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

Many-membered Carbon Rings. XII. Stereochemical Studies of Some *gem*-Dimethylcyclononane Derivatives[1]

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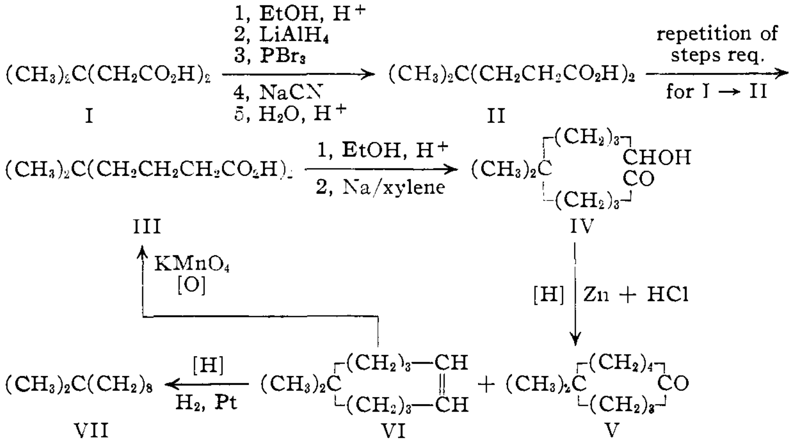
RECEIVED JUNE 15, 1955

The molecular flexibility of the nine-membered carbon ring has been investigated using 5,5-dimethylcyclononanone (V). A synthesis of this compound is described. Direct attempts to resolve V gave no indication of separation of stereoisomers even though well characterized optically active derivatives were obtained. Conversion of V to 5,5-dimethylcyclononanol (VIII) and the resolution of the latter has been achieved. Oxidation of the optically active alcohols VIII afforded inactive ketone V. It is concluded that nine-membered carbon rings of this type are incapable of retaining dissymmetric conformations at room temperature.

It is well known that molecular dissymmetry may arise from the restriction of rotation about single bonds. The optically active biphenyls probably comprise the most thoroughly studied group of compounds of this type. Inspection of molecular models shows that a nine-membered carbon ring lacks both a plane and center of symmetry and that restriction of rotation about carbon–carbon single bonds affords dissymmetric conformations. In 1938, Marvel and Glass[4] from a consideration of Stuart models, predicted the possible optical isomerism of cyclononanone. They were, however, unable to separate optical isomers. This result may, of course, have simply reflected the difficulty in accomplishing a resolution with the small amount of material available at the time. These workers concluded that Stuart models failed to present a true picture of the flexibility of the cyclononanone molecule. The shortcomings of Stuart models are now generally recognized and from the more exact Fisher–Taylor–Hirschfelder models it can be seen that in cyclononanone the hydrogen atoms are not sufficiently bulky to prevent free rotation about carbon–carbon single bonds. The actual conversion of one dissymmetric form of cyclononanone to its enantiomorph appears to be possible.

If restriction of free rotation could be achieved by the introduction of sufficiently large substituents into the nine-membered ring, without creating an asymmetric center, the possibility of actually isolating optical isomers resulting from the intrinsic dissymmetry of the nine-membered ring might be realized. The ketone 5,5-dimethylcyclononanone (V) seemed to possess the necessary requirements. Fisher–Taylor–Hirschfelder models of this compound showed crowding to a degree sufficient to prevent conversion of any dissymmetric conformation to its enantiomorph without rupture of the ring. For these reasons V has been synthesized and subjected to a careful stereochemical study.

