slowly to a stirred suspension of **2** (2.04 g, 15.9 mmol) in 30 mL of THF at -10 °C. The mixture was stirred at room temperature for 1 h, during which time it became clear. The pale yellow solution was then cooled to -30 °C. Lithium diphenylphosphide[20] (3.03 g, 15.9 mmol) was added dropwise over a period of 30 min. The solution was allowed to warm gradually to room temperature, and then it was stirred for 5 h (TLC control). The solvent was removed under vacuum. The residue was taken up in pentane and fractionated rapidly (10 min) through 3 in. of degassed silica gel (Merck, 35-70mesh), with pentane/THF = 9/1 (200 mL), by means of a frit under vacuum-argon line. Removal of the solvent gave **5** (4.80 g, 68% yield) as a light yellow viscous oil. (The phosphine **5** is extremely sensitive to oxygen. The oxide precipitated by stirring **5** in pentane for a few minutes at room temperature in an open flask; mp 121-123 °C; $^{31}P\{^1H\}$ NMR δ +27.9, +28.3). A trace of the phosphine oxide may be eliminated from **5** by dissolving it in pentane; IR (neat) 3050 (s), 2960 (vs), 2910 (vs), 2850 (vs), 1950 (w), 1885 (w), 1810 (w), 1730 (m), 1650 (m), 1580 (m), 1475 (s), 1430 (vs), 1375 (m), 1315 (m), 1270 (m), 1180 (m), 1095 (s), 1065 (m), 1025 (s), 990 (m), 910 (w), 840 (m), 740 (vs), 695 (vs) cm^{-1}; ^1H NMR (C_6D_6) δ 0.99 (d, CH_3, 6.0 Hz), 1.49-1.55 (m, CH_2), 1.60 (s, CH_3), 1.65 (br s, CH_3), 1.74 (br s, CH_3), 1.80-1.90 (m, CH_2), 2.28 (m, CH), 7.13-7.22 (m, Ph-*m*,*p*), 7.36-7.53 (m, Ph-*o*); $^{13}C\{^1H\}$ NMR (C_6D_6) δ [11.5, 11.8, 13.0, 13.3, 14.7, 14.8] (CH_3), [23.3, 24.0] (CH_2 β to P, $J_{^{31}P-^{13}C}$ = 11.5 Hz), [32.0, 33.3] (CH_2 α to P, $J_{^{31}P-^{13}C}$ = 18.1 Hz), [56.1, 58.4] (CH), [128.4-149.0] (aromatic and olefinic carbons); $^{31}P\{^1H\}$ NMR (C_6D_6) δ -16.4, -16.9; MS, *m*/*e* (relative intensity) 334 (55, M^+), 319 (91), 213 (18), 183 (84), 149 (29), 121 (47), 77 (100).

Registry No. **1**, 4249-10-9; **2**, 87781-76-8; **3**, 125050-56-8; **4**, 125050-57-9; **5**, 125050-59-1; $TsO(CH_2)_2Cl$, 80-41-1; Ph_2PCl, 1079-66-9; $Ph_2P^-Li^+$, 4541-02-0; 2,3,4,5-tetramethylcyclopent-2-enol, 82061-20-9.

(20) Lithium diphenylphosphide was prepared by reaction of *n*-BuLi with diphenylphosphine in pentane.

Reactivites of Some Allylic Hydroperoxides toward Allylic Rearrangement and Related Reactions

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The allylic rearrangement has been studied of the hydroperoxides that are formed when singlet oxygen reacts with epicholesterol, $\Delta^{9,10}$-octahydronaphthalene, 2,3-dimethylbut-2-ene, cyclopentylidenecyclopentane, and cyclohexylidenecyclohexane. The reactivity in this sense decreases in the above sequence. 1-(Cyclopent-1-enyl)cyclopentyl hydroperoxide rearranges only slowly, but in the presence of triplet oxygen it reacts to give 1-(5-hydroperoxycyclopent-1-enyl)cyclopentyl hydroperoxide, and 1-(cyclohex-1-enyl)cyclohexyl hydroperoxide does not rearrange and shows only the reaction with oxygen to give 1-(6-hydroperoxycyclohex-1-enyl)cyclohexyl hydroperoxide. The various factors that affect the rates of these reactions are discussed. It is suggested that the reactivity and regioselectivity in the autoxidation which leads to the formation of dihydroperoxides implies that the reaction involves not the usual two-step propagation sequence, but a three-step sequence in which the chain carriers are a cycloalkenyl radical, a cycloalkenylperoxyl radical, and a cycloalkylperoxyl radical.

Introduction

Over three decades ago Schenck and co-workers demonstrated that 5α-hydroperoxycholest-6-en-3β-ol (**1**) formed in the reaction of singlet oxygen with cholesterol rearranges in a nonpolar solvent during about 1 day to give the corresponding Δ^5-7α-hydroperoxide (Scheme I).[2] Since this discovery, a dozen or so further examples of this phenomenon, in which an allyl hydroperoxide rearranges to its allylic isomer, have been identified.[3-5] Three others in particular that we have studied are the methyl- and ethyloctalin hydroperoxides[3] (**2**, **3**) and the hydroperoxide (**4**) derived from valencene.[4]

These rearrangement reactions are well established to proceed via the corresponding allylperoxyl radical.[2-6] In general, the product of singlet oxygenation rearranges to the product of triplet oxygenation. Under an atmosphere of $^{18}O_2$, the hydroperoxides **1** and **4**[4,6] and that derived from oleic acid[5] incorporate no labeled oxygen during the rearrangement. This, together with the observation that the reactions of the hydroperoxides (**1**-**4**) occur suprafacially, suggests that the rearrangements follow a sigmatropic, nondissociative mechanism (Scheme II).[4-6]

The reactivity, however, of various cyclic systems studied is sensitive to structure, and the detailed mechanism is not clear. For example, the 5α-hydroperoxides derived from the O-methyl, O-trimethylsilyl and O-acetyl derivatives of cholesterol rearrange much more readily than **2**, the hydroperoxide derived from cholesterol itself.[6] Further, the mechanism of the related rearrangement of β-(acyloxy)-alkyl radicals appears to be different in cyclic and acyclic systems.[7]

In an attempt to understand further some of the structural factors that affect the reactivity, we have now examined the rearrangement of a number of allyl hydro-

