Allylic Hydroperoxides Formed by Singlet Oxygenation of Cholest-5-en-3-one

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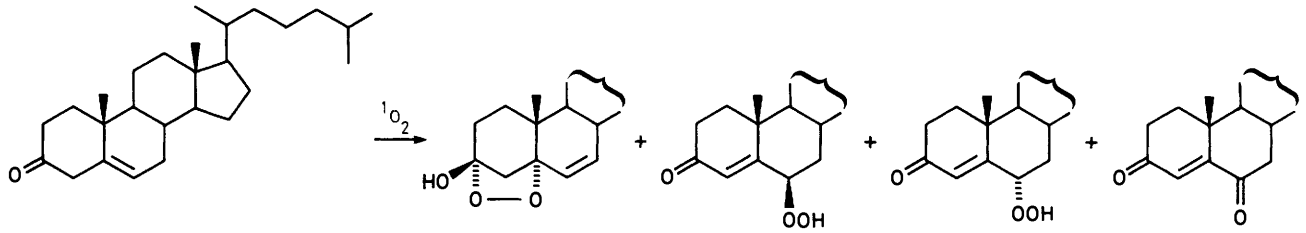
Cholest-5-en-3-one (**I**) reacts with singlet oxygen to give the hemiperketal (**II**) (*ca.* 55%), the epimeric 6β- and 6α-hydroperoxides (**III**) and (**IV**) (*ca.* 30 and 8% respectively), and the dione (**V**) (*ca.* 7%). The hemiperketal (**II**) does not undergo an allylic rearrangement in solution, but the hydroperoxides (**III**) and (**IV**) epimerise by a radical chain mechanism.



(I) (II) (III) (IV) (V)

Stereochemical problems connected with this system have been probed by carrying out parallel experiments and molecular mechanics calculations on the corresponding derivatives of methyloctahydronaphthalenone as model compounds.

Allyl compounds react with singlet oxygen with migration of the double bond, to give allyl hydroperoxides which can then undergo rearrangements and epimerisation reactions.[1] The example which has been studied most thoroughly is cholesterol (**1**) which gives the Δ^6-5α-hydroperoxide (**2**), which in a non-polar solvent rearranges to the Δ^5-7α-hydroperoxide (**3**) and then to the Δ^5-7β-hydroperoxide (**4**) (Scheme 1).[2]

Both rearrangements are well established to take place through the corresponding allylperoxyl radicals. The supra-facial rearrangement (**2**)→(**3**) does not involve exchange of the peroxidic oxygen with an atmosphere of $^{18}O_2$, whereas the epimerisation (**3**)→(**4**) does involve exchange,[3] and it has been suggested that the former reaction proceeds by a non-dissociative, probably pericyclic process,[3,4] and the latter involves a dissociative mechanism.[3,5]

We find that in *O*-derivatives of cholesterol the relative tendency of the 5α-hydroperoxides to undergo the allylic rearrangement is very dependent on the nature of the *O*-substituent.

Relatively little work has been carried out on the reaction of cholest-5-ene-3-one (**5**) with singlet oxygen, or indeed of any other βγ-unsaturated ketones.[1,6,7]

The 6β- and 6α-hydroperoxycholest-4-en-3-ones (**6**) and (**7**) have been identified as the major products of the autoxidation ($^3O_2$) of the ketone (**5**).[8–11] In Schenck's original work on the photo-oxygenation ($^1O_2$) of (**5**) he isolated the 6β-hydroperoxide (**6**) in 7.2% yield.[12] This has been misquoted in ref. 7 as being the 5α-hydroperoxide in 72% yield; as far as we can determine, no 5-oxygenated product has ever been identified. In later work, photo-oxygenation has been reported to give, after reduction, the 6β- and 6α-alcohols (**8**) and (**9**), the enedione (**10**), and the dienone (**11**).[9,12,13] It was suggested that (**6**) and (**7**), the precursors of (**8**) and (**9**), are formed through a competing free radical ($^3O_2$) pathway, and that (**11**) might be formed through an elimination reaction involving a 5-hydroperoxide.[9]

A few acyclic βγ-unsaturated ketones have been studied in a similar way,[1,13,14] but there appears to be no report of the hydroperoxides which are formed undergoing the equivalent of either the allylic rearrangement or the epimerization which is shown in Scheme 1. However, the rearrangement has recently been reported of the hydroperoxides (**12**) which are obtained from the reaction of singlet oxygen with αβ-unsaturated ketones (Scheme 2).[15]

We report here a study of the peroxides which are formed by the reaction of singlet oxygen with cholest-5-en-3-one, and their tendency to undergo allylic rearrangement and epimerisation. A parallel briefer study has been carried out on methyloctalenone as a model system.

Results and Discussion

Singlet photo-oxygenation of cholest-5-en-3-one (**5**) in methanol–dichloromethane or pyridine with Rose Bengal as a photosensitizer, and in the absence or presence of 2,6-di-t-butyl-4-methylphenol (DTBMP) as a radical trap gave the products shown in Scheme 3 and Table 1.

The peroxides (**13**) and (**6**) were reduced with triphenylphosphine to the corresponding hydroxycholestenones (**14**) and (**8**). To assist in determining the structures, the hydroperoxides (**6**) and (**7**) were also prepared by autoxidation ($^3O_2$) of cholestenone (**5**) by Cox's method.[10]

The structures of the products were identified by 400 MHz ^1H NMR, ^{13}C NMR, MS, and IR spectroscopy, as described below.