The ketone V was synthesized *via* the scheme



β,β-Dimethylglutaric acid (I), obtained by hypohalite oxidation of dimedone,[5] was homologated to γ,γ-dimethylpimelic acid *via* its diester, the derived glycol, dibromide and dinitrile. The over-all yield of this bis-homologation was 62–65%. Treatment of 3,3-dimethyl-1,5-pentanediol with anhydrous hydrogen bromide instead of phosphorus tribromide produced 4,4-dimethyltetrahydropyran rather than the desired dibromide. Upon repeating the bis-homologation reaction sequence, II was converted to δ,δ-dimethylazelaic acid (III) in 72–75% over-all yield. Attempted bis-homologation by a malonic ester synthesis using 1,5-dibromo-3,3-dimethylpentane as well as various attempts to carry out Grignard reactions with this dibromide were unsuccessful. A standard acyloin cyclization of the diethyl ester of III gave the acyloin IV in excellent yield (66–70%).[6] Reduction of IV to the cyclic ketone V using zinc and concd. hydrochloric and acetic acid was never completely satisfactory as there was always formed a substantial amount of 6,6-dimethylcyclononene (VI) together with the acetate of the original acyloin IV. The best procedure, using commercial zinc dust, afforded 60% of V, 20% of VI and 10% of IV-acetate. VI absorbed 99.5% of one molecular equivalent of hydrogen when reduced with Adams catalyst and gave

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[1] For the preceding paper in this series see A. T. Blomquist and J. Wolinsky, THIS JOURNAL, **77**, 5423 (1955).

[2] Abstracted from part of the dissertations presented by E. S. Wheeler in June, 1952, and Y. Chu in September, 1955, to the Graduate School of Cornell University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[3] Charles Kendall Adams Senior Fellow, Cornell University, 1954–1955.

[4] C. S. Marvel and D. B. Glass, THIS JOURNAL, **60**, 1051 (1938).

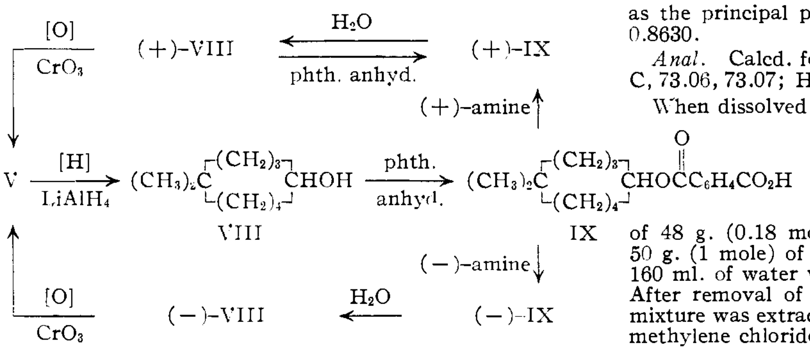
[5] J. Walker and J. K. Wood, *J. Chem. Soc.*, **89**, 598 (1906).

[6] It should be noted that cyclization here is apparently facilitated by the presence of the *gem*-dimethyl group. Using azelaic ester the maximum yields of azeloin realized were *ca.* 35–40% (see A. T. Blomquist, L. H. Liu and J. C. Bohrer, THIS JOURNAL, **74**, 3643 (1952)).

the acid III on oxidation with potassium permanganate. The infrared absorption spectrum of VI, showing maxima at 6.04, 10.25 and 13.72 μ, indicated that it was a mixture of *cis* and *trans* isomers. The structure of the acyloin acetate was assigned solely on the basis of its infrared spectrum which showed absorption maxima at 5.77, 5.88 and 8.05 μ. When pure zinc dust was used in the reduction of IV, an 80% yield of VI was obtained. The ketone V was purified conveniently by conversion to its crystalline semicarbazone followed by regeneration using oxalic acid.

Derivatives of V with (+)- and (−)-δ-(α-phenylethyl) semicarbazide[7] and (+)-5-(α-phenylethyl) semioxamazide[8] were prepared and subjected to fractional crystallization. In all cases sharp melting, crystalline derivatives were obtained which showed no evidence of resolution. This behavior of V with the aforementioned resolving agents gave some preliminary indication of the non-rigidity of the nine-membered ring in V. Nevertheless, this was still not regarded as conclusive evidence of flexibility as it is well known that the resolution of carbonyl compounds, containing *bona fide* asymmetric centers, is frequently difficult.[9] Therefore, a more definite demonstration of ring flexibility in V was sought.

