# Some Reactions of Levopimaric Acid Dioxide

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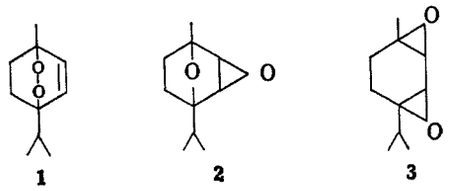
The conversion of levopimaric acid transannular peroxide to levopimaric acid dioxide has been accomplished by treatment with ferrous sulfate as well as thermally. The reaction of the dioxide with acids and bases has been examined and a 1,4:2,3-dioxide structure has been proposed for this compound based on the results obtained. The reaction of levopimaric acid with *m*-chloroperbenzoic acid in aqueous ethanol was found to give 12-$\alpha$-hydroxyabietic acid and 8$\alpha$,12$\alpha$-dihydroxy-$\Delta^{13}$-dihydroabietic acid.

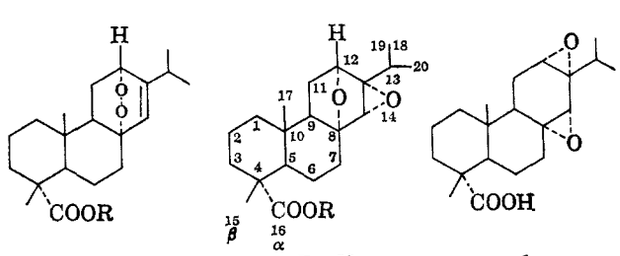
The photosensitized oxidation of $\alpha$-terpinene has been shown to give ascaridole.[2] The same reaction, when applied to levopimaric acid, gave the expected transannular peroxide.[3] When ascaridole (1) is heated in refluxing xylene, a dioxide is obtained (isoascaridole) for which two different structures have been proposed (2 and 3). The 1,4:2,3-dioxide structure (2) was



1 2 3

initially advanced for the compound.[4-6] Later workers accumulated evidence for the 1,2:3,4-dioxide structure[7-9] (3). Still other work may be interpreted in terms of either structure.[10-11] An examination of yields, however, leads to the definite possibility that isoascaridole may actually be a mixture of the two different compounds (2 and 3) as has been considered.[8]

Levopimaric acid transannular peroxide was accordingly refluxed in xylene. A pure compound was obtained,[12] which was tentatively assigned structure 6.



**4a**, R = H
**b**, R = $CH_3$

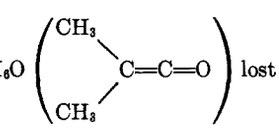
**5a**, R = H
**b**, R = $CH_3$

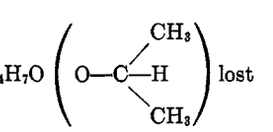
**6**

In the present communication we wish to describe some chemical reactions of the dioxide which suggest that, of the two structures, **5** can be considered to be more probable at the present time.

The mass spectrum of the methyl ester of levopimaric acid dioxide was run. The following peaks were observed which can be interpreted as indicated below:

*m/e* 348, parent peak, P − 16 = 332 or oxygen lost

P − 70 = 278 or $C_4H_6O$  lost

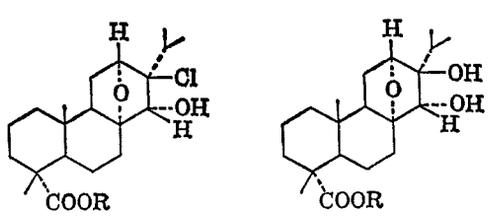
P − 71 = 277 or $C_4H_7O$  lost

This would tend to confirm the assumption that one of the oxygen atoms is attached to a carbon bearing an isopropyl group. Structure **5** might be supported over **6** by the fact that a single oxygen atom is lost and a fragment from which two oxygen atoms are lost is essentially absent from the spectrum.

Levopimaric acid dioxide was found to be relatively stable toward base. It was refluxed for 50 hr in excess cyclohexylamine and was recovered unchanged.

On the other hand, the dioxide was found to react smoothly with acids. Reaction of the dioxide with an excess of hydrogen chloride in ether gave a product containing one atom of chlorine and one secondary hydroxyl group. The infrared spectrum of the cyclohexylamine salt confirmed the fact that the second oxygen atom was not a ketone function. Thus, the two oxide groups in the dioxide would appear to be very different in reactivity.

Treatment of the chloro compound with dilute aqueous alkali very rapidly (3 min) converted the chlorohydrin back to the starting dioxide. On the basis of these results the structure of the dioxide is tentatively assigned as being an 8,12:13,14-dioxide of constitution **5**, and the chlorohydrin of constitution **7**.



**7a**, R = H
**b**, R = $CH_3$

**8a**, R = H
**b**, R = $CH_3$

(1) (a) Research conducted while pursuing a postdoctoral resident research associateship under the auspices of the National Academy of Sciences National Research Council. (b) Or ɔ of the laboratories of the Southern Utilization Research and Development Division (SURDD), Agricultural Research Service, U. S. Department of Agriculture.

(2) G. O. Schenck and K. Ziegler, *Naturwissenschaften*, **32**, 157 (1944); **33**, 356 (1951).