To provide simpler models, more amendable to calculation, the oxidation of the methyloctahydronaphthalenone (**15**) was studied in the same way, and the products which were identified are shown in Scheme 4. For consistency, in this section we have numbered the skeleton of the naphthalenone (**15**) in the same way as that of cholestenone (**5**). The correct systematic numbering is used in the Experimental section.

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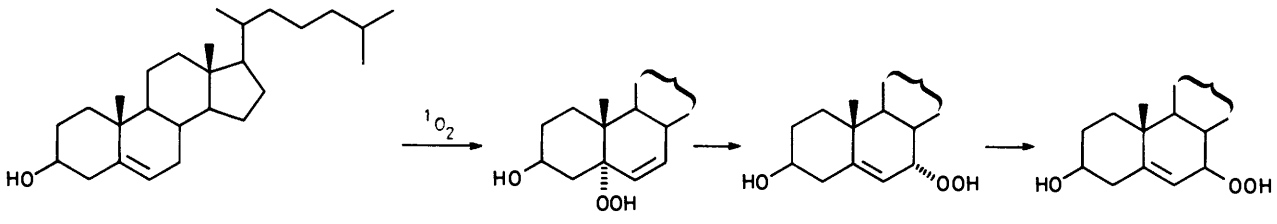
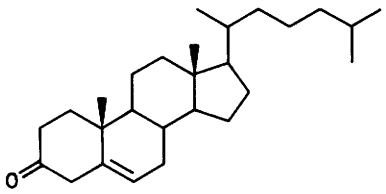
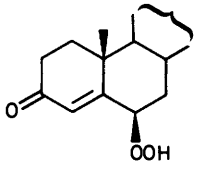


(1) (2) (3) (4)

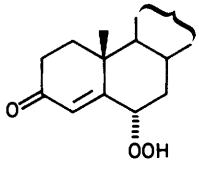
Scheme 1.



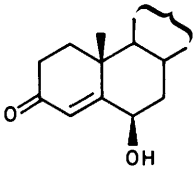
(5)



(6)



(7)



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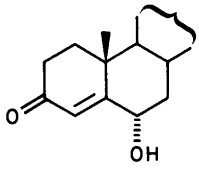

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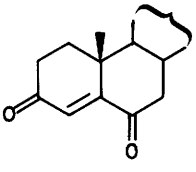

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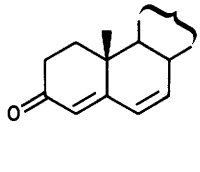
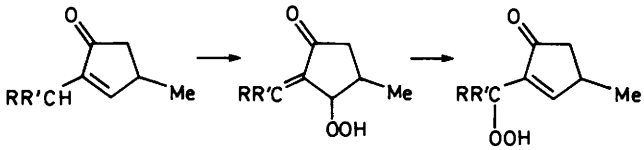


(11)

The distribution of products from (**15**) is very similar to that of the products from cholestenone (**5**) as shown in Table 1. This implies that the relative energies of the transition states and of the products in the two series of compounds are very similar, and that it is valid to base conclusions related to the compounds in Table 1 on calculations carried out on the simpler structures in Scheme 1.

The hemiperketal (**13**) which results from attack of singlet oxygen at the 5α-position, and which we find to be the principal product, has not been identified previously. The olefinic region of the ^{1}H NMR spectrum of (**13**), and of the alcohol (**14**) which is formed on reduction, showing in each the presence of two olefinic protons, is illustrated in Figure 1. The cyclic structure is



(12)

Scheme 2.

Table 1. Products from the singlet oxygenation of cholest-5-en-3-one (**5**).

	Product (%)			
Solvent	(**13**)	(**6**)	(**7**)	(**10**)
CH_2Cl_2–MeOH	52	29	9	5
Pyridine	57	17[a]	6	8
CH_2Cl_2–MeOH +13 mol % DTBMP	55	32	8	4
CH_2Cl_2–MeOH +25 mol % DTBMP	52	30	9	9

[a] Plus 11% of the corresponding 6β-alcohol (**8**).

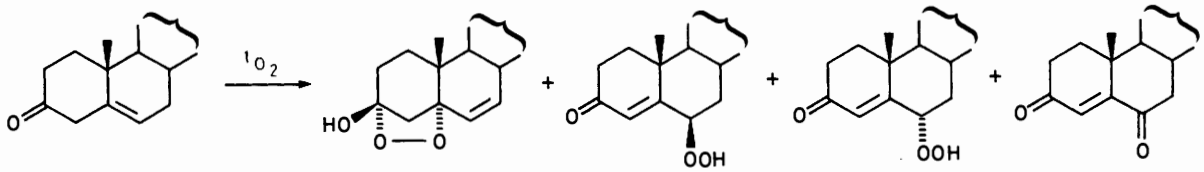
shown by, particularly, the absence of the carbonyl stretching frequency from the IR spectrum and the absence of the ^{13}C signal of the carbonyl group from the ^{13}C NMR spectrum. Similar evidence establishes the structures of the methyloctalinone analogue (**16**). Some other 3-hydroperoxy ketones have been reported to form similar hemiperketals,[7] but others (*e.g.* those shown in Scheme 2)[15] exist in the open form.

