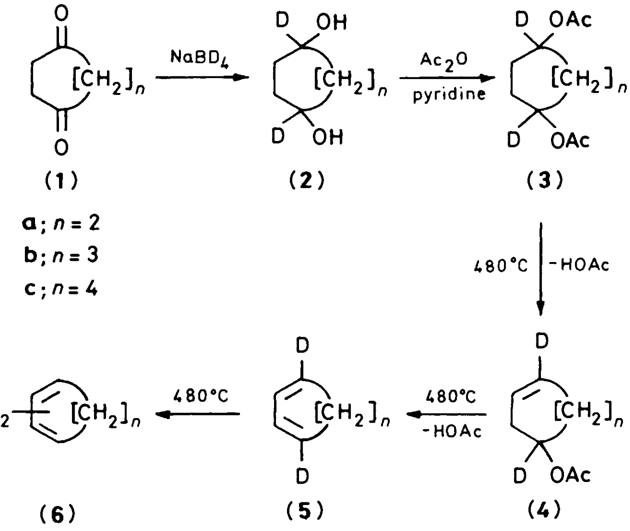
Use of Deuteriation, Endoperoxidation, and ^2H Nuclear Magnetic Resonance Spectroscopy to Demonstrate Thermal [1,5] Sigmatropic Rearrangements in Cycloalka-1,3-dienes

A. J. Bloodworth* and Henny J. Eggelte
Christopher Ingold Laboratories, Chemistry Department, University College London, 20 Gordon Street, London WC1H 0AJ

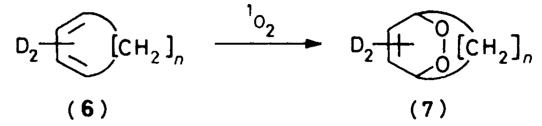
The ^2H n.m.r. spectra of the mixtures of endoperoxides obtained by photo-oxygenation of pyrolysed 1,4-diacetoxy-1,4-dideuteriocyclo-hexane, -heptane, and -octane demonstrate that 1,5-migrations of hydrogen and deuterium in the corresponding dideuteriated cycloalka-1,3-dienes proceed to equilibrium in less than 5 s at 480 °C.

Although the occurrence of [1,5] sigmatropic migrations of hydrogen is now widely accepted,[1] the experimental evidence for such migrations in deuteriated C_6—C_8 cycloalka-1,3-dienes is poor. Thus, thermal scrambling of the deuterium label of 5-deuteriocyclo-octa-1,3-diene was detected by observing a change in the ratio of the ^1H n.m.r. peak areas for vinylic, allylic, and homoallylic protons from 1:0.75:1 to 1:1:1.[2] The evidence for scrambling in monodeuteriocyclohepta-1,3-diene rested on i.r. and Raman spectra, which indicated the presence of only vinylic deuterium in the starting material but of similar amounts of vinylic and non-vinylic deuterium after thermolysis.[3] There do not appear to have been any studies with deuteriated cyclohexa-1,3-dienes.

We now report the use of ^1H-decoupled ^2H n.m.r. spectroscopy to detect [1,5] sigmatropic rearrangements in deuteriated C_6—C_8 cycloalka-1,3-dienes. This method provides a more direct and more complete analysis of the deuterium scrambling than has been achieved hitherto. Furthermore, by isolating the scrambled dienes as their singlet oxygen adducts (endoperoxides), we have obviated the need for tedious g.l.c. separations to remove the isomeric cycloalka-1,4-dienes that are produced competitively during the synthesis of the conjugated isomers.



Scheme 1.



Scheme 2.

