Oxymetallation. Part 11.[1,2] Synthesis of Cyclic Secondary Alkyl Peroxides *via* the Peroxymercuration of α,ω-Dienes
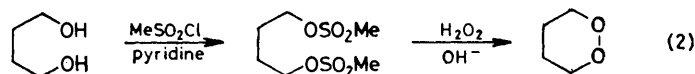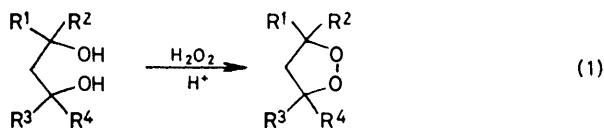
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Six cyclic peroxides of the form $O-(XCH_2)CH[CH_2]_nCH(CH_2X)-O$ [X = HgCl (1), H (2), or Br (3) ; $n = 1$ (a) or 2 (b)] have been prepared in high yield *via* the reaction of penta-1,4-diene or hexa-1,5-diene with hydrogen peroxide and mercury(II) nitrate. The new compounds are identified by ^1H and proton-decoupled ^{13}C n.m.r. spectroscopy and additionally by mass spectrometry where X = H or Br; compound (1a) isomerises to a β-oxo-alcohol when dissolved in pyridine. The 1,2-dioxacyclopentanes are obtained as approximately equimolar mixtures of *cis*- and *trans*-isomers whereas the 1,2-dioxacyclohexanes contain about three times as much *trans*- as *cis*-isomer. The configurations are assigned on the basis of ^{13}C and ^1H n.m.r. chemical shifts and variable-temperature n.m.r. spectra.

PRINCIPAL methods for synthesising cyclic peroxides involve autoxidation, photo-oxygenation, or nucleophilic displacement with hydrogen peroxide. Of these, only nucleophilic displacement can be used to make simple 1,2-dioxacyclo-pentanes and -hexanes, and conventional variations of the method are intrinsically unsuitable for preparing cyclic *secondary* alkyl compounds. The acid-catalysed reaction of 1,3-diols with concentrated hydrogen peroxide [equation (1)] has provided a series of 1,2-dioxacyclopentanes with tertiary carbon atoms next to the peroxide linkage [3-5] and

3,3,6,6-tetramethyl-1,2-dioxacyclohexane has been prepared by an analogous route.[3] The displacement of methylsulphonyl groups by basic hydrogen peroxide has afforded the unsubstituted 1,2-dioxacyclohexane [equation (2) [6,7]].

Even in these structurally favourable cases the yields are often no better than 30% [3,6,7] but when the bis-(methanesulphonate) method was used to synthesise the secondary compounds 3-methyl-5-(2-phenylethyl)-1,2-dioxacyclopentane and 3,5-bis-(2-phenylethyl)-1,2-dioxacyclopentane the yields fell to 7 and 0.5%, respectively.[8]

$$ (1) $$

$$ (2) $$

[1] Part 10, A. J. Bloodworth and M. E. Loveitt, *J.C.S. Perkin I*, 1977, 1031.

[2] Preliminary account, A. J. Bloodworth and M. E. Loveitt, *J.C.S. Chem. Comm.*, 1976, 94; corrigendum: *cis* and *trans* should be interchanged throughout.

[3] R. Criegee and G. Paulig, *Ber.*, 1955, **88**, 712.

[4] W. Adam and N. Durán, *J.C.S. Chem. Comm.*, 1972, 279.

[5] W. Adam and N. Durán, *J. Org. Chem.*, 1973, **38**, 1434.

[6] R. Criegee and G. Müller, *Chem. Ber.*, 1956, **89**, 238.
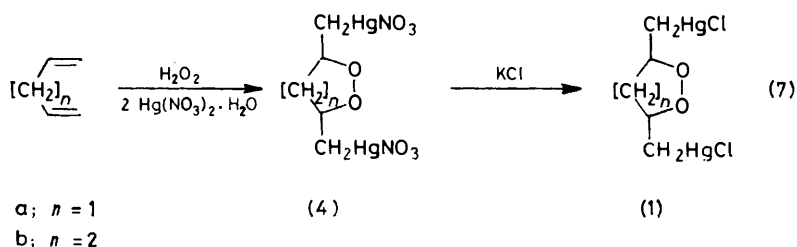
[7] H. D. Holtz, P. W. Solomon, and J. E. Mahan, *J. Org. Chem.*, 1973, **38**, 3175.

[8] P. M. Jacobs and A. H. Soloway, *J. Org. Chem.*, 1974, **39**, 3427.

