The rate of the isomerization process is affected by temperature and per cent. of catalyst. The solidification point decreases from 100° (for pure IV) to a minimum of about 0°, under any of the following conditions.

Time, hr.	Temp., °C.	P_2O_5, %
36	200	0.5
5	200	1.0
2	200	1.5
1	230	1.0
84	170	1.0

The product obtained after 4 hours heating at 194° with 1% P_2O_5 contained 60% III. This mixture was fractionally crystallized and the crystals obtained were crystallized twice from toluene to yield essentially pure III (m.p. 57°; mixed m.p. with authentic III, 58°). The product obtained after 7 hr. heating at 194° was liquid at room temperature. However, crystals tended to form on standing.

2. **With Sulfuric Acid.**—Six hundred grams of IV was heated at 200° for 18 hr. with 6 g. of sulfuric acid. The product was vacuum distilled as above to yield 570 g. of liquid distillate and 29 g. of residue. The neutralization equivalent of the distillate was 76.0.

Complete Isomerization of IV.—Six hundred grams of IV was heated at 200° with 9 g. of phosphorus pentoxide for 48 hr. The product was distilled at 5–9 mm. and 140–145° to yield 481 g. of solid distillate and 87 g. of tarry residue. Neutralization equivalent of the distillate was 76.2, m.p. 71–72°.

Determination of Isomer Concentration by Infrared Absorption.—Two 1000-g. samples of IV were agitated with 10 g. of P_2O_5 at 180 and 194°, respectively. Fifty-gram samples were withdrawn after various time intervals and distilled rapidly *in vacuo* at 150°. Samples of distillates were dissolved in chloroform (5.00 g./100 ml.) and their infrared absorption spectra determined using a Baird spectrophotometer. The relative concentrations of the various isomers were determined by comparison of these spectra with the spectra of the pure isomers (dissolved in chloroform, (5.00 g./100 ml.)). A principal absorption band was selected for each material such that there was no substantial interference from other isomers (Fig. 1). Compound I was determined by measuring the absorbancy of the bands at 7.9 μ referred to 7.7 μ basing point, *versus* the absorbancy for the pure isomer; II was determined using the 8.9 μ band referred to a base line constructed tangent to the inflection points near 8.8 and 9.0 μ; III, by using the 9.9 μ band referred to a base line tangent to the inflection points near 9.0 and 12.0 μ; IV, by using the band at 10.1 μ referred to a basing point at 10.0 μ. The results are shown graphically for the two temperatures in Fig. 2.

Acknowledgment.—The authors wish to express their gratitude to Messrs. B. M. Helfaer and E. B. Punnett for their helpful suggestions and advice and to Dr. Wesley Minnis for his guidance and encouragement during the course of this research. The assistance and suggestions of Mr. Richard Seeber, Dr. A. Semetsov and Mr. Richard Spaunburgh are acknowledged as well.

BUFFALO 5, NEW YORK

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS UNIVERSITY, THE STATE UNIVERSITY OF NEW JERSEY]

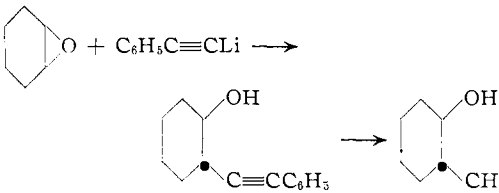
The Cyclization of Optically Active 2-(2-Phenylethyl)-cyclohexanol

BY RODERICK A. BARNES AND ARTHUR D. OLIN[1]

RECEIVED DECEMBER 27, 1955

Optically active *trans*-2-(2-phenylethyl)-cyclohexanol has been prepared and cyclized with 90% sulfuric acid. The formation of optically active *cis*-1,2,3,4,4a,9,10,10a-octahydrophenanthrene eliminates both the olefin and tertiary carbonium ion as possible intermediates in this reaction. In addition to the expected ketone, there resulted from the oxidation of the cyclization product, a substance which has been characterized as an unsaturated ketone; a possible mechanism for its formation has been suggested.

As a result of previous studies on the cyclization of 2-arylethylcyclohexanols,[2] it was suggested that one of three intermediates may react with the aromatic nucleus depending on the experimental conditions and the reactivity of the nucleus. In order to obtain information which could serve to further elucidate the mechanistic details of these cyclizations, it was believed necessary to prepare optically active alcohols of known stereochemical configuration. The first of the required alcohols, the *trans* form of 2-(2-phenylethyl)-cyclohexanol (III), has been prepared from cyclohexene oxide.



