Registry No.—1, 13240-40-9; 2, 61788-23-6; 3, 61788-24-7; 4, 17954-06-2; 5, 61788-25-8; 6, 61788-26-9; 7, 61788-27-0; 8, 61788-28-1; 9, 61788-29-2; diethylamine, 109-89-7; butylamine, 109-73-9; aniline, 62-53-3; benzylamine, 100-46-9; phenethylamine, 64-04-0; *o*-chlorophenylamine, 95-51-2; *o*-bromophenylamine, 615-36-1; dibenzylamine, 103-49-1.

Supplementary Material Available. Infrared, NMR, and analytical data for compounds 2-9 (2 pages). Ordering information is given on any current masthead page.

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Remote Oxidation in the Fe(II)-Induced Decomposition of a Rigid Epidioxide[1a]

Werner Herz,*[1b] Robert C. Ligon,[1b] James A. Turner,[1b] and John F. Blount[1c]

Department of Chemistry, The Florida State University, Tallahassee, Florida 32306, and Research Division, Hoffmann-La Roche Inc., Nutley, New Jersey 07110

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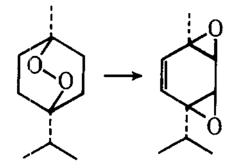
Reaction of the diterpenoid epidioxide **5** with ferrous sulfate gave by remote oxidation the tetrahydrofuran **14a** and the olefin **18a** and by reduction the diol **6**. Structures of **14a** and **18a** were established by a combination of chemical and physical methods and were confirmed by x-ray diffraction of a derivative of **14a**. The mechanism of the Fe(II)-induced remote oxidation of epidioxides which actually involves the Fe(II)–Fe(III) redox system is discussed. The $FeSO_4$–$Cu(OAc)_2$ system also caused remote oxidation in the decomposition of **5**. Highest yields of remote oxidation products were produced by $VO(AcAc)_2$. An unusual isomerization of a 12-chloro derivative of **5** was discovered.

The thermal rearrangement of unsaturated epidioxides to diepoxides, exemplified by the conversion of ascaridole (**1**) to **2**[2,3] and of the epidioxide **3a** of levopimaric acid to **4**,[4] has assumed importance not only because of its use in the preparation of the long-elusive arene dioxides and trioxides,[5,6] but also because of the discovery of naturally occurring diepoxides[7-9] and the tumor-inhibitory activity of this functionality.[9] The rearrangement can also be induced photolytically;[10] it is less well known that it can also be effected by ferrous ion at much lower temperatures[11] and that, at least in the case of **3**, this procedure leads to greatly improved yields.



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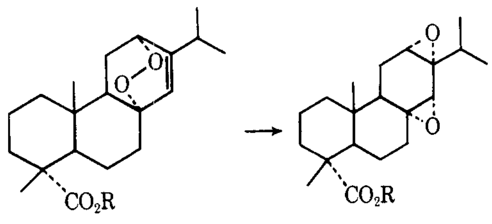
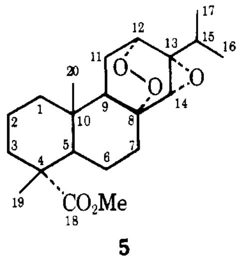


3a, R = H
b, R = Me

4a, R = H
b, R = Me

The mechanism proposed for the thermal and photolytic reaction involves homolytic fission of the O–O bond followed by attack of the oxygen atoms on the double bond and cyclization. No mechanism has been proposed for the Fe(II)-induced reaction, but in light of the usual one-electron reduction of the O–O bond by Fe(II),[12] one may conclude that the radical anion chemistry displayed by hydroperoxides and dialkyl peroxides without proximate double bonds is altered to *apparent* diradical chemistry in the unsaturated endoperoxide by oxidation of the initially formed anion radical.

Earlier[13] we had prepared the epoxidic epidioxide **5** from **3b** and were now interested in the behavior of this saturated endoperoxide under the influence of Fe(II). This resulted in approximately equal amounts of diol **6**[13] and two new isomeric compounds of formula $C_{21}H_{32}O_5$. Structure elucidation of these substances revealed that they had been formed by a new type of remote oxidation reaction. The details of this discovery constitute the subject of this communication.



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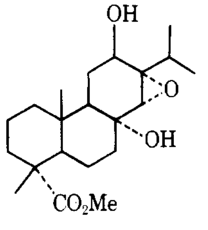

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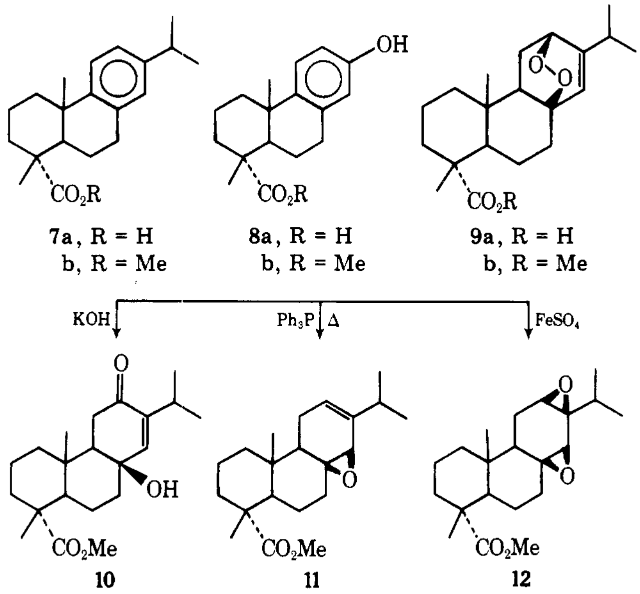
Results

Preparation of Starting Material. Reaction of sodium levopimarate with singlet oxygen by the original procedure[14] gave variable yields (30–50%) of **3a**; other products which have not previously been identified were dehydroabietic acid (**7a**, 18%, formed either by disproportionation or dehydration of the 1,4-glycol **6**), the podocarpic isomer **8a** (5%), the diepoxide **4a** (2.5%, presumably the result of thermal rearrangement of **3a** under the reaction conditions), and 2.5% of the new epidioxide **9a**, apparently the first example of a Diels–Alder adduct formed from the more hindered "folded" side of levopimaric acid.[15] The most efficient procedure for the preparation of starting material was reaction of methyl levopimarate with singlet oxygen which furnished 65% of **3b**, 14% of **7b**, and 2% of **9b**. The structure of the new epidioxide **9b** in whose NMR spectrum the C-10 methyl signal exhibited a dramatic downfield shift of 0.64 ppm relative to that of **3b** was established by transformations to **10**, **11**, and **12** which are similar to those previously used for **3b**.[4] In all these substances the C-10 methyl frequency is "normal", instead of being shielded as in derivatives of **3b**.



Reaction of Epidioxide of Methyl Levopimarate with $FeSO_4$. Reaction of **5**[13] with $FeSO_4$ in aqueous tetrahydrofuran gave three substances which were separated chromatographically. The product of medium polarity (31%) was the known diol **6**.[13] The least polar substance A ($C_{21}H_{32}O_5$, 28%) was a hydroxy ester (IR bands at 3545 and 1712 cm^{-1}) which retained the isopropyl group of the starting material (NMR spectrum) as well as the 13,14-epoxide (sharp singlet at 3.28 ppm) and had a new hydroxyl group (presumably α oriented due to the stereochemistry of the starting material) attached to C-12 (multiplet at 4.03 ppm). The fifth oxygen atom of the empirical formula was that of an ether one of whose termini was obviously attached to C-8. The other terminus was assumed to be either C-9 as in **13**, or C-5 as in **14** (Scheme I).

Formation of such a substance could be rationalized by assuming initial cleavage and reduction by Fe(II) of the O–O bond to a radical anion C or D (Scheme I).[12] Abstraction of H-9 by the oxy radical of C (1,3-hydrogen transfer) or D (1,4-hydrogen transfer), oxidation of the radical at C-9 by Fe(III), and combination of the carbonium ion at C-9 with the hydroxyl or oxygen anion at C-8 would have led to **13**. Alternatively, abstraction of H-5 by the oxy radical of C (1,5-hydrogen transfer), oxidation of C-5, and recombination with hydroxyl at C-8 would have led to **14**.

The most polar substance B (33%, $C_{21}H_{32}O_5$) was a dihydroxy ester (IR bands at 3520, 3458, and 1740 cm^{-1}) whose IR spectrum showed retention of the isopropyl group, a singlet at 3.03 ppm typical of H-14 in the various 13,14-epoxides under study, a multiplet at 4.16 ppm attributed to the presence of a hydroxyl group on C-12, and a triplet at 5.67 ppm which indicated the presence of a trisubstituted olefin. Structural possibilities included **16**, formed by deprotonation of a carbonium ion generated from **13** by acid-catalyzed ring