We felt it necessary to check the epimeric structures of (**6**), (**7**), (**8**), (**9**), (**17**), and (**18**) because the evidence on which the assignment of the structure of (**6**) and (**7**) is based is indirect[16] and it implies that singlet oxygen reacts at C-6 in (**5**) preferentially at the β-face which might be thought to be shielded by the 10β-methyl group.

Molecular mechanics (MM2) calculations were carried out on the alcohols (**20**) and (**21**) derived from the hydroperoxides (**17**) and (**18**).

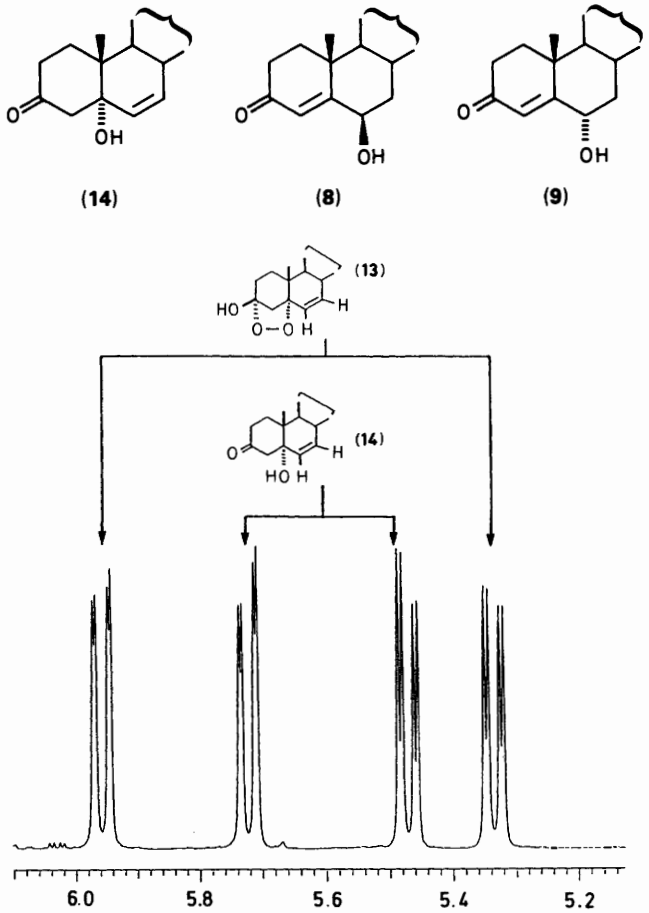
The energy-minimised structures which result are illustrated in Figure 2 and have strain energies of 15.45 and 14.81 kcal mol^{-1} respectively. The dihedral angles (φ) and the calculated ^3J coupling constants between the C*H*(OH) proton and the vicinal axial-equatorial pair of methylene protons are φ_{ea} 63°, $^3J_{ea}$ 3.4 Hz, φ_{ee} 53°, $^3J_{ee}$ 2.7 Hz in (**20**) and φ_{aa} 173°, $^3J_{aa}$ 11.2 Hz, φ_{ae} 55°, $^3J_{ae}$ 4.7 Hz in (**21**).

These calculated values of ^3J are to be compared with the measured values for the hydroperoxides (**6**) and (**7**), and (**17**) and (**18**), and for the alcohol (**8**) from (**6**), which are given in Table 2. The relevant regions of the ^{1}H NMR spectra of (**6**) and (**7**) are illustrated in Figure 3. The replacement of an OH group by an OOH group would not be expected to affect the conformation of the rings. It will be seen that there is a very good correspondence between calculated and observed coupling constants. We conclude from this that the alcohols (**20**) and (**21**) do indeed serve as good stereochemical models for the hydroperoxides (**17**) and (**18**), and (**6**) and (**7**), and that the



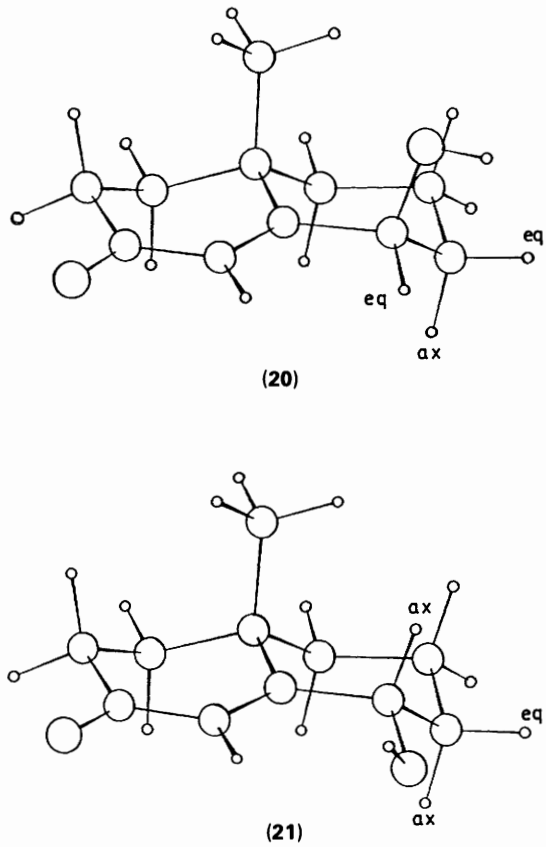
(5) (13) (6) (7) (10)

Scheme 3.