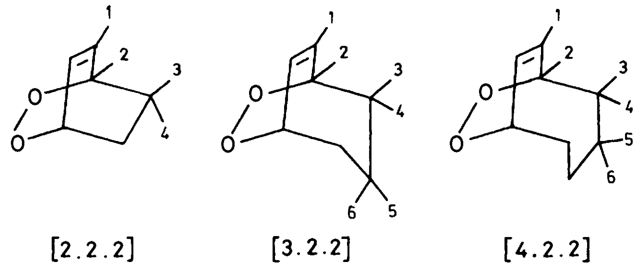
Results and Discussion

The method by which the labelled cycloalka-1,3-dienes were prepared is shown in Scheme 1. Cycloalkane-1,3-diones (**1**)[4] were reduced with sodium borodeuteride and the resultant diols (**2**) were acetylated. The 1,4-diacetates (**3**), each a mixture of *cis*- and *trans*-isomers, were pyrolysed[5] at 480 °C with contact times of 3—5 s. This afforded the 1,4-dideuteriocycloalka-1,3-dienes (**5**) under conditions where [1,5] sigmatropic rearrangements also took place, so that the specifically labelled dienes (**5**) were not observed; instead the scrambled mixtures (**6**) were obtained directly. However, in the pyrolysis of the cyclohexane diacetate (**3a**), we recovered some starting material and also obtained compelling spectroscopic evidence for the formation of the intermediate monoacetate (**4a**). This not only provides support for the pathway of thermolysis outlined in Scheme 1, but also confirms that no molecular rearrangements take place before the second molecule of acetic acid is eliminated.

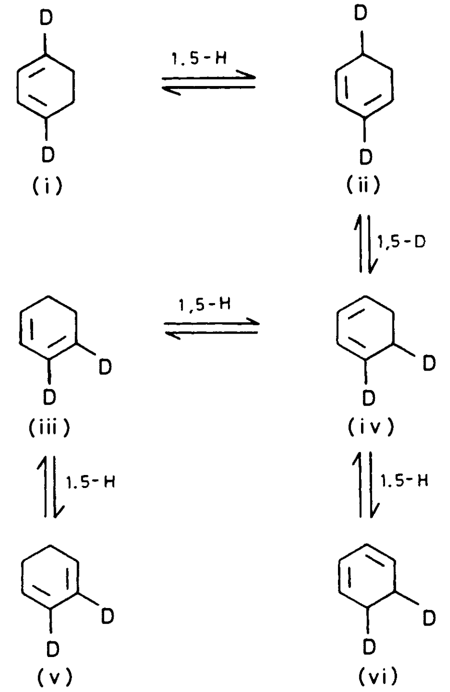
Of course the pyrolyses additionally afforded non-conjugated cycloalkadienes, but we circumvented the need to carry out separations by converting the conjugated species (**6**) into the corresponding endoperoxides (7) (Scheme 2). This was conveniently achieved by dye-sensitized photo-oxygenation, which is known to proceed without molecular rearrangements.[6] The endoperoxides (**7a**—**c**), each a mixture of several isomeric dideuteriated species (see later), were then readily isolated as crystalline solids by chromatography on silica.

Mass spectra confirmed that each endoperoxide contained two deuterium atoms, and the ^1H-decoupled ^2H n.m.r. spectrum of each endoperoxide mixture showed the number of lines and intensities expected for complete scrambling of the deuterium labels, *i.e.* each spectrum accurately reflected the number and relative abundance of the different sites at which deuterium can reside (see Scheme 3).

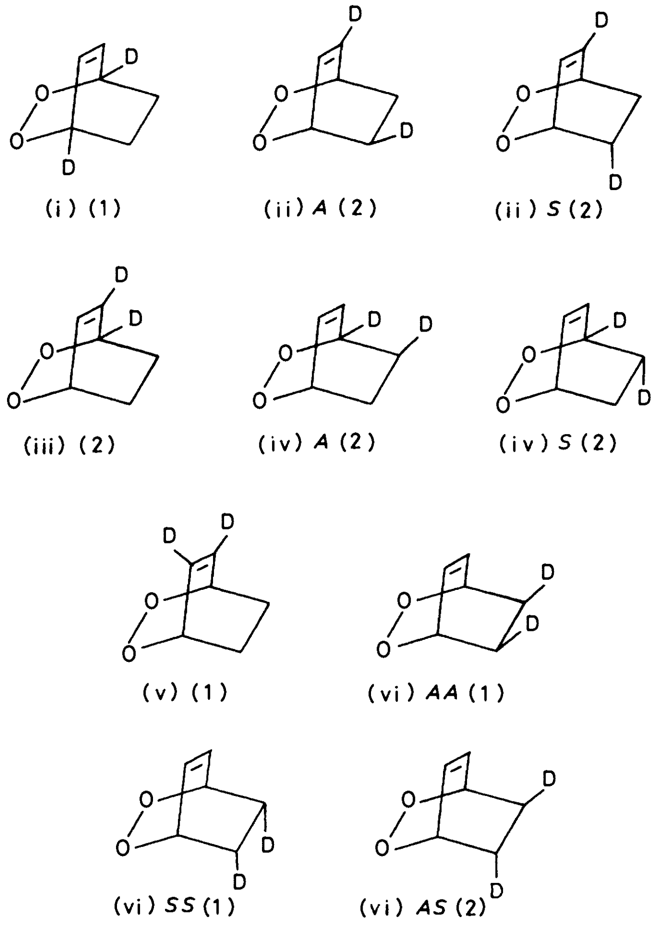
Thus, the [2.2.2] endoperoxide possesses four pairs of sites and the spectrum of the endoperoxide mixture (**7a**) consisted of four lines of equal intensity at appropriate chemical shifts (δ 6.62, 4.49, 2.17, and 1.37). Similarly, the six different sites and their relative abundancies in the [3.2.2] and [4.2.2] endoperoxides were reflected in the six-line spectra obtained for endoperoxide mixtures (**7b**) and (**7c**), with equal line intensities for (**7c**) (δ 6.22, 4.70, 2.13, 1.92, 1.79, and 1.61), and relative



