In an attempt to remove the molecule of water, the analytical sample was crystallized thrice from benzene and dried 32 hr. a 100° and 0.5 hr. at 140° under vacuum over phosphorus pentoxide. A sublimation of the compound was also tried without success.

Anal. Found: C, 60.63, 60.82; H, 5.28, 5.56.

4,6-Dicarbomethoxy-2-spirocyclopentyl-9,11-dimethyl-11a-hydroxyoxazolino[4,5-*b*]phenoxazine (28). A. By Photolysis.—A solution of 40 mg. of **15** in 225 ml. of benzene and 75 ml. of methanol was photolyzed following the procedure for compound **12**. Solvent was removed under reduced pressure and the residue in a minimum of benzene, was allowed to stand in an icebox for several hours. The yellow product (12 mg.) which separated was washed several times with small amounts of benzene until t.l.c. showed a single spot. The gummy residue from the benzene filtrate was subjected to preparative t.l.c. on a 20 × 20 cm. silica gel G plate with 20% acetone in chloroform to yield approximately 4 mg. of **7**.

B. From 7.—The oxazoline **28** was formed in trace amounts only, as indicated by t.l.c. when its preparation was attempted from reduced **7** and cyclopentanone; most of the unreacted **7** was recovered from the reaction mixture.

An analytical sample of **28** was prepared by passing its chloroform solution through a short column of alumina (activity IV) and crystallization from ethyl acetate: m.p. 180° (darkening); λ_{max}^{MeOH} 222 mμ (ε 12,388), 244 (21,237), 270 (14,158), 312 (9733), 376 (20,352); ν_{max}^{KBr} 3430, 2950, 2875, 1715, 1675, 1622, 1560 cm.$^{-1}$; n.m.r. 2.30, 2.90 (ring protons), 5.92, 6.10 (O-methyl), 7.61, 7.93 (ring methyl), 8.04 (methylene). The compound was insufficiently soluble in deuteriochloroform; therefore, the signals due to the amino and hydroxyl protons were not observed.

Anal. Calcd. for $C_{23}H_{24}N_2O_7$: C, 62.72; H, 5.49. Found: C, 62.42; H, 5.60.

4,6-Dicarbomethoxy-2-spirocyclohexyl-9,11-dimethyl-11a-hydroxyoxazolino[4,5-*b*]phenoxazine (29). A. By Photolysis.—A solution of 40 mg. of **16** in 225 ml. of benzene and 75 ml. of methanol was photolyzed following the procedure for compound **12**, and the oxazoline **29** (36%) and 2-aminophenoxaz-3-one **7** (13.5%) were isolated from the photolysis mixture.

B. From 7.—The same compound **29** was prepared in 36.6% yield in the same manner as oxazoline **28** by using cyclohexanone instead of acetone. The analytical sample of **29** was prepared by crystallization from ethyl acetate: m.p. 189–192°; λ_{max}^{MeOH} 222 mμ (ε 15,520), 240 (24,649), 268 (17,346), 310 (11,868), 376 (23,736); ν_{max}^{KBr} 3430, 2940, 2860, 1720, 1705, 1675, 1620, 1560 cm.$^{-1}$; n.m.r. 2.32, 3.06 (ring protons), 5.95, 6.20 (O-methyl), 7.65, 7.98 (ring methyl), 8.30 (methylene). The compound was insufficiently soluble in deuteriochloroform; therefore, the signals due to the amino and hydroxyl protons were not observed.

Anal. Calcd. for $C_{24}H_{26}N_2O_7$: C, 63.42; H, 5.77; N, 6.14. Found: C, 63.29; H, 6.02; N, 6.25.

Hydrolysis of Oxazolines 26, 28, and 29.—A solution of 15 mg. of oxazoline **26** in 10 ml. of methanol was treated with 2 ml. of 2 *N* hydrochloric acid and heated for 10 hr. at 55°. On allowing the reaction mixture to stand overnight at room temperature, dark red crystals (3 mg.) of 2-hydroxyphenoxaz-2-one (**8**), identified by t.l.c., mixture melting point, and infrared spectrum, were obtained. The filtrate was neutralized with sodium bicarbonate solution and extracted with chloroform. The residue from the dried chloroform extract was chromatographed on a short column of alumina (activity IV) with chloroform to yield 3 mg. of pure 2-aminophenoxaz-3-one **7**.

The same compound **7** could be isolated from the acid hydrolysis of **28** and **29** under similar conditions.

Acknowledgment.—We take pleasure in thanking Dr. M. E. Wall, director of this laboratory, for his encouragement and support throughout the course of this work.

Resin Acids. IV. 12-Hydroxyabietic Acid and Its Reduction[1]

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12α-Hydroxyabietic acid has been obtained by reaction of levopimaric acid with hypochlorous acid in basic solution. The structure was proved by independent synthesis from levopimaric acid peroxide. Hydrogenation furnished two dihydro derivatives and one tetrahydro derivative whose structure and stereochemistry were established. The o.r.d. curves of 12-keto-8α-H-abietanes are discussed.

In an earlier paper[1] it was demonstrated that the structure of a hydroxyabietic acid obtained by selenium dioxide oxidation of abietic acid was not 12-hydroxyabietic acid as originally proposed[5] but 9α-hydroxyabietic acid (**1**). We now report the preparation of authentic 12α-hydroxyabietic acid (**2**), proof of its structure, and a study of its reduction.

When levopimaric acid (**3**) was dissolved in dilute base and treated with hypochlorous acid, there was formed in 35% yield a substance, $C_{20}H_{20}O_3$, m.p. 164–166°, $[\alpha]^{24}D$ −146°, which was obviously a hydroxy acid (formation of a methyl ester which exhibited hydroxyl absorption in the infrared) and differed from the isomeric substance prepared by selenium dioxide oxidation of abietic acid.[1,5]

The ultraviolet spectrum of the new hydroxy acid was essentially identical with the ultraviolet spectrum of abietic acid and exhibited maxima at 236, 242, and 250 mμ (ϵ_{max}^{242} 24,800). The n.m.r. spectrum,[6] in addition to resonances at 1.07, 1.10 (doublets, J = 7, of isopropyl side chain), 0.77 (C-10 methyl), and 1.24 p.p.m. (C-4 methyl), had two signals in the vinyl region which were very similar to analogous signals in the n.m.r. spectrum of abietic acid, one relatively complex resonance at 5.50 corresponding to H-7 and a second sharp singlet at 5.85 p.p.m. corresponding to H-14. In addition there was a broad one-proton peak at 4.28 p.p.m. characteristic of a proton geminal to a hydroxyl group.