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

(4) H. Thomas and W. Dobke, *Arch. Pharm.*, **268**, 128 (1930).

(5) J. L. Simonsen and L. N. Owen, "The Terpenes," Vol. I, 2nd ed, Cambridge University Press, London, England, 1953, pp 446-451.

(6) A. S. Danilova and G. U. Pigulevskii, *Zh. Obshch. Khim.*, **33**, 2076 (1963); *Chem. Abstr.*, **59**, 10130 (1963).

(7) O. Runquist, *Dissertation Abstr.*, **16**, 2313 (1956).

(8) M. Matic and D. A. Sutton, *J. Chem. Soc.*, 349 (1953).

(9) A. S. Danilova, *Zh. Org. Khim.*, **1**, 521 (1965); *Chem. Abstr.*, **63**, 1819 (1965).

(10) A. S. Danilova and A. I. Kol'tsov, *Zh. Org. Khim.*, **1**, 965 (1965); *Chem. Abstr.*, **63**, 7045 (1965).

(11) A. S. Danilova, *Zh. Org. Khim.*, **1**, 1754 (1965); *Chem. Abstr.*, **64**, 3603 (1966).

(12) W. H. Schuller, J. C. Minor, and R. V. Lawrence, *Ind. Eng. Chem. Prod. Res. Develop.*, **3**, 97 (1964).

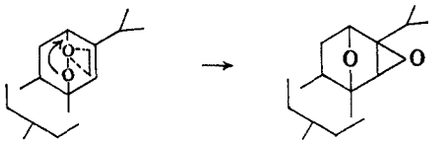
The assignment of the $\alpha$ configuration to the peroxy group in **4** is well established.[13,14] The first-order character of the reaction[12] supports the notion that the rearrangement of the transannular peroxide to a dioxide is intramolecular in nature and that both groups would thus remain in the $\alpha$ configuration. The chlorohydrin (**7**) almost certainly has the hydroxyl located on $C_{14}$ based on the analysis for secondary hydroxyl. The chlorine would then be located in the $\beta$ configuration, or in a *trans* configuration with respect to the hydroxyl group, based on the observation that the attacking anion almost always attacks the protonated epoxide ring from the rear[15-17] (axial attack from the backside). The rapidity of the conversion of the chlorohydrin (**7a**) back to the dioxide (**5a**) in the presence of base is in accord with the expected behavior of *trans*-diaxial halohydrins.[16]

The dioxide **5a** was then found to react smoothly with aqueous sulfuric acid to give a crystalline product in which only one of the oxide rings had opened and which contained only one secondary hydroxyl. The infrared spectrum of the cyclohexylamine salt ruled out the possibility of ketone formation. Again, the very different reactivity of the two oxide groups in the dioxide was apparent. The molecular rotations of the acids, esters, and cyclohexylamine salts of the chlorohydrin and the glycol were essentially the same, strongly indicating that the stereochemistry of the glycol is as indicated in **8a**.

The 8,12:13,14-dioxide structure postulated for **5** well accommodates the experimental findings and the known chemistry of the two kinds of oxide groups present. The stability of the 1,4-oxide or tetrahydrofuran structure toward acidic and basic reaction conditions is well known.[18,19] The stability of 1,2-epoxides ring substituted with several alkyl groups in the presence of base is also known.[20] The ready cleavage of 1,2-epoxides, ring substituted with several alkyl groups, in the presence of acid is well documented.[15] *Both* oxide groups in a 1,2:3,4-dioxide would thus be expected to open in the presence of acid. Instead, the opening of only one oxide ring is observed, as described above.

The dioxide **5a** was dehydrogenated with palladium on carbon at 350° and retene was obtained, indicating that no rearrangement of the resin acid skeleton had taken place during the thermal rearrangement of the peroxide to the dioxide.

It has been reported[21,22] that treatment of ascaridole (**1**) with ferrous sulfate resulted in the formation of the 1,4-oxy-2,3-glycol, postulated as passing through the intermediate 1,4:2,3-dioxide (**2**). Accordingly, levopimaric acid transannular peroxide was treated with ferrous sulfate at room temperature, and a 90% yield of pure levopimaric acid dioxide (**5a**) was obtained. This result also strengthens the assignment of the structure **5a** to levopimaric acid dioxide and would support the notion that no carbon skeleton rearrangement occurs during either reaction. It was of interest to note that this rearrangement did not take place in the presence of nickelous acetate, cuprous chloride, sodium bisulfite, potassium dihydrogen phosphate, ferric sulfate, or sodium bisulfate, respectively. The lack of reaction in the presence of acid salts rules out the possibility that the rearrangement is due to a simple acid catalysis. The rearrangement of the peroxide to a dioxide may properly be called an intramolecular disproportionation. A similarity to the mechanism of Fenton's reagent might seem to exist, in the presence of ferrous iron. A possible pathway for the thermal and the ferrous sulfate initiated rearrangement is pictured below.



