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Resin Acids. XXIV. Intramolecular Functionalizations of 11-Oxygenated Abietanes and Podocarpanes[1]

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The transformation of dehydroabietonitrile and podocarpic acid to 11-hydroxy- and 11-ketoabietanes and podocarpanes is described. Key reactions were metal–amine reductions of 12-methoxydehydroabietic acid, *O*-methylpodocarpic acid, 12-acetoxy-9(11)-abietenes, and 12-acetoxy-9(11)-podocarpenes. Hypoiodite reaction and oxidative cyclization of the C-11 alcohols and photochemical isomerizations of the C-11 ketones followed by oxidative cleavage resulted in functionalization at C-1 and C-18 of the resin acid skeleton. Differences in product distribution and ease of ether cleavage between this work and observations in the steroid series are attributed to the absence of an axial substituent on C-13. Chiroptical properties of two new isomers of methyl levopimarate are discussed in terms of the helicity rule.

Our previous studies on the partial synthesis of more complex diterpenoids from readily available resin acids were directed mainly at the introduction of modifications which permitted construction of tetracyclic and pentacyclic ring systems. Since many diterpenes of interest can be construed as being derived from 1-hydroxylated intermediates or are actually functionalized on ring A or on the C-10 methyl group, whereas most resin acids are not, it was desirable to test whether functionalization reactions developed in the steroid series[2-4] were also applicable to 11-oxygenated resin acid derivatives.

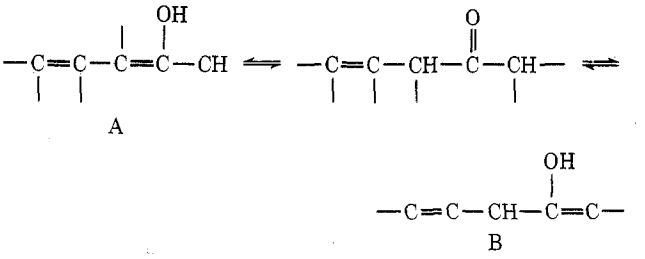
The synthesis of some 11-oxygenated abietanes was reported earlier,[5] but the low yields precluded further study of the products. In the present communication we describe the synthesis of 11-oxygenated abietanes and podocarpanes by a different route and report results of functionalization reactions which differ to some extent from observations in the steroid series.

Results and Discussion

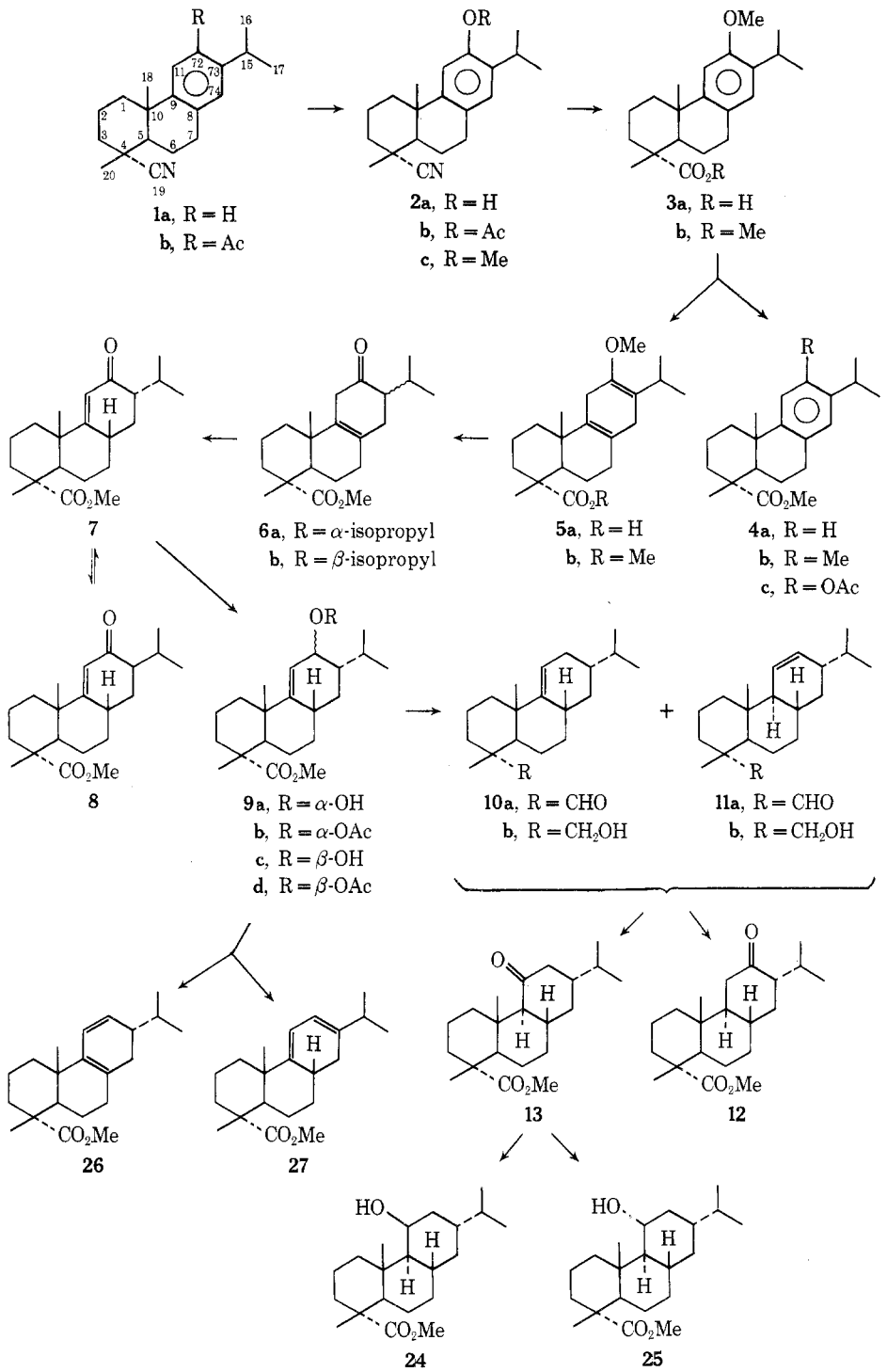
Synthesis of 11-Oxygenated Abietanes. Our first target was the α,β-unsaturated ketone **7** (Scheme I) which should result from dissolving metal reduction of 12-methoxydehydroabietic acid (**3a**). Since the previously described[6] route to **3a** proceeded only in poor overall yield, the following reaction sequence to **3a** was adopted. Dehydroabietonitrile (**1a**) underwent Friedel–Crafts acylation in 92% yield to **1b**[7] which gave a 76% yield of **2b** on treatment with 40% peracetic acid in chloroform. Hydrolysis to **2a** (quantitative yield, 1% HCl–MeOH, room temperature), methylation to **2c** (80% yield, *t*-BuOH, $K^+t\text{-}OBu^-$, CH_3I) and, finally, hydrolysis (NaOH, diethylene glycol–water, 170°) gave an 88% yield of **3a**.

Considerable effort was devoted to a study of the Birch reduction of **3a** with lithium, ethylamine, and *tert*-amyl alcohol (high-speed stirring).[8] This was followed by acidification and ether extraction of the product mixture, methylation of the acidic extract, treatment with 0.5% hydrochloric acid in methanol under carefully defined conditions (*vide infra*) to induce hydrolysis of **5b** and isomerization of **6** without equilibrating[9] **7** and **8**, and finally acetylation of the crude product to permit subsequent separation of the by-product **4b** from **7** and **8** in the form of **4c**. Chromatography of the product mixture gave **4a** (10%), **3b** (14%), **4c** (18%), **7** and **8** (4:1 ratio, 60% combined yield). The properties of **7** and **8** corresponded to those reported in our earlier publications.[9]

Hydrolysis and rearrangement of **5b** with 0.5% HCl could be followed closely by tlc. A new compound, presumably **6**, was formed rapidly and rearranged gradually to form a mixture of **7** and **8**. When the reaction mixture was worked up immediately after disappearance of **6** (2 hr), the ratio of **7** to **8** was 4:1; when the acid concentration was increased or the mixture was exposed to acid for a longer period, the ratio of **7** to **8** approached the equilibrium ratio (1:1).[9] Now acid-catalyzed enolization of β,γ-unsaturated ketones to conjugated enols of type A, which may be followed by rearrangement to α,β-unsaturated ketones, proceeds much faster than enolization to unconjugated enols of type B;[10] hence rearrangement of the double bond of **6** should proceed faster than epimerization of the isopropyl group. Consequently the 4:1 ratio of **7** to **8**



Scheme I



reflects the ratio of the initially obtained C-13 epimers of **6**, since **6** is the product of kinetically controlled protonation at the α carbon and favors axial addition of the proton to the least hindered side of the enol ether.[11a] Dreiding models (Figure 1) reveal that that conformation of **5b** which would yield **6a** by protonation from the β side is preferred over the conformation which would yield **6b** by protonation from the α side because 1,3 interactions between the two hydrogens at C-11 and the C-18 methyl and the C-1 methylene group are minimized. The observed preference for the formation of **6a**, and therefore **7**, was fortunate, since in a trans-anti-trans-fused perhydrophenanthrene a β-oriented isopropyl group could compete with the C-10 methyl group for functionalization from the C-11 position and thus negate the proposed reaction sequence.

With the α,β-unsaturated ketone **7** in hand, its further transformation to the desired alcohols **24** and **25** (Scheme I) could be studied. $NaBH_4$ reduction of **7** gave a mixture of alcohols, one of which (**9c**) could be isolated in crystalline form. The configuration of the hydroxyl function was

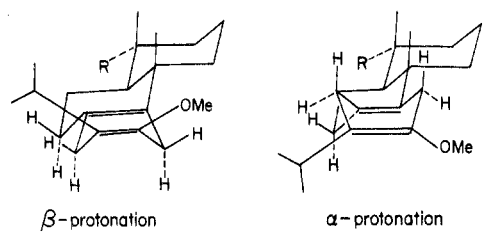
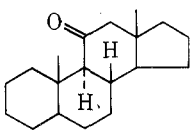


Figure 1. Conformations of **5b**.

apparent from the half-height width of the H-11 resonance at 5.32 ppm (5 Hz) and the shape of the H-12 resonance at 4.08 ppm (d br, $J_{12,13}$ = 9 Hz), which indicated that the H-11–H-12 dihedral angle was near 90°. By contrast the H-12 signal of the epimer **9a** was a broad peak ($W_{1/2}$ = 22 Hz). Reduction of the mixture of allylic acetates **9b** and **9d** with lithium in ethylamine gave a mixture of isomeric aldehydes **10a** and **11a** and alcohols **10b** and **11b**, in 87% yield (ratio of $\Delta^{9(11)}$ to Δ^{11} olefins was 5:1). Hydroboration–oxidation of this mixture followed by oxidation with Jones reagent and methylation afforded the known ketone **12** of established stereochemistry[9] (8% yield), and a new ketone **13** (64% yield) whose stereochemical assignment is based on the following observations. The chemical shift of the C-10 methyl signal (1.08 ppm) is almost the same as that of **14** (Scheme II, 1.09 ppm)[5] and is in consonance with Zürcher's rules[12] which are based on the observed influence of substituents on the chemical shift of angular methyl groups in steroids. A broadened absorption at 2.16 ppm ($W_{1/2}$ = 9 Hz) was assigned to the two C-12 protons and a broadened doublet at 2.48 ppm (J = 12 Hz) to the β proton at C-11 which is strongly shielded by the 11-ketone. Similar resonances in the region 2.1–2.6 ppm are displayed by **14** and by **15**,[13] the resonance due to the C-1β proton having been identified by deuterium exchange.



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The CD curve of ketone **13** displayed a negative Cotton effect ($[\theta]_{294}$ = −1050). Ketone **14** also exhibited a negative Cotton effect, although 11-keto steroids with trans B/C ring junctions display weak positive/Cotton effects.[14] The reasons for this apparent discrepancy have been discussed previously.[5] Finally, the mass spectral fragmentation of **13** was similar to that reported for **15**,[15] if allowance is made for the presence of substitution at C-4, the presence of the isopropyl group, and the absence of ring D. Ketone **15** undergoes a McLafferty rearrangement followed by three fragmentations, one of which is responsible for the base peak. An analogous process can explain the formation from **13** of three major peaks at m/e 139, 153, and 165.

