Studies on Resin Acids. IV. The Structure, Stereochemistry, and Reactions of Some Dihydroabietic Acids[1]

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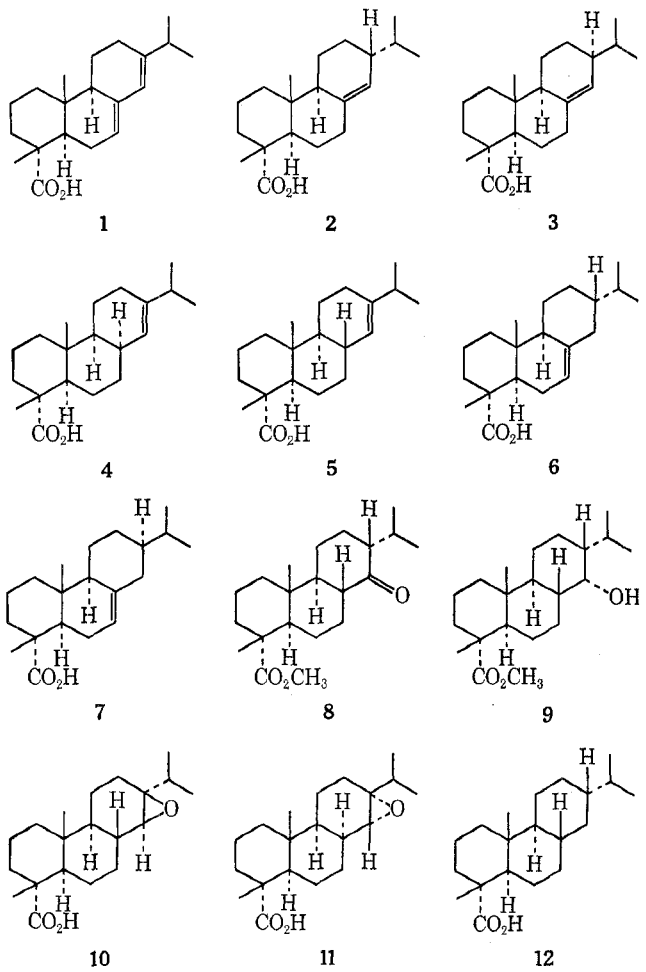
Unequivocal syntheses of 8α-abiet-13-en-18-oic (**4**), abiet-13-en-18-oic (**5**), and abiet-7-en-18-oic acids (**6**) are described. The stereochemical course of various reactions of these compounds as well as those of the two abiet-8-(14)-en-18-oic acids (**2** and **3**) are discussed.

Direct reduction of abietic acid (**1**) by either chemical or catalytic methods may, in theory, give rise to six different dihydro acids (**2**–**7**). At the time this work was initiated, the structure and stereochemistry of only one of these acids (**2**) was known with certainty,[1,3] although a number of other dihydroabietic acids had been prepared and characterized.[4] Following the initiation of this work, we learned that acids **3**, **5**, and **6** had been obtained and identified in addition to **2** from the lithium–ammonia reduction of abietic acid,[5] and structure **7** had been assigned to one of the acids obtained by Velluz, *et al.*[4b] In earlier work in this laboratory, structure **4** had been assigned to the Δ^{13}-dihydro acid, which is present to the extent of *ca.* 15% in most samples of **2** prepared by reduction of abietic acid;[1] however, Burgstahler, Marx, and Zinkel[5] present rather convincing evidence that this impurity is in fact **5**. The earlier assignment of stereochemistry was based on the course of the rearrangement of an epoxide obtained in low yield from the oxidation of a sample of **2** obtained in the usual manner.[1] In order to reconcile this discrepancy, and also to confirm the structural and stereochemical assignments made by Burgstahler, *et al*,[5] the preparation of acids **4**–**6** by unambiguous routes has been carried out.



The synthesis of **5** was accomplished by first reducing the known[1,5] methyl 14-oxoabietan-18-oate (**8**) with sodium borohydride to give the 14α (axial) alcohol (**9**) contaminated with a small quantity of another alcohol, presumably the 14β-ol. The nmr spectrum of **9** was in accord with that expected for an axial alcohol, with H-14 appearing as a broadened singlet at δ 3.72 and the C-10 methyl peak at relatively high field (δ 0.84) as expected for a compound with a *trans* B,C-ring fusion.[1] Dehydration of this alcohol with phosphorus oxychloride–pyridine and hydrolysis of the esters afforded a mixture of the corresponding acids, from which **5** contaminated with a few per cent of **2** could be obtained. The nmr spectrum of **5** was in agreement with the assigned structure, showing the C-10 methyl signal at δ 0.86. Reaction of **5** with *m*-chloroperbenzoic acid gave epoxide **10**, which was markedly different from that reported earlier and assigned structure **11**.[1] By analogy with the hydrogenation of **5**, which affords almost exclusively abietan-18-oic acid (**12**),[1,5] and hydroboration of the methyl ester of **5**, which gives methyl 14β-hydroxyabietan-18-oate (**13**), it is assumed that **10** is the β oxide.

While this work was in progress, Cross and Myers obtained a glycol from the osmylation of the usual mixture of **2** and **4** or **5**[6] to which they assigned structure **14**; however, when acid **5** was treated with osmium tetroxide, a glycol was obtained which was identical with that prepared by Cross and Myers.[7] The nmr spectrum of this glycol showed H-14 as a doublet with a coupling constant of 9 Hz, indicating a *trans*-diaxial relationship between H-8 and H-14, and on

(1) Part III: J. W. Huffman, T. Kamiya, L. H. Wright, J. J. Schmid, and W. Herz, *J. Org. Chem.*, **31**, 4128 (1966). This work was supported in part by Career Development Award GM-5433 from the National Institutes of Health and was presented at the Fifth International Symposium on the Chemistry of Natural Products, London, July 1968.

(2) Abstracted in part from the dissertation presented by J. A. Alford in partial fulfillment of the requirements for the Ph.D. degree, Clemson University, Dec 1968.

(3) A. W. Burgstahler and J. N. Marx, *Tetrahedron Lett.*, 3333 (1964).