**4a** **5a**

The nmr spectra, as summarized in Table I, support the above structural assignments. The proton of the secondary alcohol in the halohydrin ester (**7b**) shows up clearly in carbon tetrachloride solution and is split by the proton attached to the same carbon as the hydroxyl. This tertiary proton is in turn split by the hydroxyl proton. Exchange with deuterium oxide eliminates the hydroxyl proton signals and the tertiary hydrogen doublet collapses into a clean singlet in the same region. The glycol (**8a**) exhibits a downfield shift of the $C_{10}$ methyl from the average value of 0.80–1.00 to 1.31 ppm. The halohydrin (**7a**) exhibits a smaller downfield shift by comparison, to 1.15 ppm. This larger shift in the case of the glycol (**8a**) is presumably due to the affect of the $C_{13}$-$\beta$ hydroxyl. An inspection of Dreding stereomodels shows that this hydroxyl group is in fairly close proximity to the $C_{10}$ methyl. It has been reported[23] that a hydroxyl located in a 1,3-diaxial position to a methyl group results in significant downfield shifts of the C-methyl group signal. The nmr spectrum of levopimaric acid dioxide methyl ester can be interpreted in terms of structure **5b**.

The permanganate oxidation of levopimaric acid in alkaline solution is reported[24,25] to give an 8,12-oxy-13,14-glycol of unassigned stereochemistry. Based on the principal of $\alpha$ attack in the resin acid series[13,14] and the fact that hydroxylation by permanganate results in *cis*-glycol formation, the structure of this compound is believed to be as indicated in **9**.

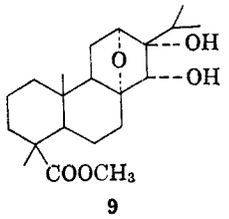
Reaction with dry hydrogen chloride in ether is reported[24] to give a chlorohydrin which is probably of configuration **10** since it clearly is not the same chlorohydrin as **7b**. Thus replacement of the hydroxyl with

(13) W. H. Schuller and R. V. Lawrence, *J. Am. Chem. Soc.*, **83**, 2563 (1961).
(14) W. Herz, H. J. Wahlborg, W. D. Lloyd, W. H. Schuller, and G. W. Hedrick, *J. Org. Chem.*, **30**, 3190 (1965).
(15) R. E. Parker, *Chem. Rev.*, **59**, 737 (1959).
(16) E. L. Eliel, N. L. Allinger, S. J. Angyal, G. A. Morrison, "Conformational Analysis," Interscience Publishers, Inc., New York, N. Y., 1965, pp 100–102.
(17) W. A. Waters, "Mechanisms of Oxidations of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1964, p 43.
(18) N. D. Cheronis and T. S. Ma, "Organic Functional Group Analysis," Interscience Publishers, Inc., New York, N. Y., 1964, p 169.
(19) E. K. Gladding and C. B. Purves, *J. Am. Chem. Soc.*, **66**, 76 (1944); R. Paul, *Bull. Soc. Chem. France*, **53**, 417 (1933); R. Paul, *Compt. Rend.*, **208**, 587 (1939); E. K. Gladding and C. B. Purves, *J. Am. Chem. Soc.*, **66**, 76 (1944).
(20) G. Berti, B. Macchia, and F. Macchia, *Tetrahedron Letters*, 3421 (1965).
(21) E. K. Nelson, *J. Am. Chem. Soc.*, **33**, 1404 (1911).
(22) D. Braun, B. T. Davis, T. G. Halsall, and A. R. Hands, *J. Chem. Soc.*, 4492 (1962).
(23) K. Kuriyama, E. Kardo, and K. Tori, *Tetrahedron Letters*, 1485 (1963).
(24) J. Simonsen and D. H. R. Barton, "The Terpenes," Vol. 3, Cambridge University Press, London, England, 1952, pp 438–439.
(25) H. Wienhaus and B. Marchland, *Chem. Ber.*, **91**, 401 (1958).

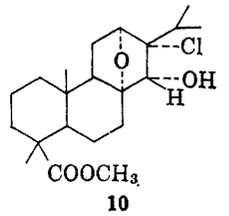
TABLE I
CHEMICAL SHIFTS OF SELECTED PROTONS[a]

