Synthesis, Resolution, and Stereochemistry of 5-Hydroxy-10-alkyl-$\Delta^{1(9)}$-2-octalones[1]

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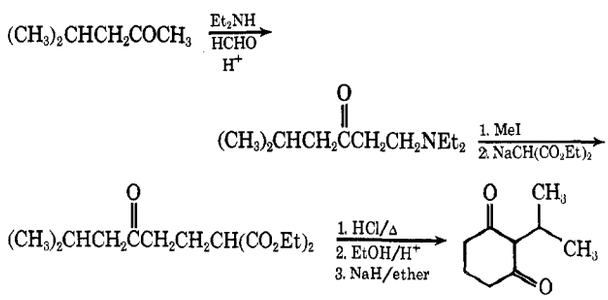
Received October 14, 1971

The 5-hydroxy-10-methyl- (ethyl- and isopropyl-) $\Delta^{1(9)}$-2-octalones (2) have been prepared and the corresponding phthalate half esters have been resolved by means of their brucine salts. From the ORD and CD data, (+)-5β-hydroxy-10β-alkyl-$\Delta^{1(9)}$-2-octalones and (−)-5α-hydroxy-10α-alkyl-$\Delta^{1(9)}$-2-octalones have been assigned the 5*S*,10*S* and 5*R*,10*R* configurations, respectively.

In connection with a current project dealing with the synthesis of optically active cyclic olefins,[1b] it became necessary to synthesize, resolve, and determine the absolute configuration of the title compounds before proceeding with this project. Syntheses of chiral steroid synthetic intermediates, such as **1** and **2**, have been accomplished by resolution,[3-6] microbiological reductions,[7] and most recently by "chiral induction.[8]" In view of the various diversified routes of resolution, it was deemed desirable to find a simple, suitable chemical resolution of **2** and to attempt their structural correlation *via* ORD and CD.

The starting 2-methyl-[9] and 2-ethyl-[10]-1,3-cyclohexanediones were prepared by the previously outlined routes. The 2-isopropyl-1,3-cyclohexanedione was synthesized by an improved five-step sequence of Bhattacharyya[11] in an overall 30% yield (Scheme I). The application of this scheme for the synthesis of 2-*tert*-butyl-1,3-cyclohexanedione was successful until the terminal cyclization stage. None of the desired product was isolated; the details of this reaction course will be published elsewhere.

SCHEME I



The Robinson annelation sequence, that is, the Michael addition of methyl vinyl ketone to 2-methyl-1,3-cyclohexanedione followed by dehydration, gave (50%) the known (±)-methyl bicyclic diketone **1a**.[12] An alternate route utilizing the intermediate pyrrolidine enamine was used for the synthesis of racemic **1b** and **1c**. This latter route seems to be preferable for the bulkier 2-alkyl substituted 1,3-cyclohexanediones in order to increase the activity of the carbonyl compound toward the initial Michael-type addition.

The saturated carbonyl group **1a** has been stereoselectively reduced with either sodium borohydride[13] or lithium tri-*tert*-butoxyaluminum hydride to afford the α,β-unsaturated keto alcohol **2a** (Scheme II). Although **2a** is an oil,[14] both **2b** and **2c** are crystalline solids. The stereochemistry of the hydroxyl group in **2a** has been adequately established, since the attacking hydride will approach the 1-keto group from the less hindered α side; therefore, the β-equatorial configuration of the hydroxyl function in **2b** and **2c** seems justifiable. The nmr spectra of **2** also showed a doublet of doublets (J = 7 and 7 Hz) for the >C**H**OH proton. These data correspond to the β-equatorial assignment of the hydroxyl group and are in rather good agreement with nmr data reported for steroids.[15]

The resolution of **2** can be accomplished by their initial conversion to the corresponding hydrogen phthalates by standard procedures, and then subsequent reso-

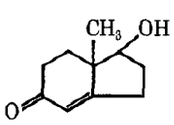
(1) (a) Part 1. Chiral Cyclic Olefins. (b) Presented in part at the Southwest Regional Meeting of the American Chemical Society, Tulsa, Okla., Dec 1969, ORGN 30; and 161st National Meeting of the American Chemical Society, Los Angeles, Calif., March 1971, ORGN 33.

(2) To whom correspondence should be addressed.

(3) L. Velluz, G. Nominé, G. Amiard, V. Torelli, and J. Cérède, *C.R. Acad. Sci.*, **257**, 3086 (1963).

