ring have been noted by Albert.[1] So far as we are aware, however, this is the first case in which a substituent has been added to the 6 position, presumably by addition to a double bond in the partially reduced ring, with subsequent further reoxidation.[2]

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(1) A. Albert, "Current Trends in Heterocyclic Chemistry," A. Albert, G. M. Badger and C. W. Shoppee, eds., Academic Press, Inc., New York, N. Y., 1958, p. 20.

(2) This work was supported by the Rockefeller Foundation, the Robert A. Welch Foundation, Houston, Texas, and the National Science Foundation.

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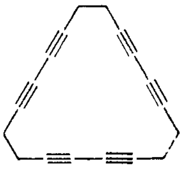
UNSATURATED MACROCYCLIC COMPOUNDS. VI. THE SYNTHESIS OF CYCLOÖCTADECA-1,3,7,9,13,15-HEXAENE-5,11,17-TRIYNE, A COMPLETELY CONJUGATED EIGHTEEN-MEMBERED RING CYCLIC SYSTEM[1]

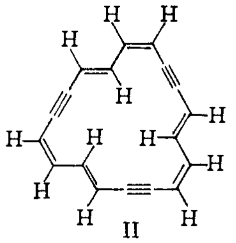
Sir:

It has been shown that the oxidative coupling of terminal diacetylenes may lead to large-ring polyacetylenes.[2,3] We have also found that certain linear 1,5-enynes $(-C\equiv C-CH_2CH_2-CH=CH-)$ and 1,5-diynes $(-C\equiv C-CH_2CH_2-C\equiv C-)$ undergo ready prototropic rearrangement on being treated with potassium *t*-butoxide in *t*-butyl alcohol, to yield, respectively, the corresponding conjugated trienes and dienynes.[4] A combination of these reactions appeared to provide a route to fully conjugated monocyclic large-ring systems and this objective has now been realized.

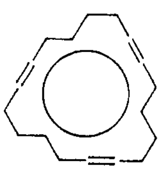
Cycloöctadeca-1,3,7,9,13,15-hexayne (I) (obtained in *ca.* 6% yield by the oxidation of 1,5-hexadiyne with cupric acetate in pyridine)[4] on treatment with potassium *t*-butoxide in *t*-butyl alcohol at 90° for 25 minutes rearranged in *ca.* 50% yield to a new substance, $C_{18}H_{12}$, which after chromatography on alumina crystallized from pentane as large brown plates, m.p. 190–192° (dec.; sample placed on block at 185°) (found: C, 94.71; H, 5.06). This substance is assigned the fully conjugated unstrained planar structure II [cycloöctadeca-1,7,13-(*cis*)-triene-3,9,15-(*trans*)-triene-5,11,-17-triyne],[5] derived from I by prototropic rearrangement of each 1,5-diyne to a 1,3-dien-5-yne unit. This structure follows from its properties as well as from an alternative method of preparation.[6]



I



II



IIa

The ultraviolet spectrum in isoöctane showed maxima at 245, 254, 322, 334, 365, 385, 400 and 434 mμ (ϵ = 18,800, 14,700, 98,000, 160,000, 8,700, 11,700, 15,200 and 1,080) and in benzene at 329, 342, 391, 407 and 441 mμ (ϵ = 95,000, 155,000, 12,000, 15,200 and 1,100). The infrared spectrum (KBr) showed bands at 3.30(w), 4.63(w), 4.75(w), 7.06(w), 7.78(m), 8.19(w), 8.40(w), 9.06(w), 10.32 (s), 10.81(s), 11.86(s) and 13.20(s) μ. Hydrogenation in dioxane over platinum yielded cycloöctadecane, m.p. and mixed m.p. 72–73°, showing that no transannular reaction had occurred during the rearrangement.

The hexaene-triyne II contains a continuous molecular orbital and may be written as IIa.[7] It contains 18 π-electrons in conjugation and is the first conjugated monocyclic system known with more than the classical sextet. The substance complies with Hückel's rule for aromatic stability in cyclic molecular orbitals [presence of $(4n + 2)$ conjugated π-electrons],[8] although the carbon-carbon bonds are of course not all equivalent as would be required for maximum stability. As expected, II is a reasonably stable compound as judged by its method of formation in satisfactory yield, the exhibition of a melting point (with decomposition) near 200°, the fact that it can be kept with little change for several days at room temperature in light and air, etc.

In practice it was found most convenient to carry out the oxidation of 1,5-hexadiyne as before,[1] rearrange the total reaction product with potassium *t*-butoxide and chromatograph. In this way 0.41 g. of pure II was obtained simply from 15 g. of 1,5-hexadiyne. In addition other colored conjugated hydrocarbons were formed, the structures of which are being investigated.

We are grateful to Prof. R. B. Woodward and the late Prof. W. E. Moffitt for valuable discussions.