We observed previously[5] that attack of diborane on **16** occurred preponderantly from the β side (Scheme II) and that oxidation of the resulting alcohol mixture yielded cis ketone **20** in 80% yield. Ketone **20** was epimerized by base to the more stable trans ketone **14**. In the present work no cis ketone **23** was isolated when **10** was subjected to a similar reaction sequence. Examination of Dreiding models (see Figure 2) suggests that attack of diborane on **10** and on **16** should occur predominantly from the β side, but that α attack on **10** is less obstructed than α-attack on **16**. β Attack on **10** would yield alcohol **22**, which, if rings B and C were in chair conformations, should orient the isopropyl group axially, thus resulting in a strong interaction with the C-7 methylene group. Flipping the B and/or C ring into a boat conformation would not significantly reduce the interaction, nor would oxidation to the cis ketone **23** reduce the strain. Thus alcohol **22** and ketone **23** are expected to be of higher energy than **18** and **20**, respectively. On the other hand, formation from **23** of a $\Delta^{9(11)}$-enol or enolate would relieve more strain than formation of a similar compound from **20**; thus steric acceleration should cause **23** to enolize faster, with eventual conversion to the thermodynamically favored trans ketone **13**, than

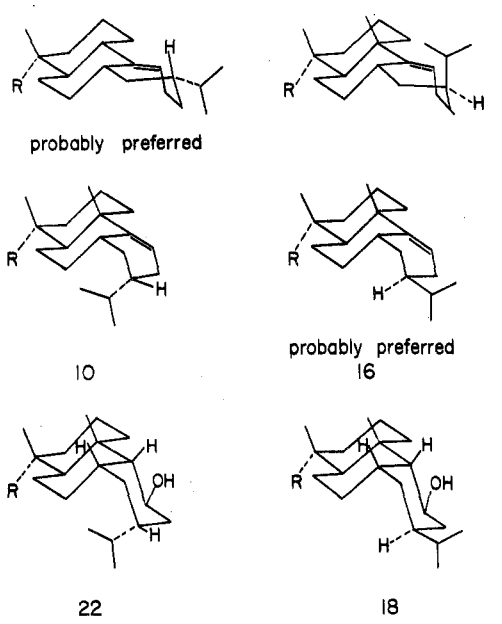
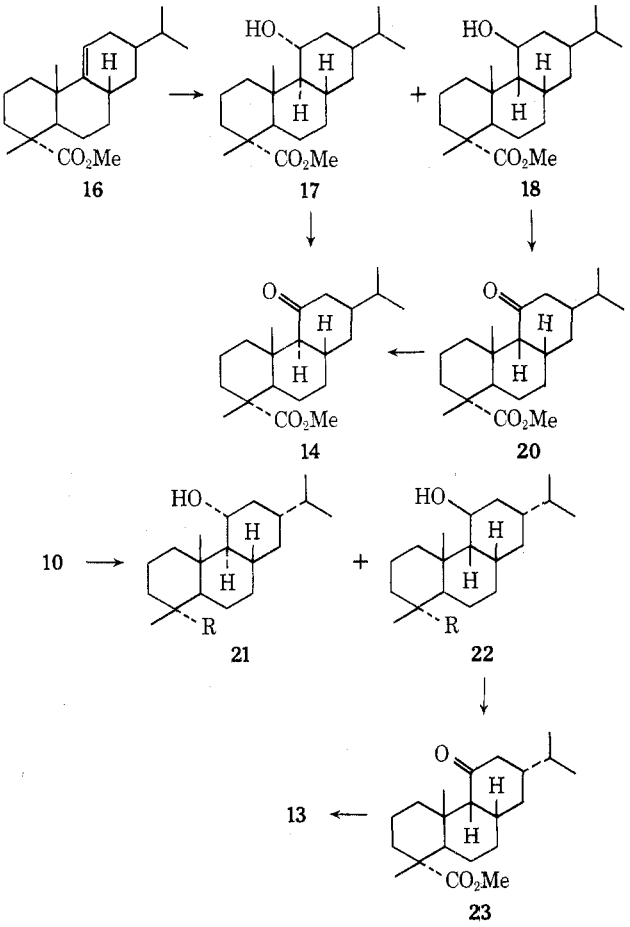


Figure 2. Hydroboration of **10** and **16**.

20. It is therefore not surprising that any cis ketone **23** obtained by oxidation of the alcohol mixture formed from olefin **10** is isomerized to the more stable ketone **13** more rapidly than **20** is isomerized to **14**.

Scheme II



Although the hindered ketone group of **13** was not affected by $NaBH_4$ in methanol at room temperature, reduction with $NaBH_4$ in THF and aqueous NaOH furnished the desired two epimeric alcohols **24** and **25** (85%, 11:9 ratio). The C-10 methyl resonance of the major alco-

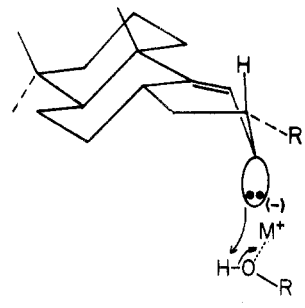


Figure 3. Anions from hydrogenolysis of 9b, 9d, and 32b.

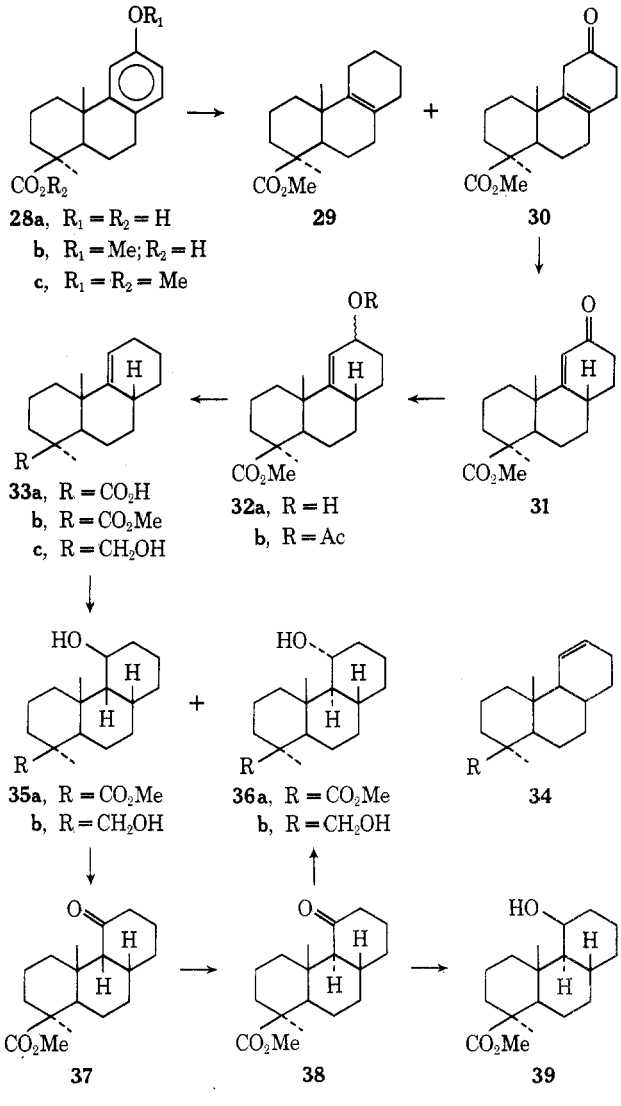
hol 24 (Scheme I) exhibited a chemical shift (1.16 ppm) near the value (1.14 ppm) previously[5] observed for the C-13 epimer and $W_{1/2}$ (11 Hz) of the H-11 signal at 4.31 ppm was characteristic of an equatorial proton coupled to two axial protons (H-9α, H-12α) and one equatorial proton (H-12β). The C-10 methyl resonance of the minor alcohol 25 at 1.03 ppm was near the value reported[5] for its C-13 epimer. The H-11 resonance at 3.64 ppm, under the three-proton singlet of the methyl ester function, was made visible by use of the Eu(fod)$_3$ shift reagent; $W_{1/2}$ (20 Hz) was characteristic of an axial proton coupled to two axial protons (H-9α and H-12α) and one equatorial proton (H-12β). Further evidence for the assigned stereochemistry was a broadened doublet at 2.39 ppm (J = 12 Hz) attributed to H-1β which is deshielded by the α-oriented hydroxyl group.

Synthesis of 11-Oxygenated Podocarpanes. The proposed reaction sequence for the synthesis of these compounds (Scheme III) was identical with that adopted in the abietic acid series. *O*-Methylpodocarpic acid (**28b**) was reduced with lithium in liquid NH_3–THF with *tert*-amyl alcohol as the proton source. Methylation of the crude product with diazomethane, rearrangement with 5% HCl in methanol, and chromatography afforded **29** (26%),[16] methyl *O*-methylpodocarpate **28c** (3%) and the two ketones **30** and **31** (52%). The less polar unconjugated ketone **30** could be isomerized to the more polar ketone **31**, which had the expected spectral properties.[17,18] $NaBH_4$ reduction of **31** gave a single allylic alcohol **32a** (or a mixture of epimeric allylic alcohols which could not be separated).[19] Conversion to the acetate **32b** followed by hydrogenolysis with lithium in ethylamine gave a mixture of **33a** (21%), characterized as **33b**, and **33c** (46%). The nmr spectra of these compounds in the vinyl region were similar to the nmr spectra of **10a** and **10b**, an observation which indicated that little if any Δ^{11} isomer **34** was present. An explanation of this result is the following.

In the hydrogenolysis leading to the podocarpenes **33a** and **33c**, approach of the bulky proton source (*tert*-amyl alcohol) to the most stable conformation of the planar allylic carbanion (Figure 3) from the α side is relatively unhindered and the $\Delta^{9(11)}$ olefin should be formed in high yield as actually observed. In the carbanion leading to the abietenes **10** and **11**, on the other hand, the α-oriented isopropyl group partially obstructs α approach of the bulky proton source and should therefore reduce the preference for formation of the more stable $\Delta^{9(11)}$ olefin.

Hydroboration–oxidation of the mixture of **33b** and **33c** followed by oxidation with chromic acid–acetic acid and subsequent methylation with diazomethane gave two keto esters which were difficult to separate. The less polar substance (20% yield) was assigned structure **37** with a cis B/C ring junction because it was isomerized by acid; the second more polar keto ester **38** was obtained in 55% yield. The characteristically deshielded resonances of H-12 and H-1β (*vide supra*) were masked by signals of other protons deshielded by the axial carbomethoxy

Scheme III



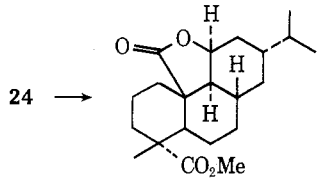
group, but the CD curve (Θ_{295} = −4360) was in harmony with the proposed stereochemistry. The groups of **38** which provide negative contributions are similar to those of keto ester **13**. However, there are two important differences. The positive contribution of the isopropyl group is no longer present and the axial carbomethoxy group located in the upper right rear octant probably provides an additional negative contribution. The Cotton effect of **38** should therefore be somewhat more negative than that of **13**, as was actually observed. Moreover, three major peaks in the mass spectrum of **13** at m/e 97, 110, and 123 correspond to the fragmentations observed in the mass spectra of **13** and **15**.

As described in the previous section, the main direction of diborane attack on **33** should be from the β side. The cis B/C alcohol **35** and cis ketone **37** obtained from it should be of lower energy than the corresponding abietanes **22** and **23** because of the absence of an axially oriented isopropyl group. Enolization of **37** (and its isomerization to **38**) would therefore result in relief of less strain and should therefore be slower than enolization (and isomerization) of the corresponding cis ketone **22** of the abietane series. On the other hand, cis ketone **37** should enolize and isomerize faster to the more stable trans ketone **38** than cis ketone **18** enolizes and isomerizes to trans ketone **14**, for **14** has an axial isopropyl group and should be of higher energy than **38**. However, the actual isomer ratios obtained after hydroboration–oxidation in the podo-

carpane series are not strictly comparable to the isomer ratios in the abietane series because of the need for a more strongly acidic medium to achieve oxidation of the axial carbinol function in the podocarpanes **35a** and **36a**. Hence oxidation of the crude alcohols of the podocarpane series may have been accompanied by partial epimerization.