(14) (8) (9)

Figure 1. Olefinic region of the 400 MHz, ^1H NMR spectrum of the peroxide (13) and the corresponding alcohol (14).



(20) (21)

Figure 2. Calculated molecular configurations for the alcohols (20) and (21).

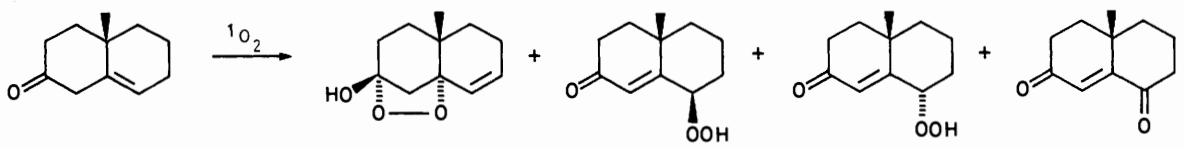
assignment of the α and β configuration to these hydroperoxides and to their corresponding alcohols is correct as shown.

The most notable points about the data in Table 1 are first that the principal product (13) (> 50%) which we detect, which results from attack of singlet oxygen at the 5α-position, has not been detected previously; second, that attack at the 7 position occurs principally at the β rather than the α face, despite steric shielding by the 10β-methyl group; and, third, that the presence of di-t-butylmethylphenol has no significant effect on the rate or the products of the reaction.

In previous work,[9] it seems likely that the 5α-hydroperoxide suffered elimination of hydrogen peroxide to give the 4,6-dien-3-one (11) which we do not detect.

The distribution of products observed in the reaction of the enones (5) and (15) with singlet oxygen can be rationalised by considering the various conformations available to (15). Figure 4 shown in (22) and (23) and two most stable conformers of (15), and their relative strain energies as calculated by the MM2 method.

If it is assumed that singlet oxygenation occurs *via* a 6-membered ene-type concerted transition state, and an appropriate transition state geometry is employed,[17] it is clear



58 % 30 % 6 % 6 %

(15) (16) (17) (18) (19)

Scheme 4.

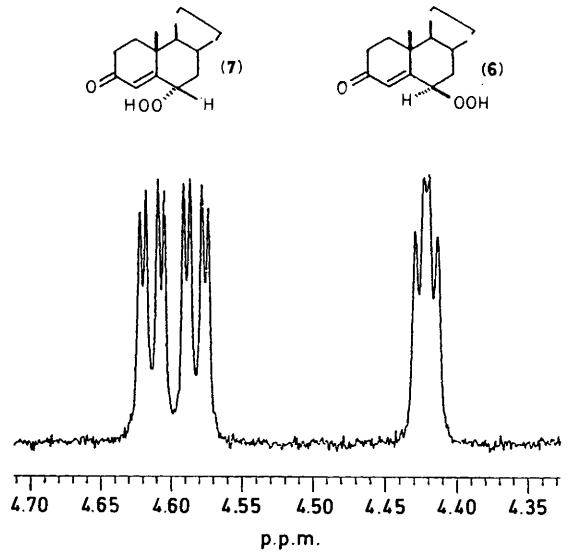


Figure 3. 6-H Region of the NMR spectrum of a 2:1 mixture of the epimeric hydroperoxides (**6**) and (**7**).

that attack at position 5 in (**22**) from the α-face will proceed through a transition state as represented in (**24**) to give the hydroperoxide which cyclises to the hemiperketal (**16**). It is not surprising that this should be the major product, as the β-face is sterically shielded by the methyl substituent, and because the β-hydrogen at position 6 is equatorial and inaccessible to the concerted mechanism.

Attack at position 6 in (**22**) on the β-face, is depicted in (**25**). This will be disfavoured by the proximity of the methyl substituent, but this will be offset somewhat by the developing stabilising conjugation between the O=C and C=C groups in the product. Even less favourable will be attack at the α-face of position 4, because as shown in (**26**), this must occur *via* the less stable conformer (**23**), as (**22**) lacks the necessary axial α-hydrogen at the 4-position.

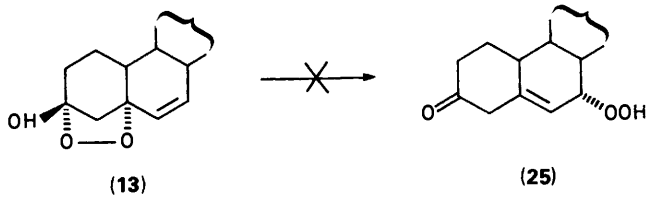
Similar conclusions are reached if one assumes a perepoxide intermediate[17] rather than the concerted mechanism.

The fact that the phenol has no effect on the reaction establishes that the process involves the non-radical reaction of singlet oxygen, rather than the homolytic chain reaction which has sometimes been invoked previously.[9]

We then examined the peroxides (**13**), (**6**), and (**7**) derived from cholestenone (**5**) for the equivalents of the allylic rearrangement and epimerization reactions which are familiar with the hydroperoxides derived from cholesterol (Scheme 1).[2,3]

The hemiperketal (**13**), which might be expected to behave as the masked 5α-hydroperoxide, showed no tendency to rearrange to the 7α-hydroperoxide (**25**) (Scheme 5).

