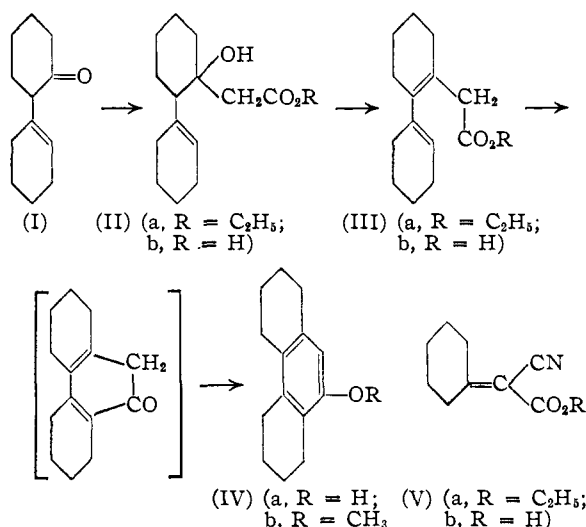


[CONTRIBUTION FROM THE POLYTECHNIC INSTITUTE OF BROOKLYN]

A New Synthesis of 9-Hydroxy-*sym*-octahydrophenanthreneBY PHANINDRANATH BAGCHI,¹ FELIX BERGMANN^{1a} AND D. K. BANNERJEE²

A common method for the synthesis of polycyclic ring systems consists in the cyclization of a saturated side-chain bearing a carboxyl group. This method has been applied to γ -aryl³- and γ -cyclohexenyl-butyric acids.⁴ However, an old observation of Fittig⁵ shows that unsaturated side chains may also be useful. β -Styrylacetic acid is converted thermally to α -naphthol, and a similar observation has been reported by Linstead⁶ for 2-phenylcyclohexylidenecyanoacetic acid. It was, therefore, of interest to determine whether this type of reaction would apply also to dienic acids.

As a suitable system we intended to prepare 1,1'-dicyclohexenyl-2-acetic acid (IIIb),^{6a} which we expected to cyclize to 9-hydroxy-*sym*-octahydrophenanthrene (IVa) according to the scheme



Reformatsky's method, when applied to the system cyclohexenylcyclohexanone (I) and ethyl bromoacetate, gave an 83% yield of the hydroxy ester (IIa). The latter could be dehydrated either by phosphorus pentoxide in benzene or by thionyl chloride in a pyridine-ether mixture (yield 76 and 78%, respectively). The dienic acid (IIIb) was cyclized by phosphorus pentoxide in

benzene, after a number of other methods proved to be inferior. It was essential to sustain vigorous stirring throughout the cyclization and to add the dehydrating agent in small portions over an extended period. The phenol (IVa)^{7,6} was obtained in 44% yield. The method was considerably simplified by saponifying the hydroxy ester (IIa) and treating the crude hydroxy-acid (IIb) directly with phosphorus pentoxide. The over-all yield (IIa \rightarrow IVa) was 35% as compared to 30% in the more elaborate process described before.

The phenol (IVa), its acetate and its 10-bromo derivative (VIIIa) all showed properties identical with the corresponding compounds described in the literature, and the methyl ether (IVb) was found to be identical with the corresponding derivative of Bachmann⁸ by direct comparison.

A second compound suitable for cyclization, was obtained by condensation of (I) with ethyl cyanoacetate. Three products were isolated from the reaction mixture: (i) ethyl cyclohexylidenecyanoacetate (Va) (26%); (ii) ethyl 2-(Δ^1 -cyclohexenyl)-cyclohexylidene-cyanoacetate (VI) (44%); (iii) 9-hydroxy-10-cyano-1,2,3,4,5,6,7,8-octahydrophenanthrene (VIIa) (\sim 1%). The first product (V) was obtained in each run, even when the starting material (I) was purified scrupulously and a constant boiling middle fraction was used for the reaction. It is thus beyond doubt that (V) originates from a reversed aldol condensation, occurring either before or after condensation with ethyl cyanoacetate.

