Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 64.83; H, 9.12.

Reaction of 14 with $FeSO_4$. Reaction of 0.300 g of 14 with 0.500 g of $FeSO_4 \cdot 7H_2O$ for 1 h, followed by removal of THF and the usual workup, gave a gum. TLC showed several spots but only one product was formed in substantial amount. Preparative TLC (17:3 ether-hexane) resulted in isolation of this substance **16** in semicrystalline form, wt 125 mg (42%). Its IR spectrum showed strong hydroxyl absorption at 3380 cm^{-1}; the NMR spectrum (270 MHz) after D_2O exchange had signals at 4.11 t (J = 4 Hz, H-3), 3.76 dd (J = 5.5, 11 Hz, H-6), 3.38 d (J = 5 Hz, H-2), 1.47 (C-1 methyl), 0.99 d and 0.92 ppm d (isopropyl methyls).

Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.40; H, 9.74. Found: C, 64.45; H, 9.89.

Registry No.—**2**, 61616-15-7; **3**, 61616-16-8; **4**, 61570-80-7; **5**, 61570-81-8; **6**, 55955-53-8; **7**, 61664-34-4; **8**, 61616-17-9; **9**, 61570-82-9; **10**, 61570-83-0; **11**, 61570-84-1; **12**, 61570-85-2; **13**, 61617-12-7; **14**, 61616-18-0; **15**, 61616-19-1; **16**, 61616-20-4; α-phellandrene, 99-83-2; $FeSO_4$, 19468-88-3.

References and Notes

(1) Supported in part by a grant from the National Science Foundation (GP-12582).

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(8) The relatively poor yield of isolated products was probably due to the difficulty in extracting the two highly polar substances from aqueous solution.

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(19) The reaction should not be confused with the now well-known thermal rearrangement of epidioxides to diepoxides. The thermal reaction requires higher temperatures and is carried out in a nonpolar solvent. Similarly, the base-catalyzed rearrangement[20] of epidioxides to γ-hydroxy-α,β-unsaturated ketones, etc., differs fundamentally from the transformations described in this report.

(20) N. Kornblum and H. E. De La Mare, *J. Am. Chem. Soc.*, **73**, 880 (1951).

(21) When the double bond is absent and the epidioxide bridge is attached to at least one tertiary center, stabilization of the initial oxidation products may occur by intramolecular hydrogen transfer followed by oxidation at the remote site as in the case of **1**,[2] or by loss of an alkyl radical which undergoes subsequent oxidation as in the case of dihydroascaridole epidioxide.[18] Therefore an alternative to the direct oxidation of the anion radicals by Fe(II) to give **5** and **6** may be loss at a hydrogen atom which is subsequently oxidized by Fe(III).[21a] (a) **Note Added in Proof.** The possible implications of the Fe(II)-induced decomposition of such epidioxides for prostacyclin and thromborane biosynthesis are discussed in a separate report: J. A. Turner and W. Herz, *Experientia*, in press.

(22) Experimental details have been specified in ref 2.

Fe(II)-Induced Decomposition of Unsaturated Cyclic Peroxides Derived from Butadienes. A Simple Procedure for Synthesis of 3-Alkylfurans

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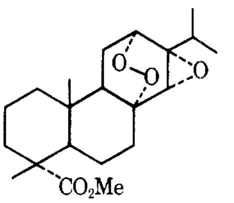
3,6-Dihydro-1,2-dioxins, prepared by reaction of 2-substituted 1,3-butadienes with singlet oxygen, furnish 3-alkylfurans in high yield when treated with ferrous sulfate. The mechanism and limitations of the reaction are discussed. The overall sequence, particularly the last step which involves a redox reaction under extremely mild conditions, may be a model for the biogenesis of naturally occurring 3-alkylfurans.

Fe(II)-induced decomposition of the epidioxide 1 resulted in the unexpected formation of remote oxidation products as the result of intramolecular hydrogen abstraction by the initially formed anion radical.[2] In an attempt to extend this reaction to other substrates with geometries suitable for 1,5-hydrogen transfer[3] we have studied the reaction of Fe(II) with several epidioxides derived from terpenoids which incorporate a 2-alkyl-1,3-butadiene residue. While the original objectives were not realized we have discovered a simple method for making 3-substituted furans which is synthetically useful and may mimic the path by which such substances are formed in nature.

