THE SYNTHESIS OF CONDENSED RING COMPOUNDS. III. A HEXAHYDRONAPHTHALENE DERIVATIVE FROM A DIENEYNE

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In the preceding paper (1) it was shown that 1,3,5-hexatriene might serve as the basis of a general synthetic method for condensed ring compounds of angular construction, such as steroids, since it was possible to secure, as the principal product of its addition to a cyclohexene, a derivative of 1-vinyloctahydronaphthalene with the annular double bond probably in the 2,3-position. The utility of this intermediate in the synthesis of angular polycyclic compounds would depend on its ability to isomerize to a 1-vinyl-1-octalin which could then add a dienophile. Before the feasibility of this procedure could be tested, we had observed that a 1,5-diene-3-yne can add two molecules of dienophile to give a crystalline product and it has now been found that this addition proceeds in the manner required for the synthesis of compounds of the type sought.

In 1933 Blomquist and Marvel (2) found that both 4,7-di-*n*-propyl-3,7-decadiene-5-yne and 6,9-dimethyl-5,9-tetradecadiene-7-yne added two moles of maleic anhydride in boiling xylene. Since the products of reaction did not crystallize, the solution in xylene was heated with aqueous alkali. Neutralization of the alkaline extract gave products with the composition $R_4C_{14}H_{10}O_8$ but, as these were amorphous, no attempt was made to characterize them further.

We have now heated 2,5-dimethyl-1,5-hexadiene-3-yne (I) with maleic anhydride at 130°. From the reaction-mixture a crystalline product, $C_{16}H_{14}O_6$, was isolated. If the two moles of maleic anhydride added one after the other in the manner of a Diels-Alder reaction, then III and IV would be the expected structures.² The intermediate II has not been

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² Providing that any 1-isopropenyl-3-methyl-1,2-cyclohexadiene-5,6-anhydride, formed as a primary adduct, rearranges before a second mole of maleic anhydride adds.

isolated. This is not surprising since II at 130° should add maleic anhydride readily, or it might polymerize.



The new compound, $C_{16}H_{14}O_6$, melts at 262–263° and is a dianhydride. It dissolves slowly in boiling water and the solution is acid. A barium salt may be precipitated from the solution in aqueous sodium hydroxide. The adduct dissolves slowly in cold ethanol. A tetraethyl ester, $C_{24}H_{34}O_8$, was formed by heating with ethanol. The presence of olefin linkages was indicated by reduction of permanganate, addition of bromine, and catalytic hydrogenation with palladium.

Structure IV was eliminated as a possibility, since after heating the dianhydride with palladium-charcoal an easily sublimable hydrocarbon, $C_{12}H_{12}$, with a naphthalene-like odor was obtained. The melting points of the hydrocarbon (77°) and its picrate agree closely with those reported in the literature (12, 13) for 1,5-dimethylnaphthalene. The hydrocarbon has been shown to be 1,5-dimethylnaphthalene by a mixed melting point determination with a specimen prepared from *o*-bromotoluene.³ The

³ This method, not hitherto used for the synthesis of 1,5-dimethylnaphthalene, and the intermediate compounds will be described elsewhere.

crystalline adduct is therefore a 1,5-dimethylhexahydronaphthalene-3,4, 7,8-dianhydride. Structure III, however, is probably not correct. Spectroscopic examination of the solutions obtained by dissolving the dianhydride in boiling water or cold ethanol indicate the presence of two con-

Comparison of Absorption Spectra with those of Known Compounds (3)			
COMPOUNDS	SOLVENT	λ max (Å)	¢
2,4-Cholestadiene.		2,670, 2,750	5,500
3,5-Cholestadiene.		2,400	14,000
4,6-Cholestadiene.		2,380	24,000
Maleic acid	Ethanol	2,100	13,000
Ethylene		1,800	10,000
1,5-Hexadiene.	\mathbf{E} thanol	<1,850	20,000
Tetracarboxylic acid, C ₁₆ H ₁₈ O ₈	Water	2,450	21,000
Tetraethyl ester, C24H34O8	Ethanol	2,470	22,000