The ultraviolet and n.m.r. spectra suggested that the new substance was either 6- or 12-hydroxyabietic acid.

(1) Previous paper: W. Herz and H. J. Wahlborg, *J. Org. Chem.*, **30**, 1881 (1965).

(2) Department of Chemistry, The Florida State University. Work at The Florida State University supported in part by a grant from the National Science Foundation (GP-1492).

(3) Abstracted from a dissertation submitted in partial fulfillment of the requirements for the Ph.D. degree, April 1965.

(4) Naval Stores Laboratory, Olustee, Fla. One of the laboratories of The Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

(5) L. Fieser and W. P. Campbell, *J. Am. Chem. Soc.*, **60**, 159 (1938).

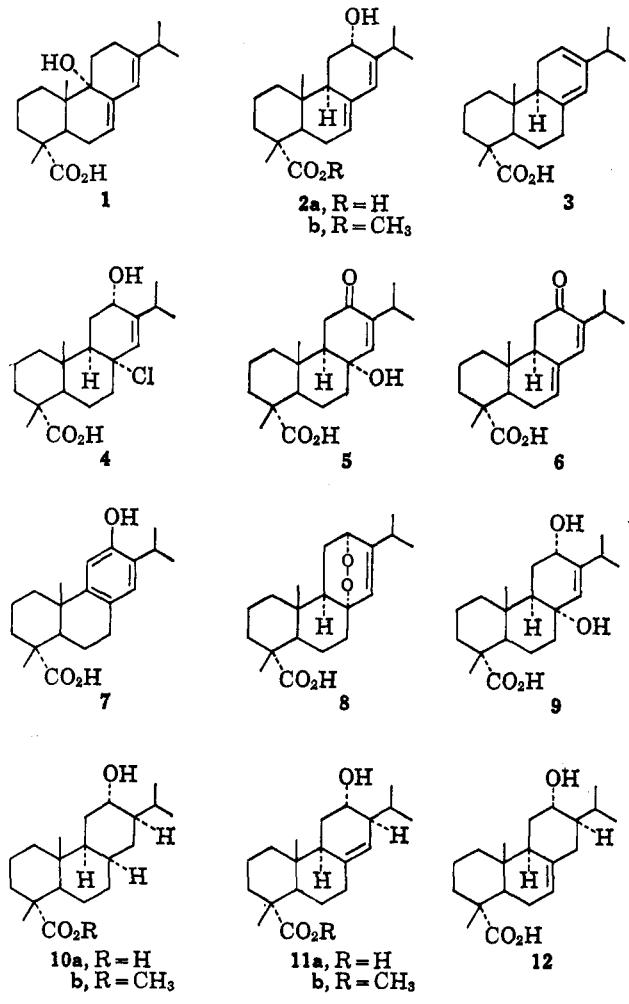
(6) N.m.r. spectra were run in deuteriochloroform, unless otherwise specified, on a Varian A-60 spectrometer purchased with the aid of a grant from the National Science Foundation to The Florida State University. Frequencies are given in parts per million with tetramethylsilane serving as internal standard. Multiplicities are expressed by conventional symbols.

The second possibility seemed considerably more likely if the reaction involved not oxidation, but conjugate addition to levopimaric acid. This would initially furnish $\Delta^{13(14)}$-8α-chloro-12α-hydroxyabietenoic acid (**4**) with the stereochemistry predicated on the more facile approach of the reagent from the α side as in the Diels–Alder reaction.[7] Subsequent elimination of hydrogen chloride under the basic reaction conditions then would yield 12α-hydroxyabietic acid, elimination toward C-7 instead of toward C-9 being preferred in related situations.[8,10]

Attempts to convert the new hydroxy acid to the known 12-hydroxydehydroabietic acid[9] or 12-ketoabietic acid (**6**)[9] failed, but its preparation by another route established its structure. Isolation of **2a** from the complex mixture resulting from the hydrogenation of levopimaric acid peroxide (**8**) which also yielded **9** led to two important conclusions. First, since **8** had previously been transformed into **7**, the location of the hydroxyl group is fixed at C-12. Second, the orientation of the hydroxyl group is now certainly α since backside approach is required for the relatively bulky dye-oxygen intermediate proposed[11b,c] for the photosensitized oxidation of levopimaric acid.[9,11a] Photosensitized oxidations of steroids which have steric requirements similar to resin acids proceed from the backside[12] and the parallelism between photochemical 1,4 addition of oxygen and 1,4-addition of maleic anhydride which adds to levopimaric acid from the α side[7] has been noted.[11]

With the structure of the hydroxy acid established as **2a** we were interested in studying its hydrogenation because of related work then in progress.[1] The results will now be detailed.

Catalytic hydrogenation of **2a** with platinium oxide in ethanol at atmospheric pressure yielded a mixture consisting of three hydroxy acids which were separated by chromatography over silicic acid.[13] Compound A, m.p. 229–230°, $[\alpha]^{25}D$ + 45°, appeared to be a tetrahydro derivative (elementary analysis of A and its methyl ester, absence of n.m.r. signals characteristic of vinyl and allylic protons, negative tetranitromethane test) whose hydroxyl group (infrared spectrum, n.m.r. signal at 6.56 p.p.m.—intensity two protons—characteristic of exchange between hydroxyl and carboxyl groups) was equatorial (broad resonance at 3.80 p.p.m. —half-height width 28 c.p.s.—characteristic of an axial proton flanked by two other protons). Structure



10a was tentatively assigned to A and evidence for its correctness will be presented in the sequel.

