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CYCLIC POLYOLEFINS. XXVI. CONVERSION OF CYCLOÖCTATETRAENYL PHENYL KETONE TO AN ACYCLIC TETRAENE

by

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CYCLIC POLYOLEFINS. XXVI. CONVERSION OF CYCLOÖCTATETRAENYL PHENYL KETONE TO AN ACYCLIC TETRAENE.*

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Received ________________

Cycloöctatetraenyllithium (I) has been converted to bicycloöctatetraenyl (II) by coupling in the presence of cobaltous chloride, and to cycloöctatetraenyl phenyl ketone (III) by reaction with benzonitrile followed by hydrolysis of the intermediate imine. The ketone III was characterized by formation of a 1:1 complex with silver nitrate, a 2,4-dinitrophenylhydrazone, and by hydrogenation to benzylcycloöctane and to 1-cycloöctenyl phenyl ketone. Reduction of III with lithium aluminum hydride formed cycloöctatetraenylphenylcarbinol (V). On reaction with phenylmagnesium bromide, the ketone III underwent ring opening and yielded the acyclic ketone, 1,9-diphenylnona-2,4,6,8-tetraen-1-one (VI) (20%), identical with a sample prepared from 7-phenylhepta-2,4,6-trienal and acetophenone.

Further investigation of cycloöctatetraenyllithium (I), prepared by halogen-metal interchange from bromocycloöctatetraene and *n*-butyllithium,[1,2]

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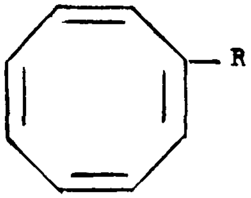
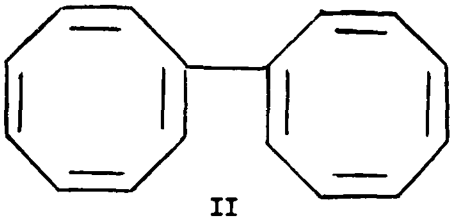
(1) A. C. Cope and M. Burg, *This Journal*, *74*, 168 (1952).
(2) A. C. Cope, M. Burg and S. W. Fenton, *ibid.*, *74*, 173 (1952).

showed the presence as a by product in its preparation of a yellow, crystalline hydrocarbon that proved to be bicycloöctatetraenyl (II). By adding a catalytic amount of cobaltous chloride to an ether solution of I, a 24% yield of II was obtained, in a reaction analogous to the coupling of phenyllithium or *n*-butyllithium in the presence of cobaltous chloride.[3]

The structure of II was established by quantitative hydrogenation to bicycloöctyl, which was identified by comparison with a sample prepared by a different method.[4]



I, R = Li
III, R = COC_6H_5
V, R = $CH(OH)C_6H_5$



II

The reaction of the lithium compound I with benzonitrile at -70° formed an unstable imine that yielded cycloöctatetraenyl phenyl ketone (III) on hydrolysis (57% yield overall from bromocycloöctatetraene). The ketone III

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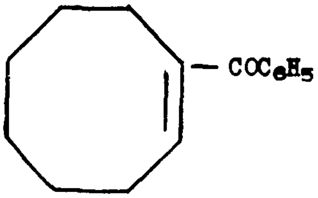
(3) M. S. Kharasch, D. W. Lewis and W. B. Reynolds, *ibid.*, **65**, 498 (1943).

(4) A. C. Cope and F. A. Hochstein, *ibid.*, **72**, 2519 (1950).

was isolated by distillation as an orange liquid that solidified and melted at 38-39.5° after recrystallization. It formed a crystalline 1:1 complex with silver nitrate, from which the ketone could be regenerated, and a red 2,4-dinitrophenylhydrazone. Quantitative hydrogenation of the ketone III in the presence of 10% palladium on Norit resulted in absorption of six molar equivalents of hydrogen and formed benzylcycloöctane. Hydrogenation of III in the presence of 1% palladium on calcium carbonate yielded 1-cycloöctenyl phenyl ketone (IV), which was identified by comparison (through the 2,4-dinitrophenylhydrazone) with a sample prepared from 1-cycloöctenyllithium[2] and benzonitrile. Reduction of the ketone III with lithium aluminum hydride yielded cycloöctatetraenylphenylcarbinol (V) (89%), which was characterized by its infrared spectrum bands at 2.78 and 2.93μ) and by quantitative reduction in the presence of palladium on Norit with the absorption of five molar equivalents of hydrogen, forming benzylcycloöctane.



