ORGANIC AND BIOLOGICAL CHEMISTRY

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY]

Optical Rotatory Dispersion Studies. XIX.[1] 8-Methylhydrindanones[2]

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The synthesis of (−)-*trans*-8-methylhydrindan-5-one (X) and of (+)-*trans*-8-methylhydrindane-2,5-dione (VIII) from an intermediate (I) of known absolute configuration is described. Rotatory dispersion measurements indicate that no major conformational distortion is produced in the cyclohexanone ring by the *trans* fusion with a cyclopentane ring. The bearing of this observation on the stereochemistry of B-norcholestanone (XIII) is discussed and the rotatory dispersion curves of a pair of *cis*- and *trans*-4-keto-hydrindanes is also reproduced. The rotatory dispersion curve of (+)-*trans*-8-methylhydrindane-2,5-dione (VIII) represents the summation of the two individual chromophores acting independently without vicinal interaction.

The most important reason for the rapid extension of the rotatory dispersion technique[4] to a variety of organic molecules has been the conclusion that the majority of the results derived from a study of steroidal and other polycyclic ketones[5]—of known stereochemistry and rigid conformation—could in fact be ascribed largely to the immediate bicyclic environment around the carbonyl chromophore. This postulate was established by synthesizing[6,7] a number of optically active decalones, octalones and hydrindanones of known absolute configuration and comparing the shape[8] of their rotatory dispersion curves with that of steroid standards. The sensitivity of the rotatory dispersion curve of a given cyclic ketone to stereochemical alterations was first established in the steroid series[9] and the characteristic shape ascribed to 5α-(A/B *trans*) and 5β-(A/B *cis*) 3-ketosteroids was also found[7] in the *trans*- and *cis*-decalone series. It was of considerable interest, therefore, to determine whether this observation would also hold true when the size of the adjacent ring is altered and, for reasons outlined below under "Rotatory Dispersion Results," the key substance required for this study was the previously unknown, optically-active *trans*-8-methyl-5-hydrindanone (X).

Synthetic Studies.—Since it was indispensable that the absolute configuration of our final product be known, it was decided to start with (+)-*trans*-2-keto-10-methyl-$\Delta^{3,6}$-hexahydronaphthalene (I)[10] whose absolute configuration[11] was established because of the transformation[12] of its (−)-antipode[13] into a natural steroid. Reduction of I with lithium in liquid ammonia[14] provided (+)-*trans*-Δ^6-10-methyl-2-octalone (II) accompanied by some of the alcohol IIIa and a small amount of a high melting dimer, which on the basis of its spectral and optical rotatory dispersion properties is assigned tentatively structure IV. Further reduction of the octalone II with lithium aluminum hydride furnished *trans*-Δ^6-10-methyl-2-octalol (IIIa), which also could be obtained in one step by sodium–ethanol treatment of the parent ketone I. The alcohol IIIa represented the key intermediate for the subsequent transformations since the isolated double bond offered a point of attack for ring opening and contraction.

Initial experiments were conducted with the acetate IIIb which was subjected to ozonolysis[15] followed by treatment with hydrogen peroxide in acetic acid. The resulting crystalline hydroxy dibasic acid VIa was pyrolyzed with barium hydroxide, since this method of ring closure worked[6] satisfactorily with the corresponding dibasic acid lacking the hydroxyl function. However, none of the desired *trans*-5-hydroxy-8-methylhydrindanone (VII) could be isolated, apparently due to either lactonization or dehydration. Consequently, the acid VIa was transformed to the hydroxy dimethyl ester VIb in the hope that Dieckmann condensation would yield the hydroxy ketone VII. The only recognizable product proved to be the lactonic methyl ester V, whose structure was proved by elementary analysis, infrared examination and the fact that it exhibited only a plain[16] positive dispersion curve. As demonstrated below, the *trans*-8-methyl-hydrindan-2-one derivative VII possesses a powerful, single positive Cotton effect[16] curve and even traces of the cyclization product could, therefore, be detected by examination of the rotatory dispersion curve.

These abortive experiments showed that the

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[1] Paper XVIII, C. Djerassi and L. E. Geller, *Tetrahedron*, in press (1958).

[2] Supported by grant No. CY-2919 of the National Cancer Institute, National Institutes of Health, U. S. Public Health Service.

[3] Recipient of a Fulbright travel grant, on leave from the University of Kyoto, Japan.

[4] For leading references see C. Djerassi, *Bull. soc. chim. France*, 741 (1957).

[5] For most recent work and references to earlier studies from this laboratory, see: (a) C. Djerassi, O. Halpern, V. Halpern, O. Schindler and C. Tamm, *Helv. Chim. Acta*, **41**, 250 (1958); (b) C. Djerassi, O. Halpern, V. Halpern and B. Riniker, THIS JOURNAL, **80**, 4001 (1958).