The ratio of the yields of products varied according to the conditions employed during distillation. The higher the distillation temperature, the higher the proportion of (VIIa) formed. This could also be confirmed by direct conversion of (VI) into (VIIa) under the influence of heat (yield 50%) or in boiling acetamide as solvent (yield 72%). This type of cyclization is similar to the one observed by McRae,⁹ Cope¹⁰ and Linstead.⁶

The structure of (VII) was established in two ways: The nitrile (VII) was "denitrated" to (IVa) by a mixture of zinc, zinc chloride and sodium chloride at 300°. ¹⁰ 9-Methoxy-10-bromo-octahydrophenanthrene (VIIIb) was converted into (VIIa) by cuprous cyanide. It is remarkable that this reaction was accompanied by demethylation. An analogous observation was made during "denitration" of (VIIb) by zinc dust.

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(3) Kipping and Hill, *J. Chem. Soc.*, **75**, 144 (1899); Cook and Hewett, *ibid.*, 373 (1934).

(4) Cook and Lawrence, *ibid.*, 1637 (1935).

(5) Fittig and Erdman, *Ber.*, **16**, 43 (1883); *Ann.*, **227**, 242 (1838).

(6) Linstead, Whetstone and Levine, *THIS JOURNAL*, **64**, 2014 (1942).

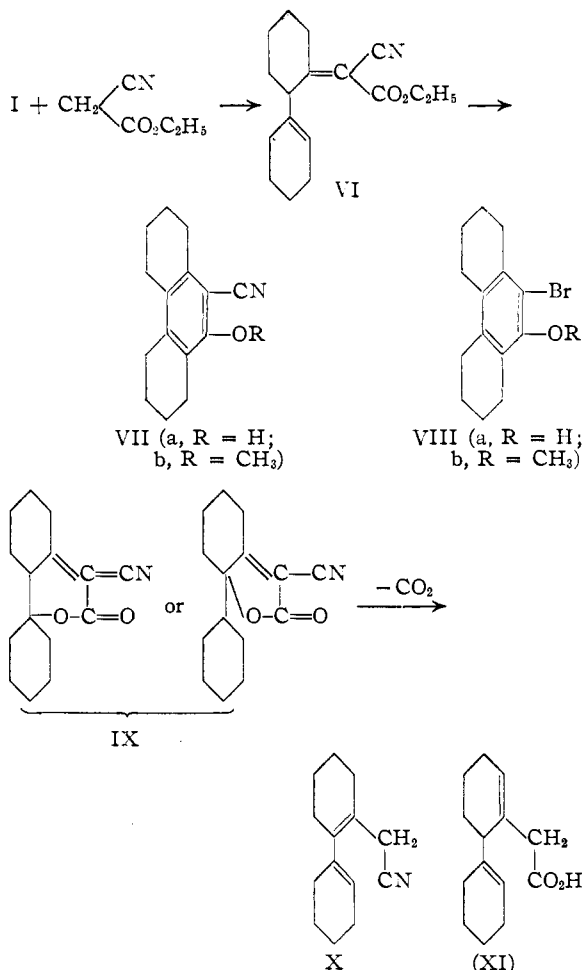
(6a) About the exact structure of this compound see the following discussion.

(7) v. Braun and Bayer, *Ber.*, **58**, 2667 (1925).

(8) Bachmann and Ness, *THIS JOURNAL*, **64**, 536 (1942). The authors wish to thank Prof. Bachmann, who kindly carried out the determination of mixed m. p.'s.

(9) McRae and Marrion, *Can. J. Res.*, **15B**, 480 (1937); **18B**, 265 (1940).

(10) Cope, Hofmann, Wyckoff and Hardenberg, *THIS JOURNAL*, **63**, 3452 (1941).



Acid hydrolysis of (VI) gave the lactone (IX), which was insoluble in sodium bicarbonate solution, but dissolved in warm sodium hydroxide solution, from which only the lactone could be recovered upon acidification. The lactonic structure was confirmed by decarboxylation to 1,1'-dicyclohexenyl-2-acetonitrile (X).

Ethyl cyclohexylidene-cyanoacetate, as shown by Kon and Nutland,¹¹ possesses the structure (Va) in view of its oxidative degradation to cyclohexanone and the exaltation shown by its molecular refraction. Decarboxylation of (Vb), however, gives a β,γ -unsaturated nitrile. In the case of compound (VI), it is possible that one or both of the double bonds are conjugated with the cyano-ester grouping. This problem was investigated by means of absorption spectra.