TABLE I



Figure I. Absorption Curves of the Tetracarboxylic Acid (O) and Tetraethyl Ester (\bullet)

jugated double bonds distributed over two rings as shown in Figure I and Table I. It is unlikely that conjugation of one of the carbon-carbon double bonds with one or two carboxyl groups could explain the observed maxima, although data (3) for comparison are available only for acyclic compounds. It is more probable that the two carbon-to-carbon double bonds are in conjugation. By migration of a single hydrogen atom in III, structures V and VI could be formed. A comparison with data (3) for 2,4-, 3,5-, and 4,6-cholestadienes indicates V as the more probable structure, but this cannot be taken as final because V represents a derivative of 4,8-hexalin whereas the known data relate to 3,5- and 4,6-cholestadienes, derivatives of 1,8-hexalin. Of the twenty-one isomeric hexahydronaphthalenes, only two, the 1,2,6,7,8,8a- and the 1,2,3,5,6,7-hexahydro- isomers contain heteronuclear conjugated double bonds. V is derived from the latter hydrocarbon and there is no reason to expect a derivative of the former from this reaction.

The crystalline compound from the dieneyne and maleic anhydride is therefore probably one of the stereoisomers of 1,5-dimethyl-2,3,4,6,7,8hexahydronaphthalene-3,4,7,8-tetracarboxylic acid (dianhydride) Va or Vb with cis attachment to the ring of the carbonyls within each of the anhydride groups.



It is unlikely that the *cis*-anhydride formed primarily in the Diels-Alder reaction would be transformed by heat into a *trans*-anhydride, since Baeyer (4) found that *trans*-1,2,3,6-tetrahydrophthalic anhydride is converted to the *cis*-isomer at 210°. A decision between the two structures Va and Vb would be of great interest in further defining the stereochemical

course of the Diels-Alder reaction (5) and experiments directed towards this end are in progress.⁴

The mechanism of the addition of a dienophile to a 1,3-eneyne must differ in some respect from the addition to a 1,3-diene, since in the latter process a new ring can form without migration of a hydrogen atom. Dane and co-workers (6) have added maleic anhydride to 1-ethynyl-6-methoxy-3,4-dihydronaphthalene and have formulated their product as VII. Thus the original 1,3-eneyne system appears in the adduct as a 1,3-diene system made up of the same carbon atoms. Migration of a hydrogen atom must have occurred during the formation of the new ring. The same would hold for their second case (7) in which methyl propiolate was the dienophile and a new benzene ring was formed during addition.



⁴ It is proposed that Va be referred to as the 3x, 4x, 7y, 8y- or simply xxyy-isomer, and Vb as the racemic xxxx-isomer. This system will be subsequently employed in



If the mechanism of the Diels-Alder addition proposed by Robinson (8) is extended to energy processes A and B are conceivable. It will be seen that the hydrogen attached to the triply bonded carbon does not migrate in any of these hypothetical processes and hence it might be inferred that the energy need not contain such hydrogen in order to add a dienophile. This is borne out by the addition to 2,5-dimethyl-1,5-hexadiene-3-yne

designating the various stereoisomers of more complicated types. Thus for the unsymmetrical molecule III, four stereoisomers would come up for consideration. These are the r-xxxxx-, r-xxxyy- and r-xxyy-isomers. The third prefix (x or y) refers to the configuration of the hydrogen at the 4a position.

reported in this paper. One would predict on the same basis that a compound like 1,1-dimethyl-1-butene-3-yne would not add, since the 1-carbon has no hydrogen to supply during ring formation. It will be of interest to investigate the intermediate case of an eneyne in which the 1-carbon has but one hydrogen. The compounds studied by Blomquist and Marvel (2) are of this type, but these may have presented difficulty for other reasons.