Scheme 3. Sites for deuteriation in the [2.2.2], [3.2.2], and [4.2.2] endoperoxides



Scheme 4. Cyclohexa-1,3-dienes (**6a**)



Scheme 5. [2.2.2] Endoperoxides (**7a**)

intensities of 2:2:2:2:1:1 for (**7b**) (δ 6.32, 4.57, 1.85, 1.79, 1.50, and 1.29).

To appreciate fully the significance of these ^{2}H n.m.r. spectra it is necessary to consider in detail the identities of all the isomeric endoperoxides that must be present, in order to account for the complete scrambling observed. Scheme 4 shows the six dideuteriocyclohexa-1,3-dienes (**6a**) that can arise by [1,5] sigmatropic rearrangements. At equilibrium, a statistical distribution of these will be present, *i.e.* [(i) + 4(ii) + 2(iii) + 4(iv) + (v) + 4(vi)].* They will give rise to the ten endoperoxides shown in Scheme 5, since the saturated sites are now distinguishable as being *anti* (*A*) or *syn* (*S*) to the dioxygen bridge. The labelling of these endoperoxides is designed to indicate the diene from which each is derived together with the *anti* or *syn* nature of any deuterium atoms on the dimethylene bridge. The numbers in parentheses after the labels indicate the statistical distribution expected from singlet oxygenation of the equilibrium mixture of dienes (**6a**).

By summing the numbers of each of the four types of deuteron (olefinic, bridgehead, *anti*, and *syn*),† it is immediately apparent that only the *complete* mixture of endoperoxides given in Scheme 5 can account for the observed ^{2}H n.m.r. spectrum in which all peaks are of equal intensity. Thus, dideuteriation, endoperoxidation, and ^{2}H n.m.r. spectroscopy together demonstrate that [1,5] sigmatropic rearrangements involving migrations of both hydrogen and deuterium around a cyclohexa-1,3-diene ring proceed rapidly to equilibrium at 480 °C.