I III

The reaction of cyclohexene oxide with either sodium or potassium phenylacetylide failed completely, perhaps due to the insolubility of these salts in the organic solvents which were used. Lithium phenylacetylide did react; however the maximum yield was only 21%. The acid phthalate of alcohol I could not be resolved with brucine, cinchonine or quinine. Finally, treatment of the acid phthalate with *d*-α-phenylethylamine yielded a salt which was readily recrystallized to constant rotation. The levorotatory form of alcohol I, obtained by decomposition of the salt, was easily reduced by hydrogen and platinum to the desired optically active 2-(2-phenylethyl)-cyclohexanol. Alcohols I and III must have the *trans* configuration because the opening of the oxide ring is certainly a bimolecular displacement.

A sample of inactive alcohol III prepared by hydrogenation of unresolved I yielded a phenylurethan melting at 117.5–118.5°. The 2-(2-phenylethyl)-cyclohexanol prepared by sodium and alcohol reduction[3] of 2-(2-phenylethyl)-cyclohexanone probably was mostly the *trans* isomer since its phenylurethan was reported[3] to melt at 115–116°. Although stereospecific reduction of ketones by lithium aluminum hydride frequently has been ob-

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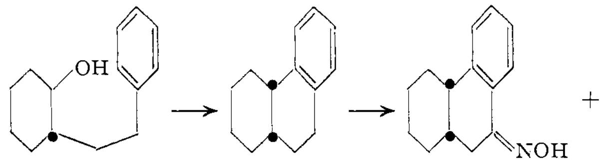
(1) Abstracted from a thesis presented by A. D. Olin to the Graduate School for the Ph.D. degree, December, 1955.

(2) R. A. Barnes, THIS JOURNAL, **75**, 3004 (1953); R. A. Barnes and M. T. Beachem, *ibid.*, **77**, 5388 (1955).

(3) J. C. Bardhan and S. C. Sengupta, *J. Chem. Soc.*, 2520, 2278 (1932).

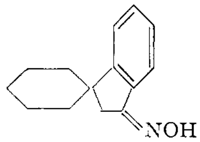


III IV V

$C_{14}H_{15}ON$
VI

served, experiments using 2-(2-phenylethyl)-cyclohexanone produced a mixture of isomeric alcohols whose phenylurethans were not readily separable.[4]

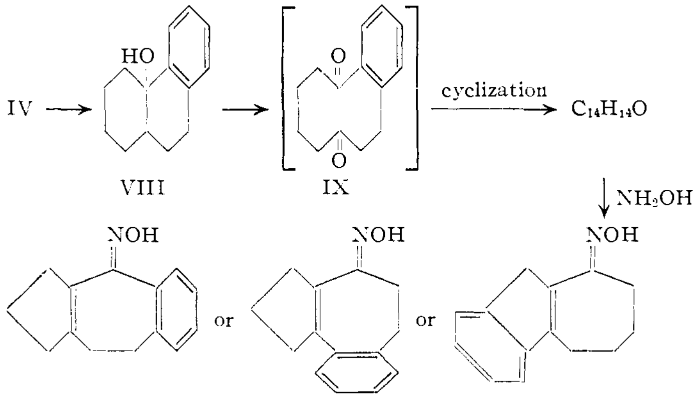
Both optically active and inactive samples of alcohol III were cyclized using 90% sulfuric acid; the active alcohol yielded a levorotatory cyclization product. In order to determine the structure of the cyclization product, it was oxidized, the ketonic products separated and the oximes prepared. The oximes were chromatographed on a column of silica gel to yield two major crystalline products. From the inactive alcohol one product was identified as the oxime of *cis*-9-oxo-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (V). The corresponding oxime from the active alcohol was optically active and moreover was dextrorotatory $[\alpha]_D$ +39.50, clearly indicating that the optical rotation could not possibly result from the presence of unchanged starting material, $[\alpha]_D$ −56°. The second component of the oxime mixture in both cyclizations was an optically inactive oxime, m.p. 191–192°. This substance has been reported[5,6] previously and was believed to be derived from the spirane which is a possible cyclization product of either 1- or 2-(2-phenylethyl)-cyclohexanol. Later work[7] has proved that the authentic oxime of spiroketone VII melts at 137°.