(1) Ramsay Memorial Research Fellow.
(2) Schenck, G. O.; Neumüller, O. A.; Eisfeld, W. *Justus Liebigs Ann. Chem.* **1958**, *618*, 202.
(3) (a) Schenck, G. O.; Neumüller, O. A.; Eisfeld, W. *Angew. Chem.* **1958**, *70*, 595. (b) Eisfeld, W. Diplomarbeit, Univ. Göttingen, 1959. (c) Lythgoe, B.; Trippett, S. *J. Chem. Soc.* **1959**, 471. (d) Schenck, G. O.; Gollnick, K.; Buchwald, G.; Schroeter, S.; Ohloff, G. *Justus Liebigs Ann. Chem.* **1964**, *674*, 93. (e) Brill, W. F. *J. Am. Chem. Soc.* **1965**, *87*, 3286. (f) Nickon, A.; Mendelson, W. L. *Can. J. Chem.* **1965**, *43*, 1419. (g) Gollnick, K. *Adv. Photochem.* **1968**, *6*, 1. (h) Schulte-Elte, K.-H.; Fracheboud, M. G.; Ohloff, W. Ger. Pat. 2035901/1971; Swiss Pat. 553141/1974. (i) Fox, J. E.; Scott, A. I.; Young, D. W. *J. Chem. Soc., Perkin Trans. 1* **1972**, 799. (j) Ohloff, G. *Pure Appl. Chem.* **1975**, *43*, 481. (k) Brill, W. F. *J. Chem. Soc., Perkin Trans. 2* **1984**, 621. (l) Davies, A. G.; Kinnart, W. *J. Chem. Res., Synop.* **1989**, *22*. (m) Kwon, B.-M.; Kanner, R. C.; Foote, C. S. *Tetrahedron Lett.* **1989**, *30*, 903.
(4) (a) Avila, D. V.; Davies, A. G.; Davison, I. G. E. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1847. (b) Davies, A. G.; Davison, I. G. E. *J. Chem. Soc., Perkin Trans. 2* **1989**, 825.
(5) Porter, N. A.; Wujek, J. S. *J. Org. Chem.* **1987**, *52*, 5085.
(6) Beckwith, A. L. J.; Davies, A. G.; Davison, I. G. E.; Maccoll, A.; Mruzek, M. H. *J. Chem. Soc., Chem. Commun.* **1988**, 475; *J. Chem. Soc., Perkin Trans. 2* **1989**, 815.
(7) Beckwith, A. L. J.; Duggan, P. J. *J. Chem. Soc., Chem. Commun.* **1988**, 1000.

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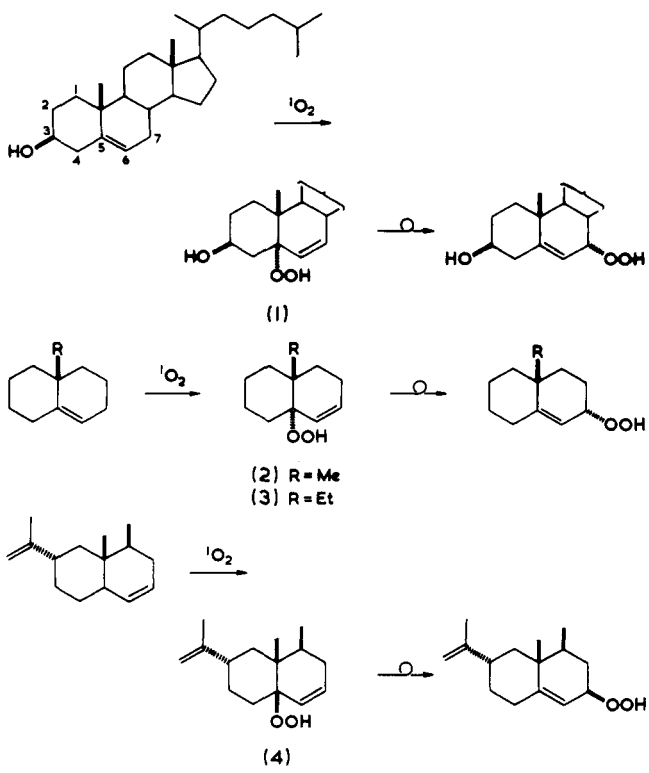
Scheme I

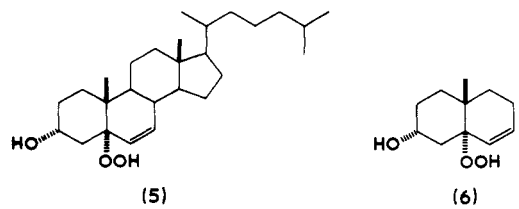


Scheme II

peroxides in which different structural features might be expected to affect the reactivity, and we report the reactions of the hydroperoxides obtained in the singlet oxygenation of cholest-5-en-3α-ol (epicholesterol, **7**), 1,2,3,4,5,6,7,8-octahydronaphthalene (**10**), 2,3-dimethylbut-2-ene (**14**), cyclohexylidenecyclohexane (**21**), and cyclopentylidenecyclopentane (**33**).

Results and Discussion

As simple ethers and esters derived from cholesterol give rise to hydroperoxides that are more reactive[6] than the parent system (**1**), we felt that the configuration at position 3 might also be important. It might be expected that in the hydroperoxide **5** derived from epicholesterol, in which the groups at positions 3 and 5 are both α (axial), the rearrangement might occur more rapidly because of destabilising steric interactions. Indeed, molecular mechanics (MM2) calculations[8] (see later) support this view. Figure 1 depicts the MM2 calculated structure of 8aα-hydroperoxy-7α-hydroxy-3,4,4a,5,6,7,8,8a-octahydronaphthalene (**6**), an analogue of the epicholesterol 5α-hydroperoxide (**5**), and the 1,3-diaxial disposition of groups is clearly displayed.



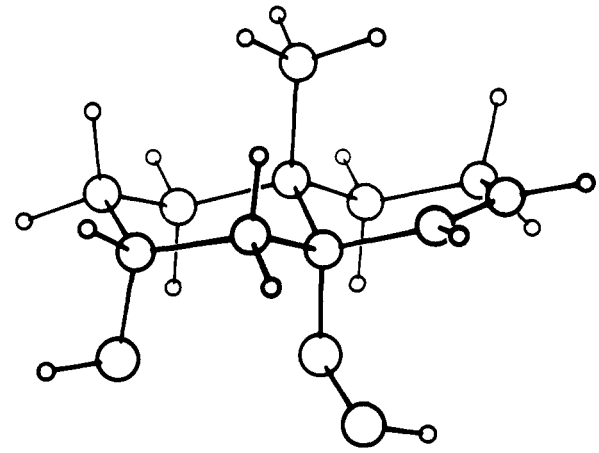
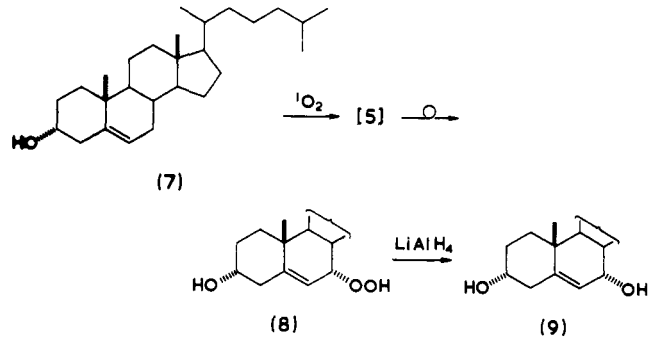


Figure 1. *Structure of the hydroperoxide* **6** *as calculated by MM2.*

Scheme III



Epicholesterol[9] (**7**) in pyridine containing Rose Bengal was stirred under oxygen and irradiated by a sodium lamp for 3 h. To our surprise, the ^1H NMR spectrum showed the absence of the expected 5α-hydroperoxide **5** and the formation of only the 7α-hydroperoxide **8**. This was confirmed by reduction of **8** to the corresponding diol **9** with lithium aluminum hydride (Scheme III).