Until a compound II has been found, another mechanism for the formation of V must be considered. It is conceivable that V is not formed from III and that II is not an intermediate at all. Using again Robinson's conception (8) of the general mechanism of diene additions, the dimethylhexadieneyne, being a perfectly symmetrical molecule, might add two molecules of maleic anhydride at the same instant to give VIII, which then could cyclize directly to V. No migration of hydrogen occurs according to this scheme. A formal analogy to this mode of addition is presented by the addition of two moles of hydrogen chloride to divinylacetylene observed by Coffman *et al.* (9). Here no intermediate allene was isolated. Could it be that an unsymmetrical dienophile would add in the same manner as hydrogen chloride?

Still another possibility, quite aside from ionic mechanisms, is perhaps worth considering. The primary adduct from I and maleic anhydride may be the allene IX. This may exist long enough to add another mole of maleic anhydride, which addition would result in the direct formation of V. Such a mechanism involves no migration of hydrogen. Some support for the idea of IX as an intermediate is furnished by the discovery of Favorskii (14) that 1,2-cycloheptadiene is sufficiently stable to be isolated.





EXPERIMENTAL

2,5-Dimethyl-3-hexyne-2,5-diol and 2,5-dimethyl-1,5-hexadiene-3-yne. The glycol, m.p. 95°, was prepared by the method of Kazar'yan (10), modified by taking the theoretical proportion of acetone, instead of half that quantity as stated in the original paper. The dieneyne, b.p. 38-43° (22 mm.), $n_{\rm D}^{\rm m}$ 1.4854, was prepared from the glycol by the procedure of Mitchell and Marvel (11).

Addition of maleic anhydride to $2, \delta$ -dimethyl-1, δ -hexadiene-3-yne. All the experiments were done at 130° in sealed tubes in which the air was replaced by carbon dioxide. The dieneyne was taken in excess and usually no other solvent was added. In one experiment where benzene was employed as solvent the dianhydride V was not found among the products. These have not yet been fully investigated. One is a substance much less stable toward heat than V. The yield of V was improved by using maleic anhydride which had been twice distilled. This precaution also prevented the formation during the reaction of a benzene-insoluble amorphous product which made difficult the separation of products. Analysis of the old undistilled sample of maleic anhydride used in some of these experiments indicated a content of about 10% of maleic acid.

In a typical run, 3 g. of twice distilled maleic anhydride and 4.7 g. (1.5 moles) of 2,5-dimethyl-1,5-hexadiene-3-yne were heated together for 2 hours. After cooling, the oil (about 3 g. consisting apparently of unchanged and dimerized dieneyne) was separated from the crystals, which were quite pure after one recrystallization from acetone, 1.1 g. (representing 24% of the maleic anhydride taken), m.p. 256-258°. Recrystallization from ethyl acetate or acetone-benzene gave V, m.p. 262-263° (uncorr.; tubes placed in bath previously heated to 220°).

Anal.⁵ Calc'd for C₁₆H₁₄O₆: C, 63.55; H, 4.67.

Found: C, 63.55; H, 4.79.

When undistilled maleic anhydride was taken, the crystalline product did not separate readily and it was necessary to resort to continuous extraction for several days with benzene in order to separate it from amorphous material.

The mother liquors, which contain three-fourths of the maleic anhydride taken, or products therefrom, remain to be investigated. Saponification with sodium hydroxide followed by neutralization with hydrochloric acid gave a product melting indefinitely around 250°, which appears to be an acid related to III or V.

Anal. Calc'd for C₁₆H₁₈O₈: C, 56.78; H, 5.36.

Found: C, 56.45; H, 6.07.

No compound corresponding to structure II has been found; and, indeed, it is questionable whether such a substance would be stable alone at 130°. Certainly it would add maleic anhydride very rapidly.