VII


The microanalytical results for oxime VI were in much better agreement with the values calculated for formula $C_{14}H_{15}ON$ than the formula $C_{14}H_{17}ON$ (oxime V or VII).[8] The ultraviolet spectrum of oxime VI also indicated that the oximino group was conjugated with a longer unsaturated system than oxime V. The formation of an unsaturated ketone is believed to result from an unexpected reaction of chromic acid on the *asym*-octahydrophenanthrene and not from spirane in the cyclization product. The attack by chromic acid on a tertiary hydrogen adjacent to a benzene ring is not surprising.[9] Also there is some evidence that tertiary alcohols such as VIII are directly oxidized by chromic acid.[10] The final step, the cyclization of diketone IX, is similar to a key step in the synthesis of azulene.[11]

An oxidation by chromic acid which follows a path very similar to that suggested for IV has been observed with triacetyldihydroveratramine.[12] The abnormal oxidation product which is obtained readily cyclizes to yield a naphthol; this is exactly analogous to the formation of VIa, VIb or VIc from IX.

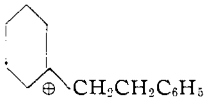
If this explanation for the formation of VI is accepted,[13] then it may be concluded that the *cis-asym*-octahydrophenanthrene is the major cyclization product from alcohol III.[14] The fact that the product from the optically active alcohol was still optically active provides definite proof that neither olefin X nor carbonium ion XI are intermediates in the cyclization of III to yield the *cis*-octahydrophenanthrene. This leaves for consideration oxonium ion XII, carbonium ion XIII and bridged ion XIV as intermediates which could retain optical activity. It is apparent from the geometry of the alcohol III that if XII is the intermediate the *cis*-octahydrophenanthrene would result.



VIII IX

VIa VIb VIc

X



XI

The previously reported results[2] have clearly indicated that the oxonium ion cannot be the intermediate in the cyclization of tertiary alcohols. If a secondary alcohol were to cyclize by this mechanism, essentially a displacement of a water molecule by the aromatic nucleus, increasing the reactivity of the ring should facilitate the process. Such an alcohol of increased reactivity, 2-[2-(2,5-dimeth-

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[4] C. Weizmann, E. Bergmann and L. Haskelberg, *Chemistry & Industry*, 587 (1937), have reported that a Guerbet reaction produced a 2-(2-phenylethyl)-cyclohexanol which was characterized by means of its phenylurethan, m.p. 143–144°.

[5] D. Perlman, D. Davidson and M. T. Bogert, *J. Org. Chem.*, **1**, 288, 300 (1936).

[6] J. W. Cook, C. L. Hewett and A. M. Robinson, *J. Chem. Soc.*, 168 (1939).

[7] M. Levitz, J. Perlman and M. T. Bogert, *J. Org. Chem.*, **6**, 105 (1941); L. H. Schwartzman, *ibid.*, **15**, 517 (1950).

[8] This observation was also reported by J. W. Cook, C. L. Hewett and C. A. Lawrence, *J. Chem. Soc.*, 71 (1936).

[9] *p*-Cymene yields *p*-toluic acid and *p*-methylacetophenone when treated with chromic and sulfuric acids; see H. Meyer and K. Bernhauer, *Monatsh.*, **53** and **54**, 729 (1929).

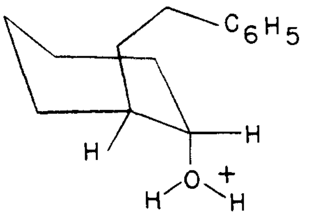
[10] L. F. Fieser and J. Szmuszkovicz, THIS JOURNAL, **70**, 335 (1948).

[11] A. G. Anderson, Jr., and J. H. Nelson, *ibid.*, **73**, 232 (1951), and Pl. A. Plattner and A. St. Pfau, *Helv. Chim. Acta*, **19**, 858 (1936).

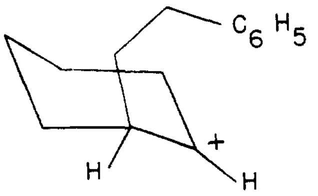
[12] N. L. Hosansky, Ph.D. Thesis, Rutgers University, 1953.

[13] Experiments designed to prove the structure of VI are in progress and these results as well as a study of related oxidations at tertiary positions will be the subject of a future communication.

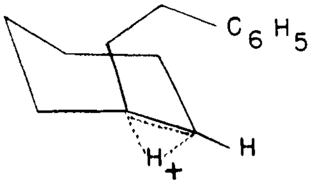
[14] Although Bardhan and Sengupta, ref. 3, previously cyclized alcohol II, no evidence for the stereochemistry of their product was obtained.