Substance B, the second compound eluted from the chromatogram, m.p. 186.5–187.5°, $[\alpha]^{25}D$ +27°, and substance C, the last component, m.p. 188–189°, $[\alpha]^{25}D$ +37°, were dihydro derivatives, as indicated by the analyses and strong end absorption in the ultraviolet. Methylation of C, whose n.m.r. spectrum exhibited signals characteristic of one hydrogen on the carbon carrying hydroxyl (complex band at 3.92) and one vinyl hydrogen (unresolved multiplet at 5.38 p.p.m.) gave a methyl ester, m.p. 127–128°, $[\alpha]^{25}D$ +51°, which was identical with the major alcohol produced by the hydroboration–oxidation reaction of methyl levopimarate with disiamylborane.[14] The stereochemistry of this substance has not been specified but can now be depicted as **11a**. Since hydroboration proceeds in a *cis* manner, since oxidation of the boron–carbon bond proceeds with retention,[15] and since the hydroxyl group of **2a** has been shown to be α, H-13 of C and **11b** must be α and the isopropyl group must be β. This is also the stereochemistry which one would have predicted if one took into consideration the steric factors governing (a) catalytic hydrogenation of **2a** and (b) hydroboration of methyl levopimarate by the bulky disiamylborane, a process particularly sensitive to steric factors.

(7) W. D. Lloyd and G. W. Hedrick, *J. Org. Chem.*, **26**, 2029 (1961); L. H. Zalkow, R. A. Ford, and J. P. Kutney, *ibid.*, **27**, 3535 (1962); W. A. Ayer, C. E. McDonald, and J. B. Stothers, *Can. J. Chem.*, **41**, 1113 (1963); N. J. Halbrook, R. V. Lawrence, R. Dressler, R. Blackstone, and W. Herz, *J. Org. Chem.*, **29**, 1017 (1964).

(8) For example, $\Delta^{13(14)}$-8α-hydroxy-12-ketoabietenoic acid (**5**) when refluxed for a few minutes with acetic acid yields 12-ketoabietic acid (**6**).[9]

(9) R. N. Moore and R. V. Lawrence, *J. Am. Chem. Soc.*, **81**, 458 (1959).

(10) Compounds resulting from 1,4 addition of hypochlorous acid to levopimaric acid in the opposite sense, *i.e.*, deriving from $\Delta^{13(14)}$-8α-hydroxy-12α-chloroabietenoic acid might also be formed but have not yet been isolated from the reaction mixture.

(11) (a) R. N. Moore and R. V. Lawrence, *J. Am. Chem. Soc.*, **80**, 1438 (1958); (b) W. H. Schuller, R. N. Moore, and R. V. Lawrence, *ibid.*, **82**, 1734 (1960); (c) W. H. Schuller and R. V. Lawrence, *ibid.*, **83**, 2563 (1961).

(12) G. D. Laubach, E. C. Schreiber, E. J. Agnello, and K. J. Brunings, *ibid.*, **78**, 4746 (1956).

(13) The three main components accounted for about 85% of starting material. There was also some less polar hydrogenolysis product which was eluted first. The amount of A never exceeded 15% at atmospheric pressure, but A predominated at higher pressures (35 p.s.i.). The ratio of B to C was always 1:2. Hydrogenation of **2a** in acetic acid at 21 p.s.i. resulted almost entirely in hydrogenolysis and was followed by further reduction.

(14) W. G. Dauben and R. Coates, *J. Org. Chem.*, **28**, 1698 (1963).

(15) H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962.

Compound B had significant n.m.r. signals at 4.10 (hydrogen α to hydroxyl) and 5.32 p.p.m. (vinyl proton, shape comparable to H-7 resonance of abietic acid), resisted oxidation by means of manganese dioxide[16] and dichlorodicyanoquinone,[17] and was therefore tentatively formulated as **12** (exclusive of stereochemistry at C-13). Oxidation with chromium oxide–pyridine furnished an unconjugated ketone D, m.p. 164–165°, $[\alpha]^{25}D$ +193°, λ_{max} 288 mμ (ϵ 141), infrared band at 1715 cm.$^{-1}$, n.m.r. signal at 5.59 p.p.m. (vinyl proton), which definitely eliminated C-13–C-14 as the locus of the double bond.

Ketone D on being refluxed with methanolic sodium methoxide was converted to an isomeric ketone E, m.p. 154–156°, $[\alpha]^{25}D$ +100°, which still exhibited one broadened n.m.r. peak characteristic of a vinyl proton and had no ultraviolet chromophore indicative of a conjugated ketone. On the basis of these properties and the following argument, compound B can be assigned formula **12**.

There are, *a priori*, three possible structures for ketone D, *viz.*, **13**, **14**, and **15**. The first of these is ruled out on two counts. In **13** the isopropyl side chain is quasi-equatorial and would not be expected to epimerize to the thermodynamically less stable isomer **16**. Rather, **13** would be expected to isomerize to the conjugated ketone under the influence of base. This has already been demonstrated by the complete conversion of the β,γ-unsaturated ketone derived from **11b**, whose structure can now be written as **16**, to the α,β-unsaturated ketone **17**.[14]

The second possibility, **14**, can be ruled out as well. In this molecule the isopropyl group occupies the thermodynamically more stable quasi-equatorial orientation also and would not be expected to isomerize.

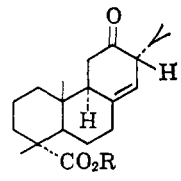
The conversion of D to E cannot involve a double-bond migration to the possibly more stable C-8–C-9 or C-13–C-14 positions since E is not an α,β-unsaturated ketone and has one vinyl proton. Therefore the only change which can occur during the transformation of D to E is epimerization of an unstable β-oriented isopropyl side chain to the α configuration which leads to the conclusion that E is **14**, that D is **15**, and that B must be **12**.

We now proceed to the evidence which unequivocally established the first hydrogenation product A as the tetrahydro derivative **10a**. Treatment with ruthenium tetroxide[18] converted **10b** to a keto ester (infrared bands at 1720 and 1710 cm.$^{-1}$) which was also prepared by chromic acid oxidation of **10a** to a keto acid and subsequent methylation. If hydrogenation proceeds from the α side, as has now been demonstrated for the two dihydro derivatives, compound A is **10a** and the derived keto acid is **18a**.

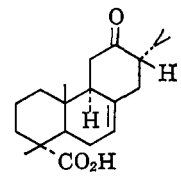
This relationship was put on a secure basis by the following experiments. Hydrogenation of **11a**, whose isopropyl side chain is β, with platinum oxide in acetic acid yielded **10a**. Hence, the isopropyl groups of **10a** and **18a** are β oriented. Second, **18a** was not epimerized by treatment with sodium methoxide in methanol. Hence, the isopropyl group of **18a**, and therefore of **10a**, occupies the more stable equatorial position. This requires that H-8 be α, since then and only then can the isopropyl side chain be stable, equatorial, and β, and completely defines the stereochemistry of compound A.

