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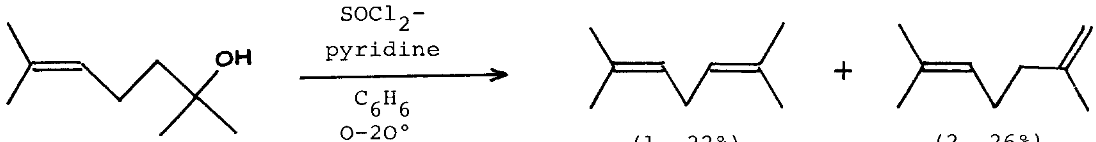
THE FORMATION AND SUBSEQUENT CYCLISATION OF NOVEL HYDROPEROXIDES FROM A 1,4- AND A 1,5-DIENE

Howard A.J. Carless* and Richard J. Batten
Department of Chemistry, Birkbeck College, Malet Street, London WC1E 7HX

Summary: The preparation of the unsaturated hydroperoxides(3,4,5,6 and 7) by the sensitized photo-oxidation of the 1,4-diene(1) and the 1,5-diene(2) is described, together with the attempted free-radical cyclisation of these.

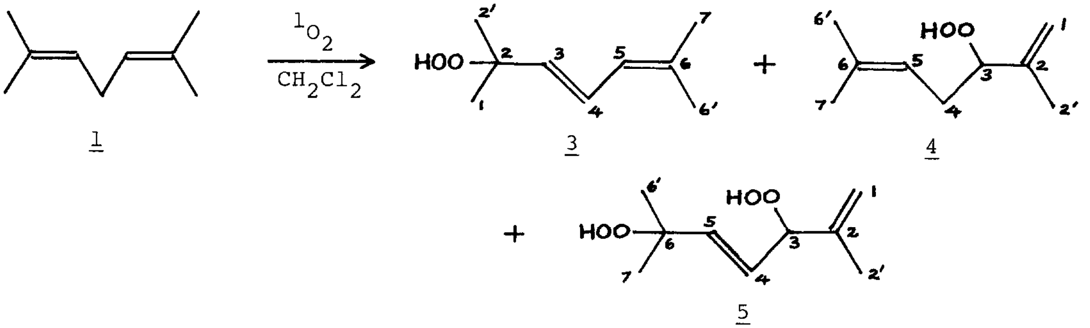
Unsaturated hydroperoxides have been implicated as intermediates in the biosynthesis of prostaglandins[1] and during lipid oxidation in vegetable oils.[2] A common feature of these hydroperoxides is that they are derived from poly-olefins containing a *cis*,*cis*-1,4-diene system. Although there has been much investigation of long chain poly-olefins,[3] short chain 1,4-dienes have received little attention. We chose to synthesise hydroperoxides by reaction of photochemically-generated singlet oxygen ($^1O_2$) with 2,6-dimethylhept-2,5-diene(1). The symmetry of 1 limits the number of possible monohydroperoxides to only two. Compound 1 was formed together with 2,6-dimethylhept-2,6-diene(2) by a modification of the published procedure:[4]



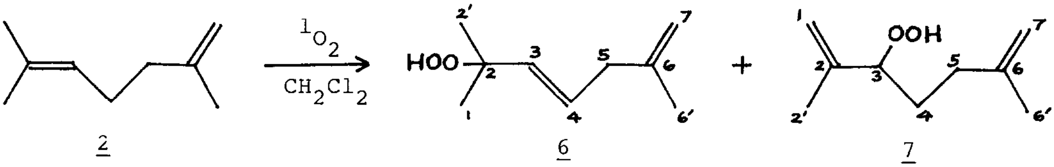
(1, 22%) (2, 26%)

1 and 2 were separated by column chromatography using silica impregnated with 10% silver nitrate.

Sensitized photo-oxidation of 1 (tetraphenylporphine, O_2, CH_2Cl_2, -50°C, 2h) afforded the monohydroperoxides (3,21%) and (4, 13%) together with a more polar product (5,11%), which were isolated by flash chromatography.[5] Spectral characterisation of these compounds[6] supported the assignment of 5 as a dihydroperoxide derived by further reaction of 4 with singlet oxygen.



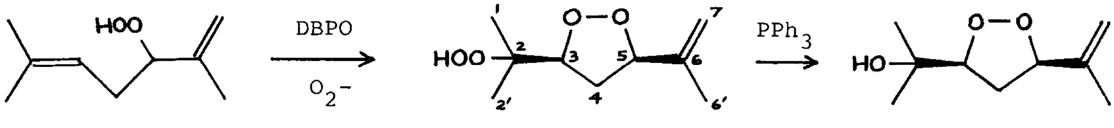
Hydroperoxides derived from 1,5-dienes are of interest because of their role in the photodegradation of such polymers as poly(isoprene) or rubber.[7] A similarly sensitized photo-oxidation of the diene 2 (4h) yielded the monohydroperoxides (6,23%) and (7,25%).[6]