Scheme I

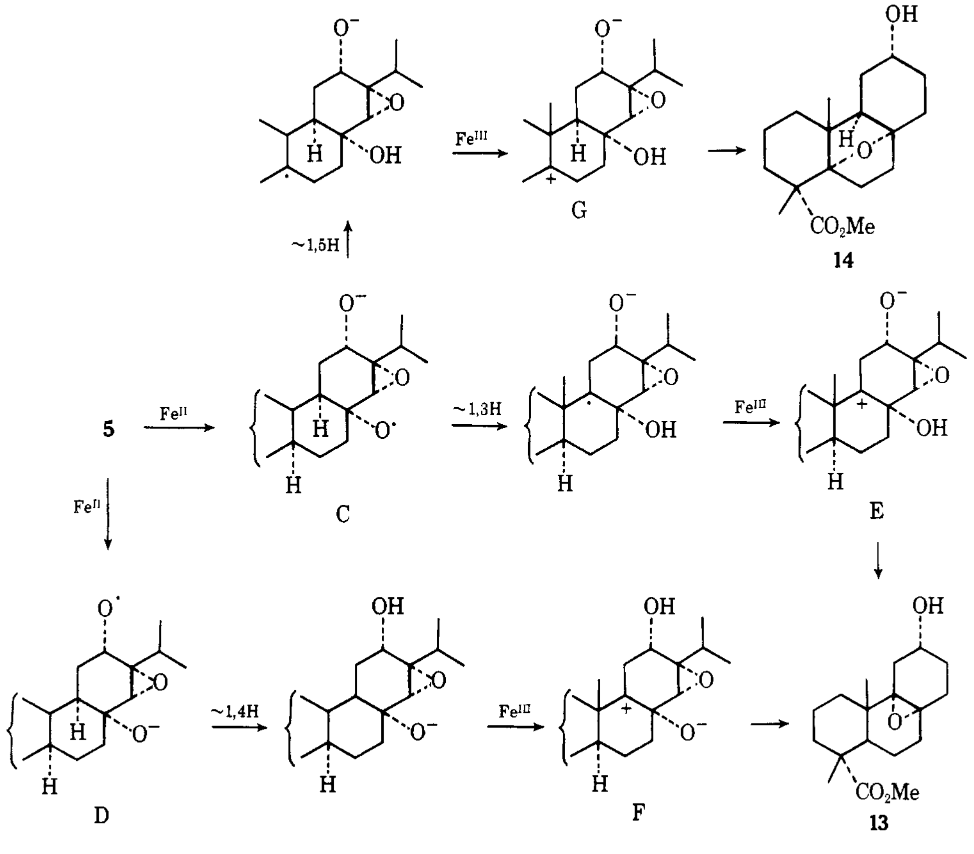
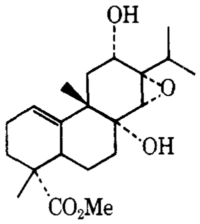


Table I. NMR Spectra of 14a, 21, 22, and 23[a]

Registry no.	Compd	H-12	H-14	H-16,[b] H-17[b]	H-18[b]	H-19[b]
61597-81-7	**14a**[c]	4.02 m ($W_{1/2}$ = 8.5 Hz)	3.29	0.82 d, 1.01 d (7)	0.97	1.29
61597-82-8	**21**[c]	4.24 m ($W_{1/2}$ = 18 Hz)	3.37 d (1)	0.83 d, 0.94 d (7)	0.98	1.29
61617-19-4	**22**[c]	4.38 m ($W_{1/2}$ = 8.5 Hz)	3.26	0.82 d, 1.01 d (7)	0.97	1.29
61617-20-7	**23**[d]	4.00 m ($W_{1/2}$ = 18 Hz)	3.23 d (1)	0.89 d, 0.92 d (6.5)	0.97	1.27

[a] In $CDCl_3$. Values in parts per million relative to Me_4Si. Coupling constants in hertz. [b] Three protons. [c] At 90 MHz. [d] At 60 MHz.

opening and methyl migration, **17** from **13** by acid-catalyzed ring opening and deprotonation, or **18** by deprotonation of ion G (Scheme I).



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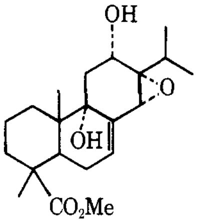

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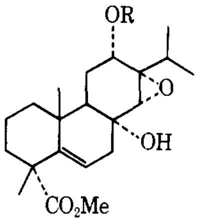


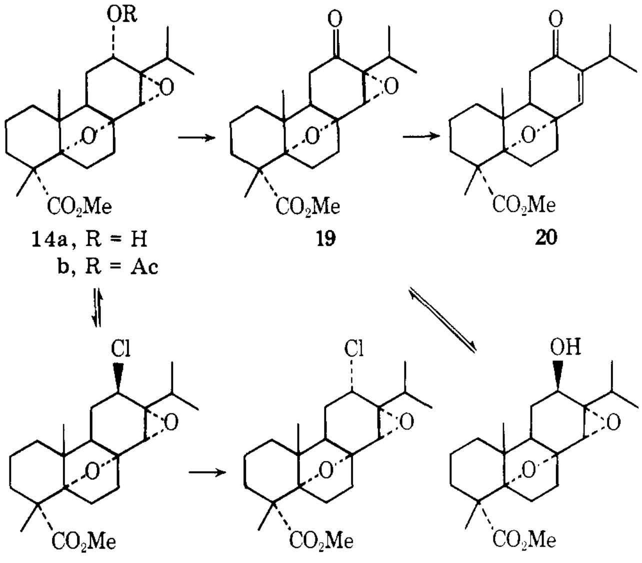
18a, R = H
b, R = Ac

These possibilities were corroborated by the ^{13}C NMR spectrum of B, which displayed five quartets one of which, at 52.5 ppm, corresponded to the methoxyl, five triplets, five doublets one of which, at 119.9 ppm, corresponded to -CH═, and two, at 66.1 and 63.7 ppm, corresponded to C-12 and C-14, and six singlets. Of the latter, a frequency at 178.2 ppm represented the carbonyl group, a signal at 150.3 ppm corresponded to >C═, and two at 78.1 and 68.9 ppm represented C-8 and C-13 (for a fuller discussion of the ^{13}C NMR spectrum see below).

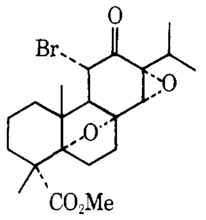
Since 1,5-hydrogen transfer in alkylperoxy radicals is more favorable than 1,4 or 1,3 transfer,[16] since 1,5-hydrogen transfer is predominant in carbon and alkoxy radicals,[17] and since in fact 1,5-hydrogen transfer completely dominates the intramolecular chemistry of radicals in relatively rigid polycyclic systems owing to a combination of the entropy factor and the requirement for collinearity,[17] formulas **14a** and **18a** seemed a priori considerably more plausible for substances A and B produced by the Fe(II)-induced decomposition of **5**. Chemical studies leading to the verification of this hypothesis will now be described; in the discussion we anticipate the final results for the sake of simplicity.

Structural Studies on A. Oxidation of A (**14a**) with Jones reagent afforded **19**, whose IR spectrum indicated the absence of hydroxyl groups, but which retained the epoxide (NMR singlet at 3.53 ppm). Reduction of **19** with chromous chloride yielded an α,β-unsaturated ketone **20** [IR bands at 1728 and 1667 cm^{-1}, narrowly split (1 Hz) doublet at 6.87 ppm characteristic of a proton attached to the β position of an α,β-unsaturated ketone]. Just as in the case of **10**, the splitting of H-14 arose from allylic coupling to H-15 whose signal was a broadened septet at 2.82 ppm; this could be shown by double irradiation experiments.

These observations confirmed the nature of the functional groups at C-12 through C-14 and confirmed that C-8 was quaternary. Subsequent work was directed at dehydration of **14a** since introduction of an 11,12 double bond would result in appearance of H-11 as a doublet of doublets if formula **14a** were correct. In the event, treatment of **14a** with $POCl_3$ or $SOCl_2$ resulted in 91% (respectively 81%) conversion to a chloride **21** (for stereochemistry vide infra). Several attempts to dehydrochlorinate **21** with Li_2CO_3–DMF, $CaCO_3$–DMF, or Dabco–DMF resulted primarily in conversion (60–75% yield) to an isomeric chloride **22** and smaller amounts (16–18% yield) of alcohol **14a**.



14a, R = H
b, R = Ac
19
20
21
22
23



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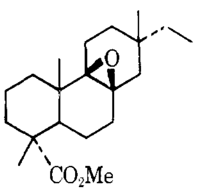

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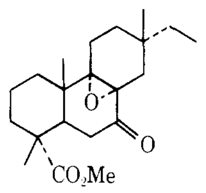

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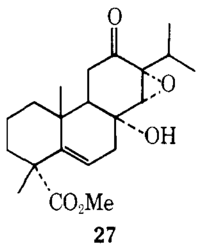


27

To establish the stereochemistry of the two isomeric chlorides, the NMR spectra were compared with the NMR specta of the pair of alcohols **14a**, which must have an α-oriented hydroxyl group, and its epimer **23**, which was the exclusive $NaBH_4$ reduction product of **19** where α-attack would be expected. The data which are summarized in Table I show that the NMR spectra of **21** and **23** are essentially superimposable except for the shift of H-14, as expected; therefore **21** is the β and **22** is the α isomer. This is also indicated by the half-height widths of the H-12 signals which show that the substituents on C-12 are quasi-axial in **19a** and **22** and quasi-equatorial in **21** and **23**. Consequently, $POCl_3$ or $SOCl_2$ treatment of **14a** has resulted in inversion and $LiCO_3$, $CaCO_3$, and Dabco in DMF treatment of **21** has produced an unusually facile halide inversion. Chlorination of alcohols with thionyl chloride is known to proceed with inversion, but there are few

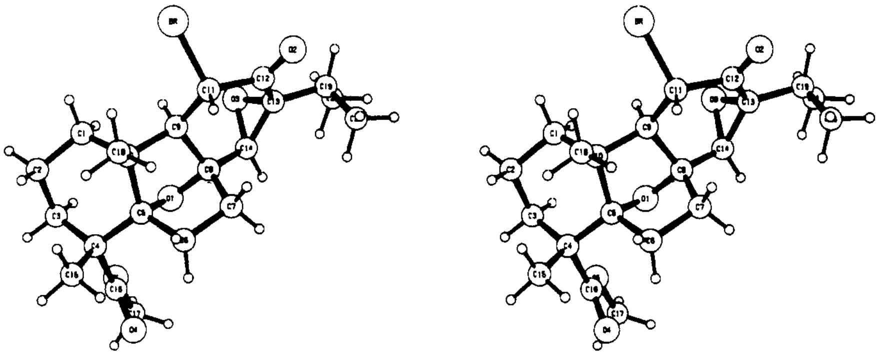


Figure 1. Stereoscopic view of **24**. Atoms are shown as arbitrary spheres.