This may be because the hemiperketal itself cannot sustain the necessary chain process, or because there is insufficient of the hydroperoxyketone in equilibrium with the perketal, or because the 5α-hydroperoxide itself is intrinsically immobile. As the mobilities of the various derivatives of cholesterol[3,18] are not properly understood, further speculation seems unjustified.



(**13**) (**25**)

Scheme 5.

Table 2. Observed values of ^3J.

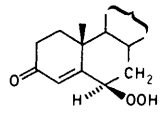
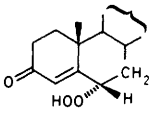
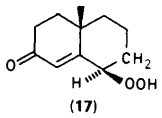
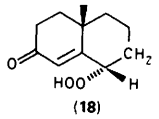
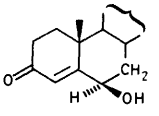
Compound		^3J/Hz
 (**6**)	ea	4.09
	ee	2.28
 (**7**)	aa	12.44
	ae	5.30
 (**17**)	ea	3.36
	ee	2.68
 (**18**)	aa	12.35
	ae	5.33
 (**8**)	ea	4.10
	ee	2.28

Table 3. Epimerization of compound (**6**) in $CDCl_3$ at room temperature.

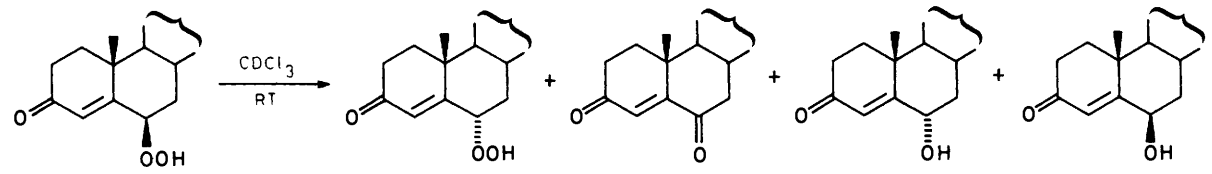
	Composition of mixture (%)				
Time (h)	(**6**)	(**7**)	(**10**)	(**9**)	(**8**)
24	85	11	3.5	—	—
72	68	26	6	—	—
96	57	34	9	—	—
126	43	39	9.3	2.5	2
195	35	36	17	4	5
291	21	30	28	12	8
400	6	13	38	26	16
450	4	10	42	27	16

On the other hand, the 6α- and 6β-hydroperoxides (**6**) and (**7**) and the corresponding hydroperoxides (**17**) and (**18**) undergo slow epimerization with some concomitant decomposition. This process can readily be distinguished in the ^1H NMR spectra as shown in Figure 3. The results of a typical experiment are shown in Table 3.

Cox[10] did not detect this epimerisation when the 6β-hydroperoxide (**6**) was recrystallised from ether at different rates over a 3-week period.

The 6β-alcohol (**8**) was identical with the product obtained by reducing the 6β-hydroperoxide (**6**) with triphenylphosphine, and the 6α-alcohol (**9**) showed the same NMR spectrum as reported in the literature. The ketone (**10**) and the α- and β-alcohols (**9**) and (**8**) may be formed as decay products of the secondary 6α- and 6β-peroxyl radicals.

When the rearrangement was followed for a 1:1.94 or 1.63:1 mixture of (**6**) and (**7**), the composition in each case reached a value of *ca.* 1:1.5 during 20 h. It appears therefore that (**6**) and



(6) (7) (10) (9) (8)

Scheme 6.

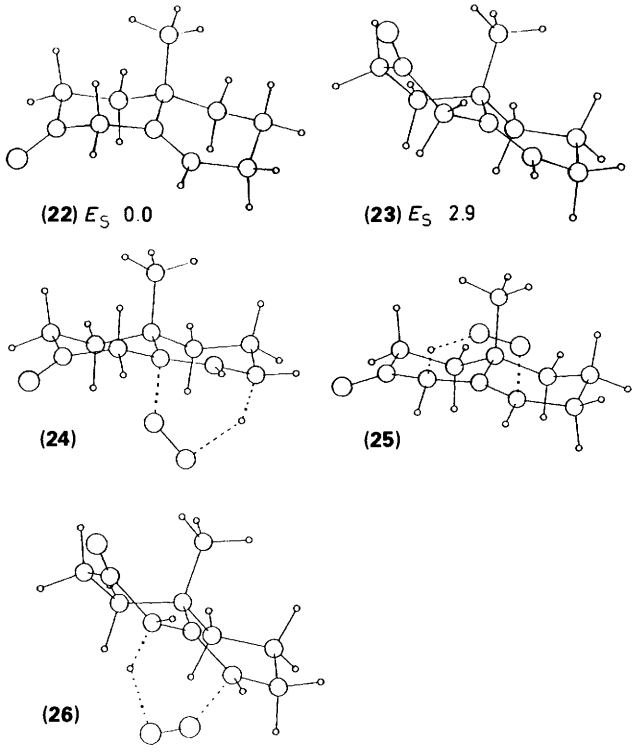


Figure 4. Molecular configurations as calculated by MM2. (**22**) and (**23**): the most stable conformations of (**15**); energies in kcal mol^{-1}. (**24**): Attack of $^1O_2$ at the 5α position of (**22**). (**25**): Attack of $^1O_2$ at the 6β position of (**22**). (**26**): Attack of $^1O_2$ at the 6α position of (**23**).