XII

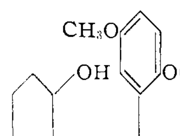


XIII



XIV

oxyphenyl)-ethyl]-cyclohexanol (XV) has been observed[3] to yield a 3:1 mixture of spirane and octahydrophenanthrene (*cis*?). Since alcohol XV, obtained by reduction of the ketone with $LiAlH_4$, was probably a mixture of *cis* and *trans* forms, the spirane may have resulted only from the *cis*-alcohol. Thus it can be concluded that, if the oxonium ion is an intermediate at all, it can be important only for secondary alcohols in which the hydroxyl and 2-arylethyl groups are *trans*.



XV

The loss of a water molecule from XII would be expected to lead directly to carbonium ion XIII and with subsequent migration of hydrogen XIV could result.

Those cyclizations in the tertiary alcohol series which yield *trans*-octahydrophenanthrenes[3,15] are all cyclizations under more drastic conditions (higher concentration of acid or higher temperature) than usual; these are believed most likely to involve a carbonium ion intermediate. Since the *trans* isomer is the more stable,[16] it should be formed if the transition state for the cyclization is similar to the product. Although models are of somewhat limited value in clarifying situations of this kind, Fisher–Hirschfelder models show that the aryl group can most readily approach the planar carbonium ion to yield the *trans* product.

If carbonium ion intermediates do indeed yield mainly the *trans* isomers, then *cis*-1,2,3,4,4a,9,10,10a-octahydrophenanthrene must result from alcohol III either by the displacement mechanism or by reaction of the phenyl nucleus with bridged ion XIV.

Experimental[17]

***trans*-2-(2-Phenylethynyl)-cyclohexanol** (I).—Phenylacetylene (40 g., 0.4 mole) was added dropwise, with stirring, to a solution of butyllithium (0.4 mole) in 600 ml. of dry ether. When the initial exothermic reaction had subsided, cyclohexene oxide (40 g., 0.4 mole) was added in one portion and the solution was refluxed for 19 hr.

The cold reaction mixture was decomposed with ice-water and the ether layer separated and dried over magnesium sulfate. The solvents as well as unreacted cyclohexene oxide and phenylacetylene were removed under aspirator vacuum (*ca.* 20 mm.) and the residue distilled from a low side-arm flask to yield a viscous liquid product (21.5 g.), b.p. 121–129° (0.4 mm.). This material crystallized when triturated with a small quantity of hexane. The solid obtained in this way was recrystallized from hexane to produce 17.5 g. (21%) of alcohol I which melted at 63–64°.

Anal. Calcd. for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.88; H, 7.78.

Acid Phthalate II of Alcohol I.—A mixture of alcohol I (6 g.) and freshly sublimed phthalic anhydride (5 g.) in a flask equipped with a calcium chloride tube was stirred and heated at 110° for 25 hr. The brownish viscous oil which resulted was dissolved by shaking for several hours with 5% sodium carbonate solution. Any traces of unreacted alcohol or diester were removed by benzene extraction of the aqueous solution. Acidification with 6 *N* hydrochloric liberated the acid phthalate as an oil which was extracted with benzene. The benzene solution was concentrated and the residue stirred with hexane to yield 7.53 g. (72%) of product, m.p. 105–109°. Recrystallization from hexane raised the melting point to 109–111°.

Anal. Calcd. for $C_{22}H_{20}O_4$: C, 75.84; H, 5.79. Found: C, 75.82; H, 5.76.

Resolution of Acid Phthalate II.—Acid phthalate II (10.3 g.) was dissolved in dry ether (24 ml.) with slight warming and treated with *d*-α-phenylethylamine[18] (3.7 g.) in dry ether (6 ml.). This mixture almost completely solidified in a few minutes. The mixture of salts was repeatedly recrystallized from minimum amounts of 95% ethanol. The progress of the resolution was followed by observing the optical rotation (1% solution in chloroform) and the melting point. The purest sample obtained had $[\alpha]_D$ $-69°$ and melting point 156–162°. Those crystalline crops which had a melting point up to 158° and $[\alpha]_D$ $-50°$ were considered to be sufficiently resolved for further work. A total of 2.45 g. of material of this purity was isolated.