[6] C. Djerassi, R. Riniker and B. Riniker, *ibid.*, **78**, 6362 (1956).

[7] C. Djerassi and D. Marshall, *ibid.*, **80**, 3986 (1958).

[8] This gross comparison can be refined considerably by comparing molecular rotatory dispersion curves (see W. Klyne and C. Djerassi, *Angew. Chem.*, **69**, 683 (1957)) and this will be discussed in detail in a future paper with Dr. W. Klyne (Postgraduate Medical School, London).

[9] C. Djerassi and W. Closson, THIS JOURNAL, **78**, 3761 (1956).

[10] We are greatly indebted to Dr. W. S. Knowles (Monsanto Chemical Co., St. Louis, Mo.) for a generous gift of a precursor of I.

[11] Throughout the present paper all structural formulas are intended to depict absolute configurations using the standard steroid notation.

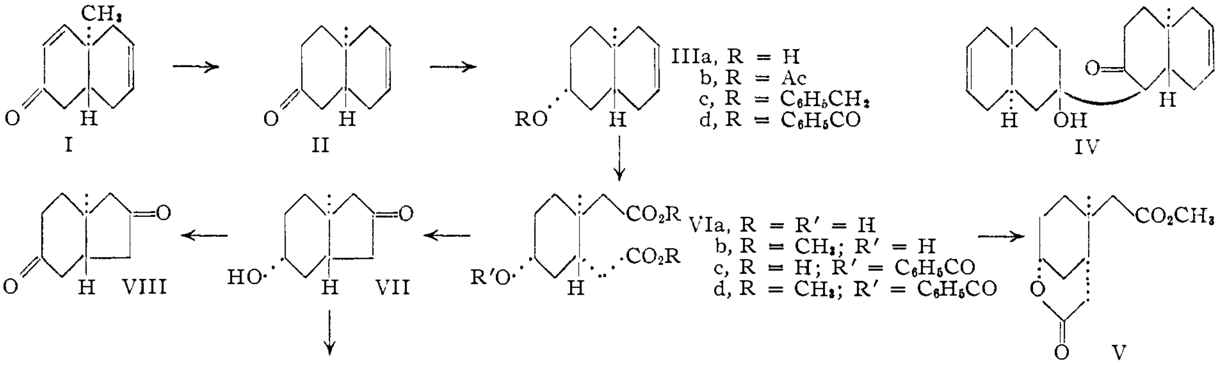
[12] L. B. Barkley, M. W. Farrar, W. S. Knowles, H. Raffelson and Q. E. Thompson, THIS JOURNAL, **76**, 5014 (1954).

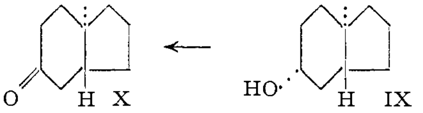
[13] A. J. Speziale, J. A. Stephens and Q. E. Thompson, *ibid.*, **76**, 5011 (1954).

[14] *Cf.* F. Sondheimer, O. Mancera, G. Rosenkranz and C. Djerassi, *ibid.*, **75**, 1282 (1953).

[15] The ozonolysis was not performed on the alcohol itself since it probably would have been oxidized to the corresponding ketone (see C. Djerassi, E. Farkas, L. H. Liu and G. H. Thomas, *ibid.*, **77**, 5330 (1955), footnote 11).

[16] For nomenclature see C. Djerassi and W. Klyne, *Proc. Chem. Soc.*, 55 (1957).





hydroxyl function had to be protected by a grouping which would be resistant to the alkaline conditions prevailing in the Dieckmann condensation. One candidate would have been the benzyl ether IIIc, which was actually prepared, but since Woodward, Barton and collaborators[17] had observed that a benzoate is not affected by vigorous treatment with potassium *t*-butoxide, the benzoate IIId was selected as the preferred intermediate for the subsequent synthetic steps. Ozonolysis and careful decomposition of the ozonide provided the crystalline benzoyloxy dibasic acid VIc which was converted to the dimethyl ester VId and then subjected to Dieckmann condensation with potassium *t*-butoxide in benzene solution. The intermediate β-keto ester was not isolated and the total product was subjected to acidic cleavage conditions whereupon the hydroxy ketone VII was secured as a crystalline solid. Oxidation with chromium trioxide led to (+)-*trans*-8-methylhydrindane-2,5-dione (VIII), while Wolff–Kishner reduction of VII followed by oxidation of the resulting *trans*-8-methylhydrindan-5-ol (IX) gave the desired (−)-*trans*-8-methylhydrindan-5-one (X), characterized as the crystalline 2,4-dinitrophenylhydrazone.