V was reduced to 5,5-dimethylcyclononanol (VIII), thus introducing an asymmetric carbon atom in the nine-membered ring. If the ring itself could retain its dissymmetric conformation, a mixture of two racemic modifications should result. The alcohol VIII gave a sharp melting acid phthalate IX which was resolved with (+)- and (−)-α-phenylethylamine. Hydrolysis of the resolved acid phthalates gave the (+)-alcohol VIII, m.p. 15–17°, [α]D +29.2 ± 0.4° (*c* 11, chloroform) and the (−)-alcohol VIII, m.p. 16–17°, [α]D −30.4 ± 0.4° (*c* 11, chloroform). Oxidation of the optically active alcohols VIII with chromic oxide at room temperature gave the ketone V which was found to be optically inactive in both cases.



In order to demonstrate that "*epimerization*" had not occurred in the hydrolysis of (+)- and (−)-IX, (+)-VIII was treated with phthalic anhydride and gave a quantitative yield of (+)-IX, identical in all respects with the original sample of (+)-IX.

The observation that the stereochemically homogeneous alcohols gave inactive ketone V and that only two stereoisomeric alcohols VIII and acid phthalates IX were obtained suggests the conclusion that "nine-membered ring dissymmetry" in 5,5-dimethylcyclononanone is absent at room temperature. Although medium-sized carbon ring compounds (8 to 12 members) do exhibit some unique properties attributable to their "*internal strain*,"[10,11] they are incapable of retaining specific conformations at room temperature. Equilibria between the various possible conformations are always attained.

Experimental Part[12]

Materials.—β,β-Dimethylglutaric acid (I) was obtained from dimedone[13] by hypohalite oxidation.[5] Diethyl β,β-dimethylglutarate, b.p. 89–90° (2 mm.), n^{20}_D 1.4278, was prepared in 94% yield by the method used for diethyl adipate.[14]

3,3-Dimethyl-1,5-pentanediol.—A solution of 200 g. (0.93 mole) of diethyl β,β-dimethylglutarate in 200 cc. of anhyd. ether was added as rapidly as possible to a stirred mixture of 50 g. (1.32 moles) of lithium aluminum hydride and 1.8 l. of anhydrous ether. The mixture was stirred for one hour after completion of addition, 200 ml. of water was carefully added to hydrolyze the complex, and filtered from the precipitated inorganic salts. From the combined ether filtrate and washings there was obtained 110 g. (90%) of the glycol, b.p. 95–98° (0.25 mm.), n^{20}_D 1.4575 [lit.[15] b.p. 132° (1 mm.)].

1,5-Dibromo-3,3-dimethylpentane. A.—Into a solution of 264 g. (2.0 moles) of 3,3-dimethyl-1,5-pentanediol in 250 ml. of glacial acetic acid heated at 130°, a rapid stream of anhydrous hydrogen bromide was passed for 5–6 hr. The lower layer of the cooled reaction mixture was washed with 20% sodium carbonate solution, then with water and finally distilled *in vacuo* to give 350–368 g. (68–71%) of the dibromide, b.p. 80–81.5° (1.3 mm.), n^{20}_D 1.5078, d^{20}_4 1.5320.

Anal. Calcd. for $C_7H_{14}Br_2$: C, 32.56; H, 5.43; *M*D, 50.1. Found: C, 32.68, 32.86; H, 5.68, 5.76; *M*D, 50.0.

B.—Following a procedure described previously using phosphorus tribromide[16] the dibromide was obtained in 98% yield.

4,4-Dimethyltetrahydropyran.—Treatment of the pentanediol with anhyd. hydrogen bromide in the absence of solvent acetic acid afforded 4,4-dimethyltetrahydropyran as the principal product, b.p. 125–127°, n^{20}_D 1.4268, d^{20}_4 0.8630.

Anal. Calcd. for $C_7H_{14}O$: C, 73.63; H, 12.36. Found: C, 73.06, 73.07; H, 12.17, 12.43.

When dissolved in an equal volume of glacial acetic acid and treated with anhyd. hydrogen bromide the pyran gave 3,3-dimethyl-1,5-dibromopentane.

