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THERMAL AND PHOTOCHEMICAL REACTIONS OF UNSATURATED BICYCLIC ENDOPEROXIDES

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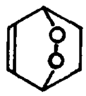
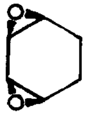
Abstract: Thermal, and especially photochemical, rearrangement of the endoperoxides (1) and (5)-(11) gives βγ-epoxycycloalkanones as primary products, accompanied by the expected *syn*-diepoxides.

Unsaturated endoperoxides [*e.g.*(1)] are readily available by reaction of singlet oxygen ($^1O_2$) with conjugated dienes.[1] Such endoperoxides have proved extremely useful in synthesis, being convertible to a wide variety of stereospecifically oxygenated compounds.[2] One commonly used transformation has been the thermal rearrangement of diene endoperoxides to *syn*-diepoxides *e.g.*[(1)→(2)],[3] which has proved a key step in the synthesis of crotepoxide[4] and stemolide.[5] Thermal diepoxide formation is generally found, although there have been occasional indications that other accompanying products may also be formed in such reactions.[6,7]

Uv irradiation of both saturated[8] and unsaturated bicyclic peroxides[9] has also received attention. Using short wavelengths of irradiation, unsaturated endoperoxides (especially those derived from aromatic compounds[10]) can revert to diene and dioxygen.[11] However, in most cases, the photochemical reactions of endoperoxides result from an initial O-O bond breaking, to give products similar to those of thermolysis. Two early reports of unsaturated endoperoxide photolysis suggested that βγ-epoxyketone [*e.g.*(3)] formation was feasible in certain cases.[6,12] We now present direct evidence that βγ-epoxyketones are generally formed (often as the major products) on thermolysis or photolysis of unsaturated bicyclic peroxides.


(1)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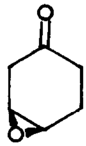
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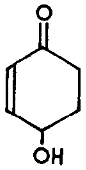
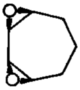
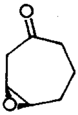
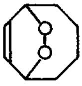
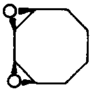
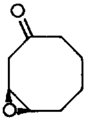
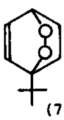
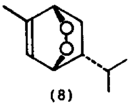
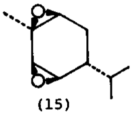
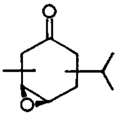
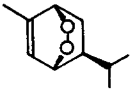
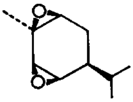
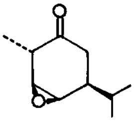
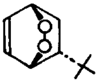
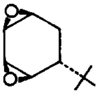
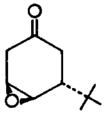
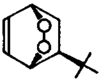
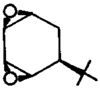
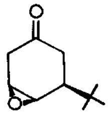


(4)

Heating the endoperoxide (1) in toluene solution under reflux led to a reaction product whose ^1H and ^{13}C nmr spectra clearly showed it to be a mixture of two components, in the ratio *ca* 1:2. The minor component was the expected diepoxide (2), subsequently isolated by silica gel chromatography of the mixture. The major component, which was easily converted by acids, bases or silica gel to hydroxyenone (4), was identified as the βγ-epoxycyclohexanone

TABLE. Products from Thermolysis and Photolysis of Endoperoxides.

Endoperoxide	Diepoxide (D)	Epoxyketone (E)	Products	Ratio (D:E)	Footnotes
(1)	(2)	(3)	Δ	35:65	
			hν	28:72	
 (5)	 (12)	 (19)	Δ	90:10	
			hν	33:67	
 (6)	 (13)	 (20)	Δ	-	*a*
			hν	35:65	
 (7)	 (14)	 (21)	Δ	65:35	*b*
			hν	53:47	
 (8)	 (15)	 (22)	Δ	58:42	*c,d*
			hν	24:76	
 (9)	 (16)	 (23)	Δ	31:69	*d*
			hν	22:78	
 (10)	 (17)	 (24)	Δ	83:17	*e*
			hν	80:20	
 (11)	 (18)	 (25)	Δ	29:71	*e*
			hν	25:75	

[a] Compound (6) proved more thermally stable; heating in xylene at 140°C gave both diepoxide and degradation products.