Finally, comments are in order on the results which were encountered when an attempt was made to apply the optical rotatory dispersion method to the solution of the stereochemistry of **18a** prior to the chemical correlation described in the previous paragraph.

Some years ago Bible and Burtner[20] were faced with the problem of assigning configurations to two saturated ketones resulting from the hydrogenation and subsequent oxidation of podocarpic acid. Application of the octant rule[21] to molecular models of all four possible B/C-ring arrangements led to the conclusion that, if chair conformations prevail, only the *trans*-8β,9α isomer should exhibit a positive Cotton effect. Dauben and Coates[14] oxidized **11b** to the β,γ-unsaturated ketone **16b** which was isomerized by base to **17** and then reduced to **19** (stereochemistry at C-13 surmised as equatorial). Their assumption that conversion of **16b** to **17** should result in the more stable *trans*-8β-9α-B/C ring fusion was supported by the observation that the o.r.d. curve of **19** exhibited the positive Cotton effect predicted by the octant rule regardless of the orientation of the isopropyl group. Dauben and Coates concluded that the earlier[20] deductions regarding the



13a, R = H
b, R = CH_3



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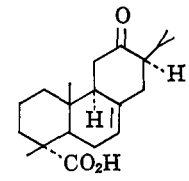

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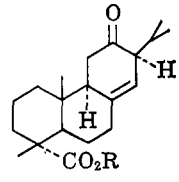
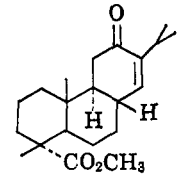


16a, R = H
b, R = CH_3



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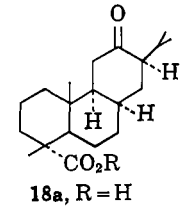
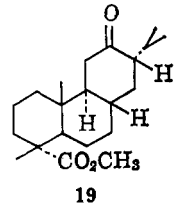


18a, R = H
b, R = CH_3



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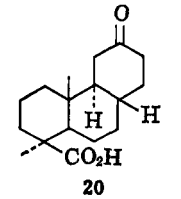

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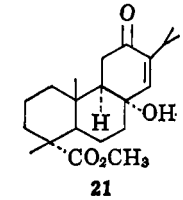

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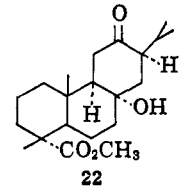

22

(16) N. L. Wendler, R. P. Graver, C. S. Snoddy, Jr., and F. W. Bollinger, *J. Am. Chem. Soc.*, **79**, 4481 (1957).

(17) D. Burn, V. Petrow, and G. O. Weston, *Tetrahedron Letters*, **No. 9**, 14 (1960).

(18) This reagent was employed to demonstrate the absence of a tetrasubstituted double bond by chemical means[19] but also accomplished the oxidation of the secondary alcohol group to the ketone.

(19) G. Snatzke and H. Fehlhaber, *Ann.*, **663**, 123 (1963).

(20) R. Bible and R. Burtner, *J. Org. Chem.*, **26**, 1174 (1961).

(21) C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., Inc., New York, N. Y., 1960.

sign of the o.r.d. curves in this series are not affected by the presence of the isopropyl group.

If these conclusions are correct, it would be expected that the o.r.d. curve of **18b** should exhibit a negative Cotton effect if H-8 is α (as has already been established by the transformations discussed earlier) and that it should be positive if H-8 is β. However, contrary to expectations, the o.r.d. curve of **18b** exhibited a positive Cotton effect (a = 14.3).

We can first assume that the assignment based on chemical evidence is incorrect and that the o.r.d. curve as normally interpreted correctly reflects the stereochemistry of the compound in question. Then the keto ester previously assigned formula **18b** must be **19** (isopropyl side chain stable, equatorial, and β) and the compound of Dauben and Coates its unstable C_{13} epimer (isopropyl group axial and α). However, the latter was not affected by sodium methoxide in boiling methanol. Hence, the structural assignments of **18b** and **19** are correct,[22] and the o.r.d. curve of **18b** reflects a distortion of ring C from the normal chair conformation.[23]

Of the several conformations which would account for the positive Cotton effect two—ring C boat and ring B boat-ring C chair—are clearly ruled out by the large interactions which would be introduced. The conformation which appears most favorable is the "five-atoms-in-a-plane" form invoked[24] to explain the inversion of the Cotton effect in 4,4-dimethyl-3-keto steroids. This conformation appears to reduce the nonbonded interactions of **18b** to a minimum while still predicting a positive Cotton effect.

The conclusion that the o.r.d. curve of **18b** must be anomalous found unexpected support from the following experiment. Chromatographic separation of the products from the oxidation of **11b** with Jones reagent yielded the main previously reported[14] product **16b** and a hydroxy ketone, m.p. 135°, $[\alpha]D$ +29°, λ_{max} 235 mμ (ϵ_{max} 6140). Direct comparison with an authentic sample of **21**, previously prepared[9] by base-catalyzed decomposition of levopimaric acid peroxide, established identity. Hydrogenation of **21** furnished a hydroxy ketone for which the stereochemistry implicit in **22** may be derived. The configuration of the C-8 hydroxyl must be α, since **21** was originally prepared from the peroxide whose oxygen atoms have been shown to be attached to the α side. H-13 must be α because hydrogenation of the C-13–C-14 double bond must proceed from the α side, the β base being too hindered for adsorption on the catalyst surface.[25]

Since **22** differs from **18b** only in the substitution of C-8 α-OH for C-8 α-H, the factors causing conformational distortion in **18b** should also be present in **22** and manifest themselves in the o.r.d. curve. This was found to be the case. Just like **18b**, **22** exhibited a positive Cotton effect (a = 4.2), although the amplitude was smaller.

Experimental[26]

12α-Hydroxyabietic Acid (2a).—A slurry of 9.5 g. of levopimaric acid, 1.9 g. of potassium hydroxide, and 150 ml. of distilled water was stirred until most of the levopimaric acid dissolved. The solution was cooled to 18° and 50 ml. of 0.6 N hypochlorous acid (Clorox) was rapidly added with vigorous stirring. After 10 min. 3.5 g. of phosphoric acid in 25 ml. of water and 200 ml. of ether was added. The ether layer was separated, washed with water, and dried, concentrated to 15 ml., and diluted with 10 ml. of petroleum ether. The product slowly crystallized, yield 3.4 g. It was recrystallized from aqueous ethanol and ether–petroleum ether, m.p. 164–166°, $[\alpha]^{24}D$ −146° (c 1.78), infrared bands at 3600 and 1700 cm.$^{-1}$. The n.m.r. spectrum exhibited signals at 0.77 (C-10 methyl), 1.07d and 1.10d (J = 7, isopropyl group), 1.24 (C-4 methyl), 4.28c (H-12), 5.50c (H-7) and 5.58 p.p.m. (H-14).