Table II. Crystal Data for 24

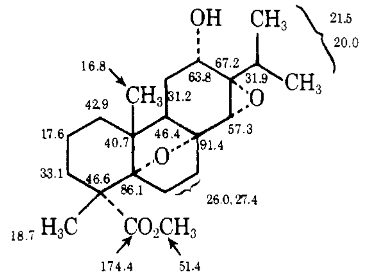
Formula $C_{21}H_{29}BrO_5$
a = 6.106 (2) Å
b = 10.868 (2) Å
c = 31.175 (8) Å
Space group $P2_12_12_1$, Z = 4
d_{calcd} 1.416 g cm^{-1}

precedents for the conversion of alicyclic alcohols to chlorides with POCl$_3$.[18,19] The unusual epimerization **21** → **22** is dealt with in a separate section below.

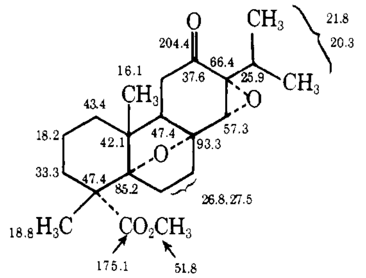
Although efforts to prepare a Δ^{11} derivative had failed, positive evidence for structure **14a** could be adduced in the following manner. Treatment of **19** with pyridinium bromide perbromide afforded a bromo ketone **24** whose NMR spectrum displayed a sharp doublet (J = 12 Hz) at 4.04 ppm for the proton on carbon carrying the bromine atom. This eliminated the alternative structure derived from **13** which should have exhibited a singlet. The large value for $J_{9,11}$ showed that H-9 and H-11 were trans diaxial and that the C-11 bromine atom was equatorial as shown in the formula.

Additional evidence in favor of formula **14a** derives from the ^{13}C NMR spectrum of A, which exhibits the requisite number of quartets (five, one of which is the methoxyl carbon at 51.4 ppm), triplets (six), doublets (four), and singlets (six, one of which is the carbonyl carbon at 174.4 ppm). It contains five other signals below 50 ppm, i.e., three singlets at 91.4, 86.1, and 67.2 ppm and two doublets at 63.8 and 57.3 ppm. The doublets must be assigned to C-12, the hydroxylated carbon, and to C-14 carrying an epoxidic oxygen. A considerable body of information has now accumulated which shows that epoxidic carbons carrying no other heteroatoms rarely, if ever, absorb at frequencies below 75 ppm,[20] whereas α carbons of substituted tetrahydrofurans absorb at considerably lower field.[21] Thus the singlets at 91.4 and 86.1 ppm are quite incompatible with formula **13**, but support formula **14a**. This conclusion is corroborated by the ^{13}C NMR spectra of two 8,9-epoxypimaranes **25** and **26**[22] whose epoxidic carbons resonate at 63.4 and 70.2 ppm (for **25**) and at 64.9 and 71.9 ppm (for **26**).

Assignments of frequencies in the ^{13}C NMR spectrum of **14a** are shown below. Comparison with the data of Wenkert and Buckwalter[23a] for other resin acids permitted identification of most signals except for three triplets (27.4, 26.0, and 31.2 ppm of C-6, C-7, and C-11), two doublets (57.3 and 63.8 ppm of C-12 and C-14), and two singlets (86.1 and 91.4 ppm of C-5 and C-8). Comparison with the ^{13}C NMR spectrum of **19** allowed assignment of the C-11, C-12, and C-14 signals. Two of the unassigned triplets of **14a** remained relatively unchanged, while the third underwent a downfield shift (31.2 → 37.6), hence was assignable to C-11. The remaining two triplets were assigned to C-6 and C-7, a distinction between them being impossible on the basis of shift arguments. Of the two unassigned doublets of **14a**, one underwent a profound downfield shift (63.8 → 204.4), hence was that of C-12. The only other signal of **14a** which was appreciably shifted on oxidation of **14a** to **19** was that of C-15 (31.9 → 25.9). This is not surprising since the models indicate that C-15 is situated in the shielding cone of the carbonyl π system.



14a[a]



19[a]

[a] Assignments at C-5 and C-8 may be interchanged.

Clearly the only structure compatible with the evidence presented so far is **14a**. There remained, however, the question of stereochemistry at C-10. If formation of a radical anion of type C (Scheme I) were the initial step in the pathway leading to intramolecular hydrogen transfer, fragmentation of anion radical C to H and recombination as sketched in Scheme II could conceivably lead to epimerization at C-9 via anion radical I. Anion radical J could not be involved, however, as products resulting from attack on the C-10 methyl group[23b] were not observed. To eliminate the ambiguity at C-9, an x-ray diffraction study of the bromo derivative **24** was undertaken.

X-Ray Analysis of 24. Crystal data for **24** are listed in Table II. Figure 1 is a stereoscopic drawing of the molecule which confirms the proposed structure and shows that C-9 has not undergone epimerization. Tables III, IV, and V containing bond lengths, bond angles, and certain torsion angles are available as supplementary material.

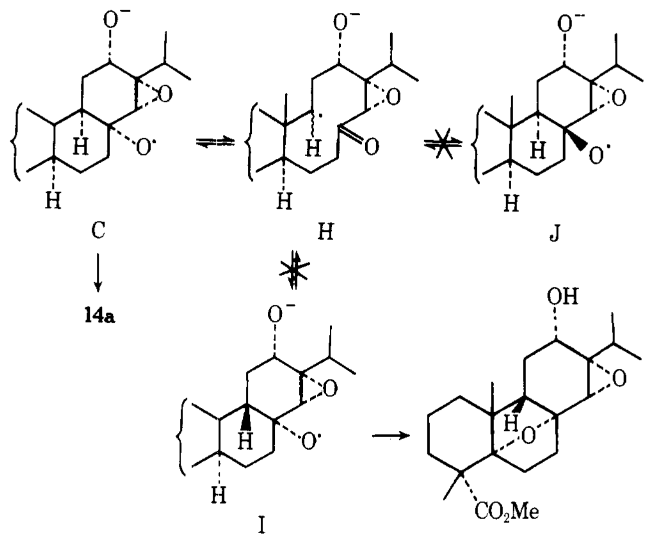
Examination of molecular models of **14a**, **21**, and **22** now suggests a reason for their resistance toward E2 elimination. When the C-12 substituent is α oriented, obstruction of the

Table VI. NMR Spectrum of 27 (270 MHz)[a]

H-6	5.65 dd ($J_{6,7\alpha}$ = 2.8, $J_{6,7\beta}$ = 7.4 Hz)
H-7a	2.36 dd ($J_{7\alpha,7\beta}$ = 16.8 Hz)
H-7b	2.52 dd
H-9	2.03 dd br ($J_{9,11\alpha}$ = 2.7, $J_{9,11\beta}$ = 8.3 Hz)
H-11α	2.31 dd ($J_{11\alpha,11\beta}$ = 15.3 Hz)
H-11β	3.01 dd
H-14	3.36 d ($J_{9,14}$ = 1 Hz)
H-15	2.38 sept (J = 7 Hz)
H-16,[b]H-17[b]	0.90 d, 0.98 d (J = 7 Hz)
H-19[b]	1.34
H-20[b]	0.88
OMe[b]	3.72
OH	3.21 br

[a] In $CDCl_3$. Values in parts per million downfield from internal Me_4Si. Unmarked signals are singlets. [b] Three protons.

Scheme II



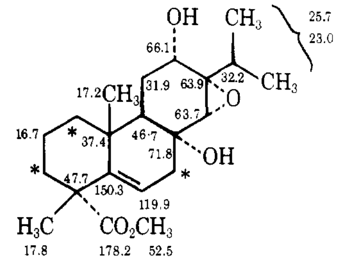
β face by the C-10 methyl group and H-7β effectively blocks attack by base on H-11β. When the C-12 substituent is β oriented as in **21**, the proper orientation for E2 elimination would result in distortion of ring C to a half-chair in which there is severe interaction between H-7β and the C-12 substituent. An attempt to prepare the Δ^{11} olefin by dehydration of **14a** under E1 condition (refluxing acetic acid) which do not require trans-antiparallel geometry resulted only in formation of **14b** (68% yield), presumably because of the difficulty in inducing a positive charge on C-12.

Structure of B. With the structure of A firmly established as **14a**, formula **18a** for B seemed more plausible than ever on mechanistic grounds and was supported by the 270-MHz spectrum of its acetate **18b**. The allylic region clearly showed two sharp doublets of doublets at 2.27 and 2.42 ppm (H-7a and H-7b) which constituted the AB part of an ABX system (J_{AB} = 15.9 Hz), the X part (H-6) being represented by a doublet of doublets at 5.66 ppm in the vinylic region (J_{AX} = 2.7, J_{BX} = 7.4 Hz). The multiplicity of the A and B signals was inconsistent with formulas **16** and **17**, but in conformity with **18**. The remaining low-field signals resembled those of **14b**, a one-proton doublet of doublets at 5.49 ppm (H-12) being coupled to H-11 ($J_{11\alpha,12}$ = 5.2, $J_{11b,12}$ = 10 Hz) and a sharp singlet at 3.04 ppm being identifiable with H-14.

Attempted dehydration of **18a** led to complex mixtures as did its ozonolysis. Oxidation of **18a** with Jones reagent furnished the α-keto epoxide **27** which yielded complex mixtures on treatment with $POCl_3$ or chromous chloride. However, the 270-MHz NMR spectrum of **27** (Table VI) furnished compelling evidence for the structure as postulated.