(4) (a) R. Lombard and J. Ebelin, *Bull. Soc. Chim. Fr.*, 930 (1953). (b) L. Velluz, G. Muller, A. Petit, and J. Mathieu, *ibid.*, 401 (1954). (c) For a review of work reported prior to 1950, see J. Simonsen and D. H. R. Barton, "The Terpenes," Vol. 3, Cambridge University Press, 1952, pp 374–445.

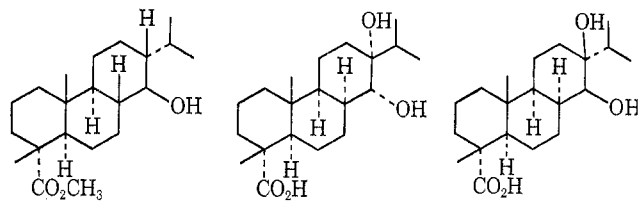
(5) (a) J. N. Marx, Ph.D. Dissertation, University of Kansas, Sept 1965. (b) A. W. Burgstahler, J. N. Marx, and D. F. Zinkel, *J. Org. Chem.*, **34**, 1550 (1969). We would like to thank Professor Burgstahler for sending us a copy of this manuscript prior to its publication.

(6) B. E. Cross and P. L. Myers, *J. Chem. Soc.*, *C*, 471 (1968).

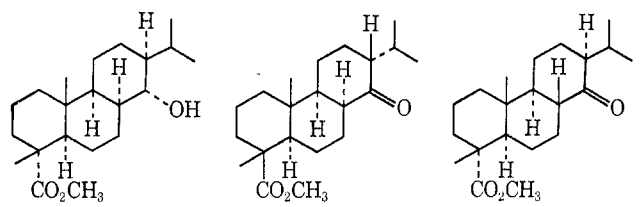
(7) We would like to thank Professor Cross for a sample of this compound.

this basis it must be 13β,14β-dihydroxyabietan-18-oic acid (**15**).[8]

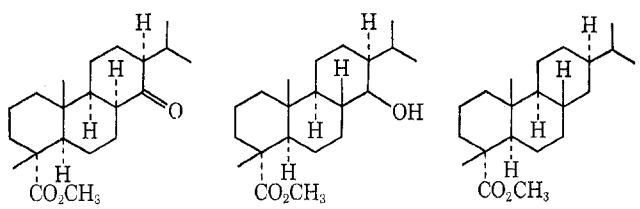
In order to clarify the nature and origin of the epoxide assigned structure **11**, an unambiguous synthesis of **4** and its epoxide was attempted. Hydroboration–oxidation of the methyl ester of **3**[5] gave a mixture of a hydroxy ester and a glycol. This hydroxy ester and its acetate showed C-10 methyl signals in the nmr at δ 1.00 and 1.10, respectively, indicative of a *cis* B,C-ring fusion.[1] Since it is well known that diborane adds to olefins in a *cis* fashion, this compound must be methyl 14α-hydroxyy-8α,13β-abietan-18-oate (**16**), and on this basis of the nmr spectrum the glycol is the 18-ol corresponding to **16**.



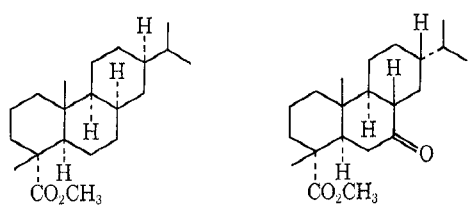
13 **14** **15**



16 **17** **18**



19 **20** **21**



22 **23**

In an effort to confirm the stereochemistry of **16** by chemical means, the 14 tosylate was prepared, with the intention of effecting the conversion of **16** into 8α,13β-abietan-18-oic, acid, using the method described earlier.[1] However, lithium aluminum hydride reduction of the tosylate followed by oxidation with Jones reagent afforded **3** as the only isolable product, the result of elimination of tosylate, rather than displacement by hydride. Lithium–ammonia reduction of the tosylate proceeded with cleavage of the sulfur–oxygen bond and reduction of the ester function to give the glycol obtained as a by-product in the hydroboration of **3**. The examination of models of the tosylate of **16** indicates that the 14 position is extremely hindered to the approach of a reagent from the β side, and this may explain the failure of these reactions to afford the desired product.

In a further effort to confirm the structure and stereochemistry of **16**, it was oxidized to a ketone, employing conditions which were assumed to preclude isomerization at either enolizable position (C-8 or C-14).[9] However, the rotatory dispersion curve of this compound showed a negative Cotton effect of moderate amplitude (−31), rather than the positive Cotton effect predicted by the octant rule for a ketone with a *cis* B,C-ring fusion. The nmr spectrum of this ketone showed a C-10 methyl signal at δ 0.87, intermediate between the position of the corresponding signals for methyl 14-oxoabietan-18-oate (**8**, δ 0.96[1]) and methyl 14-oxo-8α-abietan-18-oate (**17**, δ 0.72[1]). On the basis of the rotatory dispersion curve of this ketone, and the fact that it was isomerized to the stable isomer **8** by base, it was tentatively assigned the 8β,13β-14-oxo structure (**18**), resulting from epimerization at C-8 during oxidation.[10] However, compound **18** was subsequently prepared by Herz and coworkers[11] by an unambiguous route and found to be different from the compound described above. Since there are only four possible ketones with a gross structure corresponding to **8**, and since three of these, **8**, **17**, and **18**, are known,[1,11] the oxidation product of **16** is probably methyl 14-oxo-8α,13β-abietan-18-oate (**19**). This assignment of stereochemistry was further confirmed by a comparison of the chemical-shift differences of the C-10 methyl in compounds **8**, **17**, **18**, and **19**, when the spectra were run in benzene-d_6 and chloroform-*d*. From these data, which are summarized in Table I, it can be seen that Δδ for

TABLE I
C-10 CHEMICAL-SHIFT DATA FOR METHYL 14-OXOABIETAN-18-OATES[a]

	Solvent	
Ketone	Chloroform-*d*	Benzene-d_6
8	0.96,[b] 0.97[c]	0.75,[d] 0.77[c]
17	0.72[b]	0.63[d]
18	0.97[c]	0.70[c]
19	0.87	0.75

[a] All values reported as parts per million relative to tetramethylsilane. [b] Reference 1. [c] Reference 11. [d] J. W. Huffman and T. Kamiya, unpublished work.

the isomers with a *trans* ring fusion is −0.21 and −0.27 for **8**[11,12] and **18**,[11] respectively, while Δδ for **17** is −0.09.[12] A similar comparison of chemical-shift differences for the compound assigned structure **19** was −0.12, indicating that the B,C-ring fusion is *cis*. The anomalous rotatory dispersion curve of **19** may be caused by any one of several factors, but is most probably due to some form of deformation of ring C, brought about by the severe steric interaction between C-14 and the C-10 angular methyl group.