A five-fold improvement in the yield of 3-methyl-5-(2-phenylethyl)-1,2-dioxacyclopentane was recently achieved by carrying out the nucleophilic displacement with potassium superoxide and a crown ether in dimethyl sulphoxide.[9,*]

In recent years we have developed a new route to acyclic dialkyl peroxides which is particularly suitable for preparing secondary alkyl compounds. The method involves the combination of peroxymercuration and hydrogenodemercuration and has been used to provide t-butyl secondary alkyl peroxides [equation (3)[10]] in much higher yields than are afforded by conventional

$$RCH{:}CH_2 \xrightarrow[Bu^tOOH]{HgX_2} XHgCH_2CHROOBu^t \xrightarrow[OH-]{NaBH_4} CH_3CHROOBu^t \quad (3)$$

routes. We have also shown [1] that if hydrogen peroxide is used in the peroxymercuration stage then the β-mercurioalkyl hydroperoxide that is generated can itself function as the nucleophile in a subsequent addition [equation (4)]. The assumption underlying this work

$$H_2O_2 \xrightarrow[HgX_2]{RCH{:}CH_2} XHgCH_2CHROOH \xrightarrow[HgX_2]{RCH{:}CH_2} (XHgCH_2CHRO)_2 \quad (4)$$

was that by linking the two alkene functions together in an appropriate αω-diene, this system could be modified to provide a synthesis of cyclic peroxides in which both carbon atoms adjacent to oxygen are secondary [equation (5)].

of intramolecular alkoxymercuration and aminomercuration are both well established.[11] Furthermore they appear to proceed *only* if 5- or 6-membered ring formation results, but if this can occur, it is strongly preferred to any competing intermolecular reactions. This augured well for the proposed synthesis of 3,5-bis(mercuriomethyl)-1,2-dioxacyclopentane [equation (5), $n = 1$] and 3,6-bis(mercuriomethyl)-1,2-dioxacyclohexane [equation (5), $n = 2$].

We now report the peroxymercuration of penta-1,4-diene and hexa-1,5-diene and the isolation of the resulting cyclic secondary alkyl peroxides in high yield as the organomercury chlorides (1). We also describe how subsequent demercurations [equation (6)] provide excellent yields of the corresponding dimethyl-1,2-dioxacycloalkanes (2) and bis(bromomethyl)-1,2-dioxacycloalkanes (3).

RESULTS AND DISCUSSION

Peroxymercuration.—(a) *Choice of mercury*(II) *salt.* Although we employed mercury(II) trifluoroacetate to prepare acyclic bis-β-mercurioalkyl peroxides [1] [equation (4); $X = CF_3CO_2$], attempts to extend its use to the diene systems met with only moderate success. With hexa-1,5-diene the procedure adopted in the earlier work with alkenes [1] afforded 56% of crude 3,6-bis-(trifluoroacetoxymercuriomethyl)-1,2-dioxacyclohexane [equation (5); $n = 2$, $X = CF_3CO_2$], but n.m.r. spectroscopy revealed the presence of impurities and the yield was halved in the process of isolating the pure organomercury chloride. No cyclic peroxide could be isolated

(5)

(6)

(3)   (1)   (2)   a; $n = 1$

b; $n = 2$

The scheme of equation (5) requires that the unsaturated hydroperoxide initially formed should participate in the previously unknown process of intramolecular peroxymercuration. The analogous reactions

from a similar reaction with penta-1,4-diene, and the i.r. spectrum of the product suggested that extensive trifluoroacetoxymercuration had taken place.

Originally mercury(II) trifluoroacetate was introduced

* *Note added in proof.* It has now been reported (M. F Salomon and R. G. Salomon, *J. Amer. Chem. Soc.*, 1977, **99**, 3500) that 1,2-dioxacyclopentane, 3,5-dimethyl-1,2-dioxacyclopentane, and 1,2-dioxacyclohexane can be prepared by the reaction of appropriate alkyl bis(trifluoromethanesulphonates) with bis(tributyltin) peroxide; the method also affords 1,2-dioxacycloheptane and -octane.

[9] E. J. Corey, K. C. Nicolaou, M. Shibasaki, Y. Machida, and C. S. Shiner, *Tetrahedron Letters*, 1975, 3183.

[10] (a) D. H. Ballard, A. J. Bloodworth, and R. J. Bunce, *Chem. Comm.*, 1969, 815; (b) D. H. Ballard and A. J. Bloodworth, *J. Chem. Soc.* (C), 1971, 945; (c) A. J. Bloodworth and G. S. Bylina, *J.C.S. Perkin I*, 1972, 2433; (d) A. J. Bloodworth and I. M. Griffin, *J. Organometallic Chem.*, 1974, **66**, C1; (e) A. J. Bloodworth and I. M. Griffin, *J.C.S. Perkin I*, 1975, 195.

[11] H. Straub, K. P. Zeller and H. Leditschke, ' Houben-Weyl. Methoden der Organischen Chemie,' Band XIII/2b Metallorganische Verbindungen: Hg, Thieme Verlag, Stuttgart, 1974, pp. 153, 160, 188, 308.

in place of mercury(II) acetate in peroxymercuration because the fluorines attenuate the nucleophilicity of the carboxylic acid and anion and eliminate or reduce competing acyloxymercuration.[10d,e] The initial results with dienes suggested that we needed to use a mercury(II) salt with an anion of still lower nucleophilicity. We elected to try $Hg(NO_3)_2 \cdot H_2O$ because it is commercially available and because there is evidence [11] that the products of intramolecular alkoxymercuration are far more stable towards strong acids than are acyclic oxymercurials.

The change to mercury(II) nitrate proved highly successful and enabled us to isolate the organomercury chlorides (1) from both hexa-1,5-diene and penta-1,4-diene in yields of over 80% on a 5 mmol scale [equation (7)].