Anal. Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50; neut. equiv., 318. Found: C, 75.33; H, 9.36; neut. equiv., 320.

The methyl ester **2b** was prepared with ethereal diazomethane and recrystallized from ether–petroleum ether, m.p. 88–90°, $[\alpha]^{25}D$ −117°, infrared bands at 3500 (hydroxyl) and 1720 cm.$^{-1}$ (ester). The n.m.r. spectrum exhibited the same peaks as **2a**, but had an additional methoxyl signal at 3.66 p.p.m.

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.85; H, 9.71. Found: C, 75.71; H, 9.59.

A solution of **2b** in dry ether at −78° was saturated with ketene, mixed with freshly distilled boron trifluoride etherate, allowed to stand at −78° for 1 hr., and made basic with ammonium hydroxide solution. The ether layer was separated, washed, dried, and removed *in vacuo;* the residue was chromatographed over alumina. The eluted acetate which was homogeneous (t.l.c., n.m.r. spectrum) could not be induced to crystallize. It had n.m.r. signals at 0.80 (C-10 methyl), 1.02d and 1.03d (J = 6.5, isopropyl), 1.25 (C-4 methyl), 2.04 (acetate), 3.64 (methoxyl), 5.53c (two protons, H-7 and H-12), and 6.00 p.p.m. (H-14). Exposure of the acetate to N-bromosuccinimide in boiling carbon tetrachloride followed by treatment with potassium acetate in acetic acid resulted in material which consisted mainly of methyl Δ^6-dehydroabietate and some methyl dehydroabietate (n.m.r. spectrum, ultraviolet peak at 260 mμ characteristic of methyl Δ^6-dehydroabietate[27]).

Hydrogenation of Levopimaric Acid Peroxide.—A solution of 3.01 g. of levopimaric acid peroxide (**8**)[11a] in 20 ml. of ethanol was reduced with 0.015 g. of platinum oxide at atmospheric pressure. Hydrogen uptake leveled off after 3.5 hr. when 0.64 mole equiv. of hydrogen had been absorbed. The solution was filtered, diluted with water to incipient turbidity at 60°, warmed slightly until clear, and allowed to stand. There precipitated 1.9 g. of crystalline material and a second crop of oil which solidified on seeding but could not be recrystallized satisfactorily. One recrystallization of the first crop from ethanol furnished long needles of **9**, 0.33 g. (11%), m.p. 217–218°. Another recrystallization raised the melting point to 218–219° dec. (with gas evolution), $[\alpha]^{25}D$ − 14.4° (c 0.18, absolute ethanol), infrared

(22) The formation of **19** by catalytic hydrogenation of **17** implies adsorption on the catalyst surface from the ordinarily more hindered β face. Inspection of a Dreiding model of **17** indicates that in this instance the β face is less hindered.

(23) Evidence for a nonchair form can also be obtained from the n.m.r. spectrum. A Dreiding model of **18b** in which ring C is strictly in the chair form shows quite clearly that the C-10 methyl group would be situated within the shielding cone of the carbonyl. However, the C-10 methyl resonance exhibits the normal chemical shift (0.81 p.p.m.) which would seem to indicate that the carbonyl group is oriented away from the C-10 methyl group. The model also shows that ring C would be positioned in close proximity to the substituents on the β face of **18b**, particularly the C-10 methyl group. Although **20** which exhibited the predicted negative Cotton effect[20] experiences the same compression (the inverted configuration at C-4 should not affect the conformation of ring C appreciably), it lacks the bulky isopropyl group whose presence in **18b** may produce sufficiently large nonbonded interactions to distort the chair conformation.

(24) N. L. Allinger and M. DaRooge, *Tetrahedron Letters*, 676 (1961); *J. Am. Chem. Soc.*, **84**, 4561 (1962).

(25) The n.m.r. spectrum of **21** shows that the C-10 methyl group is situated directly over the double bond and that hydrogen transfer must occur from the opposite side. The spectrum exhibits a methyl resonance at 0.65 p.p.m. characteristic of a shielded C-10 methyl group. A similar situation occurs in Diels–Alder adducts of levopimeric acid where the C-13–C-14 double bond is forced into close proximity to the C-10 methyl group, thus inducing a diamagnetic shift of 0.25 p.p.m.[7]

(26) Melting points are uncorrected. Analyses were carried out by Dr. F. Pascher, Bonn, Germany. Infrared spectra were determined in chloroform solution, ultraviolet spectra and rotations in 95% ethanol unless otherwise specified. Petroleum ether was low boiling (b.p. 30–60°). Chromatograms were run on Alcoa F-20 alumina neutralized with ethyl acetate or Mallinckrodt 100-mesh silicic acid. O.r.d. curves were run by Dr. L. Tether on a Rudolph recording spectropolarimeter.

(27) G. Dupont, R. Dulou, and C. Thibault, *Compt. rend.*, **236**, 2408 (1953).

bands (Nujol) at 3390 and 3290 cm.$^{-1}$, ultraviolet end absorption.

Anal. Calcd. for $C_{20}H_{32}O_4$: C, 71.39; H, 9.59; sec. -OH, 5.1; neut. equiv., 336. Found: C, 71.34; H, 9.50; sec. -OH, 5.5; neut. equiv., 338.

The second crop from the recrystallization of **9** was recrystallized from ethanol and furnished an additional 0.15 g. of **9**, total wt. 0.48 g. (15%). The mother liquor of this crystallization was diluted with water, warmed until clear, and allowed to stand. There precipitated 0.51 g. (17%) of **2a**, m.p. 161.5°. Several recrystallizations raised the melting point to 163.5–165.5°, $[\alpha]^{25}D$ −152° (*c* 0.77), mixture melting point with material from hypochlorite reaction undepressed, infrared and n.m.r. spectra superimposable.