The formation of epidioxides by reaction of homo- and semiannular 1,3-dienes with singlet oxygen is well known,[4] but the preparation of unsaturated cyclic peroxides (3,6-dihydro-1,2-dioxins) from acyclic 1,3-dienes is a relatively new development.[5-7] Very recently, Matsumoto and Kondo[8] examined the reaction of singlet oxygen with a number of acyclic monoterpenoid 1,3-dienes and suggested the following order of reactivity of olefins toward singlet oxygen: trisubstituted monoolefin > 1,3-diene with alkyl substituent at the 2 position > 1,1-disubstituted olefins. Since singlet oxygen is an electrophilic reagent and since mono- and disubstituted olefins react very sluggishly with singlet oxygen,[4] the order of reactivity of olefins toward singlet oxygen suggested by Matsumoto and Kondo[8] can probably be extended as follows: tetrasubstituted monoolefins > trisubstituted monoolefins > 1,3-diene ≫ disubstituted monoolefin and monosubstituted olefin.

Results

As initial substrates for the reaction with ferrous ion we selected the dioxides 3 and 6 from β-myrcene (2) and the epoxide 5.[8,9] Treatment of 3 with ferrous sulfate in aqueous tetrahydrofuran surprisingly furnished only one product (TLC analysis) which was isolated in 81% yield. The IR spectrum displayed hydroxyl absorption as well as bands at 1500 and 880 cm^{-1} characteristic of furans. The 270-MHz



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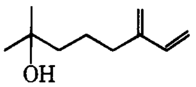

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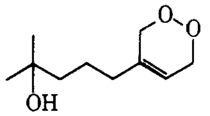

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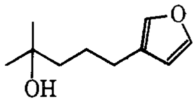

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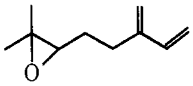

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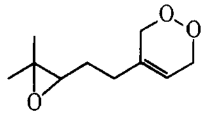

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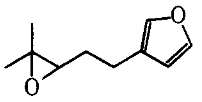

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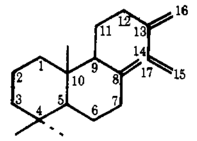

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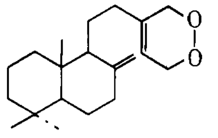

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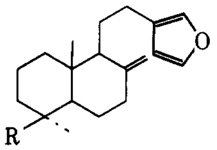
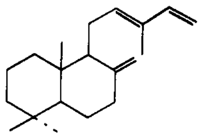
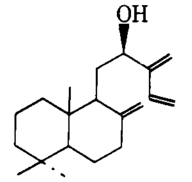


10a, R = Me
b, R = CO$_2$H



11



12

NMR spectrum displayed the typical ABX pattern of a 3-substituted furan (one-proton multiplet of β proton at 6.2 ppm, one-proton multiplet at 7.13 ppm, and one-proton multiplet at 7.25 ppm, J = 1.8 Hz, of the α protons), a two-proton triplet at 2.41 ppm (J = 7 Hz) of the furfurylic protons, and a six-proton siglet at 1.18 ppm. The downfield signals were in good agreement with those reported for 3-hydroxy-2-methyl-5-(3-furyl)-1-pentene;[10] hence the product must be **4**.

Dioxide **6** reacted with ferrous ion in analogous fashion to furnish the furan **7** whose NMR spectrum exhibited the furan resonance at 7.36 (t), 7.26 (m), and 6.29 ppm (m) and the methyl signals at 1.23 and 1.30 ppm. The epoxidic proton signal occurred as a triplet (J = 6 Hz) at 2.77 ppm; two-proton triplets at 2.63 and 1.85 ppm were assigned to H-5 and H-4, respectively.

Two additional substances were examined to determine whether furan formation was a general consequence of the reaction of 3,6-dihydro-1,2-dioxins with Fe(II). These were the naturally occurring labdatrienes sclarene (**8**) and *trans*-biformene (**11**) which can also be prepared, together with *cis*-biformene, from manool.[11]

Reaction of **8** with singlet oxygen gave a relatively poor yield (29%) of peroxide **9**, presumably due to the facility with which the diene polymerizes in air.[11,12] The spectroscopic properties of **9** (see Experimental Section) were in accord with the proposed formulation. Treatment of **9** with ferrous sulfate gave in essentially quantitative yield furan **10a** whose NMR spectrum exhibited the H-17 resonances as broadened singlet at 4.55 and 4.84 ppm and the usual three furan signals, as well as three methyl singlets at 0.79 and 0.68 ppm. The downfield portion of the spectrum was very similar to that of lambertianic acid (**10b**).[13,14]