The sodium borohydride reduction of **19** gave essentially one hydroxy ester, which was different from the known 8α,13β,14α-ol (**16**), and was also neither

(8) B. E. Cross and P. L. Myers [*J. Chem. Soc.*, *C*, 711 (1969)] have independently reached the same conclusions. See also ref 5b.

(9) E. J. Corey and R. A. Sneen, *J. Amer. Chem. Soc.*, **78**, 6269 (1956).

(10) Burgstahler, *et al.* (ref 5b), have concluded that this compound is **18**. However, on subsequent reinvestigation this structure has been revised to **19** (A. Burgstahler, personal communication).

(11) W. Herz, personal communication. We would like to thank Professor Herz for carrying out the comparison of these ketones.

(12) Footnote *d*, Table I.

of the epimeric methyl 14-hydroxyabietan-18-oates (**9** and **13**). The nmr spectrum of this alcohol showed a relatively shielded C-10 methyl signal at δ 0.88, indicating a *trans* B,C-ring fusion, and H-14, although at rather low field for an axial proton (δ 3.38), appeared as a very diffuse multiplet ($W_{1/2}$ = 15 Hz), which indicates that this compound has an equatorial hydroxyl group. The only structure consistent with these data is methyl 14β-hydroxy-13β-abietan-18-oate (**20**), and comparison with a sample of this material prepared by Herz and coworkers confirmed this assignment of stereochemistry.[13] An examination of models of **19** indicates that attack by borohydride would be expected to occur from the α side of the molecule to give a 14β-hydroxy ester. However, in this compound there is an extremely severe steric interaction between the angular methyl and hydroxyl group, and under the conditions of the reaction C-8 is isomerized prior to reduction.

With the structure and stereochemistry of **16** clarified, an attempt was made to prepare the still unknown 8α-abiet-13-en-18-oic acid (**4**). Treatment of hydroxy ester **16** with phosphorus oxychloride–pyridine led to a 1:1 mixture of the methyl esters of **3** and a new acid, presumably **4**. Chromatography of this mixture on silver nitrate–silica gel led to the separation of the isomers; however, the methyl ester of the new acid could be obtained only in *ca.* 90% purity. The nmr spectrum of this ester agreed well with that expected for **4**, with H-14 appearing as a multiplet at δ 5.20 and the C-10 methyl protons at δ 0.91.[14] The stereochemistry of the new unsaturated ester was further confirmed when it was found that hydrogenation of the 1:1 mixture of $\Delta^{(8,14)}$ and Δ^{13} esters obtained from the dehydration gave a 1:2 mixture of methyl 13β- (**21**) and 8α,13β-abietan-18-oate (**22**). Since **3** is known to afford a mixture of **21** and **22** (containing 62% **21**[5b]) on hydrogenation, and since **4** would be expected to give nearly exclusively **22**, the hydrogenation data indicate that the new acid is indeed **4**. Reaction of the methyl ester of **4** with *m*-chloroperoxybenzoic acid gave a complex mixture of products; however, a lack of material precluded a detailed study of the course of this reaction. Although it has not been possible to isolate acid **4** from the lithium–ammonia reduction of abietic acid, the reported physical and chemical properties of the compound assigned structure **11** strongly indicate that this compound must indeed be the α oxide derived from **4**, and that acid **4** must be present in the reduction mixture.

During the course of their work on the reduction of abietic acid, Burgstahler and Marx reported the isolation of a 1:1 mixture of abiet-7- and -13-en-18-oic acids (**6** and **5**)[5a] from which the Δ^7 acid was subsequently obtained in pure form by chromatography.[5b] In an effort to effect an alternate separation, we have converted the mixture of acids into the methyl esters and subjected this mixture to hydroboration–oxidation. Chromatography of this mixture gave no effective separation, and it was consequently oxidized to the mixture of 7 and 14 ketones (**23** and **8**). Although this mixture again could not be resolved by chromatography, advantage was taken of the known reluctance of **8** to form carbonyl derivatives[1,5,6] and the mixture was converted into an easily separable mixture of **8** and the oxime of **23**. Hydrolysis of this oxime gave pure **23**, which was identical with a sample prepared by the method of Cross and Myers.[6] The rotatory dispersion curve of **23** showed a negative Cotton effect curve of moderate amplitude, in agreement with the assigned structure.[15] The gross structure of **23** and its stereochemistry at C-13 were confirmed by reduction under Wolff–Kishner conditions to abietan-18-oic acid (**12**). In an effort to convert **23** into the desired abiet-7-enoic acid, it was reduced to a mixture of stereoisomeric 7-ols; however, attempted dehydration with phosphorus oxychloride–pyridine gave an intractable mixture. This conversion was effected *via* the Bamford–Stevens reaction of the tosylhydrazone of **23**, which gave, although in mediocre yield, **6**, the spectral properties of which were in agreement with the indicated structure. Finally, **6** was isolated from its mixture with **5** by recrystallizing their (−)-α-phenethylamine salts.

During the course of this work it became quite clear that the so-called "rule of α attack," which is of considerable utility in the steroid series,[16] is not valid in the dihydroabietic acid series. It has already been noted[1] that additions to the 8,14 double bond in **2** occur almost exclusively from the β side, while this work indicates that in 13β-abiet-8(14)-en-18-oic acid (**3**) additions proceed to a considerable extent from the β side of the molecule.[17] In the Δ^{13} olefins the course of addition reactions is governed by the stereochemistry of C-8, with the 8β isomer (**5**) undergoing virtually exclusive β attack,[6,8] while the 8α isomer (**4**) reacts preferentially (and predictably) from the α face. Insufficient data are available to permit any generalizations concerning the stereochemistry of additions to the Δ^7-abietenes.