$NaBH_4$ reduction of **38** in refluxing THF containing NaOH yielded alcohols **36a** and **39**, which were very difficult to separate, in approximately equal amounts. Structures were assigned by nmr spectroscopy, the C-10 methyl resonance of **39** being more deshielded (0.92 ppm) than that of **36** (0.82 ppm) and $W_{1/2}$ of H-11 in **39** (8 Hz) being considerably smaller than $W_{1/2}$ of H-11 in **36** (20 Hz).[20]

Functionalization Reactions. A. The Lead Tetraacetate–Iodine Reagent. Reaction of lead tetraacetate–iodine with **24** in cyclohexane gave a mixture (tlc) which on oxidation with Jones reagent afforded a complex mixture (tlc). Preparative tlc resulted in isolation of a lactone **40** (49%), obviously produced by oxidation of the corresponding hemiketal, whose infrared (carbonyl bands at 1760 and 1722 cm^{-1}) and nmr spectra (lack of the C-10 methyl signal, broadened one-proton resonance of H-11 at 4.77 ppm, $W_{1/2}$ = 7 Hz) were consonant with the proposed structure. The downfield shift of the H-11 signal indicated esterification; its half-height width showed that it had remained α and equatorial. Moreover, the model indicated that the C-4 methyl group was located within the deshielding influence of the lactone function, thus accounting for the downfield shift of the C-4 methyl resonance to 1.54 ppm. A similar lactone **41** was isolated in 40% yield after oxidation of the crude product obtained by lead tetraacetate–iodine oxidation of **39**. Disappearance of the C-10 methyl signal, downfield shift of the H-11 resonance, and a new infrared frequency at 1762 cm^{-1} (γ-lactone) supported the structure proposal.



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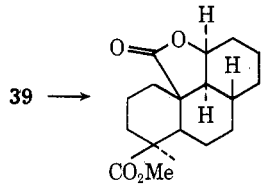

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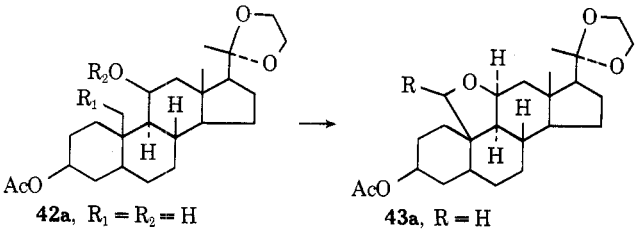
These results are slightly at variance with previously reported results in the steroid series, but can be easily rationalized in terms of the mechanism proposed for the hypoiodite reaction[2-4] and in fact serve to buttress it. Oxidation of the 11β-hydroxypregnane derivative **42a** afforded[21]

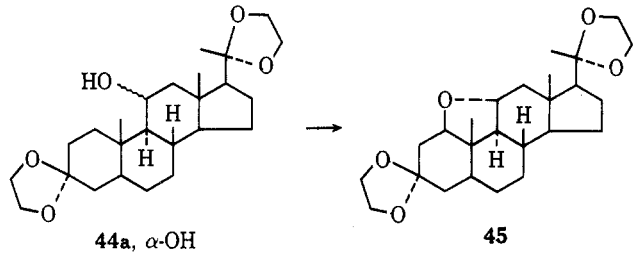


42a, $R_1 = R_2 = H$
b, $R_1 = I; R_2 = H$
c, $R_1 = R_2 = I$

43a, R = H
b, R = OH
c, R = I

ether **43a**, hemiketal **43b**, and C-18 functionalized products, although formation of an ether normally requires colinearity of iodine, carbon, and oxygen in the first intermediate, an iodohydrin, of the general reaction scheme and this condition is not fulfilled in the case of **42b** and the corresponding iodohydrins from **24** and **39**. In the case of **42a**, the formation of **43a** has been ascribed to steric factors which interfere with formation of hypoiodite **42c**, the precursor of **43c** and thence of **43b**, a situation which opens the way to a competing ring closure of **42b** to **43a**, "probably by an ionic mechanism."[3] In the case of **24** and **39**, the absence of an axial C-13 methyl group removes the obstacle to formation of the second hypoiodite corresponding to **42c** and allows the reaction to take a normal course, although the presence of a small amount of ether **49** (*vide infra*) corresponding to **43a** in the steroid series in the crude reaction product cannot be excluded. Similarly, if products are present which are the result of a "billiard-ball" reaction[22] on the axially oriented C-4 methyl group of **24**, they could not be isolated.

Subjection of **25** to the hypoiodite reaction yielded a complex mixture, none of whose components could be isolated or characterized. In the steroid series, hypoiodite reaction of the 11α-hydroxypregnane derivative **44a** resulted in functionalization at C-1 and formation of ether **45**.[23] The complexity of products in the case of **25** may

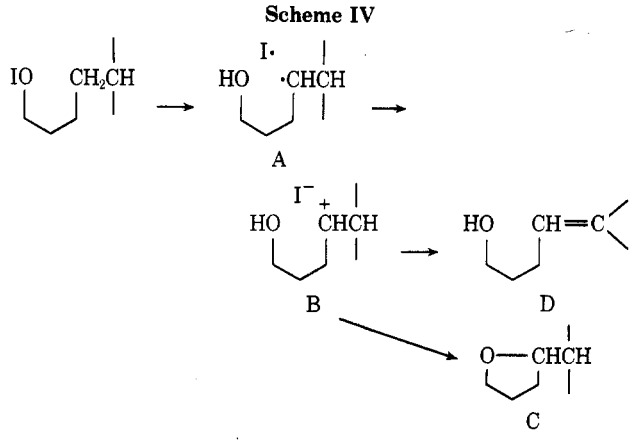


44a, α-OH
b, β-OH

45

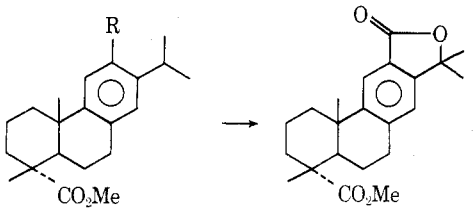
conceivably be rationalized in terms of the reaction sequence proposed for substitution on secondary and tertiary carbon.[3,4] If combination of the initially formed radical A (Scheme IV) with iodine is hindered, as in the radical resulting from decomposition of the hypoiodite of **25** and subsequent hydrogen transfer, electron transfer may lead to an ion pair B which can form an ether C by an ionic mechanism or stabilize itself by elimination of a proton to D. In the case of the resin acids, elimination of a proton from C-1 might be favored because a 1,2 double bond forces ring A into a quasi-boat conformation which relieves the strong 1,3 interaction between the C-10 methyl group and the axial substituent on C-1. Further possible complicating transformations of such olefinic alcohols under the influence of lead tetraacetate–iodine have been discussed.[3,4]

Scheme IV



Because of the disappointing results with **25**, no attempt was made to carry out a similar reaction on the analogous podocarpane derivative **36a**. However, the outcome of another hypoiodite reaction not directly related to the work so far described in this section merits brief discussion.

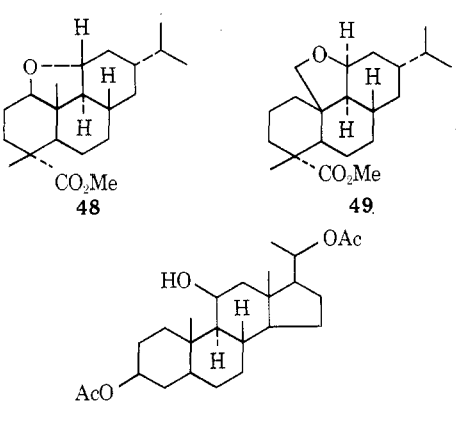
Cambie and Franich[24] have reported the successful functionalization of the isopropyl group of a dehydroabietic acid derivative by conversion of **46a** to **47** on treatment with lead acetate in benzene. The availability of **46b** and its facile conversion to a mixture of epimeric alcohols **46c**[25] suggested that hypoiodite oxidation of **46c** might provide another entry to C-15 functionalized resin acids. However, the product of this reaction was quite unexpectedly the lactone **47** (55% yield). This is obviously the result of a fragmentation of the originally formed O radical which is followed by oxidation of the fragmentation product **46d** to **46a** and subsequent functionalization at C-15 as observed previously.[24] The activation energy for intramolecular hydrogen abstraction reaches a minimum in rigid systems with a C–O distance of 2.5–2.7 Å.[4] In **46c**, however, the C–O distance (measured from Dreiding models) is 2.25 Å. The closeness of the reacting centers reduces their ability to orient properly for hydrogen abstractions and greatly increases the chance for the competing fragmentation to **46d**.



46a, R = CO_2H
b, R = Ac
c, R = $CHCH_3$ (OH)
d, R = CHO

47

B. Oxidative Cyclization with Lead Tetraacetate. Because the hypoiodite reaction failed to yield the desired 1,11 ethers, attention was turned to oxidative cyclization with lead tetraacetate, for in rigid, hindered systems this reaction is believed to produce ethers without generation of carbonium ions.[2,4,26] Indeed, treatment of **25** with $Pb(OAc)_4$ in cyclohexane afforded two ethers. The more polar substance (33% yield) was assigned structure **48** in view of its nmr spectrum, which retained the three-proton singlets of the C-10 methyl (0.84 ppm), the C-4 methyl (1.28 ppm), and the carbomethoxyl group (3.65 ppm). A two-proton resonance hidden under the latter was made visible by the $Eu(fod)_3$ shift reagent and resolved into a doublet of doublets (H-1α) which was coupled to H-2β (J = 8.5 Hz) and H-2α (J = 5.5 Hz), and a doublet of triplets (H-11β) which was coupled to H-9α (J = 10 Hz), H-12α (J = 10 Hz), and H-12β (J = 5 Hz). The less polar product (40% yield) was formulated as **49**, presumably the result of a reversible fragmentation leading to epimerization of starting material during $Pb(OAc)_4$ treatment,[3] because the nmr spectrum displayed only two methyl singlets at 0.95 (C-4 methyl) and 3.66 ppm (carbomethoxyl), a one-proton resonance characteristic of an equatorial H-11 proton (4.24 ppm, $W_{1/2}$ = 7 Hz) similar to H-11 of **24**, and an AB quartet centered at 3.80 ppm characteristic of the two hydrogens on C-20.

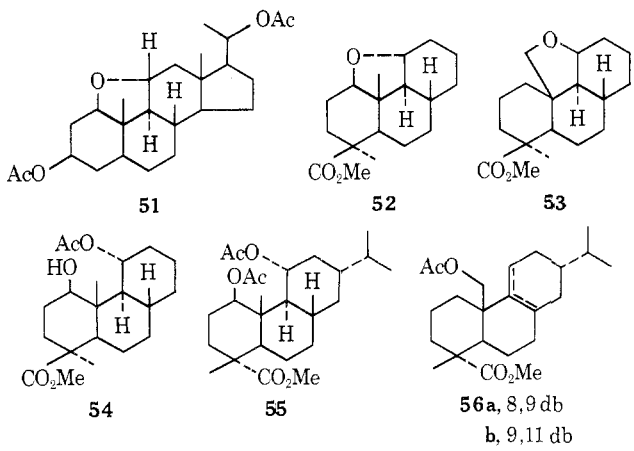


The products from **25** indicate that partial isomerization of an equatorial alcohol (**25**) to an axial alcohol (**24**) has taken place. By contrast, lead tetraacetate treatment of the equatorial alcohol **44a** furnished only the 1β,11α ether **45**[27a] without epimerization, whereas the axial 11β-hydroxy steroid **50** gave, in addition to 11β,18 and 11β,19 ethers, the 1β,11α ether **51**[28] by partial epimerization of an axial to an equatorial alcohol.