According to the order of reactivity of olefins toward singlet oxygen presented earlier, one of the conjugated double bonds of **11** would be expected to undergo preferential "ene" reaction. Indeed, the reaction of **11** with singlet oxygen was complete after only 2.5 h and, after reduction of the hydroperoxide with triethyl phosphite, the triene alcohol **12** was obtained in 43% yield.[16] The NMR spectrum exhibited three methyl singlets, a doublet of doublets at 6.34 ppm (J = 18 Hz) assigned to H-14, multiplets at 4.50 and 4.83 ppm (H-17), and a multiplet at 4.34 ppm (H-12). A partially obscured broadened doublet at 5.37 ppm (J = 8 Hz) was identifiable with the resonance of H-15a trans to H-14, whereas a somewhat broadened signal at 4.94 ppm was one-half of a doublet centered at 5.08 ppm (H-15b cis to H-14), the other half being completely hidden. Two narrowly split doublets (J = 1 Hz) at 5.18 and 5.10 ppm were due to the resonance of H-16. These assignments are in good agreement with the NMR spectrum of sclarene (see Experimental Section). Evidence for the configuration of the hydroxyl group depicted in the formula will be presented subsequently.

Table I. Downfield Portion of NMR Spectra of 14a–c

	14a[a]	**14b**[b]	**14c**[b]
H-17a	4.47	4.48	4.72
H-17b	4.85	4.86	4.88
H-16 H-15	7.32 d (1.6)	7.3 m	7.3 m
H-14	6.36 t (1.6)	6.37 m	6.37 m
H-12	4.69 dd (9, 3)	4.71 m	4.78 m

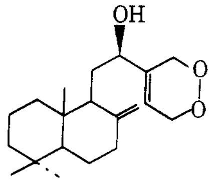
[a] At 270 MHz in CDCl$_3$. [b] At 60 MHz in CDCl$_3$, quoted from ref 17.

Table II. H-17 Resonances of Selected 12-Hydroxylabdanes[a]

	12	**13**	**15a**[b]	**15b**[b]
H-17a	4.54	4.39	4.40	4.72
H-17b	4.83	4.83	4.83	4.88

[a] At 60 MHz. [b] Quoted from ref 18.

Reaction of **12** with singlet oxygen gave the expected peroxide **13** in 54% yield whose NMR spectrum (see Experimental Section) was in accord with the proposed formula. Treatment of **13** with ferrous sulfate furnished the crystalline furan **14a** in quantitative yield. The NMR spectrum of **14a** is presented in Table I together with spectra of the very similar labdanoic acids **14b** and **14c**.[17] The striking similarity between the NMR spectra of **14a** and **14b** (cf. shifts of H-17a and H-12) permits the deduction that the configuration of the new furan, and therefore that of **12** and **13**, at C-12 is R. Additional evidence is furnished by Table II in which the H-17 resonances of compounds **12** and **13** are compared with those of **15a** and **15b**.



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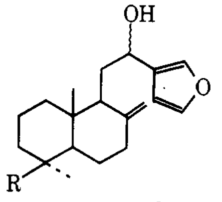
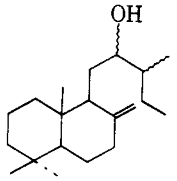
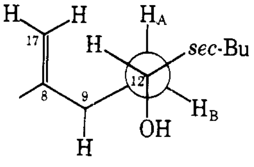


14a, R = Me, –OHβ (12R)
b, R = CO$_2$H, –OHβ (12R)
c, R = CO$_2$H, –OHα (12S)

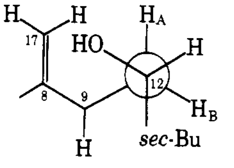


15a, –OHβ (12R)
b, –OHα (12S)

The coupling constants of H-12 in the NMR spectrum of



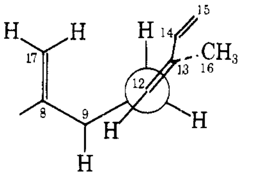
A



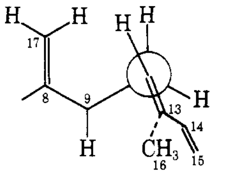
B

14a are consistent with the contention[18] that in 12*R*-hydroxylabdanes conformation A is more highly populated than conformation B. The large coupling constant ($J = 9$ Hz) is expected for the anti arrangement of H-12 and H-11$_B$; the smaller one (3 Hz) is typical for the gauche relationship between H-12 and H-11$_A$.