| Compound | Solvent | Isopropyl methyls, $J$ = 6–7 cps | $C_{10}$ methyl | $C_4$ methyl | Methoxyl | $H_{12}$ | $H_{14}$ | Other |
|---|---|---|---|---|---|---|---|---|
| vtla[b] | $CDCl_3$ | 1.00 d, 1.13 d | 1.13 | 1.34 | ... | 2.30 t | 5.75[c] | |
| **4a** | $CCl_4$ | 1.08 d, 1.13 d | 0.58 | 1.14 | ... | 4.48 m | 5.82[c] | |
| **4a** | Pyridine | 1.09 d, 1.09 d | 0.59 | 1.37 | ... | 4.75 m | 5.98[c] | |
| **5b** | $CCl_4$ | 0.88 d, 1.08 d | 0.89 | 1.17 | 3.67 | 2.70[d] m | 2.89 | |
| **5b** | $CDCl_3$ | 0.90 d, 1.08 d | 0.88 | 1.18 | 3.62 | 2.84[d] m | 3.01 | |
| **7a** | Pyridine | 1.09 d, 1.15 d | 1.15 | 1.41 | ... | 3.41 t | 3.95 | |
| **7b** | Pyridine | 1.07 d, 1.14 d | 1.08 | 1.25 | 3.60 | 3.38 t | ... | |
| **7b** | $CCl_4$ | 1.00 d, 1.10 d | 1.05 | 1.15 | 3.61 | 3.31 t | 3.42 d, $J$ = 10 | 2.59 d, $J$ = 10, $C_{14}$ hydroxyl |
| **7b** | $CCl_4 + D_2O$ | 1.00 d, 1.11 d | 1.06 | 1.16 | 3.62 | 3.31 t | 3.54 | $C_{14}$ hydroxyl signals disappear in 2.59 region |
| **8a** | Pyridine | 1.08 d, 1.18 d | 1.31 | 1.48 | ... | 3.49 t | 3.64 | |
| **8a** | Pyridine + $D_2O$ | 1.10 d, 1.17 d | 1.30 | 1.18 | ... | 3.60 t | 3.72 | |
| **16a** | Pyridine | 1.17 d (6H) | 0.90 | 1.41 | ... | 4.23 br | 5.62[c] | |
| **16b** | $CCl_4$ | 0.88 d, 0.91 d | 0.78 | 1.16 | 3.62 | 3.76 br | 5.21[c] | 3.12, $C_8$ hydroxyl; 3.30 br, $C_{12}$ hydroxyl |
| **16b** | $CCl_4 + D_2O$ | 0.79 d, 0.89 d | 0.78 | 1.16 | 3.61 | 3.80 br | 5.20[c] | Hydroxyl signals disappear at 3.12 and 3.30 |

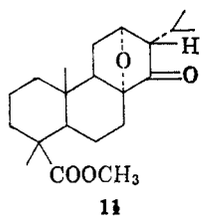
[a] Nmr spectra were run on a Varian A-60 spectrometer. Frequencies are given in parts per million with tetramethylsilane serving as internal standard. Multiplicities are expressed by conventional symbols. $J$ values are in cycles per second. [b] Valence tautomer of levopimaric acid: W. H. Schuller, R. N. Moore, J. B. Hawkins, and R. V. Lawrence, *J. Org. Chem.*, **27**, 1178 (1962). [c] Vinyl hydrogen. [d] Total area 1 proton; best approximation is a doublet superimposed upon a second doublet.



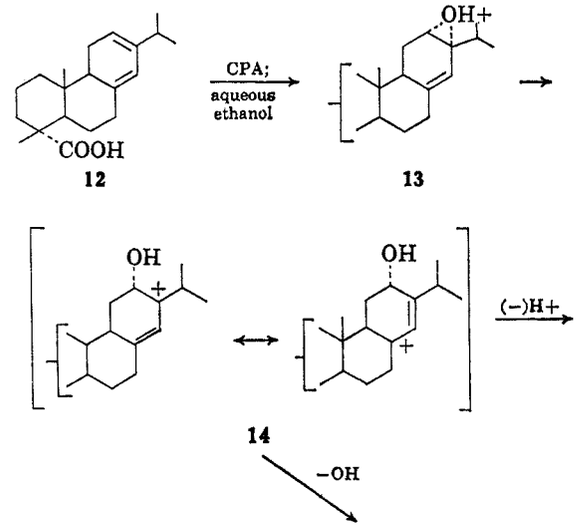

**9**




**10**




**11**




chlorine must take place with retention of configuration. The treatment of the chlorohydrin, **10**, with sodium hydroxide results in the rapid formation of the ketone, **11**, rather than the oxide, owing to *cis* arrangement of the hydroxyl and chlorine atoms.[16] Consideration of Dreiding stereomodels indicates that the isopropyl group would be most stable in the $\alpha$ position in **11**.

It was next considered of interest to prepare, if possible, a levopimaric acid dioxide by direct epoxidation and to determine if it were identical with the dioxide obtained from the rearrangement of levopimaric acid transannular peroxide. Accordingly, the reaction of levopimaric acid with *m*-chloroperbenzoic acid (CPA) was carried out in a variety of organic solvents. No crystalline products could be obtained. A run was made in 80% aqueous ethanol, and a good yield of a mixture of 12$\alpha$-hydroxyabietic acid[14] (**15a**) and 8$\alpha$,12$\alpha$-dihydroxy-$\Delta^{13}$-dihydroabietic acid[14] (**16a**) was obtained. A likely explanation for the course of the reaction is pictured below. The attachment of all hydroxyls in the $\alpha$ configuration in the two compounds further reflects the steric crowding of the $\beta$ side of the resin acid molecule and the preference for $\alpha$ attack.[13,14,17] The nmr spectra of methyl 8$\alpha$,12$\alpha$-dihydroxy-$\Delta^{13}$-dihydroabietate (**16b**) substantiate the structure assigned to this compound.

## Experimental Section[26]

**Levopimaric Acid Dioxide *via* Thermal Rearrangement of Transannular Peroxide 5.**—The *t*-butylamine salt of the dioxide was prepared[12] of $[\alpha]^{25}D$ −60.5° (*c* 0.5); no infrared bands were found in the 5.5–6.0-$\mu$ region (no ketone). The free acid (**5a**) was regenerated using a 1:1 molar amount of phosphoric acid–amine or preferably by using a saturated solution of boric acid.