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(1) Part V, see F. Sondheimer, Y. Amiel and R. Wolovsky, THIS JOURNAL, **79**, 4247 (1957).

(2) F. Sondheimer, Y. Amiel and R. Wolovsky, *ibid.*, **78**, 4178 (1956); **79**, 4247, 5817, 6263 (1957); *Proc. Chem. Soc.*, 22 (1957).

(3) G. Eglinton and A. R. Galbraith, *Chem. and Ind.*, 737 (1956); *Proc. Chem. Soc.*, 350 (1957).

(4) *Cf.* E. R. H. Jones, M. C. Whiting, *et al.*, *J. Chem. Soc.*, 3197, 3201, 3208, 3212 (1954).

(5) For a discussion, but not the realization, of syntheses of related cyclic planar conjugated vinylacetylenes, see T. J. Sworski, *J. Chem. Phys.*, **16**, 550 (1948).

(6) F. Sondheimer, Y. Amiel and Y. Gaoni, THIS JOURNAL, **81**, 1771 (1959).

(7) *Cf.* W. von E. Doering and L. H. Knox, *ibid.*, **74**, 5683 (1952).

(8) E. Hückel, *Z. Physik*, **70**, 204 (1931); "Grundzüge der Theorie ungesättigter und aromatischer Verbindungen," Verlag Chemie, Berlin, 1938.

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UNSATURATED MACROCYCLIC COMPOUNDS. VII.[1] SYNTHESIS OF CYCLOÖCTADECA-1,3,7,9,13,15-HEXAENE-5,11,17-TRIYNE FROM 1,5-HEXADIYN-3-OL

Sir:

It has been shown recently that macrocyclic polyacetylenes can be prepared simply by the oxidative coupling of certain terminal diacetylenes.[2] A possible approach to the synthesis of completely conjugated macrocyclic unsaturated compounds involved the coupling of the hitherto unknown 1,5-hexadiyn-3-ol (I) and subjecting any

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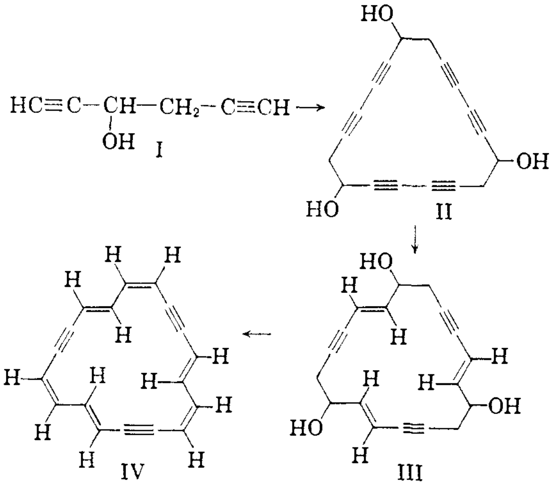
(1) Part VI, F. Sondheimer and R. Wolovsky, THIS JOURNAL, **81**, 1771 (1959).

(2) F. Sondheimer, Y. Amiel and R. Wolovsky, *ibid.*, **78**, 4178 (1956); **79**, 4247, 5817, 6263 (1957); G. Eglinton and A. R. Galbraith, *Chem. and Ind.*, 737 (1956); *Proc. Chem. Soc.*, 350 (1957).

cyclic products to partial reduction and dehydration. We have now found that this type of sequence can be carried out successfully and by its use we have effected a second synthesis of the fully conjugated cycloöctadeca-1,7,13-(*cis*)-triene-3,9,-15-(*trans*)-triene-5,11,17-triyne (IV) already described.[1]

1,5-Hexadiyn-3-ol (I) [b.p. 72–73° (20 mm.), n^{25}_D 1.4755; found: C, 75.96; H, 6.56; acetylenic H, 2.06] was prepared in 50–60% yield by the reaction of propargylaldehyde with propargylmagnesium bromide[3a] or with propargyl aluminum bromide[3b] at −30 to −10°. The conditions are critical (details will be given in the full paper) and



1,4-hexadiyn-3-ol [HC≡C—CH(OH)—C≡C—CH_3] [b.p. 82–84° (20 mm.), n^{25}_D 1.4765; found: C, 76.57; H, 6.59; acetylenic H, 1.04] is formed when the reaction with propargyl magnesium bromide is carried out at 20°.

Oxidative coupling of I with cupric acetate in pyridine[2] (2.5 hr., 40°) gave a brown amorphous poly-ol containing α-diacetylene groupings ($\lambda^{MeOH}_{max.}$ 231, 244, 251 and 257 mμ; ε = 610, 920, 1020 and 1120, per C_6 unit). The infrared spectrum of the corresponding poly-acetate indicated it to be partly cyclic, as judged by the relative intensities of the α-diacetylene and terminal acetylene bands. By analogy[2] the poly-ol therefore presumably contains the symmetrical cyclic trimer II (two racemic forms possible) as well as other cyclic products. Attempts to purify the poly-ol (or the derived acetate or tetrahydropyranyl ether) were unsuccessful and often resulted in explosive decomposition, even at room temperature.

