The products of *trans*-CHDMDA oxidation which were identified support the premise of hydroperoxide **3** and its associated alkoxy radical **5** as major intermediates (Scheme I).

Whether **5** arises from thermolysis of **3** or from a nonterminating reaction of peroxy radicals during the oxidation cannot be determined with the limited data of this investigation. The rapid autocatalysis of the oxidation and the near zero order in added initiator suggest a facile cleavage of **3** to radicals. The unidentified products found by the glpc analysis are assumed to result from ring cleavage of radical **5** to radical **7** and so on or, possibly, from radical attack at the secondary ring hydrogens of the CHDMDA.

The amount of acid titrated in the oxidized *trans*-CHDMDA mixture increases almost proportionately to increasing conversion. However, the production of **4** falls far short of accounting for the acid formed (top line of Scheme I), even if it is assumed that the formaldehyde is quantitatively oxidized to formic acid.[1] Clearly, there are other sources of carboxylic acid in the oxidation mechanism.

The results of this and other investigations indicate that a multiplicity of products may be generated from the autoxidation of simple bifunctional esters. Much more work will be required to identify and authenticate all of the elementary steps of the oxidation mechanism of esters.

Registry No.—**4**, 33904-15-3; *trans*-1,4-cyclohexylenedimethylene diacetate, 10412-78-9; 4-*oxo*-methylenecyclohexylmethyl acetate, 33904-17-5.

Resin Acids. XXIII. Oxidation of Levopimaric Acid with Potassium Permanganate and Osmium Tetroxide[1,2]

WERNER HERZ* AND R. C. LIGON

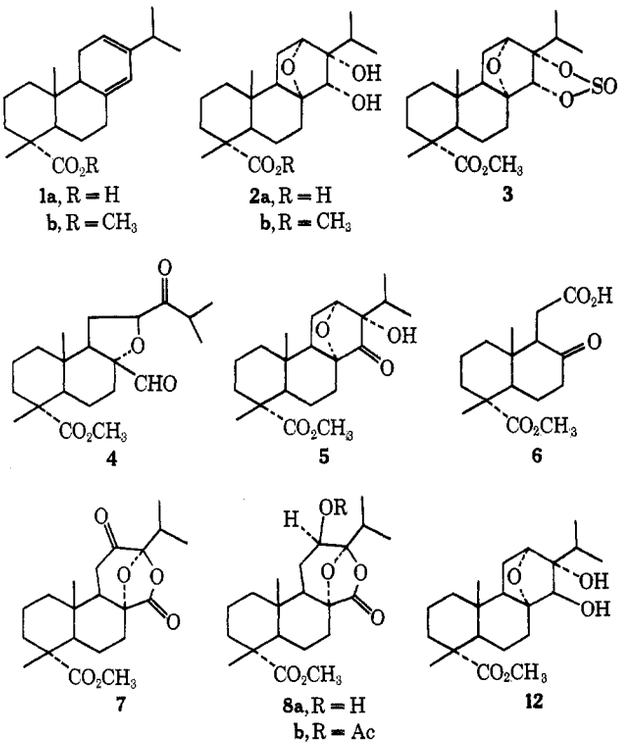
Department of Chemistry, The Florida State University, Tallahassee, Florida 32306

Received October 29, 1971

Structures have been deduced for the products resulting from the $KMnO_4$ and osmium tetroxide oxidation of levopimaric acid. The major product of $KMnO_4$ oxidation is 8α(12α)-oxido-13α,14α-dihydroxyabietan-18-oic acid (**2a**). The compounds produced by osmium tetroxide of methyl levopimarate are methyl 8α,14α-dihydroxyabiet-12-en-18-oate (**16**), methyl 12α,13α-dihydroxyabiet-8(14)-en-18-oate (**13**), and methyl 8α,12α,13α,14α-tetrahydroxyabietan-18-oate (**15**). The preparation of other enediols, epoxydiols, and tetraols derived from levopimaric acid is described.

Structure **2a** (exclusive of stereochemistry) was proposed after prolonged controversy[3] by Wienhaus and Marchand[4] for the major product resulting from the oxidation of levopimaric acid (**1a**) with aqueous permanganate. This formula has been generally accepted, but the evidence for the gross structure was not decisive and the stereochemistry assigned to it more recently on a provisional basis[5] remained unproved.[6] In the present communication we produce conclusive proof for formulation of this substance as **2a**. We also show that earlier structure assignments[8] for the diols obtained by osmylation of methyl levopimarate (**1b**) require correction.

Potassium Permanganate Oxidation.—The nmr spectrum of **2b**, obtained in 30% yield by oxidation of levopimaric acid followed by esterification, was in excellent agreement with the gross structure assigned to it by the German workers.[4] The presence of a secondary hydroxyl group on a carbon next to two tertiary centers and of an ether oxygen linking a tertiary and secondary carbon atom next to a methylene group was indicated by a doublet (J = 3 Hz) at 4.05 ppm, which collapsed to a singlet on addition of D_2O, and a multiplet at 3.30 ppm. The cis nature of the diol was easily established by the formation of a sulfite ester



(1) Previous paper: W. Herz and V. Baburao, *J. Org. Chem.*, **36**, 3899 (1971).

(2) Supported in part by grants from the National Science Foundation (GP-12582) and the Petroleum Research Fund, administered by the American Chemical Society (508-A1).

(3) For a review of work prior to 1953, see J. Simonsen and D. H. R. Barton, "The Terpenes," Vol. III, 2nd ed, Cambridge University Press, New York, N. Y., 1952, p 438; Vol. V, 1957, pp 604–610.

(4) H. Wienhaus and B. Marchand, *Chem. Ber.*, **91**, 401 (1958).

(5) H. Kanno, W. H. Schuller, and R. V. Lawrence, *J. Org. Chem.*, **31**, 4138 (1966).

(6) Especially so since the structure of levopimaric acid dioxide, whose transformation products were compared with the transformation products of **2a**, has had to be revised.[7]

(7) W. Herz, R. C. Ligon, H. Kanno, W. H. Schuller, and R. V. Lawrence, *J. Org. Chem.*, **35**, 3338 (1970).