In a second experiment, utilizing 1.05 g. of levopimaric acid peroxide in 200 ml. of ethanol, hydrogen uptake stopped after absorption of 1 mole equiv. of hydrogen (3 hr.). There was isolated 0.23 g. (22%) of **9** and 0.27 g. (26%) of **2a**.

Hydrogenation of 2a.—A solution of 0.4 g. of **2a** in 200 ml. of ethanol was reduced with 0.07 g. of prereduced platinum oxide at atmospheric pressure in a microhydrogenator. Hydrogen uptake ceased after absorption of 1 mole equiv. of hydrogen. The solution was filtered and concentrated, and the residue dissolved in benzene and chromatographed over 15 g. of silicic acid. Elution with ether–benzene (1:11) gave, in order, 0.075 g. of 12α-hydroxy-8α,13αH-abietanoic acid (**10a**), 0.075 g. of Δ^7-12α-hydroxy-13αH-abietenoic acid (**12**), and 0.2 g. of $\Delta^{8(14)}$-12α-hydroxy-13αH-abietenoic acid (**11a**).

The first fractions from the above chromatogram were recrystallized from chloroform and ethanol–water. **10a** had m.p. 229–230°, $[\alpha]^{25}D$ +45°. The n.m.r. spectrum exhibited signals at 0.82d (*J* = 6) and 0.93d (*J* = 7, isopropyl group), 1.02 (C-10 methyl),[28] 1.20 (C-4 methyl), and 3.80 p.p.m. [unresolved multiplet (H-12)].

Anal. Calcd. for $C_{20}H_{34}O_3$: C, 74.49; H, 10.63; O, 14.89. Found: C, 74.65; H, 10.73; O, 14.81.

The methyl ester was prepared by mixing **10a** with ethereal diazomethane. The product was recrystallized from methanol–water, m.p. 164–165°.

Anal. Calcd. for $C_{21}H_{36}O_3$: C, 74.95; H, 10.78; O, 14.26. Found: C, 75.17; H, 11.02; O, 13.66.

Acetylation of **10a** with ketene by the method described in the previous section furnished an acetate which melted at 220.5–221.5° after several recrystallizations from methanol–water.

Anal. Calcd. for $C_{22}H_{36}O_4$: C, 72.49; H, 9.36; O, 17.56. Found: C, 72.69; H, 9.46; O, 18.11.

The middle fractions from the above chromatogram were recrystallized from methanol–water. Pure **12** had m.p. 186.5–187.5°, $[\alpha]^{25}D$ +27° (*c* 1.06). The n.m.r. spectrum exhibited signals at 0.83 and 0.93 (superimposed doublets of isopropyl group), 0.83 (C-10 methyl), 1.23 (C-4 methyl), 4.10c (H-12) and 5.32 p.p.m. (br, H-7).

Anal. Calcd. for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06; O, 14.98. Found: C, 74.77; H, 9.79; O, 15.12.

The last fractions of the chromatogram containing **11a** were combined and recrystallized from ethanol–water, m.p. 188–189°, $[\alpha]^{25}D$ +37° (*c* 1.04). The n.m.r. spectrum exhibited signals at 0.80 (C-10 methyl), 0.92d (*J* = 6) and 0.98d (*J* = 6, isopropyl group), 1.20 (C-4 methyl), 3.93c (H-12), and 5.42 p.p.m. (broadened singlet, H-14).

Anal. Calcd. for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06; O, 14.98. Found: C, 74.77; H, 9.79; O, 15.12.

The methyl ester **11b** was recrystallized from ethanol–water: m.p. 124–125°, $[\alpha]^{22}D$ +35° (*c* 1.04); lit.[14] m.p. 126–127.5°, $[\alpha]D$ +56°. The low rotation was ascribed to contamination by methyl levopimarate, $[\alpha]^{25}D$ −268°, formed by partial dehydration of **11a** or **11b** during the recrystallization from the high-boiling polar solvent. Several recrystallizations from ether–petroleum ether then furnished material, m.p. 127–128°, $[\alpha]^{25}D$ +51°, infrared bands at 3620 and 1725 cm.$^{-1}$, identical in all respects with the major product produced by the hydroboration of methyl levopimarate (*vide infra*). The n.m.r. spectrum was superimposable on that of **11a**, but had an additional methoxyl resonance at 3.68 p.p.m.

Anal. Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25; O, 14.35. Found: C, 75.35; H, 10.39; O, 14.23.

Hydrogenation of 1.5 g. of **2a** in 100 ml. of acetic acid with 0.3 g. of platinum oxide at 20 p.s.i. followed by filtration and dilution with water resulted in precipitation of 0.9 g. of product which after recrystallization from ethanol–water had m.p. 170–174°; $[\alpha]D$ +8° probably represented a somewhat impure tetrahydroabietic acid, several isomers of which are reported in the literature[30]; n.m.r. signals at 0.80 and 0.89 (broadened doublet of isopropyl group), 0.87 (C-10 methyl) and 1.19 p.p.m. (C-4 methyl). There were no signals characteristic of vinylic or allylic protons.

Δ^7-12-Keto-13αH-abietenoic Acid (15).—One milliliter of the standard Sarett reagent (made by adding 0.3 g. of chromium trioxide to 3 ml. of pyridine) was added to a solution of 0.1 g. of **12**. After 10 hr. the solution was acidified with dilute hydrochloric acid and extracted with ether. The ether extract was thoroughly washed, dried, and evaporated. The crude product from two runs was chromatographed over 10 g. of alumina. Elution with benzene–ether (2:1) furnished 0.15 g. of **15** which was recrystallized from acetone, yield 0.09 g., m.p. 164–165°, $[\alpha]^{25}D$ +193° (*c* 1.04), λ_{max} 288 mμ (ϵ_{max} 141). The infrared spectrum had one broad band centered at 1715 cm.$^{-1}$ (ketone and carboxyl). The n.m.r. spectrum exhibited signals at 0.83 and 0.92 (slightly broadened doublet of isopropyl group) superimposed on the C-10 methyl resonance at 0.92, 1.26 (C-4 methyl), and 5.59 p.p.m. (br, H-7); o.r.d. curve (*c* 0.11, methanol) $[\alpha]_{589}$ +101°, $[\alpha]_{310}$ +2680°, $[\alpha]_{268}$ −1512°.

Anal. Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50; O, 15.07. Found: C, 74.93; H, 9.28; O, 15.87.

