

NOTES

Photochemical rearrangement of diene endoperoxides^{1, 2}

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It has been shown that the direct irradiation of cyclic peroxides such as ascaridole, and those derived from cyclohexadiene, 1,3,5,5-tetramethylcyclohexadiene, and levopimaric acid methyl ester rearrange on irradiation. The bisepoxides are obtained, as in the thermal rearrangement, together with, where the structure permits, the ketoepoxide. The reaction can be induced by triplet-triplet energy transfer.

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The discovery (1, 2) in nature of a *cis* bisepoxide, crotepoxide (1) raised the problem of a general mode of synthesis of substances containing such functional groups. An obvious method was the thermal rearrangement of endoperoxides. The most studied of these is ascaridole (2), which on such treatment has been shown (3, and references there cited) to give isoascaridole (3), but other examples are available in alicyclic chemistry (4, 5). An objection to the use of this procedure was that the temperature needed (*ca.* 140°) might well be such as to lead to decomposition of the product should it be substituted with sensitive groups. An alternative mode of rearrangement was therefore sought.



The photolytic rearrangement of peroxides derived from the oxidation of acenes has been a subject of study by Dufraisse, Rigaudy and their school (6, 7 and references cited). Recently the rearrangement has been extended into the naphthalene series (8), as exemplified by the transformation of 4 into 5. It was therefore possible that the simple endoperoxides of type 2 might also rearrange. The irradiation of acyclic peroxides was already known (9, 10) to lead to photolysis, and evidently if the intermediate species so generated were the same as in the thermolysis then the same transformation should be expected (11).

Indeed, it was found that ascaridole (2) and peroxides derived from 1,3,5,5-tetramethylcyclohexadiene (6), cyclohexadiene (7), and levopimaric acid methyl ester (8) all behaved in essentially the same manner on irradiation through Pyrex or at 366 nm as on heating. In all cases a bisepoxide was obtained, but this was accompanied, where the structure permitted, by the corresponding ketoepoxide. The latter was unstable with respect to the corresponding keto alcohol, and chromatographic treatment usually yielded the latter.

A number of incidental points of interest emerge. Ascaridole has, as have most peroxides, a long tail in the u.v. absorption spectrum which reaches beyond 360 nm. In ascaridole this absorption is intensified somewhat as compared with normal peroxides and there appears to be a maximum at 233 nm of low intensity ($\epsilon \sim 166$). The origin of this is conjectural, but it presumably implies interaction of the oxygen lone pairs with the double bond, perhaps in the antibonding orbital. It was possible that this interaction might allow the conversion of ascaridole to isoascaridole without passing through any intermediate biradical. This would then suggest participation of

¹Photochemical synthesis: Part 34.

²Publication No. 10 from the Photochemistry Unit.

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some excited singlet state. Some qualitative experiments were undertaken to ascertain if this were so.

It was found, however, that irradiation of solutions of ascaridole or of 8 in the presence of any of the sensitizers, Michler's ketone, phenanthrene, or triphenylamine (such that the sensitizers absorbed essentially all the light), gave a faster conversion to products than did direct irradiation under the same conditions. Presumably, then, the triplet was a possible pathway though not necessarily the only one. However, the complementary quenching experiments were more difficult to perform. Essentially the problem was to find a quencher which did not absorb more than the peroxide. The acyclic dienes were possible candidates and indeed appeared to quench the reaction. But careful measurements of the extinction coefficient near 366 nm indicated that the dienes had residual absorption which required quantitative yield measurement to give decisive information. A similar experiment was performed with di-tert-butyl nitroxide as quencher by irradiation at 334 nm. In this case the yields were estimated by t.l.c. using a densitometer. The results (see the Experimental section) indicated, apparently beyond the limits of error, that quenching was occurring. Such a result is surprising and cannot be regarded as definitive since a number of points remain unclear. The possibility of singlet quenching, known to be possible with di-*tert*-butyl nitroxide (19) cannot be excluded. Assuming diffusion controlled quenching the lifetime of a species showing the degree of "quenchedness" observed can be calculated to be of the order of $10^{-9}-10^{-10}$ s.

The absorption spectrum of peroxides may result from the overlapping of two lone-pair orbitals with resulting splitting of so-formed π levels into bonding and antibonding, both filled. The transition may then be $\pi^* \rightarrow \sigma^*$. The quenching then requires that this state be not immediately dissociating, but yet that it may efficiently become so, since the quantum yield of peroxy radicals from di-*tert*-butyl peroxide and other peroxides is unity even in solution. The significance of the experiment is thus unclear.