The diol **9** has been reported as a minor product in the oxidation of cholesterol with soybean lipoxygenase[10] but was characterized only by TLC and by the mass spectrum of the corresponding bis(trimethylsilyl ether).

High resolution (400 MHz) ^1H NMR spectroscopy of **9** shows that the proton at position 7 (δ 4.12) is coupled to the single olefin proton at position 6 (δ 5.70) and to the proton at position 8. Decoupling of the olefin proton indicates ^3J (H7–H8) is 4.2 Hz, confirming that H-7 is equatorial, and therefore that the hydroxyl and hydroperoxyl groups in structures **9** and **8** are axial.

If it is accepted that the singlet oxygenation of **7** proceeds to give the 5α-hydroperoxide **5**, as it does with all other derivatives of cholesterol that have been investigated, then rearrangement to **8** proceeds very rapidly. Isolation of **8** establishes that the rearrangement of **5**, like that of **1**–**4**, occurs suprafacially.

When the oxygenation was carried out in the presence of 2,6-di-*tert*-butyl-4-methylphenol or galvinoxyl (ca. 10 mol %), known radical inhibitors that should inhibit any possible radical chain reaction of **7** with triplet oxygen, or of the rearrangement of **5** to **8**, again only the 7α-hydroperoxide **8** could be detected.

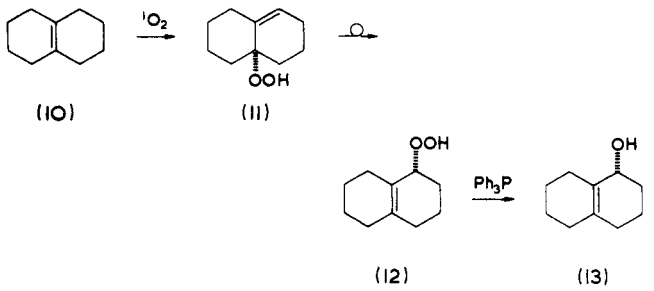
It is clear that epicholesterol 5α-hydroxyperoxide (**5**) rearranges extremely rapidly, faster than any other cho-

(8) (a) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127. Burkert, U.; Allinger, N. L. *Molecular Mechanics*, ACS Monograph Series; American Chemical Society: Washington, DC, 1982.

(9) Corey, E. J.; Nicolaou, K. C.; Shibasaki, M.; Machida, Y.; Shiner, C. S. *Tetrahedron Lett.* **1975**, 3183.

(10) Aringer, L.; Nordström, L. *Biomed. Mass Spectrom.* **1981**, *8*, 183.

Scheme IV



lesterol derivative studied to date. Rapid rearrangement of **5** is consistent with the MM2 calculations (see later) on the relative stabilities of the reactant and product peroxyl radicals, but this factor does not necessarily affect the overall rate of reaction.

The elementary reactions in the rearrangement of a tertiary hydroperoxide to a secondary or primary hydroperoxide are

$$\mathrm{ROOH} \xrightarrow{R_i} \mathrm{ROO^\bullet} \quad (1)$$

$$\mathrm{ROO^\bullet} \xrightarrow{k_r} \mathrm{R'OO^\bullet} \quad (2)$$

$$\mathrm{R'OO^\bullet + ROOH} \xrightarrow{k_p} \mathrm{R'OOH + ROO^\bullet} \quad (3)$$

$$2\mathrm{R'OO^\bullet} \xrightarrow{2k_t} \text{products} \quad (4)$$

where ROOH and R'OOH represent initial and rearranged hydroperoxides respectively, R_i is the rate of initiation, and k_p and k_t are the rate constants for chain propagation and termination, respectively.[6]

As the termination rate constants for alkylperoxyl radicals are normally in the sequence primary > secondary ≫ tertiary, termination will predominantly be between R'OO• radicals as indicated. This leads to the kinetic expression

$$-\mathrm{d[ROOH]}/\mathrm{d}t = k_p[\mathrm{ROOH}](R_i/2k_t)^{1/2} \quad (5)$$

which has been shown to be obeyed in the rearrangement of cholesterol 5α-hydroperoxide (**1**).[6] The overall rate of the reaction is thus a complex function of the rates of initiation, termination, and propagation steps, and the rate constant, k_r, of the elementary reaction ROO• → R'OO• is not necessarily involved.

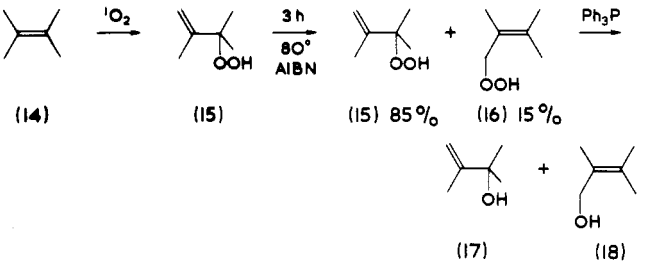
If under other structural conditions, termination occurred by self-reaction of the initial peroxyl radicals ROO• with the rate constant k_t, the overall rate would become dependent on the rearrangement rate constant k_r by eq 6.

$$-\mathrm{d[ROOH]}/\mathrm{d}t = k_r(R_i/2k_t)^{1/2} \quad (6)$$

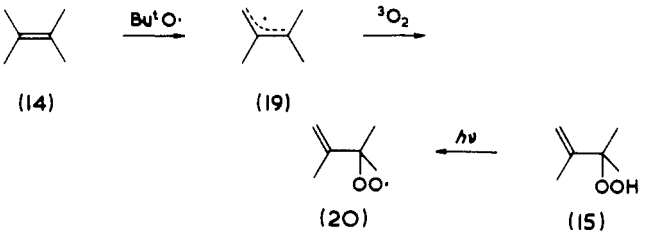
We next turned our attention to another cyclic system, the hydroperoxide derived from Δ^9-octalin (**10**), 4a-hydroperoxy-1,2,3,4,4a,5,6,7-octahydronaphthalene (**11**). This system, while being similar to the cholesterol-based hydroperoxides, differs in that rearrangement is expected to occur in a ring that is more conformationally mobile than those based on cholesterol.