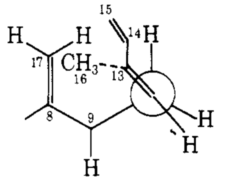
The predominant formation of the 12*R* hydroperoxide in the reaction of **11** with singlet oxygen can be rationalized in a manner similar to that used to explain the preferred direction of nucleophilic attack on the ketone precursor **16** of **15a** and **15b**.[18] If eclipsed conformations of the isoprene moiety are excluded, three conformations, C, D, and E, are theoretically possible for **11**. But E can be ruled out because of severe interactions between either H-9 and H-16 or H-1 and H-16, even if there were considerable torsion around the 9,11 bond. In conformation C, H-17$_A$ shields C-12 from the left and attack by oxygen should occur only from the direction yielding the 12*R* hydroperoxide, whereas in conformation D the opposite situation prevails and formation of the 12*S* isomer would be expected. Preferential formation of **15a** by nucleophilic attack on **16** was rationalized[18] by noting that in the transition states the carbonyl oxygen is forced toward H-17$_A$ and that the transition state from D would be of higher energy than the transition state from C because of the smaller distance between H-17$_A$ and the oxygen atom. This effect should not be as pronounced in **11** as in **16** since C–H bonds are shorter than C=O. However, it should also be noted that C has the more favorable anti arrangement of the two large groups while D is gauche. Also D of **11** has an additional interaction between H-16 and H-9 not present in D of **16**.



C



D

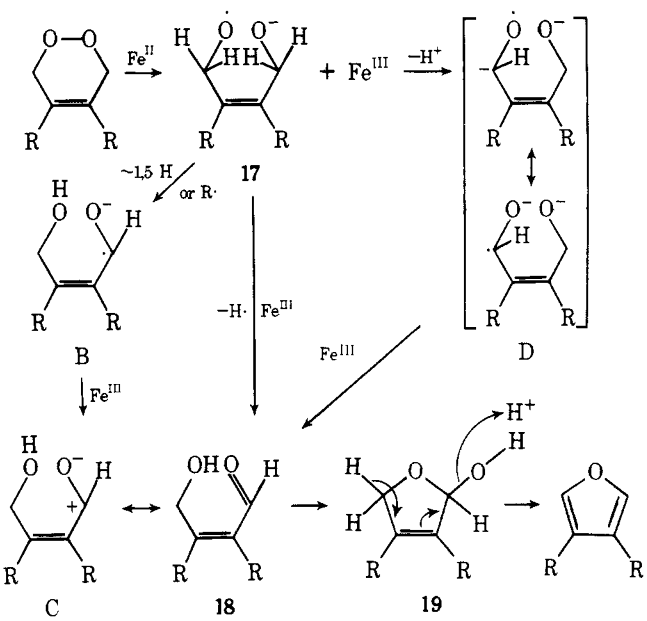


E

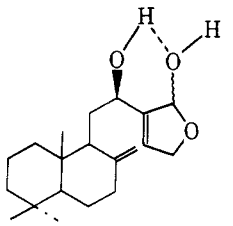
Discussion

The mechanism by which furans are formed in one step and in excellent yield from 3,6-dihydro-1,2-dioxins by reaction with ferrous ion is probably analogous to the formation of hydroxy ketones in the phellandrene series.[3] Thus cleavage of the O–O bond would result in the radical anions **17** (Scheme I). Several possibilities exist for the conversion of **17** to final product. The most attractive one involves intramolecular hydrogen abstraction leading to anion radical B which is oxidized by Fe(III) to C equivalent to hydroxy aldehyde **18**. The latter is expected to cyclize to hemiacetal **19**. Loss of a proton from **17** and concomitant oxidation of the oxy radical [or more likely the allylic carbon radical by Fe(III)] to D followed by proton loss or fragmentation by loss of a hydrogen atom and oxidation would also furnish **18** but seems less plausible. It should be noted that fragmentation by loss of H· and oxidation of the latter to H^+ is mechanistically equivalent to loss of H^+ and simultaneous oxidation of the radical. Hydrogen atom abstraction by another radical within the system is also a possibility; an example of this would be air oxidation of **17** to **18**. Dehydration of **18** to the furan is presumably catalyzed by either the Lewis acid Fe(III) or by a proton within the system. The reactions were usually worked up by extraction of an ethereal solution of the product mixture with dilute aqueous acid to facilitate removal of Fe(III) which is almost insoluble in neutral aqueous solution. However, dehydration of **19** does not occur during this procedure since TLC showed complete conversion to furan prior to workup.