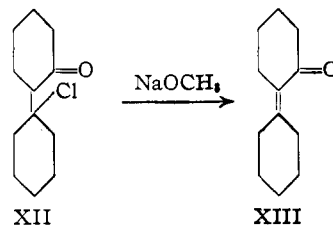
Although in α,β -unsaturated acids and esters absorption bands are not as sharply defined as in α,β -unsaturated ketones, it is possible, within a closely related group of compounds, to define the exact position of double bonds, e. g., α -cyanoacrylate shows a maximum at 2200 Å., the corresponding β -methyl derivative at 2300 Å. ($\log \epsilon =$

(11) Kon and Nutland, *J. Chem. Soc.*, 3102 (1926).

4.0). α -Cyanosorbate and its δ -methyl derivative have maxima at 2820 and 3020 Å., respectively.¹² Inspection of Fig. 1 demonstrates the close relationship between (Va), (Vb), (VI) and (IX) (λ_{max} at 2350 Å., $\log \epsilon = 4.0$ –4.1). Furthermore, as all the three compounds are β,β -disubstituted carboxyl derivatives, their absorption maximum corresponds approximately to that of β -methyl- α -cyanoacrylate. It is thus clear, that in (VI) only one double bond is conjugated with the ester group, the other being located inside the second ring.

The spectra of the acetic acids and acetonitriles are represented in Fig. 2. Cyclohexenylacetonitrile, acid (IIIb) and its ester again form a close group with absorption maxima < 2200 Å. In view of the fact that dicyclohexenyl itself has a maximum at 2360 Å. ($\log \epsilon = 4.25$)¹³ and that acids of the abietic type, in which the butadienic structure is not conjugated with the carboxyl group, possess maxima at 2400–2500 Å.,¹⁴ it is quite certain that the acid (IIIb) does not possess the expected 1,1'-dicyclohexenyl ring structure, but is to be represented rather as (XI). However, the nitrile (X), showing an appreciable absorption over the entire range of 2200–2700 Å. ($\log \epsilon = 3.8$ –3.3), may contain partially conjugated structures.

In this connection, it is also of interest to discuss the structure of cyclohexenylcyclohexanone. Kon¹¹ assumed for this ketone the non-conjugated structure (I), in equilibrium with a small amount of cyclohexylidenecyclohexanone (XIII). Evans and Gillam¹⁵ concluded from the fact that (I) shows an absorption of $\epsilon = 800$ at $\lambda = 2540$ Å. "This low intensity of absorption suggests the predominance of an unconjugated isomer." Recently Reese¹⁶ prepared (XIII) in crystalline form by dehydrochlorination of (XII) by means of sodium methoxide in methanol. Therefore he ascribed to the "liquid isomer" the β,γ -unsaturated structure (I). The absorption spectrum of our preparation, obtained by dehydrochlorination of (XII) by means of methanolic potassium hydroxide, is given in Fig. 3. The liquid shows two absorption maxima, $\lambda_1 < 2200$ Å., $\lambda_2 = 2450$ Å. The value of λ_2 is near to that of α,β,β -trisubstituted α,β -unsaturated ketones,^{15,17} but ϵ_2 is only



(12) Andrews, Cristol, Lindenbaum and Young, *THIS JOURNAL* **67**, 715 (1945).

(13) Booker, Evans and Gillam, *J. Chem. Soc.*, 1453 (1940).

(14) Harris and Sanderson, *THIS JOURNAL*, **70**, 334 (1948).

(15) Evans and Gillam, *J. Chem. Soc.*, 815 (1941).

(16) Reese, *Ber.*, **75**, 384 (1942).

(17) Woodward, *THIS JOURNAL*, **63**, 1123 (1941).

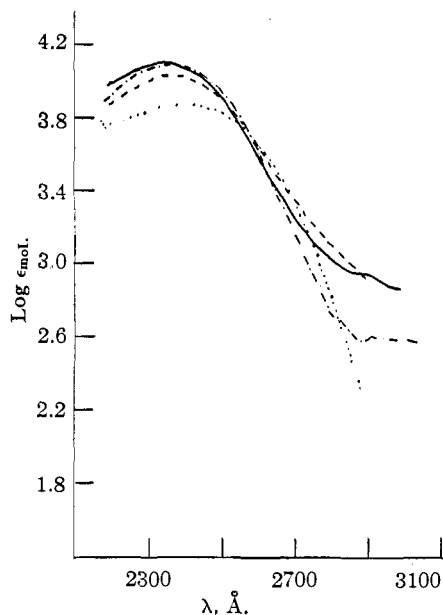


Fig. 1—Ultraviolet absorption spectra of cyclohexylenecyanoacetic acid (Vb)——; ethyl cyclohexylidenecyanoacetate (Va)-----; ethyl 2-cyclohexenylcyclohexylidenecyanoacetate (VI)-----; lactone (IX).....