(26) Melting points are uncorrected. All rotations in 95% ethanol, unless otherwise specified. Analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

The free acid was prepared of $[\alpha]^{25}D$ −76° (*c* 0.4) and exhibited no characteristic absorption from 220–230 mμ in 95% ethanol, in acid, and in basic solution; $\lambda_{max}$ ($CHCl_3$ solution) 5.93 μ, no absorption in the 3-μ region; $\lambda_{max}$ (Nujol mull) 3.12 and 5.85 μ, the band in the 3-μ region being similar to the band observed for neoabietic acid in a Nujol mull and which is not present in solution.[13] The methyl ester[12] (**5b**) of $[\alpha]^{25}D$ −72.4° (*c* 0.60) exhibited no infrared bands in the 3-μ region (no OH).

TABLE II
MASS SPECTRUM OF METHYL ESTER OF LEVOPIMARIC ACID DIOXIDE[a,b]

| *m/e* | % of base peak | *m/e* | % of base peak |
|---|---|---|---|
| 270 | 42.2 | 330 | 74.9 |
| 271 | 49.3 | 331 | 21.8 |
| 273 | 33.1 | 332 | 6.1 |
| 277 | 10.7 | 333 | 26.1 |
| 278 | 23.1 | 348 | 39.5 |
| 287 | 25.1 | | |
| 288 | 31.4 | | |
| 289 | 47.9 | | |
| 301 | 56.2 | | |
| 302 | 23.0 | | |
| 305 | 32.6 | | |
| 306 | 26.0 | | |
| 312 | 22.3 | | |
| 315 | 18.8 | | |

[a] Molecular weight calcd 348.2, found 348.2. [b] Base peak, *m/e* 199.

**Levopimaric Acid Dioxide *via* Ferrous Sulfate Rearrangement of Transannular Peroxide (5a).**—A solution of 0.16 g of ferrous sulfate heptahydrate (0.376 g-atom based on peroxide, 0.00056 mole) dissolved in 0.5 ml of water was added dropwise to a solution of 0.50 g (0.0015 mole) of levopimaric acid transannular peroxide (**5a**) in 4.0 ml of peroxide-free dioxane (solution exhibited pH 4.2). A white solid precipitated out of solution and an exotherm to 36° occurred. After 1 hr at room temperature, 7 ml of water was added. The solid dissolved, a syrup came out of solution which crystallized on rubbing and cooling, yield 0.45 g (90%), $[\alpha]^{25}D$ −79.0° (*c* 1.27), no change in rotation or recrystallization from methanol; infrared spectrum in Nujol mull and in chloroform solution was essentially identical with the spectra of levopimaric acid dioxide (**5a**) prepared thermally above.

*Anal.* Calcd for $C_{20}H_{30}O_4$: C, 71.8; H, 9.0; O, 19.1. Found: C, 71.9; H, 9.2; O, 19.0.

The above experiment was repeated using 0.00056 mole of each of the following salts in place of ferrous sulfate (the pH of the solution, where measured, is given in parentheses): nickelous acetate, cuprous chloride, sodium bisulfite, sodium bisulfate (2.2), potassium dihydrogen phosphate (5.5), and ferric sulfate (2.1). In all cases, the product was isolated and found to be essentially unreacted levopimaric peroxide based on optical rotation and infrared spectrum.

**Dehydrogenation of Levopimaric Acid Dioxide.**—A mixture of 50 mg of levopimaric dioxide (**5a**) and 50 mg of palladium on carbon (5%) was placed in a small test tube and heated in a fluidized sand bath to 350°. No effort was made to prevent loss of material due to volatilization. The product distilled up onto the walls of the tube and was repeatedly washed down with ether, the ether was removed under a nitrogen stream, and the mixture was heated further. Heating was continued in this fashion for a total of 115 min. Extraction of the residue with ether gave 5.9 mg of impure retene: $\lambda_{max}$ (95% ethanol) 249 (α 64.8), 257 (α 70.5), 277 (α 25), 286 (α 19.3), 299 mμ (α 18.2). [Pure retene exhibits $\lambda_{max}$ 250 (α 210), 257.5 (α 290), 279 (α 60), 287.5 (α 48), 300 mμ (α 60).]

**The Reaction of Levopimaric Dioxide with Hydrogen Chloride in Ether.**—A solution of 2 g of levopimaric acid dioxide (**5a**) in 88 ml of 0.2 *N* dry hydrogen chloride in ether was allowed to stand at room temperature until the rotation became constant ($[\alpha]^{25}D$ +25°, 3 hr). After 24 hr the rotation had not changed further. The solution was washed with water until neutral and decolorized with carbon, and the ether was removed, 1.93 g, $[\alpha]^{25}D$ +21° (*c* 0.6, 95% ethanol). Recrystallization of the chlorohydrin (**7a**) from acetonitrile and then from acetone to a constant rotation of $[\alpha]^{25}D$ +48.6° (*c* 0.5) was carried out: MD +180; 0.58 g (26.4%); mp 169–170° dec; no characteristic absorption from 220 to 320 mμ in 95% ethanol, in alkali, and in acid solution; $\lambda_{max}$ (Nujol mull) 2.85 (s), 3.10–3.17 (s), 5.80 (s), 5.92 (s) μ; $\lambda_{max}$ (chloroform solution) 2.87 (m) (OH), 5.92 (s) (acid) μ.