The crystalline product C16H14O6 is insoluble in cold water, but dissolves slowly in

⁵ All analyses by Arlington Laboratories, Arlington, Virginia.

hot water to give an acid solution. A few mg. in acetone decolorized potassium permanganate slowly (15 minutes) and a suspension in acetic acid reacted with bromine at 25° somewhat more slowly than cholesteryl acetate. The bromide (?) which was obtained by precipitation with water melted above 310°. A single experiment indicated that 1.5 moles of hydrogen are absorbed in ethanol in the presence of palladium; 77.5 mg. dianhydride, 9.8 cc. hydrogen, 747 mm., 27°, 2 hours.

Preparation of a tetraethyl ester from the dianhydride $C_{16}H_{14}O_6$. The dianhydride dissolved slowly in ethanol at 25°. Twenty-three cubic centimeters of ethanol was added to 101 mg., let stand 20 hours, warmed on the steam-bath 5 minutes to complete solution, and cooled. No solid separated. Evaporation of the ethanol (steam-bath, 50 minutes) in a stream of nitrogen gave an oil which crystallized on addition of benzene. Twenty cubic centimeters of benzene was added, the mixture boiled for a few minutes, filtered, and the insoluble part recrystallized from benzene-acetone (30:1); colorless crystals, m.p. 163-165° (corr.).

Anal. Calc'd for C24H34O8: C, 63.98; H, 7.16.

Found: C, 63.95; H, 6.99.

Dehydrogenation to 1,5-dimethylnaphthalene. The dianhydride (841 mg.) was heated at 230-325° for 30 minutes with 244 mg. of palladium (12%) on charcoal. Rapid production of gas and water occurred at 285-325°. The temperature was then maintained at 325-355° for one hour. During the reaction some colorless solid appeared in the receiver as a result of steam distillation. The solid products of reaction were extracted successively with ether and sodium hydroxide solution. Partition between ether and aqueous sodium hydroxide gave 50 mg. of material soluble in ether. Evaporation of the ether gave a crystalline residue which formed a picrate, m.p. 130-131° (corr.); 1,5-dimethylnaphthalene picrate (12), m.p. 137-138°.

Anal. Calc'd for C₁₂H₁₂·C₆H₃O₇N₃: N, 10.90. Found: N, 10.49, 10.50.

More 1,5-dimethylnaphthalene was obtained by acidification of the alkaline solution, distillation of the precipitated acids with calcium hydroxide, steam distillation of the condensate thus obtained, and recrystallization of the steam distilled products from methanol. The hydrocarbon thus obtained had the m.p. 76° (corr.); literature, Veselý and Štursa (12), 77-78°, Anderson and Short (13), 80-80.5°. It did not depress the m.p. (77-78°) of 1,5-dimethylnaphthalene prepared from obromotoluene.

Anal. Calc'd for C12H12: C, 92.31; H, 7.69.

Found: C, 92.25; H, 7.65.

The same hydrocarbon was obtained by another procedure. The dianhydride was dissolved in aqueous sodium hydroxide, the solution precipitated with barium hydroxide, and the dried barium salt heated at 450-500° with palladium-charcoal and two moles of barium hydroxide octahydrate.

SUMMARY

1. 2,5-Dimethyl-1,5-hexadiene-3-yne adds two molecules of maleic anhydride to give a crystalline substance, $C_{16}H_{14}O_6$, which can be converted to 1,5-dimethylnaphthalene by heating with palladium-charcoal.

2. The new compound is probably 1,5-dimethyl-2,3,4,6,7,8-hexa-hydronaphthalene-xxyy-3,4,7,8-tetracarboxylic acid (dianhydride) or r-1,5-dimethyl-2,3,4,6,7,8-hexahydronaphthalene-xxxx-3,4,7,8-tetracarboxylic acid (dianhydride).

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3. This dianhydride forms the tetraethyl ester with great ease by merely heating with ethanol.

4. The mechanism of the addition of dienophiles to energy and dienergy is discussed.

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