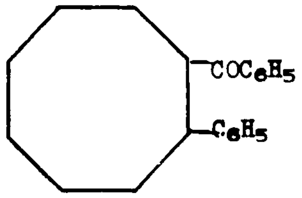
IV

Since III is a conjugated unsaturated ketone, it could react with a Grignard reagent either by addition to the carbonyl group to form a tertiary alcohol, or by addition to the conjugated system, forming a ketone. The reaction of III with phenylmagnesium bromide formed a mixture, from which a yellow crystalline ketone $C_{21}H_{18}O$ (VI) was isolated in 20% yield. Although VI was expected to be a phenylcycloöctatrienyl phenyl ketone from its analysis and method of preparation, quantitative hydrogenation in the presence of 1%

palladium on calcium carbonate resulted in absorption of four molar equivalents of hydrogen, and yielded a saturated liquid ketone (VII). This result excluded the possibility that VI could be a cycloöctatriene derivative. It also furnished evidence arguing against a cycloöctatetraene structure for VI,[5] because most cycloöctatetraene derivatives (including the ketone III) absorb three molar equivalents of hydrogen under these conditions and yield substituted cycloöctenes. Further evidence against the formulation of VI as a cycloöctatetraene derivative was obtained by synthesis of one of the stereoisomers of 2-phenylcycloöctyl phenyl ketone (VIII) from 1-cycloöctenyl phenyl ketone (IV) and phenylmagnesium bromide; VIII had entirely different properties from the saturated ketone VII obtained from VI by hydrogenation.

$C_6H_5(CH_2)_8COC_6H_5$

VII



VIII

The ultraviolet absorption spectrum of VI (Fig. 1) provided the essential information indicating its structure, for the principal absorption band occurred at a wave length ($\lambda_{max.}$ 401 mμ, ε 54,000), indicating the presence

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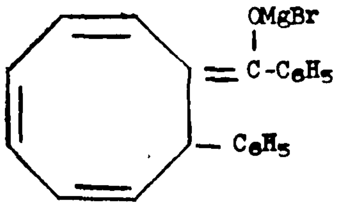
(5) A phenylcycloöctatetraenyl phenyl ketone might be formed from the addition product of III and phenylmagnesium bromide by loss of the elements of magnesium bromohydride, as phenylcycloöctatetraene is formed from cycloöctatetraene and phenyllithium; see A. C. Cope and M. R. Kinter, *This Journal*, 73, 3424 (1951).

of a long conjugated system. On this basis it appeared probable that VI was 1,9-diphenylnona-2,4,6,8-tetraen-1-one, formed by ring opening of the enolate (IX) produced by 1,4-addition of phenylmagnesium bromide to the ketone III. This supposition was supported by the fact that the melting point reported[6] for 1,9-diphenylnona-2,4,6,8-tetraen-1-one was identical with that found for VI.



IX

The structure of VI was confirmed by synthesis of an authentic sample by condensation of 7-phenylhepta-2,4,6-trienal[7] with acetophenone. The authentic

$$C_6H_5(CH{=}CH)_3CHO + CH_3COC_6H_5 \xrightarrow{NaOH} \underset{VI}{C_6H_5(CH{=}CH)_4COC_6H_5}$$

sample of VI was shown to be identical with VI obtained from III and phenylmagnesium bromide by comparison of melting points and mixed melting points of the ketone samples and their 2,4-dinitrophenylhydrazones, and by comparison of

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[6] F. Straus, Ann., 393, 313 (1912).

[7] M. Korach and W. Bergmann, J. Org. Chem., 14, 118 (1949).

the ultraviolet and infrared spectra of VI from the two sources. The saturated ketone obtained by hydrogenation of VI accordingly is 1,9-diphenylnonan-9-one (VII). If the double bonds in VI are all *trans*, as is probable from the method of synthesis of the authentic sample, the conversion of III to VI involves rearrangement of *cis* to *trans* ethylenic linkages if III has a boat (*cis*) configuration.