[b] 1-t-Butylcyclohexa-1,3-diene prepared from 4-t-butylcyclohexanone, *via* the enone (E.W. Garbisch, Jr., *J. Org. Chem.* 1965, *30*, 2109), lithium aluminium hydride reduction and 1,4-dehydration using 2,4-dinitrobenzenesulphenyl chloride (H.J. Reich and S. Wollowitz, *J. Am. Chem. Soc.*, 1982, *104*, 7051).

[c] Two isomeric epoxyketones (22) formed.

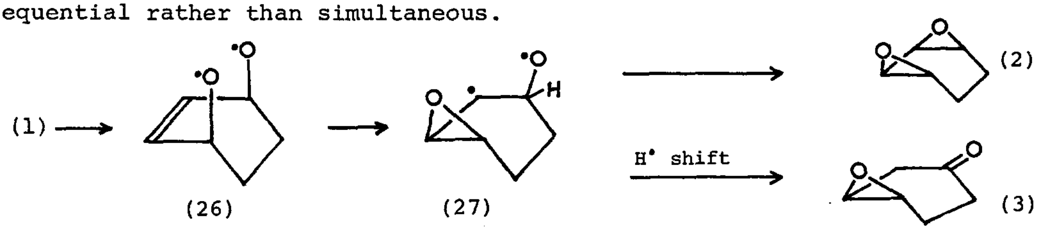
[d] Prepared from α-phellandrene: J.A. Turner and W. Herz, *J. Org. Chem.*, 1977, *42*, 1895.

[e] Endoperoxides prepared from 4-t-butylcyclohexene, *via* the diene (P.F. King and L.A. Paquette, *Synthesis*, 1977, 279); (10) $\delta_H(CDCl_3)$ 0.82(9H,s), whereas (11) $\delta_H(CDCl_3)$ 1.00(9H,s); the configuration of these endoperoxides was shown by reduction of each to the corresponding 2-t-butylcyclohexane-1,4-diols, and comparison of ^{13}C nmr shifts with those of *cis*- and *trans*-2-t-butylcyclohexanols.

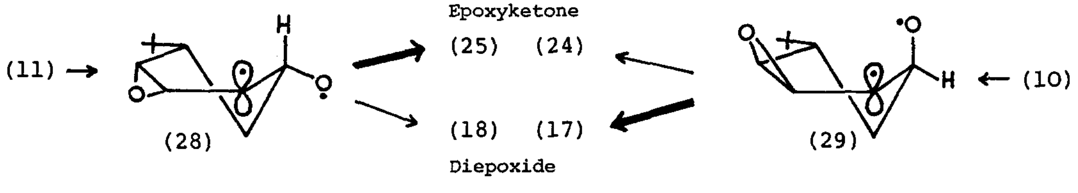
(3) by comparison with an authentic sample synthesised by photo-oxidation of the corresponding βγ-epoxyalcohol.[13] Photolysis of the endoperoxide (1) in benzene solution also gave a reaction mixture consisting of (2) and (3), although the proportion of epoxyketone (3) was increased (see Table).[14]

The formation of βγ-epoxyketones either by thermolysis or by photolysis was found to be quite general for the bicyclic peroxides (5)-(11), although the ratio of diepoxide to epoxyketone varied widely, as shown in the Table. Carbon-13 nmr spectra of the βγ-epoxyketones revealed a carbonyl group (208-211 p.p.m.) and two epoxide carbons (*ca.* 50-60 p.p.m.) in each case.[15] The epoxyketones (19)-(25) were thermally stable at 110°C, and could generally be analysed by g.l.c. without appreciable isomerisation to hydroxyenones. However, chromatography of the reaction mixtures yielded diepoxide and the corresponding γ-hydroxy-αβ-cycloalkenones as the only isolated products.[16]