The protons α to the carbonyl group (H-11α and H-11β) were clearly doublets of doublets as required by formula **27**. Irradiation at the frequency of H-11α collapsed the signal of H-11β to a doublet and established the identity of H-9 as a doublet of doublets at 2.03 ppm which was broadened by "W" coupling to H-14, a phenomenon frequently encountered in this series of compounds (cf. Table I). The signal of the olefinic proton (H-6) at 5.65 and two signals at 2.36 and 2.52 ppm represented a second ABX system of the type $QQC{=}CHCH_2Q$ where Q must represent a quaternary center since A, B, and X were not coupled to other protons and since the magnitude of J_{AB} (16.8 Hz) corresponded to a geminal coupling constant. This information can be accommodated only by **27**; hence **18a** is the structure of the precursor B.

The ^{13}C NMR spectrum of **18a** (see below) is in accord with the postulated structure. Frequencies were assigned by comparison with **14a** and **19**. The two downfield doublets at 66.1 and 63.7 ppm were tentatively assigned to C-12 and C-14, respectively, by noting that C-12 is further downfield in **14a** than C-14 (63.8 vs. 57.3 ppm). The possible effect of a hydroxyl instead of an ether oxygen on C-8 was not considered in making this assignment; it is conceivable, but not likely, that the deshielding effect of a C-8 hydroxyl group could reverse the assignments. The singlets at 68.9 and 71.9 ppm were tentatively assigned to C-13 and C-8, respectively, by noting that C-13 occurred at 67.2 and 66.4 ppm in **14a** and **19**. Although the C-3 triplets of **14a** and **19** occurred near 33 ppm, the effect of replacing the 5–8 ether bridge by a 5,6 double bond on C-1 and C-3 was uncertain; no attempt was made therefore to assign the three triplets at 36.5, 33.5, and 32.2 ppm to C-1, C-3, and C-7, specifically.

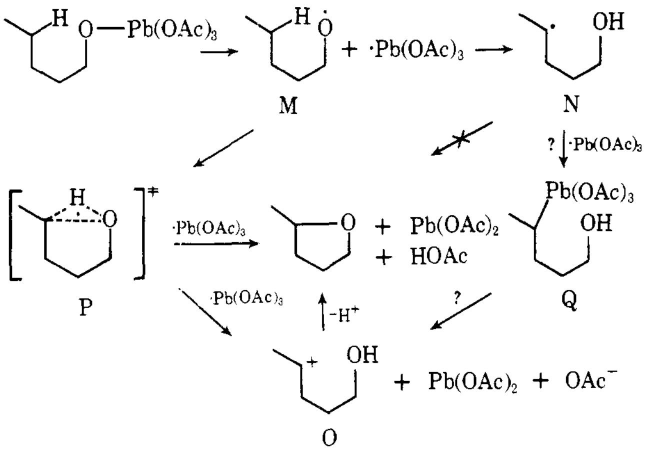


18a (*see Discussion)

Discussion

Formation of the unexpected "long range" oxidation products **14a** and **18a** on treatment of **5** with $FeSO_4$ is a new variant of the functionalizations and remote oxidations which proceed through oxy radicals generated through homolysis of an O–X bond, such as the lead tetraacetate oxidation of alcohols,[24] the lead tetraacetate–iodine reaction,[25] the photolysis of nitrites (Barton reaction), the cleavage of hydroperoxides with ferrous sulfate and cupric acetate,[26] and others.[17] A tentative pathway to **14a** and **18a** has already been adumbrated in Scheme I. In the lead tetraacetate oxidation where an oxy radical M formed by homolytic cleavage of a lead alkoxide[24,25] induces 1,5-hydrogen transfer (Scheme III) and which may be taken as a close analogy to the reaction under discussion here, direct displacement of hydrogen on oxygen by the ensuing carbon radical N is considered unfavorable[25] and other pathways which can generate tetrahydrofurans have been suggested. In rigid systems like **5**, where intramolecular hydrogen abstraction is very favorable, ether formation apparently proceeds without intervention of carbonium ions O (equivalent to G of Scheme I) and it is postulated that a three-centered radical species of type P is directly oxidized to tetrahydrofuran. In aliphatic systems, carbonium ions of type O, presumably also formed by oxidation of P, appear to be present and may either cyclyze to tetrahydrofurans or be

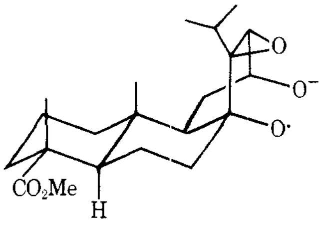
Scheme III



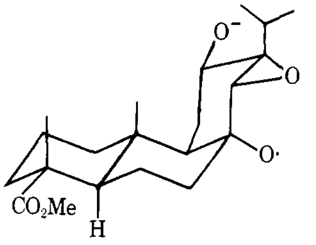
deprotonated to olefins. The intermediacy of a species Q which could subsequently decompose to O has not been conclusively established.

Evidence for an oxidation step in the ferrous ion reaction of **5** was obtained by varying the concentration of Fe(II) (Table VII). Reduction of **5** to either of the anion radicals C or D (Scheme I) requires 1 molar equiv of Fe(II) whereas reduction of **5** to **6** requires 2. Table VII shows that reaction of **5** with only 0.5 molar equiv of ferrous ion (entries 6 and 7) resulted in practically complete conversion to **6**, **14a**, and **18a**. Since at least 1.54 molar equiv of ferrous ion is required for complete conversion to the amounts of **6**, **14a**, and **18a** in entries 6 and 7, an oxidation step requiring the regeneration of ferrous ion must be involved. Inclusion of an oxidation step in the mechanism is consistent with the previously mentioned view that direct displacement of an oxygen-bound hydrogen by a carbon radical to generate tetrahydrofuran **14a** is unfavorable. Scheme I includes such an oxidation step which for simplicity's sake is listed as proceeding via carbonium ion G.

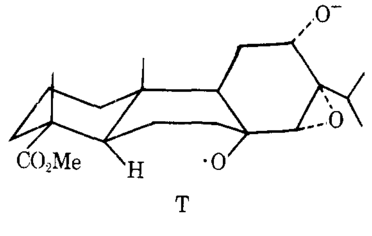
In the case under discussion, there are three conceivable conformations for radical anion C. Clearly hydrogen abstraction from C-5 cannot occur in the chair-chair-boat conformation R initially formed from **5**, the C–O bond distance being ~4.1 Å and the equatorial C–O bond pointing away from the C–H bond which is to be attacked. In the all-chair arrangement S which is a priori expected to be the most stable conformation, the C–O distance and the geometry for H abstraction are equally unfavorable. However, in the chair-boat-chair conformation T, the C–O distance is 2.6 Å, within the specified limits,[25] and although the transition state for 1,5-hydrogen transfer would not be chairlike,[17] the geometry is suitable for ready collinear attack on H-5 by the oxy radical on C-8.



R



S



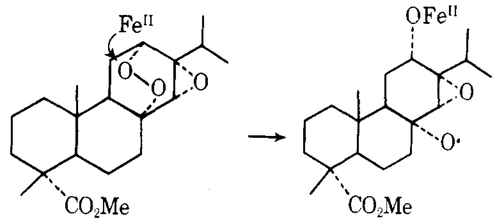
T

Table VII. Reaction of 5 with Various Concentrations of FeSO$_4$[a]

Entry	[Fe(II)] molar equiv	Yield, % 6	14a	18a	Total recovery
1	10.00	32.5	28.0	33.5	94.0
2	2.00	35.0	33.5	29.0	97.5
3	2.00	34.0	32.0	30.5	96.5
4	1.00	34.0	35.0	27.5	96.5
5	1.00	31.5	32.5	30.0	94.0
6	0.50	28.0	40.0	27.0	95.0
7	0.50	26.0	38.5	26.0	90.5
8	0.25	26.0[b] 16.5[c]	36.0[b] 23.0[c]	25.0[b] 16.0[c]	92.0[d]

[a] See Experimental Section for details. [b] Yields based on amount of **5** which reacted. [c] Overall yields. [d] includes recovered **32** (see Experimental Section).

Two questions concerning the mechanism of reaction of **5** with ferrous ion remain. First, to what extent are the two anion radicals C and D formed, and second, what is the mechanism of oxidation at C-5 by Fe(III) in the radical ensuing from hydrogen transfer in T? Table VII shows that the ratio of long-range oxidation products **6** and **14a** to reduction product **18a** remains essentially constant over a 40-fold range of concentration of FeSO$_4$ (60/33 in entry 1 and 68/27 in entry 6 represent the two extremes, a difference which is probably statistically not very significant because 5–6% of starting material remained unaccounted for in each case). That the percentage of reduction product remains essentially the same even in the presence of very small amounts of Fe(II) can be accounted for by assuming that in the presence of FeSO$_4$, the ratio C/D is approximately 2:1. C undergoes intramolecular hydrogen transfer and eventual oxidation as soon as it is formed whereas D can undergo only reduction to **6** by ferric ion produced in the remote oxidation step. This suggests that the C-12 oxygen atom of **5** is reduced preferentially by Fe(II). The exact mode of O–O bond rupture of peroxides by FeSO$_4$ is not known but could involve nucleophilic attack by Fe(II) on C-12 oxygen, thus resulting in the alkoxide–ferric complex **28** which is similar to that generally written for the reaction of acyclic peroxides with cuprous ion.[26,27] The preferential formation of one radical anion is consistent with the observation that reaction of ferrous ion with alkyl hydroperoxides principally yields alkoxy radicals and hydroxyl ions.[28] Steric factors, electronic factors, or relative stabilities of the oxy radicals and oxy anions involved could all account for this; in the present case, preferential attack by ferrous ion on the C-12 oxygen for steric reasons to give an alkoxide–ferric complex **28** similar to that written for reaction of acyclic peroxides with cuprous ion[26,27] seems plausible, but is at variance with the preferred attack[13] by triphenylphosphine on the C-8 oxygen of **5**, where the oxygen is removed as triphenylphosphine oxide.



5 **28**

Walling[29] has suggested that ease of reduction of carbon radicals parallels the stability of the carbanion formed and suggests that this reduction occurs by an outer-sphere electron transfer. The same may hold for the peroxide reduction as well.