Dichloromethane was the solvent used for peroxymercurations with mercury(II) trifluoroacetate [1] and has

alkane (1) as a white precipitate. Details of compounds (1) are provided in Table 1 together with data for the cyclic peroxides prepared from them by hydrogeno- and bromo-demercuration (see later).

The fact that pure 3,5-bis(chloromercuriomethyl)-1,2-dioxacyclopentane (1a) is obtained in such high yield indicates that the reaction with penta-1,4-diene is very clean. The corresponding 1,2-dioxacyclohexane (1b) was isolated in lower yield and was not analytically pure, but examination of the crude organomercury nitrate [13]C n.m.r. spectroscopy (see next section) revealed no additional products.

(b) *Characterisation of the bis(mercuriomethyl)-1,2-dioxacycloalkanes.* As in the identification of earlier peroxymercurials [1,10] we have relied heavily on n.m.r. spectroscopy to establish the structures of the new compounds.

The [1]H n.m.r. spectra (Table 2) are complex for two

(7)

a; n = 1
b; n = 2

(4)   (1)

been retained for the reactions with $Hg(NO_3)_2 \cdot H_2O$ even though this salt is at best only sparingly soluble. The high strength (*ca.* 80%) hydrogen peroxide is added to a vigorously stirred suspension of $Hg(NO_3)_2 \cdot H_2O$ in dichloromethane followed immediately by the diene.

reasons. First, each product is obtained as a mixture of diastereoisomers in which the mercuriomethyl groups are either *cis* or *trans* with respect to the ring (see later). Thus each peroxymercurial gives rise to a [1]H n.m.r. spectrum that is the sum of the non-identical spectra of

TABLE 1

1,2-Dioxacycloalkanes prepared *via* reaction of αω-dienes with hydrogen peroxide and mercury(II) nitrate

$$XCH_2-CH \underset{O-O}{\overset{/[CH_2]_n\diagdown}{\diagup}} CH-CH_2X$$

Compound	n	X	% *trans*-Isomer [a]	M.p. (°C)	Found (%) C	H	Calc. (%) C	H	Yield [b] (%)
(1a)	1	HgCl	50	119—121 (decomp.)	10.3	1.4	10.5	1.4	92
(2a)	1	H	50	Liquid [c]	58.4	9.85	58.8	9.85	68 [d,e]
(3a)	1	Br	60	Liquid	23.0	3.2	23.1	3.1	51
(1b)	2	HgCl	95	183 (decomp.)	12.35	1.85	12.3	1.7	26 [f]
(2b)	2	H	80	Liquid [c]	62.85	10.65	62.05	10.4	72 [d]
(3b)	2	Br	75	63—70 [g]	25.8	3.65	26.3	3.7	75

[a] Calculated (to nearest 5%) from proton-decoupled [13]C n.m.r. spectrum assuming equal responses for corresponding carbons of the isomers; checked from [1]H n.m.r. spectrum where possible. [b] Based on diene. [c] Purified by g.l.c. [d] Of crude product indicated by analytical g.l.c. to contain *ca.* 90% of required peroxide. [e] For crude product, Found: C, 59.7; H, 10.0%. [f] From $Hg(O_2CCF_3)_2$; $Hg(NO_3)_2 \cdot H_2O$ afforded 82% of crude organomercury chloride (75% *trans*), m.p. 158—162 °C (decomp.) (Found: C, 11.2; H, 1.55%, suggesting the presence of about 10% of inorganic material). [g] Recrystallisation from CH_2Cl_2-pentane at −10 °C afforded pure *trans*-isomer, m.p. 91—92 °C.

It is important to get the diene into the system quickly otherwise mercury(II) nitrate and hydrogen peroxide react to evolve oxygen. An insoluble oil is formed which is presumably a very concentrated solution of the organomercury nitrate (4) in nitric acid. Treatment of an aqueous solution of this oil with potassium chloride affords the bis(chloromercuriomethyl)-1,2-dioxacyclo-

the individual diastereoisomers. Secondly, both exocyclic and endocyclic methylene protons are magnetically non-equivalent and with the methine protons attached to the asymmetric carbons constitute ABX systems. Owing to this complexity it was often difficult to identify unambiguously the satellites arising from coupling with naturally occuring [199]Hg nuclei.

The complication arising from non-equivalence of methylene protons is removed in the proton-decoupled ^{13}C n.m.r. spectra (Table 3), and these readily permit the ratios of isomers to be determined (Table 1). The crude organomercury nitrates were examined by ^{13}C n.m.r. spectroscopy and these data are included in Table 3.

in part by the base-induced cleavage that takes place in pyridine solution [e.g. equation (8), $X = CF_3CO_2$].[1] A similar reaction [equation (9)] occurs with compound (1a). This was monitored by ^1H n.m.r. spectroscopy and was essentially complete after 4 days at room temperature. The product had a broad singlet (^1H