***l*-*trans*-2-(2-Phenylethylethynyl)-cyclohexanol** (Ia).—The salt (2.43 g.) from the previous experiment was suspended in benzene (30 ml.) and shaken with 5% hydrochloric acid. The benzene solution was concentrated to yield the acid phthalate which crystallized on cooling, but remelted at room temperature. No further attempt was made to purify this substance; it was hydrolyzed directly by heating on the steam-bath for an hour with 20% sodium hydroxide (5 ml.) and ethanol (5 ml.). The alcohol was removed from the diluted hydrolysis mixture by extraction with benzene. When the benzene extract was concentrated and the residual oil taken up in a small amount of hexane and seeded with a crystal of racemic alcohol, there was obtained 200 mg. of Ia, m.p. 49–53°, $[\alpha]_D$ $-56.3°$ (*c* 1, chloroform). From the mother liquor an additional 450 mg. of product, m.p. 35–38°, $[\alpha]_D$ $-48.3°$ (*c* 1, chloroform) was obtained.

***l*-*trans*-2-(2-Phenylethyl)-cyclohexanol** (IIIa).—Alcohol Ia (2.145 g.) obtained by combination of several fractions ($[\alpha]_D$ $-41°$ to $-56.3°$) was dissolved in absolute alcohol (25 ml.) and hydrogenated at 30 p.s.i. using a platinum oxide catalyst (53.6 mg.). The hydrogenation was complete in 2 hr., and after the catalyst was filtered and the solvent removed, a crystalline residue remained. This solid, m.p. 60–65°, was recrystallized from hexane to yield two crops, $[\alpha]_D$ -55.3 and $-56.4°$, yield 1.44 g. The analytical sample melted at 64.5–66°.

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(15) R. A. Barnes and M. D. Konort, THIS JOURNAL, **75**, 303 (1953), and H. V. Maddox, Ph.D. Thesis, Rutgers University, 1953.

(16) J. W. Cook, N. A. McGinnis, A. S. Mitchell, *J. Chem. Soc.*, 286 (1944), have found that aluminum chloride would cause isomerization of *cis*-1,2,3,4,4a,9,10,10a-octahydrophenanthrene to the *trans* isomer, which therefore must be the more stable isomer.

(17) Microanalyses were by W. Manser, Zurich, Switzerland, and melting points were determined using the Kofler hot-stage.

(18) This was resolved with malic acid, see A. W. Ingersoll, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 506.

Anal. Calcd. for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.18; H, 9.84.

***d,l-trans*-2-(2-Phenylethyl)-cyclohexanol** (III). **A.**—Unresolved alcohol I (3.7 g.) was reduced by the same procedure as for the optically active alcohol Ia. The product was evaporatively distilled at 115–140° (0.1 mm.) to yield 3.1 g. of liquid whose infrared spectrum had no absorption band in the carbon–carbon triple bond region (*ca.* 4.5 μ).

A sample of this alcohol was treated with phenyl isocyanate to yield a crystalline phenylurethan, m.p. 112–115°. Two recrystallizations from hexane raised the melting point to 117.5–118.5°.[3]

Anal. Calcd. for $C_{21}H_{25}O_2N$: C, 77.98; H, 7.79. Found: C, 77.79; H, 7.88.

B.—2-(2-Phenylethyl)-cyclohexanone (20.2 g., 0.1 mole) prepared by acid hydrolysis[19] of ethyl 2-oxo-1-(2-phenylethyl)-cyclohexancarboxylate, was dissolved in dry ether (25 ml.), and this solution added dropwise to a slurry of lithium aluminum hydride (2 g., 0.05 mole) in dry ether (100 ml.). This mixture was stirred for an hour and the excess hydride decomposed with ethyl acetate (10 ml.). Dilute sulfuric acid (75 ml., 10%) was added to the cold reaction mixture and the product extracted with ether. The ether solution was dried and concentrated and the residue distilled to yield 8.3 g. (37%) of I which boiled at 115° (0.23 mm.), n^{25}_{D} 1.5373.

Neither benzoyl chloride nor *p*-nitrobenzoyl chloride formed a crystalline ester when allowed to react with I. A solid phenylurethan, m.p. 93–110°, was obtained, but this product was not purified by either recrystallization or chromatography on alumina.

Cyclizations.—The procedure of Perlman, Bogert and Davidson[5] was employed. **A.** From alcohol IIIa (1.44 g.) and 90% sulfuric acid (5.2 ml.), there was obtained 827 mg. (63%) of cyclized product which was evaporatively distilled at 83–85° (0.08 mm.), n^{23}_{D} 1.5500, $[\alpha]_D$ −4.3° (*c* 1%, chloroform).