The methyl ester was prepared with diazomethane in the usual manner and melted at 90–91° after recrystallization from methanol–water. Its n.m.r. spectrum had the same signals as **15** and an additional methoxyl resonance. Isomerization with sodium methoxide furnished the noncrystalline ester of **14**.

Δ^7-12-Keto-13βH-abietenoic Acid (14).—A solution of 0.1 g. of **15**, 0.05 g. of sodium, and 25 ml. of methanol was refluxed for 5 hr. in a nitrogen atmosphere, cooled, diluted with water, acidified, and extracted with ether. The ether extract was washed, dried, and evaporated and the residue chromatographed over 5 g. of alumina. Elution with benzene–ether gave, after recrystallization from petroleum ether, 0.05 g. of **14**, m.p. 142–146°. Further recrystallizations from methanol–water raised the melting point to 154–156°, $[\alpha]^{25}D$ +100° (*c* 0.37). The n.m.r. spectrum had signals at 0.89d (*J* = 7) and 0.92d (*J* = 7, isopropyl group), 0.91 (C-10 methyl), 1.29 (C-4 methyl), and 5.58 p.p.m. (c, H-7).

Anal. Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50; O, 15.07. Found: C, 75.20; H, 9.57; O, 15.31.

The methyl ester could not be obtained in crystalline form. Its n.m.r. spectrum had the same signals as that of **14** and an additional methoxyl resonance at 3.68 p.p.m.

12-Keto-8α,13αH-abietanoic Acid (18a).—A solution of 1.0 g. of **10a** in 22 ml. of ice-cold acetone was oxidized with 1.1 ml. of Jones' reagent (aqueous chromic acid) with cooling and stirring. After 10 min. a little methanol was added, and the solution was diluted with water and extracted with ether. The ether extract was washed and dried and the residue recrystallized from ether–petroleum ether and methanol–water to yield 0.6 g. of **18a**: m.p. 176–178°; n.m.r. signals at 0.85d and 0.92d (*J* = 7, isopropyl group), 0.85 (C-10 methyl), and 1.15 p.p.m. (C-4 methyl).

Anal. Calcd. for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06; O, 14.98. Found: C, 74.66; H, 9.79; O, 15.41.

The methyl ester **18b** was prepared with diazomethane in the usual manner. One recrystallization from methanol–water furnished **18b**: m.p. 116°; $[\alpha]^{23}D$ +41° (*c* 1.37); o.r.d. curve (*c* 0.195, methanol) $[\alpha]_{589}$ +21°, $[\alpha]_{305}$ +398°, $[\alpha]_{269}$ −29°; infrared bands at 1710 (ketone) and 1720 cm.$^{-1}$ (ester); n.m.r.

(28) This represents a downfield shift of approximately 0.2 p.p.m. when this signal is compared with the C-10 methyl resonance of tetrahydroabietic acids not containing a hydroxyl group.[29] Because the hydroxyl and the C-10 methyl group are separated by four carbon atoms, the only arrangement which can account for the paramagnetic shift is a *cis*-8α,9α-B/C ring fusion in which ring C occupies the chair conformation. All other combinations do not orient the 12α-hydroxyl group sufficiently close to affect the C-10 methyl group. This is of course the stereochemistry which was deduced earlier on chemical grounds.

(29) J. C. W. Chien, *J. Am. Chem. Soc.*, **82**, 4762 (1960), and unpublished work at The Florida State University.

(30) J. Simonsen and D. H. R. Barton, "The Terpenes," Vol. 3, Cambridge University Press, Cambridge, 1952, pp. 374–480; R. Lombard and J. Ebelin, *Bull. soc. chim. France*, **20**, 930 (1953); L. Velluz, G. Muller, A. Petit, and J. Mathieu, *ibid.*, **21**, 401 (1954); E. Royals, W. Bailey, and R. Kenney, *J. Org. Chem.*, **23**, 151 (1958); A. Burgstahler and J. N. Marx, *Tetrahedron Letters* 3333 (1964).

signals at 0.85d and 0.92d (J = 7, isopropyl), 0.85 (C-10 methyl), 1.17 (C-4 methyl), and 3.63 p.p.m. (methoxyl).

Anal. Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.57; H, 10.25.

This substance was also obtained by oxidation of 0.06 g. of **10b** with an excess of ruthenium tetroxide in carbon tetrachloride.[31] After 1 hr. at room temperature the solution was filtered and mixed with a few drops of methanol, filtered again, washed with water, dried, and evaporated. Recrystallization of the residue from methanol–water furnished 0.03 g. of **18b**, m.p. 115–116°.

A solution of 0.1 g. of **18b** was refluxed with sodium methoxide in methanol for 6 hr. The recovered material was recrystallized from methanol–water, yield 0.07 g., identical in all respects with starting material.

Hydroboration of Methyl Levopimarate.—The major product, prepared by following the directions of Dauben and Coates,[14] melted at 123–124°, $[\alpha]^{25}D$ +53° (*c* 1.08), lit.[14] 126–127.5°, $[\alpha]D$ +56°, and was identical in all respects with the sample of **11b** prepared by methylation of **11a** from the hydrogenation of **2a**. The minor product[14] melted at 131–132°, lit.[14] m.p. 133–134°. The n.m.r. spectrum exhibited signals at 0.80 (C-10 methyl), 0.90 and 1.09 (slightly broadened isopropyl doublet), 1.17 (C-4 methyl), 3.62 (methoxyl), and 5.12 p.p.m. (H-14).

Oxidation of 11b.—Oxidation of 1.1 g. of **11b** by the literature method[14] and chromatography of the crude product over 35 g. of neutral alumina gave, in the benzene–petroleum ether (1:1) fraction, 0.65 g. of methyl $\Delta^{8(14)}$-12-keto-13α-H-abietenoate (**16b**), which, as reported previously,[14] did not exhibit a sharp melting point. The n.m.r. spectrum indicated the presence of a single substance, signals at 0.88 and 0.98 (superimposed doublets of isopropyl group), 0.98 (C-10 methyl), 1.20 (C-4 methyl), 2.40 (H-13?), 3.70 (methoxyl), and 5.52 p.p.m. (d, J = 3, H-14). Elution with benzene–petroleum ether (3:1) and benzene gave small amounts of gum. Elution with benzene–ether (20:3) gave 0.265 g. of methyl $\Delta^{13(14)}$-8α-hydroxy-12-ketoabietenoate (**21**) which after recrystallization from high-boiling petroleum ether melted at 135°, $[\alpha]^{23}D$ +29°, λ_{max} 235 mμ (ϵ_{max} 6140). The n.m.r. spectrum had signals at 0.65 (C-10 methyl), 1.01d and 1.04d (J = 7, isopropyl group), 1.13 (C-4 methyl), and 3.68 p.p.m. (methoxyl). Admixture of an authentic sample of **21**, m.p. 135°, $[\alpha]D$ +28°, prepared by the literature method[9] gave no melting point depression, and the n.m.r. spectra of the two samples were identical.