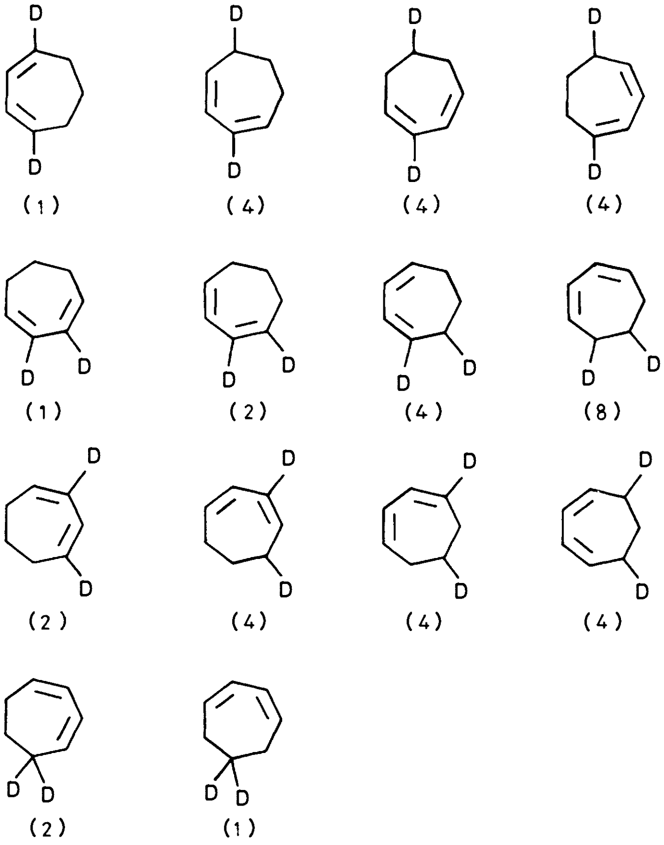
Since the equilibrium mixture (Scheme 4) contains 1,2-dideuteriated cyclohexadienes [(iii)—(vi)] in addition to the 1,4-dideuteriated species [(i) and (ii)], it should be possible to obtain the same result by thermolysing a 1,2-dideuteriated isomer. The pyrolysis of *cis*-5,6-dideuteriocyclohexa-1,3-diene has been reported,[7] but the investigation centred on the distribution of deuterium in the benzene formed by dehydrogenation. In the light of our results, it seems safe to assume that the equilibration outlined in Scheme 4, entering now *via* structure (vi) rather than structure (i), will be complete before any substantial amount of dehydrogenation takes place.‡ The mechanism of thermal dehydrogenation of cyclohexa-1,3-diene is believed to involve a radical chain process,[8] which amounts to

---

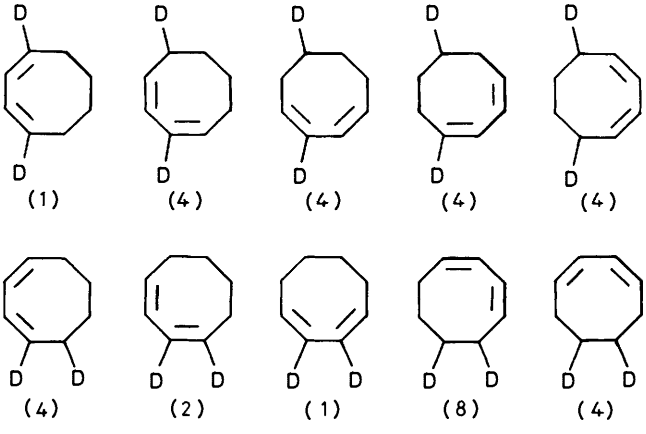
* Calculated by summing the numbers of equivalent structures in the cycle of sigmatropic rearrangements that returns the molecule to its original form, remembering that there are two possibilities whenever a deuterium atom occupies a saturated site.

† The isotope effect upon ^{2}H n.m.r. chemical shifts of even a vicinal deuterium atom is expected to be negligible.

‡ The ^{1}H n.m.r. spectrum of our pyrolysate indicated the presence of benzene, but this amounted to less than 10% of the total hydrocarbon product and, in any case, it probably arises mainly from cyclohexa-1,4-diene, which dehydrogenates more readily than the conjugated diene.



Scheme 6. Cyclohepta-1,3-dienes (**6b**)



Scheme 7. Cyclo-octa-1,3-dienes (**6c**)

a stepwise, and therefore non-stereospecific, 1,2-elimination. Random 1,2-eliminations from the equilibrium mixture of the dideuteriated cyclohexa-1,3-dienes [(i) + 4(ii) + 2(iii) + 4(iv) + (v) + 4(vi)] (see before) is calculated to yield a mixture containing 56% of $[^2H_2]$benzene, 38% of $[^2H_1]$benzene, and 6% of $[^2H_0]$benzene. The reported experimental figures were 63%, 29%, and 6% respectively.[7] The discrepancy can be accounted for by the operation of a small isotope effect.