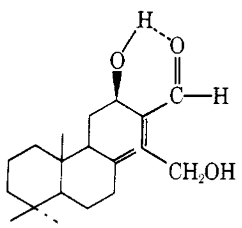
Scheme I



An interesting observation was made in the preparation of **14a** from **13**. After addition of Fe(II) to **13**, TLC indicated complete disappearance of **13** and the formation of two new substances. One, less polar than **13**, was identified as **14a**; the second, more polar substance was converted completely to **14a** on stirring overnight. Hence the polar product was either the hemiacetal **20** or the hydroxyaldehyde **21**, both of which should be stabilized by hydrogen bonding. No attempt was made to isolate the intermediate since hemiacetals of type **19** (Scheme I) readily dehydrate upon chromatography.[7,19]



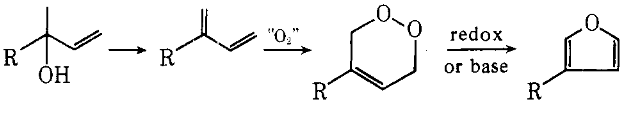
20



21

3,6-Dihydro-1,2-dioxins have served previously as starting materials for the preparation of substituted furans.[5,7,10,21,22] However, the yields of 3-substituted furans by the Fe(II) method are excellent, comparable to those obtained[22] by base-catalyzed rearrangement and dehydration of 3,6-dihydro-1,2-dioxins and superior to those achieved by thermal dehydration.[7,21] The one-step reaction is simple to carry out, is often complete on addition of Fe(II), and can be carried out in aqueous solvents in the presence of air. By-products were not observed. Use of the procedure is probably limited only by the availability of the appropriate diene and its ability to undergo the required Diels–Alder type reaction with singlet oxygen. As was mentioned earlier and was found in the case of *trans*-biformene, dienes with trisubstituted double bonds can be expected to undergo preferentially an "ene" reaction.

The biogenetic implications of the formation of furans from acyclic dienes via peroxides have been noted[7,8,21] and demonstrated in biomimetic syntheses of naturally occurring furans.[7,21] Of particular importance is the circumstance that allylic alcohols coexist with dienes naturally (e.g., manool, the biformenes, and sclarene). Hence a possible biogenetic scheme for the formation of furans may be the following:



The redox system discovered in the course of this work is particularly attractive as a model for the last step in this scheme.

Experimental Section[23]

General Procedures. I. Photolyses. A. A solution of the olefin and sensitizer was irradiated in a Hanovia-type reactor using a Sylvania DVY-tungsten halogen projection lamp as an internal light source. The lamp was operated at 60–70 V and was cooled with a stream of air. A stream of oxygen was bubbled through the reaction mixture which was cooled by a water jacket between the lamp and the vessel containing the mixture.

B. A solution of the diene and *meso*-tetraphenylporphine in CCl_4 in a vessel cooled by a water jacket was irradiated with a 30-W sodium vapor lamp placed outside the vessel while oxygen was bubbled through the reaction mixture. These directions were supplied by Dr. Matsumoto.

C. A solution of the diene and sensitizer in a vessel surrounded by a water jacket was irradiated with a 150-W incandescent lamp placed near the vessel while oxygen was bubbled through the reaction mixture.

II. Reaction of Peroxides with $FeSO_4$. A solution of $FeSO_4{\cdot}7H_2O$ in distilled water was added all at once to a stirred solution of the peroxide in THF. Brown ferric salts precipitated immediately and the reactions were generally complete at this stage. The solvent was usually removed at reduced pressure, and the residue diluted with water and acidified to facilitate removal of the water-insoluble ferric salts. The mixture was extracted with ether and the washed and dried ether extracts removed to yield crude product.