The nature of the products suggests that when the biradical is formed, and a methine hydrogen(s) exist on the carbon(s) bearing oxygen addition (to give **15**) to the double bond takes place faster than hydrogen migration (Scheme 1). For the second step, if the reaction proceeds via a triplet, a spin inversion is required. It may be that this

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delays the closure to the bisepoxide sufficiently to allow the hydrogen migration to compete.³

An alternative possible explanation is that the bisepoxide is first formed and is then further rearranged. The thermal rearrangement of epoxides to ketones has been observed as have exceptions (12), but such rearrangements are not known to occur photochemically with light of such long wavelength⁴ in the absence of an additional vicinal chromophore (such as a ketone carbonyl). In control experiments the bisepoxides appeared stable, which suggests that the 1,3-biradical 15 rearranges directly to the ketoepoxide at least in the photochemical process. That the relative proportions of the products have a rough parallel in the thermal and photochemical processes suggests that the same is true for the thermal process. In addition thermal or photochemical rearrangement of the bisepoxides should not be restricted to just one of the pair, nor restrict the direction of opening to essentially one sense.

Experimental

Ascaridole

Ascaridole was distilled (56–57° at 0.17 mm) and gave a single spot on t.l.c. It showed λ_{max} 233 nm, ε 188. It was further purified by the method of Halsall (14). Repeated purification gave material with $\varepsilon = 166$ which was unchanged on further chromatography. Isoascaridole was prepared by heating a solution of ascaridole in refluxing xylene for 4 h followed by chromatography.

³This raises the interesting possibility that the ketone may first be formed in the triplet state.

NOTES

Irradiation of Ascaridole

(a) A solution of 100 mg ascaridole in cyclohexane (10 ml) was degassed by nitrogen purge (30 min). The solution was then irradiated through Pyrex for 6 h (85 W G.E. mercury medium pressure arc). The t.l.c. indicated the absence of ascaridole and the presence of isoascaridole as the only detectable substance. The isolated oil (85%) was identified as isoascaridole by comparison of i.r. and n.m.r. spectra which were identical.

Irradiation of ascaridole in methanol gave identical results.

(b) Solutions of ascaridole (32 mg) in (i) cyclohexane (ii) dioxan and dioxan containing (iii) 150 mg phenanthrene, (iv) 100 mg Michler's ketone, (v) 160 mg triphenylamine, (vi) 5 mg hexadiene-2,4, (vii) 11 mg hexadiene-2,4, and (viii) 22 mg hexadiene 2,4 were simultaneously irradiated on a merry-go-round (15) using a 450 W medium pressure mercury source and filters (Corning 760 and 052) to permit transmission in the 366 nm region. After 3 h irradiation the presence of isoascaridole was detectable in small amounts by t.l.c. in tubes (i) and (ii), and in decreasing amounts in tubes (vi) to (viii). In the latter the isoascaridole was barely detectable. Tubes (iii) to (v) showed the presence of large amounts of isoascaridole. In the case of tube (iv) the products were isolated and the isoascaridole (yield \sim 50 %) identified by comparison of its i.r. spectrum with that of an authentic specimen. Control experiments showed that isoascaridole itself was stable under the conditions of the experiment.

(c) Solutions of ascaridole (ca. 125 mg) in methanol (5 ml) were prepared and di-t-butyl nitroxide (ca. 35 mg) added to half, such that greater than 90% of the incident light was absorbed by the ascaridole. The light from the 200 W high pressure mercury arc was passed through the following filters (i) NiSO₄.6H₂O (saturated solution), 2 cm, (ii) CS 7-51, (iii) naphthalene, 12.8 g/1 isooctane, 1 cm. This system gave 30 % transmission at 334 nm < 2 % at 320 nm and <5% at 355 nm. The product was estimated by t.l.c., standardized charring and relative intensities measured on the plates by a densitometer after moistening with Nujol. The irradiation was followed over 13 h. The amount of quenching at the end of this time in two separate experiments was 30 and 45% where reproducibility of the analysis appeared to be $\pm 10\%$. The agreement between the separate experiments is not good, but the fact of quenching appears to be beyond experimental error.

Cyclohexa-1,3-diene Endoperoxide

This was prepared by the method of Murray and Kaplan (16). The endoperoxide was first obtained as a waxy solid, but after sublimation was crystalline in form. However, some benzenoid material was present. The procedure of Foote *et al.* (17) also, in our hands gave material having some benzenoid absorption. Separation by t.l.c. eliminated this impurity but some diene absorption ($\lambda_{max} \sim 230$ nm) remained. This could not effectively be further purified and was used as such.

Irradiation

(a) A solution of 125 mg of the endoperoxide (6) in 25 ml cyclohexane was irradiated as described for ascaridole (1.5 h). The mixture was separated by t.l.c.

