XX XXI

separation by cooling to dry ice temperatures and stirring were unsuccessful.

This acetylenic alcohol differs from all the other acetylenic compounds described in the present work in that it does not form an insoluble silver acetylide in ammoniacal silver nitrate.

The presence of the triple bond in these ethynyl cyclohexanols introduces certain difficulties in their dehydration. Chemical agents which are sufficiently strong to effect dehydration invariably bring about simultaneous destruction of the triple bond. The dehydration of 1-ethynyl-cyclohexanol-1 has been described twice[19,20] in the literature, and in both cases the dehydration was accomplished catalytically; alumina was employed in one case and aluminum sulfate in the other. No analytical data for 1-ethynyl-cyclohexene-1 have been reported in the literature beyond a series of widely differing physical constants. These are listed in Table II for comparison with the data obtained in the present work.

Mousseron[21] has reported the preparation of 1-ethynyl-cyclohexene-1 by treatment of acetylcyclohexene with phosphorus pentachloride, with subsequent elimination of the elements of hydrogen chloride with sodamide, but experimental details and analytical data are lacking.

The lack of chemical evidence for the existence of this enyne in the reports listed above is perhaps significant, since all low-boiling fractions obtained by the dehydration of ethynyl cyclohexanols in this laboratory using aluminum phosphate on pumice as the catalyst have been found to possess values for active hydrogen ranging from less than 0.1 to 0.9, although the boiling points and hydrogenation values of these fractions are almost identical to those of the enynes. A value for active hydrogen less than 1.0 indicates that some decomposition or

TABLE II

Physical Constants of 1-Ethynylcyclohexene-1

Investigator	b.p.	n_D	d	$\lambda_{max.}$	$\varepsilon_{mol.}$	C	H	Zer.
Baeyer Patents[19]	148-151°	1.4922 (20°)	--	--	--	--	--	--
Carothers[20]	40-43° (12mm.)	--	--	--	--	--	--	--
Mousseron[21]	--	1.4648 (25°)	0.855 (25°)	--	--	--	--	--
Braude[22]	--	--	--	2240 Å	6000	--	--	--
Azerbaev[23]	148-151°	--	0.9001 (22°)	--	--	--	--	--
Present work	52-53° (30mm.)	1.4934 (25°)	0.8843	2240 Å	13465	90.44	9.52	1.0
Theory	--	--	--	--	--	90.50	9.50	1.0

rearrangement has occurred in the course of the dehydration.

By reducing to a minimum the time of contact of the catalyst and the vapors of the cyclohexanol and operating at a temperature of 290-295°, conversions up to 52% per pass of 1-ethynylcyclohexanol-1 and of the liquid form of 2-methyl-1-ethynylcyclohexanol-1 into low-boiling fractions with values for active hydrogen of 0.9 have been effected. When the solid form of the 2-methyl-1-ethynylcyclohexanol-1 was subjected to identical treatment, conversions of about 17% per pass into fractions with values of active hydrogen of 0.5 were obtained.

Finally, the enynes from representative dehydrations of the ethynyl cyclohexanols XVII A and XVII B were purified by the precipitation of their silver derivatives and subsequent decomposition of the acetylides with ammonium thiocyanate.

No method of dehydrating 2,6,6-trimethyl-1-ethynylcyclohexanol-1 in satisfactory yields was found. By treating this compound with a mixture of succinic anhydride and meta-phosphoric acid, Milas and MacDonald[8] have prepared a substance in 7% yield which analyzed well, but no attempt was made to elucidate the structure.

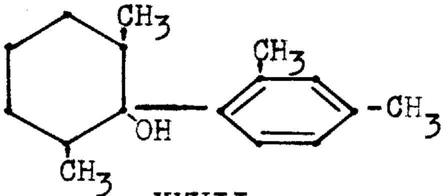
The catalytic method described above and used to such advantage in the dehydration of the simpler ethynyl cyclohexanols proved entirely useless in this case; the acetylene group originally present in the molecule was entirely destroyed. Other workers[4] in this laboratory have investigated as dehydrating agents the use of acetic anhydride, p-toluene sulfonic acid, magnesium sulfate, phthalic anhydride, potassium acid sulfate, aluminum oxide on pumice, calcined alum on pumice, alumina and aluminum sulfate, barium oxide, thoria on pumice, succinic anhydride, alone and dissolved in dibutyl phthalate, and mixtures of succinic anhydride and sulfuric acid and also zinc chloride.

Other reagents investigated include iodine as a catalytic agent and ortho-phosphoric acid. The hydroxyl of the cyclohexanol was replaced by a chlorine atom and the mixture of compounds obtained[24] treated with sodamide in liquid ammonia, but the product contained no active hydrogen.

This cyclohexanol was treated with two moles of ethyl magnesium bromide; one mole of tert-butyl alcohol was added to the compound formed, and the product pyrolyzed. Only a very small yield of enyne was obtained. This experiment was repeated, with the difference that only one mole of the Grignard reagent was added, which reacted with the hydroxyl group preferentially, according to the experience of this laboratory. When the product was heated to 200° using diphenyl ether as a solvent, no enyne was obtained.

The difficulty encountered in the attempts to dehydrate this compound stem from the facts that on one hand, the hydroxyl group is hindered by the methyl groups, and on the other hand, there is present in the triple bond a group extremely sensitive to the stringent conditions necessary to overcome the effects of the hindrance.