TABLE 2

^1H N.m.r. spectra of 1,2-dioxacycloalkanes

Compound	n	X	Solvent	Isomer [a]	CH_2X	CH	$[CH_2]_n$
(1a)	1	HgCl	C_5H_5N [b]	cis	7.7 (d)	5.1 (m)	7.8 (m)
				trans	7.85 (d)		
(2a)	1	H	CCl_4	cis	8.74 (d) [c]	5.75 (ddq)	8.29 (dt) [d] / 7.23 (dt) [e]
				trans	8.78 (d) [c]	5.70 (tq)	7.81 (t) [f]
(3a)	1	Br	$CDCl_3$	cis and trans	6.44 (m)	5.35 (m)	7.37 (m)
(1b)	2	HgCl	C_5H_5N	cis	7.7 (d) [c]	5.5 (br m)	8.1 (br m)
				trans	7.95 (d) [c,g]		
(2b)	2	H	CH_2Cl_2	cis	8.84 (d) [c]	5.94 (m)	8.44 (m)
				trans	9.02 (d) [h]		
(3b)	2	Br	$CDCl_3$	cis	6.40 (m) [i]	5.69 (m)	8.02 (m)
				trans	6.61 (d) [c]		

n and X as in Table 1.

[a] See text for basis of assignment. [b] Spectrum recorded immediately after preparing solution. [c] ^3J 6.0 Hz. [d] ^2J 11.5 Hz, ^3J 6.5 Hz. [e] ^3J 7.2 Hz. [f] ^3J 6.7 Hz. [g] $^2J(^{199}Hg-^1H)$ 241 Hz. [h] ^3J 7.0 Hz. [i] AB part of ABX spectrum.

TABLE 3

Proton-decoupled ^{13}C n.m.r. spectra of 1,2-dioxacycloalkanes

Compound	n	X	Solvent	Isomer [a]	CH_2X	CH	$[CH_2]_n$
					δ [b] (p.p.m.)		
(4a)	1	HgNO$_3$	D_2O-HNO$_3$	cis	26.69	81.65	52.49
				trans	26.46	82.41	51.40
(1a)	1	HgCl	C_5H_5N [c]–CDCl$_3$	cis	31.60 [d]	81.96 [e]	53.65
				trans			53.42
(2a)	1	H	$CDCl_3$	cis	19.25	77.30	49.34
				trans	18.40	77.04	48.61
(3a)	1	Br	$CDCl_3$	cis	32.51	79.68	43.59
				trans	31.34	80.35	43.49
(4b)	2	HgNO$_3$	D_2O-HNO$_3$	cis	28.09 (?)	80.34	32.62
				trans	25.88	81.02	33.25
(1b)	2	HgCl	C_5H_5N [c]–C$_6$D$_6$	cis	28.80	79.53	34.27 [h]
				trans	30.75 [f]	80.02 [g]	
(2b)	2	H	$CDCl_3$	cis	18.18	76.30	27.04
				trans	18.79	77.08	31.58
(3b)	2	Br	$CDCl_3$	cis	23.48	79.57	30.61
				trans	27.30	80.19	

n and X as in Table 1.

[a] See text for basis of assignment. [b] Downfield from internal Me$_4$Si; spectra of compounds (4a) and (4b) were referenced to internal 1,4-dioxacyclohexane [δ(Me$_4$Si) 67.39]. [c] 70% v/v. [d] $^1J(^{199}Hg-^{13}C)$ 1 783 Hz. [e] $^2J(^{199}Hg-^{13}C)$ 62 Hz. [f] $^1J(^{199}Hg-^{13}C)$ 1 757 Hz. [g] $^2J(^{199}Hg-^{13}C)$ 72 Hz. [h] $^3J(^{199}Hg-^{13}C)$ 112, $^4J(^{199}Hg-^{13}C)$ 19 Hz.

Comparison with model compounds, notably the acyclic bis-β-mercurioalkyl peroxides,[1] indicate that the chemical shifts and ^{199}Hg coupling constants (^1H and ^{13}C) and multiplicities (^1H) are entirely consistent with

n.m.r.) at τ 6.8, assigned to ClHgCH_2CO by comparison with ClHgCH$_2$COCH$_3$ (CH_2 at τ 6.9),[1] and a signal (^{13}C n.m.r.) at δ 68.8, assigned to CH(OH) by comparison with RCH(OH)CH$_2$HgCl [CH at δ 61.7 (R = H) or 77.0

$$(XHgCH_2CHMeO)_2 \xrightarrow{\text{pyridine}} XHgCH_2COMe \ + \ MeCH(OH)CH_2HgX \qquad (8)$$

$$ClHgCH_2-CH{\overset{\displaystyle /CH_2\backslash}{\underset{\displaystyle O-O}{}}}CH-CH_2HgCl \xrightarrow{\text{pyridine}} ClHgCH_2COCH_2CH(OH)CH_2HgCl \qquad (9)$$
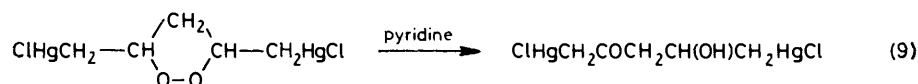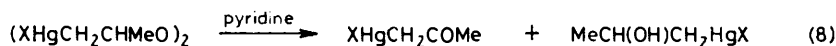
the proposed structures. The i.r. spectra of the organo-mercury chlorides showed no absorptions in the OH-stretching region, thus confirming the absence of hydro-peroxides.