⁴The irradiation of epoxides at 254 mm has been recorded (13) but beyond this wavelength there is insufficient absorption for reaction to occur under normal conditions of irradiation.

(eluant ether:benzene, 1:4). Two main products were isolated:

(i) The alcohol (9) (28 mg; 22%), v_{max} (CHCl₃) 3600, 3400, 1680 cm⁻¹; λ_{max} (cyclohexane) 220 nm (ϵ 6700). Vinylic protons were present in the n.m.r. spectrum at δ 6.95 and 5.92. These protons were not present in the n.m.r. spectrum of the crude irradiation mixture.

Anal. Calcd. for C₆H₈O₂: C, 64.27; H, 7.19. Found: C, 63.87; H, 7.29.

(ii) The bisepoxide (10) (35 mg; 27%). This substance was optically transparent (210-300 nm) and showed no hydroxyl or carbonyl absorption in the i.r. spectrum. The n.m.r. spectrum showed signals in the region δ 3.0–3.3 for four protons and at 1.77 for a similar number.

Anal. Calcd. for C₆H₈O₂: C, 64.27; H, 7.19. Found: C, 63.71; H, 7.48.

(b) Irradiation of a nitrogen-flushed solution of 102 mg of the endoperoxide in 20 ml methanol at -70° for 7 h gave 9 and 10 in 24 and 29% yield respectively.

Thermal Rearrangement

A solution of 245 mg of the endoperoxide in 6 ml xylene was refluxed for 3 h. The reaction product, which appeared cleaner than that obtained by irradiation, consisted essentially of 9 and 10. Separation by t.l.c. gave 45 and 36% respectively, of these substances.

1,3,5,5-Tetramethyl-1,3-cyclohexadiene Endoperoxide

The diene (2 g) in 200 ml methanol containing 35 mg Rose Bengal was irradiated (300 W tungsten lamp) with the concomitant passage of oxygen. The endoperoxide (7) was partly purified by chromatography and t.l.c. (0.82 g; 41 %) but contained small amounts of a heteroannular diene (λ_{max} 236) which was a contaminant of the starting material.

Irradiation

A solution of 200 mg endoperoxide in 200 ml cyclohexane on irradiation (6 h) gave two major products and several substances in minor amounts which were not further investigated. The two main products were isolated by t.l.c. One was the enone 11, v_{max} (CHCl₃) 3600, 3400, and 1685 cm⁻¹; λ_{max} (MeOH) 228 nm (ϵ 7600).

Anal. Calcd. for C10H16O2: C, 71.39; H, 9.59. Found: C, 70.75; H, 9.30.

The second substance was the bisepoxide (12) n.m.r (CDCl₃) δ: 2.88H (1H, S), 2.56 (1H, S), 1.53 (3H, S), 1.31 (3H, S), 1.02 (3H, S), and 0.97 (3H, S).

The methylene group appeared as an AB centered approximately at 1.42 ($J \sim 15$ Hz), but only the outside two of the four peaks were resolved, one of the center two being a shoulder on the 1.31 singlet and the other being observed by the 1.53 singlet.

Anal. Calcd. for C₁₀H₁₆O₂: C, 71.39; H, 9.59. Found: C, 71.48; H, 9.77.

Methyl Levopimarate Endoperoxide (8)

(a) This was prepared by the method of Schuller and Lawrence (18). Irradiation of 210 mg in 60 ml cyclohexane (5 h) gave two main products. Separation by t.l.c. gave: (i) 78 mg of 13 (30%) m.p. 147-148°. Recrystallization from methanol gave material of m.p. 149-150°; v_{max} (CCl₄) 1725, 1705, 1245 cm⁻¹.

Anal. Calcd. for C21H32O4: C, 72.38; H, 9.26. Found: C, 72.60; H, 9.31.

(ii) The bisepoxide, 14, 63 mg (31%), m.p. 118-119° unchanged on further crystallization from methanol v_{max} (CCl₄) 1725, 1245 cm⁻¹.

Anal. Calcd. for C21H32O4: C, 72.38; H, 9.26. Found: C, 72.53; H, 9.45.

(b) Thermal rearrangement of 75 mg of the endoperoxide in 7 ml refluxing xylene for 8 h gave 13 and 14 in 41 and 29% yields respectively.

(c) Solutions of the endoperoxide (35 mg) in (i) cyclohexane, (ii) dioxane, and dioxane containing (iii) 120 mg Michler's ketone, (iv) 150 mg phenanthrene, and (v) 150 mg triphenylamine were irradiated on a merry-go-round as described for ascaridole. After 2 h the presence of the irradiation products was readily detectable in tubes (iii) to (v) but not in (i) and (ii). After 6 and 18 h the difference was more marked (at least a factor of 10).

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