The formation of VI from the ketone III and phenylmagnesium bromide is the first case in which a reaction of a cycloöctatetraene derivative has been observed to result in ring opening with the formation of an acyclic tetraene. The driving force for the unusual carbon-carbon cleavage that occurs may result from the stability of the conjugated system of VI compared to the enolate IX, and the degree to which IX is strained by the stereochemical requirements of the structure.

Study of ring opening reactions of cycloöctatetraene derivatives is being continued, as is the use of cycloöctatetraenyllithium for the synthesis of substituted cycloöctatetraenes.

Experimental[8]

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(8) Melting points are corrected and boiling points are uncorrected. We are indebted to Dr. S. M. Nagy and his associates for analyses. ~~Infrared spectra were determined with a Baird Double Beam Infrared Recording Spectrometer, Model B, fitted with a sodium chloride prism.~~ Ultraviolet spectra were determined with a Cary Ultraviolet Recording Spectrophotometer, Model 11 MS. All reactions involving organometallic compounds were carried out under an atmosphere of dry nitrogen.

Bicycloöctatetraenyl (II). - To a solution containing 0.038 mole of *n*-butyllithium[9] in 90 ml. of dry ether was added 7.00 g. (0.038 mole) of bromocycloöctatetraene[1] in 15 ml. of ether at -65°. After stirring for 1 hour at -70°, 0.25 g. (5 mole %) of anhydrous cobaltous chloride was added, the cooling bath was removed, and the mixture was stirred at room temperature for 40 hours. It was then poured onto ice, and the ether layer, after washing with 5% hydrochloric acid and 5% sodium bicarbonate, was dried over sodium sulfate and concentrated. On cooling, 0.60 g. of bicycloöctatetraenyl (II) was obtained as a yellow solid. Short-path distillation of the residual liquid at 100° (0.1 mm.) yielded an additional 0.35 g. of II and 0.88 g. of an unidentified orange oil, n_D^{25} 1.5388. The two crops of crude II (0.95 g., 24%) were combined and recrystallized from ether as shining yellow plates m.p. 125.4-126.5°.

Anal. Calcd. for $C_{16}H_{14}$: C, 93.15; H, 6.84. Found: C, 92.87; H, 7.02.

Hydrogenation of 122 mg. of II in 10 ml. of glacial acetic acid in the presence of 100 mg. of prereduced platinum oxide catalyst resulted in the absorption of 104% of 8 molar equivalents of hydrogen. After separation of the catalyst, the acetic acid was neutralized with 15% sodium hydroxide solution, and the mixture was extracted with pentane. The extracts were dried over sodium sulfate and the pentane was removed. Short-path distillation of the residue yielded 88 mg. (67%) of bicycloöctyl as a colorless oil, n_D^{25} 1.5008, m.p. 10-11°. A mixed m.p. with a sample prepared by a different method[4] which had n_D^{25} 1.4998 was not depressed, and the infrared spectra of the two samples were identical.

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(9) H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. E. Dunn and L. S. Miller, *This Journal*, **71**, 1499 (1949).

Cycloöctatetraenyl Phenyl Ketone (III). - To a stirred solution of n-butyllithium prepared from 15.1 g. of n-butyl bromide and 1.53 g. of lithium wire in 110 ml. of dry ether, and cooled to -70° in a Dry Ice-trichloroethylene bath, was added 14.2 g. of bromocycloöctatetraene[1] in 15 ml. of dry ether over a period of 15 minutes. The red mixture was stirred for 1 hour at -70°, and then 7.95 g. of benzonitrile in 15 ml. of ether was added over a period of 20 minutes, at a temperature below -65°. The cooling bath was removed and when the temperature reached 0-20° the mixture was poured onto ice. The aqueous phase was extracted with two 15-ml. portions of ether, and the ketimine was extracted rapidly from the combined ether solutions with two 50-ml. and five 30-ml. portions of 5% hydrochloric acid without attempting careful phase separation. The acid extract was heated on a steam bath for 35 minutes, cooled, and extracted with ether. After drying over magnesium sulfate, the ether extract was concentrated and distilled through a semi-micro column.[10] The distillation separated 3.62 g. of a low-boiling fraction consisting of valerophenone (from the reaction of n-butyllithium with benzonitrile) from 9.15 g. (57%) of cycloöctatetraenyl phenyl ketone (III), an orange oil, b.p. 96° (0.06 mm.), n_D^{25} 1.5930-1.5980, which eventually partially crystallized. It was recrystallized from petroleum ether and then melted at 38.0-39.5°.