The poly-ol (or derivatives) could not be partially hydrogenated catalytically, but reduction with lithium aluminum hydride in boiling tetrahydrofuran yielded a brown mass with spectral data [$\lambda^{MeOH}_{max.}$ 228 mμ (ε = 11,000 per C_6 unit); $\lambda_{max.}$ 10.44 μ] compatible with the presence of *trans*-enyne chromophores. This method usually causes reduction only of acetylenic bonds adjacent to hydroxyl groups to *trans*-double bonds[4] and the mixture is therefore presumed to contain the trienetriyne-triol III besides other substances. Finally dehydration with phosphorus oxychloride–pyridine at 20° or with potassium bisulfate in boiling acetic anhydride–acetic acid gave a material which without purification showed the ultraviolet maxima at 322, 335, 384 and 399 mμ (isoöctane) typical of the fully conjugated hexaene-triyne IV[1]. Chromatography yielded IV as sole crystalline material, brown plates, m.p. 190–192° (dec.). It was identified with the previously described substance[1] by the complete identity of the infrared and ultraviolet spectra as well as by hydrogenation to cycloöctadecane. The crude poly-ol prior to lithium aluminum hydride reduction under the same dehydration conditions gave no material with high-intensity ultraviolet absorption.

The presently described synthesis of the completely conjugated eighteen-membered ring hexaene-triyne provides additional evidence for the structure IV.[1] The over-all yield by this new route is, however, inferior to that given by the previous method[1] which is a better one from the preparative standpoint.

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[3] *Cf.* (a) M. Gaudemar, *Ann. chim.* (*Paris*), 190 (1956); (b) 204 (1956).

[4] *Inter al.*, J. D. Chanley and H. Sobotka, THIS JOURNAL, **71**, 4140 (1949); K. R. Bharucha and B. C. L. Weedon, *J. Chem. Soc.*, 1584 (1953); E. B. Bates, E. R. H. Jones and M. C. Whiting, *ibid.*, 1854 (1954).

THE ENZYMATIC SYNTHESIS OF ANTHRANILIC ACID FROM SHIKIMIC ACID-5-PHOSPHATE AND L-GLUTAMINE[1]

Sir:

Anthranilic acid, an intermediate in the biosynthesis of tryptophan in microörganisms,[2,3] has been shown to be derived from shikimic acid.[4,5] It has now been possible to demonstrate, in a cell-free extract of *Escherichia coli* mutant B-37,[6] that shikimic acid-5-phosphate[7,8] (I) and L-glutamine are converted to anthranilic acid (Table I).

Of all the amino donors tried, L-glutamine was the most effective. In addition, aza-L-serine and 6-diazo-5-oxo-L-norleucine, known inhibitors of reactions in which L-glutamine participates,[9] inhibit the present conversion. With L-glutamine as the amino donor shikimic acid alone was ineffective, and addition of ATP gave only a conversion of 18% in contrast to the almost quantitative conversion of shikimic-5-P.[10] Compound Z1 (prob-

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[1] This work was supported by a grant from the National Institutes of Health, United States Public Health Service.

[2] C. Yanofsky, in "Amino Acid Metabolism" (W. D. McElroy and B. Glass, eds.), The Johns Hopkins Press, Baltimore, Md., 1955, pp. 930–939.

[3] C. Yanofsky, *J. Biol. Chem.*, **224**, 783 (1957).

[4] B. D. Davis in *Advances in Enzymology*, **16**, 287–295 (1955).

[5] E. L. Tatum, S. R. Gross, G. Ehrensvärd and L. Garnjobst, *Proc. Natl. Acad. Sci.*, **40**, 271 (1954).

[6] A tryptophan requiring mutant blocked in the conversion of anthranilic acid to indole-3-glyceryl phosphate.

[7] U. Weiss and E. S. Mingioli, THIS JOURNAL, **78**, 2894, 1956.

[8] Abbreviations: shikimic acid-5-phosphate, shikimic-5-P; Tris, 2-amino-2-hydroxymethyl-1,3-propanediol; ATP, adenosine triphosphate; DPN⁺, DPNH, oxidized and reduced form of diphosphopyridine nucleotide; TPN⁺, triphosphopyridine nucleotide; SA, shikimic acid.

[9] B. Levenberg, I. Melnick and J. M. Buchanan, *J. Biol. Chem.*, **225**, 163 (1957).

[10] Presumably these extracts can phosphorylate SA, albeit poorly.