A similar case[25] is that of 1-(2,4-dimethylphenyl)-2,6-dimethyl-1-cyclohexanol (XXVI), which could not be dehydrated by potassium acid sulfate at 190-200° or with boiling acetic anhydride. The corresponding cyclohexene



XXVII

was obtained in 81% yield[26] when XXVII was refluxed with anhydrous oxalic acid at 200-220° for one hour.

When 2,6,6-trimethyl-1-ethynylcyclohexanol-1 was heated with anhydrous oxalic acid at 160°, an acidic distillate was formed which, when neutralized, washed, dried, and fractionated yielded a small amount of material possessing an acetylenic hydrogen atom. This material was purified through its silver derivative, and the analysis of the product agreed well with that of the desired enyne. An ultra-violet absorption spectrum of the substance indicated a weak absorption in the expected region. When the compound was ozonized, no geronic acid 2,4-dinitrophenylhydrazone was obtained. The material obtained by the ozonization did exhibit a positive iodoform test; this fact indicates the existence of a double bond adjacent to the carbon atom in the ring containing one methyl group.

The subsequent step in the scheme of synthesis, which was the first step common to both phenylacetylene and the cyclohexenynes was the formation of the corresponding Grignard reagents. In the case of the cyclohexenynes, both purified and crude fractions were used; a Zerewitinoff determination provided a convenient index of the amount of enyne present. Condensation with chloroacetone followed the recommendations of Kyriakides[27], who determined the optimum conditions for the addition of a Grignard reagent to the carbonyl group of chloroacetone for the minimizing of the reaction involving the chlorine atom. Hydrolysis of the complex leads to the formation of the chlorohydrins.

Reactions involving the formation of a Grignard reagent of phenylacetylene frequently do not follow entirely the anticipated course[28,29]. The chlorohydrin from a pure sample of this hydrocarbon could not be purified by fractionation as in the case of the chlorohydrins derived from the cyclohexenynes. Various conditions of experimental procedure led to the same unsatisfactory analytical results. The only by-product which was isolated and identified was diphenyldiacetylene, which was obtained from the residue of a second distillation of the chlorohydrin. However, when the crude phenylacetylene chlorohydrin was dehydrochlorinated, an epoxy compound was obtained, the analysis of which agreed with the theoretical.

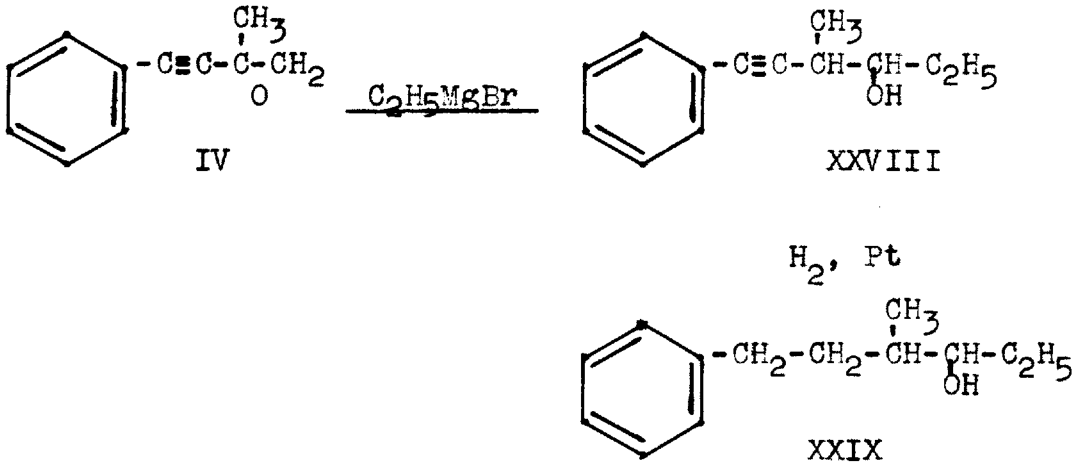
None of these chlorohydrins formed solid derivatives when they were treated with 3,5-dinitrobenzoyl chloride according to the procedure of Koelsch and McElvain[30].

Dehydrochlorination of the chlorohydrins was effected by treatment with powdered potassium hydroxide in quantities two to three times that of theory. Sodamide was equally effective, but a milder base such as triethylamine was completely ineffective.

The epoxy compounds could be rearranged by hydrochloric acid, and 2,4-dinitrophenylhydrazones of the aldehydes thus formed were prepared.

Since the ultimate use of these epoxy compounds will involve reaction with a Grignard reagent, ethyl magnesium bromide was added to 1-phenyl-3-methyl-3-epoxybutyne-1 (IV). An unsaturated alcohol was obtained (XXVIII). It is known that a Grignard reagent[9a,b,c] reacts with an unsymmetrically substituted epoxy compound to form a secondary rather than a tertiary alcohol.

When a hydrogenation value of this alcohol was determined using pure acetic acid as a solvent and platinum as a catalyst, three double bonds and one triple bond were indicated; there was no evidence of replacement of the hydroxyl group by hydrogen. However, when a larger quantity of the unsaturated alcohol was hydrogenated in absolute **ethanol** containing about 2% pure acetic acid as a solvent and platinum as the catalyst, apparently only the triple bond was saturated. Again, there was no evidence of hydrogenolysis of the hydroxyl group.