(**7**) are in equilibrium. Similarly, a 1.09:1 mixture of (**17**) and (**18**) appeared to give an equilibrium mixture with the composition 1.8:1 after 150 h. These results are in accord with the MM2 calculations (see above) on the α- and β-alcohols (**17**) and (**18**) which showed that the α-configuration was slightly the more stable.

When 20 mol % of 2,6-di-t-butyl-4-methylphenol was added as a free radical inhibitor to a solution of the 6β-hydroperoxide (**6**) in $CDCl_3$, no epimerization to (**7**) nor decomposition to (**10**), (**9**), or (**8**) could be detected by NMR during 105 h. This establishes that the epimerization is a radical chain process, and supports the suggestion that (**10**), (**9**), and (**8**) are products of the chain termination of the secondary alkylperoxyl radicals. The epimerization probably follows a dissociative mechanism similar to that which was proposed for the epimerization of the 7α-hydroperoxide derived from cholesterol [(**3**)→(**4**)].

Experimental

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ using a Varian XL-200 or VXR-400 spectrometer, and IR spectra using a Perkin-Elmer PE 983 instrument. Electron ionization mass spectra were obtained using a VG 7070H instrument.

Molecular mechanics calculations were carried out using the MM2 program (QCPE 423).

Cholest-5-en-3-one (**5**).—This compound was prepared by Fieser's method[19] and showed the following characteristics: m.p. 122–125 °C (lit.,[19] 124–129 °C); $\delta_H(CDCl_3)$ 0.69 (3 H, s, 18-Me), 0.84 (6 H, d, *J* 6.59 Hz, 26- and 27-Me), 0.90 (3 H, d, *J* 6.53 Hz, 21-Me), 2.79 (1 H, dd, *J* 16.43 and 1.93 Hz, 2-H), 3.27 (1 H, dm, *J* 16.55 and 0.63 Hz, 2-H), and 5.32 (1 H, m, 6-H); $\delta_C(CDCl_3)$ 122.9 (C-6), 138.5 (C-5), and 209.7 (C-3), consistent with the literature.[20]

Photo-oxygenation of (**5**).—A solution of cholest-5-en-3-one (0.5 g) and Rose Bengal (*ca.* 0.01 g) in a mixture of methanol and dichloromethane (1:1, v/v) in a water-cooled flask was irradiated for 5 h with light from a 400 W sodium lamp at a distance of 5 cm. The solvent was removed at room temperature on the rotary evaporator and the residue was chromatographed on Merck silica gel 60 (70–230 mesh) using a 1:1 mixture of ether and pentane as eluant, giving in sequence the following compounds.

Cholest-4-ene-3,6-dione (**10**), m.p. 120–123 °C (lit.,[9] 124–126 °C), $\delta_H(CDCl_3)$ 0.71 (3 H, s, 18-Me), 0.85 (3 H, d, *J* 6.56 Hz, 27- and 26-Me), 0.87 (3 H, d, *J* 6.60 Hz, 26- or 27-Me), 0.92 (3 H, d, *J* 6.48 Hz, 21-Me), 2.50 (3 H, m, 2- and 7-H), 2.67 (1 H, dd, *J* 15.90 and 4.09 Hz, 2- or 7-H), and 6.16 (1 H, s, 4-H); $\delta_C(CDCl_3)$ 125.4 (C-4), 161.1 (C-5), 199.5 (C-6 or C-3), and 202.4 (C-3 or C-6).

3α,5α-Epidioxycholest-6-en-3β-ol (**13**). M.p. 137–139 °C; δ_H 0.68 (3 H, s, 18-Me), 0.848 (3 H, d, *J* 6.56 Hz, 27- or 26-Me), 0.853 (3 H, d, 26- or 27-Me) 0.87 (3 H, s, 19-Me), 0.90 (3 H, d, *J* 6.53 Hz, 21-Me), 2.25 (1 H, dd, *J* 11.33 and 2.60 Hz, 4-H), 3.05 (1 H, br, OH), 2.48 (1 H, d, *J* 11.29 Hz, 4-H), 5.34 (1 H, dd, *J* 9.76 and 2.71 Hz, 7-H), 5.95 (1 H, dd, *J* 9.77 and 1.56 Hz, 6-H); δ_C 89.0 (C-5), 107.6 (C-3), 123.3 (C-7), 140 (C-6); *m/z* (70 eV) 416 (M^+), 401 (M^+ − Me), and 383 (M^+ − OOH); ν_{max}(Nujol) 3 401 (OH str.), 1 706 (C=O str.), and 1 637 (C=C str.) Found: C, 77.7; H, 10.9. $C_{27}H_{24}O_3$ requires C, 77.8; H, 10.7%.