(8) B. Marchand, *Chem. Ber.*, **91**, 407 (1958).

3 and by facile cleavage of **2b** with lead tetraacetate to a product which had properties commensurate with formula **4**. The nmr spectrum of **4** displayed the signal of the C-10 methyl group at relatively high field. This value is reasonable if the C-10 methyl group is in a 1,3-diaxial relationship to the new aldehyde carbonyl, a situation possible only if the oxide bridge of **2b** is α oriented.

To confirm this deduction and to establish the relative orientation of the hydroxyl groups to the oxide bridge, attempts were made to oxidize **2b** to the ketol **5**. These experiments met with little success at first.[9] Acidic Cr(VI) reagents led to products arising from cleavage of the diol grouping. The main product (70%) was identified as the keto acid ester **6**, which has been obtained more directly by Lemieux–Rudloff and RuO_4–$NaIO_4$ oxidation of **1b**,[10] by exhaustive ozonolysis of **1b** followed by oxidative work-up,[10] and by lead tetraacetate–Jones oxidation of **2b**.[10] Two other compounds which were formed in variable amounts also resulted from cleavage of the diol system and contributed to an understanding of the path by which **6** was formed.

One of these had structure **7** on the basis of the empirical formula $C_{21}H_{30}O_6$ and spectral data. The infrared spectrum exhibited three carbonyl bands at 1790, 1732, and 1721 cm^{-1}, indicating the presence of strained lactone, ketone, and ester groups. The presence of a ketone was further verified by the CD curve. Since the nmr spectrum displayed no resonance below 2.6 ppm other than that of the methyl ester function, the only possible structure was **7**. The stereochemistry of **7** was inferred from that subsequently deduced for the starting material **2b** and was corroborated by the weak positive Cotton effect, which is in excellent agreement with the octant diagram (Figure 1).

The third product, $C_{21}H_{32}O_6$, isolated from the chromic acid oxidation of **2b**, was also produced by reduction of **7** with sodium borohydride and could therefore be assigned formula **8a**. Its nmr spectrum had a new broad multiplet at 3.80 ppm ($W_{1/2}$ = 20 Hz) which sharpened on addition of D_2O and appeared as a doublet of doublets (J = 10, 6 Hz) at 4.97 ppm in the nmr spectrum of **8b**. Inspection of a model of **7** indicates that hydride attack should occur on the α face of the molecule and produce a β-oriented hydroxyl group. This is in accord with the nmr spectrum of **8b**. The observed couplings (10, 6 Hz) fall within the ranges expected for axial–axial (8–13 Hz) and axial–equatorial (2–6 Hz) couplings for six-membered rings in the chair conformation.[11]

Chromic acid induced cleavages of vicinal secondary–tertiary diols have been reported previously,[12] although oxidation to a hydroxy ketone is usually the dominant reaction. In the case of **2b**, however, inspection of the model shows that the two hydroxyl groups are ideally suited for formation of a cyclic chromate ester, the initial step in the path by which ditertiary 1,2-glycols are cleaved.[13,14]

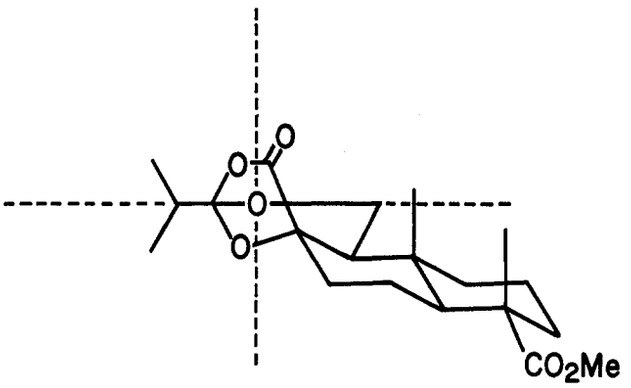
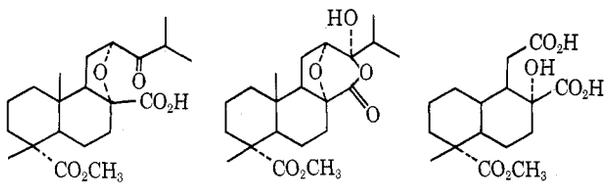


Figure 1.—Octant diagram of **7**.



9 **10** **11**

The desired ketol **5** was eventually prepared in low yield by the method of Walker,[12] which employs manganous ion to suppress the cleavage reaction. Subsequently the yield of **5** was improved by utilizing chromium trioxide–acetic anhydride in benzene.[15] The C-10 methyl resonance of **5** appeared at 0.71 ppm, a chemical shift similar to that of **4**. Inspection of models showed that the C-10 methyl group is in the shielding cone of the carbonyl group at C-14 only if the oxide bridge is α oriented. The CD curve of the ketol exhibited a negative Cotton effect, which is in accord with the octant diagram (Figure 2).

Sodium borohydride reduction of **5** afforded a new diol **12**[19] which must differ from **2b** at C-14. This was confirmed by the infrared spectrum, which indicated a trans relationship of the two hydroxyl groups (two bands at 3420 and 3310 cm^{-1}, nonbonded and bonded hydroxyl). The C-10 methyl group, whose signal appeared at 0.93 ppm, was deshielded by 7 Hz in comparison with the C-10 methyl group of **2b**. It follows[20] that the C-14 hydroxyl group of **12** is β and

(9) Oxidations which require removal of the proton at C-14 by a base in the initial step (Pfitzner–Moffat, Albright–Goldman, and modifications thereof) resulted in complete recovery of starting material. Inspection of molecular models indicates that, if the stereochemistry is as depicted in **2b**, approach to H-14 by a base is severely restricted by the C-10 methyl group. Attempts to oxidize **2b** with Sarett's or Collins' reagent also resulted in recovery of starting material. The reason for this is not readily apparent but may be due to an increase in the bulk of the oxidizing agent (association of two pyridine molecules with the chromium species) which inhibits formation of a chromate ester.