(4) Z. G. Hojos, D. R. Parrish, and E. P. Oliveto [*Tetrahedron*, **24**, 2039 (1968)] have recently resolved the related 7,7a-dihydro-1-hydroxy-7a-methyl-5(6*H*)-indanone (i).

(5) W. R. Adams, O. L. Chapman, J. B. Sieja, and W. J. Welstead, Jr., *J. Amer. Chem. Soc.*, **82**, 162 (1966), partially resolved 10-methyl-$\Delta^{1(9)}$-2-octalone (ii) by fractional recrystallization of the *d*-camphor-10-sulfonic acid salt of the pyrrolidine enamine of ii.



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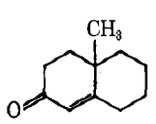


ii

(6) Also see A. J. Speziale, J. A. Stevens, and Q. E. Thompson, *ibid.*, **76**, 5011 (1954).

(7) (a) V. Prelog and W. Acklin, *Helv. Chim. Acta*, **39**, 748 (1956); (b) W. Acklin, V. Prelog, and D. Zäch, *ibid.*, **41**, 1416, 1424, 1428 (1958); (c) V. Prelog, U. S. Patent 2,833,694 (1959); *Chem. Abstr.*, **58**, 3179*d* (1959); (d) V. Prelog, Swiss Patent 366,530 (1964); *Chem. Abstr.*, **60**, 431*c* (1964); (e) H. H. Weston, *Helv. Chim. Acta*, **47**, 575 (1964).

(8) U. Eder, G. Sauer, and R. Weichert, *Angew. Chem., Int. Ed. Engl.*, **10**, 496 (1971).

(9) (a) H. Schick, G. Lehmann, and G. Hilgetag, *ibid.*, **6**, 80 (1967); (b) H. Schick and G. Lehmann, *J. Prakt. Chem.*, [4] **38**, 361 (1968); (c) A. B. Mekler, S. Ramachanchan, S. Swaninathan, and M. S. Newman, *Org. Syn.*, **41**, 56 (1961).

(10) N. Stetter and W. Diericks, *Ber.*, **85**, 61 (1952).

(11) P. C. Bhattacharyya, *J. Indian Chem. Soc.*, **42**, 467 (1965).

(12) (a) S. Swaminathan and M. S. Newman, *Org. Syn.*, **41**, 38 (1961); (b) M. S. Newman and A. B. Mekler, *J. Amer. Chem. Soc.*, **82**, 4039 (1960); (c) S. Swaminathan and M. S. Newman, *Tetrahedron*, **2**, 88 (1958); (d) P. Wieland and K. Miescher, *Helv. Chem. Acta*, **33**, 2215 (1950).

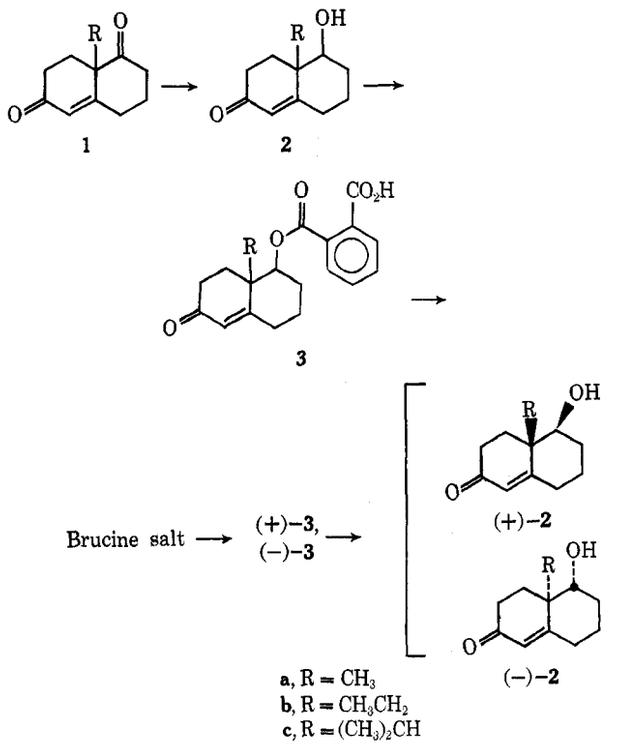
(13) (a) C. B. C. Boyce and J. S. Whitehurst, *J. Chem. Soc.*, 2680 (1960); (b) J. D. Cocker and T. G. Halsall, *ibid.*, 3441 (1957).