Further proof of structure was obtained by the reduction of each hydroperoxide with triphenylphosphine to give the corresponding known allylic alcohols: 3 → 8;[8] 4 → 9;[9] 6 → 10;[10] 7 → 11.[11] Reduction of the dihydroperoxide 5 gave the corresponding diallylic alcohol which decomposed upon silica column chromatography. A significant feature of these reactions is that the terminal methylene group of 2 appears to be much less reactive than the isopropylidene group towards singlet oxygen, an observation which has been predicted on theoretical grounds.[12]

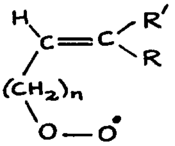
We next investigated the cyclisation of these unsaturated hydroperoxides under the influence of free radicals, using di-tertiary-butyl peroxyoxalate (DBPO)[13] as a source of *t*-butoxy radicals. It has been shown that DBPO induces the abstraction of the hydroperoxide hydrogen leading to peroxy radicals, which further react with suitable double bonds present.[14]

Monohydroperoxide (4) when stirred for 19h at room temperature with 0.4 equivalents of DBPO in oxygenated benzene solution (0.02M) gave the cyclised product (12,20%), whose structure was assigned by spectral characterisation[15] and by reduction with triphenylphosphine to give the tertiary alcohol (13). The formation of a 3,5-disubstituted *cis*-1,2-dioxolane ring is in accord with the *cis*-selectivity observed in the cyclisation of hydroperoxides derived from methyl linoleate[16] and methyl linolenate.[17] The other hydroperoxides (3,6 & 7) did not cyclise under the above reaction conditions.



4 12 13

This result is to be expected since exo-ring closure 14 → 15 is kinetically favoured over the endo-process 14 → 16 in intramolecular free-radical reactions.[18]



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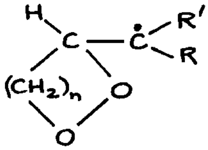
(n≤4)



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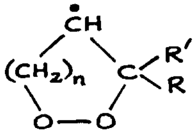

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With hydroperoxides (3,6 and 7) formation of a dioxolane by exo-ring closure is prohibited.

We are currently investigating the free-radical cyclisation of other unsaturated hydroperoxides.

References

1. N.A. Porter, "Free Radicals in Biology", ed. W.A. Pryor, Academic Press, New York, 1980, 4, 261.
2. A.H. Clements, R.H. Van den Engh, D.J. Frost, K. Hoogenhout and J.R. Nooi, J.Am.Oil Chem.Soc., 1973, 50, 325.
3. See, e.g., N.A. Porter, L.S. Lehman, B.A. Weber and K.J. Smith, J.Am.Chem. Soc., 1981, 103, 6447; E.N. Frankel, W.E. Neff and D. Weisleder, J. Chem. Soc., Chem. Commun., 1982, 599.
4. S.M. Baba, H.H. Mathur and S.C. Bhattacharyya, Tetrahedron, 1966, 22, 903.
5. W.C. Still, M. Kahn and A. Mitra, J.Org.Chem., 1978, 43, 2923.
6. 3, R_f 0.41(diethyl ether-hexane, 1:3); IR(film):3390, 1657cm^{-1}; ^{1}H-NMR(200MHz,CDCl$_3$)δ:1.41(6H,s, H-1,H-2'), 1.82(6H,s,H-6',H-7), 5.65(1H,d,J16Hz,H-3), 5.87(1H,d,J11Hz,H-5), 6.49(1H,dd,J11 and 16Hz,H-4), 7.47(1H,s,OOH): ^{13}C-NMR(15MHz,CDCl$_3$):137.0(C-6), 133.5, 127.6(C-4), 124.6, 82.6(C-2), 26.1, 24.5, 24.5, 18.4 ppm.

   4, R_f 0.49(diethyl ether-hexane, 1:3); IR(film):3400, 1651cm^{-1}; ^{1}H-NMR(200MHz,CDCl$_3$)δ:1.67(3H,s,H-2'), 1.76(3H,s,H-7), 1.81(3H,s,H-6'), 2.19(2H,m,H-4), 4.35(1H,t,J8Hz,H-3), 5.05(3H,m,H-1,H-5), 8.02(1H,s,OOH); ^{13}C-NMR(15MHz,CDCl$_3$):143.8(C-2), 134.3(C-6),119.4(C-5),114.3(C-1). 89.6(C-3), 30.0(C-4), 25.7 (C-6'), 17.9 (C-2'), 17.5(C-7) ppm.

   5, R_f 0.41(diethyl ether-hexane, 2:3): IR(film):3390, 1652cm^{-1}; ^{1}H-NMR(200MHz,CDCl$_3$)δ:1.36(6H,s,H-6',H-7), 1.76(3H,s,H-2'), 4.78(1H,d,J8Hz,H-3), 5.01,5.04(2H,m,H-1), 5.66(1H,dd,J8 and 16Hz,H-4), 5.89(1H,d,J16Hz,H-5), 7.96(1H,s,OOH), 8.44(1H,s,OOH); ^{13}C-NMR (15MHz,$CDCl_3$):142.6(C-2), 139.0(C-4), 127.1(C-5), 114.6(C-1), 89.2(C-3), 82.1(C-6), 24.3(C-6'), 24.0(C-7), 18.5(C-2') ppm.