Δ^9-Octalin (**10**) was caused to react with singlet oxygen in the usual fashion.[11] The hydroperoxide **11** was unchanged after 72 h in deuteriochloroform at room temperature, but in carbon tetrachloride at 40 °C, 80% of the rearranged 1-hydroperoxy-1,2,3,4,5,6,7,8-octahydronaphthalene (**12**) was obtained after 141 h. The hydroperoxide **12** was characterized by reduction to the known alcohol **13**[12] (Scheme IV).

Scheme V



Scheme VI



This rearrangement was accelerated by di-*tert*-butylperoxy oxalate and inhibited by 2,6-di-*tert*-butyl-4-methylphenol.

It is interesting that this rearrangement is somewhat slower than that for the hydroperoxides derived from valencene (**4**),[4] 9-methyl- or 9-ethyloctalin (**2**, **3**)[3] or cholesterol (**1**).[2-6]

Having demonstrated that two cyclic systems studied do rearrange, although at rather different rates, we chose to examine a situation in which rearrangement, if seen, would occur in an acyclic system. Tetramethylethylene (**14**) appeared to afford us this opportunity. Like the octalin hydroperoxide (**11**), the hydroperoxide derived from **14**, 2,3-dimethyl-2-hydroperoxybut-3-ene (**15**) has been reported by Schenck and co-workers,[11] although no mention of any rearrangement was made.

The hydroperoxide **15** was prepared by the method of Schenck.[11] It was unchanged when a solution in chloroform or carbon tetrachloride was kept for 48 h at room temperature in the absence or presence of di-*tert*-butylperoxy oxalate. Similarly no change was observed at 40 °C, but in deuteriochloroform at 80 °C with AIBN (azobis(isobutyronitrile)) as initiator, the ^{1}H NMR spectrum showed 15% conversion to the primary hydroperoxide **16**. This was confirmed by reduction of the mixture of **15** and **16** to the known alcohols **17**[11] and **18**[13] (Scheme V). Similar results were obtained when a solution of **15** was kept for 9 h at 80 °C in the absence of AIBN. Prolonged heating resulted in decomposition.

When di-*tert*-butyl peroxide was photolyzed in the presence of the alkene **14**, the ESR spectrum of the allylic radical **19** could be observed, a(3 H) 16.0, a(3 H) 12.8, a(3 H) 3.0, a(2 H) 12.7 G, g 2.0026, in agreement with previous reports.[14] Admission of oxygen into the ESR tube caused this spectrum to be replaced by a strong singlet associated with the peroxyl radical **20**, ΔH_{pp} 3.0 G, g 2.0151. No signal

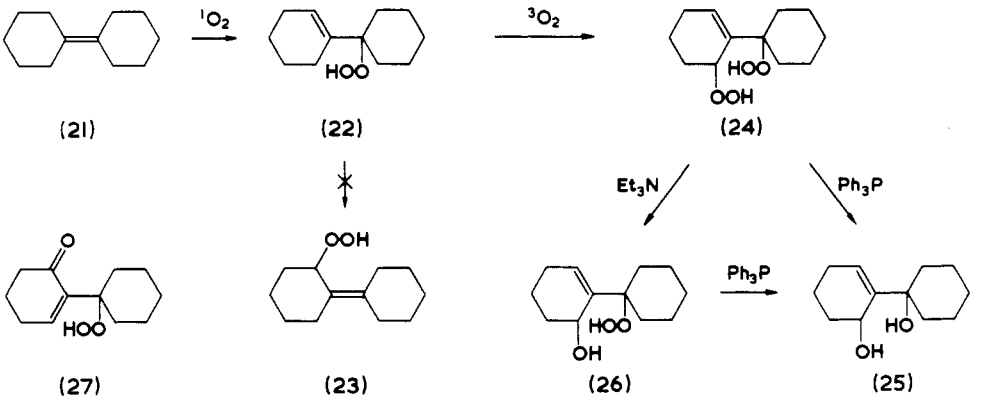
(11) Schenck, G. O.; Schulte-Elte, K.-H. *Justus Liebigs Ann. Chem.* **1958**, *618*, 185.

(12) Burgstahler, A. W.; Nordin, I. C. *J. Am. Chem. Soc.* **1961**, *83*, 198.

(13) Okada, K.; Kiyooka, F.; Nakanishi, E.; Hirano, M.; Ohno, I.; Matsuo, N.; Matsui, M. *Agric. Biol. Chem.* **1980**, *44*, 2595.

(14) Linder, R. E.; Winters, D. L.; Campbell Ling, A. *Can. J. Chem.* **1976**, *54*, 1405.

Scheme VII



that might be ascribed to the primary alkylperoxyl radical corresponding to **16**, with an expected hyperfine coupling of a(2 H) of about 4 G, could be detected. The same peroxyl radical (**20**) was observed when the hydroperoxide **15** was photolyzed in deuteriochloroform at −50 °C (Scheme VI).

It is interesting to note that tetramethylethylene (**14**) reacts with triplet oxygen to give principally the tertiary hydroperoxide **15**.[15] Our detection of only the tertiary peroxyl radical **20** in the ESR experiment is in agreement with this. Mayo has reported that reduction of the autoxidation mixture obtained from **14** gave the alcohols **17** and **18** in the ratio 18:1.

Our observation that the hydroperoxide **15** rearranges to the extent of only 15% at 80 °C is therefore consistent with the general observation that singlet oxygenation products tend to rearrange to the triplet oxygenation products.

We find that rearrangement of **15** to **16** occurs much less readily than that for the cyclic hydroperoxides studied. Part of the reason for this may be that the rearrangement of **15** gives a primary hydroperoxide, in which the termination rate constant k_t (eq 4), will be large, reducing the overall rate of rearrangement as expressed in eq 5.

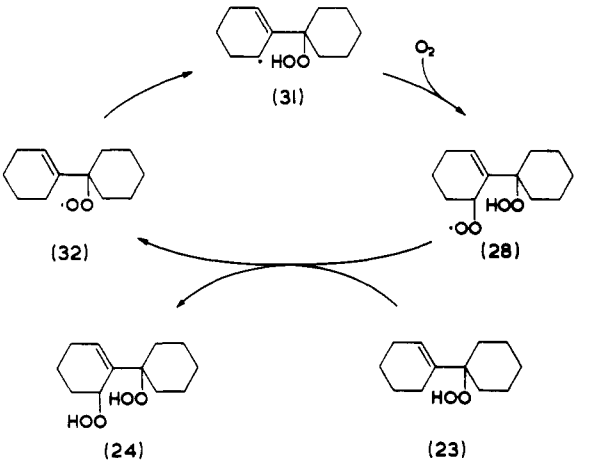
Hoping to alleviate any problems associated with chain termination, we decided to investigate the chemistry of the hydroperoxide derived from cyclohexylidenecyclohexane (**21**), in which rearrangement is expected to give a secondary allylperoxyl radical, with slower termination rate constant, k_t.