(14) The anhydrous oil solidified on exposure to moisture; the hydrate can be recrystallized with difficulty from ether,[13a] mp 58–59°.

(15) D. H. Williams and N. S. Bhacca, *J. Amer. Chem. Soc.*, **86**, 2742 (1964).

lution as a typical carboxylic acid.[16] Although Pasteur's method of resolution is commonly employed, the use of chiral amines, *e.g.*, (+)-1-phenylethylamine, (+)-1-(1-naphthyl)ethylamine, and dehydroabietyl amine,[17] failed in our hands to afford separable diastereoisomeric salts. The successful resolution of **3** was accomplished with the use of brucine in acetone, or less preferably benzene. After several recrystallizations, nearly pure specimens of the diastereoisomeric salts of **3a** can be achieved, although after one recrystallization *ca.* 50% optical purity is obtained. No attempts were made herein to prepare pure samples of these salts. Simple extraction of the alkaloid with cold dilute hydrochloric acid regenerated the chiral phthalate half esters (+)- or (−)-**3**.

SCHEME II



The removal of the phthalate group is a facile process *via* treatment with dilute aqueous base. It was found, however, that on prolonged contact with base the freed chiral **2** easily rearranged to 1-hydroxy-4-alkyl-5,6,7,8-tetrahydronaphthalene, which is the product of a diene–phenol-type rearrangement.[18] To avoid this unwanted side reaction, a heterogeneous mixture of dilute aqueous base containing **3** and ether was rapidly stirred at 0–10° with constant addition and removal of the product contained in the ether extract. After several minutes of such continuous extraction, the product was isolated in high yield and contaminated with little or no rearranged material.

Structural Correlations.—As alluded to earlier,[19] the characteristic shapes of ORD, as well as CD, curve of a given α,β-unsaturated ketone should be governed predominantly by the unsaturated chromophore rather than by any additional substituents unless certain conformational factors interfere. Since the structure of (+)-**2a** appears to be substantiated[7a,20] as (5*S*,10*S*)-5-hydroxy-10-methyl-$\Delta^{1(9)}$-2-octalone and the ORD curve measured,[20] it could serve as an excellent standard for the assignment of the configurations of the angular alkyl function in **2b** and **2c**.

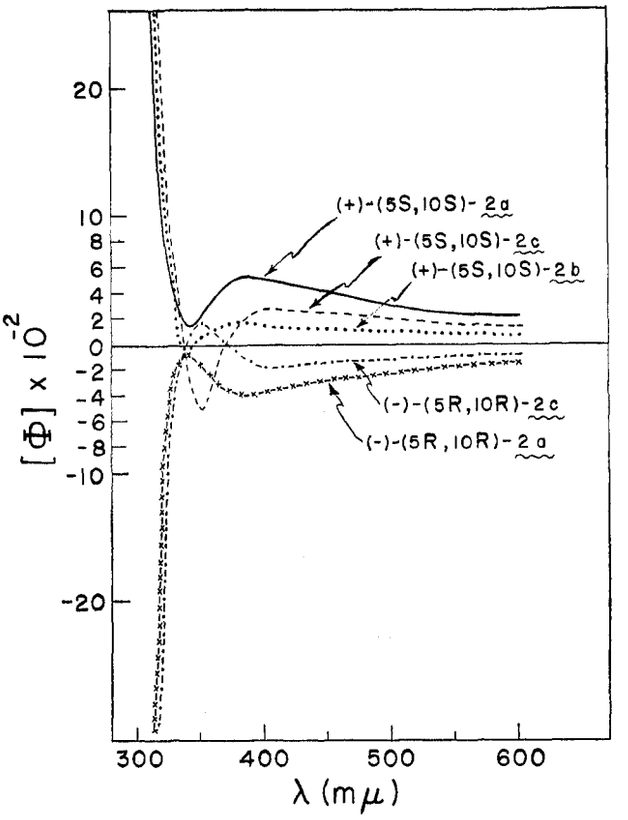


Figure 1.—Optical rotatory dispersion curves of 5-hydroxy-10-alkyl-$\Delta^{1(9)}$-2-octalones (methanol).

In Figures 1 and 2 are reproduced the ORD and CD curves, respectively, of (+)-**2** and (−)-**2**. Since (+)-**2b** and (+)-**2c** differ only in the size of the angular alkyl substituent, it is evident that except for some amplitude changes, the ORD and CD curves are nearly identical with those of (+)-**2a**, thus establishing the congeneric absolute configurations. Similarly, the dispersion curves of (−)-**2** are of a mirror image relationship to that of (+)-**2a** and, therefore, possess the opposite configuration.

