maintain the mixture at reflux. The solution was then heated under reflux for 1 hr. and distilled to give 30 g. (58%) of dimethyl 2-[(dimethylamino)(ethoxy)methylene]-3-methylenesuccinate, b.p. 121–124° (0.5 mm.), n^{20}_D 1.5270.

Anal. Calcd. for $C_{12}H_{19}NO_5$: C, 56.0; H, 7.5; N, 5.5. Found: C, 56.1; H, 7.5; N, 5.5.

1,1-Dipiperidinoethylene with Dimethyl Acetylenedicarboxylate.—Dimethyl acetylenedicarboxylate (7.8 g., 0.055 mole) was added in portions to 1,1-dipiperidinoethylene (10.6 g., 0.055 mole) in 25 ml. of ether with cooling to keep the temperature at 25–30°. Chilling and filtration of the reaction mixture gave 15 g. (82%) of dimethyl 2-(dipiperidinomethylene)-3-methylenesuccinate, m.p. 101–102°.

Anal. Calcd. for $C_{18}H_{28}N_2O_4$: C, 64.3; H, 8.4. Found: C, 64.6; H, 8.6.

Determination of the Configuration of C-9 in Levopimaric Acid[1]

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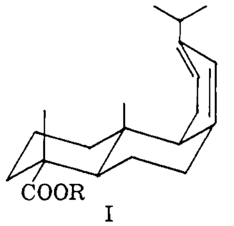
Although the gross structure of levopimaric acid has been well known for many years,[3] the stereochemistry of the material is known with less certainty. The absolute steric arrangement of C-4, C-5, and C-10 (steroid numbering) was established by conversion of levopimaric acid to abietic acid which, in turn, has been related to lanosterol.[4,5] In agreement with these results is the more recent work relating pimaric acid, which has been related to abietic acid,[6,7] to cholesterol.[8]

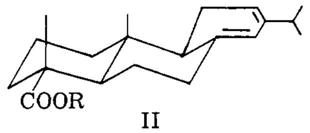
The configuration of C-9 in levopimaric acid has been more difficult to determine with certainty because the position is allylic to the reactive diene system and most interconversion studies have involved acid-catalyzed reactions. If the stereochemistry of this center were the less stable arrangement, these chemical studies might well have led to inversion of the center. Nevertheless, much chemical evidence has been presented in favor of an *anti*-backbone for levopimaric acid. For the most part the α-configuration at C-9 has been assigned by correlation with abietic and neoabietic acids,[9–11] the configuration in the latter materials having been assigned on the basis of conformational concepts and rotatory dispersion studies.[3,12,13] Recent investigations of the maleic anhydride adduct of levopimaric acid[14] also were best interpreted by assuming a C-9 α-configuration.

Purely physical methods also have been employed by various workers interested in this stereochemistry question. By comparison of the molecular rotations of levopimaric acid and $\Delta^{2,4}$-cholestadiene, it was concluded that the C-9 hydrogen has a β-orientation.[12] More recently it has been established that the direction of the skew of the diene rather than the configuration of the allylic center determines the sign of the Cotton curve of an optically active cyclohexadiene.[15] Using this concept, it was concluded that, if levopimaric acid did possess a 9α-configuration, the diene containing ring must assume a folded conformation (I) rather than the expected extended form II.[15] Surface film measurements were well in accord with this hypothesis.[16]

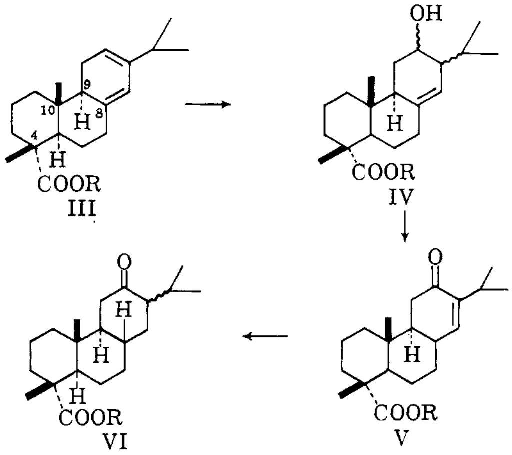
With such an accumulation of data, the α-assignment at C-9 appears preferable. However, since a rather unusual conformation is required to explain the dispersion curve, an unequivocal determination would be desirable. In the course of another study, we have obtained the unsaturated keto ester V which has permitted settlement of this stereochemistry problem.