The ^2H n.m.r. spectra obtained for the [3.2.2] and the [4.2.2] endoperoxide mixtures (**7b** and **c**) similarly require that the corresponding cycloalka-1,3-dienes are equilibrated *via* thermal 1,5-migrations of hydrogen and deuterium under the conditions of pyrolysis. The cycloheptadiene is the more complicated case, the sigmatropic rearrangements giving rise to the distribution of compounds shown in Scheme 6. The $[1,4-^2H_2]$, $[1,2-^2H_2]$, $[1,3-^2H_2]$, and $[1,1-^2H_2]$ dienes afford seven, seven, eight, and two isomeric endoperoxides, respectively, making 24 in all, and accounting for the observed statistical distribution of the six types of deuteron.

Sigmatropic rearrangements in the cyclo-octadiene give rise to the simpler equilibrium mixture shown in Scheme 7. The $[1,4-^2H_2]$ and $[1,2-^2H_2]$ dienes each afford ten isomeric endoperoxides and the complete mixture contains equal numbers of the six types of deuteron, thereby once again accounting for the observed ^2H n.m.r. spectrum.

Experimental

^1H-Decoupled ^2H n.m.r. spectra (31 MHz) were measured with a Varian XL200 spectrometer for solutions in CCl_4 with $CDCl_3$ as internal reference; the chemical shifts quoted are in p.p.m. from $(CD_3)_4Si$, assuming δ 7.27 for $CDCl_3$. ^1H N.m.r. spectra (60 MHz) and ^1H-decoupled ^{13}C n.m.r. spectra (20 MHz) were recorded with Perkin-Elmer R12 and Varian CFT20 spectrometers, respectively, for solutions in $CDCl_3$ or CCl_4 with $SiMe_4$ as internal reference, or in D_2O with CH_3CN (δ_C 1.3) as internal reference. Mass spectra were obtained with a VG 7070 F/H mass spectrometer plus Finnigan INCOS data system.

Preparation of 1,4-*Dideuteriocycloalkane*-1,4-*diols* (**2**).—A solution of $NaBD_4$ (1.4 g, 33 mmol) in aqueous NaOH (1M; 60 cm^3) was added to cyclohexane-1,4-dione (6.5 g, 58 mmol) and the mixture was stirred overnight. Continuous extraction with diethyl ether then afforded the diol (**2a**) (5.5 g, 80%), $\delta_C(D_2O)$ 66.9 [t, $^1J(^2H-^{13}C)$ 21.5 Hz], 65.1 [t, $^1J(^2H-^{13}C)$ 20.5 Hz], 29.7, and 27.0.

A solution of $NaBD_4$ (0.5 g, 12 mmol) in aqueous NaOH (1M; 25 cm^3) was added to a solution of cycloheptane-1,4-dione (3.15 g, 25 mmol) in tetrahydrofuran (25 cm^3) and the mixture was stirred for 2 h. Continuous extraction with diethyl ether then afforded the diol (**2b**) (2.86 g, 87%), $\delta_C(D_2O)$ 72.6 [t, $^1J(^2H-^{13}C)$ 21 Hz], 72.1 [t, $^1J(^2H-^{13}C)$ 21 Hz], 37.8, 37.2, 31.8, 30.9, 19.8, and 18.6.

$NaBD_4$ (0.165 g, 3.9 mmol) was added to a solution of cyclo-octane-1,4-dione (0.540 g, 3.9 mmol) in ethanol (20 cm^3) and the mixture was stirred overnight. The ethanol was then removed at a water pump and the residue dissolved in water (20 cm^3). Extraction with dichloromethane (6 × 20 cm^3) afforded the diol (**2c**) (0.480 g, 85%), $\delta_C(CDCl_3)$ 71.0 [t, $^1J(^2H-^{13}C)$ 21.9 Hz, 2C], 33.3, 33.0, 30.4 (2C), 22.7, and 22.3.

Preparation of 1,4-*Diacetoxy*-1,4-*dideuteriocycloalkanes* (**3**).—A mixture of 1,4-dideuteriocyclohexane-1,4-diol (1.9 g, 16 mmol) and acetic anhydride (3.5 g, 34 mmol) in pyridine (5 cm^3) was heated at 90 °C for 2 h, and the product was partitioned between hydrochloric acid (2M) and dichloromethane. The dichloromethane layer was washed with aqueous $NaHCO_3$ and dried ($MgSO_4$), and the solvent was removed at a water pump to afford the diacetate (**3a**) (2.97 g, 91%), $\delta_H(CDCl_3)$ 2.0 (s, 6 H) and 2.2—1.3 (m, 8 H); $\delta_C(CDCl_3)$ 170.0, 169.9, 70.5 [t, $^1J(^2H-^{13}C)$ 22.5 Hz], 69.7 [t, $^1J(^2H-^{13}C)$ 22.8 Hz], 28.0, 27.3, and 21.1.