Experimental Section[18]

Methyl 14α-Hydroxyabietan-18-oate[19] (**9**).—To a solution of 18.0 g of keto ester **8** in 500 ml of methanol at 0° was added 20.0 g of sodium borohydride in small portions over a period of 10 min. The solution was stirred for an additional 40 min at room temperature. The volume of the methanol was reduced by one-half with the aid of an aspirator, and the mixture was poured into water, extracted with chloroform, and dried. Removal of sol-

(13) W. Herz, personal communication. We would like to thank Professor Herz for a sample of **20**.

(14) The angular methyl group in this compound lies above the plane of the double bond and would be expected to appear at somewhat higher field than if this were not the case. The C-10 methyl signal of methyl 8α-abiet-12-en-18-oate also appears at δ 0.91.[1]

(15) P. Crabbe, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1965, p 44.

(16) L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, p 14, and references cited therein.

(17) W. Herz and R. N. Merrington [*J. Org. Chem.*, **30**, 3198 (1965)] have already noted that additions to methyl pimar-8(14)-en-18-oate acid led to a mixture of 8α and 8β isomers.

(18) Melting points were determined on a Thomas–Hoover melting point apparatus and are uncorrected. Infrared spectra were taken as films or potassium bromide pellets on a Perkin-Elmer Model 137 spectrophotometer. Vapor phase chromatographic analyses were performed on an F & M Model 810 chromatograph, utilizing a 6 ft × 0.125 in. column packed with SE-30 on Chromosorb W. Nuclear magnetic resonance spectra were recorded on a Varian Associates Model A-60 nuclear magnetic resonance spectrometer using deuteriochloroform as solvent and tetramethylsilane as an internal standard. Signals are given in parts per million relative to this standard. Optical rotatory dispersion curves were determined in methanol with a Jasco Model ORD/UV-5 spectropolarimeter. Rotations at the sodium D-line were determined in 95% ethanol using a Rudolph Model 70 polarimeter. Analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

(19) This preparation was originally carried out by Dr. T. Kamiya.

vent *in vacuo* yielded an oil which crystallized on trituration with hexane. Recrystallization from the same solvent afforded 14.3 g (79%) of white needles: mp 104–106°; $[\alpha]D$ +14° (*c* 0.900); nmr 3.72 (br s, H-14), 1.18 (C-4 methyl), 0.92 (d, J = 7 Hz, isopropyl), and 0.84 ppm (C-10 methyl).

Anal. Calcd for $C_{21}H_{36}O_3$: C, 74.95; H, 10.78. Found: C, 74.98; H, 10.69.

Abiet-13-en-18-oic Acid (5).—To a solution of 14.0 g of alcohol **9** in 50 ml of pyridine was added 14.0 g of phosphorus oxychloride. The mixture was protected from moisture with a calcium chloride drying tube and heated on a steam bath for 7 hr. The solution was cooled and carefully poured over 150 g of ice–water, and the excess pyridine was neutralized with hydrochloric acid. The mixture was extracted with methylene chloride, washed with water, and dried. Removal of the solvent afforded 13.1 g (98%) of oil, the nmr spectrum of which indicated that it contained about 10% 8(14) isomer. A solution of 16.0 g of this oil and 40.0 g of anhydrous lithium iodide in 150 ml of dry collidine was heated at reflux under nitrogen for 18 hr. The solution was cooled, poured into 250 ml of ice–water, neutralized with concentrated hydrochloric acid, extracted with methylene chloride, washed with water, and dried. Removal of the solvent afforded 10.0 g of white solid. The nmr spectrum indicated that the mixture contained 90% the desired compound plus 10% 8(14) isomer. After three recrystallizations from acetone, the nmr indicated that the solid product was richer in the 8(14) isomer (**2**), and the filtrates were converted into the diamylamine salt, which was recrystallized three times from acetone. Regeneration of the acid with acetic acid and subsequent recrystallization from acetone afforded 2.4 g of abiet-13-en-18-oic acid:[20] mp 162–164°; $[\alpha]D$ −7.2° (*c* 1.092) (lit.[5b] mp 146–147°; $[\alpha]D$ +6°); nmr 5.09 (br s, H-14), 1.18 (C-4 methyl), 0.97 (d, J = 7 Hz, isopropyl), and 0.86 ppm (C-10 methyl).

Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 79.12; H, 10.80.

Epoxidation of Abiet-13-en-18-oic Acid.—To a solution of 1.5 g of the acid in 25 ml of methylene chloride at 0° was added slowly and in small portions 1.1 g of *m*-chloroperbenzoic acid. The solution was stirred overnight at room temperature and then heated at reflux for 7 hr. The solution was washed twice with 25 ml of 10% sodium bisulfite solution, three times with saturated sodium bicarbonate, and once with water, and dried over magnesium sulfate. After removal of solvent, there was obtained 1.4 g of oil which crystallized from 2-butanone. Recrystallization from acetone afforded 0.75 g of **10** as white needles: mp 226–228°; $[\alpha]D$ +11.2° (*c* 1.163); nmr 2.82 (s, H-14), 1.16 (C-4 methyl), 0.95 (d, J = 6 Hz, isopropyl), and 0.82 ppm (C-10 methyl).

Anal. Calcd for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 74.73; H, 9.87.