*Anal.* Calcd for $C_{20}H_{31}ClO_4$ C, 64.8; H, 8.4; Cl, 9.6; O, 17.2; neut equiv, 371; secondary alcohol, 4.6. Found: C, 64.6, 64.7; H, 8.3; Cl, 9.6; O, 17.0; neut equiv, 370; secondary alcohol *via* acetic anhydride–pyridine method (110–120° for 12 hr in a bomb tube), 4.9.

The reaction was repeated in refluxing ether containing a large excess of dry hydrogen chloride. The rotation was constant after 3 hr. Refluxing was continued for 20 hr. The same product was obtained as described above in 32% yield of analytically pure material.

The cyclohexylamine salt was prepared in acetone and recrystallized from 95% ethanol to a constant rotation of $[\alpha]^{25}D$ +36.0° (*c* 0.4%); MD +169; yield 80%; mp 175–176° dec; no characteristic absorption from 220 to 320 mμ; $\lambda_{max}$ (Nujol mull) 2.87 (m) (OH), 6.14 (m), and 6.60 (s) (salt) μ, no bands in 5.5–6.0-μ region (no ketone).

*Anal.* Calcd for $C_{26}H_{44}ClNO_4$: C, 66.4; H, 9.4; Cl, 7.5; N, 3.0; O; 13.6; neut equiv, 470. Found: C, 66.3; H, 9.4; Cl, 7.4; N, 2.9; O, 13.7; neut equiv, 473.

The methyl ester of the chlorohydrin (**7b**) was prepared with diazomethane in ether. It was recrystallized to a constant rotation of $[\alpha]^{25}D$ +45.4° (*c* 0.43) from aqueous methanol; MD +174; yield 85%; mp 121–123°; no characteristic absorption from 220 to 320 mμ; $\lambda_{max}$ (Nujol mull) 2.86 (m) (OH), 2.90–2.98 (m) (OH), 5.82 (s) (ester) μ.

*Anal.* Calcd for $C_{21}H_{33}ClO_4$: C, 65.5; H, 8.6; Cl, 9.2; O, 16.6. Found: C, 65.7; H, 8.8; Cl, 9.4; O, 16.5.

**Reaction of 13β-Chloro-14α-hydroxy-8,12α-epoxyabietic Acid (7a) with Base.**—A solution containing 0.85 g of chlorohydrin (**7a**) dissolved in 200 ml of 0.1 *N* aqueous sodium hydroxide was prepared. The reaction was over in 3 min as determined by the change in optical rotation (final $[\alpha]^{25}D$ −63°). After 1 hr the solution was adjusted to pH 6.5 with aqueous phosphate buffer solution and ether extracted exhaustively. The ether solution was water washed, dried, and stripped to dryness: yield 0.70 g of $[\alpha]^{25}D$ −68.5° (c 0.57). The product was recrystallized twice from ethyl ether, with no further change in optical rotation on further recrystallization from aqueous acetonitrile: 0.50 g (82%), $[\alpha]^{25}D$ −80° (*c* 0.34), mp 176–177° dec, no characteristic absorption from 220 to 320 mμ; infrared absorption spectrum in chloroform and in a Nujol mull was identical with the infrared absorption spectrum of authentic levopimaric acid dioxide (**5a**).

*Anal.* Calcd for $C_{20}H_{30}O_4$: C, 71.8; H, 9.0; O, 19.1; neut equiv, 334. Found: C, 71.6; H, 9.1; O, 19.3; neut equiv, 334.

*t*-Butylamine salt had $[\alpha]^{25}D$ −60.5° (*c* 0.50), mp 183–186° dec; infrared spectrum was essentially the same as the infrared spectrum of an authentic sample of the *t*-butylamine salt of levopimaric acid dioxide.

Methyl ester **5b** had $[\alpha]^{25}D$ −75° (*c* 0.43), yield 82%, mp 121°; a mixture melting point with an authentic sample of the methyl ester of levopimaric acid dioxide was not depressed; infrared spectrum of the methyl ester was essentially identical with the infrared spectrum of an authentic sample.

**Reaction of Levopimaric Acid Dioxide with Aqueous Sulfuric Acid (8a).**—To a solution of 30 ml of dioxane and 30 ml of 0.4% aqueous sulfuric acid was added 1.0 g of levopimaric acid dioxide (**5a**). The reaction was over in *ca.* 100 min at room temperature as indicated by the change in optical rotation (final $[\alpha]^{25}D$ +36°). The reaction was first order with respect to diepoxide for the entire period. After 3 hr 100 ml of water was added and the solution was extracted exhaustively with ether. The ether solution was washed with water until neutral, decolorized with activated carbon, and stripped to give 1.02 g of solid of $[\alpha]^{25}D$ +23.2° (*c* 0.95). The crude 13β,14α-dihydroxy-8,12α-oxyabietic acid (**8a**) was recrystallized from aqueous methanol to a constant rotation of $[\alpha]^{25}D$ +47.8° (*c* 0.4); MD +168; 0.29 g, 29%; mp 235° dec; no characteristic absorption from 220 to 320 mμ; $\lambda_{max}$ (Nujol mull) 2.92 (m) (OH), 2.97 (m) (OH), 5.85 (shoulder), 5.96 (s) (acid) μ.