γ,γ-Dimethylpimelonitrile and γ,γ-Dimethylpimelic Acid (II).—A mixture of 48 g. (0.18 mole) of 1,5-dibromo-3,3-dimethylpentane, 50 g. (1 mole) of sodium cyanide, 150 ml. of ethanol and 160 ml. of water was refluxed for 12 hours under nitrogen. After removal of most of the alcohol by distillation, the mixture was extracted with methylene chloride. From the methylene chloride layer 30 g. of the crude nitrile was obtained. A distilled sample showed b.p. 155–157° (7 mm.) [lit.[15] b.p. 155–157° (7 mm.)].

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(7) I. V. Hopper and F. J. Wilson, *J. Chem. Soc.*, 2483 (1928).

(8) N. Leonard, *J. Org. Chem.*, **15**, 42 (1950).

(9) For a description of unsuccessful attempts to resolve (±)-camphor and (±)-3-methylcyclohexanone see A. J. Little, J. McClean and F. J. Wilson, *J. Chem. Soc.*, 336 (1940). An interesting review of the difficulties encountered in the resolution of carbonyl compounds is given by R. B. Woodward, T. P. Kohman and G. C. Harris, This Journal, **63**, 120 (1941).

(10) V. Prelog, *J. Chem. Soc.*, 420 (1950).

(11) H. C. Brown, R. S. Fletcher and R. B. Johannesen, This Journal, **73**, 212 (1951).

(12) All melting points are corrected, all boiling points are uncorrected. Rotations were measured in chloroform solution at room temperature except where indicated.

(13) A. H. Blatt, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 200.

(14) Reference 13, p. 264.

(15) R. F. Miller and R. Adams, This Journal, **58**, 787 (1936).

(16) A. T. Blomquist and J. Verdol, *ibid.*, **77**, 1806 (1955).

The crude nitrile was hydrolyzed by refluxing overnight with a mixture of 40 ml. each of water, concd. sulfuric acid and glacial acetic acid. The mixture was poured onto crushed ice and the solid precipitate was collected. The crude acid weighed 33 g. (94%). A sample recrystallized from water showed m.p. 85.5–86° (lit. m.p. 83°).[17]

Diethyl γ,γ-Dimethylpimelate.—The crude acid II (330 g., 1.75 moles) was esterified using the alcohol–toluene–water azeotropic distillation method. The yield of pure ester was 320 g. (72% from 1,5-dibromo-3,3-dimethylpentane), b.p. 102–103° (0.7 mm.), n^{20}_{D} 1.4394, d^{20}_{4} 0.9854 (lit.[15] n^{20}_{D} 1.5632, d^{20}_{4} 0.9732).

Anal. Calcd. for $C_{13}H_{24}O_4$: C, 63.90; H, 9.90; sapn. no., 122.0; M_D, 65.5. Found: C, 63.86; H, 9.85; sapn. no., 120.6; M_D, 65.4.

4,4-Dimethyl-1,7-heptanediol.—Diethyl γ,γ-dimethylpimelate (160 g., 0.65 mole) was reduced with lithium aluminum hydride (50 g., 1.3 moles) as described above. There was obtained 93 g. (90%) of the glycol, b.p. 128° (1.2 mm.), n^{20}_{D} 1.4620, d^{20}_{4} 0.9390.

Anal. Calcd. for $C_9H_{20}O_2$: C, 67.45; H, 12.58. Found: C, 67.61; H, 12.61.

1,7-Dibromo-4,4-dimethylheptane.—A. Using the hydrogen bromide method described previously, from 20 g. (0.125 mole) of the glycol, 32 g. (89.5%) of the dibromide was obtained. B. Using the phosphorus tribromide procedure, from 186 g. (1.16 moles) of the glycol 309 g. (94%) of the dibromide was obtained, b.p. 96.5–98° (1 mm.), n^{20}_{D} 1.5018, d^{20}_{4} 1.4145.

Anal. Calcd. for $C_9H_{18}Br_2$: C, 37.76; H, 6.29; M_D, 59.3. Found: C, 37.87; H, 6.41; M_D, 59.5.