From the ORD and CD curves, (+)-**2** and (−)-**2** are assigned the (5*S*,10*S*) and (5*R*,10*R*) configurations, respectively.

(16) For a recent review concerning the methods of optical resolution, see P. H. Boyle, *Quart. Rev., Chem. Soc.*, **25**, 323 (1971).

(17) W. J. Gottstein and L. C. Cheney, *J. Org. Chem.*, **30**, 2072 (1965), described the isolation of dehydroabietyl amine from Amine D, which was generously supplied by Hercules Powder Co.

(18) J. B. Jones, J. D. Leman, and P. W. Marr, *Can. J. Chem.*, **49**, 1604 (1971), and references cited therein.

(19) See (a) C. Djerassi, *Bull. Soc. Chim. Fr.*, 741 (1957); (b) C. Djerassi, "Optical Rotatory Dispersion: Application to Organic Chemistry," McGraw-Hill, New York, N. Y., 1960, p 83; (c) P. Crabbe, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," Holden-Day, San Francisco, Calif., 1965, p 191.

(20) C. Djerassi, J. Osiecki, and W. Herz, *J. Org. Chem.*, **22**, 1361 (1957).

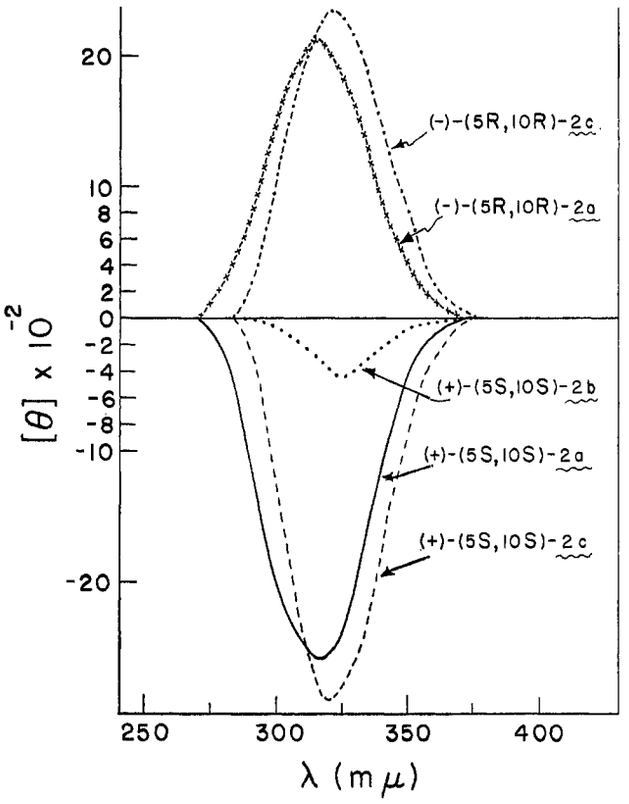


Figure 2.—Circular dichroism curves of 5-hydroxy-10-alkyl-$\Delta^{1(9)}$-2-octalones (methanol).

Experimental Section[21]

1,6-Dioxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (**1a**) was prepared from 2-methyl-1,3-cyclohexanedione,[9] mp 204–206° (lit.[9b] mp 204–206°), as previously outlined,[11] mp 49–50° (lit.[12a] mp 47–50°).

(±)-5-Hydroxy-10-methyl-$\Delta^{1(9)}$-2-octalone (**2a**) was prepared (89%) by the method of Boyce and Whitehurst,[13a] bp 135–136° (0.05 mm) [lit.[13] bp 140° (0.25 mm)].

2-Ethyl-1,3-cyclohexanedione was prepared[10] (31%) by alkylation of 1,3-cyclohexanedione with ethyl iodide, mp 172–175° (lit.[10] mp 178°).