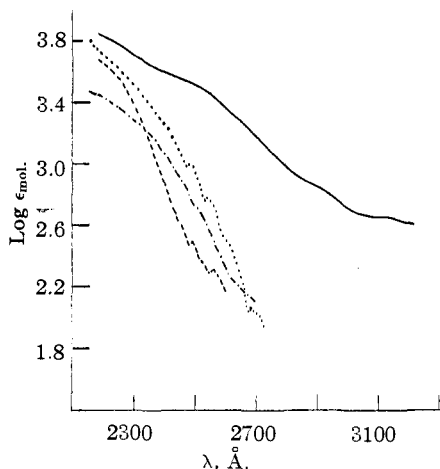


Fig. 2—Ultraviolet absorption spectra of cyclohexenylacetoneitrile-----; dicyclohexenylacetic acid (IIIb).....; ethyl dicyclohexenylacetate (IIIa)-----; dicyclohexenylacetoneitrile (X)——.

2.7, indicating that only part of the molecular species can be represented by (XIII).

Experimental¹⁸

Cyclohexenylcyclohexanone (I) was prepared in 80% yield following essentially the procedure of Wallach,¹⁹ methanolic caustic potash being used for dehydrochlorination of the intermediate chloroketone.

Condensation of (I) with Ethyl Bromoacetate.—Strips of zinc foil were activated by washing consecutively with

(18) All melting points are uncorrected.

(19) Wallach, *Ber.*, **40**, 70 (1907).

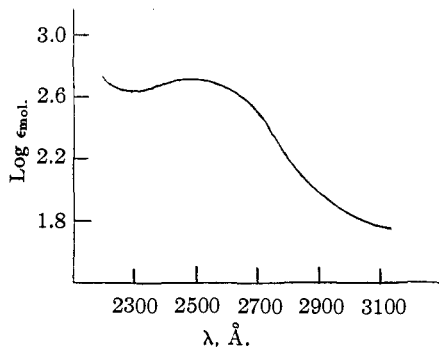


Fig. 3—Ultraviolet absorption spectrum of cyclohexenylcyclohexanone (I).

5% sodium hydroxide, water, 2% hydrochloric acid, water, ethanol and finally with ether. When cyclohexenylcyclohexanone (22 g.), ethyl bromoacetate (30 g.) and zinc (11.5 g.) in benzene (90 cc.) were heated on a water-bath, a vigorous reaction set in. Thereafter the mixture was refluxed for one hour, the dark brown liquid decanted from the unreacted zinc and treated with cold dilute hydrochloric acid. The benzene solution was washed with water, dried over calcium chloride and fractionated. The yield of (IIa) was 83%; b. p. 144–146° (1.5 mm.); n_D^{25} 1.4960.

Anal. Calcd. for $C_{16}H_{26}O_3$: C, 72.2; H, 9.8. Found: C, 72.1; H, 9.6.

Dehydration to Ethyl 1,1'-Dicyclohexenyl-2-acetate (IIIa): (a) **Pyridine-Thionyl Chloride Method.**—To a stirred solution of the hydroxy ester (24.5 g.) in pyridine (18 cc.) and anhydrous ether (100 cc.), cooled to 0°, was added dropwise thionyl chloride (9 cc.). The mixture was left overnight and then decomposed with cold water containing a small amount of hydrochloric acid. The ether layer was washed with water and dried over calcium chloride. Distillation gave (IIIa) as a colorless oil of b. p. 114–115° (1.5 mm.) in 78% yield; n_D^{25} 1.5006.

Anal. Calcd. for $C_{16}H_{26}O_2$: C, 77.4; H, 9.7. Found: C, 77.3; H, 9.6.

(b) **Phosphorus Pentoxide Method.**—The hydroxy ester (24 g.) and phosphorus pentoxide (16 g.) in dry benzene (100 cc.) were refluxed for three and a half hours. The benzene layer was decanted, the sirupy pentoxide decomposed with water and extracted with benzene. The combined benzene layers were washed, dried and fractionated. The product (IIIa) obtained in 76% yield was identical with the one described before.