These differences can be rationalized by comparing the steric interactions experienced by α- and β-oriented hydroxyl functions in steroids **44a** and **44b** (or **50**) with those in the abietanes **24** and **25**. The equatorial 11α-hydroxyl group in both steroids and abietanes is rigidly positioned near the C-1 methylene group such that the C–O distance is 2.5 Å (measured on Dreiding models). The interaction between the 11α-hydroxyl group and the C-1 methylene of **44a** and **25** should therefore be approximately equal to the 1,3-diaxial interaction between the axial 11β-hydroxyl and the C-10 angular methyl group of **44b** or **50** and **24**, for in these substances the C–O distance is also 2.5 Å. In the case of steroid **44b** (or **50**), the axial hydroxyl experiences an additional 1,3-diaxial interaction with C-19; hence the axial alcohol is of higher energy than the equatorial alcohol to which it might be expected to epimerize.

Abietane **24**, on the other hand, should be of approximately the same energy as **25**. Both alcohols might, therefore, be expected to produce a mixture of epimers when exposed to oxidative cyclization with lead tetraacetate. This was observed experimentally; treatment of **24** with lead tetraacetate gave a mixture of **48** (13%) and **49** (54%).[29]

In analogy with the results in the abietane series, podocarpane **36a** furnished 1β,11α ether **52** in 33% yield and 11β,19 ether **53** in 38% yield. Treatment of podocarpane **35a** with lead tetraacetate–cyclohexane also gave **52** (40%) and **53** (30%).



Oxidation of ethers **49** and **53** (CrO_3–HOAc–Ac_2O) resulted in disappointingly poor yields of lactones **40** and **41**, presumably because of the obstruction presented to the oxidizing agent by the axial group at C-4. Cleavage of **52**

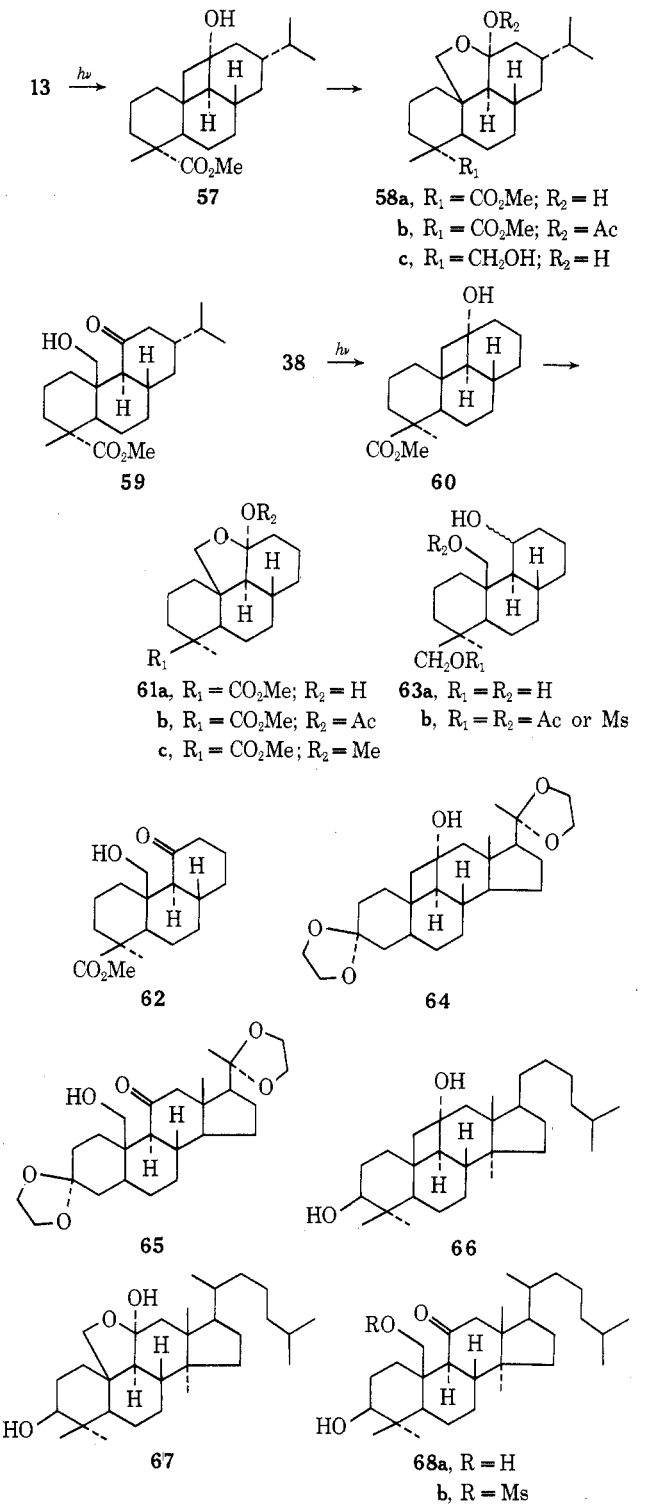
with acetic anhydride–boron trifluoride etherate[30] furnished a complex mixture from which **54** was isolated in 34% yield. Structure assignment was based on the observation that the one-proton resonance at lowest field (5.00 ppm, $W_{1/2}$ = 18 Hz) corresponded to that of H-11 in **36a** and that the chemical shift and coupling constant of a second signal (triplet at 3.56 ppm, J = 8 Hz), made visible with the shift reagent Eu(fod)$_3$, were characteristic of H-1α.[31] An analogous cleavage reaction of **48** gave **55** in 38% yield. BF_3 cleavage of **49** gave a mixture of **56a** and **56b**.

The preceding results indicate that while oxidative cyclization of 11-hydroxyabietanes and podocarpanes with lead tetraacetate proceeds quite efficiently, the reaction is not as selective as in the steroid series, since the direction of functionalization is not dependent on the original configuration of the 11-hydroxyl group.

C. Photoisomerization of 11-Ketones. Irradiation of **13** (quartz apparatus, Corex filter[33]) resulted in quantitative conversion to the cyclobutanol **57**, as indicated by disappearance of the ketone frequency from the ir spectrum, the appearance of OH absorption, and the disappearance of the C-10 methyl signal from the nmr spectrum. Cleavage of **57** with $Pb(OAc)_4$[34] did not furnish the expected hydroxy ketone **59**, but the hemiketal acetate **58b**, which could be hydrolyzed to **58a** and reduced ($LiAlH_4$–ether) to **58c**. Similarly, photoisomerization of **38** provided **60**, which was cleaved to **61b**. The latter was hydrolyzed to **61a**, which was stable in the hemiketal form. **58a** and **60a** were resistant toward oxidation attempts; reduction of **61a** ($LiAlH_4$–THF) furnished the triol **63a**, which could not be converted to derivatives in which the primary hydroxyl groups were protected selectively.

Hemiketal acetates have been isolated as products of the lead tetraacetate cleavage of certain strained tertiary alcohols,[35] but not from steroidal or triterpenoid cyclobutanols corresponding to **57** and **60**. The product formed by lead tetraacetate cleavage of **64** exists entirely in the hydroxy ketone form **65**.[34] Lead tetraacetate treatment of cyclobutanol **66** from 11-oxolanostanol, on the other hand, yields a hemiketal **67** which can be opened with base to the keto mesylate **68b**.[36] Attempts to duplicate this reaction with **61a** resulted only in recovery of starting material or formation of **61c**.

These differences in the hemiketal–hydroxy ketone equilibrium of the diterpenoids **58a** and **61a**, the steroid **65**, and the triterpenoid **67** can be rationalized as follows. (1) Formation of a hemiketal will reduce the interaction between an axial substituent at C-4 and the substituted C-10 methyl group by incorporating the hydroxyl group in a ring, thus favoring the hemiketal over the hydroxy ketone form. (2) Formation of a hemiketal introduces a new interaction between an axial substituent on C-13 and the axial substituent on C-11, thus favoring the hydroxy ketone over the hemiketal form. In steroid **65**, the absence of an axial substituent on C-4 and the presence of an axial substituent on C-13 both favor the hydroxy ketone form. In triterpenoid **67** the presence of an axial C-4 substituent shifts the equilibrium toward the hemiketal, but the presence of an axial substituent on C-13 permits displacement of the equilibrium toward **68a** under appropriate circumstances. In diterpenoids **58a** and **61a**, the presence of an axial C-4 substituent and the absence of an axial C-13 substituent conspire to favor the hemiketal forms over the hydroxy ketone forms **59** and **62** to such an extent that formation of derivatives of the latter is difficult, if not impossible. This result has so far interfered with utilization of the present route to C-10 methyl functionalized diterpenoids, although the photoisomerization reactions proceeded in high yield.



New Isomers of Levopimaric Acid. The availability of the acetates **9** from the synthesis of the 11-oxygenated abietanes suggested the possibility of conversion to the methyl levopimarate isomer **27** (Scheme I), which is of interest because of its chiroptical properties. This substance lacks the interactions which are probably responsible[37] for the "folded" conformation of levopimaric acid, originally invoked[38] to account for its deviation from what is now known as the cisoid helicity rule;[39] moreover, it is conceivable that **27** may be a component of the complex mixture which constitutes pine oleoresin.

In fact, pyrolysis of **9b** and **9d** by the method of Girotra and Zalkow[40] afforded a mixture of dienes **26** and **27** which was extremely difficult to separate. Very small amounts of pure samples were eventually obtained by re-

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Experimental Section[41]

(41) For details concerning methods, see footnote 32 of Ref. 1.

12-Acetyldehydroabietonitrile (1b)[7].--To a solution of 26.8 g of dehydroabietonitrile (Hercules Inc.) in 200 ml of tetrachloroethane cooled to 0° (dry atmosphere) was added 10 ml of acetyl chloride and 26.5 g of aluminum chloride. The mixture was stirred at 0° for 24 hr, poured into water and extracted with $CHCl_3$. The washed and dried extract was evaporated; the residue was recrystallized from methanol-water, yield 27.5 g of 1b, mp 157.5-158°, $[\alpha]_D^{25}$ + 97.0° (c, 0.320; 95% ethanol), ir bands at 2247 (nitrile) and 1692 cm^{-1}; nmr signals at 1.18 (C-10 methyl), 1.26d (J=6.5 Hz, isopropyl), 1.40 (C-4 methyl), 2.50 (methyl ketone), 7.00 and 7.26 ppm (aromatic protons).

Anal. Calcd for $C_{22}H_{29}NO$: C, 81.69; H, 9.04; N, 4.33. Found: C, 81.61; H, 9.19; N, 4.54.

12-Acetoxydehydroabietonitrile (2b).--A mixture of 10 g of 1b in 30 ml of $CHCl_3$ and 90 ml of 50% peracetic acid was stirred for 48 hr in the dark, poured into water and extracted with ether. The washed and dried ether extract was evaporated and the residue was recrystallized from ethanol-water, yield of 2b 8 g, mp 137.5-139°, ir bands 2250 (nitrile) and 1770 cm^{-1} (ester); nmr signals at 1.18d (J=6.5, isopropyl), 1.19 (C-10 methyl), 1.42 (C-4 methyl) 2.30 (acetate), 6.86 and 7.05 ppm (aromatic protons).

Anal. Calcd for $C_{22}H_{29}NO_2$: C, 77.84; H, 8.61; N, 4.13. Found: C, 77.83; H, 8.69; N, 4.17.

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12-Hydroxydehydroabietonitrile (2a).--A solution of 0.5 g of 2b in 20 ml of CH_3OH and 2.7 ml of conc. HCl was allowed to stand for 24 hr at room temperature, diluted with water and extracted with ether. The washed and dried ether extract was evaporated; the residue (quantitative yield of 2a) was recrystallized from methanol-water, mp of 2a 205.5-207°, $[\alpha]_D^{25}$ + 34.4° (c, 0.329, 95% ethanol), ir bands 3430 (-OH) and 2248 (-CN), nmr signals at 1.16 (C-10 methyl), 1.21d (J=6.5 Hz, isopropyl), 1.39 (C-4 methyl) 6.54 and 6.82 ppm (aromatic protons).