δ,δ-Dimethylazelaonitrile and δ,δ-Dimethylazelaic Acid (III).—Using the procedure described previously, from 220 g. (0.77 mole) of 4,4-dimethyl-1,7-dibromoheptane, there was obtained 127 g. (93%) of the dinitrile, b.p. 146° (0.9 mm.), n^{20}_{D} 1.4540, d^{20}_{4} 0.9200.

Anal. Calcd. for $C_{11}H_{18}N_2$: C, 74.11; H, 10.18; N, 15.71. Found: C, 73.93; H, 10.21; N, 15.41.

The crude nitrile (from 309 g., 1.09 moles of dibromide) was hydrolyzed by the procedure described previously. The yield of crude III was 230 g. (97.5%), m.p. 60–65°. A sample of the acid purified through its sodium salt showed m.p. 68.0–69.5°.

Anal. Calcd. for $C_{11}H_{20}O_4$: C, 61.09; H, 9.32; neut. equiv., 108.0. Found: C, 61.22; H, 9.32; neut. equiv., 109.7.

Diethyl δ,δ-Dimethylazelate.—Esterification of crude III (230 g., 1.06 moles) using the method described previously gave 248.5 g. (86%) of the pure ester, b.p. 102° (0.05 mm.), n^{20}_{D} 1.4412, d^{20}_{4} 0.9562. The over-all yield from 1,7-dibromo-4,4-dimethylheptane was 83%.

Anal. Calcd. for $C_{15}H_{28}O_4$: C, 66.14; H, 10.36. Found: C, 66.20; H, 10.48.

6,6-Dimethylcyclononanol-2-one (IV).—The cyclic acyloin IV was obtained in 66–70% yield from diethyl δ,δ-dimethylazelate following a standard procedure,[18] using a mixture of xylene–toluene (3:1) as solvent. Cyclizations were carried out on 0.3 to 0.5 molar scale and the product obtained showed b.p. 88–91° (1–1.2 mm.), n^{20}_{D} 1.4845, d^{20}_{4} 1.0177.

Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94; M_D, 52.4. Found: C, 72.06; H, 10.88; M_D, 52.0.

5,5-Dimethylcyclononanone (V).—Following the reduction procedure described for the conversion of azeloin to cyclononanone,[19] IV (25.8 g., 0.14 mole) was subjected to zinc dust (90%) reduction. The crude product was distilled through an 83-cm. Podbielniak column to give three main fractions: fraction 1, b.p. 104–107° (35 mm.), which absorbed 75% of one molecular equiv. of hydrogen on quantitative hydrogenation; fraction 2, b.p. 132–135° (33 mm.), was relatively pure ketone V, n^{20}_{D} 1.4718, (11.9 g., 51%); fraction 3, b.p. 135–137° (5 mm.), contained mainly the acyloin acetate. Fraction 2 (crude V) was further purified through its semicarbazone, m.p. 172–173°.

Anal. Calcd. for $C_{12}H_{23}N_3O$: C, 63.97; H, 10.31; N, 18.65. Found: C, 63.74, 63.87; H, 10.43, 10.33; N, 18.60, 18.86.

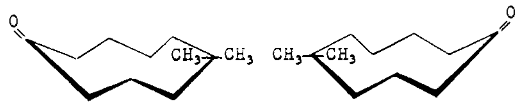

Fig. 1.—Enantiomorphs of 5,5-dimethylcyclononanone.

The ketone V was regenerated by refluxing 21 g. (0.091 mole) of the semicarbazone and 30 g. (0.33 mole) of oxalic acid in 200 ml. of water for 12 hours. The mixture was cooled and extracted with ether. From the ether layer 13.1 g. (87%) of pure V was obtained, b.p. 104° (8.5 mm.), n^{20}_{D} 1.4714, n^{25}_{D} 1.4696, d^{20}_{4} 0.9389.

Anal. Calcd. for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.59, 78.66; H, 11.91, 11.99.