Epidioxide of Myrcenol (3). This substance was prepared from myrcenol[24] by procedure A (solvent methylene chloride–5% methanol, sensitizer rose bengal[8]) and by procedure B. The reactions were run until TLC showed nearly complete consumption of starting material (usually 18–24 h). The rate of reaction was approximately the same by either procedure, but it was very difficult to remove the tetraphenylporphine used in procedure B. The crude mixture was evaporated to dryness and chromatographed over Florisil or silica gel. The product **3** was rechromatographed prior to further use.

Epidioxide of Epoxymyrcene (6). Epoxymyrcene (**5**) was prepared from β-myrcene by the literature method.[8] Procedures A and B were used with equal success; the sensitizer was separated from **6** by column chromatography.

5-(3-Furyl)-2-methylpentan-2-ol (4). A solution of 0.753 g of $FeSO_4{\cdot}H_2O$ in 20 mL of water and 0.500 mg of **3** in 15 mL of THF was stirred for 2 h and worked up as described in the general reaction procedure except that the reaction mixture was not acidified. Chromatography furnished 0.367 g (81%) of **4** (viscous liquid) which had an odor resembling that of myrcenol: IR bands at 3390, 1500, and 880 cm^{-1}; NMR signals at 7.25 t (J = 1.8 Hz) and 7.13 m (H-2′ and H-5′), 6.20 m (H-4′), 1.18 ppm (two superimposed methyl singlets). At 270 MHz, the H-5 signal was resolved into a triplet at 2.41 ppm (J = 7 Hz). For analysis, the product was repurified by preparative TLC.

Anal. Calcd for $C_{10}H_{16}O_2$: mol wt, 168.1149. Found: mol wt (MS), 168.1165.

2,3-Epoxy-5-(3′-furyl)-2-methylpentane (7). Reaction of 0.500 g of **6** and 0.700 g of $FeSO_4{\cdot}7H_2O$ in the manner described in the previous paragraph and chromatography of the crude product over 25 g of silica gel gave 0.418 g (92%) of **7** as a volatile liquid homogeneous on TLC, which had IR bands at 3125–3090, 1550, and 880 cm^{-1}; NMR signals at 7.36 t (J = 1.7 Hz) and 7.27 m (H-2′ and H-5′), 6.29 m (H-4′), 2.77 t (J = 6 Hz, H-3), 2.63 t (somewhat distorted, J = 7 Hz, H-5), 1.83 c (H-4), 1.30 and 1.20 ppm (two methyl singlets).

Anal. Calcd for $C_{10}H_{14}O_2$: mol wt, 166.0993. Found: mol wt (MS), 166.1004.

Dehydration of Manool. 8, 11, and *cis*-biformene were prepared from manool and separated by the procedure of Carman and Dennis.[11]

15,16-Epidioxy-8(17),13-labdadiene (9). This peroxide was prepared from 0.550 g of sclarene by procedure A (solvent 250 mL of CH_2Cl_2–5% methanol, sensitizer 20 mg of rose bengal, time 24 h). Analytical TLC of the mixture showed complete reaction, with one major spot and a more polar streak. The solvent was removed at reduced pressure; the residue was taken up in $CHCl_3$, filtered, and evaporated. Preparative TLC of the crude product (solvent 1:19 ether–hexane) gave 177 mg (29%) of **9** which crystallized on drying. Further purification by preparative TLC raised the melting point to 37–39 °C; IR bands at 3070 and 1638 cm^{-1}; NMR signals at 5.62 m (H-14), 4.82 br ($W_{1/2}$ = 4 Hz), and 4.56 br (H-17), 4.47 c (4 protons, H-15 and H-16), and 0.87, 0.80, and 0.68 ppm (C-4, C-10 methyls).

Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 79.00; H, 10.43.

In another run, 0.500 g was oxygenated for only 15 h. Chromatography gave 150 mg of sclarene and 157 mg of **9** (28%, but 40% based on recovered diene).

15,16-Epoxy-8(17),13(16),14-labdatriene (*anti*-Daniellane, 10a). Reaction of 0.100 g of **9** in 10 mL of THF with 0.100 g of $FeSO_4{\cdot}7H_2O$ in 8 mL of water was slow, presumably because of the low solubility of **9** in the aqueous medium. TLC showed complete reaction after 1 h. The mixture was not acidified. The crude residue obtained after the usual workup was chromatographed over 20 g of silica gel: yield 93 mg (99%) of **10a**; IR bands at 3050, 1635, 1495, and 874 cm^{-1}; NMR signals at 7.31 t (J = 1.8 Hz) and 7.17 m (H-15 and H-16), 6.23 m (H-14), 4.84 br ($W_{1/2}$ = 4 Hz) and 4.55 br ($W_{1/2}$ = 4 Hz, H-17), 0.86, 0.79, and 0.68 ppm (C-4 and C-10 methyls). The analytical sample was repurified by preparative TLC.