Anal. Calcd. for $C_{15}H_{12}O$: C, 86.48; H, 5.81. Found: C, 86.51; H, 6.04.

Hydrogenation of 143 mg. of III in 7 ml. of 95% ethanol in the presence of 150 mg. of 10% palladium on Norit resulted in the absorption of

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(10) C. W. Gould, Jr., G. Holzman and C. Niemann, Anal. Chem., 20, 361 (1948).

98% of 6 molar equivalents of hydrogen. Short-path distillation at 0.1 mm. of the residue left after separation of the catalyst and removal of the solvent yielded 57 mg. of benzylcyclooctane, n_D^{25} 1.5251, the infrared spectrum of which was identical with that of an authentic sample[11] which had n_D^{25} 1.5244.

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[11] A. C. Cope and J. E. Krueger, to be published.

The ketone III (213 mg.) also was hydrogenated in 15 ml. of dry benzene in the presence of 200 mg. of 1% palladium on calcium carbonate. The reaction was interrupted after 3 molar equivalents of hydrogen had been absorbed, and the catalyst and solvent were removed. Comparison of the infrared spectrum of the pale yellow oil (145 mg., n_D^{25} 1.5548) obtained by short-path distillation of the residue with that of an authentic sample of 1-cyclooctenyl phenyl ketone (IV) indicated that the reduction product was slightly impure IV.

The impure product was dissolved in ethanol and treated with 2,4-dinitrophenylhydrazine reagent.[12] Since the crude derivative would not solidify, the mixture was diluted with water and extracted with ether. The ether solution was dried over magnesium sulfate and the ether was removed. The residue (80 mg.) was dissolved in 1:1 benzene-ligroin and chromatographed on a 22 x 2-cm. column of 1:1 silicic acid-Supercel which had been washed with ether followed by ligroin. Development of the chromatogram with 30 ml. of 1:1

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[12] R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds", John Wiley and Sons, Inc., New York, N. Y., 1948, p. 171.

benzene-ligroin gave a broad orange lower band and two faint yellow bands. The material obtained by elution of the lower band with ether was recrystallized twice from ethanol-ethyl acetate (including treatment with Darco) and yielded the 2,4-dinitrophenylhydrazone of 1-cycloöctenyl phenyl ketone (IV), m.p. 159-161°, and mixed m.p. with an authentic sample described below, 161-162°.

Silver Nitrate Complex of Cycloöctatetraenyl Phenyl Ketone. - To a hot solution of 1.60 g. of III in 10 ml. of absolute ethanol was added 1.31 g. of powdered silver nitrate. The solution was heated for 15 minutes, filtered, and cooled in an ice bath. An oil separated which solidified on scratching, yielding 2.62 g. (90%) of the silver nitrate complex of III as pale yellow needles, m.p. 120-122° (dec.). One recrystallization from absolute ethanol raised the m.p. to 121.4-122.0° (dec.)

Anal. Calcd. for $C_{15}H_{12}O.AgNO_3$: C, 47.63; H, 3.20; Ag, 28.54.
Found: C, 47.68; H, 3.28; Ag, 28.19.

The ketone III was regenerated by adding 10 ml. of concentrated ammonium hydroxide with stirring to 1.52 g. of the complex suspended in 30 ml. of water. The mixture was extracted with ether, the ether extracts were dried over magnesium sulfate, and the ether was removed. Short-path distillation of the residue at 0.1 mm. yielded 0.62 g. of analytically pure III, n_D^{25} 1.6104, d_4^{25} 1.095.

The 2,4-Dinitrophenylhydrazone of Cycloöctatetraenyl Phenyl Ketone was prepared by adding 2,4-dinitrophenylhydrazine reagent[11] to III dissolved in ethanol. The crude derivative was recrystallized from 1:1 ethanol-ethyl acetate, yielding the red 2,4-dinitrophenylhydrazone of III, m.p. 178.7-179.8°.