6,6-Dimethylcyclononene (VI).—A suspension of 100 g. of pure zinc dust (Standard 122, New Jersey Zinc Co.) in 194 ml. of glacial acetic acid was mixed thoroughly with stirring, IV (36.8 g., 0.2 mole) and 2 g. of copper acetate were introduced. From a dropping funnel, 250 ml. of concd. hydrochloric acid was added over a period 1.5 hr., during which time the reaction flask was surrounded by a cool water-bath. After the addition was complete, the reaction mixture was heated to reflux for 0.5 hr., cooled in ice and diluted with water. After the usual procedure for isolation of organic products, the mixture was distilled to give 24.4 g. (80%) of VI, b.p. 117–120° (70 mm.), n^{25}_{D} 1.4714. A portion of the sample was redistilled at 105–105.5° (40 mm.), n^{25}_{D} 1.4716, d^{25}_{4} 0.8531.

Anal. Calcd. for $C_{11}H_{20}$: C, 86.76; H, 13.24. Found: C, 86.73, 86.55; H, 13.07, 13.19.

On quantitative hydrogenation, this sample absorbed 99.5% of one molecular equivalent of hydrogen. One gram of the once-distilled VI was dissolved in 5 ml. of acetone (freshly distilled over potassium permanganate). To this solution was added with swirling 60 ml. of a 5% potassium permanganate solution. The reaction mixture was warmed on a steam-bath for 15 min., and cooled to room temperature. Sulfur dioxide was bubbled into the mixture until the solution was just colorless. Upon acidification and extraction with methylene chloride, a colorless oily residue was obtained from the methylene chloride layer. The oil was crystallized from hexane to give 400 mg. of III, m.p. 69–70°.

1,1-Dimethylcyclononane (VII).—Compound VI (5 g.) was subjected to catalytic hydrogenation with 100 mg. of platinum oxide in 20 ml. of ethanol in a Parr hydrogenation apparatus. After the removal of catalyst and solvent, 3.5 g. of the hydrocarbon VII was obtained by distillation; b.p. 104.5° (36 mm.), n^{25}_{D} 1.4604, d^{25}_{4} 0.8402.

Anal. Calcd. for $C_{11}H_{22}$: C, 85.63; H, 14.37. Found: C, 85.43, 85.57; H, 14.18, 14.36.

Attempted Resolutions of V. A. V-(+)-δ-(α-Phenylethyl) Semicarbazone.—A clear solution of 2.16 g. (0.01 mole) of (+)-δ-(α-phenylethyl) semicarbazide hydrochloride[20] and 1.62 g. of sodium acetate trihydrate in 10 ml. of methanol and 5 ml. of water was added to a solution of 3.36 g. (0.02 mole) of V in 10 ml. of methanol. The mixture was kept in a water-bath at 50° and gradually allowed to cool to room temperature. After standing in the refrigerator for 5 days, a first crop of solid derivative[21] (1.2 g., m.p. 95–103°) was collected. Recrystallization from absolute ethanol or hexane raised the melting point to 107.5–109.5°, $[\alpha]_D$ $-52.7 \pm 0.8°$ (*c* 5, abs. ethanol). Further crops were collected from the mother liquors. These showed no variation in m.p. or specific rotation.

Anal. Calcd. for $C_{20}H_{31}N_3O$: C, 72.90; H, 9.48; N, 12.76. Found: C, 73.05; H, 9.41; N, 13.02.

After three crops of similar crystals had been collected, the mother liquor was concentrated to an oily residue which was dissolved in ether and washed with water. The residue obtained on evaporating the dried ether solution was chromatographed on grade-3 alumina. After eluting with pentane 1 g. of optically inactive V was obtained. The semicar-

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[17] G. Komppa, *Ber.*, **62B**, 1371 (1929).

[18] A. T. Blomquist, R. E. Burge and A. C. Sucsy, THIS JOURNAL, **74**, 3636 (1952).

[19] A. T. Blomquist, L. H. Liu and J. C. Bohrer, *ibid.*, **74**, 3643 (1952).

[20] F. J. Wilson, I. V. Hopper and A. B. Crawford, *J. Chem. Soc.*, **121**, 866 (1922).

