

[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY AT CORNELL UNIVERSITY]

Many-membered Carbon Rings. VII. Cyclooctyne

BY A. T. BLOMQUIST¹ AND LIANG HUANG LIU²

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Cyclooctyne has been obtained by the alkali-catalyzed oxidative decomposition of 1,2-cyclooctanedione dihydrazone. Its structure is indicated by its infrared absorption spectrum and by chemical behavior upon ozonolysis, catalytic reduction and hydration.

Recently it was shown that the application of classical methods to the synthesis of simple cyclic acetylenes in the intermediate carbocyclic range, cyclononyne¹ and cyclodecyne,³ failed to give pure acetylene free of other unsaturated compounds. This observation prompted a study of cyclooctyne whose synthesis from 1-bromo-2-chlorocyclooctene was reported by Domnin.⁴ That Domnin had at hand pure cyclooctyne is doubtful. It has been shown that his method of synthesis produces a mixture of allene and acetylene when applied to the C₁₀-carbocycle. The refractive index and density of his hydrocarbon are inconsistent with the values for such properties reported for the very closely related simple cyclic acetylenes, olefins and paraffins.^{1,3,5} Finally, the chemical evidence in support of the cyclooctyne structure for his hydrocarbon is insufficient. In fact, all of the properties of Domnin's cyclooctyne may be accounted for better on the assumption that the hydrocarbon was a mixture of cyclooctene and cyclooctane.

Cyclooctyne, free from the isomeric 1,2-cyclooctadiene and other unsaturated hydrocarbons, has been obtained by the alkali-catalyzed oxidative decomposition of 1,2-cyclooctanedione dihydrazone. Purification of the hydrocarbon, achieved by distillation and chromatographic adsorption, was followed by refractive index and infrared spectrum measurements.

The infrared spectrum of cyclooctyne having n_D^{20} 1.4850 and d_4^{20} 0.868 was determined. Characteristic absorption at 4.53 μ (C \equiv C stretching) was observed similar to that found for cyclononyne and cyclodecyne.⁶ This sample of cyclooctyne absorbed 102% of two molar equivalents of hydrogen upon quantitative reduction and gave only suberic acid upon ozonolysis. Upon hydration it was converted to cyclooctanone, characterized as its semicarbazone.

That cyclooctyne is probably highly strained was indicated by its explosive reaction with phenyl azide.

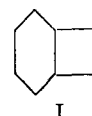
The cyclic intermediates suberoin and suberil required for the synthesis have not been previously described.^{6a} They were obtained by modification of methods previously described for similar derivatives of the C₉- and C₁₀-carbocycles.^{1,3} Their infra-

red spectra were determined and they corresponded closely to those of the related C₉- and C₁₀-homologs.^{1,3}

The preparation of suberoin by the acyloin condensation of diethyl suberate proved to be particularly troublesome when carried out following the procedure used for azeloin and sebacoins.^{1,3} During the condensation the reaction mixture became so gelatinous that it was impossible to maintain effective stirring and the tendency for charring to occur became quite marked. By carrying out the condensation in a refluxing mixture of toluene and xylene and by careful control of the rate of addition these difficulties were eliminated and suberoin was obtained in satisfactory yield.

Suberoin was characterized as its semicarbazone and *p*-phenylazobenzoate while suberil was converted to its quinoxaline derivative, its dihydrazone, and oxidized to suberic acid using periodic acid.

The isolation of cyclooctyne free from oxygen containing compounds required careful exclusion of air as the acetylene was very prone to react with oxygen. Also in the course of isolating the acetylene certain observations indicated that there was a tendency for cyclooctyne to rearrange to a more stable isomeric hydrocarbon showing less unsaturation. This may possibly be the bicyclooctene I.



Further studies related to these observations are in progress.

Experimental Part⁷

Suberoin (2-Hydroxycyclooctanone).—The procedure previously described for the preparation of sebacoins³ was modified in order to avoid the formation of a thick gelatinous reaction mixture which could be stirred only with extreme difficulty and which readily charred when heated. The use of a mixture of toluene and xylene as a reaction solvent eliminated these difficulties. For 115 g. (0.5 mole) of pure diethyl suberate a mixture of 1190 ml. of xylene and 310 ml. of toluene was used as the solvent. The ester was added carefully over a six-hour period. Decomposition of the reaction mixture was carried out with 50 ml. of methanol followed by 240 ml. of 50% aqueous acetic acid. From ten preparations a suberoin fraction showing b.p. 70–81° (2 mm.) was obtained in 50–56% yield. After two redistillations, suberoin showing b.p. 75° (1.5 mm.) and m.p. 53–57° was obtained in 35% yield.^{7a}

(7) Melting points are corrected and boiling points are uncorrected except where indicated. The infrared spectra were determined with a Perkin-Elmer double beam infrared spectrophotometer, model 21, using a sodium chloride prism. Pure liquid samples of varying thickness were used in the determinations.