1,6-Dioxo-8a-ethyl-1,2,3,4,6,7,8,8a-octahydronaphthalene.—A solution of 20 g (0.143 mol) of 2-ethylcyclohexanedione, 12 g (0.169 mol) of pyrrolidine, and 100 ml of benzene was refluxed for 12 hr using a Dean–Stark trap. The benzene and excess pyrrolidine were then removed under reduced pressure. To the crude air-sensitive enamine was added 15 g (0.212 mol) of methyl vinyl ketone in 100 ml of benzene followed by a solution of 20 ml of acetic acid, 20 ml of water, and 10 g of sodium acetate. The mixture was refluxed with stirring for 6 hr under nitrogen. The reaction mixture was cooled and extracted with benzene. The extract was washed with four 10-ml portions of 10% aqueous hydrochloric acid, then once with saturated sodium bicarbonate, dried over anhydrous magnesium sulfate, and concentrated to give 14 g of an orange oil. The oily crude product was chromatographed on 200 g of Merck alumina eluting with 10% ether in petroleum ether (bp 30–60°) and upon *in vacuo* concentration gave a semisolid, which was vacuum distilled giving (52%) a colorless, crystalline diketone, mp 58–62°. Recrystallization from ether–petroleum ether (bp 30–60°) gave an analytical sample of **1b**, mp 66–67° (lit.[22] mp 67.5–68.5°).

(21) Melting points were recorded in sealed capillary tubes on a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra were determined on a Perkin-Elmer 137-B spectrophotometer. Nmr spectra were determined on a Varian Associates Model A-60A spectrometer; chemical shifts are given in parts per million relative to TMS as an internal standard. Optical rotatory dispersion (ORD) and circular dichroism (CD) spectra were determined on a Durrum-Jasco spectropolarimeter, Model J-20. Analyses were performed by Mr. R. Seab in these laboratories.

(22) M. Los, U. S. Patent 3,321,489 (1967); *Chem. Abstr.*, **68**, 195442c (1968).

(±)-5-Hydroxy-10-ethyl-$\Delta^{1(9)}$-2-octalone (**2b**) was prepared (92%) by the ethanolic sodium borohydride reduction of the diketone **1b** following the procedure of Boyce and Whitehurst:[13a] bp 140–144° (0.05 mm); mp 87–88° [lit.[22] bp 165° (0.8 mm); mp 88.0–89.5°]; ir (neat) 1670 (C=O), 1625 (C=C), and 3450 cm^{-1} (OH); nmr (CCl_4) δ 0.96 (CH_3CH_2–, t, J = 7 Hz, 3 H), 3.7 (CH_3CH_2–, q, J = 7 Hz, 2 H), 5.99 (–CH=C<, s, 1 H), and 3.8 (CHOH, dd, J = 7.7 Hz, 1 H).

Preparation of 2-Isopropyl-1,3-cyclohexanedione. A.—A solution of 4-methyl-2-pentanone (75 g, 0.75 mol), diethylamine hydrochloride (106 g), paraformaldehyde (29 g), concentrated hydrochloric acid (1.5 ml), and absolute ethanol (600 ml) was refluxed for 6 hr with stirring under nitrogen. The yellow solution was diluted with water (500 ml) and extracted with ether (2 × 250 ml); then the aqueous solution was neutralized with sodium hydroxide (200 ml, 5 *N*) and extracted with ether (3 × 25 ml each). The ethereal extract was washed with a saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*, and distillation afforded (60%) the pungent-smelling 1-diethylamino-5-methylhexan-3-one, bp 69–76° (1–2 mm) [lit.[11] bp 93–94° (6 mm)].

B.—An ethereal solution of the above 1-diethylamino-5-methylhexan-3-one and excess methyl iodide was stirred for 7 hr at room temperature. The crude quaternary iodide was separated and dried *in vacuo*, yield 195 g. Further purification was not attempted nor necessary.

C.—The above crude methiodide (195 g, 0.595 mol) dissolved in 100 ml of anhydrous ethanol was added dropwise to diethyl sodiomalonate, prepared from diethyl malonate (105.6 g, 0.66 mol) and sodium (15.8 g) in 400 ml of absolute ethanol. After the addition, the mixture was heated with stirring for 10 hr. The reaction mixture was poured into ice water and extracted with chloroform, dried over anhydrous magnesium sulfate, and concentrated, giving (62%) an yellow oil, which was vacuum distilled to afford the keto diester: bp 143–152° (1–2 mm) [lit.[11] by 145–150° (4 mm)]; nmr (CCl_4) δ 0.92 (Me_2CH, d, J = 7 Hz, 6 H), 1.25 (CH_3CH_2O–, t, J = 7 Hz, 6 H), 3.52 (Me_2CH–, t, J = 7 Hz, 1 H), and 4.16 (CH_3CH_2O, q, J = 7 Hz, 4 H).