[21] The initial crystallization of this derivative required one month.

bazone derivative of this sample of V showed m.p. 171–173.5° and $[\alpha]_D$ 0.

B. **V-(−)-δ-(α-Phenylethyl) Semicarbazone.**[20]—The procedure used here was essentially the same as that described immediately above. A one to one mole ratio of the ketone and the (−)-semicarbazide reagent was used. A 0.01-mole run gave 1.4 g. of crystals as the first crop, m.p. 107–109°, $[\alpha]_D$ +52.2 ± 0.8° (*c* 5, abs. ethanol).

Anal. Calcd. for $C_{20}H_{31}N_3O$: C, 72.90; H, 9.48; N, 12.76. Found: C, 73.07; H, 9.47; N, 12.91.

The active derivative (1.2 g.) was decomposed by stirring with 5.5 g. of oxalic acid and 40 ml. of water at room temperature for two weeks. The solvent was evaporated *in vacuo*. The residue after chromatographing on grade-3 alumina gave a ketone fraction with zero rotation.

C. **V-(+)-5-(α-Phenylethyl) Semioxamazone.**—To a solution of 3.4 g. (0.02 mole) of V in 50 ml. of dry benzene was added 2.1 g. (0.01 mole) of (+)-5-(α-phenylethyl) semioxamazide[8] and a crystal of iodine. The reaction mixture was refluxed for 5 min. The solution was concentrated and cooled. Six crops of solid derivative were collected, m.p. 106–108°, $[\alpha]_D$ +106.5° (*c* 1.5). Recrystallization from hexane–benzene gave soft needles, m.p. 108–109°, $[\alpha]_D$ +107.2 ± 1° (*c* 2).

Anal. Calcd. for $C_{21}H_{31}N_3O_2$: C, 70.55; H, 8.74; N, 11.76. Found: C, 70.63, 70.39; H, 8.55, 8.82; N, 12.34, 12.07.

After a total of 2.2 g. of the solid derivative had been collected, the mother liquor was sucked down to dryness. The residue was chromatographed on grade-3 alumina, as before, to give 1 g. of the unreacted V, $[\alpha]_D$ 0 (neat). A sample of V regenerated from the active semioxamazone derivative, $[\alpha]_D$ +107.2° (*c* 1.5), was also optically inactive.

5,5-Dimethylcyclononanol Acid Phthalate (IX).—Compound V (9 g.) diluted with 10 ml. of ether was reduced with 2 g. of lithium aluminum hydride in 40 ml. of anhydrous ether in the usual manner. About 10 ml. of water was added to decompose the complex. After following the usual isolation procedure, 10 g. of crude VIII was obtained. The yield was essentially quantitative. Treatment of this crude VIII with 8.8 g. of phthalic anhydride by heating at 110° in 20 ml. of dry toluene for 12 hr. gave crude IX. After recrystallization there was obtained 14 g. (75%) of IX, m.p. 111–112°. An additional 3 g. of IX was obtained from the mother liquor.

Anal. Calcd. for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.50; H, 8.22.

Resolution of IX.—A mixture of 18 g. (0.059 mole) of IX and 7.07 g. (0.059 mole) of (+)-α-phenylethylamine in 65 ml. of acetone was warmed gently on a hot-plate until the solution became clear. On standing at room temperature 20 g. of solid salt deposited, m.p. 110–129°. Fractional recrystallization of this salt from acetone until the least soluble fractions showed no further change in m.p. or optical rotation gave 5 g. of the (+)-acid-(+)-base salt as fine needles, m.p. 126–129.5°, $[\alpha]_D$ +8.0 ± 1° (*c* 5). A large excess of 10% aqueous hydrochloric acid was added to a solution of the 5 g. of active salt in the minimum amount of warm ethanol. Upon cooling, (+)-IX deposited and showed m.p. 120–121.5°, $[\alpha]_D$ +8.9 ± 0.8° (*c* 6). After recrystallization from hexane 3.5 g. of (+)-IX, unaltered in m.p. or optical rotation, was obtained.