Hydrogenation of Abiet-13-en-18-oic Acid.—A solution of 0.100 g of the acid **5** in 19 ml of acetic acid was hydrogenated with 0.050 g of platinum oxide at 59 psi and room temperature. The reaction mixture was filtered through Celite and the product was precipitated by the addition of water. Recrystallization from aqueous acetone gave 0.075 g of abietan-18-oic acid (**12**), mp and mmp 178–180°.[1]

Hydroboration of Methyl Abiet-13-en-18-oate.—To a solution of 0.450 g of the methyl ester (prepared from the acid and ethereal diazomethane) in 10 ml of dry diglyme was added 0.100 g of sodium borohydride. The reaction was cooled in an ice bath and 0.050 g of freshly distilled boron fluoride etherate in 2 ml of diglyme was added over a period of 30 min. The reaction mixture was allowed to warm to room temperature and stirred for 4 hr. A few drops of water followed by 3 ml of 10% sodium hydroxide and 3 ml of 30% hydrogen peroxide were added slowly. The mixture was stirred overnight and poured into 25 ml of water. The precipitate was collected and recrystallized from hexane to give 0.310 g (70%) of product, mp 134–135°, identified as methyl 14β-hydroxyabietan-18-oate (**13**) by mixture melting point (134–135°) and by comparison of the infrared spectra with that of an authentic sample.[1]

13β,14β-Dihydroxyabietan-18-oic Acid (15).—To a solution of 0.150 g of **5** in 2.5 ml of pyridine was added 0.200 g of osmium tetroxide. The black solution was allowed to stand for 72 hr at room temperature. An additional 15 ml of pyridine, 15 ml of water, and 0.5 g of sodium bisulfite were added, and the solution was vigorously stirred for 2 hr. The pyridine was neutralized with concentrated hydrochloric acid, and the resulting precipitate was collected. Two recrystallizations from ether–hexane afforded 0.095 of glycol: mp and mmp 183–184°; ir spectrum identical with that of the material prepared by Cross and Myers;[6] nmr (pyridine) 3.39 (d, J = 9 Hz, H-14), 1.39 (C-4 methyl), 1.10 (d) and 0.98 (d, J = 7 Hz, isopropyl), and 0.94 ppm (C-10 methyl).

Methyl 14α-Hydroxy-8α,13β-abietan-18-oate (16).—To a solution of 10.0 g of methyl 13β-abiet-8(14)-en-18-oate[5] (**3**) in 150 ml of dry diglyme was added 2.0 g of sodium borohydride. The reaction was cooled in an ice bath and 8.4 g of freshly distilled boron trifluoride etherate was added over a 1-hr period. The gelatinous reaction mixture was allowed to warm to room temperature and stirred for 4 hr. A few drops of water followed by 50 ml of 10% sodium hydroxide and 50 ml of 30% hydrogen peroxide were added cautiously. The mixture was stirred overnight and poured into water. The white precipitate, yield 10.0 g, mp 100–110°, was dried, dissolved in hexane–benzene (1:4), and chromatographed on Merck acid-washed alumina. Elution with hexane–benzene (1:4) gave 0.78 g of starting ester. Elution with methylene chloride–benzene (1:4) gave 7.26 g (69%) of hydroxy ester **16**, which was recrystallized from hexane: mp 136–138°; $[\alpha]D$ −11.7° (*c* 1.109); nmr 3.62 (m, H-14), 1.19 (C-4 methyl), 1.00 (C-10 methyl), and 0.90 (d) and 0.80 (d, J = 7 Hz, isopropyl).

Anal. Calcd for $C_{21}H_{36}O_3$: C, 74.95; H, 10.87. Found: C, 74.77; H, 10.81.

The 14 acetate, mp 122–123°, $[\alpha]^{23}D$ −47.3° (*c* 1.053), was formed in the usual manner and was recrystallized from methanol: nmr 5.21 (m, H-14), 1.20 (C-4 methyl), 1.11 (C-10 methyl), and 0.90 (d) and 0.80 (d, J = 7 Hz, isopropyl).

Anal. Calcd for $C_{23}H_{38}O_4$: C, 72.98; H, 10.12. Found: C, 72.79; H, 10.23.

Elution with methylene chloride–methanol (19:1) gave 1.83 g of diol. Two recrystallizations from methanol gave crystals, mp 155–157° (lit.[5b] mp 155–157°), $[\alpha]D$ +7.5° (*c* 1.594), which held tenaciously to solvent and failed to give satisfactory analytical data.

Anal. Calcd for $C_{20}H_{36}O_2 \cdot CH_3OH$: C, 74.07; H, 11.84. Found: C, 74.59; H, 11.96.

Methyl 14α-Tosyloxy-8α,13β-abietan-18-oate.—To a solution of 5.0 g of hydroxy ester **16** in 15 ml of pyridine was added 3.75 g of *p*-toluenesulfonyl chloride. The solution was stirred overnight at room temperature and poured into water. The precipitate was recrystallized from cold acetone to give 6.80 g (93%) of tosylate, mp 112–113°, $[\alpha]D$ −21.5° (*c* 1.024).

Anal. Calcd for $C_{28}H_{42}O_5S$: C, 68.55; H, 8.63. Found: C, 68.31; H, 8.54.

Attempted Preparations of 8α,13β-Abietan-18-oic Acid (22). A.—To a solution of 3.0 g of tosylate in 90 ml of absolute ether was added 1.50 g of lithium aluminum hydride. The reaction mixture was heated at reflux for 18 hr and cooled, the excess hydride was decomposed with water, and the mixture was acidified with 10% hydrochloric acid. The ether layer was washed, dried, and evaporated, and the residue was dissolved in hexane and passed through a column of 50 g of Merck acid-washed alumina. Evaporation of the hexane eluant furnished 1.57 g (88%) of material which could not be induced to crystallize. The nmr spectrum exhibited a one-proton singlet at 5.5 ppm, indicating that elimination had taken place. A 0.5-g portion of this material was dissolved in 20 ml of acetone, mixed with 2 ml of Jones reagent, and stirred for 30 min. The mixture was poured into water, extracted with methylene chloride, and dried. After removal of solvent, there was obtained 0.45 g of the colorless oil. Crystallization of the oil from acetone afforded 0.25 g of 13β-abiet-8(14)-en-18-oic acid (**3**), mp 148–149°. The nmr spectrum of the residual oil from the evaporation of the mother liquors was identical with that of 13β-abiet-8(14)-en-18-oic acid.

B.—A solution of 1.0 g of tosylate in 20 ml of ether was added to 75 ml of liquid ammonia. To this solution was added 0.5 g of lithium and the blue reaction mixture was stirred for 1 hr. Sufficient anhydrous ethanol was added to destroy the blue color, the reaction mixture was allowed to stand overnight, and 50 ml of water was added. The mixture was extracted with methylene chloride and dried, and the solvent was removed to give 0.48 g (76%) of product, mp 155–157°. The infrared and nmr spectra of the product were identical with those of the diol obtained from hydroboration of methyl 13β-abiet-8(14)-en-18-oate.