III. EXPERIMENTAL PART

III. EXPERIMENTAL PART

Styrene Dibromide.-- A sample of commercial styrene was purified by the method of Price and Adams[31]. It was brominated by the procedure of Evans and Morgan[32], except that the bromine was not dissolved in ether before it was added to the hydrocarbon. The product melted at 74-75° (corr.); Zincke[33] reports the dibromide as melting at 74-74.5°.

Phenylacetylene.-- Styrene dibromide was dehydrobrominated with sodamide in liquid ammonia in the manner first used by Nieuwland, Vaughn, and Vogt[34]. The yield was less than half that reported by these workers. N_D^{25} 1.5459, the value obtained by these workers, n_D^{26} 1.5461.

o-Methylcyclohexanol.-- Five hundred g. (4.55 moles) of o-cresol, obtained from the Barrett Company and redistilled, boiling at 184.5-185.5°, was placed in a high-pressure bomb, 10 g. of Raney nickel[35] was added, the hydrogenation apparatus assembled, and hydrogen added to the system at 2200 lbs. pressure at 150°. Hydrogen was added as it was absorbed over a period of four days. At the end of this time the apparatus was cooled and dismantled, and the catalyst removed from the solution by filtration. The solution was washed with 100 ml. of 5% sodium hydroxide solution and the cyclohexanol separated, washed twice with 100 ml. of water and dried over magnesium sulfate. The alcohol distilled at 165°; 540 g. (80% yield) was obtained.

o-Methylcyclohexanone (XVI).-- One kg. (8.77 moles) of o-methylcyclohexanol prepared as described above (E.K.C. practical grade was also used subsequently with similar results) was added to a solution of 310 ml. of concentrated sulfuric acid and 1075 ml. of water in a 5 l. 3-necked flask equipped with a stirrer and immersed in a bath of running tap water. The stirrer was started and a cold solution of 310 ml. of concentrated sulfuric acid, 1075 ml. of water, and 1075 g. (3.6 moles, 10.8 equivalents) of technical sodium dichromate was added dropwise at a rate slow enough to hold the temperature below 40°. Stirring was continued for two hours after all the oxidant had been added.

The solution was then extracted twice with 500 ml. of ether, the combined extracts washed with 300 ml. of water, and neutralized with a 5% solution of potassium hydroxide. The ether layer was then dried over magnesium sulfate. Distillation through a 40-in. packed column at atmospheric pressure yielded 786 g. of product boiling at 160.5-161.0° (79% based on the o-methylcyclohexanol); n_D^{25} 1.4465 (literature value[36], n_D^{20} 1.4480).

Dimethylcyclohexanone.-- By the procedure described in detail by Greenlee and Henne[37], 277 g. (7.1 moles) of sodamide was prepared in a 5 l. flask, and the ammonia replaced with 3 liters of anhydrous ether. A one-liter dropping funnel was substituted for the glass inlet tube and the dry ice condenser was replaced by an Allighn condenser. The flask was immersed in an ice bath, and 756 g. (6.75 moles) of o-methylcyclohexanone was added dropwise at a rate sufficient to maintain a vigorous but not violent reflux. When all the ketone had been added the ice bath was removed and the slurry stirred at room temperature for twelve hours; it was then refluxed on a steam bath for three hours.

At the end of this time the flask was again cooled in an ice bath and 850 g. (6.75 moles) of dimethyl sulfate was added dropwise to the stirred slurry slowly enough that a gentle reflux was maintained. When the addition was complete the gray mass was stirred at room temperature for four hours.

The contents of the flask were hydrolyzed cautiously with 1.5 l. of water, the ether layer separated, and the water layer extracted twice with 200 ml. of ether. The combined ether layers were washed once with 100 ml. of 10% hydrochloric acid, once with 50 ml. of 5% sodium bicarbonate solution, and twice with 100 ml. of water.

The ether was removed at reduced pressure and the crude ketone shaken in a separatory funnel with 200 ml. of saturated sodium bisulfite solution. The layers were separated with the help of 150 ml. of ether, and the ether layer washed twice with 100 ml. of water. It was dried over magnesium sulfate.

Finally, the ketone was fractionated through a 40-in. packed column at atmospheric pressure. The material distilling at 165-167° was taken as dimethylcyclohexanone; this fraction weighed 558 g., a yield of 65.5% based on the o-methylcyclohexanone; n_D^{25} 1.4460. Haller and Cornubert[10] report $n_D^{20.5}$ 1.4480.

2,6,6-Trimethylcyclohexanone (XX).-- The third methyl group was introduced into the cyclohexanone ring by a procedure identical to that just described, except that anhydrous benzene was used as a solvent in order that a higher refluxing temperature could be obtained; also, the extraction with sodium bisulfite was eliminated. A volume of ether equal to about one-tenth that of the benzene used was added first to the suspension of sodamide in liquid ammonia to prevent freezing of the benzene.

Thus, 432 g. (3.4 moles) of dimethylcyclohexanone was added to 133 g. (3.5 moles) of sodamide in two liters of anhydrous benzene, and was methylated with 428 g. (3.4 moles) of dimethyl sulfate.