A possible mechanism for the reactions is shown below, assuming that diepoxide and epoxyketone are both formed from the biradical (26). Ring closures of the latter to give diepoxide (2) are in competition with the 1,2-hydrogen shift required to yield epoxyketone (3). Since no cyclohexane-1,4-dione is formed from (1), it would appear that the first ring closure is rapid, to give 1,3-biradical (27), and that the epoxide ring closures are sequential rather than simultaneous.



Conformational factors obviously play an important role in determining the product distribution, as shown by the different results found for the two t-butyl endoperoxides (10) and (11). If the intermediate biradicals (28) and (29), from the isomers (11) and (10) respectively, adopt the half-chair conformations shown, then the required 1,2-hydrogen shift in (28) is facilitated by the nearly parallel arrangement of the p electron on carbon with the adjacent axial C-H bond. Hence (11) leads mainly to epoxyketone (25), whereas (10), with an equatorial C-H bond in the biradical (29), prefers ring closure to diepoxide (17). In a 1,5-biradical, it has been shown that there is a relative ease of ~20:1 favouring abstraction of axial rather than equatorial hydrogen adjacent to a radical centre in the cyclohexyl ring.[17]



A clear trend was observable from the results in the Table: *photolysis generally gave a greater proportion of epoxyketone than thermolysis;* this effect was most remarkable in the [3.2.2] system (5). Thus, it seems that the photochemically-derived biradicals [*e.g.* (27)] are more prone to give a hydrogen shift (or less prone to ring closure) than the thermally-derived species. However, the excited state involved in these reactions needs investigation.

The ability of unsaturated bicyclic endoperoxides to give βγ-epoxycycloalkanones in the present examples suggests that it would be worth investigating their possible involvement in the known catalytic rearrangements of endoperoxides in the presence of palladium(O) complexes,[18] ruthenium(II) species[19] and cobalt(II) porphyrins.[20]

References and Notes

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14. *General conditions.* Thermolysis (Δ): endoperoxide (*ca.* 0.1-0.3 *M*) heated under reflux in toluene (b.p. 111°C), 3-8 h, followed by rotary evaporation to remove solvent. Photolysis (hν): medium-pressure mercury arc lamp, pyrex apparatus, endoperoxide (*ca.* 0.05-0.1 *M*) in benzene or pentane solution, irradiated under nitrogen.
15. ^{13}C NMR data (CDCl$_3$):
    (19) 207.6, 55.5, 50.4, 44.3, 43.1, 27.6 and 18.1 p.p.m.;
    (20) 210.4, 55.4, 52.9, 43.3, 42.3, 27.1, 24.5 and 23.9 p.p.m.;
    (21) 208.8, 64.4, 53.6, 39.1, 36.1, 33.3, 25.8 and 21.6 p.p.m.;
    (22) 208.6, 58.6, 57.0, 48.4, 44.9, 29.8, 26.5, 23.8, 22.4 and 18.5 p.p.m, other isomer at 210.9, 58.0, 55.6, 42.6, 41.6, 38.3, 30.7, 20.2, 19.7 and 13.5 p.p.m.;
    (23) 211.0, 54.8, 54.6, 41.8, 39.8, 37.4, 31.4, 19.7, 19.4 and 14.1 p.p.m.;
    (24) 208.5, 52.2, 52.2, 48.7, 41.4, 31.8, 27.8 and 26.0 p.p.m.;
    (25) 208.2, 52.3, 48.8, 43.4, 37.9, 37.3, 33.2 and 27.6 p.p.m.
16. *cf.* F. Delay and G. Ohloff, *Helv. Chim. Acta*, 1979, *62*, 2168.
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