D.—A solution of the above keto diester (100 g, 0.37 mol), 200 ml of concentrated hydrochloric acid, and 200 ml of water was refluxed for 48 hr under nitrogen. The reaction mixture was extracted with methylene chloride; then the organic layer was extracted with a 10% sodium hydroxide solution. The aqueous extract was acidified with concentrated hydrochloric acid and extraction with methylene chloride to give the crude keto acid, nmr ($CDCl_3$) δ 0.88 (Me_2CH–, d, J = 7 Hz, 6 H) and 11.25 (CO_2H, s, 1 H). After concentration, the crude keto acid was dissolved in 500 ml of absolute ethanol with 1 g of *p*-toluenesulfonic acid, and then refluxed for 24 hr. After removal of the excess ethanol, the oily residue was vacuum distilled, affording (92%) ethyl 5-keto-7-methyloctanoate: bp 93–97° (1.0–1.5 mm) [lit.[11] bp 120–122° (5 mm)]; nmr ($CDCl_3$) δ 0.90 (Me_2CH–, d, J = 7 Hz, 6 H), 1.21 (CH_3CH_2O–, t, J = 7 Hz, 3 H), and 4.15 (CH_3CH_2O, q, J = 7 Hz, 2 H).

E.—An ethereal solution of ethyl 5-keto-7-methyloctanoate (90 g, 0.5 mol) was added dropwise to a stirred suspension of 30 g (50% oil dispersion, 0.75 mol) of sodium hydride in anhydrous diethyl ether (400 ml). The stirred mixture was refluxed for 8 hr under nitrogen. The reaction mixture was cooled to 5° and acidified with dilute hydrochloric acid. The ethereal layer was washed with water, dried over anhydrous magnesium sulfate, and concentrated to give (80%) a white solid, which was recrystallized from benzene giving analytically pure 2-isopropyl-1,3-cyclohexanedione: mp 150–151° (lit.[11] mp 140–143°); nmr (D_2O) δ 0.75 and 1.1 (Me_2CH, d, J = 7 Hz, 6 H).

Anal. Calcd for $C_9H_{14}O_2$: C, 70.13; H, 9.09. Found: C, 70.19; H, 9.04.

1,6-Dioxo-8a-isopropyl-1,2,3,4,6,7,8,8a-octahydronaphthalene.—The procedure used for **1b** was followed giving (58%) the crude diketone, which was vacuum distilled affording a pale yellow oil, bp 140–150° (0.5 mm). Recrystallization from anhydrous diethyl ether gave analytically pure diketone: mp 64–65°; nmr ($CDCl_3$) δ 0.85 and 0.99 (Me_2CH, J = 7 Hz, d, 6 H), 5.97 (–CH=C<, s, 1 H), and 1.5–3.0 (m, 11 H); ir ($CHCl_3$) 1720, 1670, and 1620 cm^{-1}.

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.73; H, 8.76. Found: C, 75.53; H, 8.59.

(±)-5-Hydroxy-10-isopropyl-$\Delta^{1(9)}$-2-octalone was prepared (93%) in a manner similar to that for the reduction of **1b**: bp

162–166° (1.3 mm); mp 85–87° from ether–petroleum ether; nmr ($CDCl_3$) δ 0.85 and 1.22 (Me_2CH, d, J = 7 Hz, 6 H), 3.0 (–OH, s, 1 H), 3.82 (>CHOH, dd, J = 7.5 Hz, each, 1 H), and 5.91 (HC=C<, s, 1 H); ir (neat) 3500, 1665 cm^{-1}.

Anal. Calcd for $C_{13}H_{20}O_2$: C, 75.01; H, 9.68. Found: C, 75.01; H, 9.54.

(±)-5-Hydroxy-10-methyl-$\Delta^{1(9)}$-2-octalone Hydrogen Phthalate.—A solution of phthalic anhydride (68.8 g, 0.46 mol), (±)-5-hydroxy-10-methyl-$\Delta^{1(9)}$-2-octalone (80 g, 0.445 mol), and anhydrous pyridine (160 ml) was stirred under nitrogen at room temperature for 24 hr. The solution was poured onto ice and acidified with 6 *N* hydrochloric acid. The white precipitate was filtered, dried *in vacuo* overnight, and recrystallized from acetone, affording the crystalline hydrogen phthalate: 109.2 g; mp 205–206°; nmr ($CDCl_3$) δ 1.31 (CH_3–, s, 3 H), 4.9 (>CHO, dd, J = 6, 6 Hz, 1 H), 5.88 (HC=C<, s, 1 H), 7.5–8.0 ($C_{aromatic}$ H, m, 4 H), and 9.04 (–CO_2H, s, 1 H).