Anal. Calcd for $C_{20}H_{27}NO$: C, 80.76; H, 9.15; N, 4.71. Found: C, 80.58; H, 9.35; N, 4.80.

12-Methoxydehydroabietonitrile (2c).--To a solution of potassium t-butoxide, prepared from 1 g of potassium, and 100 ml of t-butyl alcohol (nitrogen atmosphere) was added 3 g of 2a. When solution was complete, 10 ml of CH_3I was added slowly with stirring for 5 hr. The solvent was removed at reduced pressure, and the residue was taken up in ether. The washed and dried ether extract was evaporated and the residue was recrystallized from ethanol-water, yield of 2c 2.53 g, mp 95-96°, $[\alpha]_D^{25}$ + 115° (c, 0.494, 95% ethanol), ir bands 2247 cm^{-1} (nitrile), nmr signals at 1.22d (J=6.5 Hz, isopropyl), 1.23 (C-10 methyl), 1.43 (C-4 methyl), 3.86 (methoxyl), 6.82 and 7.04 ppm (aromatic protons).

Anal. Calcd for $C_{21}H_{29}NO$: C, 80.98; H, 9.38; N, 4.50 Found: C, 81.05; H, 9.25; N, 4.49.

12-Methoxydehydroabietic Acid (3a).--A mixture of 2 g of 2c, 20 ml of diethylene glycol, 0.5 ml of H_2O and 1 g of NaOH was heated with stirring (nitrogen atmosphere) for 16 hr at 170°. The condenser was temporarily removed to drive off water and replaced. The mixture was refluxed at 200° for 6 hr, cooled, poured into H_2O and extracted with ether. The aqueous layer was acidified and extracted with ether. The washed and dried ether extract was evaporated and the residue recrystallized from ethanol-water, yield 1.82 g of 3a, mp 205-205°, $[\alpha]_D^{25}$ + 29.0° (C, 0.517, 95% ethanol), ir bands 3400 br (-OH) and 1640 cm^{-1} (carboxyl), nmr signals at 1.20d (J=6.5 Hz, isopropyl), 1.25 (C-10 methyl) 1.28 (C-4 methyl), 3.80 (methoxyl), 6.80 and 6.92 ppm (aromatic protons).

Anal. Calcd for $C_{21}H_{30}O_3$: C, 76.33; H, 9.15; O, 14.52. Found: C, 76.70; H, 9.28; O, 14.59.

Birch reduction of 3a.--A)[42] To a solution of 0.3 g of 3a in 3.78 ml of dry t-butylalcohol was added 300 ml of ethylamine, dried and condensed by having been passed through a U-tube containing glass wool and KOH and a dry ice-isopropyl alcohol condenser. 0.48 g of Li wire was added in two portions with stirring; this was followed by 4.4 ml of t-butyl alcohol. The reaction mixture was *stirred at reflux until the lithium was consumed and ethylamine* was driven off with the aid of a stream of nitrogen. The residue was dissolved in water, acidified with NH_4Cl followed by 10% HCl and extracted with ether. The washed and dried ether layer was evaporated and methylated with diazomethane. Tlc showed the presence of 7 spots. Preparative tlc permitted the isolation of two pure

(42) A. W. Burgstahler and L. R. Worden, J. Am. Chem. Soc., 86, 96 (1964).

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compounds; 1) Methyl vinyl ether 5b (44% yield), gum, ir bands 1720 cm^{-1} (ester), nmr signals at 0.97d (J= 7 Hz, isopropyl), 1.07 (C-10 methyl), 1.25 (C-4 methyl), 3.58 (ester methoxyl), 3.72 ppm (ether methoxyl); 2) Methyl 12-hydroxydehydroabietate 4b (13% yield), mp 157-158°, nmr signals at 1.20 (C-10 methyl), 1.25d (J=6Hz, isopropyl, 1.30 (C-4 methyl), 3.64 (methoxyl), 6.60 and 6.81 ppm, (aromatic protons), identical with material obtained by hydrolysis of 2a in the manner described above for 2c followed by methylation.

B) In a 1 l. 3-necked, round-bottom creased flask fitted with a dry ice-isopropyl alcohol condenser and a high speed (6000 rpm) stirrer was placed 1g of 3a in 200 ml of dry ethylamine. Addition of 35 ml of dry t-amyl alcohol was followed by addition of 1.84 g (43 fold excess) of Li wire with high speed stirring. To prevent appearance of a dark blue color, an additional 35 ml of t-amyl alcohol was added. After consumption of lithium, ethylamine was removed as before, water was added to the residue and the solution acidified with 10% HCl. The aqueous mixture was immediately extracted with ether, the washed and dried ether extracts were evaporated and the residue was methylated with diazomethane. The methyl ester was taken up in 20 ml of MeOH containing 0.27 ml of conc. HCl, allowed to stand at room temperature for 2 hr (tlc control to monitor disappearance of 5b), poured into water and extracted with ether. The washed and dried ether extracts were evaporated and the residue was dissolved in a 1:1 mixture of acetic anhydride-pyridine. After standing overnight at room temperature, the mixture was poured into water, neutralized with solid $NaHCO_3$

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and extracted with ether. The washed and dried ether extracts were evaporated and the residual mixture was separated by preparative tlc. The following substances were isolated in increasing order of polarity: 1) Methyl dehydroabietate, 9a (10% yield), mp 62-63°, $[\alpha]_D^{25}$ (c, 0.314, 95% ethanol), identical with an authentic sample: 2) Methyl 12-methoxydehydroabietate, 3b (14%), physical properties identical with those of an authentic sample; 3) Methyl 12-acetoxydehydroabietate, 4c (18% yield), physical properties identical with those of an authentic sample; 4) Methyl 12-oxo-abiet-9(11)-en-18-oate, 7 (48% yield), mp 104-105°, $[\alpha]_D^{25}$ + 47° (c, 0.250, $CHCl_3$), ir and nmr spectra superimposable on those of material obtained previously[9]; 5) Methyl 12-oxo-13S-abiet-9(11)-en-18-oate, 8 (12% yield), mp 94-95°, $[\alpha]_D$ + 163° (c, 0.30, $CHCl_3$), ir and nmr spectra superimposable on those of material obtained previously[9].

Methyl 11a- and 11S-abiet-9(11)-en-18-oate (9a and 9c).--A solution of 0.403 g of 7 in 10 ml of methanol was reduced with 0.48 g of $NaBH_4$ and worked up in the usual manner. Recrystallization of the crude alcohol mixture, yield 0.40 g, from hexane afforded 9c, $[\alpha]_D^{25}$ -54.0° (c, 0.368, 95% ethanol); ir bands at 3340 and 1720 cm^{-1}; nmr signals at 0.80d and 0.94d (J=6 Hz, isopropyl), 1.06 (C-10 methyl), 1.16 (C-4 methyl), 3.64 (methoxyl), 4.02d (J=9 Hz, H-12a), 5.32 (w_h=5 Hz, H-11).

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.41; H, 10.25; O, 14.35. Found: C, 75.32; H, 10.33; O, 14.27.

The presence of 9a in the alcohol mixture was revealed by the observation in the nmr spectrum of a broad resonance at 4.08 (w_h=22 Hz, H-12S).

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Acetylation of the crude alcohol mixture with acetic anhydride-pyridine followed by the usual work-up gave a mixture from which 9d was isolated by recrystallization from hexane, mp 106-107°, $[\alpha]_D^{25}$ -82.8° (c, 0.389, 95% ethanol); ir band at 1727 cm^{-1} (double intensity); nmr signals at 0.79d and 0.91d (J=7Hz, isopropyl), 1.07 (C-10 methyl), 1.18 (C-4 methyl), 2.05 (acetate, 3.62 (methoxyl), 5.15 (w_h = 5 Hz, H-11), 5.27d (J=9 Hz, H-12a).

Anal. Calcd for $C_{23}H_{36}O_4$: C, 73.37; H, 9.64; O, 17.00. Found: C, 73.30; H, 9.65; H, 16.90.

Methyl 11-Oxo- and 12-Oxoabietan-18-oate (13 and 12).--To 10 ml of purified dry ethylamine in a flask fitted with a dry ice-isopropyl alcohol condenser was added 0.550 g of Li wire followed immediately by 0.456 g of the mixture of 5b and 9d dissolved in the minimum amount of THF. The dark blue mixture was stirred for 1.5 hr; this was followed by addition of 20 ml of dry t-amyl alcohol to destroy the excess metal. The usual work-up described in part A of the Birch reduction of 3a gave a residue which could be separated by preparative tlc into two fractions. The less polar material (21% yield) was a mixture of 10 and 11a in a 5:1 ratio, which had nmr signals at 0.80d (J=5.5, isopropyl), 1.08 (6 H, C-4 and C-10 methyls), 5.37 C and 5.62 br (w_h = 11 and 3 Hz, H-11 and H-12), 9.20 ppm (-CHO). The more polar fraction (66%) was a mixture of 10b and 11b in a 5:1 ratio, nmr signals at 0.80 (C-4 methyl), 0.86d (J=7 Hz, isopropyl), 1.04 (C-10 methyl), 3.25 (2 H, center of AB quartet of H-18), 5.40 c and 5.65 br (w_h = 10 and 3 Hz, H-11 and H-12). To a solution of 0.176 g of the mixture of alcohols and aldehydes in 4 ml of ether was added (nitrogen atmosphere) 0.74 g of BF_3-etherate

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followed by 0.16 g of $LiAlH_4$ in 10 ml of ether. After addition of 10 ml of ether and one hr of stirring, a satd. solution of Na_2SO_4 was added dropwise until a granular white precipitate had formed. Solid anh. Na_2SO_4 was added to absorb excess water, the mixture was stirred for one hr and filtered, the precipitate being washed thoroughly with hot THF. The combined filtrate and washings were evaporated; the residue was dissolved in 40 ml of ethanol containing 0.20 g of NaOH and oxidized with 2 ml of 30% H_2O_2. After 10 min at room temperature and 5 min on the steam bath, the mixture was poured into water and extracted with ether. The washed and dried ether extract was evaporated and the residue was oxidized with Jones' reagent, methylated with diazo*methane and separated by preparative tlc into two fractions.*

Methyl 12-oxoabietan-18-oate (12), mp 98-99°, was isolated in 8% yield; its properties were identical with properties reported previously[6, 43, 44].

(43) W. G. Dauben and R. Coates, J. Org. Chem., 28, 1698 (1963).
(44) W. Herz, H. J. Wahlborg, W. D. Lloyd, W. H. Schuller, and G. W. Hedrick, J. Org. Chem., 30, 3190 (1965).

Methyl 11-oxoabietan-18-oate (13) was obtained in 64% yield, mp. 105.5-106.5°, $[\alpha]_D^{25}$ -24.6° (C, 0.480, 95% ethanol); ir bands at 1720 and 1706 cm^{-1}; nmr signals at 0.84d (J=6 Hz, isopropyl), 1.08 (C-10 methyl), 1.15 (C-4 methyl), 2.16 2p, (w_h = 9 Hz, H-12), 2.48d (J=12 Hz, H-18), 3.62 ppm (methoxyl); uv λ_{max} 292 nm (ε 43); CD curve θ_{294} -1050 (C, 0.00609 g/l, CH_3OH).

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Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.41; H, 10.25; O, 14.35. Found: C, 75.19; H, 10.33; O, 14.50.

Methyl 11a- and 11S-Hydroxyabietan-18-oate (25 and 24).--To 0.050 g of 13 in 10 ml of THF containing 0.86 ml of 5% NaOH solution was added 0.186 g of $NaBH_4$. The mixture was refluxed for 9 hr, poured into water and worked up in the usual way. The crude product was separated by preparative tlc into two fractions. The less polar material (42% yield) was 24, mp 101-102°, $[\alpha]_D^{25}$ -10.9° (C, 0.331, 95% ethanol); ir bands at 3500 and 1720 cm^{-1}; nmr signals at 0.84d (J=6 Hz, isopropyl), 1.16 (C-10 methyl), 1.20 (C-4 methyl), 3.64 (methoxyl), 4.31 (w_h = 10 Hz, H-11a).