Acyclic bis-β-mercurioalkyl peroxides were identified

(R = Ph)].[12] Compound (2a) was much more stable in pyridine and did not change appreciably during 5 days at room temperature.

In addition to their synthetic importance, the reactions

[12] A. J. Bloodworth and R. Peters, unpublished results.

with sodium borohydride and bromine discussed below provide additional evidence for the structures of the organomercury compounds.

*Hydrogenodemercuration.*—Analytical g.l.c. (silicone oil) indicated that the products obtained in almost

Presumably the unsaturated alcohols (5) arise through partial deoxymercuration followed by reduction of the resultant unsaturated hydroperoxide [equation (11)]. This contrasts with the behaviour of t-butyl peroxymercurials which afford epoxides as the byproducts,[10c]

(1) a; $n = 1$
     b; $n = 2$

(2) (90%)   (5) (10%)

(10)

(11)
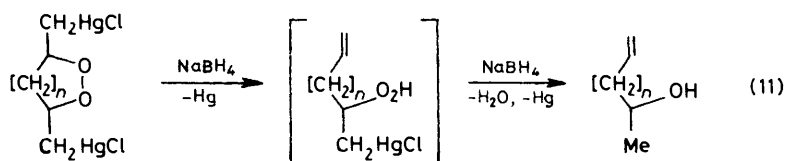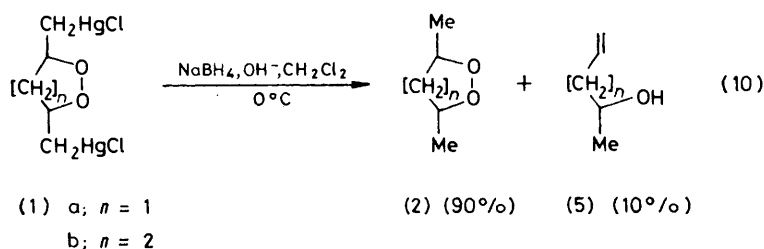
quantitative yield by reducing each peroxymercurial (1) with sodium borohydride are mixtures containing a major and a minor component. Each major component (*ca.* 90% of the mixture) was isolated by preparative g.l.c. (silicone oil) and identified by ^{1}H and proton-decoupled ^{13}C n.m.r. spectroscopy (Tables 2 and 3) as

but the occurrence of borohydride-induced deoxymercuration has been reported previously for other oxymercurials.[13]

The observed fragmentation patterns are summarised in the Scheme. Speculation on the detailed mechanism of ion fragmentations is not warranted but the formation
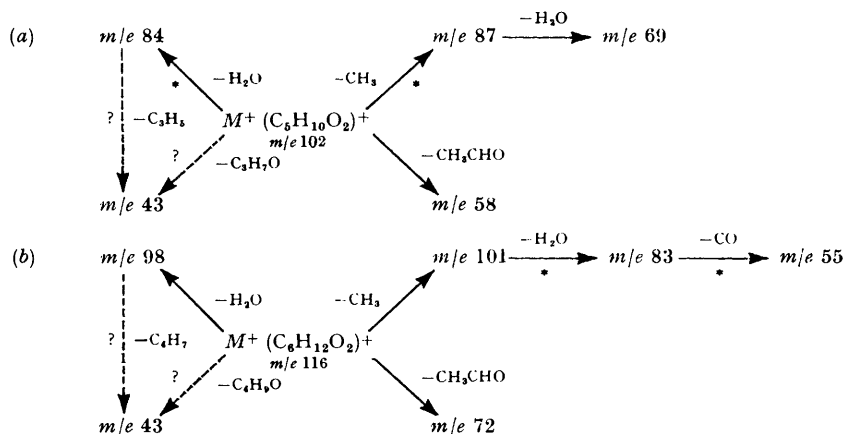
SCHEME   Mass-spectral fragmentation pattern for (*a*) 3,5-dimethyl-1,2-dioxacyclopentane (2a) and (*b*) 3,6-dimethyl-1,2-dioxacyclohexane (2b)

* Neutral loss supported by observation of the appropriate metastable ion.

the dimethyl-1,2-dioxacycloalkane (2) (Table 1). The minor component of the product from compound (1a) was shown to be pent-4-en-2-ol by comparing its g.l.c. retention time, ^{1}H n.m.r. spectrum, and ^{13}C n.m.r. spectrum with those of an authentic sample; by analogy it seems probable that the minor component of the product from compound (1b) was hex-5-en-2-ol. Thus the outcome of the reduction is summarised in equation (10).

of $(M - 15)^+$ and $(M - 44)^+$ ions can be envisaged as taking place *via* β-scission in the species produced by cleavage of the peroxide linkage in the molecular ion. On the other hand the formation of $(M - 18)^+$ and $(CH_3CO)^+$ ions appears to require rearrangements involving hydrogen migrations.