I



II



Selective hydroboration of methyl levopimarate (III) with disiamylborane[17] gave mainly one unsaturated alcohol (IV) in 40% yield. Oxidation of IV to the ketone followed by base-catalyzed isomerization of the double bond into the α,β position afforded the conjugated isomer V. Hydrogenation of V yielded the saturated ketone VI which showed a positive Cotton curve.[18] Application of the Octant Rule showed that only with a *trans* 8β,9α B/C ring fusion would

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[1] This work was supported in part by grant no. A-709, U. S. Public Health Service.

[2] National Science Foundation Cooperative Predoctoral Fellow, 1960–1962.

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[18] We are indebted to Professor C. Djerassi for determination of the optical rotatory dispersion curve.

such a Cotton result be expected.[19,20] Accordingly the hydrogen on C-9 must have an axial (α) orientation in the ketone VI. Since none of the reactions and conversions from levopimaric acid should affect the geometry at C-9, this center must be α in the resin acid itself.

Experimental[21]

Hydroboration of Methyl Levopimarate.—A 300-ml., three-necked, round-bottomed flask was equipped with an addition funnel and a mechanical stirrer. The third neck was covered with a serum cap to permit removal of aliquots by means of a syringe. The system was flushed with dry nitrogen and cooled in an ice bath. Sodium borohydride (2.04 g., 0.054 mole) and a solution of 9.52 g. (0.132 mole) of 2-methyl-2-butene in 25 ml. of dry diglyme were placed in the cooled flask and a solution of 9.36 g. (0.066 mole) of boron trifluoride etherate in 25 ml. of dry diglyme was added, with stirring, over a period of 30 min. The mixture was allowed to stir for an additional 15 min. and then allowed to stand at ice temperature for 12 hr.

A solution of methyl levopimarate (prepared from 9.04 g. of levopimaric acid,[22] $[\alpha]^{16}\mathrm{D}$ $-252°$, $\lambda_{\max}$ 272 mμ (ϵ 6500), by reaction with excess diazomethane) in 25 ml. of dry diglyme was added, at 0°, to the above reagent over a period of 45 min. The course of the reaction was followed by observing the disappearance of the maximum in the ultraviolet. After 5 days, about 50% of the diene had been consumed. At this time, an additional 33 mmoles of disiamylborane was added to the reaction mixture. At the end of 4 additional days the optical density in the ultraviolet had dropped to 10% of the original absorption.

To the reaction mixture there was added, slowly (frothing), 30 ml. of 3 N sodium hydroxide solution followed by the addition of 40 ml. of 30% hydrogen peroxide. The mixture was stirred at 0° for 1 hr. and then at room temperature for 2 hr. The reaction was diluted with water and the product extracted with benzene. The benzene solution was washed with water, acidic 5% ferrous sulfate solution, water, and then dried. The solvent was removed under reduced pressure and the white waxy product dried overnight at 70° (5 mm.), yield 10.0 g.

The crude product was chromatographed on 300 g. of activity III alumina. Elution with pentane separated diglyme and nonhydroxylated material. Elution with pentane–benzene (3:1 and 5:2) gave a total of 795 mg. of a minor alcohol. Pentane–benzene (2:1) yielded mixtures of two alcohols and elution with pentane–benzene (1:1), benzene, and benzene–ether (20:1) gave 4.79 g. of a major alcohol. Elution with ether yielded 200 mg. of a diol which was not examined further.

The major alcohol was recrystallized from methylcyclohexane, yield 4.01 g. (40%), m.p. 120–125°. This material was shown to be homogeneous by thin layer chromatography on silica gel (pentane–ether 1:1). An analytical sample was obtained by repeated crystallization from both methylcyclohexane and from methanol, m.p. 126.0–127.5°, $[\alpha]^{25}\mathrm{D}$ $+56°$ (c 1.49), $\epsilon_{205}^{\mathrm{EtOH}}$ 10,000. Major peaks in the n.m.r. were found at τ 4.62, 6.08, and 6.34.

Anal. Calcd. for $C_{21}H_{34}O_3$ (334.48): C, 75.40; H, 10.25. Found: C, 75.45; H, 10.48.

The major alcohol was acetylated with acetic anhydride in pyridine and the crude product chromatographed on alumina. The acetate was recrystallized from aqueous methanol, m.p. 85.5–86.5°, $[\alpha]^{25}\mathrm{D}$ $+60°$ (c 2.00), $\epsilon_{205}^{\mathrm{EtOH}}$ 9300. The n.m.r. spectrum showed peaks at τ 4.72, 5.08, 6.38, and 8.05.

Anal. Calcd. for $C_{23}H_{36}O_4$ (376.52): C, 73.36; H, 9.64. Found: C, 73.08; H, 9.52.