Anal. Calcd for $C_{21}H_{36}O_3$: C, 74.95; H, 10.78; O, 14.26. *Found: C, 75.05; H, 10.86; O, 14.19.*

The more polar material (34% yield) was 25, mp 88-89°, $[\alpha]_D^{25}$ +8.1° (C, 0.510, 95% ethanol); ir bands at 3400 and 1718 cm^{-1}; nmr signals at 0.86d (J=6 Hz, isopropyl), 1.02 (C-10 methyl), 1.20 (C-4 methyl), 2.39d (J=12 Hz, H-18), 3.64 (methoxyl), 3.64 (w_h = 20 Hz, made visible by using $Eu(fod)_3$, H-11S).

Anal. Calcd for $C_{21}H_{36}O_3$: C, 74.95; H, 10.78; O, 14.26. Found: C, 75.10; H, 10.85; O, 13.97.

Pyrolysis of Acetates 9b and 9d.--A solution of the mixture of allylic acetates, wt. 0.483 g, in 5 ml of benzene was added dropwise to a column filled with glass helices and kept at 300°, while a nitrogen stream was passed upward through the column. When addition was complete the nitrogen stream was stopped. After 30 min, the column was allowed to cool and washed with ether. Removal of solvent and chromatography furnished 0.091 g of starting

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material and 0.206 g (84%) of a diene mixture which proved difficult to separate. Chromatogrphay over silica gel impregnated with silver nitrate yielded methyl dehydroabietate due to disproportionation. Eventually, repeated continuous solvent flow preparative tlc permitted separation of the dienes 26 and 27 (1:5 ratio). The less polar substance, methyl 8,11-abietadien-18-oate (26) was noncrystalline and had $[\alpha]_D^{25}$ +65.5° (C, 0.578, 95% ethanol); nmr signals at 0.96d (J=6.5 Hz, isopropyl), 1.08 (C-10 methyl), 1.27 (C-4 methyl), 3.72 (methoxyl), 5.88 (2p, center of AB quartet of H-11 and H-12, J=10 Hz); uv λ_{max}246, 253, 267sh nm (ε 3230, 3170, 2620), λ_{min} 250 nm (ε 3160), Ord curve (C, 7.8 x 10^{-5} g/ml) ϕ_{310} +2630, ϕ_{285} +5780, ϕ_{260} 0, ϕ_{245} -3800.

Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.90; H, 10.19; O, 10.11. Found: C, 79.94; H, 10.13; O, 9.68.

The more polar methyl 9(11),12-abietadien-18-oate (27) was also non-crystalline and had $[\alpha]_D^{25}$ -25.8° (C, 0.538, 95% ethanol), nmr signals at 1.02d (J=7 Hz, isopropyl), 1.08 (C-10 methyl), 1.22 (C-4 methyl), 3.62 (methoxyl), 5.60 br (2H, w_h = 2 Hz, almost coinciding center lines of AB system, H-11 and H-12); uv λ_{max} 260sh, 268, 280, 287.5 sh nm (ε 3300, 3840, 3560, 1950), λ_{min} 273.5 (ε 3500); Ord curve (C, 1.04 x 10^{-4} g/ml), ϕ_{310} -1220, ϕ_{296} - 2600, ϕ_{282} 0, ϕ_{275} +3050, ϕ_{250} 0, ϕ_{222} -1010.

Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19; O, 10.11. Found: C, 79.84; H, 10.07; O, 9.29.

Birch Reduction of O-Methylpodocarmic Acid[18].--To 600 ml of purified ammonia was added a solution of 10 g of 28b (prepared by methylation of the sodium salt of 28a with a limited amount of dimethylsulfate and separation of 28c in the usual manner) in

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120 ml of THF followed by 125 ml of t-amyl alcohol and then 5 g of Li wire. The mixture was stirred until the Li was consumed, 100 ml of MeOH was added and the ammonia was allowed to evaporate on a water bath. The remaining material was diluted with water, acidified with 10% HCl and extracted with ether. Evaporation of the washed and dried ether extracts gave a gum which was methylated with diazomethane, stirred overnight with 5% HCl in methanol to hydrolyze the vinyl ether and to rearrange the β,γ-unsaturated ketone, poured into water and extracted with ether. The washed and dried ether extracts were evaporated; chromatography gave the following fractions: 1) Methyl podocarp-8(9)-en-19-oate 29 (26% yield), mp 82-83°; $[\alpha]_D^{25}$ +190° (C, 0.400; 95% ethanol; ir band 1710 cm^{-1}; nmr signals at 0.78 (C-10 methyl), 1.19 (C-4 methyl) and 3.60 ppm (methoxyl). A similar substance, desoxytetrahydropodocarpinol, has been isolated as a minor product from the Li-NH_3-t-butyl alcohol reduction of O-methylpodocarpinol[16].

Anal. Calcd for $C_{18}H_{28}O_2$: C, 78.31; H, 10.21; O, 11.58. Found: C, 78.91; H, 10.42; O, 11.75.

2) Methyl O-methylpodocarpate 28c (3% yield), mp 128-129°, $[\alpha]_D^{25}$ +132° (C, 0.511, 95% ethanol), identical with an authentic sample.

3) Methyl 12-oxopodocarp-8(9)-en-19-oate, 30 (1.3%), a gum, ir band at 1710 cm^{-1}, nmr signals at 0.78 (C-10 methyl), 1.21 (C-4 methyl) and 3.62 ppm (methoxyl). Treatment with 5% HCl in methanol caused rearrangement to 31.

4) Methyl 12-oxopodocarp-9(11)-en-19-oate 31 (52% yield), mp 107-108°, $[\alpha]_D^{25}$ -12.4° (C, 0.500, 95% ethanol), ir bands 1710 and 1664 cm^{-1}, nmr signals at 0.97 (C-10 methyl), 1.20 (C-4 methyl), 3.66 (methoxyl) and 5.86d (J=2.5 Hz, H-11), uv λ_{max} 238 nm (ε 17000). The mp of this compound prepared by a more circuitous route, is reported as 116-118°[16].

Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.03; O, 16.53. Found: C, 74.36; H, 8.98; O, 16.90.

Methyl 12-Hydroxypodocarp-9(11)-en-19-oate (32a).--$NaBH_4$ reduction of 1 g of 31 in the manner described for 7 gave a gummy alcohol, possibly a mixture of epimers, which was homogeneous on tlc. It had ir bands at 3380, 1720 and 1650 cm^{-1}, nmr signals at 0.87 (C-10 methyl), 1.15 (C-4 methyl), 3.63 (methoxyl), 4.16 (w_h = 18 Hz, H-12) and 5.42 br (w_h = 5 Hz, H-11).

Acetylation with acetic anhydride-pyridine gave a gummy product 32b which was homogeneous on tlc, ir bands at 1735 (double strength) and 1650 cm^{-1}; nmr signals at 0.89 (C-10 methyl), 1.15 (C-4 methyl), 2.01 (acetate), 3.63 (methoxyl), 5.24 c (H-12) and 5.34 br (H-12).

Hydrogenolysis of 32b.--Reductive cleavage of 0.622 g of 32b in 200 ml of ethylamine and a little THF with 0.730 g of Li wire in the manner described for the mixture of 5b and 8d followed by preparative tlc of the crude product gave podocarp-9(11)-en-19-oic acid 33a (21% yield) by partial hydrolysis of the initially-formed 33b under Birch conditions; which was remethylated to gummy 33b. The latter had an ir band at 1720 cm^{-1} and nmr signals at 0.83 (C-10 methyl), 1.14 (C-4 methyl) and 3.62 ppm (methoxyl). The major product was podocarp-9(11)-en-19-ol 33c, mp 97-99°, $[\alpha]_D^{25}$-35.5° (C, 0.395, 95% ethanol), ir band at 3370 cm^{-1}, nmr signals at 0.93 (C-10 methyl), 1.00 (C-4 methyl), 3.60 (2p, center of AB quartet of H-19, J=10 Hz), and 5.36 ppm (w_h = 9 Hz, H-11).

Anal. Calcd for $C_{17}H_{26}O$: C, 82.20; H, 11.36; O, 6.44. Found: C, 82.22; H, 11.63; O, 6.30.

Methyl 11-Oxopodocarpan-19-oate (38) and Methyl 9β-11-Oxopodocarpan-19-oate (37).--Hydroboration-oxidation of 0.315 g of a mixture of 33b and 33c with 0.961 g of BF_3-etherate and 0.190 g of $LiAlH_4$, as described in the abietane series, followed by oxidation of the crude alcohol mixture with 5 ml of a solution of 5 g of CrO_3 in 10 ml of H_2O and 90 ml of acetic acid for 9 hr, methylation of the ketoacid mixture with CH_2N_2 and preparative tlc gave, in the less polar fraction, gummy ketone 38 (20% yield) which could be isomerized to 37 on treatment with a 5% solution of NaOH in CH_3OH, ir band at 1720 cm^{-1}, nmr signals at 0.80 (C-10 methyl), 1.16 (C-4 methyl) and 3.63 ppm (methoxyl). The more polar ketone 37 (35% yield) had mp 104-105°, $[\alpha]_D^{25}$ +22.2° (C, 0.577, 95% ethanol) ir bands at 1720 and 1705 cm^{-1}, nmr signals at 0.95 (C-10 methyl), 1.16 (C-4 methyl) and 3.63 ppm (methoxyl); uv λ_{max} 295 nm (ε 31.6); CD curve (C 0.00585 g/ml, CH_3OH), $[\theta]_{295}$ +4360.

Anal. Calcd for $C_{18}H_{28}O_3$: C, 79.93; H, 9.65; O, 16.41. Found: C, 73.88; H, 9.74; O, 16.32.

Methyl 11α-Hydroxy- and 11β-Hydroxypodocarpan-19-oate (36a and 39).--Reduction of 0.3 g of 37 with sodium borohydride gave a 1:1 mixture of C-11 epimeric alcohols which was difficult to separate. Partial separation was achieved by continuous solvent flow preparative tlc using benzene as solvent. The alcohol band

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JOC-11-13

which broadened as it moved upward, was divided into 4 parts. Pure alcohols were obtained from the first and fourth part. The less polar α-hydroxy isomer 36a had mp 103-104°, $[\alpha]_D^{25}$ +7.0° (C, 0.343, 95% ethanol), ir bands at 3470 and 1710 cm^{-1}, nmr signals at 0.82 (C-10 methyl), 1.17 (C-4 methyl), 3.62 (methoxyl), and 3.62c (w_h = 20 Hz, revealed by conversion to the acetate, H-11β).

Anal. Calcd for $C_{18}H_{30}O_3$: C, 73.43; H, 10.27; O, 16.30. Found: C, 73.23; H, 10.48; O, 16.18.

The more polar β-hydroxy isomer 39 had mp 77-78°, $[\alpha]_D^{25}$ +40.3 (C, 0.201; 95% ethanol); ir bands at 3500 and 1710 cm^{-1}; nmr signals at 0.92 (C-10 methyl), 1.17 (C-4 methyl), 3.64 (methoxyl), and 4.89 ppm (w_h=8 Hz, H-11α).

Anal. Calcd for $C_{18}H_{30}O_3$: C, 73.43; H, 10.27; O, 16.30. Found: C, 73.23; H, 10.44; O, 15.92.

Hypoiodite Reactions on 24.--A solution of 0.088 g of 24 in 130 ml of cyclohexane containing 0.53 g of $Pb(OAc)_4$, 0.360 g of $CaCO_3$ and 0.0725 g of I_2 was irradiated with a 70 watt incandescent lamp and refluxed (due to the heat of the lamp) for 90 min with stirring. After cooling, the mixture was filtered and the residue washed thoroughly with hexane. The combined organic layers were washed with 5% sodium thiosulfate, the wash solution was extracted with ether and the extract combined with the organic layers which were then washed with H_2O, dried and evaporated. The residue was oxidized with Jones' reagent and worked up in the usual manner. Preparative tlc of the crude product furnished lactone 40 (49% yield) which had mp 127-128°, $[\alpha]_D^{25}$ -15.5° (c 0.554, 95% ethanol), ir bands at 1760 and 1722 cm^{-1}, nmr signals at 0.86d (J=5, 10 and 10 Hz, H-11β).