*Anal.* Calcd for $C_{20}H_{32}O_5$: C, 68.2; H, 9.2; O, 22.7; secondary hydroxyl, 4.8; neut equiv, 352.5. Found: 3, 68.3; H, 9.0,

22.9, secondary hydroxyl by acetic anhydide–pyridine method 5.1; neut equiv, 352.5.

The cyclohexylamine salt of the glycol was prepared in acetone. It was recrystallized from 95% ethanol to a constant rotation of $[\alpha]^{25}D$ +35.6 (*c* 0.3); MD +161; 96%; mp 255–265° dec; no characteristic absorption from 220 to 320 mμ; $\lambda_{max}$ (Nujol mull) 2.89 (3) (OH), 6.14 (s) and 6.56 (s) salt) μ, no bands in 5.5–6.0-μ region (no ketone oxygen).

*Anal.* Calcd for $C_{26}H_{45}NO_5$: C, 69.1; H, 10.0; N, 3.1; O, 17.7; neut equiv, 451. Found: C, 69.1; H, 10.1; N, 3.3; O, 17.8; neut equiv, 448.

The methyl ester of the glycol (**8b**) was prepared in ether using diazomethane. It was recrystallized from aqueous methanol to a constant rotation of $[\alpha]^{25}D$ +42.2° (*c* 0.61); MD +154; yield 89%; mp 149–150°; no characteristic absorption from 220 to 320 mμ; $\lambda_{max}$ (Nujol mull) 2.82 (w) (OH), 2.87 (m) OH), 2.97 (m) OH), 5.84 (s) (ester) μ.

*Anal.* Calcd for $C_{21}H_{34}O_5$: C, 68.8; H, 9.4; O, 21.8. Found: C, 68.8; H, 9.2; O, 21.6.

**Reaction of Levopimaric Acid Dioxide with Bases.**—A solution of 0.1 g of levopimaric acid dioxide **5a** was dissolved in 20 ml of dimethylamine (25% in water). No change in optical rotation was observed in 8 days. The solution was heated under a reflux condenser at 65° for 5 hr. No change in optical rotation was observed.

A solution of 1.0 g of levopimaric acid dioxide in 45 g of redistilled cyclohexylamine was refluxed (134°) under prepurified nitrogen for 50 hr. No change in optical rotation was observed. The amine was stripped off under reduced pressure and the free acid was liberated with a 1:1 mole ratio of $H_3PO_4$:amine. The free dioxide was recovered in 95% yield of $[\alpha]^{25}D$ −72° (*c* 0.43). The infrared spectrum in chloroform was essentially identical with the spectrum of the starting material.

A solution of 0.5 g of levopimaric acid dioxide was dissolved in 50 ml of 4 *N* aqueous sodium hydroxide. No change occurred at room temperature over a period of several days. A slow reaction occurred on refluxing the solution, the initial value of $[\alpha]^{25}D$ −68 leveling off at $[\alpha]^{25}D$ −18° after 14 hr. The product could not be crystallized.

**Permanganate Oxidation of Levopimaric Acid.**—The methyl ester of the 1,4-oxyglycol (**9**) was obtained, mp 182° (lit.[24] mp 183°), $[\alpha]^{25}D$ +13.3° (c 1.12, methanol) [lit.[24] $[\alpha]^{25}D$ +13.3° (methanol)], $\lambda_{max}$ (Nujol mull) 3.03 μ (s) (OH). The chlorohydrin (**10**) was prepared: mp 169.5–170° (lit.[24] mp 167°, $[\alpha]^{25}D$ +39.8° (*c* 0.83), $[\alpha]^{25}D$ +41.8 (*c* 0.91, methanol); $\lambda_{max}$ (Nujol mull) 2.92 (m) (OH), 5.87 (s) (ester) μ; no characteristic absorption from 220 to 320 mμ.

**Reaction of *cis*-Chlorohydrin (10) with Sodium Hydroxide.**—To a solution of 0.75 g (0.00202 mole) of the *cis*-chlorohydrin (**10**) in 5 ml of purified dioxane was added 1 ml of 0.5 *N* aqueous sodium hydroxide, solution had pH 9. A second milliliter was added; a slight exotherm was noted to 30°; solution pH fell to 7. Then 1.0 ml of 2 *N* aqueous sodium hydroxide was added (excess) plus 20 ml of dioxane and 7 ml of water. The rotation changed from $[\alpha]^{25}D$ +33° to $[\alpha]^{25}D$ −56° and remained at the latter point for 2 hr. The solution was diluted with excess water, the syrup was rubbed and chilled until it crystallized, 0.56 g (83%), $[\alpha]^{25}D$ −86.4° (*c* 0.80). After recrystallization from methanol the ketone (**11**) exhibited $[\alpha]^{25}D$ −87.7° (*c* 1.0); mp 91–91.5°; no characteristic absorption from 220 to 320 mμ at 0.16 g/l.; $\lambda_{max}$ (Nujol mull) no absorption in 3-μ region (no OH), clearly resolved doublet in carbonyl region at 5.81 (s) and 5.90 (s) (ester and ketone carbonyl) μ.