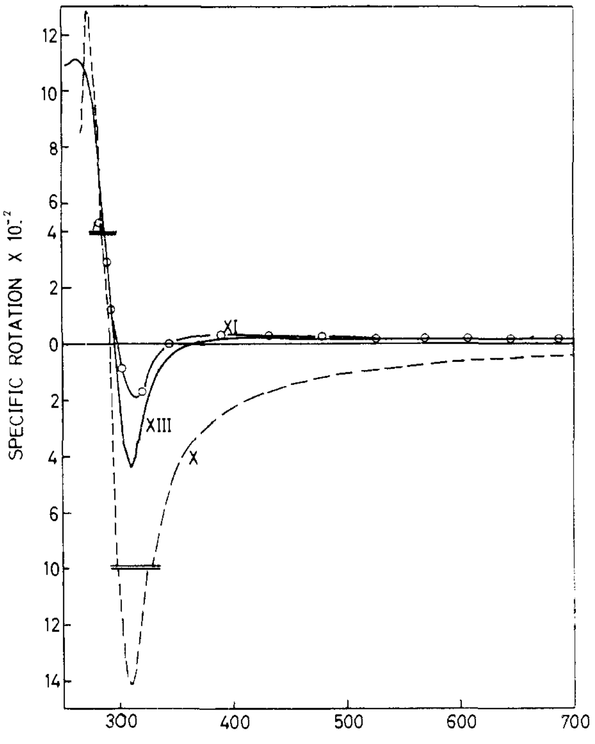


Fig. 1.—Optical rotatory dispersion curves of (−)-*trans*-8-methylhydrindan-5-one (X) (methanol), (+)-*cis*-8-methylhydrindan-5-one (XI) (dioxane) and B-norcholestan-3-one (XIII) (methanol).

Optical Rotatory Dispersion Results.—Racemic *cis*-8-methylhydrindan-5-one (XI) has been synthesized by Conroy[18] starting with *cis*-2-methyl-2-carboxycyclopentane-1-acetic acid.[19] By resolving the latter with brucine and carrying the (+)-antipode of the dibasic acid through the same synthetic scheme,[18] Conroy and Cohen[20] prepared (+)-*cis*-8-methylhydrindan-5-one (XI) and its rotatory dispersion curve[6] is reproduced in Fig. 1. Its shape[21] is typical of 5β-3-ketosteroids[9] or *cis*-9-methyl-3-decalone[7] and consequently the (+)-antipode was assigned[6] the absolute configuration implied[11] in formula XI. This in turn meant that contraction of the non-oxygenated ring in *cis*-9-methyl-3-decalone to a five-membered ring does not affect the characteristic shape of the "coprostanone" curve. Since a *trans* fused hydrindane system is probably somewhat strained, it was not certain *a priori* whether this conclusion would also apply to the *trans* series, but an inspection of Fig. 1 shows that this is clearly the case. The rotatory dispersion curve of (−)-*trans*-8-methylhydrindan-5-one (X) closely resembles—both in shape and amplitude—that[6] of the six-membered homolog (−)-*trans*-9-methyl-3-decalone (XII) and it is evident, therefore, that no major conformational distortion is produced by the *trans* fusion.

In the light of these observations, it is noteworthy that the rotatory dispersion curve (Fig. 1) of B-norcholestan-3-one (XIII)[22] is clearly of the 5β-type and consequently in disagreement with the assigned[22] 5α-stereochemistry. The evidence presented by Dauben and Fonken[22] is very suggestive of a 5α-orientation but it is not rigorous since it is

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(17) R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. J. Ives and R. B. Kelly, *J. Chem. Soc.*, 1131 (1957).

(18) H. Conroy, THIS JOURNAL, **74**, 3046 (1952).

(19) K. D. Errington and R. P. Linstead, *J. Chem. Soc.*, 666 (1938).

(20) H. Conroy and E. Cohen, *J. Org. Chem.*, **23**, 616 (1958).

(21) The amplitude in this case is not very significant since it is not certain whether the substance was completely resolved.

(22) W. G. Dauben and G. J. Fonken, THIS JOURNAL, **78**, 4736 (1956).