The ketone was fractionated through a 40-in. packed column at atmospheric pressure. The material distilling at 174-176° possessed a strong odor of sulfur dioxide;

it was washed once with 50 ml. of 5% potassium hydroxide, once with 50 ml. of water, dried over magnesium sulfate, and fractionated through a 1-ft. packed column at 20 mm. pressure. The desired ketone, distilling at 69-71.5°, weighed 322 g. This is 52.3% of theory, based on the dimethylcyclohexanone; n_D^{25} 1.4465. Haller and Cornubert[10] report n_D^{18} 1.4493.

1-Ethynylcyclohexanol-1 (XIII).--- A solution of sodium acetylide was prepared by the addition of 92 g. (4.0 moles) of clean sodium to 2.5 l. of liquid ammonia at -50° in a 5 l. 3-necked flask equipped with a mercury sealed stirrer and gas inlet tube, through which was passed acetylene, washed with water and dried with sulfuric acid and phosphorus pentoxide. Cyclohexanone (392 g., 4.0 moles) (obtained from duPont and fractionated) dissolved in 400 ml. of dry ether was added dropwise with stirring over a period of three hours. The solution was then allowed to stand overnight at -50°. At the end of that time the ammonia was removed by evaporation at room temperature, and the resulting mush was hydrolyzed by the addition with cooling of 250 g. of tartaric acid dissolved in 700 ml. of water. An additional 500 ml. of water and 1 l. of ether was added. The acidification of the mixture was completed by the addition of 6 N sulfuric acid. The mixture of acid salts formed by the neutralization may not be dissolved entirely by the amount of water present, so at this point it may be convenient to remove any solid material present by filtration.

The layers were then separated, the water layer extracted twice with 100 ml. of ether and the ether layer washed twice with 100 ml. of water. The combined ether layers were dried with magnesium sulfate. Distillation of the ethynylcyclohexanol through a 40-in. packed column at 21 mm. yielded 287 g. of product boiling at 79-81°, a yield of 58% based on the cyclohexanone.

This material solidified completely on standing; m.p. 31-32°. Marvel _et al_[38] report m.p. 31-32°.

2-Methyl-1-Ethynylcyclohexanol-1 (XVII).-- The preceding set of directions was followed using 560 g. (5.0 moles) of _o_-methylcyclohexanone and 130 g. (5.6 moles) of sodium with proportionately larger quantities of the other reagents. The product distilling at 98-105° at 45 mm. weighed 464 g., a yield of 67% based on the original ketone. The crystals which appeared upon cooling for 12 hrs. at 0° weighed 227 g.; the separated liquid weighed 225 g. The solid, after recrystallization from petroleum ether, melted at 61.0-61.5° (corr.); the liquid portion was redistilled and boiled at 84.0° at 17 mm. Wang and Hu[15] report 60° and 85° at 18 mm. respectively.

2,6,6-Trimethyl-1-Ethynylcyclohexanol (XXI).-- In an identical manner, 560 g. (4.0 moles) of 2,6,6-trimethylcyclohexanone was treated with sodium acetylide formed from 92 g. (4.0 moles) of sodium metal. The material after hydrolysis and drying was fractionated through a forty-in. packed column at 20 mm. pressure, the desired cyclohexanol distilling at 90-95°. A yield of 524 g. was obtained, corresponding to 79.0% based on the trimethylcyclohexanone.

An analytical sample was obtained by treating 30 g. of this product with a solution of 60 g. of silver nitrate in 35 ml. of water; the acetylide was precipitated by the addition of 50 ml. of alcohol. The solid was removed by filtration, washed with 60 ml. of 50% alcohol, and sucked free from excess moisture. It was then suspended in 250 ml. of water, 50 ml. of ether added, and the solid decomposed with 50 g. of ammonium thiocyanate. The water layer was separated and washed once with 25 ml. of ether. The combined ether layers were washed once with 20 ml. of 1% sodium chloride solution and dried over sodium sulfate.

The acetylenic cyclohexanol was fractionated at 20 mm. pressure through a 1-ft. packed column. The fraction distilling at 88-90° weighed 21 g.; n_D^{25} 1.4740; d_4^{25} 0.9300; MR_D (calc.) 50.32; MR_D (obs.) 50.25.

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.91; Act. H, 2.0

Found: C, 79.51; H, 10.86; Act. H, 2.0

Dehydration of the Ethynylcyclohexanols.-- The apparatus used for the dehydration of these cyclic alcohols consisted of a glass tube 2.5 cm. in diameter and 24 cm. long. The length of the tube (20 cm.) containing the catalyst, a mixture of 5 parts of pumice to 1 part of aluminum phosphate, was inside an electric furnace. The alcohol was placed in an ordinary round-bottomed flask connected to the tube by a ground glass joint and heated independently of the furnace. Vapors of the unchanged alcohol and the dehydrated product passed from the catalyst into a spiral water condenser attached to a suction flask immersed in an ice-salt mixture. A dry ice trap, manometer, and oil pump completed the experimental arrangement.

In a typical dehydration, the alcohol was introduced into the flask and the apparatus assempled completely. The furnace was heated to 290-300° under pressure diminished just enough that the water evaporated from the catalyst did not drop into the alcohol. The alcohol was simultaneously heated to a temperature above its boiling point at the diminished pressure to be used in the dehydration. When this temperature was reached, the pressure was lowered to 175-180 mm. and the vapors of the alcohol allowed to distill over as rapidly as possible. The condensate was collected, ether added to aid in the separation of the water and hydrocarbon layers, the water layer removed, and the ether dried over magnesium sulfate. About 1 hr. was required for each 75 g. of material passed through the column.