(20) Glpc data indicate that our material contains *ca.* 9% $\Delta^{8(14)}$ isomer: Dr. D. F. Zinkel, personal communication.

Methyl 14-Oxo-8α,13β-abietan-18-oate (19).—To a solution of 1.50 g of chromium trioxide, 1.50 g of sodium dichromate, and 2.4 ml of acetic acid in 12 ml of water was added 1.50 g of hydroxy ester **16** in 45 ml of benzene at 0°. The reaction mixture was stirred at 0° for 2 hr and at room temperature for 18 hr. The organic layer was separated, washed with water, and dried over magnesium sulfate. After removal of the drying agent and the solvent, there was obtained 1.5 g (100%) of white solid. Recrystallization from hexane and then methanol furnished the analytical sample: mp 79–80°; nmr 1.20 (C-4 methyl), 0.92 (d) and 0.82 (d, J = 7 Hz, isopropyl), and 0.87 ppm (C-10 methyl); mmp (with the 8β,13β isomer) 45–56°; ORD $[\phi]_{589}$ −250°, $[\phi]_{311}$ −2400°, $[\phi]_{287}$ 0°, $[\phi]_{274}$ +770°.

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.19; H, 10.11.

A 0.5-g sample of this ketone in 10 ml of methanol containing 0.5 g of potassium hydroxide was heated at reflux for 30 min and poured into water, and the precipitate was collected. Recrystallization from methanol afforded 0.4 g (80%) of material, mp 79–80°. A mixture melting point with methyl 14-oxoabietan-18-oate (**8**) was 79–80°. Infrared and nmr spectra were identical with those of an authentic sample of this material.

Methyl 14β-Hydroxy-13β-abietan-18-oate (20).—To a solution of 0.050 g of **19** in 3 ml of 95% ethanol was added 0.050 g of sodium borohydride, and the reaction mixture was heated at reflux 2.5 hr. The clear solution was cooled, diluted with 12 ml of 5% hydrochloric acid, extracted with ether, washed thoroughly with water and saturated sodium chloride, and dried, and the solvent was removed to give 0.050 g of crystalline residue. Tlc (silica gel G, 5% ethyl acetate in benzene) showed the presence of nonpolar material, and 0.043 g of the solid was taken up in benzene and chromatographed on silica gel. Elution with 1% ethyl acetate–benzene gave 0.002 g of nonpolar material, while the later fractions with ethyl acetate–benzene mixtures gave first 0.011 g of impure alcohol and then 0.024 g (48%) of **20**, which was homogeneous to tlc and showed nmr signals at 3.47 (m, $W_{1/2}$ = 15 Hz, H-14), 1.18 (s, C-4 methyl), 1.09 and 0.90 (d, J = 6 Hz, isopropyl), and 0.90 ppm (s, C-10 methyl). The analytical sample, mp 130–131°, was crystallized from hexane. This material was identical (mixture melting point and nmr) with a sample prepared by Herz, *et al.*[13]

Anal. Calcd for $C_{21}H_{36}O_3$: C, 74.95; H, 10.78. Found: C, 74.68; H, 10.84.

8α-Abiet-13-en-18-oic Acid (4).—To a solution of 0.30 g of methyl 14α-hydroxy-8α,13β-abietan-18-oate (**16**) in 3 ml of pyridine was added 0.5 ml of phosphorus oxychloride. The reaction mixture was heated overnight on a steam bath, cooled, and slowly added to 15 ml of ice–water. The excess pyridine was neutralized with concentrated hydrochloric acid and the mixture was extracted with ether, washed, and dried. Removal of the solvent yielded 0.272 g (92%) of semicrystalline material. The nmr spectra of this material indicated that it was a 1:1 mixture of the abiet-8(14)- and-13-en-8-oates. A 0.265-g portion of this material was taken up in hexane and chromatographed on 25 g of silver nitrate impregnated silica gel. Elution with 4:1 hexane–benzene gave 0.091 g of **3**, while later fractions with the same solvent pair gave first 0.020 g of a mixture and then 0.094 g of nearly pure (*ca.* 80% by nmr) **4** as the methyl ester. This material showed nmr signals at 5.21 (m, H-14), 1.20 (s, C-4 methyl), 0.95 (d, J = 6 Hz, isopropyl), and 0.91 ppm (s, C-10 methyl). In view of the small amount of this material available and the fact that it could not be induced to crystallize, a sample was subjected to mass spectrometry in lieu of analysis and gave a parent peak at m/e 318 (calculated mol wt, 318).

Hydrogenation of Methyl 13β-Abiet-8(14)-en-18-oate (3) and 8α-Abiet-13-en-18-oate (4).—A solution of 0.05 g of the mixture of esters from above in 10 ml of acetic acid was hydrogenated in the presence of 0.05 g of Adams catalyst at 35 psi for 6 hr. The solution was filtered, diluted with water, extracted with ether, washed with water and diluted base, and dried. After removal of solvent, analysis by glc indicated the presence of two compounds (**22** and **21**) in a ratio of 2:1. These were identified by a comparison of their retention times with those of authentic samples.

Lithium–Ammonia Reduction of Abietic Acid.—The reduction and isolation of abiet-8(14)-en-18-oic acid was carried out as described previously.[1,5] From 145 g of the diamylamine salt of abietic acid, there was obtained 27.6 g (29%) of the *ca.* 4:1 mixture of abiet-8(14)-en-18-oic acid (**2**) and abiet-13-en-18-oic acid (**5**), mp 190–194°, which was used for those experiments requiring the 8(14)-unsaturated acid. From the mother liquors, employing the method of Marx, could be isolated 10.0 g (9%) of 13β-abiet-8(14)-en-18-oic acid (**3**), mp 148–150° (lit. mp 148–150°), identical with a sample prepared by the hydrogenation of levopimaric acid.[5] Regeneration of the acids from the solid mixture of salts collected prior to the isolation of 13β-abiet-8(14)-en-18-oic acid afforded an additional 40.0 g (36%) of the mixture of abiet-8(14)- and -13-en-18-oic acids, mp 187–195° after five recrystallizations. The material remaining in the mother liquors was purified through the diamylamine salt to give 0.65 g (0.6%) of abiet-13-en-18-oic acid, mp 162–164°, identical with the material mentioned above. In addition to the above compounds, 3.0 g (27%) of the 1:1 mixture of abiet-7-en-18-oic acid (**6**) and abiet-13-en-18-oic acid (**5**) (lit.[5a] mp 161–162°) was obtained.