Saponification to 1,1'-Dicyclohexenyl-2-acetic Acid (IIIb): (a) **From Acid (IIIb).**—The dienic ester (10 g.) and potassium hydroxide (4 g.) in methanol (20 cc.) were heated on a water-bath for three hours. After evaporation of the methanol, the residue was dissolved in water. After extracting any unsaponified matter with ether, the aqueous layer was acidified at 0°. A sticky, light brown precipitate was obtained, which crystallized on scratching. Two crystallizations from dilute methanol yielded the acid (IIIb) in the form of colorless prismatic blocks, m. p. 97°, yield 85%.

Anal. Calcd. for $C_{16}H_{26}O_2$: C, 76.4; H, 9.1. Found: C, 75.9; H, 9.1.

9-Hydroxy-1,2,3,4,5,6,7,8-octahydrophenanthrene (IVa): (a) **From Acid (IIIb).**—To a boiling solution of the dienic acid (10 g.) in dry benzene (150 cc.), thoroughly stirred, was added phosphorus pentoxide (15 g.) in several portions during one and one-half hours. Thereafter the mixture was refluxed for one-half hour and worked up as usual. Distillation at 150–160° (3 mm.) gave a viscous, semi-solid mass, which was dissolved in petroleum ether (90–100°). The solution deposited crystals of m. p. 130–132°, yield 44%. Two crystallizations from the same solvent gave (IVa) as prismatic columns of m. p. 134–135°.

Anal. Calcd. for $C_{14}H_{15}O$: C, 83.2; H, 8.9. Found: C, 83.2; H, 8.9.

From the mother liquor of the first crystallization some impure starting material was recovered.

The phenol (IVa) was obtained in only 8% yield, when (IIIb) was first converted into its acid chloride, treated with stannic chloride in dry carbon disulfide solution and the product dehydrochlorinated with dimethylaniline.⁴

(b) From the Hydroxy Ester (IIa).—The hydroxy ester (15 g.) and potassium hydroxide (5 g.) in water-methanol (1:2, 45 cc.) were heated on a water-bath for three hours. After removal of methanol and extraction of any unsaponified matter with ether, the solution was acidified with cold dilute hydrochloric acid. The precipitated oily acid was taken up in ether. After washing and drying, the ether was evaporated, the sirupy residue dried *in vacuo* and dissolved in dry benzene (100 cc.). To the boiling benzene solution phosphorus pentoxide (20 g.) was added portionwise during two hours, under vigorous stirring. After heating for one more hour, the mixture was worked up as before and yielded 35% of the phenol (IVa), m. p. and mixed m. p. 134–135°.

9-Methoxyoctahydrophenanthrene (IVb).—(a) The hydroxy compound (IVa) (2 g.) was warmed with 10% potassium hydroxide (20 cc.), when an insoluble potassium salt separated. It was dissolved by addition of methanol and warming. To the stirred solution dimethyl sulfate (2 cc.) was added. Upon heating an oil separated. Three more portions of potassium hydroxide (10 cc.) and dimethyl sulfate (1 cc.) were added. Upon cooling, the methyl ether (IVb) separated. Two crystallizations gave (IVb) in the form of prismatic columns, m. p. 92–93°; yield 70%.

This product did not depress the m. p. of the compound of Bachmann and Ness.⁵

(b) The phenol (IVa) (2 g.) was added to a solution of sodium (0.6 g.) in methanol (15 cc.) and methylated with methyl iodide (5 cc.) by refluxing for two hours; yield 65%.

9-Methoxy-10-bromo-*sym*-octahydrophenanthrene (VIIIb).—(a) 9-Hydroxy-*sym*-octahydrophenanthrene was brominated according to v. Braun and Bayer⁷ and the 9-hydroxy-10-bromo derivative methylated by dimethyl sulfate as described above. (VIIIb) forms minute colorless prismatic plates from methanol, m. p. 99–100°; yield 70%.

Anal. Calcd. for $C_{15}H_{19}OBr$: C, 61.0; H, 6.5. Found: C, 61.2; H, 6.6.

(b) The same compound was obtained by bromination of the methyl ether (IVb) in glacial acetic acid; yield 66%.

Condensation of (I) with Ethyl Cyanoacetate.—A mixture of cyclohexenylcyclohexanone (17.8 g.), ethyl cyanoacetate (11.3 g.), ammonium acetate (1.5 g.), glacial acetic acid (10 cc.) and benzene (40 cc.) was refluxed for eight hours, and the water formed during the reaction was separated with the help of a separator. The light brown solution was washed with water, dried and fractionated at 1.5 mm.