6β-Hydroperoxycholest-4-en-3-one (**6**). M.p. 176–179 °C (lit.,[10] 180–181 °C); $\delta_H(CDCl_3)$ 0.69 (3 H, s, 18-Me), 0.86 (3 H, d, *J* 6.64 Hz, 27- or 26-Me), 0.87 (3 H, d, *J* 6.60 Hz, 26- or 27-Me), 0.91 (3 H, d, *J* 6.56 Hz, 21-Me), 2.08 (2 H, m, 7-H), 2.38 (1 H, dm, *J* 17.23 and 3.26 Hz, 2-H), 2.52 (1 H, ddd, *J* 17.25, 14.93, and 5.04 Hz, 2-H), 4.43 (1 H, dd, *J* 4.09 and 2.28 Hz, 6-H), 5.88 (1 H, d, *J* 0.91 Hz, 4-H), and 8.41 (1 H, br, OOH); $\delta_C(CDCl_3)$ 85.9 (C-6), 129.3 (C-4), 163.7 (C-5), and 200.3 (C-3).

Other fractions gave a mixture of (**6**) and 6α- hydroperoxycholest-4-en-3-one (**7**) with $\delta_H(CDCl_3)$ 4.60 (1 H, ddd, *J* 12.44, 5.30, and 1.85 Hz, 6-H), and 6.08 (1 H, d, *J* 1.85 Hz, 4 (H).

Autoxidation of Compound (**5**).—The reaction was carried by Cox's method,[10] using cyclopentane as the solvent, to give a mixture of (**6**) (70%) and (**7**) (30%) with the same ^1H NMR spectra as reported above. By repeated chromatography this solution was enriched to contain 70% (**7**), but a pure sample of (**7**) could not be isolated.

Using these data, the yields of the products given in Table 1 were obtained using integrated ^1H NMR spectroscopy.

5α-Hydroxycholest-6-en-3-one (**14**).—The 3α,5α-epidioxide (**13**) in ether was reduced with an excess of triphenylphosphine at room temperature and the product was chromatographed on silica gel with ether–pentane (1:1, v/v) as eluant to give the 5α-alcohol (**9**), m.p. 185–188 °C; $\delta_H(CDCl_3)$ 0.66 (3 H, s, 18-Me), 0.80 (3 H, d, *J* 6.71 Hz, 27- or 26-Me), 0.81 (3 H, d, *J* 6.60 Hz, 26- or 27-Me), 0.85 (3 H, d, *J* 6.45 Hz, 21-Me), 0.10 (3 H, s, 18-Me), 1.51 (3 H, s, 19-Me), 2.22 (1 H, d, *J* 15.7 Hz, 4-H), 2.36 (2 H, dd, *J* 9.23 and 5.16 Hz, 2-H), 2.58 (1 H, dd, *J* 15.19 and 1.34 Hz, 4-H), 5.41 (1 H, dd, *J* 9.83 and 2.67 Hz, 7-H), and 5.66 (1 H, dd, *J* 9.83 and 1.30 Hz, 6-H); $\delta_C(CDCl_3)$ 75.2 (C-5), 130.9 (C-7), 134.1 (C-6), and 210.3 (C-3); *m/z* (70 eV) 400 (M^+), 382 ($M^+ - H_2O$), 367; ν_{max}(Nujol) 3 409 (OH str.), 1 710 (C=O str.), 1 456, and 1 376 cm^{-1}; *m/z* (HRMS) 400.3348 ($C_{27}H_{44}O_2$ requires 400.3341).

6β-Hydroxycholest-4-en-3-one (**8**).—This compound was prepared in the same way by reduction of 6β-hydroperoxycholest-4-en-3-one (**6**), m.p. 186–188 °C (lit.,[10] 188–189 °C); $\delta_H(CDCl_3)$ 0.69 (3 H, s, 18-Me), 0.86 (3 H, d, *J* 6.64, 27- or 26-Me), 0.87 (3 H, d, *J* 6.60 Hz, 26- or 27-Me), 0.91 (3 H, d, *J* 6.56, 21-Me), 2.08 (2 H, m, 7-H), 2.39 (1 H, dm, *J* 17.20 Hz and 3.24 Hz, 2-H), 2.52 (1 H, ddd, *J* 4.10 and 2.28 Hz, 6-H), and 5.82 (1 H, d, *J* 0.90, 4-H); $\delta_C(CDCl_3)$ 73.3 (C-6), 126.3 (C-4), 168.5 (C-5), and 200.5 (C-3).

Epimerization of the 6α- and 6β-Hydroperoxides (**6**) *and* (**7**).—The concentration of (**6**), (**7**), (**10**), (**8**), and (**9**) was monitored in $CDCl_3$ solution by integration of the olefinic ^1H NMR signals at δ 5.88 (**6**), 6.08 (**7**), 6.16 (**10**), 6.19 (**9**), and 5.82 (**8**). When (**6**) was kept in $CDCl_3$ in the presence of 2,6-di-t-butyl-4-methylphenol (12 mol %), no change was observed during 105 h.

4aβ-Methyl-3,4,4a,5,6,7-hexahydronaphthalen-2(1H)-one (**15**).—This compound was prepared by condensation of 2-methylcyclohexanone with methyl vinyl ketone to give 4α-methyl-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one[21,22] which was converted into the corresponding ethylene ketal.[21,23] This in turn, was hydrolysed in 80% acetic acid at 65 °C to give a mixture consisting of 65% of (**15**) and 35% of 4aβ-methyl-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one. The literature reports a 95% yield of (**15**). Compound (**15**) was isolated by chromatography on silica gel with ether–pentane (1:5, v/v) as eluant.