Anal. Calcd. for $C_{21}H_{16}N_4O_4$: C, 64.97; H, 4.16; N, 14.43.
Found: C, 65.11; H, 4.32; N, 14.53.

1-Cycloöctenyl Phenyl Ketone (IV).- To a stirred solution of 1-cycloöctenyllithium[2] prepared from 5.00 g. of 1-bromocycloöctene and 0.36 g. of lithium wire in 50 ml. of dry ether was added 2.68 g. of benzonitrile in 10 ml. of ether over a period of 20 minutes. The red mixture was stirred for 10 minutes after addition was complete and poured onto ice. The ether layer was extracted rapidly with four 25-ml. portions of 5% hydrochloric acid. The extracts were heated on a steam bath for 40 minutes, cooled, and extracted with ether. The ether extracts were dried over sodium sulfate, and the residue left after removal of the ether was distilled through a semi-micro column,[9] yielding 4.18 g. (75%) of 1-cycloöctenyl phenyl ketone (IV) as a faintly yellow oil, b.p. 94° (0.06 mm.), n_D^{25} 1.5620-1.5631. The mid-fractions had n_D^{25} 1.5630.

Anal. Calcd. for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 84.11; H, 8.53.

The 2,4-Dinitrophenylhydrazone of 1-Cycloöctenyl Phenyl Ketone was recrystallized from ethanol-ethyl acetate (including Darco treatment) and melted at 161.0-162.3°.

Anal. Calcd. for $C_{21}H_{22}N_4O_4$: C, 63.96; H, 5.62; N, 14.21. Found: C, 63.90; H, 5.67; N, 14.18.

Cycloöctatetraenylphenylcarbinol (V). - To a stirred suspension of 0.20 g. of lithium aluminum hydride in 20 ml. of dry ether was added a solution of 2.00 g. of cycloöctatetraenyl phenyl ketone (III) in 10 ml. of ether over a period of 15 minutes. The mixture was stirred and heated under reflux for 1 hour and then was hydrolyzed with water and 5% hydrochloric acid. The aqueous layer was extracted once with ether, and after drying over magnesium sulfate, the solvent was removed from the combined ether solutions. Short-path distillation of the residue with a heating block temperature of 110-120° (0.1 mm.) yielded 1.80 g. (89%) of cycloöctatetraenylphenylcarbinol (V) as a viscous yellow oil, n_D^{25} 1.5982.

Anal. Calcd. for $C_{15}H_{14}O$: C, 85.67; H, 6.71. Found: C, 85.76; H, 6.70.

Hydrogenation of V in the presence of palladium on Norit under the conditions described above for III resulted in the absorption of 98.5% of 5 molar equivalents of hydrogen and the formation of benzylcycloöctane, identified by comparison of its infrared spectrum with the spectrum of an authentic sample.[10]

Reaction of III With Phenylmagnesium Bromide. - To a stirred refluxing solution of phenylmagnesium bromide prepared from 3.97 g. of bromobenzene and 0.61 g. of magnesium in 30 ml. of ether was added 4.86 g. of III in 25 ml. of ether over a period of 20 minutes. A solid formed in the reaction mixture during the addition. Stirring and heating were continued for 1 hour and the mixture was then hydrolyzed by the addition of excess saturated ammonium chloride solution. The aqueous layer was extracted once with ether, and the combined ether solutions were dried over magnesium sulfate and concentrated. Two crops of crude 1,9-diphenylnona-2,4,6,8-tetraene-1-one (VI), totalling 1.23 g. (20%), were obtained. Recrystallization from ethanol yielded VI as yellow needles, m.p. 125.0-126.2°, which was undepressed on admixture with an authentic sample, described below. This unsaturated ketone was quite sensitive to atmospheric oxygen.

Anal. Calcd. for $C_{21}H_{18}O$: C, 88.08; H, 6.33. Found: C, 88.08; H, 6.42.