(10) (a) S. W. Pelletier, K. N. Iyer, C. W. Chang, and A. Ogiso, *Tetrahedron Lett.*, 3819 (1968); (b) S. W. Pelletier, K. N. Iyer, and C. W. Chang, *J. Org. Chem.*, **35**, 3535 (1970).

(11) L. M. Jackman and S. Sternhell, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, Elmsford, N. Y., 1969, p 288.

(12) B. H. Walker, *J. Org. Chem.*, **32**, 1098 (1967).

(13) J. Roček and F. H. Westheimer, *J. Amer. Chem. Soc.*, **84**, 2241 (1962).

(14) If this is so, the presumed intermediate **9** is formed *via* **4** rather than by cleavage of **5**. Rearrangement of **5** to **8a**, perhaps by way of the pseudo-acid **10**, is followed by oxidation to **7**. Further oxidation of **7** or its open-chain equivalent furnishes **11** and then **6**.

(15) The success of these experiments leads to the conclusion that at least part of the cleavage of **2b** to **6**, **7**, and **8a** is due to the presence of Cr(IV), since the reactivity of this species is suppressed under these conditions.[12,16] That Cr(IV) is responsible for oxidative cleavage of secondary alcohols which contain a quaternary center has been demonstrated recently.[17,18]

(16) K. B. Wiberg and S. K. Mukherjer, *J. Amer. Chem. Soc.*, **93**, 2543 (1971).

(17) J. Roček and A. E. Rudkowsky, *ibid.*, **90**, 2986 (1968).

(18) P. M. Nave and W. S. Trahanovsky, *ibid.*, **92**, 1120 (1970).

(19) The structure of a compound to which this formula was ascribed previously[5] has been revised.[7]

(20) R. F. Zürcher, *Helv. Chim. Acta*, **46**, 2054 (1963).

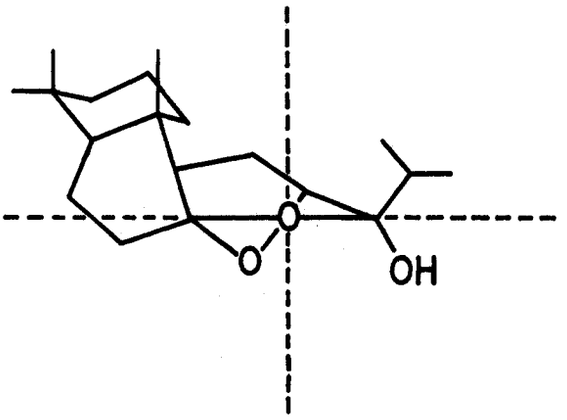


Figure 2.—Octant diagram of **5**.

that of **2b** is α. This is eminently reasonable, since inspection of models shows that hydride attack on **5** should occur exclusively from the α side. Therefore the stereochemistry of the permanganate oxidation product of levopimaric acid is correctly represented by **2a**.

Osmium Tetroxide Oxidation and Related Topics.—Marchand[8] reported that osmium tetroxide oxidation of **1b** in diethyl ether–pyridine furnished two dihydroxy esters which could be separated because the solubilities of their osmate ester–pyridine complexes differed. The major product, mp 138–140°, was assigned structure **13**; the minor product, mp 118–120°, formula **14**. Further oxidation of the major product yielded a tetraol formulated as **15**. No evidence was presented to substantiate these assignments.

Because recent work in our laboratory[1] led to the isolation and structure proof of **16**, whose melting point matched that of Marchand's major product, we repeated the osmium tetroxide oxidation of **1b** by the described method. The major product, mp 138–140° (70%), was indeed identical with **16**. The minor product, mp 112–114° (20%), was identified as **13**. A slightly broadened singlet at 5.27 ppm was characteristic of a vinyl proton at C-14, not C-12, and the presence of a multiplet at 3.87 ppm which sharpened on addition of D_2O confirmed that the secondary hydroxyl group was attached to C-12 rather than to C-14. The normal chemical shift of the C-10 methyl resonance (0.78 ppm) indicated α rather than β orientation of the two hydroxyl groups, in agreement with the rule that attack on the α face of levopimaric acid is generally preferred.

Osmylation of **1b** in anhydrous benzene furnished **16** and the tetraol **15**, mp 186–188°, which could also be prepared by further osmylation of **16**. The nmr spectrum of **15** indicated the presence of nine low-field protons, four of which disappeared after deuterium exchange. Of the remaining five, three could be assigned to the methyl ester function (singlet at 3.60 ppm), one to H-14 (singlet at 3.50 ppm), and one to H-12 (somewhat broadened triplet at 3.94 ppm).[21] Conclusive proof for the α orientation of the hydroxyl groups at C-12 and C-13 was provided by the observation that osmylation of **18**[23] and **19**,[7] both of authenticated stereochemistry, furnished **15**.[24,25]

Jones oxidation of **16** gave the ketol **21**, which could be obtained more directly from **2b** by the action of phosphoric acid in refluxing methanol, perhaps *via* β elimination of an intermediate **22**. Sodium borohydride reduction of **21** furnished **23** by attack from the less hindered α face. In accordance with the postulated stereochemistry, the C-10 methyl resonance was deshielded by 7 Hz in comparison with that of **21**.[20] Further confirmation for the orientation of the C-14 hydroxyl group was provided by the observation that **23** resisted acetylation with acetic anhydride–pyridine under conditions which afforded the 14-acetate **17** in quantitative yield. Models show that attack on the secondary hydroxyl group of **23** is severely hindered by the C-10 methyl and the axial hydrogen on C-6, while the secondary hydroxyl group of **16** is easily approached.

Osmylation of **23** gave the tetraol **24** by attack from the less hindered α side. This conclusion was supported by the appearance of the C-10 methyl resonance at 0.97 ppm. Use of Table I, which lists the approximate shielding constants for hydroxyl groups in ring C of 8α-abietanes and is derived from measurements on a number of compounds obtained in the course of our studies of resin acids, affords the same value.[27] Epoxidation of **23** yielded **25**, the stereochemistry of the oxirane being based on analogy to the osmium tetroxide oxidation and on the presence of a narrowly split triplet at 3.27 ppm (H-12). Attempts to cleave the epoxide ring with acid to form a new tetraol resulted in a complex mixture of at least seven components.