By the use of this procedure, 297 g. of 1-ethynylcyclohexanol-1 yielded on dehydration and distillation through a 40-in. packed column 150 g. of material boiling up to 47° at 13 mm. This material possessed a value for active hydrogen of 0.85, corresponding to a conversion of 52%. The higher boiling material was saved for a subsequent dehydration.

Similarly, 250 g. of the liquid form of 2-methyl-1-ethynylcyclohexanol-1 was dehydrated. On fractionation through a 40-in. packed column 103 g. of product boiling up to 55° at 20 mm. was obtained; this material had a value for active hydrogen of 0.9. The conversion was 47%.

Dehydration of 180 g. of the solid form of 2-methyl-1-ethynylcyclohexanol-1 led to the formation of 84 g. of material boiling up to 57° at 20 mm. This product had a value for active hydrogen of 0.5, corresponding to a conversion of 17%.

Purification of the Enynes.-- A portion of the crude enyne was dissolved in 10 times its weight of absolute ethanol. The desired hydrocarbon was precipitated by the addition of an alcoholic solution of ammoniacal silver nitrate containing two moles of silver per mole of enyne treated. The silver nitrate solution was prepared by adding a weight of the reagent to 5 times its weight of absolute ethyl alcohol and then adding just enough concentrated ammonium hydroxide to dissolve the solid.

The precipitated acetylide was filtered, washed with 50% alcohol and then water, and sucked free of all excess moisture. The damp solid was then slurried in a small amount of water, 50 ml. of ether added to dissolve the hydrocarbon as it was liberated, and then a fivefold excess of solid ammonium thiocyanate added. Vigorous shaking of the slurry completely decomposed the acetylide. The two layers were separated and the ether solution dried over magnesium sulfate. The enyne was subsequently fractionated through a 1-ft. packed column.

Treated in this manner, 9.0 g. of crude 1-ethynyl-cyclohexene-1 yielded 6.0 g. of the pure enyne XIV boiling at 52-53° at 30 mm. pressure; n_D^{25} 1.4934, d_4^{25} 0.8843, MR_D (calc.), 34.48, MR_D (obs.), 34.90; λ max. 2240; εmol. 13,465.

Anal. Calcd. for C_8H_{10}: C, 90.50; H, 9.50; Act. H., 1.0

Found: C, 90.44; H, 9.52; Act. H., 1.0

Similarly, 32 g. of the crude enyne from the dehydration of the liquid form of 2-methyl-1-ethynyl-cyclohexanol-1 yielded 11.0 g. of material distilling at 63.0-63.5° at 30 mm.; n_D^{25} 1.4895, d_4^{25} 0.8827, MR_D (calc.) 39.09, MR_D (obs.) 39.41; λmax. 2290; εmol. 10,000.

Anal. Calcd. for C_9H_{12}: C, 89.93; H, 10.07; Act. H., 1.0

Found: C, 89.71; H, 10.16; Act. H., 1.0

Forty g. of the crude enyne obtained by the dehydration of the solid form of 2-methyl-1-enthynylcyclohexanol-1 yielded 12.0 g. of product boiling at 63.5-64.0° at 30 mm.; n_D^{25} 1.4883, d_4^{25} 0.8820, MR_D (calc.), 39.09; MR_D (obs.), 39.26; λ max. 2290; $\mathcal{E}$mol. 11,450.

Anal. Calcd. for C_9H_{12}: C, 89.93; H, 10.07, Act. H., 1.0

Found: C, 89.75; H, 10.20; Act. H., 1.0

Ozonization of the two 2-Methyl-1-Ethynylcyclohexenes.--The following procedure is an adaption of a method developed by Strain[39]. Two g. of the purified enyne was dissolved in 50 ml. of carbon tetrachloride and ozonized for twelve hrs. at 0°. At the end of this time 60 ml. of glacial acetic acid was added to the solution and the ozonization continued as before for an additional twelve hrs. Five ml. of 30% hydrogen peroxide was then added to the solution and the whole allowed to stand at room temperature for twenty-four hrs.

The solution was then steam-distilled until about a liter of distillate was collected. The residue was made to 25 ml. in a volumetric flask; 5 ml. of this solution was treated with 25 ml. of a saturated solution of 2,4-dinitrophenylhydrazine in 6N sulfuric acid and allowed to stand at 0° for three days. The sticky solid which formed was removed by filtration, washed well with water, and dissolved in 30 ml. of warm 3% sodium bicarbonate solution. After being filtered while warm, this solution was acidified with 4N sulfuric acid and allowed to stand at 0° for sixteen hrs. The sticky solid which formed was removed by filtration and washed well with water. The dried material was dissolved in 30 ml. of cold glacial acetic acid and the derivative precipitated by the addition of 50 ml. of water. The solution on standing at room temperature for sixteen hrs. deposited light-orange needles.

The 2,4-dinitrophenylhydrazone from the ozonized enyne from the solid form of 2-methyl-1-ethynylcyclohexanol-1 melted at 132.6-133.1° (corr.); 5.0 ml. of the solution made up after ozonization yielded 0.1238 g.