These compounds had the following characteristics. 4aβ-Methyl-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one, b.p. 92–94 °C/1.1 mmHg (lit.,[21] 82–83 °C/0.7 mmHg); $\delta_H(CDCl_3)$ 1.21 (3 H, s, Me), 1.35 (2 H, m, CH_2), 1.61–1.90 (6 H, m, CH_2), 2.26 (1 H, dm, *J* 17.07 and 2.07 Hz, 3-H), 2.31–2.37 (2 H, m, 8-H), 2.50 (1 H, ddd, *J* 17.12, 14.15, and 5.75 Hz, 3-H), and 5.69 (1 H, m, 1-H).

2,2-Ethylenedioxy-4aβ-methyl-1,2,3,4,4a,5,6,7-octahydronaphthalene [after chromatography on silica with ether–pentane (1:5, v/v) as eluant]; $\delta_H(CDCl_3)$ 1.08 (3 H, s, Me), 1.45–1.67 (8 H, 4 × CH_2), 1.84 (2 H, m, 3-H), 2.10 (1 H, dd, *J* 13.90 and 2.94 Hz, 1-H), 2.48 (1 H, dq, *J* 13.90 and 2.49 Hz, 1-H), 3.94 (4 H, m, *J* 3.09, ketal CH_2), and 5.36 (1 H, quin, *J* 2.41, 8-H); $\delta_C(CDCl_3)$, 19.0, 23.7, 25.6, 31.1, 34.0, 38.4, 38.9, 41.7 (C-1), 64.2 and 64.4 (ketal) 109.7 (C-2), 122.6 (C-8), and 139.7 (C-8a).

4aβ-Methyl-3,4,4a,5,6,7-hexahydronaphthalene-2(1H)-one (**15**). δ_H 1.21 (3 H, s, Me), 1.58–1.75 (6 H, m, 4-, 5-, and 6-H), 1.93 (2 H, m, 7-H), 2.29 (1 H, dm, *J* 13.96 and 1.15 Hz, 3-H), 2.51 (1 H, ddd, *J* 14.03, 8.00, and 6.15 Hz, 3-H), 2.78 (1 H, dq, *J* 16.14 and 1.97 Hz, 1-H), 3.18 (1 H, dm, *J* 16.11 and 1.76 Hz, 1-H), 5.38 (1 H, quin, *J* 2.63 Hz, 8-H); $\delta_C(CDCl_3)$ 18.9, 23.8, 25.5, 37.8, 34.2 (C-4a), 38.1 (C-7), 38.8 (C-3), 48.5 (C-1), 123.3 (C-8), 132.8 (C-8a), and 209.2 (C-2).

Photo-oxygenation of (**15**).—The singlet oxygenation of (**15**) was carried out in the same way as described above for (**5**). After work-up, the reaction mixture was chromatographed on silica gel with ether–pentane (1:2, v/v) as eluant to give 2α,8aα-epidioxy-4aβ-methyl-1,2,3,4,4a,5,6,8a-octahydronaphthalen-2β-ol (**16**), m.p. 108–110 °C; $\delta_H(CDCl_3)$ 0.94 (3 H, s, Me), 1.30 (1 H, dm, *J* 12.50 and 2.95 Hz, 5- or 4-H), 1.40 (1 H, dd, *J* 12.10 and 5.61 Hz, 5- or 4-H), 1.75–2.15 (6 H, m, 3 × CH_2), 2.23 (1 H, dd, *J* 11.30 and 2.60 Hz, 1-H), 2.45 (1 H, d, *J* 11.27 Hz, 1-H), 3.15 (1 H, br, OH), 5.39 (1 H, dt, *J* 9.72 and 1.99 Hz, 7-H), and 6.04 (1 H, dt, *J* 9.78 and 3.45 Hz, 8-H); δ_C 20.5, 22.9, 29.7 (C-4a), 31.3, 32.9, 33.4 (Me), 47.1 (C-1), 87.9 (C-8a), 107.8 (C-2), 123.4 (C-7), 136.8 (C-8); *m/z* (HRMS) 196.112 ($C_{11}H_{16}O_3$ requires 196.110).

The rest of the material consisted of a mixture of 8β-hydroperoxy-4aβ-methyl-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one (**17**); $\delta_H(CDCl_3)$ 4.40 (1 H, dd, *J* 3.46 and 2.68 Hz, 8-H), 5.87 (1 H, s, 1-H), 8α-hydroperoxy-4aβ-methyl-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one (**18**); $\delta_H(CDCl_3)$ 4.60 (1 H, ddd, *J* 12.35, 5.53, and 1.96 Hz, 8-H), 6.08 (1 H, d, *J* 1.90 Hz, 1-H), and 4aβ-methyl-3,4,4a-5,6,7-hexahydronaphthalene-2,8-dione (**19**); $\delta_H(CDCl_3)$ 6.16 (1 H, s, 1-H). With this information, the composition of the product mixture was shown to be (**16**) 58%, (**17**) 30%, (**18**) 6%, and (**19**) 6%.

Acknowledgements

We acknowledge support from the SERC and the Ramsay Memorial Trust.

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Paper 9/03499D
Received 21*st August* 1989
Accepted 20*th October* 1989