Oxidation of radicals by Cu(II) has been extensively studied by Kochi.[30] These oxidations apparently occur by one of two inner-sphere electron transfer processes shown in Scheme IV.

Scheme IV. Oxidation of Carbon Radicals by Cupric Ion

electron-transfer oxidation:

$$R\cdot + Cu^{II}(OAc)_2 \longrightarrow \underset{\mathbf{29}}{RCu(OAc)_2} \nearrow R(-H) + Cu^{I}OAc + HOAc$$

$$\mathbf{29} \downarrow R^{+}[Cu^{I}(OAc)_2]^{-}$$

ligand-transfer oxidation: X = Hal or pseudo-Hal

$$R\cdot + Cu^{II}X_2 \longrightarrow [R{-}{-}{-}X{-}{-}{-}CuX]^{2-} \longrightarrow RX + Cu^{I}X$$

or

$$R\cdot + Cu^{II}X_2 \longrightarrow RCuX_2 \longrightarrow [R+ (Cu^{I}X_2)^{-}] \rightleftharpoons RX + Cu^{I}X$$

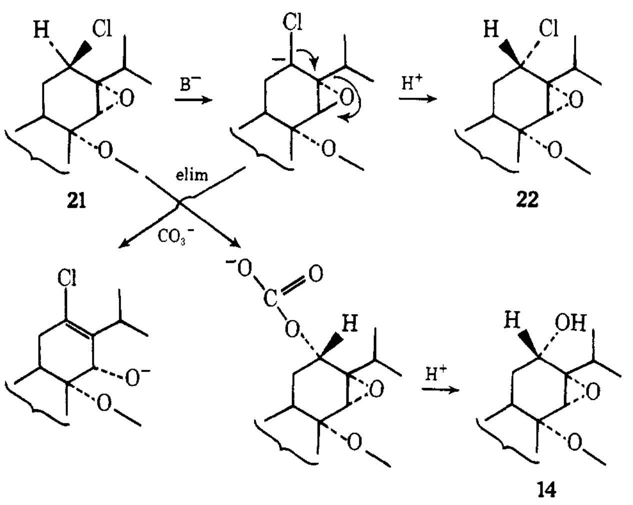
Since Fe(III) is a selective oxidizing agent which oxidizes most easily those radicals which lead to stable carbonium ions, Walling[29] has proposed that oxidation by ferric ion is an outer-sphere electron transfer yielding carbonium ion products. Furthermore, oxidation of substrates which yield highly stable carbonium ions is very fast, oxidation by Cu(II) being appreciably slower than the fastest oxidation by Fe(III). Thus, organoiron species analogous to **29** (Scheme IV) should not be present. The mechanism advanced in Scheme I for oxidation of the C-5 carbon radical proposes such an outer-sphere electron transfer. A transition state similar to P (Scheme III) proposed for oxidation of an alcohol by lead tetraacetate[24,25] is compatible with Scheme I as is the proposed oxidation–cyclization step which could occur by an outer-sphere electron-transfer oxidation by ferric ion in this transition state.

A brief study of the reaction of **5** with other one-electron oxidizing agents was undertaken with interesting results. Substance **5** remained inert toward $MnSO_4$ even on stirring overnight in a nitrogen atmosphere. Reaction with $FeSO_4$–$Cu(OAc)_2$ under the conditions used for intramolecular reactions of acyclic hydroperoxides[31] furnished a very complex mixture (TLC), possibly because the method requires the use of acetic acid as a solvent. In one experiment when the mixture was separated by laborious preparative TLC, 43% of **14a**, but only 7% of **18a**, was isolated although it had been expected that in the presence of $Cu(OAc)_2$, a reagent which usually oxidizes carbon radicals to olefinic products,[30] the major product would have been **18a**. That the solvent acetic acid was not responsible for converting **18a** to **14a** was shown in an independent experiment which resulted in recovery of **18a**.

Reaction of **5** with $VO(AcAc)_2$ in benzene gave the highest yields of long-range oxidation products (58% of **14a** and 28% of **18a**, i.e., 86% total). The remaining material (13%) was an intractable mixture intermediate in polarity between **14a** and **18a**. If **6** were present in this mixture, it must have been formed in very small yield. It appears, therefore, that in the presence of $VO(AcAc)_2$, anion radical C is either formed in much greater proportion than with $FeSO_4$ or that D if formed can equilibrate to C before it is subject to reduction.

The Isomerization 21 → 22. Because of the unusual isomerization of **21** to **22** by the various reagents mentioned previously, the reaction was studied in more detail. $CaCO_3$ in refluxing DMF afforded 57% of **22**, 15% of **14a**, and 5% of recovered **21**. $LiCO_3$ in refluxing DMF gave 70% of **22**, 17% of **14a**, and 11% of unreacted **21**.

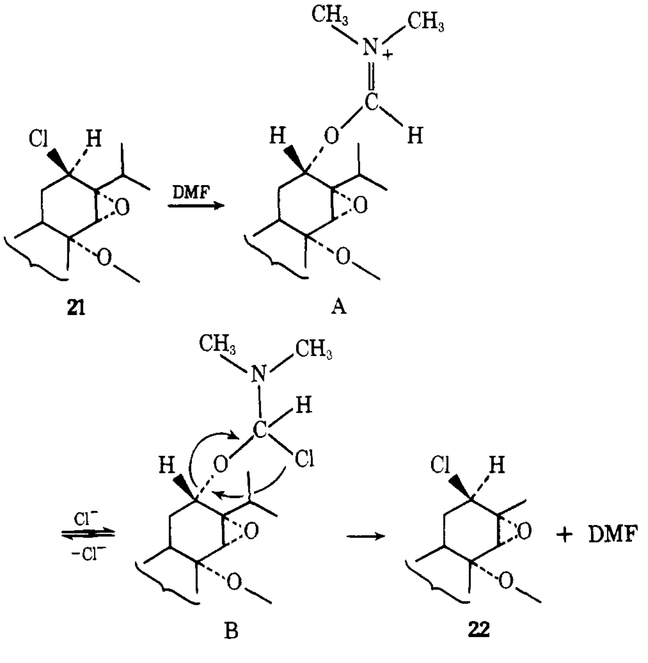
Scheme V



Two mechanisms can be written for this conversion of **21** to **22** and **14a**. The first is a base-catalyzed reaction (Scheme V) in which an anion or partial negative charge is induced α to the electron-withdrawing epoxide group. If this path were operating, the small yield of **14a** must have arisen by nucleophilic displacement of Cl^- by carbonate; on the other hand, the elimination process leading to an olefin of the type shown on the lower left might be expected to predominate.

The second mechanism might involve nucleophilic attack by the DMF oxygen atom on C-13 (Scheme VI) as in the formation of formates from tosylates by heating with DMF.[32] The iminium ion A could now combine with displaced Cl^- to give B which could undergo chlorination at C-12 by an S_Ni mechanism similar to chlorination with thionyl chloride in the absence of pyridine. If this mechanism were in operation, the added base should play no role in the isomerization, i.e., refluxing **21** in DMF alone should produce **22**. In fact, under these conditions, **22** was obtained in 67% yield together with 27% of **14a** and a very small amount of unreacted **21**. While this observation does not completely eliminate the mechanism of Scheme V, it strongly supports that of Scheme VI. The reason for the formation of **14a** instead of its formate is not entirely clear, but may be related to the concentration of water in the DMF used for the reaction. The possible implications

Scheme VI



of the surprising isomerization of 21 to 22 by DMF will be the subject of further studies.

Experimental Section[33]

Reaction of Sodium Levopimarate with Singlet Oxygen.[14] A solution of 35 g of sodium levopimarate in 400 mL of 95% ethanol was irradiated in the presence of 25 mg of methylene blue with two 150-W incandescent lamps placed near a Hanovia-type reactor and air as the oxygen source, cooling being supplied by a water jacket. After 30 h, the solvent was removed at reduced pressure; the residue was dissolved in water and extracted with ether. The water layer was acidified with 10% acetic acid and thoroughly extracted with ether. The washed and dried ether layers were concentrated at reduced pressure. The residue was dissolved in 50 mL of ethanol and mixed with 25 mL of 2-methyl-2-amino-1-propanol. The precipitate was filtered and recrystallized from ethanol, the filtrates and mother liquors being saved. The precipitate was slurried in ether and mixed with 10% acetic acid to hydrolyze the salt. The ether layer was washed, dried, and evaporated and the gummy residue was recrystallized from methanol–water to give 11.3 g (29%) of **3a**. A second run, identical with the above, gave 14 g (40%) of **3a**.

The ethanolic filtrates from the two preparations of the crude salt of **3a** were combined, hydrolyzed with 5% acetic acid, and extracted with ether. The washed and dried extracts were evaporated and the resulting gum, wt 28.7 g, was placed on 650 g of silica gel column. The following substances were eluted in order: 11 g (17%) of dehydroabietic acid, 1.25 g (1.7%) of **9a**, 8.0 g of a mixture from which 4.2 g (5.8%) of additional **3a** could be obtained by crystallization from methanol–water [the filtrate from this crystallization was evaporated and recrystallized from $CHCl_3$ to afford 3.2 g (5.4%) of impure **8a**], and lastly 1.2 g (1.7%) of **4a**.

Recrystallization of crude **9a** from methanol–water afforded material of mp 152–153 °C, which had NMR signals at 5.84 t (J = 1.5 Hz, H-14), 4.53 m (H-12), 1.22, 1.22 (C-4 and C-10 methyls), 1.09 d and 1.05 ppm d (J = 7 Hz, isopropyl methyls).

Anal. Calcd for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04; Found: C, 71.93; H, 9.12.