The minor alcohol was recrystallized from hexane and from aqueous methanol, m.p. 133.5–134.0 and 139.5–141.0°, $[\alpha]^{27}\mathrm{D}$ $-43°$ (c 1.88), $\epsilon_{205}^{\mathrm{EtOH}}$ 9000. The major peaks in the n.m.r. were at τ 4.88, 6.30, and 6.71.

Anal. Calcd. for $C_{21}H_{34}O_3$ (334.48): C, 75.40; H, 10.25. Found: C, 75.66; H, 9.98.

Methyl 12-Keto-$\Delta^{8,14}$-dihydrolevopimarate.—To a solution of the major alcohol (402 mg., 1.2 mmoles, m.p. 120–125°) in 8 ml. of C.P. acetone cooled in an ice bath there was added 0.45 ml. (1.80 mmoles) of standard chromic acid–sulfuric acid solution (prepared from 26.7 g. of chromium trioxide and 23 ml. of concentrated sulfuric acid diluted to 100 ml. with water) over a period of 5 min. The mixture was allowed to stir for an additional 3 min. and then the reaction quenched with methanol. The mixture was diluted with water and extracted with ether The ether layer was washed, dried, and then evaporated to dryness to yield 348 mg. of solid yellow material. The compound crystallized well from either hexane or methanol but little if any purification was obtained as shown by the m.p. range of 123–135° and the presence of two spots on thin layer chromatography (silica gel, pentane–ether 1:1).

The crude material was chromatographed on 10 g. of Woelm activity III alumina. Elution with pentane–benzene mixtures and with pure benzene yielded 164 mg. (41%) of the β,γ-unsaturated ketone. There also was obtained about 50 mg. of more polar material but it was not examined. The unsaturated ketone is sensitive to air and should be isomerized immediately.

The β,γ-unsaturated ketone (164 mg.) was dissolved in 15 ml. of methanol, the solution flushed with nitrogen, sodium methoxide (75 mg.) added, and the solution allowed to stir for 5 hr. under a nitrogen atmosphere. The isomerization was followed by observing the development of a maximum at 238 mμ. The reaction was stopped by addition of 10% sulfuric acid, most of the methanol was removed under reduced pressure, and the product isolated by chloroform extraction. After evaporation of the chloroform the product was chromatographed on 5 g. of activity II alumina and the eluted material recrystallized from aqueous methanol, yield 48 mg. (12% from starting alcohol), m.p. 102.0–102.5°, $[\alpha]^{25}\mathrm{D}$ $+54°$ (c 1.15), $\lambda_{\max}^{\mathrm{EtOH}}$ 238 mμ (ϵ 8800). The major n.m.r. bands were found at τ 3.78, 6.39, and 7.25.

Anal. Calcd. for $C_{21}H_{32}O_3$ (332.47): C, 75.86; H, 9.70. Found: C, 75.96; H, 9.78.

Methyl 12-Ketotetrahydrolevopimarate.—The α,β-unsaturated ketone (220 mg., 0.66 mmole) was hydrogenated in ethanol over prereduced platinum oxide (25 mg.) at atmospheric pressure. Theoretical hydrogen uptake was obtained in 90 min. The product was isolated in the usual manner and recrystallized from aqueous methanol, yield 114 mg. (51%), m.p. 98.5–99.5°, $[\alpha]^{27}\mathrm{D}$ 11 ± 1° (c 1.27). The rotatory dispersion curve (c 0.106 in methanol) showed a peak at 311 mμ (amplitude $+604°$) and a trough at 269 mμ (amplitude $-755°$).

Anal. Calcd. for $C_{21}H_{34}O_3$ (334.48): C, 75.40; H, 10.25. Found: C, 75.06; H, 10.06.

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[20] Although the isopropyl group is probably equatorial, its configuration does not affect the predictions based on the Octant Rule.

[21] All melting points were taken in evacuated sealed capillaries and are uncorrected. Optical rotations were measured in chloroform. The n.m.r. spectral data are relative to tetramethylsilane as an internal standard. Chromatographies were performed of Woelm neutral alumina which had been deactivated to the desired activity by the addition of distilled water. All analyses were conducted by the Microanalytical Laboratory, College of Chemistry, University of California.

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β-Bromocrotonolactone from the Bromination of Furoic Acid

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We wish to report the isolation, albeit in low yield, of β-bromocrotonolactone ($C_4H_3BrO_2$, m.p. 78°) from the bromination of furoic acid. The controversy[2a] regarding the early reports[3] (unconfirmed by later workers[4])

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