6, R_f 0.45(diethyl ether-hexane, 1:3): IR(film):3403, 1651cm^{-1}; ^{1}H-NMR (200MHz,$CDCl_3$)δ:1.35(6H,s,H-1,H-2'), 1.73(3H,s,H-6'), 2.75(2H,d,J8Hz,H-5), 4.69(1H,d,J1Hz,H-7), 4.74(1H,d,J1Hz,H-7), 5.65(1H,d,J15Hz,H-3), 5.68 (1H,m,H-4), 7.39(1H,s,OOH); ^{13}C-NMR(15MHz,$CDCl_3$):144.6(C-6), 135.4(C-3), 129.6(C-4), 111.2(C-7), 82.4(C-2), 40.9(C-5), 24.3, 24.3(C-1,C-2'), 22.4(C-6') ppm.

7, R_f 0.54(diethyl ether-hexane, 1:3); ^{1}H-NMR(200MHz,$CDCl_3$)δ:1.70(2H,m,H-4), 1.73(3H,s,H-2'), 1.75(3H,s,H-6'), 2.04(2H,m,H-5), 4.33(1H,t,J8Hz,H-3), 4.69(1H,d,J1Hz,H-7), 4.73(1H,d,J1Hz,H-7), 5.03(2H,m,H-1), 7.82(1H,s,OOH); ^{13}C-NMR(15MHz,$CDCl_3$):145.2(C-2), 143.8(C-6), 114.7(C-1), 110.5(C-7), 89.3(C-3), 33.7(C-4), 28.7(C-5), 22.4(C-6'), 17.1(C-2') ppm.

7. J. Chaineaux and C. Tanielian, in "Singlet Oxygen: Reaction with Organic Compounds and Polymers", ed. B.Rånby and J.F. Rebek, Wiley-Interscience, 1978, p. 164.

8. E.A. Braude and J.A. Coles, J.Chem.Soc., 1952, 1425.

9. T. Shono, T. Yoshimura and R. Oda, J.Org.Chem., 1967, 32, 1088.

10. J. Colonge and A. Varagnat, Bull.Soc.Chim.Fr., 1964(3), 561.

11. W.S. Johnson, T.J. Brocksom, P. Loew, D.H. Rich, L. Werthemann, R.A. Arnold, T. Li and D.J. Faulkner, J.Am.Chem.Soc., 1970, 92, 4463.

12. L.A. Paquette, D.C. Liotta and A.D. Baker, Tetrahedron Lett., 1976, 2681.

13. P.D. Bartlett, E.P. Benzing and R.E. Pincock, J.Am.Chem.Soc., 1960, 82, 1762.

14. N.A. Porter, M.O. Funk, D. Gilmore, R. Isaac and J. Nixon, J.Am.Chem.Soc., 1976, 98, 6000.

15. 12, R_f 0.29(diethyl ether-hexane, 1:3); IR(film):3415, 1653cm^{-1}; ^{1}H-NMR (200MHz,$CDCl_3$)δ:1.23, 1.36(6H,s,H-1,H-2'), 1.81(3H,s,H-6'), 2.50 (1H,ddd,J7,9 and 12Hz,H-4α), 2.74(1H,ddd,J7,8 and 12Hz,H-4β), 4.44 (1H,t,J8Hz,H-3), 4.70(1H,t,J8Hz,H-5), 4.98,5.09(2H,m,H-7), 8.33(1H,s, OOH); ^{13}C-NMR(15MHz,$CDCl_3$): 140.6(C-6), 114.4(C-7), 85.4, 84.8(C-3,C-5), 83.0(C-2), 40.4(C-4), 21.4,20.8(C-1,C-2'), 18.0(C-6') ppm.

13, R_f 0.23(diethyl ether-hexane, 1:2); IR(film):3440, 1652cm^{-1}; ^{1}H-NMR (200MHz,$CDCl_3$)δ:1.18, 1.27(6H,s,H-1,H-2'), 1.78(3H,s,H-6'), 2.00 (1H,s,OH), 2.54(1H,ddd,J7,8 and 12Hz,H-4α), 2.66(1H,ddd,J7,8 and 12Hz, H-4β), 4.18(1H,t,J8Hz,H-3), 4.69(1H,t,J8Hz,H-5), 4.96,5.05(2H,m,H-7)ppm.

16. E.D. Mihelich, J.Am.Chem.Soc., 1980, 102, 7141.

17. D.E. O'Connor, E.D. Mihelich and M.C. Coleman, J.Am.Chem.Soc., 1981, 103, 223.

18. Some guidelines for radical reactions:
A.L.J. Beckwith, C.J. Easton and A.K. Serelis, J.Chem.Soc., Chem.Commun., 1980, 482.

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