1,4-Dideuteriocycloheptane-1,4-diol (2.35 g) was similarly converted into the diacetate (**3b**) (3.21 g, 83%), $\delta_H(CCl_4)$ 2.0 (s, 6 H) and 2.3—1.3 (m, 10 H); $\delta_C(CDCl_3)$ 170.1, 73.5 [t, $^1J(^2H-^{13}C)$ 22.2 Hz], 73.3 [t, $^1J(^2H-^{13}C)$ 22.0 Hz], 33.9, 33.8, 27.9, 27.6, 21.3, 18.7, and 18.3.

1,4-Dideuteriocyclo-octane-1,4-diol (0.480 g) was similarly converted into the diacetate (**3c**) (0.520 g, 69%), $\delta_H(CDCl_3)$ 2.0 (s, 6 H) and 2.2—1.4 (m, 12 H); $\delta_C(CDCl_3)$ 170.2, 73.5 [t, $^1J(^2H-^{13}C)$ 22.4 Hz, 2C], 30.5, 30.1, 27.5, 27.1, 22.8, 22.5, and 21.3.

Pyrolysis of Diacetates (**3**) *and Photo-oxygenation of the Resultant Pyrolysates.*—The pyrolysis set-up consisted of a vertical Pyrex column (20 cm × 18 mm i.d.) filled with Pyrex spheres (8 mm diam.) and maintained at 480 °C by an electrical heating tape. The top of the column was fitted with a stillhead, one arm of which was used to introduce the sample and the other to take a stream of nitrogen carrier gas. The products were collected in a Büchner flask connected to the bottom of the column and cooled in a bath of solid CO_2 and acetone, but to ensure complete recovery of the pyrolysate the exit gases were then passed through a trap cooled in liquid nitrogen. The liquid diacetates (**3b** and **c**) were introduced through a septum cap by syringe; the solid diacetate (**3a**) was placed in the side arm of the stillhead and heated until it melted and flowed on to the column under gravity.

After each pyrolysis, the combined contents of the Büchner flask and the trap were dissolved in CCl_4 (20—40 cm^3), washed with aqueous $NaHCO_3$ (20—40 cm^3), and dried ($MgSO_4$). For the cycloheptane and cyclo-octane derivatives, the solution was then diluted with more CCl_4 (100 cm^3), tetraphenylporphyrin (2—5 mg) was added, and oxygen was gently bubbled through the stirred mixture while it was irradiated with a 400 W sodium lamp for 5 h and 18 h, respectively. For the cyclohexane derivative, the initial solution was trap-to-trap distilled (20 °C; 20 mmHg) and the distillate was then diluted with CCl_4 and photo-oxygenated similarly for 2 h.

Each endoperoxide mixture (**7**) was isolated by chromatography on Merck silica (70—230 mesh) with CH_2Cl_2 as eluant. The ${}^1H$ n.m.r. spectra of the endoperoxides (**7**) closely resembled those of the fully protiated compounds, the only difference being that the fine structure of the multiplets was less well defined. The ${}^1H$-decoupled ${}^{13}C$ n.m.r. spectra consisted primarily of singlets with the same chemical shifts as for the fully protiated compounds. Under the usual conditions of spectral accumulation (no pulse delay), triplets arising from carbon nuclei with an attached deuterium atom were detected only for the methylene carbon atoms, and the usual small isotope effect upon chemical shift[9] was observed. Analogous triplets for the olefinic and bridgehead carbon atoms became discernible when a pulse delay was employed, but the signals remained markedly weaker than those for the methylene carbon atoms, presumably because of the absence of any Overhauser effect. Individual results follow.