The 2,4-Dinitrophenylhydrazone of VI was prepared by dissolving 50 mg. of the ketone and 35 mg. of 2,4-dinitrophenylhydrazine in 5 ml. of boiling ethanol and adding a drop of concentrated hydrochloric acid. The solid obtained by heating for 5 minutes followed by cooling was recrystallized three times from nitromethane, yielding 18 mg. of the dark red 2,4-dinitrophenylhydrazone, m.p. 215.5-216.0°, which was undepressed on admixture with an authentic sample, described below.

Anal. Calcd. for $C_{27}H_{22}N_4O_4$: C, 69.50; H, 4.75; N, 12.00.
Found: C, 69.17; H, 4.72; N, 12.21.

An authentic sample of VI was obtained by dissolving 2.00 g. of 7-phenylhepta-2,4,6-trienal (IX)[6] and 1.92 g. of acetophenone in a mixture of 100 ml. of ethanol and 15 ml. of benzene and adding 5 ml. of 1.3% aqueous sodium hydroxide solution. After the mixture stood overnight, 3.0 g. of a yellow-orange solid, m.p. 121-125°, had precipitated. Recrystallization from ethanol yielded VI as golden-yellow needles, m.p. 124-126°.

The 2,4-dinitrophenylhydrazone of the authentic sample of VI was prepared as described above and melted at 215.5-216.5°. An attempt to prepare the phenylhydrazone from the ketone by the procedure described by Straus[6] was unsuccessful.

1,9-Diphenylnonan-1-one (VII). - The ketone VI (199 mg.) was hydrogenated in 30 ml. of methanol in the presence of 80 mg. of 1% palladium on calcium carbonate. After 0.5 hour, 4 molar equivalents of hydrogen had been taken up and the rate of absorption had greatly decreased. The reaction was interrupted, the catalyst separated, and the solvent removed. Two short-path distillations of the residue yielded 1,9-diphenylnonan-1-one (VII) as an almost colorless oil, n_D^{25} 1.5426.

Anal. Calcd. for $C_{21}H_{26}O$: C, 85.69; H, 8.90. Found: C, 85.76; H, 9.17.

The 2,4-Dinitrophenylhydrazone of VII was prepared with 2,4-dinitrophenylhydrazine and a drop of concentrated hydrochloric acid in ethanol. Since it was not easily purified by recrystallization, the crude derivative (87 mg.) was dissolved in 2 ml. of 1:1 benzene-ligroin and placed on a 25 x 1.8-cm. column of 1:1 silicic acid-Supercel which had been washed with ether followed by ligroin. Development of the chromatogram with 45 ml. of 1:1 benzene-ligroin gave a 5-mm. top band of 2,4-dinitrophenylhydrazine, a 15-mm. orange middle band, and a 100-mm. diffuse orange lower band. The material obtained by elution of the lower band with ether was recrystallized three times from ethanol-ethyl acetate and yielded 24 mg. of the 2,4-dinitrophenylhydrazone of 1,9-diphenylnonan-1-one, m.p. 114.3-115.1°.

Anal. Calcd. for $C_{27}H_{30}N_4O_4$: C, 68.32; H, 6.37; N, 11.80. Found: C, 68.36; H, 6.25; N, 11.68.

Recrystallization from ethanol-ethyl acetate of the material eluted from the middle band of the chromatogram with ether gave a very small amount of an orange solid, m.p. 243-245° (presumably a 2,4-dinitrophenylhydrazone) which was not investigated further.

2-Phenylcycloöctyl Phenyl Ketone (VIII). - To a stirred refluxing solution of phenylmagnesium bromide prepared from 6.21 g. of bromobenzene and 0.95 g. of magnesium in 40 ml. of ether was added 7.50 g. of 1-cycloöctenyl phenyl ketone (IV) in 40 ml. of ether over a period of 1 hour. The mixture, containing a white solid, was stirred and heated for 0.5 hour, and then enough saturated ammonium chloride solution was added to precipitate the magnesium salts. The ether solution was decanted and the residue was washed with ether. Sublimation at 0.1 mm. of the residue left after removal of the ether yielded 8.10 g. (79%) of 2-phenylcyclooctyl phenyl ketone (VIII) which formed long colorless needles, m.p. 136.4-137.8°, on recrystallization from ethanol.

Anal. Calcd. for $C_{21}H_{24}O$: C, 86.26; H, 8.27. Found: C, 85.93; H, 8.23.