(7a) The discrepancy in m.p. of our suberoin (53–57°) with that reported by Cope (37–38.5°), see ref. 6a, is very likely due to the presence of some suberoin dimer in our suberoin. The tendency for cyclic acyloins to dimerize has been demonstrated by J. C. Sheehan, R. C. O'Neil and M. A. White, *THIS JOURNAL*, **72**, 3376 (1950).

(1) For the preceding paper in this series see A. T. Blomquist, L. H. Liu and J. C. Bohrer, *THIS JOURNAL*, **74**, 3643 (1952).

(2) Postdoctoral Research Fellow under the du Pont grant-in-aid, 1951–1952.

(3) A. T. Blomquist, R. E. Burge, Jr., and A. C. Suesy, *THIS JOURNAL*, **74**, 3636 (1952).

(4) N. A. Domnin, *J. Gen. Chem. (U.S.S.R.)*, **8**, 851 (1938); *C. A.*, **33**, 1282 (1939).

(5) K. Ziegler and H. Wilms, *Ann.*, **567**, 1 (1950).

(6) A. T. Blomquist, *et al.*, *THIS JOURNAL*, **73**, 5510 (1951).

(6a) The preparation of suberoin from dimethyl suberate was recently described by Cope and co-workers; *ibid.*, **74**, 5884 (1952).

The infrared spectrum of suberoin was similar to that of sebacoin³ showing strong absorption at 2.92 and 5.90 μ , OH and CO stretching, respectively.

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.55, 67.39; H, 9.88, 10.01.

Suberoin semicarbazone, m.p. 179.5–180°, was obtained in 70% yield after two recrystallizations from ethanol.

Anal. Calcd. for $C_8H_{17}O_2N_3$: C, 54.25; H, 8.60; N, 21.09. Found: C, 54.23, 54.50; H, 8.53, 8.62; N, 21.02, 21.06.

Suberoin *p*-phenylazobenzoate after purification by chromatographing and recrystallizing showed m.p. 128.5–129°.

Anal. Calcd. for $C_{21}H_{22}O_3N_2$: C, 71.99; H, 6.33; N, 7.99. Found: C, 72.01, 72.03; H, 6.36, 6.40; N, 8.08, 8.10.

Suberil (1,2-Cyclooctanedione).—This α -diketone was obtained in approximately the same yield by the oxidation of suberoin using either of two reagents. Oxidation of 21.3 g. (0.15 mole) of suberoin using 60 g. (0.30 mole) of cupric acetate monohydrate in 10 ml. of methanol and 150 ml. of 50% acetic acid⁸ gave 64–70% of crude suberil showing b.p. 65.5–77° (3 mm.). Oxidation of 21.3 g. (0.15 mole) of suberoin using 28 g. (0.06 mole) of bismuth oxide in 75 ml. of acetic acid⁹ gave a 62% yield of suberil. Upon redistillation the pure diketone showed b.p. 68.8–69.5° (3 mm.). Freezing point determinations of the solid diketone after four redistillations were unsatisfactory.

The infrared spectrum of suberil was similar to those of sebacil³ and 1,2-cyclononanedione¹ showing very strong absorption at 5.86 μ , CO stretching, and weak absorption at 2.90–2.98 μ , OH stretching.

Anal. Calcd. for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.65, 68.85; H, 8.65, 8.78.

The quinoxaline derivative of suberil was prepared by the method of Leonard and Mader.¹⁰ It was obtained in 75% yield after recrystallizations from ethanol; m.p. 120.2–120.7°.

Anal. Calcd. for $C_{14}H_{16}N_2$: C, 79.20; H, 7.60; N, 13.20. Found: C, 79.06, 79.00; H, 7.62, 7.60; N, 13.20.

(8) P. Ruggli and P. Zeller, *Helv. Chim. Acta*, **28**, 741 (1945).

(9) W. Rigby, *J. Chem. Soc.*, 793 (1951).

(10) N. J. Leonard and P. M. Mader, *THIS JOURNAL*, **72**, 5388 (1950).