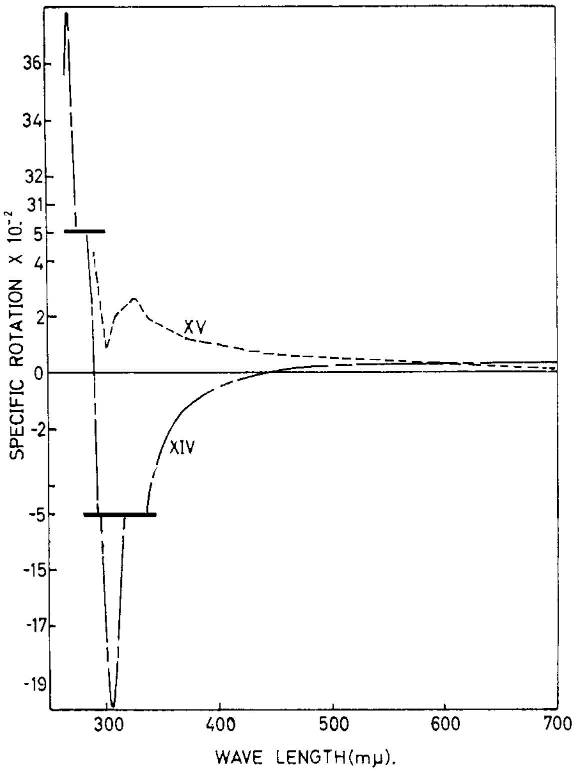

Fig. 2.—Optical rotatory dispersion curves (methanol solution) of *trans*-1-(2-iso-octyl)-8-methylhydrindan-4-one (XIV) and *cis*-1-(2-iso-octyl)-8-methylhydrindan-4-one (XV).

based on chemical and infrared spectral analogy to steroids with a six-membered B ring. It is conceivable that the additional B/C *trans* juncture in XIII precludes direct comparisons with steroids but it must be emphasized that the same argument also can be applied to the interpretation of the rotatory dispersion curve of XIII, namely, that this additional ring fusion produces a conformational distortion which does not permit direct comparison of its rotatory dispersion curve with that of the bicyclic analog X.[23] To the extent that the conformational distortion argument is valid in prohibiting rotatory dispersion comparisons, this also weakens the earlier stereochemical assignment[22] which involves the tacit assumption that the conformations of the B-norcholestane[24] and cholestane series are substantially identical. This may still be true since the rotatory dispersion is probably much more sensitive to relatively minor conformational alterations,[5b] but further chemical work on the stereochemistry (at C-5) of B-norcholestan-3-one (XIII) seems indicated.

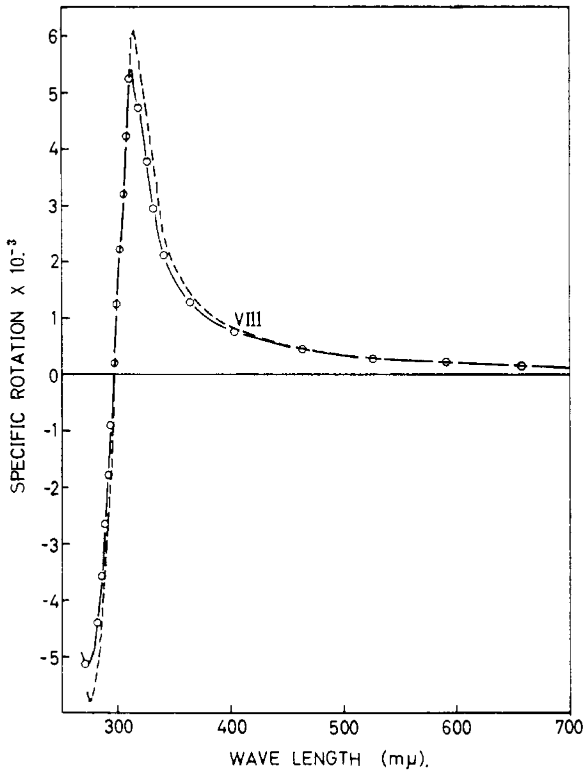

Fig. 3.—Optical rotatory dispersion (methanol) of (+)-*trans*-8-methylhydrindane-2,5-dione (VIII): solid line, observed curve; dotted line, calculated curve.

In Fig. 2 are reproduced the rotatory dispersion curves of a pair of *trans*- and *cis*-8-methylhydrindan-4-ones (XIV, XV) derived[25] from vitamin D_3. If the fact that a bulky (isoöctyl) substituent is present at C-1 can be ignored,[26] then these two curves can serve as rotatory dispersion standards for *trans*- and *cis*-8-methylhydrindan-4-ones. It should be noted that the dispersion curves of XIV and XV suggest that the kinetics of the alkaline isomerization of the *trans* (XIV) to the *cis* (XV) isomer probably can be measured very conveniently by observing the change in rotation near 305 mμ, where the specific rotations of the two isomers differ by over 2000°.

Our synthetic studies also included the preparation of (+)-*trans*-8-methylhydrindane-2,5-dione (VIII), since it was felt that its rotatory dispersion curve (Fig. 3) would offer a good example of the extent of interaction of two optically active chromophores (each possessing Cotton effects of opposite sign) situated in close proximity. In order to place this on a quantitative basis a theoretical curve is also reproduced in Fig. 3 which is constructed from the sum of the rotations of (−)-*trans*-8-methylhydrindan-5-one (X) and (−)-*trans*-8-methylhydrindan-2-one (XVI).[6,27] A comparison of the calculated and observed curves shows that they are virtually superimposable and that, therefore, there seems to be practically no interaction between the two carbonyl functions in spite of their close proximity.