Methyl 7-Oxoabietan-18-oate (23).—Hydroboration–oxidation of 3.0 g of the mixture of the methyl esters of abiet-7- and -13-en-18-oic acids was carried out as previously described to give 2.80 g of crude product which was dissolved in hexane and chromatographed on 80 g of Merck acid-washed alumina. Elution with hexane and hexane–benzene (1:1) gave 0.29 g of starting esters. The first benzene fraction gave 0.18 g of crystals, which on recrystallization afforded pure methyl 14β-hydroxyabietan-18-oate. Further elution with benzene gave 1.81 g of a mixture of this compound and a 7-hydroxy ester. Attempts to separate the mixture by rechromatography were unsuccessful, and it was converted into the mixture of the corresponding ketones.

To a solution of 8.0 g of the mixture of 7- and 14-hydroxy esters in 600 ml of acetone at 0° was added 40 ml of Jones reagent. The reaction mixture was stirred for 2.5 hr and sufficient methanol was added to destroy the excess chromic acid. The volume was reduced to 200 ml, and the reaction mixture was diluted with 500 ml of water, extracted with ether, and dried over magnesium sulfate. Removal of the drying agent and solvent afforded 7.5 g (93%) of oil which could not be crystallized. Attempts to separate the mixture by column chromatography again failed, and the ketones were separated *via* the 7-oximino compound.[21]

A solution of 8.5 g of the mixture of keto esters, 16.0 g of sodium acetate, and 28.0 g of hydroxylamine hydrochloride in 240 ml of methanol was heated at reflux overnight. The solution was cooled, poured into water, extracted with methylene chloride, washed with water, and dried over magnesium sulfate. Removal of drying agent and solvent gave 8.5 g of oily product. The oil was dissolved in benzene–hexane (1:1) and chromatographed on Merck acid-washed alumina. Elution with benzene gave methyl 14-oxo-abietan-18-oate (**8**), identical with an authentic sample.[1] Elution with benzene–methylene chloride (1:1) gave 4.1 g of the oxime of methyl 7-oxoabietan-10-oate, mp 183–185°. Recrystallization from methanol and then hexane gave the analytical sample: mp 185–186.5°; nmr 1.25 (C-4 methyl), 0.98 (C-10 methyl), and 0.87 (d, J = 6 Hz, isopropyl).

Anal. Calcd for $C_{21}H_{35}NO_3$: C, 72.12; H, 10.09; N, 4.01. Found: C, 72.36; H, 9.98; N, 4.01.

To obtain the required 7-keto compound (**23**), a solution of 0.5 g of the oxime, 20 ml of methanol, 2 ml of water, and 2 ml of concentrated sulfuric acid was heated at reflux for 80 hr. The solution was cooled, poured into water, extracted with ether, and dried. After removal of solvent, an oil was obtained which was dissolved in benzene and filtered through a short column of alumina. Recrystallization of the material eluted with benzene from pentane and then methanol gave 0.3 g (63%) of methyl 7-oxoabietan-18-oate (**23**): mp 86.5–87°; nmr 1.23 (C-4 methyl), 1.09 (C-10 methyl), and 0.88 (d, J = 6 Hz, isopropyl); ORD $[\phi]_{589}$ −260°, $[\phi]_{306}$ −3620°, $[\phi]_{282}$ 0°, $[\phi]_{270}$ +1564°. Cross and Meyers[6] report this compound as an oil; however, a sample prepared by their method was identical with that prepared by this route.

Wolff–Kishner Reduction of Methyl 7-Oxoabietan-18-oate.—A solution of 0.5 g of the keto ester, 2.0 g of potassium hydroxide, and 5 ml of anhydrous hydrazine in 60 ml of ethylene glycol was heated at 150° for 1.5 hr. The condenser was removed and the temperature was allowed to rise to 195° during a 2-hr period. The reaction was held at this temperature for an additional 1 hr. The solution was cooled, acidified with hydrochloric acid, poured into ice–water, extracted with ether, and dried. After removal of solvent, there was obtained 0.40 g of oil which crystallized from acetone to give 0.24 g (51%) of abietan-18-oic acid (**12**), mp and mmp 176–178°.[1] The infrared and nmr spectra were identical with those of an authentic sample.[1]

(21) An attempt to separate this mixture with Girard's T reagent was successful, although the product recovery was not satisfactory.

p-Toluenesulfonylhydrazone of Methyl 7-Oxoabietan-18-oate.—A solution of 0.300 g of keto ester, and 0.372 g of *p*-toluenesulfonylhydrazine in 25 ml of 0.2 *M* ethanolic hydrochloric acid was heated at reflux for 2 hr and then boiled for 19 min without the condenser. An equal volume of water was added, and the white precipitate was collected and recrystallized from aqueous methanol, affording 0.365 g (90%) of material, mp 81–82°.

Anal. Calcd for $C_{28}H_{42}N_2O_4S$: C, 66.91; H, 8.42; N, 5.57. Found: C, 66.67; H, 8.26; N, 5.31.

Abiet-7-en-18-oic Acid (6). A.—To a solution of 0.1 g of sodium in 5 ml of ethylene glycol was added 0.140 g of the *p*-toluenesulfonylhydrazone. The reaction mixture was poured into water and extracted with ether. The ether solution was extracted with 20% potassium hydroxide solution, acidified, and reextracted with ether. The solvent was removed and the resulting oil was crystallized from acetone to give 0.025 g of product: mp 166–167° (lit.[5b] mp 180–182°); nmr 5.30 (m, H-7), 1.25 (C-4 methyl), 0.87 (d, J = 7 Hz, isopropyl), and 0.82 ppm (C-10 methyl).

Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 79.04; H, 10.44.

B.—To a boiling solution of 3.0 g of the mixture of abiet-7- and -13-en-18-oic acids obtained from the reduction of abietic acid in 50 ml of acetone was added 1.4 g of (−)-α-phenethylamine; boiling was continued until the amine salt began to precipitate. The solution was cooled and the precipitate was recrystallized once from acetone, five times from ethyl acetate, and five additional times from aqueous acetone. The acid was regenerated from the salt and recrystallized three times from acetone to give 0.80 g of **6**, mp 178–180°. The infrared and nmr spectra were identical with those of abiet-7-en-18-oic acid prepared by the Bamford–Stevens reaction.

Registry No.—**3**, 17611-13-1; **5**, 17611-11-9; **6**, 77611-19-7; **9**, 22565-86-2; **10**, 22565-87-3; **15**, 22565-88-4; **16**, 22565-89-5; **16** 14 acetate, 22565-90-8; **16** 14 tosylate, 22565-91-9; **19**, 22565-92-0; **23**, 22576-93-8; **23** oxime, 22565-93-1; **23** *p*-toluenesulfonylhydrazone, 22576-94-9.

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Studies on Resin Acids. V. Preparation and Reactions of Ring-A Olefins from Dehydroabietic Acid[1]

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The lead tetraacetate decarboxylation of dehydroabietic acid has been found to give three olefins (**2**, **5**, and **6**) and the acetate of 18-norabieta-8,11,13-trien-4-ol (**7**). Hydroboration–oxidation of this mixture of olefins gives principally 18-norabieta-8,11,13-trien-19-ol (**12**) and 18-norabieta-8,11,13-trien-3α-ol (**13**), plus small quantities of 19-nor-5β-abieta-8,11,13-trien-7-one (**17**). To elucidate the structure of **17**, it was necessary to prepare 18- and 19-norabieta-8,11,13-trien-7-one by oxidation of the corresponding hydrocarbons. It was found that sodium–ammonia reduction of dehydroabietonitrile gives the 19-nor hydrocarbon (**20**), rather than 18-norabieta-8,11,13-triene as suggested originally. The structure of **17** was confirmed by its synthesis in two steps from methyl 7-oxoabieta-5,8,11,13-tetraen-18-oate (**22**).

The readily available diterpenes, dehydroabietic acid (abieta-8,11,13-trien-18-oic acid[2]) and podocarpic acid (12-hydroxypodocarpa-8,11,13-trien-19-oic acid[2]), have received considerable attention as possible precursors for the synthesis of steroids or steroid analogs.[3] The basic goal of these workers was the conversion of dehydroabietic acid (**1**) into abieta-4(18),8,11,13-tetraene,[4] which was accomplished by various methods and with varying degrees of success. The earliest workers in this area investigated the acid-catalyzed dehydration of abieta-8,11,13-trien-18-ol (**3**) and recognized that this led to mixtures of olefins.[3a,b] Later workers prepared what was described as pure **2** by either Hofmann[3c,d] or Cope[3d] eliminations carried out on 4-dimethylamino-18-norabieta-8,11,13-triene (**4**) or, alternatively, by the lead tetraacetate decarboxylation of **1**.[3e]

The single-step decarboxylation of **1** with lead tetraacetate, carried out in these laboratories some years ago and reported to lead to essentially pure **2**, is by far the most convenient of the methods employed to date for this conversion. However, subsequent reinvestigation of this reaction, making use of techniques which were not available during the course of the earlier work, indicates that the material described as **2** is actually a mixture of three olefins.[5] Repetition of the lead tetraacetate decarboxylation of dehydroabietic acid and careful analysis of the nmr spectrum indicated that the material previously described as pure **2** was in fact a mixture of **2**, abieta-3,8,11,13-tetraene (**5**), and abieta-4,8,11,13-tetraene (**6**) in a ratio of 2:2:1. In addition to a 65% yield of the olefin mixture, there was also obtained an oily acetate in 7% yield. The spectral data for this compound indicated that it was probably the same as the 4-acetoxy-18- or -19-norabieta-8,11,13-triene (**7** or **8**) re-

(1) Part IV: J. W. Huffman, J. A. Alford, and R. R. Sobti, *J. Org. Chem.*, **34**, 473 (1969). This work was supported in part by Career Development Award GM-5433 from the National Institutes of Health.

(2) The systematic method of nomenclature employed in this paper is that outlined by J. ApSimon, M. Fetizon, E. Fujita, L. Gough, W. Herz, P. R. Jefries, D. Mangoni, T. Norin, K. Overton, S. W. Pelletier, J. W. Rowe, and E. Wenkert, Abstracts, 6th International Symposium on the Chemistry of Natural Products, Mexico City, April 1969, p 35.

(3) (a) A. Brossi, H. Gutmann, and O. Jeger, *Helv. Chim. Acta*, **33**, 1730 (1950); (b) R. P. Jacobsen, *J. Amer. Chem. Soc.*, **75**, 4709 (1953); (c) H. H. Zeiss and W. B. Martin, *ibid.*, **75**, 5935 (1953); (d) J. W. Huffman and R. F. Stockel, *J. Org. Chem.*, **28**, 506 (1963); (e) J. W. Huffman and P. G. Arapakos, *ibid.*, **30**, 1604 (1965); (f) C. R. Bennet and R. C. Cambie, *Tetrahedron*, **23**, 927 (1967); (g) R. N. Seelye and W. B. Watkins, *Tetrahedron Lett.*, 1271 (1968).

(4) In the case of the workers in ref 3f, the conversion was in the podocarpic acid series.

(5) (a) A. W. Burgstahler, personal communication; A. W. Burgstahler and J. N. Marx, *J. Org. Chem.*, **34**, 1562 (1969). We would like to thank Professor Burgstahler for copies of the nmr spectra of this mixture of olefins, as well as that obtained by the method of Zeiss and Martin.[3c] We would also like to thank Professor Burgstahler for sending us a copy of his manuscript prior to publication. (b) J. F. Biellmann, R. Werrig, P. Daste, and M. Raynaud, *Chem. Commun.*, 168 (1968).