Bromodemercuration.—Bromodemercuration of acyclic peroxymercurials takes place under mild conditions and is generally a very clean reaction.[1,14] The organomercury chlorides (1) behaved similarly [equation (12)]

[13] (*a*) F. G. Bordwell and M. L. Douglass, *J. Amer. Chem. Soc.*, 1966, **88**, 993; (*b*) B. Giese, S. Gantert, and A. Schulz, *Tetrahedron Letters*, 1974, 3583.

[14] A. J. Bloodworth and I. M. Griffin, *J.C.S. Perkin I*, 1975, 695.

to provide the bis(bromomethyl)-1,2-dioxacycloalkanes (3) (Table 1). Partial separation of the diastereoisomers occurred in the isolation of compound (3a) and this enabled us to group its ^{13}C n.m.r. signals (see later).
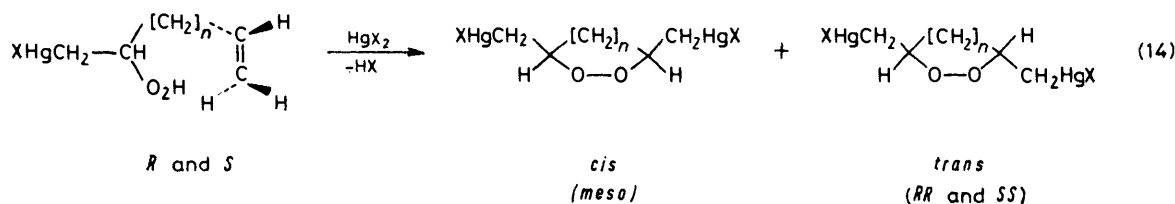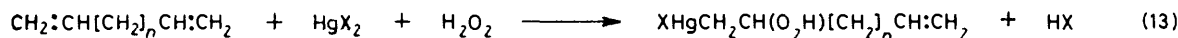
unequal amounts of the *cis*- and *trans*-isomers can be expected in general.

Using mercury(II) nitrate, the 5-membered ring peroxide was obtained as an approximately equimolar

$$(1) \quad a; \ n = 1$$
$$b; \ n = 2 \qquad\qquad (3)$$
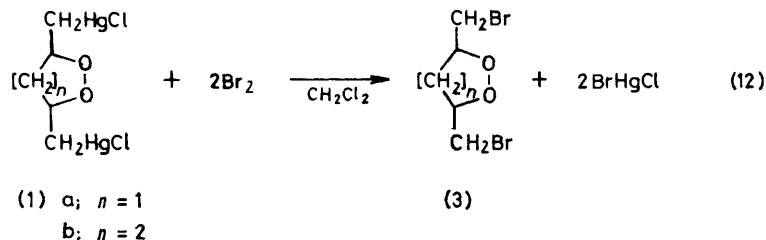
The major isomer of compound (3b) was isolated by fractional crystallisation of the 3 : 1 mixture initially obtained.

The bromodemercuration products were identified by ^1H and proton-decoupled ^{13}C n.m.r. spectroscopy (Tables 2 and 3) and by mass spectrometry. Each mass spectrum showed three molecular-ion peaks with relative intensities 1 : 2 : 1 as expected for a compound containing two bromine atoms, two base peaks with m/e corresponding to $(M - CH_2Br)^+$, and strong peaks at m/e 93 and 95 $[(BrCH_2)^+]$ and m/e 121 and 123 $[(BrCH_2CO)^+]$. Peaks corresponding to $(M - BrCH_2-CHO)^+$ and to $(M - H_2O)^+$, $(M - H_2O - CH_2Br)^+$, and $(M - H_2O - CH_2Br - CO)^+$ (see Scheme) were either absent or very weak.

mixture of isomers, while the 1,2-dioxacyclohexane contained about three times as much *trans*- as *cis*-isomer. By way of comparison the oxymercuration–reduction of hexa-1,5-diene and hepta-1,6-diene [equation (15), $n = 2$ or 3] is reported to afford dimethyloxacyclo-alkanes with isomer ratios (*cis* : *trans*) of 19 : 72 and 61 : 19, respectively.[15]

We determined isomer ratios from signal strengths in the proton-decoupled ^{13}C n.m.r. spectra (Table 3). Up to six resonances were observed for each cyclic peroxide and three correlations had to be made.

First the lines were assigned to the appropriate carbon atom (to establish the vertical correlations in Table 3). For the 1,2-dioxacyclopentanes this could be done unambiguously from chemical shifts and relative intensities

$$CH_2{:}CH[CH_2]_nCH{:}CH_2 \ + \ HgX_2 \ + \ H_2O_2 \longrightarrow XHgCH_2CH(O_2H)[CH_2]_nCH{:}CH_2 \ + \ HX \qquad (13)$$

$$R \ and \ S \qquad\qquad\qquad cis \qquad\qquad\qquad trans$$
$$(meso) \qquad\qquad (RR \ and \ SS)$$

Comparison with the mass spectra of compounds (2a and b) shows that the fragmentation pattern is greatly influenced by the presence of the bromine atoms. Loss of $Br\dot{C}H_2$ is the strongly preferred mode of homolytic β-scission in molecular ions and formation of $Br\overset{+}{C}H_2$ can be envisaged by heterolytic β-scission in either M^+ or $(M - CH_2Br)^+$; $[BrCH_2CO]^+$ is presumably formed from the rearranged molecular ion, $BrCH_2\overset{\bullet+}{C}O-[CH_2]_nCH(OH)CH_2Br$.