*Anal.* Calcd for $C_{21}H_{32}O_4$: C, 72.4; H, 9.3; O, 18.4. Found: C, 72.5; H, 9.3; O, 18.2.

The 2,4-dinitrophenylhydrazone of the ketone was prepared, mp *ca.* 206–208° dec, $\lambda_{max}$ (95% ethanol) 371 mμ (ε 16,400).

*Anal.* Calcd for $C_2H_{36}O_7N_4$: N, 10.6. Found: N, 10.8.

**Reaction of Levopimaric Acid with *m*-Chloroperbenzoic Acid.**—To a solution of 15 g (0.05 mole) of levopimaric acid (**12**) in 1275 ml of 80% aqueous ethanol was added 9.7 g of 90% *m*-chloroperbenzoic acid in 75 ml of 80% aqueous ethanol, during stirring at 27° over a 15-min period. The solution was held at 20° for an additional 2 hr. A small amount of aqueous sodium sulfite was then added. The solution was diluted with 1.5 l. of water, and extracted with ether. The ether was washed three times with 150 ml of 2% aqueous sodium bicarbonate to remove the *m*-chlorobenzoic acid, then washed with water until neutral. The solution was stripped to dryness and the residue was crystallized from aqueous ethanol to give 13.15 g (83.5%) of a crude mixture. This was dissolved in absolute ethanol and an ethanol-insoluble substance was filtered off, yield 2.67 g, (16%), $[\alpha]^{25}D$ −10° (*c* 0.11, 95% ethanol). This compound was recrystallized from a large volume of 95% ethanol to a constant rotation of $[\alpha]^{25}D$ −11.5° (*c* 0.07); no characteristic absorption was found from 220 to 320 mμ; infrared absorption spectrum was essentially identical with the infrared absorption spectrum of an authentic sample of 8α,12α-dihydroxy-$\Delta^{13}$-dihydroabietic acid (**16a**);[14] neut equiv theory 336, found 336.

The methyl ester (**16b**) was prepared in ether employing dizaomethane. It was recrystallized from aqueous acetonitrile to a constant rotation of $[\alpha]^{25}D$ −13.3° (*c* 0.18); mp 119–120°; no characteristic absorption from 220 to 320 mμ; $\lambda_{max}$ 2.88 (m) (OH), 5.87 (s) (ester) μ.

A sample of authentic 8α,12α-dihydroxy-$\Delta^{13}$-dihydroabietic acid (**16a**)[14] was treated with diazomethane in ether to give **16b**. It was recrystallized from aqueous acetonitrile to a constant rotation of $[\alpha]^{25}D$ −18.6° (*c* 0.22), mp 119–120°; a mixture melting point with the preceding ester was not depressed; the infrared spectra of the two compounds were essentially identical.

*Anal.* Calcd for $C_{21}H_{34}O_4$: C, 71.9; H, 9.8; O, 18.1. Found: C, 72.0; H, 9.8; O, 18.3.

The mother liquor, from which the ethanol-insoluble glycol had been removed, was first diluted with a small amount of water and then chilled to give 7.15 g (45%) of crude 12α-hydroxyabietic acid (**15a**), $[\alpha]^{25}D$ −127.5° (*c* 0.3). The product was recrystallized from aqueous ethanol to a constant rotation of $[\alpha]^{25}D$ −151.5° (*c* 0.4); yield 4.8 g (32%); mp 161–163° dec; neut equiv 318.2; $\lambda_{max}^{ethanol}$ 236, 242 (α 84.3), 251 mμ; infrared spectrum was essentially identical with the spectrum of an authentic sample of 12α-hydroxyabietic acid.[14]

**Conversion of 8α-12α-Dihydroxy-$\Delta^{13}$-dihydroabietic Acid (16) to 12α-Hydroxyabietic Acid (15a).**—A solution of 0.050 g of 8α,12α-hydroxy-$\Delta^{13}$-dihydroabietic acid in 30 ml of 0.1 *N* sulfuric acid in 80% ethanol was allowed to stand at room temperature for 18 hr. Then 100 ml of distilled water was added and ether extracted, the ether was washed with water until neutral removed: yield 0.048 g; $\lambda_{max}^{ethanol}$ 236, 243 (α 70), 251 mμ.[14] The reaction was repeated in 0.12 *N* hydrochloric acid in 80% ethanol. The reaction was found to be over in less than 15 min as shown by the change in optical rotation.

The reaction was repeated by dissolving 0.07 g of the glycol in 50 ml of 80% ethanol containing 0.27 g of *m*-chlorobenzoic acid. The reaction was followed by the change in optical rotation and over in *ca.* 144 hr. Excess water was added, the mixture was ether extracted, the ether was washed three times with 3.5 ml of 2% sodium bicarbonate solution to remove the *m*-chlorobenzoic acid and washed with water, and the solvent was removed to give 0.068 g: $\lambda_{max}^{ethanol}$ 236, 243 (α 45.5), 251 mμ.[14]

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