1-(Cyclohex-1-enyl)cyclohexyl hydroperoxide (**22**) was prepared by singlet oxygenation of cyclohexylidenecyclohexane (**21**).[11] No rearrangement to the isomeric hydroperoxide **23** could be detected (NMR) when **22** was kept in deuteriochloroform for 2 months at room temperature or 97 h at 40 °C, either with or without TBHN (*t*-butyl hyponitrite) as initiator in the absence of oxygen. During 3 h at 80 °C, the hydroperoxide **22** appeared to decompose.

^{1}H NMR spectroscopy showed that under air or oxygen, **22** in chloroform was converted into a dihydroperoxide with the probable structure **24**. This was confirmed by a single-crystal X-ray diffraction study of the diol[16] **25** derived by the reduction of **24** (Scheme VII).

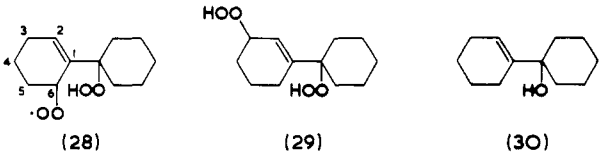
In an attempt to prepare the hydroperoxy ketone **27** by a carbonyl-forming elimination, the dihydroperoxide **24** was treated with triethylamine. To our surprise, a new compound, with a very similar ^{1}H NMR spectrum to that of the dihydroperoxide **24** was obtained. The hydroperoxyl

Scheme VIII



protons of **24** (δ 8.98, 9.12) were absent. The olefinic signal (δ 6.05, dd, J_a = 2.9 Hz, J_b = 4.7 Hz) had shifted (δ 5.88, dd, J_a = 2.8 Hz, J_b = 4.8 Hz), but not to that of the diol **25** (δ 5.83, dd, J_a = 3.2 Hz, J_b = 4.8 Hz). A similar shift was observed for the methine proton (δ 4.70 in **24** shifted to 4.55; similar proton at 4.47 in **25**). These observations, together with the fact that reduction of this compound with triphenylphosphine gave the same diol **25** as obtained by reduction the dihydroperoxide **24**, implies that **24** is reduced to the hydroxy hydroperoxide **26** by the action of triethylamine. We are not aware of any other examples in which triethylamine reduces an alkyl hydroperoxide.

Clearly hydroperoxide **22** is involved in an autoxidation process in which the peroxyl radical **28** must be one of the chain carriers, but the usual two-step propagation sequence appears to be unable to account for the regioselectivity and the reactivity. On both electronic and steric grounds the peroxyl radical **28** would be expected to react with **22** at the 3-position rather than the 6-position, to give the dihydroperoxide **29** rather than **24**.[17] Further, this hydrogen abstraction should occur as readily with the alcohol **30** as with the hydroperoxide **22**, yet when **30** was added to the autoxidizing hydroperoxide, **30** was recovered unchanged.



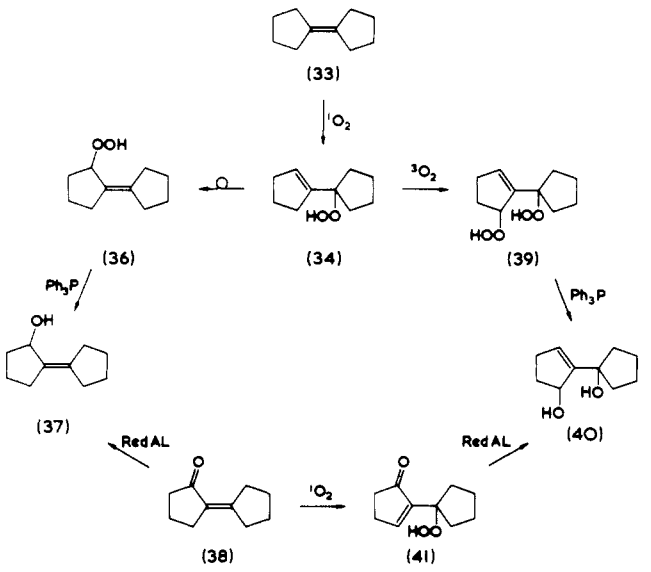
To account for this special regioselectivity and reactivity in the autoxidation of the hydroperoxide **22**, we propose

(15) Van Sickle, D. E.; Mayo, F. R.; Arluck, R. M.; Syz, M. G. *J. Am. Chem. Soc.* **1967**, *89*, 967.

(16) Davies, A. G.; Povey, D. C.; Schiesser, C. H.; Smith, G. W. Manuscript in preparation.

(17) Bateman, L. C. *Q. Rev. Chem. Soc.* **1954**, *8*, 147.

Scheme IX



that the reaction involves the novel three-step propagation cycle depicted in Scheme VIII, rather than the usual two-step propagation cycle.

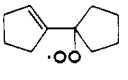
The allylperoxyl radical **28** reacts with the hydroperoxide **22** by abstraction not of allylic hydrogen but of hydroperoxyl hydrogen to give the new peroxyl radical **32**, which intramolecularly transfers allylic hydrogen to give the allylic radical **31**.

The overall reaction is rapid, as peroxyl radicals abstract hydrogen about 100 times more rapidly from a hydroperoxyl than an allylic methylene group,[18] the tertiary peroxyl radical **32** will terminate the chain less readily than the secondary peroxyl radical **28**,[18] and the intramolecular hydrogen transfer **32** → **31** is favored for steric and entropic reasons.

It is curious that **22** should become involved in a process other than rearrangement. As demonstrated, the peroxyl radical **32** is readily generated in an efficient chain. Rearrangement might not occur because the process is energetically disfavored in that the energy barrier might be large or the product thermodynamically disfavored over the starting material. The kinetics of the rearrangement might then be described by eq 6, in which k_r is small. Alternatively, the hydrogen-transfer process, occuring via a six-membered ring transition state might compete more efficiently with rearrangement, so much so as to be the only observed process.

If the hydrogen abstraction process is too efficient, then increasing the strain in the six-membered ring transition state should lead to a less efficient process and perhaps a return to rearrangement as the dominant process.

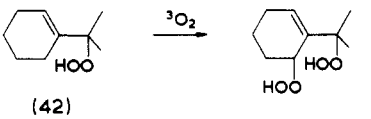
Accordingly, the hydroperoxide derived from cyclopentylidenecyclopentane (**33**), 1-(cyclopent-1-enyl)cyclopent-1-yl hydroperoxide (**34**) was prepared in the usual fashion. Inspection of models suggests that the corresponding peroxyl radical **35** is less able to abstract allylic hydrogen intramolecularly than in the six-membered ring analogue **32**.



(35)

(18) Landolt Börnstein, *Numerical Data and Fundamental Relationships in Science and Technology*; Springer Verlag: W. Berlin, 1984; Vol. 13, Part d.