TABLE I

SUBSTITUENT SHIFTS FOR C-10 METHYL GROUP IN 8α-ABIETANES[a]

Substituent	J, Hz	Ppm
8α-OH	-5.0 ± 0.5	-0.08
12α-OH	-3.5	-0.06
12β-OH	3.0	0.05
13α-OH	-1.0	-0.02[b]
14α-OH	-3.5	-0.06
14β-OH	3.0	0.05

[a] From nmr spectra run at 60 MHz in $CDCl_3$ solution on at least three compounds. Reference compound is methyl 8α-abietan-18-oate. Positive values indicate shift toward lower field. [b] Two compounds.

The C-12 epimer **27** (H-14 singlet at 5.18, H-12 multiplet at 4.38 ppm) of **19** was formed by sodium borohydride reduction of **26**[23] and underwent spontaneous dehydration at room temperature to **28** (H-14 singlet at 5.64, H-7 multiplet at 5.43, H-12 multiplet at 4.30 ppm), presumably because this relieves the severe interaction between the pseudoaxial hydroxyl

(21) The appearance of this signal was compatible neither with an α-hydroxyl (H-12 β and axial) nor a β-hydroxyl (H-12 α and equatorial) group on C-12 and may reflect distortion of ring C as has been noted in similar compounds.[22]

(22) J. W. Huffman, T. Kamiya, L. H. Wright, J. J. Schmid, and W. Herz, *J. Org. Chem.*, **31**, 4128 (1966).

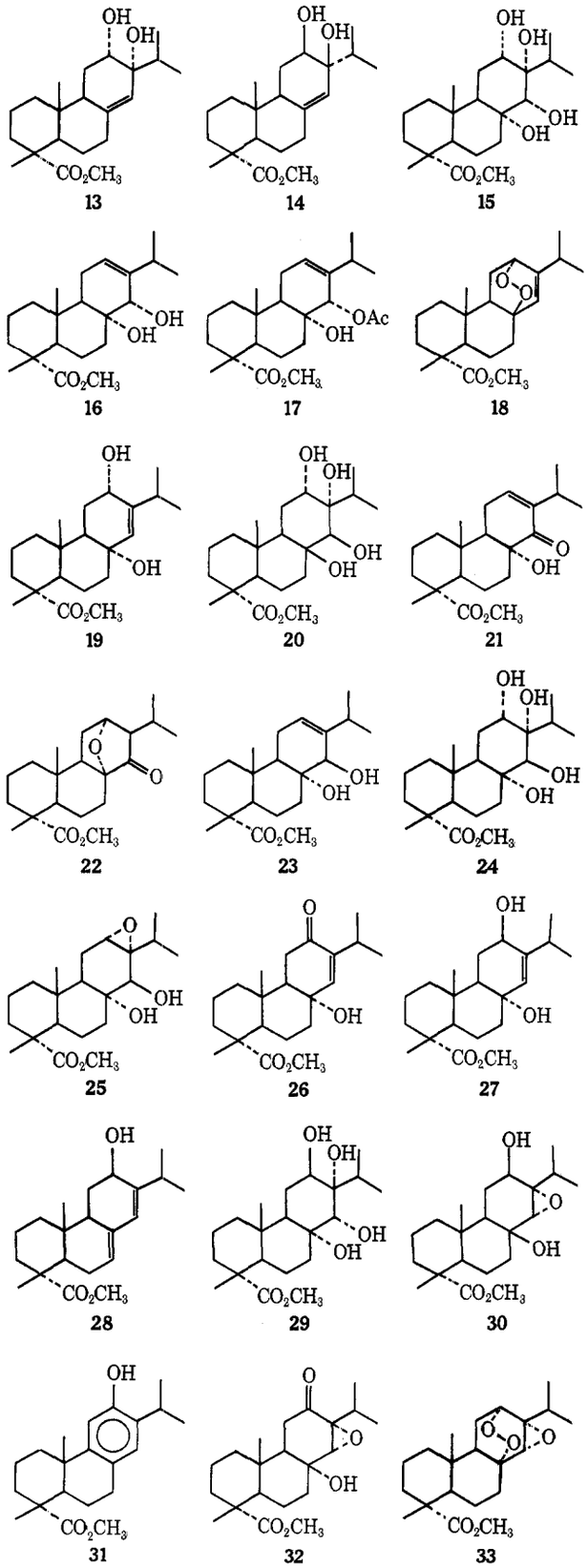
(23) R. N. Moore and R. V. Lawrence, *J. Amer. Chem. Soc.*, **80**, 1438 (1958); **81**, 458 (1959).

(24) Reductive cleavage of the transannular peroxide linkage of **18** was undoubtedly caused by the hydrogen sulfide used to cleave the osmate ester.

(25) Since it has been shown[26] that the double bond of $\Delta^{8(14)}$-abietanes is attacked from the β as well as the α face, it is reasonable to assume that the noncrystalline material obtained by Marchand[8] from the osmylation of the enediol, mp 118–120° (now shown to be **13**), was a mixture of **15** and **20**.

(26) J. W. Huffman, J. A. Alford, and R. R. Sobti, *J. Org. Chem.*, **35**, 473 (1970).

(27) Table I predicts a chemical shift of 0.86 ppm for the C-10 methyl signal of **17**. This is in good agreement with the observed value (0.88 ppm).

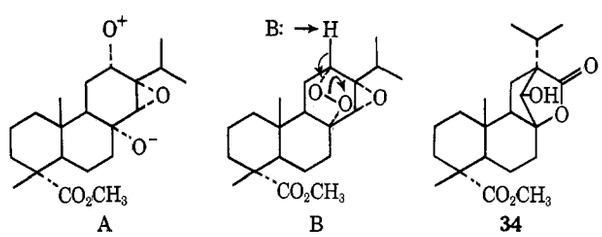


group at C-12 and the C-10 methyl group in **27**. Since **28** differs from methyl 12α-hydroxyabiet-7,13-dienoate,[28] the C-12 stereochemistry of **27** and **28** is as shown.