Oxidation of suberil with periodic acid afforded suberic acid, m.p. 140–141°, in 59% yield. A mixed m.p. determination with an authentic specimen of suberic acid showed no depression.

The dihydrazone of suberil was prepared following the method described for sebacil dihydrazone.³ The crude dihydrazone, m.p. 103–104.5°, was obtained in 93% yield. Careful recrystallization from benzene, keeping the temperature below 60°, gave the pure hydrazone (69%), m.p. 105–106°.

Anal. Calcd. for $C_8H_{16}N_4$: C, 57.11; H, 9.59; N, 33.30. Found: C, 57.40, 57.12; H, 9.46, 9.58; N, 33.00.

Cyclooctyne.—The preparation and purification procedures were similar to those for cyclononyne¹ with the following modifications. The reaction mixture was heated at 80° with a water-bath, length of heating was reduced to 5–8 hr. depending upon cessation of evolution of nitrogen, and all distillations were carried out under nitrogen.

The impure distilled acetylene was obtained in 9.3% yield. After purification by chromatographing, the pure acetylene showed b.p. 157.5–158° (740 mm.) (micro method), n_D^{20} 1.4850 and d_4^{20} 0.868 (micro method).

The infrared spectrum of cyclooctyne was similar to those of cyclononyne and cyclodecyne⁶ showing weak absorption at 4.53 μ characteristic of $C\equiv C$ stretching.

Anal. Calcd. for C_8H_{12} : C, 88.82; H, 11.18. Found: C, 88.83, 89.00; H, 10.93, 11.09.

Quantitative reduction in acetic acid using Adams catalyst required 102% of two molar equivalents of hydrogen.

Ozonolysis of 0.4 g. of cyclooctyne following the procedure used for cyclononyne¹ gave 0.43 g. of an acidic product which showed a m.p. of 138.5–140° after two recrystallizations. When this acidic product was mixed with an authentic specimen of suberic acid the m.p. was not depressed.

Hydration of 0.2 g. of cyclooctyne using the procedure described for cyclononyne¹ gave 0.2 g. of an oil of camphor-like odor. This oil was converted to a semicarbazone having m.p. 170–171°. The m.p. of a mixture of this semicarbazone and authentic cyclooctanone semicarbazone was not depressed.

When treated with phenyl azide, according to the procedure of Ziegler and Wilms,⁶ cyclooctyne reacted explosively forming a viscous liquid product which was not characterized.

ITHACA, N. Y.

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Some Reactions of 1,2-Diethoxyethylene and its Bromo Derivatives

BY S. M. McELVAIN AND CHARLES H. STAMMER¹

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The bromination product (II) of 1,2-diethoxyethylene (I) has been converted to bromodiethoxyethylene (III), which is found to add either ethanol or water in both possible directions. The intermediate addition product (IV), identical with the product from the addition of hydrogen bromide to ethoxyketene acetal, is found to be too unstable to isolate. III may be reconverted to I *via* the lithium derivative or to the dibromo derivative (VIII) of I. The distinctive pyrolysis behaviors of II, III and VIII are described. Acyl halides and phthalic anhydride promote the polymerization of I, but maleic anhydride produces a 1:1 copolymer which retains the functional groups of the monomers. Benzoyl peroxide adds stoichiometrically to I to yield the two stereoisomeric 1,2-dibenzoyloxy-1,2-diethoxyethanes (XI).

In an earlier paper² describing the preparation and properties of 1,2-diethoxyethylene (I), a few of the reactions that were used to establish its structure were indicated. The present paper reports a further study of the reactions of this compound, particularly the preparation and properties of its bromo derivatives.

The addition of bromine to I was found in the earlier experiments to occur rapidly at 0–10°, but

attempts to isolate the dibromo compound (II) were unsuccessful because of its rapid decomposition into hydrogen bromide and an intractable tar; however, II could be immediately hydrolyzed to glyoxal in high yield.² A further study of this bromination reaction has shown that II separates as a white solid when a petroleum ether solution of I is treated with bromine at –20°. This product is unstable at room temperature and attempts to purify it by recrystallization gave material of variable melting point. II reacts with ethanol to yield glyoxal tetraethylacetal³ (92%); with potas-

(1) Wisconsin Alumni Research Foundation Research Assistant, 1951–1952.

(2) S. M. McElvain and C. H. Stammer, *THIS JOURNAL*, **73**, 915 (1951).

(3) Cf. R. C. Schreyer, *ibid.*, **73**, 2962 (1951).