The infrared spectrum of VIII indicated clearly the presence of a carbonyl group (band at 5.92 μ), but the ketone did not form a 2,4-dinitrophenylhydrazone or semicarbazone under the usual conditions.

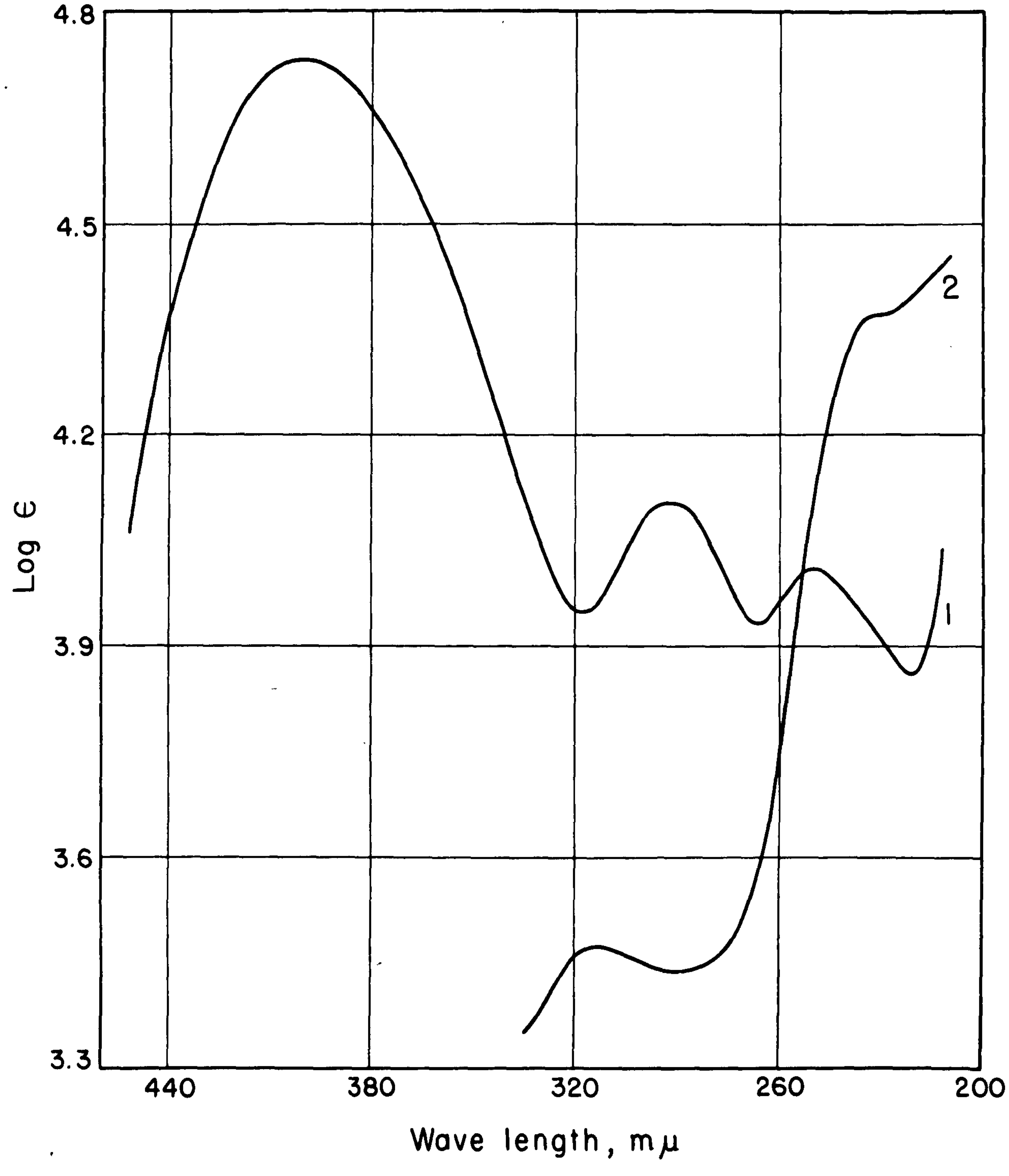

Fig. I. - Ultraviolet absorption spectra: curve 1, 1,9-diphenylnona-2,4,6,8-tetraen-1-one (VI); curve 2, bicycloöctatetraenyl (II), both in 95% ethanol.