Osmylation of **27** produced a new tetraol **29** whose nmr spectrum displayed the C-10 methyl signal at anomalously high field (0.85 instead of 0.97 ppm as calculated from Table I). We ascribe this to a conformational change in ring C from a chair to a twist-boat, which minimizes the strong interaction between the C-10 methyl and the axial 12-hydroxyl group. An analogous interaction exists in **24** between the C-10 methyl and the 14-hydroxyl group, but here the interaction would be exacerbated rather than relieved by a conformational change.

Epoxidation of **19** furnished **30**, which had spectral properties in accord with the proposed stereochemistry and exhibited surprising stability toward aqueous acid when attempts were made to convert it to a tetraol. Elevated temperature caused quantitative conversion of **30** to methyl 12-hydroxydehydroabietate (**31**).[23] Oxidation of **30** with Collins' reagent afforded **32**, a substance also obtained quite surprisingly and more conveniently by refluxing **33**[7] in xylene.

The direct thermal conversion of **33** to **32** is difficult to explain in terms of the diradical mechanism discussed for the thermolysis of endoperoxides such as ascaridol,[29,30] but can be rationalized by assuming heterolytic cleavage of the peroxide bond to the zwitterion A, which suffers loss of a proton. This speculation is supported by the observation that substitution of the more polar solvent chlorobenzene for xylene produced a notable increase in the rate of conversion of **33** to **32**. The possibility that catalysis by the glass walls of the reaction vessel might be responsible for the transformation of **33** to **32** through operation of the Kornblum–De La Mare mechanism B[31] was thought to be unlikely as addition of glass helices to increase the surface area did not result in an increased conversion rate. Moreover, it has been shown previously[7] that treatment with alkali transforms **33** into **34**, presumably *via* Favorskii rearrangement of the intermediate, not isolable **32** and subsequent lactonization; this conversion can also be catalyzed by weaker organic bases such as cyclohexylamine.



Experimental Section[32]

Methyl 8α(12α)-Oxido-13α,14α-dihydroxyabietan-18-oate (2b).—To a solution of 60 g of **1a** and 25 g of KOH in 1 l. of

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

(29) J. Boche and O. Runquist, *ibid.*, **33**, 4285 (1968).

(30) K. K. Maheshwari, P. De Mayo, and D. Wiegand, *Can. J. Chem.*, **48**, 3265 (1970).

(31) N. Kornblum and P. De La Mare, *J. Amer. Chem. Soc.*, **73**, 880 (1951).

(32) Melting points are uncorrected. Analyses were carried out by Dr. F. Pascher, Bonn, Germany. Nmr spectra were run on Varian A-60 or Bruker HFX-90 instruments in deuteriochloroform with tetramethylsilane as internal standard, unless specified otherwise. Values for line positions are expressed in parts per million from the standard, coupling constants in hertz. Signals are characterized in the usual way: d, doublet; t, triplet; br, broadened singlet; m, multiplet; c, complex band whose center is given. Singlets are not marked. Ir spectra were run on a Perkin-Elmer Model 257 spectrometer as KBr pellets unless otherwise noted. ORD curves were recorded on a Jasco Model ORD/UV-5 recording spectropolarimeter in methanol solution; rotations were measured in 95% ethanol. Mass spectra were run at 70 MeV on a Nuclide 12 in medium resolution or a MS-902 high resolution mass spectrometer. Silica gel $PF_{254+366}$ (Merck) was used for preparative tlc.

water was added 90 g of $KMnO_4$ in small portions. The mixture was stirred for 1 hr in an ice bath and for 2 hr at room temperature. The MnO_2 formed was decomposed with $NaHSO_3$, the mixture was filtered, and the filtrate was acidified with dilute H_2SO_4. The product was taken up in ether, and the solution was extracted with saturated brine, dried, and partially concentrated *in vacuo*. The concentrated ether solution was methylated with diazomethane and chilled; this resulted in precipitation of **2b**. Further work-up of the mother liquors gave a total of 21.4 g (30%) of **2b**: mp 178–180°; nmr signals at 4.05 (br, sharpens on addition of D_2O, H-14), 3.64 (methoxyl), 3.30 (m, H-12), 1.12 (C-4 methyl), 1.06 (d) and 0.90 (d, J = 7.0 Hz, isopropyl), and 0.91 ppm (C-10 methyl).

Anal. Calcd for $C_{21}H_{34}O_5$: C, 68.82; H, 9.35; O, 22.29. Found: C, 69.03; H, 9.41; O, 22.08.

The sulfite **3** was prepared by dissolving 0.5 g of **2b** in 4 ml of pyridine and adding 2 ml of thionyl chloride dropwise. After 10 min at room temperature, the mixture was poured into water and extracted with ether. The dried ether extracts were evaporated and the residue (**3**) was recrystallized from methanol: yield 0.475 g (85%); mp 153–155°; nmr signals at 5.04 (H-14), 3.68 (methoxyl), 3.32 (t, 3, H-12), 1.19 (C-4 methyl), 1.04 (d) and 1.01 (d, 7, isopropyl), and 0.81 ppm (C-10 methyl).

Anal. Calcd for $C_{21}H_{32}O_6S$: C, 61.15; H, 7.82. Found: C, 61.31; H, 7.86.

Cleavage of 2b with Lead Tetraacetate.—A solution of 0.5 g of **2b** in the minimum amount of benzene was mixed with 0.62 g of lead tetraacetate in 25 ml of benzene, stirred for 1 hr, filtered, and concentrated *in vacuo*. The residue was taken up in ether, washed, dried, and evaporated, but could not be induced to crystallize. The product (**4**) was homogeneous on tlc and had nmr signals at 9.52 (-CHO), 3.65 (methoxyl), 3.28 (m, H-12), 1.15 (C-4 methyl), 0.95 (d) and 0.89 (d, J = 6.5, Hz, isopropyl), and 0.73 ppm (C-10 methyl).