Scheme X



(42)

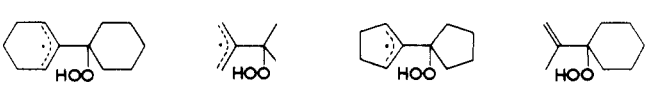
When the hydroperoxide **34** in deuteriochloroform in the absence of air was kept at 0 °C for 72 h, 18% rearrangement to (2-hydroperoxycyclopentylidene)cyclopentane (**36**) was observed by ^1H NMR spectroscopy. When the reaction was repeated at room temperature, the conversion was 25% complete after 30 h and 40% complete after 192 h. After 10 days, substantial decomposition was apparent. When the rearranged hydroperoxide **36** was treated with triphenylphosphine, the corresponding alcohol **37**, prepared independently by the reduction of 2-cyclopentylidenecyclopentanone (**38**),[19] was obtained (Scheme IX).

In the presence of air, however, the hydroperoxide **34** gave after 48 h at room temperature, the rearranged hydroperoxide **36** (27%) and some dihydroperoxide **39** (6%). The formation of **39** presumably occurs via a similar autoxidation process to that of the six-membered ring analogue **22** as depicted in Scheme VIII. When this mixture was reduced with triphenylphosphine, the diol **40** was observed in the ^1H NMR spectrum and confirmed by its independent preparation. Singlet oxygenation of the ketone **38** gave the hydroperoxy ketone **41**,[20] which, upon reduction with Red-AL (Aldrich) gave the diol **40**.

The observation that the hydroperoxide **34** rearranges, unlike its six-membered ring analogue **22**, can be accounted for in terms of a less facile intramolecular abstraction of allylic hydrogen, which becomes less competitive with the rearrangement process.

It is interesting that 1-(1-hydroperoxy-1-methylethyl)-cyclohexene (**42**) also appears to undergo exclusive and facile autoxidation to give the analogous dihydroperoxide (Scheme X),[21] supporting the view that hydrogen abstraction occurs more readily in the (cyclohexenylmethyl)peroxyl systems.

It is also interesting to note that 2,3-dimethyl-2-hydroperoxybut-3-ene (**15**), which also has intramolecularly accessible allylic hydrogen, does not become involved in any autoxidation process. Even at 80 °C in the presence of oxygen, **15** prefers (slowly) to rearrange. We believe that part of the reason for this is entropic (loss of the methyl rotor in the formation of the allylic radical **43**), part that **43** is a di-primary allylic radical while its analogues **31** and **44** are the more favorable di-secondary allylic radicals, and part that chain termination of the primary hydroperoxyl radical that is produced will be more rapid, as previously discussed. It is consistent with this that 1-(prop-1-en-2-yl)-1-hydroperoxycyclohexane (**45**) also fails to undergo autoxidation.[21]



(31) (43) (44) (45)

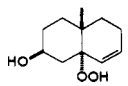
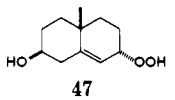
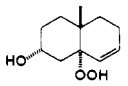
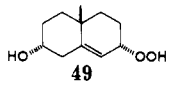
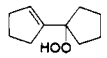
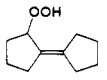
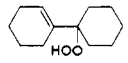
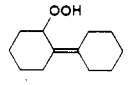
To supplement our understanding of these processes, we calculated the relative energies of the various reactant and product hydroperoxides by the molecular mechanics (MM2) method. Table I lists the optimized lowest steric

(19) Mitsui, S.; Senda, Y.; Saito, H. *Bull. Chem. Soc., Jpn.* **1966**, *39*, 694.

(20) Ensley, H. E.; Carr, R. V. C.; Martin, R. S.; Pierce, T. E. *J. Am. Chem. Soc.* **1980**, *102*, 2836.

(21) Davies, A. G.; Schiesser, C. H.; Williams, C. Unpublished work.

Table I. MM2 Steric Energies (kcal mol^{-1}) of Allylically Isomeric Hydroperoxides

ROOH	E_s	R'OOH	E_s	E_s
 **46**	18.9	 **47**	16.1	−2.8
 **6**	2.07	 **49**	17.1	−3.6
 **11**	12.4	 **12**	9.3	−3.1
 **15**	5.3	 **16**	5.2	−0.1
 **34**	20.4	 **36**	21.8	+1.4
 **22**	17.6	 **23**	21.4	+3.8

energies of a number of low energy conformers. For simplicity, the cholesterol derivatives (**1** and **5**) were modeled by their octalin analogues (**46** and **6**).

Table I shows that for all the hydroperoxides except **22** and **34**, the rearrangement is expected to be exothermic. Thus the cholesterol hydroperoxide analogue **46** is predicted to rearrange exothermically by 2.8 kcal mol^{-1}. The rearrangement of the epicholesterol hydroperoxide analogue (**6**) is predicted to be some 0.8 kcal mol^{-1} more exothermic than that of **46**, mainly because of unfavorable 1,3-diaxial interactions in **47** that do not occur in **46**. Similarly, the rearrangement of the octalin hydroperoxide (**11**) is predicted to exothermic by 3.1 kcal mol^{-1}. It is not surprising then that rearrangements are observed for **1**, **5**, and **11**.

The rearrangement of the hydroperoxide derived from tetramethylethylene (**15**) is predicted to be essentially thermoneutral, and an equilibrium between **15** and its isomer **16** might be expected to be established. We could not test this hypothesis because the hydroperoxide **15** decomposed when it was kept for a prolonged period at 80 °C, the rearranged hydroperoxide **16** could not be separated from **15** by chromatography nor could an authentic sample of **16** be prepared by other means.[22] Other acyclic allylic hydroperoxides have been established to rearrange to an equilibrium mixture.[2]

The rearrangement of the hydroperoxide **22** derived from cyclohexylidenecyclohexane is predicted to be endothermic by 3.8 kcal mol^{-1}. This reinforces our suggestion (see above) that the slowness of this step may preclude the rearrangement.

However the rearrangement of the hydroperoxide **34**, derived from cyclopentylidenecyclopentane, is also predicted to be endothermic by 1.4 kcal mol^{-1}, although the reaction to give **36** is observed to occur readily. Apart from the fact that this value borders on the limit of the accuracy of the MM2 calculation, we cannot offer an excuse for this inconsistency.

(22) Silver-assisted displacement of bromide by hydrogen peroxide on 1-bromo-2,3-dimethylbut-2-ene, which is reported to proceed by inversion of configuration, gave only **15**. See: Cookson, P. G.; Davies, A. G.; Roberts, B. P. *J. Chem. Soc., Chem. Commun.* **1976**, 1022. Sotowicz, A. Ph.D. Thesis, University of London (1982).

Conclusion

The overall rate of the rearrangement is a consequence of the interplay of various elementary reactions, the relative importance of which is strongly dependent on the molecular structure. This leads to the following generalizations.

(i) The relative overall rates of rearrangement of the systems in this study are **5** > **4** > **2** > **3** ~**1**, ~**34** > **11** > **15** > **22**.

(ii) Rearrangements that occur within a six-membered ring, such as the reactions of **1**–**5** and **11**, generally occur readily. This is presumably due to favorable geometric constraints in the initial hydroperoxide, as well as favorable termination rate constants associated with secondary peroxyl radicals.