Anal. Calcd. for $C_{13}H_{16}O_6N_4$: C, 48.14; H, 4.97,
N, 17.28; N.E., 324
Found: C, 47.97; H, 4.89, N, 16.96; N.E., 327

A 5.0 ml. aliquot portion of the solution made up after ozonization of the liquid form of the cyclohexanol yielded 0.0422 g. of the derivative; in this instance, the mixture of solution and reagent was allowed to stand only one-third as long before the derivative was filtered for the first time. The crystals melted at 132.6-133.0° (corr.); no depression was observed when a mixed m.p. was taken. N.E. 326.

Since this 2,4-dinitrophenylhydrazone is not described in the literature, it was prepared from a sample of ε-keto-n-heptylic acid synthesized by the method of Wallach[38]. The material resulting from the oxidation of 3.0 g. of o-methylcyclohexanone by 4.0 g. of chromic anhydride was steam distilled, and 50 ml. of a saturated solution of 2,4-dinitrophenylhydrazine in 6N sulfuric acid added to the residue. From this point on, the purification procedure was identical to that described above. The m.p. was 132.5° (corr.) and there was no depression when a mixed m.p. with each of the derivatives formed above was determined.

Also, a semicarbazone was prepared from each of these same solutions made up after the two ozonizations. A 2.0 ml. aliquot of the solution obtained by the ozonization of the enyne from the solid form of the ethynyl cyclohexanol formed a precipitate which melted at 145.0-146.0° (corr.); 0.0642 g. was obtained.

Two ml. of the other solution formed 0.1605 g. of derivative melting at 144.0-145.0° (corr.). There was no depression of the melting point when the two samples were mixed. Wallach[40] reports this derivative as melting at 144-145°.

Dehydration of 2,6,6-Trimethyl-1-Ethynylcyclohexanol with Anhydrous Oxalic Acid.-- Eighty g. (0.48 mole) of this cyclohexanol was added to 61 g. (0.68 mole) of anhydrous oxalic acid in a 250 ml. distilling flask equipped with a thermometer and attached to a 10-in. coil condenser. The pressure was diminished as far as possible by an aspirator and the flask was placed in an oil bath previously heated to 170°. A vigorous reaction occurred almost immediately; a cloudy distillate collected, which was resolved into two layers with the help of a few ml. of ether. The lower layer was separated and extracted once with 10 ml. of ether; the combined ether layers after being washed four times with 15 ml. of 5% sodium bicarbonate solution and twice with 15 ml. of water were dried over sodium sulfate.

The material was fractionated through a 1-ft. packed column at 30 mm. pressure; 26 g. of a colorless liquid distilled up to 75° (chiefly 72-74°). A Zerewitinoff determination on this fraction indicated a value for active hydrogen of 0.3.

This material was treated with ammoniacal silver nitrate in the manner described above, and the product fractionated; 2.1 g. of material distilled at 58-62° at 30 mm. pressure. This was a yield of 3% based on the cyclohexanol; n_D^{25} 1.4745, d_4^{25} 0.8574, MR_D (calc.), 48.33; MR_D (obs.), 48.55. Milas and MacDonald[8] report n_D^{25} 1.4755 for their product.

Anal. Calcd. for $C_{11}H_{16}$: C, 89.11; H, 10.89; Act. H., 1.0
Found: C, 88.76; H, 10.79; Act. H, 0.9

1-(Cyclohexen-1'-yl)-3-Methyl-4-Chloro-1-But-1-yn-ol-3 (XV).-- A Grignard reagent was prepared from 60 g. of crude 1-ethynylcyclohexene-1 (Act. H., 0.9, corresponding to 54 g. (0.5 mole) of the enyne) by adding a solution of it dissolved in 200 ml. of dry ether rapidly to a stirred solution of 0.5 mole of ethyl magnesium bromide cooled in an ice-salt bath. A nitrogen stmosphere was maintained continually. After the addition was complete, the solution was stirred at room temperature for twenty-four hrs. At the end of this time the solution was cooled again in an ice-salt freezing mixture, and 47.2 (0.5 mole) of chloroacetone dissolved in 200 ml. of anhydrous ether added very slowly to the rapidly stirred solution. The solution was then stirred at room temperature for six hrs. Hydrolysis was effected by 200 ml. of saturated ammonium chloride solution. The ether and water layers were separated, the water layer extracted twice with 50 ml. of ether, and the combined ether layers washed twice with 50 ml. of water. After being dried over magnesium sulfate, the ether layer was fractionated in a 1-ft. packed column; there was obtained 40 g. of very light orange colored material distilling at 110-116° at 4 mm. This amounted to a 39.5% yield based on the enyne; n_D^{25} 1.5259; d_D^{25} 1.1090; MR_D (calc.), 54.72; MR_D (obs.), 54.96.

Anal. Calcd. for $C_{11}H_{15}OCl$: C, 66.47; H, 7.56; Cl, 17.85; $\overline{\Gamma}$, 3.0; Act. H., 1.0

Found: C, 66.15; H, 7.61; Cl, 18.19; $\overline{\Gamma}$, 3.3 (Pt); Act. H., 1.0

1-(2'-Methylcyclohexen-1'-yl)-3-Methyl-4-Chloro-1-But-1-yn-ol-3 (XIX).-- With 44 g. of crude 2-methyl-1-ethynylcyclohexene-1 (Act. H., 0.9, corresponding to 39.6 g. (0.33 mole) of the enyne) the procedure described previously was followed to provide 38.0 g. of the chlorohydrin boiling at 115-130° at 4 mm. This corresponded to a yield of 54.0%; n_D^{25} 1.5360; d_4^{25} 1.1111; MR_D (calcd.), 59.34; MR_D (obs.), 59.63.