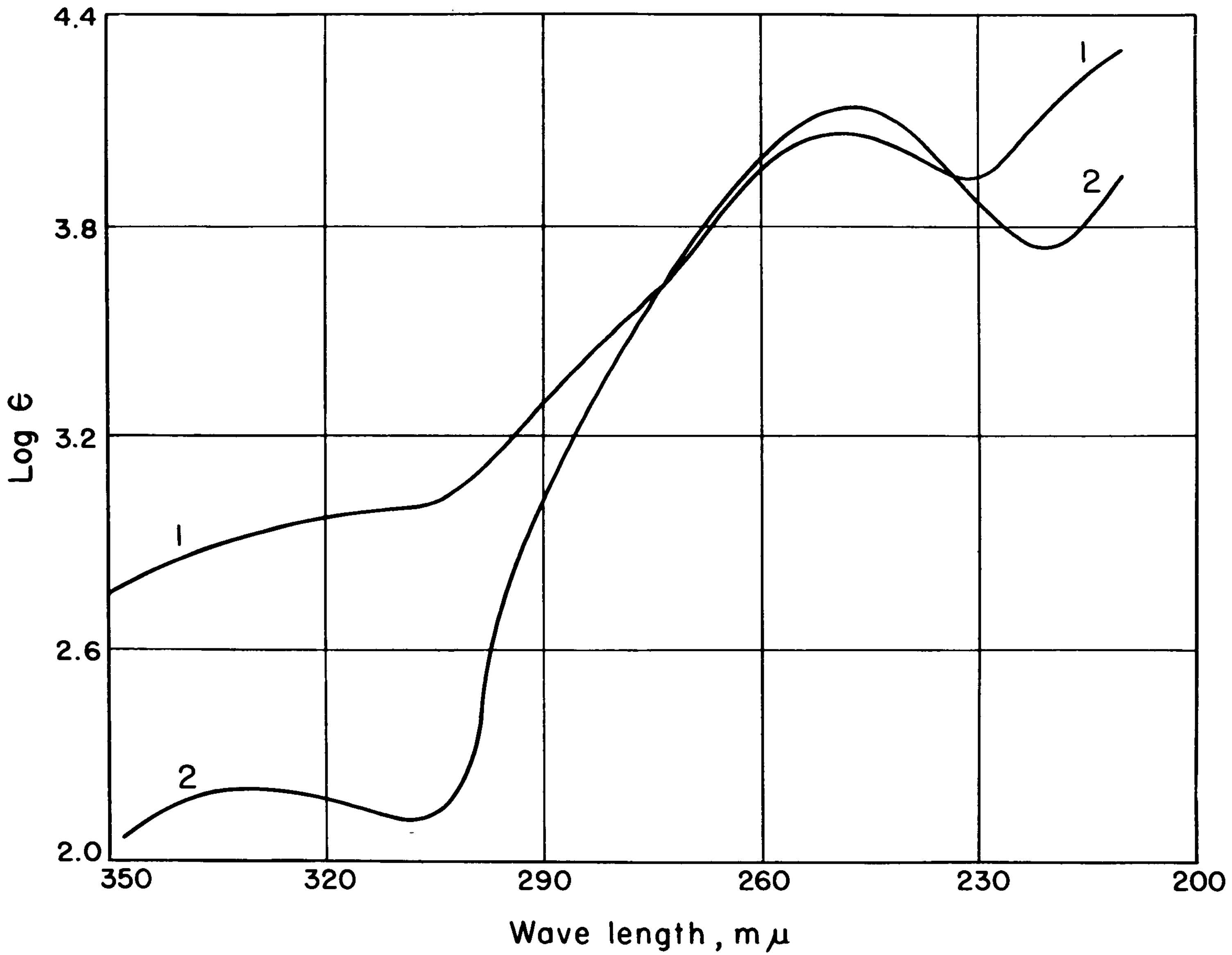

Fig. 2. - Ultraviolet absorption spectra: curve 1, cycloöctatetraenyl phenyl ketone (III); curve 2, 1-cycloöctenyl phenyl ketone (IV), both in 95% ethanol.