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.41; H, 10.25; O, 14.35. Found: C, 75.40; H, 10.21; O, 14.51.

The less polar product 41 (40% yield) had mp 127-128°, $[\alpha]_D^{25}$ +17.6° (c 0.975, 95% ethanol); ir band at 1728 cm^{-1}; nmr signals at 0.86d (J=6 Hz, isopropyl), 0.95 (C-4 methyl), 3.66 (methoxyl), 3.80 (2H, AB quartet of H-20, J=9 Hz), and 4.24 ppm (w_h = 7 Hz, H-11α).

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.41; H, 10.25; O, 14.35. Found: C, 75.38; H, 10.39; O, 14.25.

A solution of 0.035 g of 40 in 2 ml of acetic anhydride was oxidized with 6 ml of 5% CrO_3 acetic acid solution by heating on a steam bath for 12 hr. The solution was poured into H_2O, neutralized with $NaHCO_3$ and extracted with ether. The washed and dried ether extract was evaporated; the residue, a complex mixture, furnished lactone 40 after preparative tlc.

Lead tetraacetate treatment of 24 gave, after preparative tlc, ether 48 in 13% and ether 49 in 54% yield.

Lead Tetraacetate Treatment of 36a and 39.--$Pb(OAc)_4$ oxidation of 0.103 g of 36a in the usual manner gave, after preparative tlc of the crude product, the less polar ether 53 (38% yield) which had mp 71.5-72.5°, ir band at 1720 cm^{-1}, nmr signals at 1.13 (C-4 methyl), 3.60 (methoxyl), 3.61 (AB quartet of H-18, J=8 Hz), and 4.19 ppm (w_h = 7 Hz, H-11α).

Anal. Calcd for $C_{18}H_{28}O_3$: C, 73.93; H, 9.65; O, 16.41. Found: C, 74.02; H, 9.71; O, 16.03.

The more polar product (33% yield) was 52, mp 76.5-77.5°, ir band at 1724 cm^{-1}; nmr signals at 0.88 (C-10 methyl), 1.18 (C-4 methyl), 3.66 (methoxyl), 3.66m (resolved with $Eu(fod)_3$ into a doublet of doublets, J=11 and 5 Hz, H-1α, and a doublet of triplets, J=10, 10 and 4 Hz, H-11β).

Anal. Calcd for $C_{18}H_{28}O_3$: C, 73.93; H, 9.65; O, 16.41. Found: C, 74.46; H, 9.76; O, 15.83.

Oxidation of 0.030 g of 53 in the manner described for 40 gave a complex mixture from which lactone 41 was isolated in 24% yield.

Lead tetraacetate oxidation of 0.050 g of 39 furnished, after preparative tlc, ether 52 in 30 % and ether 53 in 40% yield.

BF_3-Cleavage of 48 and 52.--To an ice-cold solution of 0.025 g of 48 in 5 ml of acetic anhydride was added 5 drops of BF_3-etherate. The mixture was immediately removed from the ice bath, allowed to stand for 5 min, poured into water, neutralized with solid $NaHCO_3$, care being taken to keep the system at or below room temperature, and extracted with ether. The washed and dried ether extract was evaporated; the residue was purified by preparative tlc and furnished non-crystalline methyl 18, 11α-diacetoxyabietan-18-oate 55 in 38% yield, $[\alpha]_D^{25}$ -24.7° (c 0.425, 95% ethanol); ir band 1728 cm^{-1} (triple intensity); nmr signals at 0.84d (J=6 Hz, isopropyl), 0.87 (C-10 methyl), 1.20 (C-4 methyl), 2.06 (2 acetates), 3.66 (methoxyl), 4.72 (2H, w_h = 27 Hz, H-1α and H-11β.

Anal. Calcd for $C_{25}H_{40}O_6$: mol wt 436.2824. Found (MS) 436.2824.

Cleavage of 0.045 g of 52 with BF_3-etherate was carried out in the same manner; however, after the reaction was complete and the mixture had been diluted with water, it was warmed on the steam bath to drive off the ether. Preparative tlc of the crude product afforded a 34% yield of gummy 54 which had ir bands at 3450, 1740 and 1730 cm^{-1}; nmr signals at 1.08 (C-10 methyl), 1.25 (C-4 methyl), 2.04 (acetate), 3.56 (methoxyl), 3.56t (J=8 Hz, resolved by $Eu(fod)_3$, H-1α), and 5.00 ppm (w_h =18 Hz, H-11β).

BF_3-Cleavage of 49.--Treatment of an ice-cold solution of 0.030 g of 49 in 5 ml of acetic anhydride with 5 drops of BF_3-etherate and work-up as described for 48 gave, after chromatography, a 60% yield of a 1:1 mixture of 56a and 56b. Continuous solvent flow preparative tlc produced partial separation of the mixture into fractions which contained predominantly 56a or 56b. The less polar olefin acetate 56b had nmr signals at 0.87d (isopropyl), 1.19 (C-4 methyl), 1.95 (acetate), 3.64 (methoxyl), 4.35 (2H, center of AB quartet, H-20), and 5.44 ppm (w_h = 9 Hz, H-11). The more polar olefin acetate 56a had nmr signals at 0.87d (J=6 Hz, isopropyl), 1.22 (C-4 methyl), 2.02 (acetate), 3.66 (methoxyl), and 4.27 ppm (2H, center of AB quartet, J=11 Hz, H-20). The olefin acetate mixture was analyzed.

Anal. Calcd for $C_{23}H_{36}O_4$: C, 73.37; H, 9.64; O, 17.00. Found: C, 73.61; H, 9.63; O, 16.84.

Photoisomerization of 13.--A solution of 0.255 g of 13 and 45 ml of 95% ethanol in a quartz apparatus was purged of oxygen by means of a nitrogen stream and subsequently irradiated with uv light from a 450 watt Hanovia mercury vapor lamp passed through a Corex 9700 filter. Removal of solvent gave a quantitative yield of cyclobutanol 57, mp 182-184°, $[\alpha]_D^{25}$ +73.0 (c 0.305, 95% ethanol); ir bands at 3500 and 1720 cm^{-1}; nmr signals at 0.92d and 0.93d (J=5.5, isopropyl), 1.54 (deshielded C-4 methyl), 3.66 (methoxyl), and 4.77 ppm br (w_h = 7 Hz, H-11α).

Anal. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26; O, 18.36. Found: C, 72.10; H, 9.26; O, 18.60.

Oxidation of 0.020 g of 25 in the same manner followed by a similar oxidative work up gave a complex mixture from which no pure compounds could be isolated.

Hypoiodite reaction on 38.--Irradiation of 0.126 g of 38 in 126 ml of cyclohexane with 0.770 g of $Pb(OAc)_4$ and 0.103 of iodine followed by oxidation and work-up as described for 24 gave a complex mixture. Preparative tlc of the crude product yielded lactone 41 (40% yield) which had mp 143.5-144.5°, $[\alpha]_D^{25}$ +46.2° (c 0.511, 95% ethanol); ir bands at 1762 and 1720 cm^{-1}; nmr signals at 1.22 (C-4 methyl), 3.70 (methoxyl) and 4.73 ppm (w_h = 8 Hz, H-11α).

Anal. Calcd for $C_{18}H_{26}O_4$: C, 70.56; H, 8.55; O, 20.89. Found: C, 70.42; H, 8.66; O, 20.85.

Hypoiodite oxidation of 46c.--Reduction[25] of 3 g of methyl 12-acetyldehydroabietate in 100 ml of methanol with 0.5 g of $NaBH_4$ gave a 1:1 mixture of the epimeric alcohols 46c which could be separated by preparative tlc. The less polar alcohol, mp 120-121°, $[\alpha]_D^{25}$ +92.6 (c 0.102, 95% ethanol) had nmr signals at 1.08d and 1.12d (J=7 Hz, isopropyl), 1.11 (C-10 methyl), 1.15 (C-4 methyl), 1.36d (J=6.5 Hz, C-22 methyl), 2.30 (AB quartet of H-7), 3.12 sept (J=7, H-15), 3.58 (methoxyl), 5.169 (J=6.5 Hz, H-21), 6.90 and 7.41 ppm (aromatic protons). The more polar alcohol, mp 133.5-134.5°, $[\alpha]_D^{25}$ +44.6° (c 0.102, 95% ethanol), had nmr signals at 1.11d (6 H, isopropyl), 1.11 (C-10 methyl), 1.17 (C-4 methyl), 1.36d (J=6.5, C-22 methyl), 2.30 (AB quartet of H-7), 3.12 sept (J=7, H-15), 3.58 (methoxyl), 5.179 (J=6.5 Hz, H-21), 6.90 and 7.40 ppm (aromatic protons).

A solution of 0.1 g of the mixture of epimers in 100 ml of cyclohexane was irradiated in the presence of $Pb(OAc)_4$ and worked up as usual without the chromic acid oxidation step. Preparative tlc of the crude product gave lactone 47[24], mp 198-199°, $[\alpha]_D^{25}$ +83.0° (c 0.636, 95% ethanol); ir bands at 1751 and 1721; nmr signals at 1.21 (C-10 methyl), 1.30 (C-4 methyl), 1.61 (C-16 and C-17-methyls), 3.67 (methoxyl), 7.10 and 7.78 ppm (aromatic protons).

Anal. Calcd for $C_{22}H_{28}O_4$: C, 74.18; H, 7.81; O, 17.95. Found: C, 73.82; H, 7.81; O, 17.86.

Lead Tetraacetate Treatment of 24 and 25.--A mixture of 0.098 g of 25, 0.510 g of $CaCO_3$, 0.595 g of dry $Pb(OAc)_4$ and 150 ml of cyclohexane was refluxed for 5 hr, cooled, filtered and the residue washed with hexane. The combined filtrate and washings were washed with 5% sodium thiosulfate solution, the thiosulfate solution was extracted with ether and the combined organic layers were washed with H_2O and dried. Removal of solvent gave a mixture of two compounds which was separated by preparative tlc. The more polar product 48 (33% yield) was a gum, $[\alpha]_D^{25}$ -45.0° (c 0.450, 95% ethanol), ir band at 1720 cm^{-1}, nmr signals at 0.84 (C-10 methyl), 0.89d (J=7 Hz, isopropyl), 1.28 (C-4 methyl), 3.65 (methoxyl), 3.65m (resolved with shift reagent to show a doublet of doublets, J=8.5 and 5.5 Hz, H-1α, and a doublet of triplets,

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JOC-11-17

JOC-11-18

(J=5 Hz, isopropyl), 1.00 (C-4 methyl), 3.64 (methoxyl); no uv or CD absorption characteristic of a ketone.

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.41; H, 10.25; O, 14.35. Found: C, 75.38; H, 10.30; O, 14.56.

Cleavage of 57.-- A solution of 0.104 g of 57 in 50 ml of dry benzene containing 0.430 g of $CaCO_3$ and 0.635 g of dry $Pb(OAc)_4$ was refluxed for 16 hr, allowed to cool and worked up as described for the oxidative cyclization of 25. Preparative tlc of the crude product gave 58b (50% yield), mp 88.5-89°, band 1721 cm^{-1}, nmr signals at 0.90d (J=6 Hz, isopropyl), 1.09 (C-4 methyl), 2.07 (acetate), 3.66 (methoxyl); no uv or CD maximum characteristic of a ketone.

Anal. Calcd for $C_{23}H_{36}O_5$: C, 70.38; H, 9.24; O, 20.38. Found: C, 70.46; H, 9.34; O, 20.27.

A solution of 0.020 g of 58b in 20 ml of MeOH containing 1 g of NaOH was stirred at room temperature for 25 hr, poured into H_2O and extracted with ether. The washed and dried ether extracts were evaporated; the residue which was recrystallized from hexane gave a quantitative yield of 58a, mp 179.5-180.5°, $[\alpha]_D^{25}$ +26.6° (c 0.478, 95% ethanol); ir bands 3380 and 1720 cm^{-1}; nmr signals at 0.89d and 0.93d (J=6 Hz, isopropyl), 1.08 (C-4 methyl) and 3.64 ppm (methoxyl); no uv or CD absorption characteristic of a ketone. The substance was not affected by CrO_3-acetic acid solution.

Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78; O, 18.26. Found: C, 71.72; H, 9.98; O, 18.07.

Reduction of 0.041 g of 58b with $LiAlH_4$ in ether and work up

in the usual way gave, after chromatography, 0.043 g of 58c which had mp 117-119°, $[\alpha]_D^{25}$ +75.6° (c 0.210, 95% ethanol); ir band at 3490 cm^{-1}; nmr signals at 0.70 (C-4 methyl), 0.89d and 0.90d (J=6 Hz, isopropyl), and 3.27 ppm (2H, AB quartet of H-9, J=11 Hz).

Anal. Calcd for $C_{20}H_{34}O_3$: C, 74.99; H, 10.63; O, 14.88. Found: C, 74.18; H, 10.82; O, 15.01.

Photoisomerization of 38.--Irradiation of 0.1 g of 38 as described for 13 gave a quantitative yield of the non-crystalline cyclobutanol 60 which had $[\alpha]_D^{25}$ +149° (c 0.255, 95% ethanol); ir bands at 3400 and 1715 cm^{-1}; nmr signals at 1.14 (C-4 methyl) and 3.64 ppm (methoxyl); no uv or CD maximum characteristic of a ketone.

Anal. Calcd for $C_{18}H_{28}O_3$: mol wt 292. Found (MS): 292.

Cleavage of 60.--A solution of 0.050 g of 60 in 26 ml of dry benzene was refluxed with 0.218 g of $CaCO_3$ and 0.323 g of dry $Pb(OAc)_4$ for 12 hr and worked up as described for oxidative cyclization of 25. Preparative tlc gave 0.040 g of non-crystalline 61b which had $[\alpha]_D^{25}$ +231° (c 0.118, 95% ethanol); ir bands at 1735 and 1725 cm^{-1}; nmr signals at 1.19 (C-4 methyl), 2.02 (acetate) and 3.68 ppm (methoxyl).

Anal. Calcd for $C_{20}H_{30}O_5$: mol wt 350. Found (MS): 350.

Hydrolysis of 0.022 g of 61b in the manner described for 58b gave, after recrystallization from hexane, a quantitative yield of 61a which had mp 153-154°, ir bands at 3400 and 1730 cm^{-1}; nmr signals at 1.21 (C-4 methyl) and 3.68 ppm (methoxyl); no uv absorption characteristic of a ketone.

Anal. Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15; O, 20.75. Found: C, 70.33; H, 9.83; O, 21.03.

Attempted mesylations of 61a were unsuccessful. In an attempt to prepare a ditosylate, 0.100 g of NaH was added to 0.051 g of 61a in 50 ml of cyclohexane (nitrogen atmosphere). After gas evolution had ceased, 0.100 g of tosyl chloride was added. The mixture was stirred at room temperature for 19 hr, decomposed with 1 ml of methanol, diluted with water, acidified and extracted with ether. The washed and dried ether extracts were evaporated. Tlc of the residue yielded 0.026 g of starting material and 0.024 g of 61c, mp 65-66°, ir bands at 1724 cm^{-1}; nmr signals at 1.19 (C-4 methyl), 3.20 (methyl ether), and 3.66 ppm (methoxyl); no uv absorption characteristic of a ketone.

Anal. Calcd for $C_{15}H_{30}O_3$: C, 70.77; H, 9.38; O, 19.85. Found: C, 70.49; H, 9.48; O, 19.23.

$LiAlH_4$ reduction of 0.024 g of 61a in refluxing THF gave the non-crystalline triol 63a which had ir bands at 3380 cm^{-1} (strong); nmr signals (d_5-pyridine) at 1.07 (C-4 methyl), 3.82 (4H, AB quartets of H-18 and H-19, J=11 Hz) and 4.39 ppm (W_h = 16 Hz, H-11).

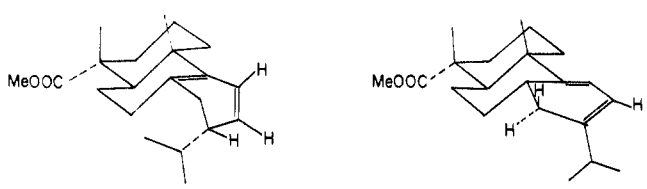
Anal. Calcd for $C_{17}H_{30}O_3$: mol wt 282. Found (MS): 282.

Mesylation of this substance resulted in complex mixtures which decomposed during attempts at chromatography.

peated continuous solvent flow thin layer chromatography; their spectroscopic properties (see Experimental Section) support the structure assignment.

The helicity rule for skewed dienes states that a strong positive Cotton effect associated with the lowest frequency cisoid diene π-π^* absorption band near 260–280 nm indicates that the diene is twisted in the form of a right-handed helix. Conversely, a strong negative Cotton effect is indicative of a left-handed twist.[39]

Diene **26** exhibited a positive Cotton effect, $[\Phi]_{285}$ 5780. Hence ring C must be in a quasi-boat conformation with the isopropyl group quasi-axial. Examination of Dreiding models (Figure 4) indicates that this conformation avoids an eclipsing interaction between the isopropyl group and H-12 and should be preferred over the half-chair form.



26 27

Figure 4. Conformations of **26** and **27**.

Diene **27** displayed a somewhat weaker *negative* Cotton effect, $[\Phi]_{296}$ −2600. In the Dreiding model of **27** the diene system of ring C is nearly planar, but flexible. The preference for a conformation at room temperature which contains a left-handed helix (Figure 4) could result from a reduction in the eclipsing interaction between the isopropyl group and the H-14 protons.

Registry No. **1a,** 31148-95-5; **1b,** 5335-58-0; **2a,** 42400-87-3; **2b,** 42400-88-4; **2c,** 42400-89-5; **3a,** 42400-90-8; **4b,** 13742-23-9; **5b,** 42400-91-9; **7,** 20104-31-8; **9a,** 42400-93-1; **9b,** 42400-94-2; **9c,** 42400-95-3; **9d,** 42400-96-4; **10a,** 42400-97-5; **10b,** 42400-98-6; **11a,** 42400-99-7; **11b,** 42401-00-3; **13,** 42401-01-4; **24,** 42401-02-5; **25,** 42401-03-6; **26,** 42401-04-7; **27,** 42401-05-8; **28b,** 10037-26-0; **29,** 42401-07-0; **30,** 24402-18-4; **31,** 24402-17-3; **32a** (α-hydroxy), 42401-10-5; **32a** (β-hydroxy), 42401-11-6; **32b** (α-acetoxy), 42401-12-7; **32b** (β-acetoxy), 42401-13-8; **33b,** 42401-14-9; **33c,** 42401-15-0; **36a,** 42401-16-1; **37,** 42401-17-2; **38,** 42401-18-3; **39,** 42401-19-4; **40,** 42401-20-7; **41,** 42401-21-8; **46c** (*R* epimer), 20149-13-7; **46c** (*S* epimer), 20149-11-5; **47,** 30906-02-6; **48,** 42401-25-2; **49,** 42401-26-3; **52,** 42401-27-4; **53,** 42401-28-5; **54,** 42401-29-6; **55,** 42401-30-9; **56a,** 42401-31-0; **56b,** 42401-32-1; **57,** 42401-33-2; **58a,** 42401-34-3; **58b,** 42401-35-4; **58c,** 42401-36-5; **60,** 42401-37-6; **61a,** 42401-38-7; **61b,** 42401-39-8; **61c,** 42401-40-1; **63a,** 42401-41-2.

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(7) We wish to thank Professor R. L. Settine, University of Alabama at Birmingham, for making available to us his unpublished directions for this preparation.
(8) Reduction of **3a** by the usual combination of reagents (Li, NH_3, THF, *tert*-butyl alcohol) was unsuccessful owing to the retarding effect of the isopropyl group (*cf.* subsequent results with **28a**).
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(20) Since the axial carbomethoxy group exerts a strong influence on the chemical shift of the C-10 methyl group, Zürcher's rules cannot

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In the case of **52**, SN2 displacement on C-1 and C-11 to which oxygen is bonded equatorially is impossible. Hence the ether linkage must open to give a carbonium ion and attack by the nucleophile at either of the two possible sites from the least hindered direction would furnish an equatorial diacetate. Hydrolysis of the C-1 acetate may have occurred during the work-up (see Experimental Section) due to assistance by the axial carbomethoxy group. On the other hand, it has been suggested by a reviewer that the C-1 oxygen being complexed to BF_3 might never have been acetylated and that the BF_3 complex was hydrolyzed during work-up.
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Resin Acids. XXV. Chromic Acid Oxidation of $\Delta^{8(9)}$-Pimaranes and Isopimaranes. Long Range Deshielding in 8,9-Epoxides[1]

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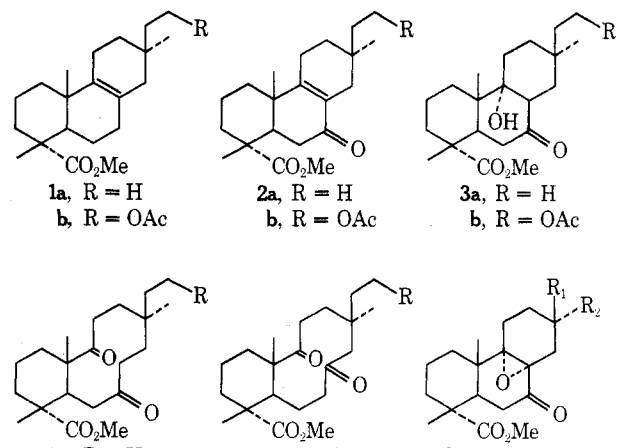
The substances formed by chromic acid oxidation of methyl pimar-8(9)-en-18-oates and isopimar-8(9)-en-18-oates have been identified as 8,9-epoxy 7-ketones. Long-range shielding effects in 8,9-epoxides of abietanes, pimaranes, and isopimaranes are discussed.

In the course of work on the synthesis of (−)-hibaene, it was noted[2] that chromium trioxide–glacial acetic acid oxidation of the pimaric acid derivatives **1a** and **1b** did not yield the hoped-for α,β-unsaturated ketones **2a** and **2b**, but gave products which contained an extra oxygen atom and did not exhibit unsaturation. These were tentatively formulated as the diketones **4**, possibly as the result of retroaldol reaction of **3** formed from **2**, or as **5**. We now report that these oxidation products actually possess the epoxy ketone structures **6a** and **6b**.

In connection with other studies, we undertook the chromic acid oxidation of methyl isopimar-8(9)-en-18-oate (**7a**). Three of the products were assigned structures **8**, **9**, and **10** on the basis of their spectroscopic properties (see Experimental Section) and corresponded to a similar set of ketones obtained by *tert*-butyl chromate oxidation of the abietane analog **7b**.[3] A fourth substance X seemed abnormal and bore a close resemblance to the "diketones" from **1a** and **1b**. However, further treatment of **10** and a still extant small sample of **2b** with acid under conditions approximating the reaction conditions under which the presumed diketones were formed resulted in recovery of starting material. Hence the theory of a retroaldol cleavage leading to **4** and **11** was abandoned. Since attempts to induce substance X and the "diketone" from **1a** to undergo an aldol condensation were also fruitless, formulas **5** and **12** seemed similarly doubtful.

To resolve the doubt, synthesis of authentic **5a**, **12a**, and the corresponding compound **12b** of the abietane series was undertaken. Osmylation of **1a**, **7a**, and **7b** afforded in each case only one ditertiary glycol **13** in high yield, presumably the result of preferred α-attack.[4] Subsequent cleavage of the diols with lead tetraacetate or periodic acid produced the three authentic diketones **5a**, **12a**, and **12b**, two of which, **5a** and **12a**, were markedly different from the substances obtained by chromic acid oxidation of **1a** and **7a**.



1a, R = H; **b**, R = OAc
2a, R = H; **b**, R = OAc
3a, R = H; **b**, R = OAc
4a, R = H; **b**, R = OAc
5a, R = H; **b**, R = OAc
6a, R_1 = Et; R_2 = Me
b, R_1 = CH_2CH_2OAc; R_2 = Me
c, R_1 = Me; R_2 = Et
d, R_1 = *i*-Pr; R_2 = H