Concentration of the mother liquor gave an additional 7.9 g, mp 189–206°, of the half ester. The fractions were combined (82%) and used without further purification.

Anal. Calcd for $C_{19}H_{20}O_5$: C, 69.50; H, 6.15. Found: C, 69.84; H, 6.58.

(±)-5-Hydroxyl-10-ethyl-$\Delta^{1(9)}$-2-octalone hydrogen phthalate was prepared in a similar manner: mp[23] 196–206°; nmr ($CDCl_3$) δ 0.89 (CH_3CH_2–, t, J = 7 Hz, 3 H), 3.8 (CH_3CH_2–, m, 2 H), 5.13 (>CHO, dd, J = 7, 7 Hz, 1 H), 6.00 (HC=C<, s, 1 H), and 7.3–8.0 ($C_{aromatic}$ H, m, 4 H).

(±)-5-Hydroxy-10-isopropyl-$\Delta^{1(9)}$-2-octalone hydrogen phthalate was prepared in a similar manner: mp[23] 204–208°; nmr ($CDCl_3$) δ 0.85 and 1.08 (Me_2CH–, d, J = 7 Hz, 6 H), 5.29 (>CHO–, dd, J = 7, 7 Hz, 1 H), 6.00 (HC=C<, s, 1 H), and 7.5–8.0 ($C_{aromatic}$ H, m, 4 H).

Resolution of (±)-5-Hydroxy-10-methyl-$\Delta^{1(9)}$-2-octalone Hydrogen Phthalate with Brucine.—A solution of brucine (204 g) in 2 l. of hot acetone was added to a solution of (±)-methyl half ester [(±)-**3a**, 116 g] in hot acetone (1 l.). The solution was concentrated to 1 l. and allowed to slowly cool overnight to ambient temperature. The resultant white solid was filtered and dried *in vacuo*, giving (49%) the brucine salt of the (±)-methyl phthalate, mp 124–126° dec. Further recrystallization from benzene did not appreciably increase the melting point, but from acetone the melting point was increased, mp 146–148° dec.

The combined mother liquors from the recrystallization of the brucine salt of the (+)-methyl half ester were concentrated *in vacuo*, affording the crude brucine salt of the enantiomeric methyl half ester, as a semicrystalline solid. Further recrystallization was not attempted.

A. (+)-(5*S*,10*S*)-5β-Hydroxy-10β-methyl-$\Delta^{1(9)}$-2-octalone Hydrogen Phthalate [(+)-3a].—The brucine salt of the (+)-methyl hydrogen phthalate (135 g) dissolved in acetone (1.2 l.) at 20°. The acetone was removed *in vacuo*, affording an aqueous supension, which was filtered, washed with water, and dried. The crude solid was recrystallized from acetone to give (+)-5β-hydroxy-10β-methyl-$\Delta^{1(9)}$-2-octalone hydrogen phthalate, 92% recovery, mp 192–196°, $[\alpha]_{600}^{25}$ +17° (MeOH). Recrystallization from acetonitrile, instead of acetone, gave poor results.

(+)-(5*S*,10*S*)-5β-Hydroxy-10β-methyl-$\Delta^{1(9)}$-2-octalone [(+)-2a].—A mixture of 47 g (0.143 mol) of (+)-methyl hydrogen phthalate dissolved in 5 *N* sodium hydroxide and ether (25 ml) was rapidly agitated at 15–20°. After several minutes, the ether was removed and additional ether was added to the basic solution. The ethereal extracts were stirred over 0.1 *N* hydrochloric acid until extraction procedure was complete; this extraction was continued every 5 min for 1 hr. The combined extracts were washed with a dilute sodium bicarbonate solution, water, and a saturated salt solution and then dried over anhydrous magnesium sulfate. After concentration, the residual oil was vacuum distilled to give the (+)-methyl hydroxy ketone: yield 14.0 g (0.078 mol); bp 128–131° (0.04 mm); $[\alpha]_{600}^{25}$ +115° (MeOH); optical purity[24] 55%; ORD data, see Figure 1; CD data, see Figure 2.

B. (–)-(5*R*,10*R*)-5α-Hydroxy-10α-methyl-$\Delta^{1(9)}$-2-octalone hydrogen phthalate [(–)-3a] was recovered in an identical manner to the corresponding levorotary brucine salt: 83% recovery; mp 200–208° (acetone); $[\alpha]_{600}^{25}$ –105° (MeOH).