(iii) If rearrangement is unfavorable, intramolecular abstraction of hydrogen may occur, leading to dihydroperoxide products. The rates of these reactions are sensitive to geometric constraints in six-membered cyclic transition states.

(iv) If the products of either rearrangement or autoxidation are primary allyperoxyl radicals, these processes are slow, presumably because these radicals take part in rapid chain termination.

Experimental Section

7α-Hydroperoxycholest-5-en-3α-ol (8). A solution of cholest-5-en-3α-ol[9] (**7**) (300 mg, 780 μmol) and Rose Bengal (ca. 5 mg) in pyridine (7 mL) was stirred under an atmosphere of oxygen, with cooling, while being irradiated with a 400-W sodium lamp at a distance of 5 cm. After 3 h the solvent was removed in vacuo and the residue chromatographed on silica, using 3:1 dichloromethane/ether as eluent, to give **8** as a fine white powder (150 mg, 46%): mp 120–120.5 °C; ^{1}H NMR ($CDCl_3$) δ 0.69 (s, 3 H), 0.87 (d, J = 6.7 Hz, 6 H), 0.90 (d, J = 7.6 Hz, 3 H), 1.12 (s, 3 H), 0.8–2.1 (m, 27 H), 4.19–4.22 (m, 1 H), 4.35 (dd, J = 2.3 Hz, 3.8 Hz, 1 H), 5.82 (dd, J = 1.1 Hz, 4.7 Hz, 1 H), 7.46 (s(br), 1 H). Similar results were obtained when the reaction was carried out in the presence of 2,6-di-*tert*-butyl-4-methylphenol or galvinoxyl (ca. 10 mol %).

Cholest-5-ene-3α,7α-diol (9). Lithium aluminum hydride (10 mg, 260 μmol) was added to a solution of **8** (18 mg, 43 μmol) in ether (2 mL) and the suspension stirred for 30 min. Ether (5 mL) and 10% hydrochloric acid (5 mL) were added, the layers were separated, and the aqueous layer was extracted with ether. The combined ether solutions were dried and the solvent was removed in vacuo to give the diol **9** as a white solid (10 mg, 52%): ^{1}H NMR ($CDCl_3$) δ 0.71 (s, 3 H), 0.88 (d, J = 6.7 Hz, 6 H), 0.91 (d, J = 7.6 Hz, 3 H), 1.16 (s, 3 H), 0.8–2.0 (m, 28 H), 4.12 (ddd, J = 4.7 Hz, 4.2 Hz, 1.9 Hz, 1 H), 4.23 (t, J = 3.1 Hz, 1 H), 5.70 (dd, J = 1.0 Hz, 4.7 Hz, 1 H); MS (18 eV) (rel intensity) 402 (12, $M^{\bullet+}$), 384 (100), 369 (66), 331 (30), 247 (19), 135 (30). $C_{27}H_{46}O_2$ requires: $M^{\bullet+}$ = 402.3498; Found: $M^{\bullet+}$ = 402.3491.

4α-Hydroperoxy-1,2,3,4,4a,5,6,7-octahydronaphthalene (11). The title compound was prepared by the method of Schenck:[11] mp 58–58.5 °C (lit.[11] mp 60 °C); ^{1}H NMR ($CDCl_3$) δ 1.11–2.38 (m, 14 H), 5.70 (m, 1 H).

Rearrangement of 11. A solution of **11** (44 mg, 260 μmol) in carbon tetrachloride (10 mL) was kept at 40 °C for 141 h, after which NMR spectroscopy indicated the presence of 80% of 1-hydroperoxy-1,2,3,4,5,6,7,8-octahydronaphthalene (**12**) in the mixture: ^{1}H NMR (CCl_4) δ 1.2–2.3 (m, 14 H), 4.23 (m, 1 H).

Triphenylphosphine (68 mg, 260 μmol) was added. After 5 min, the solvent was removed in vacuo and the residue subjected to preparative TLC, using 2:1 pentane/ether as eluent, to give 1-hydroxy-1,2,3,4,5,6,7,8-octahydronaphthalene (**13**) (12 mg, 42%) identical with an authentic sample:[12] ^{1}H NMR ($CDCl_3$) δ 1.11–2.35 (m, 14 H), 3.92 (m, 1 H).

2,3-Dimethyl-2-hydroperoxybut-3-ene (15). The title hydroperoxide was prepared by the method of Schenck:[11] ^{1}H NMR ($CDCl_3$) δ 1.37 (s, 6 H), 1.82 (m, 3 H), 4.97 (m, 1 H), 5.01 (m, 1 H), 7.54 (s, 1 H).

Rearrangement of 15. A solution of **15** (10 mg, 90 μmol) and azobis(isobutyronitrile) (AIBN, 2 crystals) in deuteriochloroform (500 μL) was heated at 80 °C for 3 h. NMR spectroscopy revealed the presence of starting material (**15**, 85%) and 2,3-dimethyl-1-hydroperoxybut-2-ene (**16**, 15%): ^{1}H NMR ($CDCl_3$) δ 1.70–1.80 (m, 9 H), 4.54 (s, 2 H), 8.12 (s(br), 1 H).

Triphenylphosphine (30 mg, 110 μmol) was added and after 5 min NMR spectroscopy showed the presence of the previously prepared 2,3-dimethylbut-3-en-2-ol[11] (**17**, 85%), ^{1}H NMR ($CDCl_3$) δ 1.35 (s, 6 H), 1.81 (m, 3 H), 4.77 (m, 1 H), 5.00 (m, 1 H), and 2,3-dimethylbut-2-en-1-ol[13] (**18**, 15%), ^{1}H NMR ($CDCl_3$) δ 1.69 (s, 3 H), 1.75 (s, 6 H), 4.13 (s, 2 H). Similar results were observed after 9 h in the absence of AIBN.

1-(Cyclohex-1-en-1-yl)cyclohex-1-yl Hydroperoxide (22). The title hydroperoxide was prepared by the method of Schenck:[11] ^{1}H NMR ($CDCl_3$) δ 1.14–1.38 (m, 2 H), 1.40–1.74 (m, 10 H), 1.74–1.95 (m, 2 H), 1.95–2.16 (m, 4 H), 5.81 (m, 1 H), 7.03 (s, 1 H).

1-Hydroperoxy-6-(1-hydroperoxycyclohex-1-yl)cyclohex-5-ene (24). A solution of **22** (430 mg, 2.19 mmol) in chloroform (5 mL) was vigorously stirred under oxygen for 3 days. The solvent was removed and the residue separated by flash chromatography using 1:19 ether/dichloromethane as eluent to give **24** as a viscous colorless oil (160 mg, 32%): ^{1}H NMR ($CDCl_3$) δ 1.18–2.42 (m, 16 H), 4.70 (t, J = 3.2i Hz, 1 H), 6.05 (dd, J = 2.9 Hz, 4.7 Hz, 1 H), 8.98 (s, 1 H), 9.12 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 15.6, 21.3, 21.8, 25.6, 25.7, 25.9, 30.4, 35.0, 77.2, 84.8, 133.4, 136.9; IR (neat) 3519, 3359, 2932, 2850, 1344 cm^{-1}.