Anal. Calcd for $C_{20}H_{30}O$: C, 83.86; H, 10.56. Found: C, 83.76; H, 10.55.

8(17),13(16),14-Labdatrien-(12*R*)-ol (12). Reaction of 0.550 g of *trans*-biformene with singlet oxygen by procedure A (solvent CH_2Cl_2–5% methanol, sensitizer 20 mg of rose bengal). After 2.5 h, 0.4 g of $P(OEt)_3$ was added and the solvent was removed at reduced pressure. The residue was purified by preparative TLC (eluent 1:9 ether–hexane). The least polar band (30 mg) was a mixture (TLC and NMR); a more polar band (101 mg), while chromatographically pure, was also a mixture by NMR criteria. These fractions were not examined further nor was a highly polar band containing $P(OEt)_3$ and other materials. A chromatographically pure band of intermediate polarity which was pure by NMR criteria was isolated as a gum (**12**): wt 226 mg (43%); IR bands at 3410, 3049, and 1628 cm^{-1}; NMR signals at 6.34 dd ($J_{14,15\text{trans}}$ = 18, $J_{14,15\text{cis}}$ = 11 Hz, H-14), 5.37 dbr (J = 18 Hz, H-15 trans to H-14), 5.08 dbr (J ~ 11 Hz, H-15 cis to H-14), 5.18 d and 5.10 d (J = 1 Hz, H-16), 4.83 br and 4.50 br (H-17), 4.38 m (H-12), 0.87, 0.79, 0.67 ppm (C-4 and C-10 methyl). Elemental analyses of this substance were not satisfactory owing to rapid decomposition; consequently it was prepared and purified just before use.

15,16-Epidioxy-8(17),13-labdadien-(12*R*)-ol (13). The reaction of 1.35 g of freshly purified **12** with singlet oxygen was carried out by procedure A (solvent CH_2Cl_2–5% methanol, sensitizer 20 mg of rose bengal) for 20 h when TLC showed the pressure of some starting material, but only one major product and small amounts of more polar fractions. The crude product was chromatographed over 100 g of silica gel; this resulted in recovery of 233 mg of **12** and isolation of 813 mg of **13** (54%, 64% based on recovered starting material) as a gum which was further purified by preparative TLC; IR bands at 3440, 3068, and 1638 cm^{-1}; NMR signals at 5.81 m (H-14), 4.83 br and 4.39 br (H-17), 4.56 m (H-15 and H-16), 4.14 m (H-12), 0.87, 0.80, and 0.66 ppm (C-4 and C-10 methyls).

Anal. Calcd for $C_{20}H_{32}O_3$: mol wt, 320.2334. Found: mol wt (MS), 320.2338.

15,16-Epoxy-8(17),13(16),14-labdatrien-(12*R*)-ol (14). After reaction of 0.100 g of **13** in 15 mL of THF with 90 mg of $FeSO_4{\cdot}7H_2O$ in 10 mL of water for 1 h, TLC indicated complete disappearance of **13** and formation of a less polar spot (**14**) and more polar material, presumably **26** or **27**. After stirring overnight, only the spot corresponding to **14** remained and had increased in intensity. After the usual workup there was obtained 99 mg of solid. Recrystallization from pentane afforded 88 mg (93%) of **14**: mp 71–72 °C; IR bands at 3415, 3125, 3113, 3062, 1635, 1500, and 872 cm^{-1}; NMR signals (270 MHz) at 7.32 d (J = 1.6 Hz, H-15 and H-16), 6.36 t (J = 1.6 Hz, H-14), 4.85 br and 4.47 br (H-17), 4.60 dd (J = 9, 3 Hz after D_2O exchange, H-12), 0.88, 0.81, and 0.68 ppm (C-4 and C-10 methyls).

Anal. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.64; H, 10.21.