Oxidation of 2b with Chromium Trioxide. A.—To a solution of 1 g of **2b** in 8 ml of acetic acid was added dropwise 0.8 g of CrO_3 in 4 ml of water and then 1 ml of sulfuric acid below 5°. The mixture was stirred for 2 hr, poured into water, and extracted with ether. The washed (bicarbonate, brine, and water) and dried ether extract gave 0.3 g of a gum. Preparative tlc resulted in isolation of two major components. The less polar material **7** was recrystallized from hexane: yield 175 mg (17%); mp 138.5–139.5°; ir 1794 (strained lactone), 1733 (ketone) and 1712, 1258 cm^{-1} (ester); nmr 3.66 (methoxyl), 1.23 (C-4 methyl), 1.00 (d, J = 7 Hz, 6 protons, isopropyl), and 1.01 ppm (C-10 methyl); ORD curve, $[\alpha]_{450}$ +18.1°, $[\alpha]_{320}$ 0°, $[\alpha]_{283}$ −197° (shoulder), $[\alpha]_{245}$ −341°, $[\alpha]_{227}$ 0° (last reading).

Anal. Calcd for $C_{21}H_{30}O_6$: C, 66.65; H, 7.99; O, 25.36. Found: C, 66.72; H, 8.01; O, 25.08.

The more polar substance **8a** was obtained after recrystallization from methanol in 90 mg (8%) yield: mp 174–176°; ir 3465, 1780, 1720, and 1250 cm^{-1}; nmr 3.80 (m, H-12), 3.65 (methoxyl), 1.22 (C-4 methyl), 1.01 (d) and 0.90 (d, J = 7 Hz, isopropyl), and 0.96 ppm (C-10 methyl). The same compound was obtained in 70 mg (70%) yield by $NaBH_4$ reduction of 100 mg of **7**.

Anal. Calcd for $C_{21}H_{32}O_6$: C, 66.29; H, 8.48; O, 25.23. Found: C, 66.31; H, 8.42; O, 25.18.

Acetylation of 0.2 g of **8a** with 3 ml of pyridine and 1 ml of acetic anhydride for 2 hr followed by the usual work-up gave **8b** as a gum which could not be induced to crystallize, but which was homogeneous on tlc.

The bicarbonate extract was acidified and extracted with ether. The usual work-up afforded an oily mixture, yield 0.64 g. Methylation with diazomethane and purification by chromatography gave a crystalline diester, mp 93–94°, yield 70%, which was identical in all respects with an authentic sample of the methyl ester of **6**.

B.—Tlc of the neutral fraction obtained by repetition of oxidation in the presence of 2 ml of a 50% solution of manganous nitrate indicated the presence of an additional component. Preparative tlc and recrystallization from methanol–water afforded 54 mg of **5**: mp 105–106°; ir 3420 (-OH), 1726 (ketone), 1712 and 1233 cm^{-1} (ester); nmr 3.68 (methoxyl), 3.59 m (H-12), 1.11 (C-4 methyl), 0.98 (d) and 0.94 (d, J = 7 Hz, isopropyl), and 0.71 ppm (C-10 methyl); ORD curve, $[\alpha]_{450}$ −22.5°, $[\alpha]_{345}$ −156°, $[\alpha]_{322}$ 0°, $[\alpha]_{293}$ +198°, $[\alpha]_{250}$ +128° (last reading).

Anal. Calcd for $C_{21}H_{32}O_5$: C, 69.20; H, 8.55; O, 21.97, mol wt, 364.2249. Found: C, 68.68; H, 8.77; O, 22.22; mol wt (mass spectrometry), 364.2277.

C.—To a solution of 0.8 g of CrO_3 in 20 ml of acetic anhydride was added 1 g of **2b** in 10 ml of dry benzene. The mixture was stirred at room temperature for 3 hr, poured into water, and extracted with ether. The washed and dried ether extracts were evaporated and subjected to preparative tlc, yield 270 mg (27%) of **4** and 310 mg (31%) of **5**.

Sodium Borohydride Reduction of 5.—A solution of 0.3 g of **5** in methanol was reduced with excess $NaBH_4$. The usual work-up gave, after recrystallization from methanol–water, 0.22 g (73%) of **12**: mp 162–163°; ir 3420, 3315 (-OH), 1722, and 1242 cm^{-1} (ester); nmr 4.73 (d br, J = 5 Hz, H-14, collapses on addition of D_2O), 3.63 (methoxyl), 3.36 (t, J = 2.5 Hz, H-12), 3.11 (d, J = 5 Hz, OH), 1.2 (C-4 methyl), 1.02 (d) and 0.90 (d, J = 7 Hz, isopropyl), and 0.93 ppm (C-10 methyl).

Anal. Calcd for $C_{21}H_{34}O_5$: C, 68.82; H, 9.35; O, 21.83. Found: C, 68.77; H, 9.42; O, 22.16.

Osmium Tetroxide Oxidation of 1b. A.—A solution of 1.4 g of **1b** in 50 ml of anhydrous benzene was oxidized with 1 g of OsO_4 for 3 days. Methanol was added and H_2S was bubbled through the solution for 1 hr. The mixture was filtered and evaporated and the residual gum was chromatographed over silica gel. The less polar material (**16**) was recrystallized from methanol, yield 0.3 g (19%), mp 138–140°. The substance was identical in all respects with **16** described in our earlier publication.[1] The more polar material (**15**) was recrystallized from hexane–ether: yield 0.17 g (10%); mp 186–188°; ir 3400 (strong) and 1722 cm^{-1}; nmr (DMSO-d_6) 3.94 (m, H-12, collapses to t br, J = 6.5 Hz, on addition of D_2O), 3.50 (m, H-14, collapses to singlet on D_2O exchange), 1.10 (C-4 methyl), 0.93 (d, J = 7 Hz, 6 protons, isopropyl), 0.86 ppm (C-10 methyl), and four -OH multiplets.

Anal. Calcd for $C_{21}H_{36}O_6$: C, 65.60; H, 9.44; O, 24.97. Found: C, 66.02; H, 9.14; O, 24.88.