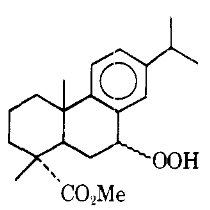
The methyl ester **9b** was prepared with diazomethane and recrystallized from methanol–water and had mp 75–74 °C; IR bands at 1718 and 1246 cm^{-1}; NMR signals at 5.85 t (J = 1.5 Hz, H-14), 4.52 m (H-12), 3.69 (methoxyl), 1.21, 1.21 (C-4 and C-10 methyls), 1.08 d and 1.05 ppm d (J = 7 Hz, isopropyl methyls).

Anal. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26. Found: C, 71.88; H, 9.30.

Phenol **8a** had NMR signals (in acetone-d_6) at 6.91 c (H-11, H-12, and H-14), 1.27 (C-4 methyl), and 1.21 (C-10 methyl); mol wt (MS) 274. Methylation with diazomethane and recrystallization from methanol–water afforded **8b**: mp 148–149 °C (lit. 147.5–148.5,[34] 149.5–150 °C[35]); IR bands at 3442 and 1278 (phenol), 1700 and 1254 (ester), 3030, 3018, 1660, 1597, 880 and 835 cm^{-1}. The 270-MHz NMR spectrum exhibited signals at 7.07 d (J = 8.5 Hz, H-11), 6.61 dd (J = 8.5, 2.8 Hz, H-12), 6.49 d (J = 2.8 Hz, H-14), 3.66 (methoxyl), 1.27 (C-4 methyl), and 1.19 ppm (C-10 methyl).

Anal. Calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39; O, 16.64. Found C, 74.93; H, 8.32; O, 16.82.

Since appreciable amounts of dehydroabietic acid were formed in this reaction, supposedly by air oxidation or disproportionation of levopimaric acid, it seemed reasonable to assume that **8a** had been formed from it by further reaction, either by air oxidation or by reaction with singlet oxygen. Air oxidation of dehydroabietic acid is known to yield **30** as the major product and only minor amounts of **31**,[36] the supposed precursor of **8a**. Thus it would have been surprising if **8a** had been formed by this route. The dehydroabietanes **7a**, **7b**, and **7c** were photooxygenated under both acidic and basic conditions, but starting material only was recovered even after several days. Hence **8a** is probably not formed from **7a** by reaction with singlet oxygen. It is also not clear why **8a** is formed from levopimaric acid under the condition of Moore and Lawrence[14] and not under neutral conditions.



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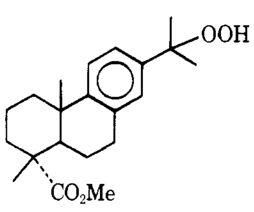


31

Reaction of Levopimaric Acid with Singlet Oxygen. The reaction of 25 g of levopimaric acid with singlet oxygen was carried out as described above (12 h, air as oxygen source). The usual workup furnished 18.4 g (48%) of **3a**. The amine salt filtrates were hydrolyzed to give 10.3 g of gum which was chromatographed over 350 g of silica gel to give 4.7 g (19%) of dehydroabietic acid, 0.8 g (2.7%) of **9a**, and an additional 2.4 g (9%) of **3a**.

Reaction of Methyl Levopimarate with Singlet Oxygen. This is the method of choice for preparation of **3b**. A solution of 10 g of methyl levopimarate in 150 mL of 95% ethanol and 10 mg of methylene blue was irradiated as above (5 h) and concentrated in vacuo. The residue was taken up in ether. The washed and dried ether extract was chromatographed over silica gel to give 7.2 g (65%) of **3b**, 1.4 g (14%) of methyl dehydroabietate, and 0.23 g of **9b**.

Methyl 8β-Hydroxy-12-oxo-13-abieten-18-oate (10). A solution of 50 mg of **9a** in 3 mL of 1 N NaOH in 95% ethanol was refluxed for 10 min, cooled, acidified with 5% acetic acid, and extracted with ether. The washed and dried extract was evaporated and the residue was recrystallized from $CHCl_3$–hexane to give 70 mg of the impure acid. Methylation of 150 mg of this material with diazomethane and recrystallization of the crude product from methanol-water afforded 135 mg (90%) of **10**: mp 107–108 °C; IR bands at 3490, 1723, 1670, and 1250 cm^{-1}; NMR signals at 6.32 d (J = 1.0 Hz), 3.65 (methoxyl), 1.21 (C-4 methyl), 1.08 (C-10 methyl), 0.98 d and 0.97 ppm d (isopropyl methyls).

Anal. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26; O, 18.36. Found: C, 72.27; H, 9.27; O, 18.35.

Methyl 8β-Epoxy-12-abieten-18-oate (11). A solution of 100 mg of **9b** and 80 mg of triphenylphosphine in n-heptane was refluxed for 3 h, cooled, filtered, and evaporated at reduced pressure. The residue was purified by preparative TLC (eluent 1:4 ether–hexane) to give 68 mg of gummy **11**. Further rechromatography gave semicrystalline material which had IR bands at 1722 and 1245 cm^{-1}; NMR signals at 5.55 m (H-12), 3.65(methoxyl), 2.79 d (J = 2.5 Hz, H-14), 1.25 (C-4 methyl), 1.08 d and 0.90 d (J = 6.5 Hz, isopropyl methyls), and 0.88 ppm (C-10 methyl).

Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.49; H, 9.60.

Methyl 8β,14β;12β,13β-Diepoxyabietan-18-oate (12). A solution of 50 mg of $FeSO_4 \cdot 7H_2O$ in 1 mL of water was added to 110 mg of **9b** in 20 mL of 3:2 THF–H_2O with stirring. Reaction was complete after 30 min. The solvent was evaporated, and the residue was diluted with water, acidified, and extracted with ether. The washed and dried ether extract was evaporated; the residue was purified twice by preparative TLC (eluent 3:7 ether–hexane), but could not be induced to crystallize, yield 76 mg (69%); IR bands at 1725 and 1245 cm^{-1}; NMR signals at 3.65 (methoxyl), 3.10 m (H-12), 2.79 br (H-14), 1.24 (C-4 methyl), 1.06 d and 0.95 d (J = 7 Hz, isopropyl methyls), 0.95 ppm (C-10 methyl).

Anal. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26. Found: C, 72.07; H, 9.69.

Reaction of 5 with Ferrous Sulfate. A. To a solution of 1.0 g of **5**[13] in 40 mL of aqueous THF was added with stirring a solution of 0.4 g of $FeSO_4 \cdot 7H_2O$ in 10 mL of water. Brown ferric compounds precipitated immediately. The mixture was stirred at room temperature for 2 h, poured into 300 mL of water, and thoroughly extracted with ether. The washed and dried ether layer was evaporated and the residue separated by preparative TLC (solvent 13:7 ether–hexane).

The least polar material was **14a**, wt 280 mg, mp 129–130 °C. It exhibited IR bands at 3545 (nonbonded hydroxyl), 1712 and 1267 cm^{-1} (ester); NMR signals at 4.03 m (sharpens to multiplet, $W_{1/2}$ = 8 Hz on D_2O exchange, H-12), 3.69 (methoxyl), 3.29 (H-14), 1.30 (C-4 methyl), 1.01 d and 0.89 d (J = 7 Hz, isopropyl methyls), 0.98 ppm (C-10 methyl).

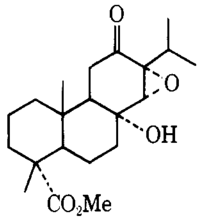
Anal. Calcd for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85; O, 21.95. Found: C, 69.28; H, 8.79; O. 21.97.

The second band was diol **6**, wt 310 mg, mp 145–146 °C, identical with authentic material.[13]

The most polar substance was **18a**, wt 330 mg, mp 161–163 °C. It had IR bands at 3520, 3458 (nonbonded and bonded hydroxyl), 1740 and 1230 cm^{-1} (ester); NMR signals at 5.76 t (J = 6 Hz, H-7), 4.16 m (sharpens on D_2O addition, H-12), 3.71 (methoxyl), 3.03 (H-14), 2.21 d (J = 6 Hz, 2 p, H-6), 1.40 (C-4 methyl), 1.05 d and 0.94 d (J = 7 Hz, isopropyl methyls), 0.97 ppm (C-10 methyl).

Anal. Calcd for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85; O, 21.95. Found: C, 68.93; H, 8.66; O, 22.19.

B. The reactions described in Table VII were carried out as described above with 200 mg of **5** in 6–10 mL of H_2O, 8 mL of THF, and the appropriate amount of $FeSO_4 \cdot 7H_2O$. The reaction was generally complete immediately after mixing, the solvent was removed at reduced pressure, and the residue diluted with water and acidified to facilitate removal of the water-insoluble ferric compounds. The mixture was extracted with ether; the washed and dried ether was evaporated and the residual gum chromatographed by preparative TLC with 13:7 ether-hexane. The three bands were extracted with boiling methanol; the solvent was removed at reduced pressure, the residues were taken up in $CHCl_3$, filtered, and concentrated to give crystalline **6**, **14a**, and **18a**. In one run with 0.25 molar equiv of $FeSO_4$ (entry 8), the product after workup was stirred overnight with silica gel in ether to decompose[37] unreacted **5** to **32**[13] before chromatography.



32

Reaction of 5 with $FeSO_4$ and $Cu(OAc)_2$. To 0.220 g of $Cu(OAc)_2 \cdot 2H_2O$ and 0.153 g of $FeSO_4 \cdot 7H_2O$ in 20 mL of glacial acetic acid was added with stirring 0.200 g of **5**. Stirring was continued for 6 h. The usual workup and chromatography revealed at least five products of which 86 mg (43%) was **14a** and 13 mg (7%) was **18a**.

Reaction of 5 with Vanadyl Acetonylacetonate. To a solution of 0.100 g of $VO(AcAc)_2$ in 25 mL of anhydrous benzene was added 0.200 g of **5**. The initially dark green solution turned red and finally dark brown. After 2 h the solvent was removed in vacuo. The residue was chromatographed in the usual fashion to yield 115 mg (59%) of **14a**, 56 mg (28%) of **18a**, and 26 mg of a mixture intermediate in polarity.