Registry No.—**3**, 57073-98-0; **4**, 61597-51-1; **5**, 29414-55-9; **6**, 56764-67-1; **7**, 61597-52-2; **8**, 511-02-4; **9**, 61597-53-3; **10a**, 61597-54-4; **11**, 10395-42-3; **12**, 61618-20-0; **13**, 61604-71-5; **14a**, 61597-55-5; myrcenol, 543-39-5; $FeSO_4$, 19468-88-3.

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Nitrones. 4.[1] Reactions of Δ^1-Pyrroline *N*-Oxides with Phosphonates. Alternative Formation of Aziridines and Enamines[2]

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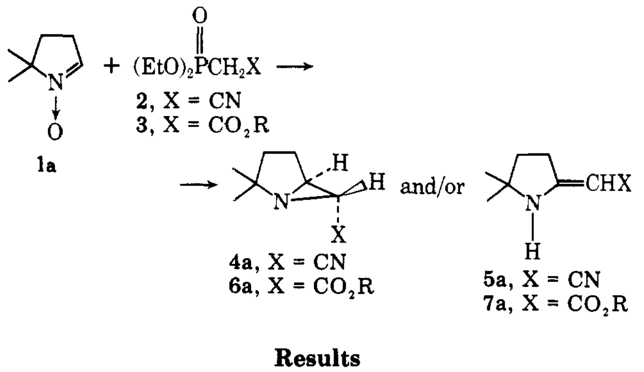
Variously methylated derivatives of Δ^1-pyrroline *N*-oxide (1) were reacted with diethyl cyanomethylphosphonate (2) and dialkyl alkoxycarbonylphosphonates **3** using sodium hydride in 1,2-dimethoxyethane or alkali metal alkoxides in alcoholic solvents. These reactions were shown to lead to 6-*exo*-cyano- and 6-*exo*-alkoxycarbonyl-1-azabicyclo[3.1.0]hexane derivatives **4** and **6**, or alternatively 2-cyanomethylene- or 2-alkoxycarbonylmethylenepyrrolidine derivatives **5** and **7**. This work describes the influence of substitution in the pyrroline *N*-oxide and of the variations in the reagents and solvents on the ratio of the products obtained in the reactions. It was found that when the reactions were carried out in 1,2-dimethoxyethane, the major product obtained was of aziridinic structure. However, using alcoholic solvents the yield of the enaminic products increased at the expense of the aziridinic products with increasing acidity of the solvent. The influence of the alkali metal cations on the course of the reaction was also studied, and it was found that lithium *tert*-butoxide promotes the formation of enaminic products as compared to sodium and potassium *tert*-butoxides.

Previously we reported that the reactions of 5,5-dimethyl-Δ^1-pyrroline *N*-oxide (**1a**) with diethyl cyanomethylphosphonate (**2**) and triethyl phosphonoacetate (**3**, R = C_2H_5) may be directed to lead to aziridines or enamines.[3,4] In this paper we wish to describe in detail the influence of substitution in the substrate and the variations in the reagents and reaction conditions on the course of this novel reaction.



1a

2, X = CN
3, X = CO_2R

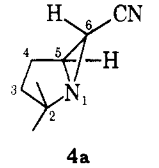
4a, X = CN
6a, X = CO_2R

5a, X = CN
7a, X = CO_2R

Results

The results from the reactions of a series of Δ^1-pyrroline *N*-oxides **1** with diethyl cyanomethylphosphonate (**2**) and dialkyl carbalkoxymethylphosphonate **3** are listed in Tables I–III. All reactions were monitored by thin layer chromatography and, when they resulted in the formation of more than one product, the mixtures were separated by chromatography. The identification of products is mainly based on their NMR spectra. Therefore it is of interest to present the significant features in the spectra of representative compounds.

The NMR spectrum of 6-*exo*-cyano-2,2-dimethyl-1-azabicylo[3.1.0]hexane (**4a**) shows the angular aziridinic hydrogen



4a

H-5 as a broad signal at δ 2.80 ppm and the second aziridinic hydrogen (H-6) as a doublet at higher field, namely at δ 1.94 ppm (J = 2.5 Hz).

We have previously suggested[5] that H-6 appears at higher field because of the shielding influence of the cis-related *N*-alkyl substituent. This assignment was subsequently confirmed by preparation of the 6-endo-deuterio derivative of **4a** using diethyl cyanomethylphosphonate-d_2. The coupling constant of H-6 indicates trans-aziridinic structure.[6]