B.—Oxidation of 2.5 g of **1b** by the procedure of Marchand[8] gave, by decomposition of the ether-soluble osmate, 2.1 g (76%) of **16**. Decomposition of the ether-insoluble osmate and recrystallization from methanol–water afforded 0.6 g (21%) of **13**: mp 112–114°; nmr 5.27 (br, H-14), 3.87 (m, H-12), 3.60 (methoxyl), 1.26 (C-4 methyl), 0.91 (d, J = 6.5 Hz, 6 protons, isopropyl), and 0.78 ppm (C-10 methyl).

Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78; O, 18.26. Found: C, 71.97; H, 9.94; O, 17.88.

Acetylation of 0.2 g of **16** in 3 ml of pyridine with 1 ml of acetic anhydride for 1 hr at room temperature followed by the usual work-up gave 0.175 g of **17**, which was recrystallized from hexane: mp 140–141°; nmr 5.77 (br, H-14), 5.60 (m, H-12), 3.61 (methoxyl), 2.13 (acetate), 1.15 (C-4 methyl), 1.01 (d, J = 7 Hz, 6 protons, isopropyl), and 0.88 ppm (C-10 methyl). Under these conditions, **23** was not acetylated and was recovered in quantitative yield.

Osmium Tetroxide Oxidation of 19.—A solution of 1.3 g of **19**[7] in 150 ml of anhydrous benzene was oxidized with 1 g of osmium tetroxide in 20 ml of benzene as described for **1b**. The organic product was recrystallized from hexane–ether, yield 0.43 g (30%), mp 186–188°, identical with **15** prepared from **1b**.

Preparation of 21.—A solution of 0.5 g of **2b** in 100 ml of methanol and 10 ml of 85% phosphoric acid was refluxed overnight, poured into water, and extracted with ether. The washed and dried ether extract yielded 0.2 g (42%) of **21**: mp 159.5–160° after recrystallization from hexane; ir 1728 and 1241 (ester) and 1668 cm^{-1} (unsaturated ketone); nmr 6.59 (t, J = 3.5 Hz, H-12), 3.69 (methoxyl), 2.20 (-OH, disappears on D_2O exchange), 1.10 (C-4 methyl), 1.04 (d) and 1.00 (d, J = 7 Hz, isopropyl), and 0.69 ppm (C-10 methyl).

Anal. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26; O, 18.36. Found: C, 72.19; H, 9.30; O, 18.50.

$NaBH_4$ Reduction of 21.—A solution of 1.5 g of **21** in methanol was reduced with excess $NaBH_4$. When tlc indicated that starting material had been consumed, the solvent was removed at reduced pressure. The residue was extracted several times with hot benzene and the undissolved material (**23**) was recrystallized from hexane: yield 1.29 g (86%); mp 124–126°; ir 3445 (strong) and 1724 cm^{-1} (ester); nmr 5.56 (t, J = 5 Hz, H-12), 3.77 (m, H-14, sharpens on addition of D_2O), 3.60 (methoxyl), 1.12 (C-4 methyl), 1.06 (d) and 1.02 (d, J = 7 Hz, isopropyl), and 0.89 ppm (C-10 methyl).

Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78; O, 18.26. Found: C, 71.78; H, 9.75; O, 18.28.

Osmium Tetroxide Oxidation of 23.—Osmylation of 1.0 g of **23** in anhydrous ether with 1 g of OsO_4 for 24 hr, followed by concentration at reduced pressure, dilution with methanol, decomposition with hydrogen sulfide, and work-up in the usual manner, gave a gum. Recrystallization from hexane–ether afforded 0.21 g (19%) of **24**: mp 197–199°; ir 3415 (strong) and 1725 cm^{-1}; nmr (DMSO-d_6) 3.85 (q, J = 5 Hz, H-12, collapses to t on D_2O exchange), 3.58 (methoxyl), 1.16 (C-4 methyl), 0.96 (d, J = 7 Hz, 6 protons, isopropyl), 0.97 ppm (C-10 methyl), and four OH multiplets.

Anal. Calcd for $C_{21}H_{36}O_6$: C, 65.60; H, 9.44; O, 24.97. Found: C, 65.44; H, 9.25; O, 24.92.

Epoxidation of 23.—A solution of 0.5 g of **23** was allowed to stand with 0.35 g of *m*-chloroperbenzoic acid at room temperature overnight and extracted with sodium bicarbonate solution, water, and saturated brine. The dried organic layer was evaporated and the residue was recrystallized from hexane: yield of **25** 0.32 g (61%); mp 156–158°; ir 3325 (strong) and 1724 cm^{-1}; nmr 3.66 (br, H-14, sharpens on addition of D_2O), 3.58 (methoxyl), 3.27 (t br, J = 2 Hz, H-12), 1.17 (C-4 methyl), 1.00 (d) and 0.88 (d, J = 7 Hz, isopropyl), and 0.90 ppm (C-10 methyl).

Anal. Calcd for $C_{21}H_{34}O_5$: C, 68.86; H, 9.35; O, 21.83. Found: C, 69.20; H, 9.39; O, 21.68.

$NaBH_4$ Reduction of 26.—Reduction of 5 g of **26**[23] with $NaBH_4$ in the manner described for **21** gave, in the hot benzene extracts, a gum which was recrystallized from hexane: yield of **27** 2.65 g (52%); mp 143.5–145°; ir 3458 (strong) and 1705 cm^{-1}; nmr 5.18 (H-14), 4.37 (m, H-12, sharpens on addition of D_2O), 3.60 (methoxyl), 1.17 (C-4 methyl), 1.03 d (J = 7 Hz, 6 protons, isopropyl), and 0.80 ppm (C-10 methyl). This material was converted to **28** on standing in chloroform solution.

Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78; O, 18.26. Found: C, 72.24; H, 9.71; O, 18.15.

Evaporation of the mother liquors of **27** produced a gum which was homogeneous (tlc) but could not be induced to crystallize and was identified as **28** spectroscopically. Its nmr spectrum exhibited signals at 5.64 (H-14), 5.33 (m, H-7), 4.30 (m, H-12, sharpens on addition of D_2O), 3.59 (methoxyl), 2.60 (m, –OH), 1.27 (C-4 methyl), 1.03 (d, J = 7 Hz, 6 protons, isopropyl), and 0.80 ppm (C-10 methyl).