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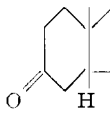
(23) It should be noted that for comparison purposes one of the curves should be inverted since X and XIII belong to enantiomeric series.

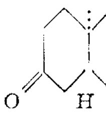
(24) It is pertinent to recall that L. F. Fieser (THIS JOURNAL, **75**, 4386 (1953)) favored a 5β-stereochemistry for certain B-norcholestane derivatives.

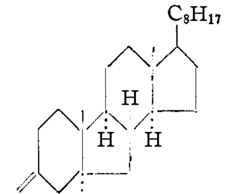
(25) See H. H. Inhoffen, G. Quinkert, S. Schütz, D. Kampe and G. F. Domagk, *Ber.*, **90**, 664 (1957).

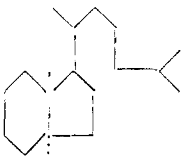
(26) This is most likely the case because even in the 15-keto steroid and 15-keto sapogenin series, where the relative stabilities of the C/D *cis* and *trans* isomers are reversed (see D. H. R. Barton and G. F. Laws, *J. Chem. Soc.*, **52** (1954), and C. Djerassi, T. T. Grossnickle and L. B. High, THIS JOURNAL, **78**, 3166 (1956)) valid rotatory dispersion comparisons (see ref. 6) can still be made.

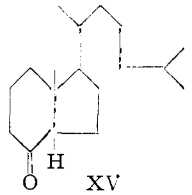
(27) In this case, the *sign* of all rotation values was, of course, inverted since XVI belongs to the antipodal series.

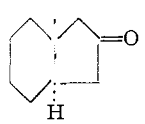

XI


XII


XIII


XIV


XV


XVI

Experimental[28]

(+)-*trans*-Δ^6-10-Methyl-2-octalone (II).[29]—Lithium (2 g.) was dissolved in 200 cc. of liquid ammonia using a Dry Ice condenser to contain the ammonia but without cooling around the flask. A solution of 4.0 g. of the unsaturated ketone I[10,13] in 100 cc. of dry ether was added dropwise over a period of 25 min. and stirring was continued for an additional 1.25 hr. The blue color of the solution was discharged by the addition of 12.0 g. of ammonium chloride, a further quantity (100 cc.) of ether was added, the condenser was removed and the bulk of the ammonia was allowed to evaporate. Finally water was added, the ether layer was separated and the aqueous solution was extracted three times with ether. The combined extracts were washed with dilute hydrochloric acid and water, dried, evaporated and the oily residue was chromatographed on 150 g. of Merck acid-washed alumina. Elution with hexane–benzene (1:1) yielded 2.9 g. of the desired ketone II, which crystallized as colorless plates (2.0 g., m.p. 32–35°) from petroleum ether at −70°. Further low temperature crystallization from pentane followed by sublimation at 0.1 mm. into a tube cooled with Dry Ice provided the pure ketone, m.p. 35–36°, $\lambda_{\max}^{\text{capill}}$ 5.80 μ; R.D. in methanol (*c* 0.095): $[\alpha]_{700}$ +25°, $[\alpha]_{589}$ +45°, $[\alpha]_{400}$ +84°, $[\alpha]_{305}$ −666°, $[\alpha]_{270}$ +1910°.

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.68; O, 9.74. Found: C, 80.54; H, 9.87; O, 9.63.

The 2,4-dinitrophenylhydrazone formed pale orange cubes, m.p. 160–164°, after crystallization from chloroform–methanol.

Anal. Calcd. for $C_{17}H_{20}N_4O_4$: C, 59.29; H, 5.85; N, 16.24; O, 18.59. Found: C, 58.99; H, 5.90; N, 16.10; O, 18.78.

Further development of the column with benzene–ether (9:1) gave 0.7 g. of the alcohol IIIa, while elution with ether–methanol (7:3) yielded 0.4 g. of a solid, which after crystallization from ethyl acetate and sublimation at 190° and 0.1 mm. exhibited m.p. 192–194°, $\lambda_{\max}^{\text{EtOH}}$ 288 mμ (log ε 1.80); $\lambda_{\max}^{\text{CHCl}_3}$ 2.80, 2.93 and 5.92 μ; R.D. in dioxane solution (*c* 0.125): $[\alpha]_{700}$ +35°, $[\alpha]_{589}$ +56°, $[\alpha]_{317.5}$ +1710°, $[\alpha]_{285}$ −1900°. These data are compatible with structure IV, but it should be noted that the Cotton effect curve is positive in contrast to the negative one of II. It is possible that a very bulky substituent at C-4 (analogous to the "4,4-dimethyl" effect (ref. 5b)) inverts the curve and this is why the linkage between the two fragments was placed from C-3 to C-4 (steroid numbering).