B. From inactive alcohol III (3.0 g.), there was obtained 2.02 g. (74%) of product which distilled at 80–87° (0.07 mm.), n^{23}_{D} 1.5509. The infrared spectra of the cyclization products from alcohol IIIa and III were superimposable.

C. 1-(2-Phenylethyl)-cyclohexanol (30 g.) was cyclized with 85% sulfuric acid (50 ml.) to yield 19.9 g. (73%) of product, b.p. 80–83° (0.4 mm.), n^{25}_{D} 1.5502.

Oxidations. **A.**—The cyclization product from inactive alcohol III (1.8 g.) was dissolved in acetic acid (17.1 ml.) and treated with a solution of chromium trioxide (2.05 g.) in 80% acetic acid (3.8 ml.). This reaction mixture was allowed to stand for 4 days, then diluted with water and the product extracted with ether. The crude ketone (1.14 g.) remaining after evaporation of the ether was purified by use of Girard reagent T[20] (1.2 g.) to yield 653 mg. (39%) of purified ketonic product.

B.—The optically active cyclization product (700 mg.) was oxidized with chromic acid as for the inactive product and the crude ketone (566 mg.) purified with Girard reagent to yield 310 mg. (44%) of ketones free of non-ketonic products.

C.—The product from the cyclization of 1-(2-phenylethyl)-cyclohexanol (14 g.) was oxidized with chromic acid as for the other hydrocarbons. The crude ketone was purified by distillation; there was obtained 9.3 g. of product which was collected at 100–120° (0.4 mm.).

Preparation and Separation of Oximes. **A.**—The ketone from the chromic acid oxidation, part C (3.67 g.), hydroxylamine hydrochloride (4 g.) and dry pyridine (40 ml.) were heated at 100° for 4 hr. The solvents were evaporated and the residue washed with water. The crude product was recrystallized several times from ethanol to yield an oxime which melted at 191–192°.

Anal. Calcd. for $C_{14}H_{17}ON$: C, 78.10; H, 7.96. Calcd. for $C_{14}H_{15}ON$: C, 78.84; H, 7.09. Found: C, 79.10; H, 6.99.

This oxime had the major maximum in the ultraviolet region at 289 mμ.

The residual oxime from the mother liquors was placed on a column of silica gel (60–200 mesh) and eluted with mixtures of hexane and benzene. The earlier fractions from the chromatography yielded material which melted in the range 90–127°; recrystallization of these fractions from ethanol–water raised the melting point to 126.5–127.5°.[21] The absorption maximum in the ultraviolet region was at 252 mμ in contrast to that of the higher melting oxime VI. The amounts of oxime V and VI obtained in this experiment are estimated to be in a ratio of 1:3.

B.—The ketone (633 mg.) from inactive *trans*-2-(2-phenylethyl)-cyclohexanol was converted to the oxime as in part A and the oxime chromatographed to yield an oxime, m.p. 121–123°. The melting point of a mixture of this oxime and that of *cis*-9-oxo-1,2,3,4,4a,9,10,10a-octahydrophenanthrene obtained in part A was 125–127°. The later fractions from the chromatography yielded oxime V identical with that obtained in part A.

C.—The active ketone (310 mg.) from *l-trans*-2-(2-phenylethyl)-cyclohexanol was treated with hydroxylamine to yield 249 mg. of oxime, which was chromatographed to yield oxime VI (*ca.* 25 mg.) and, after recrystallization, an oxime (*ca.* 100 mg.), m.p. 110–112°, $[\alpha]_D$ +39.5 (*c* 1, chloroform). The infrared spectrum of this product was superimposable on that of inactive oxime V. Further recrystallization of this oxime from aqueous ethanol raised the melting point to 117–119°.

Anal. Calcd. for $C_{14}H_{17}ON$: C, 78.10; H, 7.96. Found: C, 77.81; H, 7.92.

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[19] H. Adkins and G. F. Hager, THIS JOURNAL, **71**, 2965 (1949).

[20] A. Girard and S. Sandulesco, *Helv. Chim. Acta*, **19**, 1095 (1936).

[21] The melting point of the oxime of *cis*-9-oxo-1,2,3,4,4a,9,10,10a-octahydrophenanthrene is reported by Cook, Hewett and Robinson, ref. 6, to be 124°; this substance was also prepared by oxidation of the cyclization product from 1-(2-phenylethyl)-cyclohexanol.