Preparation of 14b. A solution of 0.200 mg in 5 mL of pyridine and 2 mL of acetic anhydride was allowed to stand overnight. The mixture was poured into water and extracted with ether. The washed and dried extracts were evaporated and the residue was recrystallized from methanol-ether to give 191 mg (86%) of **14b**: mp 231–232 °C; IR bands at 1729, 1711, 1247, and 1225 cm^{-1}; NMR signals at 5.35 m (H-12), 3.73 (methoxyl), 3.17 (H-14), 2.11 (acetate), 1.30 (C-4 methyl), 0.96 (C-10 methyl), 0.95 d and 0.85 ppm d (J = 6.5 Hz, isopropyl methyls).

Anal. Calcd for $C_{23}H_{34}O_6$: C, 67.96; H, 8.43; O, 23.61. Found: C, 67.85; H, 8.25; O, 23.82.

When an attempt was made to dehydrate 0.100 g of **5** by refluxing with 25 mL of glacial acetic acid, TLC indicated complete disappearance of starting material after 3 days. Chromatography of the crude product resulted in isolation of 76 mg (68%) of **14b**, presumably because of the difficulty in inducing a positive charge at C-12.

Methyl 5α,8α;13α,14α-Diepoxy-12-oxoabietan-18-oate (19). A. A solution of 0.100 g of **14a** in 25 mL of acetone was cooled to 0 °C and treated with Jones reagent dropwise until the orange-brownish color persisted. After 15 min ice was added and the mixture was extracted with ether. The washed and dried extract was evaporated. Recrystallization of the residue from methanol-water gave 94 mg (94%) of **19**: mp 159–162 °C; IR bands at 1710 (double strength) and 1260 cm^{-1}; NMR signals at 3.72 (methoxyl), 3.53 (H-14), 1.31 (C-4 methyl), 1.00 (C-10 methyl), 0.89 d and 0.81 ppm d (J = 7 Hz, isopropyl methyls).

Anal. Calcd for $C_{21}H_{30}O_5$: C, 69.59; H, 8.34; O, 22.07. Found: C, 69.62; H, 8.55; O, 22.01.

B. Oxidation of 50 mg of **23** in the same manner afforded 47 mg (95%) of **19**.

Methyl 5α,8α-Epoxy-12-oxo-13-abieten-18-oate (20). Chromous chloride was prepared by the literature method[38] from 10 g of Zn dust, 5 g of $CrCl_3$, and 2 mL of concentrated HCl; 14 mL of the resulting solution was added to 0.125 g of **19** in 21 mL of glacial acetic acid (CO_2 atmosphere). After 5 min the solution was poured into 150 mL of water and extracted with ether. The washed and dried ether extracts were evaporated; the solid residue was recrystallized from hexane and then from methanol to give 0.115 g (97%) of **20** which had IR bands at 1728, 1668, and 1252 cm^{-1}; NMR signals at 6.87 d (J = 1.0 Hz, H-14), 3.68 (methoxyl), 1.30 (C-4 methyl), 1.30 (C-4 methyl), 1.07 (C-10 methyl), 0.97 d and 0.95 ppm d (J = 7 Hz, isopropyl methyls).

Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73; O, 18.47. Found: C, 72.84; H, 8.56; O, 18.80.

Methyl 12β-Chloro,5α,8α;13α,14α-diepoxyabietan-18-oate (21). A. A solution of 0.200 g of **14a** in 10 mL of pyridine was cooled to 0 °C and stirred overnight with 1 mL of $POCl_3$. The mixture was cautiously diluted with ice and 50 mL of water and then extracted with ether. The washed and dried ether layers were evaporated. The solid residue was recrystallized from methanol-water to give 0.192 g (91%) of **21**, mp 137–138 °C, IR bands at 1710 and 1668 cm^{-1}. Significant peaks of the NMR spectrum are given in Table I. The mass spectrum exhibited the molecular ion at m/e 382 with a large (30%) peak at m/e 384.

Anal. Calcd for $C_{21}H_{31}O_4Cl$: C, 65.87; H, 8.16; Cl, 9.26. Found: C, 66.20; H, 8.16; Cl, 9.14.

B. Reaction of 0.200 g of **14a** with 1 mL of $SOCl_2$ in 10 mL of pyridine followed by the same workup gave 0.170 g (81%) of **21**.

Methyl 12α-Chloro,5α,8α;13α,14α-diepoxyabietan-18-oate (22). A. A solution of 0.15 g of **21** and 0.120 g of $CaCO_3$ in 25 mL of DMF was heated at reflux for 18 h. The mixture was poured into 50 mL of water and extracted with ether. The washed and dried ether layers were evaporated at reduced pressure. The residue was purified by preparative TLC (eluent 3:2 ether-hexane). The least polar product (7 mg) was unreacted **21** and the most polar product (21 mg, 15%) was **14a**. The product of intermediate polarity (86 mg, 57%) was **22** which was recrystallized from methanol and methanol-water, mp 178–180 °C, IR bands at 1713 and 1268 cm^{-1}. Significant NMR signals are listed in Table I. The mass spectrum exhibited the molecular ion at m/e 382 and a large (30%) peak at m/e 384.

Anal. Calcd for $C_{21}H_{31}O_4Cl$: C, 65.87; H, 8.16; Cl, 9.26. Found: C, 66.21; H, 8.17; Cl, 8.94.

B. A mixture of 0.175 g of **21**, 0.140 g of Li_2CO_3, and 25 mL of DMF was refluxed for 24 h and worked up in the same way. After chromatography, the yields were 122 mg (70%) of **22**, 21 mg of unreacted **21**, and 28 mg (17%) of **14a**.

C. A soltion of 10 mg of **21** and 100 mg of Dabco in 25 mL of DMF was refluxed for 6 h. TLC showed one major product (**22**, identified by NMR spectrometry) and a minor product, but the mixture was not separated.

D. A solution of 0.100 g in 25 mL of DMF was refluxed for 18 h. Chromatography after the usual workup resulted in isolation of 67 mg (67%) of **22** and 26 mg (27%) of **14a**.

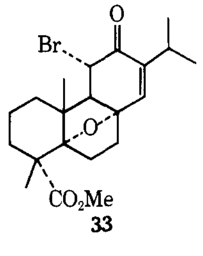
Methyl 5α,8α;13α,14α-Diepoxy-12β-hydroxyabietan-18-oate (23). To 50 mg of $NaBH_4$ in 10 mL of anhydrous methanol was added dropwise with stirring 0.300 g of **19** in 25 mL of methanol. After 1 h, the mixture was decomposed by cautious addition of 10 mL of water, acidified with dilute HCl, and extracted with ether. The washed and dried ether extract was evaporated and the residue was recrystallized from $CHCl_3$-hexane, yield 0.276 g (92%), mp 202–204 °C, IR bands at 3472, 1690, and 1275 cm^{-1}. Significant peaks of the NMR spectrum are listed in Table I.

Anal. Calcd for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85; O, 21.95. Found: C, 68.98; H, 8.73; O, 21.86.

Methyl 11α-Bromo-5α,8α;13α,14α-diepoxy-12-oxoabietan-18-oate (24). A solution of 0.300 g of **19** and 0.275 g of pyridinium bromide perbromide in 15 mL of glacial acetic acid was heated on a steam bath for 30 min, cooled, diluted with 100 mL of water, and extracted with ether. The washed and dried extract was evaporated. The residual gum was purified by preparative TLC (three elutions with 2:5 ether-hexane). The major band was isolated and rechromatographed to remove yellow impurities. Recrystallization from hexane afforded 0.193 g (53%) of **24**, mp 153–154 °C, IR bands at 1715 (double strength) and 1262 cm^{-1}. The 270-MHz spectrum exhibited signals at 4.08 d (J = 11.5 Hz, H-11), 3.72 (methoxyl), 3.60 (H-14), 2.85 dd (J = 11.5, 2 Hz, H-9), 2.48 sept (J = 7 Hz, H-15), 1.31 (C-4 methyl), 1.19 (C-10 methyl), 0.90 d and 0.86 ppm d (J = 7 Hz, isopropyl methyls). The low-resolution mass spectrum exhibited the molecular ion at m/e 440; a peak of equal intensity at m/e 442 showed the presence of Br. Single crystals for x-ray analysis were prepared by recrystallization from ethyl acetate-hexane.

Anal. Calcd for $C_{21}H_{29}O_5Br$: C, 57.15; H, 6.63; Br, 18.10. Found: C, 57.45; H, 6.58; Br, 18.63.

A minor product, isolated from the first chromatogram and rechromatographed for further purification, was recrystallized from methanol-water, yield 93 mg (27%), mp 163–164 °C. Structure **33** was



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assigned to this substance which exhibited NMR signals at 6.96 d (J = 1 Hz, H-14), 4.50 d (J = 13 Hz, H-11), 3.68 (methoxyl), 1.33 and 1.31 (C-4 and C-10 methyls), 1.01 d and 0.97 ppm d (J = 7 Hz, isopropyl methyls). The low-resolution mass spectrum exhibited the molecular ion at *m/e* 424 and a peak of equal intensity at *m/e* 426.

Anal Calcd for $C_{21}H_{29}O_4Br$: Br, 18.79. Found: Br, 18.97.

X-Ray Analysis of Methyl 11α-Bromo-5α,8α;13α,14α-diepoxy-12-oxoabietan-19-oate (19). Single crystals were prepared by recrystallization from ethyl acetate–hexane. Intensity data were measured on a Hilger-Watts diffractometer (Ni filtered Cu Kα radiation, θ–2θ scans, pulse height discrimination). The size of the crystals used for data collection was ca. 0.02 × 0.08 × 0.55 mm. Data were corrected for absorption (μ = 32.3 cm^{-1}). Of the 1661 independent reflections with $\theta < 57°$, 1061 were considered to be observed.