Anal. Calcd. for $C_{22}H_{32}O_2$: C, 80.44; H, 9.83; O, 9.74; mol. wt., 328. Found: C, 80.60; H, 9.15; O, 10.16; Rast mol. wt., 317.

***trans*-Δ^6-10-Methyl-2-octalol (IIIa).**—The above ketone II (1.48 g.) was dissolved in 50 cc. of dry ether and heated overnight under reflux with 1 g. of lithium aluminum hydride dissolved in 100 cc. of ether. The excess reagent was decomposed with ethyl acetate, a saturated aqueous solution of sodium sulfate was added followed by anhydrous magnesium sulfate and filtration. The solid was washed with ether and the filtrate and washings were combined and evaporated leaving 1.47 g. of an oil. Distillation of this oil at 3.5 mm. and a bath temperature of 120–130° provided the analytical sample of the alcohol IIIa, $\lambda_{\max}^{\text{capill}}$ 3.04 μ.

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.91; O, 9.62. Found: C, 79.09; H, 10.71; O, 10.28.

The identical alcohol (10.6 g.) was obtained[30] when 13.6 g. of the ketone I was reduced in 800 cc. of boiling ethanol with 84 g. of sodium (added over a period of 15 hr.).

The acetate IIIb was obtained in nearly quantitative yield with acetic anhydride–pyridine at room temperature and distilled as a colorless liquid at 0.2 mm. and a bath temperature of 70–75°.

Anal. Calcd. for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.62; H, 9.42.

The benzyl ether IIIc was prepared in the following fashion. The alcohol IIIa (500 mg.) was heated under reflux in an atmosphere of nitrogen for 7 hr. with 35 cc. of toluene and 70 mg. of sodium. After cooling slightly, 380 mg. of benzyl chloride was added and heating was continued for an additional 4 hr. The mixture was stirred at room temperature for 8 hr. before adding water, the organic layer was separated and distilled carefully through a small column in order to avoid losses due to co-distillation with the solvent. The fraction boiling at 125–135° and 0.05 mm. weighed 420 mg. and proved to be the desired benzyl ether IIIc, $\lambda_{\max}^{\text{capill}}$ 6.0 and 6.65 μ, $[\alpha]_D$ +57° (*c* 0.98 in $CHCl_3$).

Anal. Calcd. for $C_{18}H_{24}O$: C, 84.32; H, 9.44; O, 6.24. Found: C, 83.96; H, 9.56; O, 6.99.

The benzoate IIId was synthesized in the customary fashion with benzoyl chloride in pyridine solution and was purified by chromatography on Merck acid-washed alumina. The colorless oil eluted with hexane and hexane-benzene (7:1) was distilled at a bath temperature of 120–130° and 0.005 mm.

Anal. Calcd. for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20; O, 11.83. Found: C, 79.75; H, 7.91; O, 11.67.

***trans*-1-Methyl-4-hydroxycyclohexane-1,2-diacetic Acid (VIa).**—A 1.0-g. sample of the acetate IIIb in 30 cc. of ethyl acetate was ozonized at −70° until the solution turned blue (45 min.). A solution of 2 cc. of 30% hydrogen peroxide in 4 cc. of glacial acetic acid was added, the solvent warmed to 50°, the bulk of the ethyl acetate was removed *in vacuo* and the residue was kept overnight at 50° with a further quantity of hydrogen peroxide in acetic acid. After heating under reflux for one hour, the acetic acid was removed under reduced pressure and the viscous residue was heated under reflux for 1.25 hr. with 30 cc. of a 10% methanolic potassium hydroxide solution. The crude acid, obtained by continuous ether extraction of the acidified aqueous solution was crystallized from chloroform–acetone to yield 0.47 g. of colorless needles of the acid VIa with m.p. 148–154° (partially melting at 85–90° and then resolidifying). The analytical sample was recrystallized from the same solvent pair and exhibited m.p. 154–156°.

Anal. Calcd. for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88; O, 34.74. Found: C, 57.48; H, 8.03; O, 34.14.

Various pyrolysis experiments with barium hydroxide led to inconclusive results or recovered starting material. In one case, a small amount (*ca.* 10%) of oil was isolated which exhibited an infrared carbonyl band at 5.72 μ, consistent with a cyclopentanone, but did not show any hydroxyl absorption. A band at 6.05 μ suggested that dehydration had occurred.

The hydroxy acid was treated with ethereal diazomethane and the dimethyl ester VIb was subjected directly to Dieckmann cyclization without preparing an analytical sample. No pure product could be isolated with sodium methoxide in benzene solution, but when 300 mg. each of the dimethyl ester VIb and of sodium hydride was heated under reflux with 25 cc. of benzene and one drop of ethanol for 3 hr., there was isolated (after acidification with acetic acid) 225 mg. of neutral oil (negative ferric chloride reaction), which crystallized as colorless needles (100 mg.),

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[28] All melting points were determined on the Kofler block. We are indebted to Mrs. T. Nakano for the rotatory dispersion measurements, to Mr. K. Hutchinson for the ultraviolet absorption spectra and to Dr. H. Kovacs for the infrared spectra. The microanalyses were performed by Dr. A. Bernhardt, Mülheim (Ruhr), Germany.