Diastereoisomerism.—Hydroperoxymercuration at the first double bond of the diene will generate the unsaturated hydroperoxide as a racemic mixture [equation (13)]. The subsequent intramolecular peroxymercuration can proceed *via* electrophilic attack on either face [left or right in equation (14)] of the second double bond thereby affording diastereoisomeric cyclic products from each enantiomer of the hydroperoxide. Formation of

(the ring CH_2 gives a weaker signal than the other two carbons). For 1,2-dioxacyclohexanes any assignments that were not obvious from chemical shifts could be based on the values of $^{199}Hg-^{13}C$ coupling constants

$$(15)$$
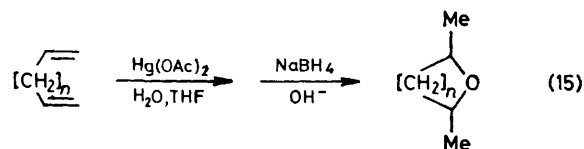
[compound (1b)] or on the α-, β-, and γ-shielding effects of the substituents $HgNO_3$ [compound (4b)] and Br [compound (3b)] as determined from the 1,2-dioxacyclo-pentanes.
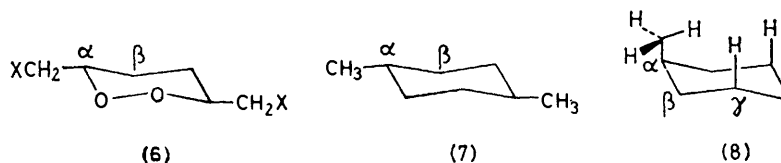
Secondly the lines were divided into two sets, each

[15] H. C. Brown, P. J. Geoghegan, J. T. Kurek, and G. J. Lynch, *Organometallic Chem. Synth.*, 1970/71, **1**, 7.

belonging to a single isomer (to establish the horizontal correlations in Table 3). This was a trivial problem where considerably different amounts of the isomers were present, as with all the 1,2-dioxacyclohexanes and with 3,5-bis(bromomethyl)-1,2-dioxacyclopentane (see Table 1). For compound (2a) an unequal mixture of isomers was obtained by reducing compound (3a) with tributylstannane [equation (16)]. The sets for compounds (1a) and (4a) were grouped by analogy with compound (3a) and may not be correct.

hydrogens [18] [see structure (8)]. These interactions similarly give rise to a shielding of the axial methyl carbon that is not experienced by an equatorial methyl carbon. Since the methyl groups of cis-1,4-dimethyl-cyclohexane spend 50% of the time in axial positions while those of the trans-isomer are essentially always equatorial, the methyl carbons of the trans-isomer resonate at lower field; the difference is found to be 2.6 p.p.m.[16] In our 3,6-dimethyl-1,2-dioxacyclohexane, where there is only one γ-methylene in the ring, the

$$\text{BrCH}_2\text{—} \underset{\text{O—O}}{\bigcirc} \text{—CH}_2\text{Br} + \text{Bu}_3\text{SnH} \longrightarrow \text{Me—} \underset{\text{O—O}}{\bigcirc} \text{—Me} + \text{Bu}_3\text{SnBr} \quad (16)$$

Finally the sets were correlated with configuration and this is discussed below.

Configurational Assignments.—(a) *1,2-Dioxacyclohexanes.* The more abundant isomer of the 1,2-dioxacyclohexane series was assigned the *trans*-configuration on the basis of comparisons with related cyclohexanes. A chair conformation (6) is envisaged, like that of the 1,4-dimethylcyclohexane (7), with the substituents spending nearly all the time in equatorial positions.

methyl carbon resonance of the major isomer appeared 0.61 p.p.m. downfield of that of the minor isomer.

A similar effect has been reported for the exocyclic CH_2OR groups of cyclohexylmethanols and their derivatives.[19] In our cyclic peroxides the downfield shift in the CH_2X resonances of the major isomer relative to those of the minor isomer were 1.95 p.p.m. when $X = HgCl$ and 3.82 p.p.m. when $X = Br$, again indicating a *trans*-configuration.

(6)   (7)   (8)

(i) *Evidence from ^{13}C n.m.r. chemical shifts.* Analysis of many chemical shift data for compounds of known stereochemistry has provided reliable methyl substituent parameters for methylcyclohexanes.[16] Since these parameters vary considerably according to whether the substituent is axially or equatorially disposed, chemical shifts of the ring carbons can be used to distinguish configurations. Furthermore it has been shown that the effects of methyl substituents on the shieldings of ring carbons in 1,3-dioxacyclohexanes are analogous to, though sometimes quantitatively different from, those for the carbocycle.[17] If we assume that the same situation applies in 3,6-dimethyl-1,2-dioxacyclohexane, then the differences in chemical shifts of the ring carbons for the two isomers indicate that the major isomer has the *trans*-configuration [(6), X = H]. Thus the resonances of C_α and C_β in the major isomer are respectively 0.78 and 4.54 p.p.m. downfield of those in the minor isomer; in the 1,4-dimethylcyclohexanes the C_α and C_β resonances of the *trans*-isomer are respectively 2.5 and 4.7 p.p.m. downfield of those of the *cis*-isomer.