The structure was solved by the heavy atom method and was refined by full matrix least squares. In the final analysis, anisotropic thermal parameters were used for the bromine atom, the oxygens, and all carbon atoms except C(19) and C(21) (see Figure 1 for numbering), and isotropic temperature factors were used for the hydrogen atoms, C(19), and C(21). The hydrogen atoms were included in the structure factor calculations but their parameters were not refined. The final discrepancy indices were R = 0.074 and R = 0.075 for the 1061 observed reflections. Except for two peaks (0.9 and 0.7 e A^{-3}) in the vicinity of the isopropyl group, there were no peaks greater than ±0.4 e A^{-3} on the final difference map. These two peaks indicate some disorder involving the isopropyl group, but no attempt was made to account for it in the calculations. Because of the large estimated standard deviations on the order of 0.02 Å, 1.5°, and 2.5°, respectively (see supplementary Tables III–V), no attempts will be made to discuss individual bond lengths, angles, and torsion angles.

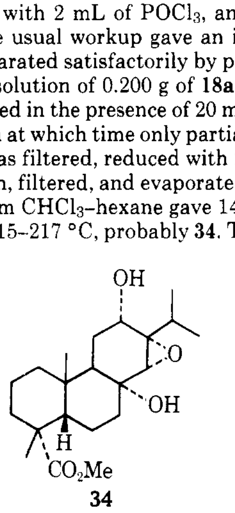
Reactions of 18a. Acetylation. Reaction of 0.150 g of **18a** in 8 mL of pyridine with 2 mL of acetic anhydride in the manner described for **14a** gave a product which could not be induced to crystallize. Purification by preparative TLC (eluent 1:1 ether–hexane) gave 0.136 g (81%) of **18b** which afforded semicrystalline material on being kept in a high vacuum. It had IR bands at 3490, 1722, and 1240 cm^{-1}; NMR signals (270 MHz) at 5.66 dd (J = 2.9, 7.4 Hz, H-6), 5.49 dd (J = 5.2, 10 Hz, H-12), 3.67 (methoxyl), 3.04 (H-14), 2.42 dd (J = 7.4, 15.9 Hz, H-7b), 2.27 dd (J = 2.9, 15.9 Hz, H-7a), 2.10 (acetate), 1.35 (C-4 methyl), 1.06 (C-10 methyl), 1.01 d and 0.87 ppm d (J = 7 Hz, isopropyl methyls). The analytical sample was purified once more by preparative TLC.

Anal. Calcd for $C_{23}H_{34}O_6$: mol wt, 406.2346. Found: mol wt (MS), 406.2346.

Ozonolysis. A solution of 0.150 g of **18a** in $CHCl_3$ was exhaustively ozonized at −78 °C. After warming to room temperature, the ozonide was decomposed by addition of 3 drops of dimethyl sulfide. Analytical TLC of the crude reaction product indicated the presence of several highly polar products; no attempt was made to isolate these substances.

Dehydration. A solution of 0.200 g of **18a** in 15 mL of pyridine was cooled to 0 °C, mixed with 2 mL of $POCl_3$, and allowed to stand overnight at 0 °C. The usual workup gave an intractable mixture which could not be separated satisfactorily by preparative TLC.

Hydrogenation. A solution of 0.200 g of **18a** in 100 mL of ethyl acetate was hydrogenated in the presence of 20 mg of 10% Pd/C at 30 psi of hydrogen for 18 h at which time only partial reduction had occurred. The solution was filtered, reduced with 20 mg of PtO_2 at 30 psi for an additional 4 h, filtered, and evaporated. Recrystallization of the solid residue from $CHCl_3$–hexane gave 146 mg (73%) of a dihydro derivative, mp 215–217 °C, probably **34**. The NMR spectrum was not well defined, but the following signals were present: 4.00 (presumably H-14), two methyl singlets at 1.30, 1.08, and two superimposed doublets at 0.93 ppm d (J = 7 Hz). The substance was isomeric with, but not identical with, **6**. Several attempts to repeat this reduction resulted only in recovery of **18a**.



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Anal. Calcd for $C_{21}H_{34}O_5$: C, 68.82; H, 9.35; O, 21.83. Found: C, 68.72; H, 9.21; O, 21.95.

Methyl 13α,14α-Epoxy-8α-hydroxy-12-oxo-5-abieten-18-oate (27). Oxidation of 0.100 g of **18a** with Jones reagent as described for **14a** followed by preparative TLC (eluent 1:1 ether–hexane) of the crude product and recrystallization from methanol–water afforded **27**, wt 89 mg (89%), mp 102–103 °C, IR bands at 3465, 1726, 1695, and 1246 cm^{-1}. The NMR spectrum is listed in Table VI.

Anal. Calcd for $C_{21}H_{30}O_5$: C, 69.59; H, 8.34; O, 22.07. Found: C, 69.67; H, 8.32; O, 22.32.

Acknowledgment. The aid of Mr. R. C. Rosanske in determining ^{13}C NMR spectra is gratefully acknowledged.

Registry No.—**3a,** 15620-98-1; **5,** 25859-65-8; **8a,** 61597-83-9; **8b,** 22465-59-4; **9a,** 18549-42-3; **9b,** 5309-31-9; **10,** 61591-76-0; **11,** 61617-17-2; **12,** 61617-18-3; **14b,** 61618-21-1; **18a,** 61597-77-1; **18b,** 61597-78-2; **19,** 61597-79-3; **20,** 61597-80-6; **24,** 61597-84-0; **27,** 61597-85-1; **33,** 61597-86-2; **34,** 61617-21-8; sodium levopimarate, 61597-87-3; levopimaric acid, 79-54-9; methyl levopimarate, 61597-88-4; $FeSO_4$, 19468-88-3.

Supplementary Material Available. Tables III, IV, and V listing bond distances, bond angles, and torsion angles of compound **24** (3 pages). Ordering information is given on any current masthead page.

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(19) The mechanism for the formation of **21** from **14a** probably involves formation of the phosphate ester of **14a** followed by nucleophilic attack by Cl^- in S_N2 fashion.

(20) For example, see recent surveys by (a) D. R. Paulson, F. Y. N. Tung, G. F. Moran, A. S. Murray, B. P. Pelka, and K. M. Vasquez, *J. Org. Chem.*, **40**, 184 (1975); (b) N. R. Easton, Jr., F. A. L. Anet, P. A. Burns, and C. S. Foote, *J. Am. Chem. Soc.*, **96**, 3945 (1974).

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Fe(II)-Induced Decomposition of Epidioxides Derived from α-Phellandrene[1]

James A. Turner and Werner Herz*

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

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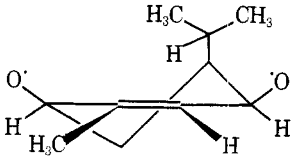
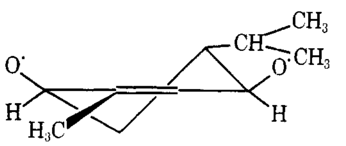
In the Fe(II)-promoted decomposition of the endoperoxides **2**, **3**, **10**, **13**, and **14** prepared from α-phellandrene, the intramolecular 1,5-hydrogen abstraction previously observed in the case of levopimaric acid epidioxide epoxide (**1**) is at best a minor pathway. Structurgs of the various products have been elucidated. A general scheme for the reactions of epidioxides with Fe(II) is presented which involves the Fe(II)–Fe(III) redox system in what superficially appears to be a series of isomerizations and provides a laboratory analogy for the PGG (or PGH) to PGF conversion.

The unexpected formation of remote oxidation products from the reaction of levopimaric acid epidioxide epoxide (**1**) with ferrous ion[2] suggested that other epidioxides might undergo similar reactions if the geometry of the peroxidic oxygen atoms were appropriate for 1,5-hydrogen transfer. Very few of the readily available epidioxides[3] fulfill this condition. In the present communication we report our results in the α-phellandrene series.

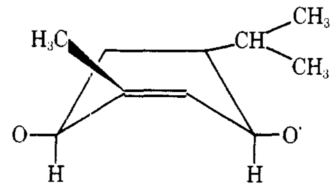
Reaction of α-phellandrene with singlet oxygen yields two epidioxides[4,5] which will be referred to as the cis peroxide **2** and the trans peroxide **3**. **3** contains a γ hydrogen (H-8) with suitable geometry and appropriate carbon–oxygen distance for abstraction by the oxygen atom on C-6 if the radical anion formed by reduction of **2**[2] could assume the half-chair conformation **2a**. The methyl hydrogens of the isopropyl side chain are available to C-3 oxygen in both half-chair and both half-boat conformers of **2**. Regardless of the conformation of the radical anion from **3**, there is no hydrogen available to the oxygen atom on C-6. But in two conformers, half-chair **3a** and half-boat **3b**, the methyl hydrogens of the isopropyl radical are accessible to the oxygen on C-3.



2a



3a



3b

Results

Reaction of trans peroxide **3** with ferrous ion in aqueous tetrahydrofuran gave a mixture of four substances (Scheme I) which were separated by preparative TLC. The least polar product (26%) was identified as the bisepoxide **4** on the basis of the following evidence. The IR spectrum had no absorption in the carbonyl or hydroxyl region. The NMR spectrum (270 MHz) exhibited a three-proton singlet at 1.51 ppm typical of methyl attached to carbon bearing an oxygen and two methyl doublets of the isopropyl group which showed that long-range oxidation at the site of the methyl groups had not occurred. A one-proton doublet ($J = 4$ Hz) at 3.12 ppm and two multiplets at 2.87 and 2.91 ppm were appropriate for H-2, H-3, and H-6. Irradiation at 3.12 ppm altered the signal at 2.87 ppm and in the reverse experiment, irradiation at 2.87 ppm collapsed the doublet at 3.12 ppm to a singlet. This allowed assignment of the three peaks at 3.12, 2.87, and 2.91 ppm to H-2, H-3, and H-6, respectively.

Scheme I