1,4-Diacetoxy-1,4-dideuteriocyclohexane (**3a**) (1.3 g) afforded the [2.2.2] endoperoxide mixture (**7a**) (0.240 g, 33%), $\delta_H(CCl_4)$ 6.7 (m), 4.55 (br s), 2.4—2.0 (m), and 1.55—1.2 (m) (*cf.* 2,3-dioxabicyclo[2.2.2]oct-5-ene[10]); $\delta_C(CDCl_3)$ 132.2, 70.8, and 21.6, and 21.3 [t, ${}^1J({}^2H-{}^{13}C)$ 20.2 Hz] (*cf.* 2,3-dioxabicyclo-[2.2.2]oct-5-ene[11]); *m/z* 114 (M^+).

The ${}^{13}C$ n.m.r. spectrum of the residue from the trap-to-trap distillation of the pyrolysate showed the following absorptions, which are assigned to the monoacetate (**4a**): $\delta_C(CDCl_3)$ 126.5 [t, ${}^1J({}^2H-{}^{13}C)$ 23.4 Hz], 123.6, 30.7, and 23.2; the remaining signals presumably overlap with those of the starting diacetate (**3a**) (see before).

1,4-Diacetoxy-1,4-dideuteriocycloheptane (**3b**) (2.6 g) afforded the [3.2.2] endoperoxide mixture (**7b**) (0.270 g, 18%), $\delta_H(CCl_4)$ 6.35 (dd), 4.55 (m), and 2.2—1.2 (m); $\delta_C(CDCl_3)$ 128.0, 77.3, 31.7, and 18.4, and 31.4 [t, ${}^1J({}^2H-{}^{13}C)$ 19.4 Hz], and 18.1 [t, ${}^1J({}^2H-{}^{13}C)$ 20.0 Hz]; *m/z* 128 (M^+).

1,4-Diacetoxy-1,4-dideuteriocyclo-octane (**3c**) (0.42 g) afforded the [4.2.2] endoperoxide mixture (**7c**) (0.037 g, 14%), $\delta_H(CDCl_3)$ 6.08 (dd), 4.72 (m), 2.0—1.6 (m), and 1.6—1.2 (m) (*cf.* 7,8-dioxabicyclo[4.2.2]dec-9-ene[12]), $\delta_C(CDCl_3)$ 128.2, 76.6, 33.2, and 24.0, and 32.8 [t, ${}^1J({}^2H-{}^{13}C)$ 19.5 Hz], and 23.6 [t, ${}^1J({}^2H-{}^{13}C)$ 21.1 Hz] (*cf.* 7,8-dioxabicyclo[4.2.2]dec-9-ene[11]); *m/z* 142 (M^+).

References

1 C. W. Spangler, *Chem. Rev.*, 1976, **76**, 187.
2 D. S. Glass, R. S. Boikess, and S. Winstein, *Tetrahedron Lett.*, 1966, 999.
3 V. A. Mironov, O. S. Chizhov, Ya. M. Kimelfeld, and A. A. Akhrem, *Tetrahedron Lett.*, 1969, 499.
4 (*a*) A. J. Bloodworth, D. S. Baker, and H. J. Eggelte, *J. Chem. Soc., Chem. Commun.*, 1982, 1034; (*b*) A. J. Bloodworth and H. J. Eggelte, *Tetrahedron Lett.*, 1984, **25**, 1525.
5 R. F. C. Brown, 'Pyrolytic Methods in Organic Chemistry,' Academic Press, New York, 1980, p. 85, and references therein.
6 A. J. Bloodworth and H. J. Eggelte in 'Singlet O_2,' ed. A. A. Frimer, C.R.C. Press Inc., Boca Raton, 1985, vol. II, ch. 4.
7 I. Fleming and E. Wildsmith, *J. Chem. Soc., Chem. Commun.*, 1970, 223.
8 S. W. Benson and R. Shaw, *J. Am. Chem. Soc.*, 1967, **89**, 5351.
9 A. J. Bloodworth and H. J. Eggelte, *J. Chem. Soc., Perkin Trans. 2*, 1984, 2069.
10 C. S. Foote, S. Wexler, W. Ando, and R. Higgins, *J. Am. Chem. Soc.*, 1968, **90**, 975.
11 W. Adam and A. J. Bloodworth, *Top. Curr. Chem.*, 1981, **97**, 121.
12 K. Kayama, M. Oda, and Y. Kitahara, *Chem. Lett.*, 1974, 345.

Received 29th August 1984; *Paper* 4/1491