6-(1-Hydroxycyclohex-1-yl)cyclohex-5-en-1-ol (25). The dihydroperoxide **24** (20 mg, 90 μmol) and triphenylphosphine (55 mg, 210 μmol) in dichloromethane (ca. 0.5 mL) were stirred for 5 min. The solvent was removed, and the residue was separated by flash chromatography using 2:3 ether/dichloromethane as eluent and recrystallized from pentane/dichloromethane to give the diol **25** as slender prisms (17 mg, 96%), mp 88–89 °C. The structure of **25** was confirmed by X-ray crystallography:[16] ^{1}H NMR ($CDCl_3$) δ 1.2–2.2 (m, 16 H), 2.6 (s(br), 1 H), 3.0 (s(br), 1 H), 4.47 (dd, J = 3.1 Hz, 4.1 Hz, 1 H), 5.83 (dd, J = 3.2 Hz, 4.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 17.2, 22.2, 25.6, 25.7, 31.6, 36.8, 37.3, 64.1, 74.4, 125.2, 143.2. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.41; H, 10.12.

Reaction of 1-Hydroperoxy-6-(1-hydroperoxycyclohex-1-yl)cyclohex-1-ene with Triethylamine. The dihydroperoxide **24** (40 mg, 180 μmol) was dissolved in chloroform (ca. 1 mL) and triethylamine (76 μL, 550 μmol) added. After 3 h the solution was diluted with chloroform and washed with 10% hydrochloric acid and water. After drying, the solvent was removed and the residue separated by flash chromatography using 1:19 ether/dichloromethane to afford starting material **24** (25 mg) and a viscous oil assigned to be the hydroxy hydroperoxide **26** (12 mg, 31%): ^{1}H NMR ($CDCl_3$) δ 1.1–2.5 (m, 18 H), 4.55 (t, J = 2.9 Hz, 1 H), 5.88 (dd, J = 2.8 Hz, 4.7 Hz, 1 H). ^{13}C NMR ($CDCl_3$) δ 15.7, 21.4, 21.9, 25.5, 25.8, 30.4, 31.7, 35.4, 62.4, 84.8, 128.9, 141.9. **26** was reduced to the diol **25** with triphenylphosphine.

1-(Cyclopent-1-enyl)cyclopentyl Hydroperoxide (34). Cyclopentylidenecyclopentane[23] (**33**) (500 mg, 3.67 mmol) and Rose Bengal (ca. 10 mg) were photooxygenated in a 1:1 mixture of methanol and 2-propanol (ca. 7 mL) as described in the preparation of **8**. The solvent was removed in vacuo and the residue purified by chromatography on silica, using 1:19 pentane/dichloromethane as eluent, to give the hydroperoxide[24] **34** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.60–2.02 (m, 10 H), 2.37 (dt, J = 7.4 Hz, 2.0 Hz, 4 H), 5.07 (quin, J = 2.1 Hz, 1 H), 7.34 (s, 1 H).

2-Cyclopentylidenecyclopentanol (37). A solution of bis(2-methoxyethoxy)aluminum hydride in toluene (3.4 M, 2.0 mL, 6.8 mmol) was added dropwise to a solution of 2-cyclopentylidenecyclopentanone[19] (**38**) (1.0 g, 6.7 mmol) in tetrahydrofuran (5 mL) cooled to 0 °C. After shaking for 5 min, the mixture was poured into water and extracted with ether, the combined extracts were dried, and the solvent was removed to give the alcohol **37** (450 mg, 44%): mp 56–58 °C (lit.[19] mp 57–59 °C); ^{1}H NMR ($CDCl_3$) δ 1.58–1.90 (m, 9 H), 2.40–2.80 (m, 3 H), 4.52 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 23.2, 26.2, 27.0, 29.9, 30.5, 31.5, 31.6, 73.6, 135.0, 139.4.

5-(1-Hydroxycyclopent-1-yl)cyclopent-4-en-1-ol (40). 2-Cyclopentylidenecyclopentanone[19] (**38**) (300 mg, 2.0 mmol) was photooxygenated as described for **34**. The hydroperoxy ketone **41** was isolated by chromatography on silica, using 1:1 ether/light petroleum ether as eluent, to give a white solid: mp 102–104 °C; IR (Nujol) 3239, 1671, 1621 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.6–1.8 (m, 6 H), 2.10 (m, 2 H), 2.54 (m, 2 H), 2.61 (m, 2 H), 7.61 (t, J = 2.7 Hz, 1 H), 9.27 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 23.9, 26.3, 35.8, 35.9, 92.1, 147.9, 161.2, 209.7. Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.55; H, 7.86.

The hydroperoxy ketone **41** (100 mg, 550 μmol) was reduced with bis(2-methoxyethoxy)aluminum hydride (1.0 mL of 3.4 M solution in toluene) as described for **37**. The diol was isolated by chromatography on silica, using 2:1 ether/light petroleum ether as eluent, and recrystallized from pentane/dichloromethane to give a white solid (30 mg, 34%): mp 85–86.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.62–1.95 (m, 8 H), 2.23 (m, 2 H), 2.45 (m, 2 H), 2.95 (s(br), 2 H), 4.95 (s, 1 H), 5.71 (m, 1 H). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.42; H. 9.72.

Rearrangement of 34. A solution of **34** (10 mg, 60 μmol) in deuteriochloroform (500 μL) in an NMR tube was degassed under vacuum by successive freeze–thaw cycles and sealed under argon. The tube was kept at 0 °C for 72 h, when NMR analysis indicated 18% rearrangement to the isomeric hydroperoxide **36**: ^{1}H NMR ($CDCl_3$) δ 4.74 (m, 1 H), 7.81 (s, 1 H). When the experiment was repeated at room temperature, the conversion was 25% after 30 h and 40% after 192 h. When the experiment was carried out under air at room temperature, the ^{1}H NMR spectrum showed 27% conversion to **36** and 6% conversion to the dihydroperoxide **39**: ^{1}H NMR ($CDCl_3$) δ 5.10 (m, 1 H), 6.11 (q, J = 2.1 Hz, 1 H), 8.73 (s, 1 H), 9.33 (s, 1 H). When triphenylphosphine was added to the tube, the ^{1}H NMR spectrum showed the presence of **37** (27%) and **40** (6%) as previously prepared.

Acknowledgment. We acknowledge support by the SERC and the Ramsay Memorial Fellowships Trust.

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(24) Kopecky, K. R.; Lopez Sastre, S. J. A. *Can. J. Chem.* **1980**, *58*, 2089.