Anal. Calcd. for $C_{12}H_{17}OCl$: C, 67.75; H, 8.06; Cl, 16.77; $\overline{\Gamma}$, 3.0; Act. H., 1.0

Found: C, 67.98; H, 8.04; Cl, 16.81; $\overline{\Gamma}$, 3.3 (Pt); Act. H., 1.0

3-Methyl-1-Phenyl-4-Chloro-1-But-1-yn-ol-3 (XXIII).-- In the same manner, 26.5 g. (0.26 mole) of phenylacetylene formed 23.5 g. of the chlorohydrin XXIII distilling at 94-96° at 1 mm. This was a yield of 52.5%; n_D^{25} 1.5624.

Anal. Calcd. for $C_{11}H_{11}OCl$: C, 67.86; H, 5.70

Found: C, 66.91; H, 5.92

1-(Cyclohexen-1'-yl)-3-Methyl-3-Epoxybutyne-1 (II).-- A solution of 27.5 g. (0.14 mole) of the chlorohydrin XV dissolved in 100 ml. of anhydrous ether was placed in a 500 ml. flask equipped with a condenser, mercury-sealed stirrer, and a calcium chloride drying tube. A nitrogen atmosphere was continually maintained. Freshly powdered potassium hydroxide (10.0 g., 0.32 mole) was added to the rapidly stirred solution at a sufficiently slow rate that the ether did not reflux. When all the alkali had been added, the reddish brown slurry was refluxed for 1 hr.

After the mixture had cooled to room temperature, the mixture of potassium chloride and excess potassium hydroxide was removed by filtration through asbestos. The ether was removed under diminished pressure and the residue distilled in a shallow 50 ml. flask with an attached 6-in. Vigreaux column. The material distilling at 85-87° at 1-2 mm. pressure was collected and fractionated through a 1-ft. packed column. The fraction boiling at 64-64.5° at 1 mm. pressure weighed 7.5 g., a yield of 33.5% based on the chlorohydrin; n_D^{25} 1.5145; d_4^{25} 0.9960; MR_D (calcd.), 47.77; MR_D (obs.), 49.01; λmax, 2320; ϵmol., 14,920.

Anal. Calcd. for $C_{11}H_{14}O$: C, 81.44; H, 8.70; Γ, 3.0

Found: C, 80.81; H, 8.63; Γ, 3.3 (Pt)

The 2,4-dinitrophenylhydrazone was formed when 0.4 g. of the epoxy compound, dissolved in 10 ml. of absolute ethanol, was mixed with 0.08 g. of 2,4-dinitrophenylhydrazine, heated to boiling on a hot plate, and rearranged by the addition of 2 drops of concentrated hydrochloric acid. The solution was refluxed for 3 min., and then water was added dropwise until a turbidity appeared. When the solution cooled to room temperature a dark orange tar appeared; this was dissolved in 10 ml. of pure acetic acid and 10 ml. of water added. The derivative appeared as an orange solid (0.75 g.), m.p. 157-158° (corr.).

Anal. Calcd. for $C_{17}H_{18}O_4N_4$: C, 59.61; H, 5.30; N, 16.37
Found: C, 59.49; H, 5.99; N, 16.28

1-(2'-Methylcyclohexen-1'-yl)-3-Methyl-3-Epoxybutyne-1 (III).-- In a manner identical to that described above, 17.5 g. (0.082 mole) of the chlorohydrin XIX was dehydrochlorinated with 13.6 g. (0.24 mole) of powdered potassium hydroxide. The preliminary distillation yielded 6.0 g. of material, and this, when fractionated as before, yielded 4.6 g. of the epoxy compound, b.p. 64-66° at 1 mm. pressure. This was a yield of 31.0%, based on the chlorohydrin; n_D^{25} 1.5058; d_4^{25} 0.9942; MR_D (calcd.), 52.39; MR_D (obs.) 52.70; λmax., 2320; εmol., 15,300.

Anal. Calcd. for $C_{12}H_{16}O$: C, 81.76; H, 9.15; Γ, 3.0
Found: C, 81.33; H, 9.24; Γ 3.2 (Pt)

The 2,4-dinitrophenylhydrazone, prepared as described above from 3 drops of the epoxy compound, melted at 158-159° (corr.).

Anal. Calcd. for $C_{18}H_{20}O_4N_4$: C, 60.66; H, 6.65

Found: C, 60.52; H, 6.34

3-Methyl-1-Phenyl-3-Epoxybutyne-1 (IV).-- This compound was formed when 17.0 g. (0.11 mole) of the chlorohydrin XXIV was treated with 11.7 g. (0.21 mole) of powdered potassium hydroxide. In this instance, the first distillation was omitted; one fractionation through a 1-ft. packed column yielded 6.0 g. of material distilling at 65-67°. This was a yield of 43.5%; n_D^{25} 1.5570; d_4^{25} 0.9968; MR_D (calcd.), 46.84; MR_D (obs.), 51.02; λmax., 2430; εmol., 19.295.