[29] The racemate already has been obtained as a by-product by R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler and W. M. McLamore, THIS JOURNAL, **74**, 4223 (1952).

[30] This reduction was carried out by Dr. B. Riniker.

m.p. 78–79°, and proved to be the **lactonic ester V**. It exhibited only a plain positive dispersion curve in dioxane solution (*c* 0.125), $[\alpha]_{589}$ +8° rising to +175° at 275 mμ, and its infrared spectrum (Nujol mull) showed no hydroxyl absorption but two carbonyl bands at 5.73 μ (lactone) and 5.80 μ (ester).

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02; O, 28.29; methoxyl, 13.70; mol. wt., 226. Found: C, 64.03; H, 7.75; O, 28.54; methoxyl, 13.35; Rast mol. wt., 207.

(−)-*trans*-1-Methyl-4-benzoyloxycyclohexane-1,2-diacetic Acid (VIc).—The ozonolysis of 2.63 g. of the benzoate IIId in 80 cc. of ethyl acetate was carried out at −70° as described above for the acetate except that ozone was passed through the solution for 2 hr. The decomposition of the ozonide was performed exactly as described above except that the final alkaline saponification was omitted. The crude acid fraction was crystallized from hexane–ethyl acetate to yield 2.84 g. of the required acid VIc, m.p. 149–152°. The analytical sample was recrystallized from the same solvent pair and dried for 20 hr. at 80° and 0.3 mm. over phosphorus pentoxide; m.p. 153–155°, $[\alpha]_D$ −30° (*c* 0.47 in methanol), $\lambda_{\max}^{CHCl_3}$ 5.78 μ.

Anal. Calcd. for $C_{18}H_{22}O_6 \cdot {}^1/_3H_2O$: C, 63.51; H, 6.71; O, 29.77. Found: C, 63.79, 63.63; H, 6.46, 6.58; O, 29.48, 29.65.

The dimethyl ester VId was obtained in over 90% yield upon methylating the dibasic acid VIc in ether containing a small amount of methanol. Crystallization from hexane–ether afforded colorless crystals, m.p. 79–80°, $[\alpha]_D$ −41° (*c* 0.61 in methanol), $\lambda_{\max}^{CHCl_3}$ 5.75 μ.

Anal. Calcd. for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23; O, 26.49; methoxyl, 17.12. Found: C, 66.05; H, 7.31; O, 26.18; methoxyl, 16.83.

(+)-*trans*-5-Hydroxy-8-methylhydrindan-2-one (VII).—A mixture of dry potassium *t*-butoxide (prepared from 0.69 g. of potassium and 50 cc. of freshly distilled *t*-butyl alcohol followed by repeated co-distillation with benzene), 0.75 g. of dimethyl ester VId and 50 cc. of dry benzene was heated under reflux with stirring for 4 hr. in an atmosphere of nitrogen. The solution was cooled, acidified with dilute sulfuric acid, extracted with benzene, washed with sodium carbonate solution,[31] water, dried and evaporated. The resulting oil (0.276 g., blue color with alcoholic ferric chloride solution) was dissolved in a mixture of 10 cc. of acetic acid, 5 cc. of concd. hydrochloric acid and 1 cc. of water and the solution was heated under reflux in a current of nitrogen. After 1.5 hr., the solvent was removed at 40° and reduced pressure, 30 cc. of 5% methanolic sodium hydroxide was added and the solution was heated under reflux for an additional 60 min. Concentration to a small volume, dilution with water and ether extraction gave, after washing and drying, 0.14 g. of a residue which crystallized spontaneously, m.p. 89–90°. Recrystallization from ether–hexane furnished colorless crystals, m.p. 92–93°, $\lambda_{\max}^{CHCl_3}$ 2.83, 2.89 and 5.70 μ; R.D. in methanol solution (*c* 0.10 to 300 mμ, 0.02 between 300 and 282.5 mμ): $[\alpha]_{700}$ +160°, $[\alpha]_{589}$ +250°, $[\alpha]_{312.5}$ +6733°, $[\alpha]_{282.5}$ −5525°.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.58; O, 19.02. Found: C, 71.13; H, 9.42; O, 19.01.