Osmium Tetroxide Oxidation of 27.—Osmylation of 1 g of **27** with 1 g of OsO_4 in anhydrous ether and work-up as described for **23** gave **29** which was recrystallized from hexane–ether: yield 0.23 g (21%); mp 220–222°; ir 3425 (strong) and 1710 cm^{-1}; nmr (DMSO-d_6) 4.1 (t br, 8, H-12), 3.60 (methoxyl, superimposed on H-14), 1.20 (C-4 methyl), 0.93 (d) and 0.88 (d, J = 7 Hz, isopropyl), 0.85 ppm (C-10 methyl), and four OH multiplets.

Anal. Calcd for $C_{21}H_{36}O_6$: C, 65.60; H, 9.44; O, 24.97. Found: C, 65.72; H, 9.16; O, 25.10.

Epoxidation of 19.—Oxidation of 1 g of **19**[7] with 0.7 g of *m*-chloroperbenzoic acid in chloroform at room temperature for 3 hr and work-up as described for **23** gave, after recrystallization from hexane, 0.55 g (52%) of **30**: mp 145–147°; ir 3478, 1705, and 1164 cm^{-1}; nmr 4.28 (t br, J = 6 Hz, H-12, sharpens on addition of D_2O), 3.66 (methoxyl), 3.02 (H-14), 1.23 (C-4 methyl), 1.04 (d) and 0.98 (d, J = 7 Hz, isopropyl), and 0.88 ppm (C-10 methyl).

Anal. Calcd for $C_{21}H_{34}O_5$: C, 68.82; H, 9.35; O, 21.83. Found: C, 68.68; H, 9.45; O, 22.08.

Reaction of 30 With Acid.—A solution of 0.5 g of **30** in 50 ml of tetrahydrofuran and 50 ml of 20% perchloric acid was stirred at room temperature for 2 days. Since tlc examination revealed that only starting material was present, the solution was refluxed on the steam bath for 3 hr, cooled, poured into water, and extracted with ether. The washed and dried ether extract was evaporated. The residual gum solidified on trituration with hexane, yield 60%, mp 156–158°, identified as methyl 12-hydroxydehydroabietate (**31**) by comparison with an authentic sample.[23] The ether mother liquors yielded an additional 30% of **31**.

Preparation of 32. A.—Oxidation of 0.5 g of **30** with Collins' reagent by the procedure of Ratcliffe and Rodehorst[33] and recrystallization of the crude product from hexane gave 0.32 g (64%) of **32**: mp 83–85°; ir 3478, 1728, 1709, and 1245 cm^{-1}; nmr 3.63 (methoxyl), 3.31 (H-14), 1.18 (C-4 methyl), 1.00 (d) and 0.96 (d, J = 7 Hz, isopropyl), and 0.85 ppm (C-10 methyl).

Anal. Calcd for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85; O, 21.95. Found: C, 68.86; H, 8.86; O, 22.09.

B.—A solution of 1 g of **33**[7] in 50 ml of *p*-xylene was refluxed for 20 hr and evaporated at reduced pressure. The residue was taken up in hot hexane and allowed to cool, whereupon crude **32** precipitated. The mother liquors were evaporated, chromatographed over a short alumina column, and evaporated to furnish additional crude **32**. Recrystallization from hexane afforded 0.71 g (71%) of **32**, mp 83–85°.

Rearrangement reactions were run simultaneously on 0.1 g of **33** in 15 ml of xylene, 15 ml of xylene packed with glass beads, and 15 ml of chlorobenzene, the progress of the reaction being followed by tlc. After 4 hr, conversion of **33** to **32** in chlorobenzene was complete, whereas the xylene runs were just beginning to show a detectable amount of **32**.

A solution of 1 g of **33** in 20 ml of cyclohexylamine was refluxed for 3 hr, poured into dilute phosphoric acid, and extracted with ether. The usual work-up and recrystallization from methanol–water afforded 0.85 g (85%) of pure **34**,[7] mp 241–243°.

Registry No.—**1a**, 79-54-9; **1b**, 3513-69-7; **2b**, 34226-16-9; **3**, 34202-06-7; **4**, 34226-17-0; **5**, 34226-18-1; **7**, 34226-19-2; **8a**, 34217-09-9; **12**, 34217-10-2; **13**, 34217-11-3; **15**, 34217-12-4; **21**, 32111-53-8; **23**, 34217-14-6; **24**, 34217-15-7; **25**, 34217-16-8; **27**, 34217-17-9; **28**, 34217-18-0; **29**, 34217-19-1; **30**, 34217-20-4; **32**, 34217-21-5; potassium permanganate, 7722-64-7; osmium tetroxide, 20816-12-0.

(33) R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, **35**, 4000 (1970).

Molecular Rotations of Steroids in Relation to Their Structures. The *S* value of a Hydrogen Atom and That of a Hydroxyl Radical

SHUKICHI YAMANA

Department of Chemistry, Kyoto University of Education, Fushimi-ku, Kyoto, Japan

Received May 14, 1971

S values of the hydrogen atom and of the hydroxyl radical vary discontinuously over a range. The particular *S* value selected from a small set of discrete values depends on influences in the remainder of the molecule which can be transmitted through a coplanar zigzag chain.

Though optical rotatory dispersion and optical circular dichroism of steroids have been investigated actively for about two decades,[1,2] many reports of molecular rotations [M]D of steroids measured at the sodium D line date from earlier periods. Therefore, it is necessary to arrange them and to try to explain (or interpret) them in the framework of a physical theory.

In 1959, Brewster applied his idea of a screw pattern

(1) C. Djerassi, "Optical Rotatory Dispersion, Applications to Organic Chemistry," McGraw-Hill, New York, N. Y., 1960.

(2) For example, see A. I. Scott and A. D. Wrixon, *Tetrahedron*, **27**, 2339 (1971).