Fraction 1. B. p. 112–114°; n_D^{20} 1.4970; yield, 5 g. of colorless oil (Va).

Anal. Calcd. for $C_{11}H_{15}O_2N$: C, 68.4; H, 7.8. Found: C, 68.1; H, 7.9.

Fraction 2: b. p. 146–148°; n_D^{20} 1.5180; yield 12 g. of a faintly yellow viscous liquid (VI).

Anal. Calcd. for $C_{17}H_{23}O_2N$: C, 74.7; H, 8.2. Found: C, 74.8; H, 8.5.

Fraction 3: residue; it was dissolved in benzene and left overnight, yielding 0.2 g. of crystals (VIIa). After repeated crystallizations from benzene or methanol,

(VIIa) was obtained as colorless prismatic columns of m. p. 215–216°.

Anal. Calcd. for $C_{14}H_{17}NO$: C, 79.3; H, 7.5. Found: C, 79.2; H, 7.4.

Like (IVa), this compound gave no color reaction with ferric chloride.

When fractionation was carried out at 7 mm. pressure, the yield of (VIIa) was 0.6 g. It was also obtained in 50% yield upon heating the ester (VI) to 210–215° for three hours and in 72% yield when (VI) was heated with an equal weight of acetamide to 200° for two hours.

The phenol (VIIa) was methylated as described above for (IVa) to give a 52% yield of (VIIb). On recrystallization from methanol prismatic columns were obtained, m. p. 105–106°.

Anal. Calcd. for $C_{15}H_{19}ON$: C, 79.7; H, 7.9. Found: C, 79.4; H, 7.9.

Denitration.—The hydroxy cyano compound (VIIa) (1 g.), zinc chloride (5 g.), zinc dust (1 g.) and sodium chloride (1 g.) were thoroughly mixed by grinding and the mixture heated to 215–225° for fifteen minutes. The mass was treated with dilute hydrochloric acid, and the residue recrystallized from methanol. The product had m. p. 212–224°, representing unchanged starting material. From the mother liquor a second crop of crystals was obtained which after repeated recrystallization from petroleum ether showed a m. p. of 133–134° and was identical with (IVa).

When the methoxy derivative (VIIb) was subjected to the same treatment, denitration was accompanied by demethylation to (IVa).

When 9-methoxy-10-bromo-*sym*-octahydrophenanthrene (VIIIb) (1.7 g.) was mixed with powdered cuprous cyanide (0.75 g.) and heated in pyridine (1 cc.) for ten hours to 215–225°, and the product directly sublimed in a high vacuum, 0.5 g. of a yellowish solid was obtained, which after repeated recrystallization from methanol showed a m. p. of 213–215°, not depressed by admixture of (VIIa).

Lactonization of (VI).—Ethyl cyclohexenylcyclohexylidene cyanoacetate (VI) (6 g.) in ethanol (60 cc.) was refluxed with concentrated hydrochloric acid (20 cc.) for four hours. Upon cooling crystals separated, which were recrystallized from methanol; prismatic plates of m. p. 171–172° (IX); yield 2 g.

Anal. Calcd. for $C_{15}H_{19}O_2N$: C, 73.5; H, 7.8; N, 5.7. Found: C, 73.4; H, 7.7; N, 5.8.

The lactone is insoluble in warm sodium carbonate solution, but dissolves in warm caustic soda or potash. Acidification reprecipitates the lactone.

When the lactone was heated to 200°, decarboxylation took place. The yellowish oil obtained in 90% yield, distilled at 114–117° (1.5 mm.) (X).

Anal. Calcd. for $C_{14}H_{19}N$: N, 7.0. Found: N, 7.4.

Absorption Measurements.—All absorption spectra were measured in 95% alcohol, using a Beckman quartz spectrophotometer.

Summary

1,1'-Dicyclohexenyl-2-acetic acid is cyclized by phosphorus pentoxide to 9-hydroxy-*sym*-octahydrophenanthrene. Ethyl cyclohexenylcyclohexylidenecyanoacetate is cyclized thermally to 9-hydroxy-10-cyano-*sym*-octahydrophenanthrene. Spectrographical analysis shows that in the dicyclohexenyl derivatives investigated usually the two double bonds are not conjugated.

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RECEIVED JUNE 26, 1948