(+)-*trans*-8-Methylhydrindane-2,5-dione (VIII).—The hydroxy ketone VII (160 mg.) was dissolved in 5 cc. of acetone, cooled in ice and an 8 *N* chromium trioxide–sulfuric acid solution[32] was added dropwise with swirling until the supernatant liquid was orange. The reaction mixture was diluted with water, extracted with ether, washed well with water, dried and evaporated. Crystallization from ether–hexane gave 100 mg. of colorless crystals, m.p. 55–57°, $\lambda_{\max}^{CHCl_3}$ 5.69 and 5.83 μ; R.D. (Fig. 3) in methanol solution (*c* 0.119 to 320 mμ, 0.023 from 320 to 267.5 mμ): $[\alpha]_{700}$ +137°, $[\alpha]_{589}$ +212°, $[\alpha]_{312.5}$ +5434°, $[\alpha]_{272.5}$ −5182°, $[\alpha]_{267.5}$ −4930°.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.96; H, 8.49; O, 19.25. Found: C, 72.20; H, 8.36; O, 18.94.

***trans*-8-Methylhydrindan-5-ol (IX).**—The hydroxy ketone VII (0.636 g.) was heated for 2 hr. with occasional shaking at 110° with 10 cc. of diethylene glycol, 0.6 g. of potassium hydroxide and 1.2 g. of 85% hydrazine hydrate. The condenser was replaced by a take-off adapter and the solution was heated for 6.5 hr. at 200°. The distillate and the reaction mixture were combined, diluted with hydrochloric acid and extracted with ether. After washing with water, drying and evaporating there remained a yellowish oil which was distilled at a bath temperature of 160–170° and 20 mm. to afford 0.57 g. of the alcohol IX as a colorless oil which showed no more carbonyl absorption in the infrared.

Anal. Calcd. for $C_{10}H_{18}O$: C, 77.86; H, 11.76; O, 10.37. Found: C, 77.53; H, 11.42; O, 10.11.

(−)-*trans*-8-Methylhydrindan-5-one (X).—The oxidation of the alcohol IX (0.796 g.) was carried out in acetone solution exactly as described above in the preparation of the diketone VIII and yielded 0.712 g. of colorless oil. This was purified by chromatography on alumina, elution with hexane–benzene (1:1) and distillation at 26 mm. and a bath temperature of 175–185°, $\lambda_{\max}^{CHCl_3}$ 5.82 μ; R.D. (Fig. 1) in methanol solution (*c* 0.15 to 300 mμ, 0.03 from 300 to 267.5 mμ): $[\alpha]_{700}$ −42°, $[\alpha]_{589}$ −64°, $[\alpha]_{310}$ −1413°, $[\alpha]_{272.5}$ +1286°, $[\alpha]_{267.5}$ +846°.

Anal. Calcd. for $C_{10}H_{16}O$: C, 78.89; H, 10.59; O, 10.51. Found: C, 78.76; H, 10.83; O, 10.50.

The yellowish-orange colored 2,4-dinitrophenylhydrazone was recrystallized from methanol–chloroform, whereupon it exhibited m.p. 135–137°, $\lambda_{\max}^{CHCl_3}$ 362 mμ, log ϵ 4.38.

Anal. Calcd. for $C_{16}H_{20}N_4O_4$: C, 57.82; H, 6.07; N, 16.86; O, 19.26. Found: C, 57.58; H, 6.07; N, 17.00; O, 19.13.

B-Norcholestan-3-one (XIII) (W. G. Dauben), R.D. (Fig. 1) in methanol solution (*c* 0.109): $[\alpha]_{700}$ +23°, $[\alpha]_{589}$ +21°, $[\alpha]_{310}$ −438°, $[\alpha]_{265}$ +1030°, $[\alpha]_{255}$ +1002°.

***trans*-1-(2-Isoöctyl)-8-methylhydrindan-4-one (XIV)** (*trans*-"**C_{18}-Ketone**") (H. H. Inhoffen), R.D. (Fig. 2) in methanol solution (*c* 0.065 to 300 mμ, 0.013 from 300–267.5 mμ): $[\alpha]_{700}$ +35°, $[\alpha]_{589}$ +23°, $[\alpha]_{305}$ −2087°, $[\alpha]_{270}$ +3792°, $[\alpha]_{267.5}$ +3561°.

***cis*-1-(2-Isoöctyl)-8-methylhydrindan-4-one (XV)** (*cis*-"**C_{18}-Ketone**") (H. H. Inhoffen), R.D. (Fig. 2) in methanol solution (*c* 0.085 to 320 mμ, 0.017 from 320–292.5 mμ): $[\alpha]_{700}$ +21°, $[\alpha]_{589}$ +42°, $[\alpha]_{325-330}$ +270°, $[\alpha]_{302.5}$ +94°, $[\alpha]_{292.5}$ +435°.

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[31] Acidification of the carbonate washes and ether extraction furnished 0.36 g. of benzoic acid.

[32] See K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946), and later papers by E. R. H. Jones and collaborators.