Methyl 12-Keto-8β,13βH-abietanoate (19).—Methyl $\Delta^{8(14)}$-12-keto-13αH-abietenoate (**16b**) was isomerized with sodium methoxide by the literature method[14] to methyl $\Delta^{13(14)}$-12-keto-8βH-abietenoate (**17**) which had n.m.r. signals at 0.93 and 1.04 (superimposed doublets of isopropyl group), 0.93 (C-10 methyl), 1.05 (C-4 methyl), 3.65 (methoxyl), and 6.32 p.p.m. (H-14) and was hydrogenated without further purification. After one recrystallization from methanol–water, the product (**19**) had m.p. 96–97°, lit.[14] m.p. 98.5–99.5°; n.m.r. signals at 0.85d and 0.89d (J = 7 and 6, isopropyl group), 0.93 (C-10 methyl), 1.22 (C-4 methyl), and 3.67 p.p.m. (methoxyl). The physical constants of this material differed from those of **18b** and the melting point was depressed on admixture of **18b**.

Anal. Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.03; H, 10.13.

A solution of **19** in methanol was refluxed for 3.5 hr. with sodium methoxide. The recovered material (65% yield) melted at 95–96° and was identical in all respects with starting material.

Methyl 8α-Hydroxy-12-keto-13αH-abietanoate (22).—A solution of 0.1 g. of **21** in 150 ml. of ethanol was hydrogenated with 0.075 g. of prereduced platinum oxide at atmospheric pressure. After the uptake of 1 mole equiv. of hydrogen, the solution was filtered and concentrated to very small volume. The product which separated on cooling weighed 0.085 g. and was recrystallized twice from methanol–water: 0.06 g.; m.p. 162–164°; o.r.d. curve (*c* 0.046, methanol), $[\alpha]_{589}$ +22°, $[\alpha]_{308}$ +350°, $[\alpha]_{276}$ +230°, $[\alpha]_{250}$ (last reading) 400°; n.m.r. signals at 0.78 (C-10 methyl), 0.84 and 0.92d (J = 7, isopropyl group), 1.15 (C-4 methyl), and 3.68 p.p.m. (methoxyl).

Anal. Calcd. for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78; O, 18.26. Found: C, 71.78, 72.11; H, 9.96, 9.62; O, 18.15, 18.40.

(31) H. Nakata, *Tetrahedron*, **19**, 1959 (1963).

Resin Acids. V. Partial Synthesis of (−)-Rimuane[1,2]

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(−)-Rimuane has been synthesized from isopimaric acid. This defines the absolute configuration of the fully saturated hydrocarbon and hence that of rimuene itself.

The chemistry of the diterpene rimuene **1** has been the subject of many communications[3] but only recently has its structure been elucidated by two groups[4,5] and placed on a firm basis by the total synthesis of *dl*-rimuene by Ireland and Mander.[6] We describe here a partial synthesis of rimuane **2** which defines the absolute configuration at every center of this fully saturated hydrocarbon and hence that of rimuene itself.

Our starting material was the known γ-lactone **5**[7] obtained in two steps from naturally occurring isopimaric acid **3**[8] of known absolute configuration (Chart I).[9] Hydrolysis of **5** with potassium hydroxide in refluxing diethylene glycol[16] afforded the acid **6** whose n.m.r. and infrared spectra confirmed the presence of a trisubstituted double bond rather than the alternate tetrasubstituted $\Delta^{5(10)}$ isomer. This acid resisted catalytic hydrogenation with such catalysts as platinum oxide in acetic acid or ruthenium dioxide in ethanol but, in the former case, traces of lactone **5** were detected by infrared spectroscopy in the recovered material. Be-

(1) Previous paper: W. Herz, H. J. Wahlborg, W. D. Lloyd, W. H. Schuller, and G. W. Hedrick *J. Org. Chem.*, **30**, 3190 (1965).

(2) Supported in part by grants from the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Foundation (GP-1962).

(3) For leading references see ref. 4.

(4) R. E. Corbett and S. G. Wyllie, *Tetrahedron Letters*, **No. 29**, 1903 (1964).

(5) J. D. Connolly, R. McCrindle, R. D. H. Murray, and K. H. Overton, *ibid.*, **No. 29**, 1983 (1964).

(6) R. E. Ireland and L. N. Mander, *ibid.*, **No. 46**, 3453 (1964).

(7) O. E. Edwards and R. Howe, *Can. J. Chem.*, **37**, 760 (1959).

(8) Isolated from WW gum rosin by the method of D. E. Baldwin, V. M. Loeblich, and R. V. Lawrence, *J. Org. Chem.*, **23**, 25 (1958).

(9) The structure and *relative* stereochemistry of isopimaric acid is represented[10,11] by **3**. Correlation[12,13] of isopimaric acid with sandaracopimaric acid, whose absolute stereochemistry has been defined by correlation with testosterone[14] and 3-acetoxyandrost-5-en-17-one,[15] therefore establishes that the *absolute* stereochemistry of isopimaric acid is also represented by **3**.

(10) W. Antkowiak, J. W. ApSimon, and O. E. Edwards, *J. Org. Chem.*, **27**, 1930 (1962).

(11) R. E. Ireland and J. Newbould, *ibid.*, **28**, 23 (1963).

(12) O. E. Edwards, A. Nicolson, and M. N. Rodger, *Can. J. Chem.*, **38**, 663 (1960).

(13) J. W. ApSimon, B. Green, and W. B. Whalley, *J. Chem. Soc.*, 752 (1961).

(14) A. K. Bose and S. Harrison, *Chem. Ind.* (London), 254 (1963).

(15) M. Fétizon and M. Golfier, *Bull. soc. chim. France*, 167 (1963).

(16) L. Van Thoi and J. Ourgaud, *ibid.*, 209 (1956).