Anal. Calcd. for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.69, 71.85; H, 8.31, 8.31.

From the combined acetone mother liquors resulting from the fractional crystallization described above there was obtained after acidification 13.7 g. of IX enriched in the (−)-isomer. This sample of IX (13.7 g.) was treated with 5.4 g. of (−)-α-phenylethylamine and the resulting salt fractionally crystallized from acetone until the least soluble fraction showed constant m.p. and optical rotation. There was obtained 6.9 g. of the (−)-acid-(−)-base salt, m.p. 127–129°, $[\alpha]_D$ −9.4 ± 0.9° (*c* 5). Regeneration of IX from this salt followed by one recrystallization from hexane gave 4.3 g. of (−)-IX as colorless prisms, m.p. 120.5–121.5°, $[\alpha]_D$ −10.0 ± 1° (*c* 6).

Anal. Calcd. for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.57, 71.76; H, 8.12, 8.33.

After regenerating IX from the accumulated acetone mother liquors of the second fractional crystallization of the (−)-acid-(−)-base salt, 8.5 g. of IX enriched in the (+)-isomer was obtained. By repeating the entire resolution with this 8.5 g. of IX there was obtained an additional 1.5 g. of (+)-IX and 1.9 g. of (−)-IX. Thus a total of 5.0 g. (55%) of (+)-IX and 6.2 g. (69%) of (−)-IX was obtained in the resolution.

(+)- and (−)-VIII.—(+)-IX (4.6 g., 0.014 mole) was refluxed with 40 ml. of 25% sodium hydroxide for two hr. From the pentane extract of the cooled alkaline mixture there was obtained 2.35 g. (97%) of crude (+)-VIII as a viscous liquid showing $[\alpha]_D$ +29.5 ± 0.25° (*c* 30). This (+)-VIII was then distilled and showed m.p. 15–17°, b.p. 76–77° (2 mm.), n^{25}_D 1.4805, $[\alpha]_D$ +29.2 ± 0.4° (*c* 11).

Anal. Calcd. for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.52, 77.82; H, 12.98, 13.05.

(−)-IX was hydrolyzed in a similar manner. From 6.1 g. of (−)-IX there was obtained 3.02 g. (93%) of pure (−)-VIII, m.p. 16–17°, b.p. 75° (2 mm.), n^{25}_D 1.4805, $[\alpha]_D$ −30.4 ± 0.4° (*c* 11).

Anal. Calcd. for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.70, 77.68; H, 12.75, 13.08.

(+)-IX from (+)-VIII.—From 1 g. of (+)-VIII treated with phthalic anhydride as described earlier for (±)-VIII there was obtained 1.8 g. (97%) of (+)-IX which showed m.p. 120–121°, $[\alpha]_D$ +8.7 ± 0.8° (*c* 6). A mixed m.p. determination with (+)-IX from the resolution experiment showed m.p. 120–121.5°.

Chromic Oxide Oxidation of (+)- and (−)-VIII.—To a solution of 2 g. of (−)-VIII in 15 ml. of acetone, freshly distilled from potassium permanganate, there was added dropwise with swirling the calculated amount of chromic acid oxidizing solution.[22] Oxidation occurred instantaneously as indicated by the change in color from orange to deep green. When the reaction was completed one extra drop of the oxidizing solution was added and the mixture let stand at room temperature for 10 minutes. The mixture, diluted with 20 ml. of water was quickly extracted with pentane. From the pentane 2 g. of V showing $[\alpha]_D$ 0 (neat) and n^{25}_D 1.4696 was obtained. Treatment with (+)-δ-(-α-phenylethyl) semicarbazide gave the (−)-semicarbazone derivative showing m.p. 107–109°, $[\alpha]_D$ −52.5 ± 0.8° (*c* 5, abs. ethanol).

A similar oxidation of 1 g. of (+)-VIII gave 0.9 g. of optically inactive V.

Ithaca, N. Y.

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[22] A. Bowers, T. G. Hallsall, E. R. H. Jones and A. J. Lemin, *J. Chem. Soc.*, 2548 (1953).