(–)-(5*R*,10*R*)-5α-Hydroxy-10α-methyl-$\Delta^{1(9)}$-2-octalone [(–)-2a] was recovered from the corresponding phthalate as outlined for the (+) isomer: yield 16 g; bp 120–130° (0.075 mm); $[\alpha]_{600}^{25}$ –84° (MeOH); optical purity[24] 41%; ORD data, see Figure 1; CD data, see Figure 2.

Resolution of (±)-5-Hydroxy-10-ethyl-$\Delta^{1(9)}$-2-octalone Hydrogen Phthalate with Brucine.—The general procedure used for the resolution of **3a** was followed using acetone solvent. No resolution could be effected if benzene was used as solvent.

(+)-(5*S*,10*S*)-5β-Hydroxy-10β-ethyl-$\Delta^{1(9)}$-2-octalone hydrogen phthalate was isolated as previously described, mp 196–206° (acetone), $[\alpha]_{600}^{25}$ +27.2° (MeOH).

(+)-(5*S*,10*S*)-5β-Hydroxy-10β-ethyl-$\Delta^{1(9)}$-2-octalone [(+)-2b] was obtained by careful saponification of the phthalate: bp 140–147° (0.06 mm); mp 74–78° (ether–petroleum ether); $[\alpha]_{600}^{25}$ +8.6° (MeOH); ORD data, see Figure 1; CD data, see Figure 2.

Resolution of (±)-5-Hydroxyl-10-isopropyl-$\Delta^{1(9)}$-2-octalone Hydrogen Phthalate with Brucine.—The general procedure outlined above was followed using acetone. The brucine salt of **3c** crystallized, mp 145–155° dec (acetone).

A. (–)-(5*S*,10*R*)-5β-Hydroxy-10β-isopropyl-$\Delta^{1(9)}$-2-octalone hydrogen phthalate was isolated from the brucine salt of **3c** as above described, mp 200–210° (acetone), $[\alpha]_{600}^{25}$ –55.3° (MeOH).

(+)-(5*S*,10*R*)-5β-Hydroxy-10β-isopropyl-$\Delta^{1(9)}$-2-octalone [(+)-2c] was isolated from (–)-**3c**: bp 60–61° (ether); $[\alpha]_{600}^{25}$ +73° (MeOH); ORD data, see Figure 1; CD data, see Figure 2.

B. (+)-(5*R*,10*S*)-5α-Hydroxy-10α-isopropyl-$\Delta^{1(9)}$-2-octalone hydrogen phthalate was obtained by saponification of the brucine salt of **3c** as previously described, mp 188–198°, $[\alpha]_{600}^{25}$ +45° (MeOH).

(–)-(5*R*,10*S*)-5α-Hydroxy-10α-isopropyl-$\Delta^{1(9)}$-2-octalone [(–)-2c] was isolated from (+)-**3c**: mp 60–62° (MeOH); $[\alpha]_{600}^{25}$ –53° (MeOH); ORD data, see Figure 1; CD data, see Figure 2.

Registry No.—**1c**, 34996-04-8; (+)-**2a**, 34996-05-9; (–)-**2a**, 34996-06-0; (±)-**2b**, 17506-54-6; (+)-**2b**, 34996-08-2; (±)-**2c**, 34996-09-3; (+)-**2c**, 34996-10-6; (–)-**2c**, 34996-11-7; (±)-**3a**, 34996-12-8; (±)-**3a** brucine salt, 34969-17-0; (+)-**3a**, 34996-13-9; (–)-**3a**, 34996-14-0; (±)-**3b**, 34996-15-1; (+)-**3b**, 34996-16-2; (±)-**3c**, 34996-17-3; (±)-**3c** brucine salt, 34996-18-4; (+)-**3c**, 34996-19-5; (–)-**3c**, 34996-20-8; 2-isopropyl-1,3-cyclohexanedione, 3401-01-2; keto diester of bp 143–152°, 3400-99-5; ethyl 5-keto-7-methyloctanoate, 3401-00-1.

Acknowledgments.—Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Research Corporation for partial support of this research. The authors are indebted to Dr. W. L. Mattice for his helpful discussions.

(23) No attempt was made to purify this sample or to obtain the analytical datum at this intermediary stage.

(24) The optical purity can be easily calculated, since Prelog and Acklin[7a] determined the absolute rotation of (+)-5β-hydroxy-10β-methyl-$\Delta^{1(9)}$-2-octalone to be +203° by enzymatic reduction of (±)-1,6-dioxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene with *Curvalaria falcata*.