Anal. Calcd. for $C_{11}H_{10}O$: C, 83.50; H, 6.37; Γ, 5.0

Found: C, 82.84; H, 6.42; Γ 5.2 (Pt)

When 23.0 g. (0.14 mole) of the chlorohydrin XXIV was dehydrochlorinated with 16.5 g. (0.42 mole) of sodamide in anhydrous ether, 7.5 g. (40.0%) of product distilling at 65-67° at 1 mm. pressure was obtained; n_D^{25} 1.5582.

Anal. Calcd. for $C_{11}H_{10}O$: C, 83.50; H, 6.37

Found: C, 82.86; H, 6.36

The 2,4-dinitrophenylhydrazone prepared from 0.40 g. of this compound and 0.08 g. of reagent weighed 0.81 g;

it melted at 96-97° (corr.).

Anal. Calcd. for $C_{17}H_{15}O_4N_4$: C, 60.17; H, 4.46; N, 16.52

Found: C, 60.10; H, 4.34; N, 15.65

3-Methyl-1-Phenyl-1-Hexyn-3-ol (XXVIII).-- A Grignard reagent was prepared from 3.2 g. of magnesium (0.133 mole) and 14.6 g. (0.133 mole) of ethyl bromide in 100 ml. of anhydrous ether. The solution was cooled in an ice bath to 0°, and 17.5 g. (0.111 mole) of the preceding epoxy compound dissolved in 40 ml. of anhydrous ether was added dropwise. After the addition was complete the mixture was stirred at room temperature for three hrs. It was then again cooled to 0° and hydrolyzed with a solution of 8 g. of ammonium chloride in 50 ml. of water. The layers were separated, the water layer extracted once with 15 ml. of ether and the combined ether layers after being washed once with 25 ml. of water were dried over magnesium sulfate.

The material was fractionated at a pressure of 1 mm. in a 1-ft. packed column; the fraction distilling at 90-94° weighed 12.0 g., a yield of 57.7% based on the epoxy compound; n_D^{25} 1.5458; d_4^{25} 0.9865; MR_D (calcd.), 58.16; MR_D (obs.), 60.34.

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.93; H, 8.57; Γ, 5.0; Act. H., 1.0

Found: C, 82.95; H, 8.55; Γ, 5.0 (Pt); Act. H., 1.0

3-Methyl-1-Phenylhexanol-3 (XXIX).-- Seven and a half g. of the preceding unsaturated alcohol was dissolved in a mixture of 100 ml. of absolute thanol and 2 ml. of pure acetic acid. Platinum catalyst (0.75 g.) was added, and the solution shaken under an atmosphere of hydrogen at 25 lb. pressure until absorption of the gas had ceased (about 1 hr.). The catalyst was removed by filtration through asbestos.

The filtrate was added in 10 ml. portions to a mixture of 150 ml. of petroleum ether and 50 ml. of a 10% salt solution. The whole was shaken in a separatory funnel, the layers separated, and the lower layer removed. A fresh 50 ml. portion of the salt solution was added, another 10 ml. sample of the filtrate introduced, and the process repeated until all the filtrate had been extracted. The combined water layers were extracted once with 30 ml. of petroleum ether and the combined ether layers extracted once with 30 ml. of a 5% sodium bicarbonate solution and once with 50 ml. of water. The solution was dried over magnesium sulfate.

The material was fractionated through a 1-ft. packed column at a pressure of 1 mm., the fraction distilling at 90-92° being taken as the hydrogenated compound. A yield of 4.3 g. was obtained, corresponding to 54.7% of theory, based on the alcohol hydrogenated; n_D^{25} 1.5020; d_4^{25} 0.9522; MR_D (calcd.), 60.16; MR_D (obs.), 61.66.

Anal. Calcd. for $C_{13}H_{20}O$: C, 81.24; H, 10.49; Γ, 3.0; Act. H., 1.0

Found: C, 81.20; H, 10.82; Γ, 3.0 (Pt); Act. H., 1.0

IV. SUMMARY

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A new acetylenic cyclohexanol, 2,6,6-trimethyl-1-ethynylcyclohexanol-1, in which the methyl groups are arranged in the same manner as those in β-ionone, has been characterized.

Two new enynes, 1-ethynylcyclohexene-1 and 2-methyl-1-ethynylcyclohexene-1 have been synthesized. It has been shown that the latter is formed when either of the pairs of stereoisomers of 2-methyl-1-ethynylcyclohexanol-1 is catalytically dehydrated.

Two enyne chlorohydrins, 1-(Cyclohexen-1'-yl)-3-methyl-4-chloro-1-but-1-yn-ol-3 and 1-(2'-methylcyclohexen-1'-yl)-3-methyl-4-chloro-1-but-1-yn-ol-3 have been prepared, and the synthesis of 3-methyl-1-phenyl-4-chloro-1-but-1-yn-ol-3 investigated.

The epoxy compounds derived from these chlorohydrins, 1-(cyclohexene-1'-yl)-, 1-(2'-methylcyclohexen-1'-yl)-, and 3-methyl-1-phenyl-3-epoxybutyne-1 respectively have been synthesized, and their structures elucidated by absorption spectra, formation of solid derivatives, and analitical data.

The alcohol formed by the reaction of a Grignard reagent with one of these epoxy compounds has been prepared and partially hydrogenated.

IV. BIBLIOGRAPHY

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BIOGRAPHY

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