The large shielding effect (*ca.* 5.4 p.p.m.) of an axial methyl group on the γ-carbon of the cyclohexane ring has been ascribed to charge polarisation in the C–H bond induced by repulsive interactions between the attached

(ii) *Evidence from ^1H n.m.r. chemical shifts.* The ^1H n.m.r. data for the exocyclic groups are also consistent with the major isomer being *trans*. The sterically induced charge polarisation that leads to shielding of axial carbons simultaneously results in *deshielding* of the attached hydrogens.[20] Thus axial CH_2X protons resonate at lower field than do equatorial ones, and *trans*-1,4-disubstituted cyclohexanes have the *upfield* absorptions.[16,19] In our 1,2-dioxacyclohexanes the CH_2X resonances of the major isomer were 0.25 (X = HgCl), 0.21 (X = Br), and 0.18 p.p.m. (X = H) upfield of those of the minor isomer.

(iii) *Evidence from variable-temperature n.m.r. spectra.* Temperature-independent n.m.r. spectra are expected for *trans*(diequatorial)-3,6-dimethyl-1,2-dioxacyclohexane (6; X = H), but it should be possible to freeze out ring inversion in the *cis*-isomer [equation (17)] and so obtain line broadening and then richer spectra at sufficiently low temperatures.

^1H N.m.r. spectra of a mixture of isomers (*ca.* 7 : 1) were recorded in the range +30 to −125 °C. At −90 °C the methyl doublet of the minor isomer was broadened much more than that of the major isomer which remained resolved at −110 °C; the methyl doublet of cis-1,4-dimethylcyclohexane coalesces at about −70 °C.[21]

Changes in the ^1H n.m.r. signal for the CH_2Br protons

[16] D. K. Dalling and D. M. Grant, *J. Amer. Chem. Soc.*, 1967, **89**, 6612; 1972, **94**, 5318.
[17] G. M. Kellie and F. G. Riddell, *J. Chem. Soc. (B)*, 1971, 1030.
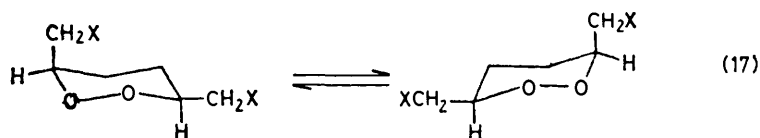[18] D. M. Grant and B. V. Cheney, *J. Amer. Chem. Soc.*, 1967, **89**, 5315.

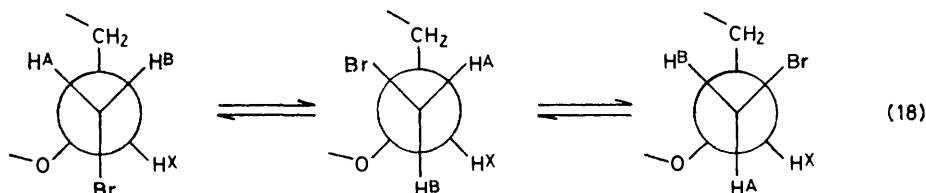[19] G. W. Buchanan, J. B. Stothers, and S-t. Wu, *Canad. J. Chem.*, 1969, **47**, 3113.
[20] B. V. Cheney, *J. Amer. Chem. Soc.*, 1968, **90**, 5386.
[21] N. Muller and W. C. Tosch, *J. Chem. Phys.*, 1962, **37**, 1167.

of the major isomer of 3,6-bis(bromomethyl)-1,2-dioxa-cyclohexane did occur in a similar variable-temperature study. However these protons constitute the AB part of an ABX system and the changes are believed to arise from changes in δ_{AB} due to modification of the rotamer

exocyclic methylene group. This is based, by analogy with the 1,2-dioxacyclohexanes, on the idea that the carbon of a pseudoaxial CH_2X group should experience a shielding due to sterically induced charge polarisation that is not felt by a pseudoequatorial group. However

(17)

populations [equation (18)]. That only 8 lines were observed for CH^AH^BBr at -85 °C is consistent with a *trans*(diequatorial) configuration; the non-equivalent CH_2Br groups of an axial–equatorial conformation could give rise to 16 lines for the *cis*-isomer at low temperature.

the same charge polarisation should deshield the attached protons, yet *trans*-(2a) has the *upfield* methyl doublet. Other factors must be influencing these chemical shifts and the assignments to compounds (1a), (3a), and (4a) should be regarded as only tentative.

(18)

Again in keeping with a *trans*-configuration there was no splitting or appreciable broadening of the three resonances in the proton-decoupled ^{13}C n.m.r. spectrum of the major isomer of compound (3b) as the temperature was lowered to -75 °C.

Although no single piece of evidence is compelling, the chemical-shift data and the variable-temperature results when taken together present a strong case for assigning the *trans*-configuration to the major isomer of the 1,2-dioxacyclohexane series.

(b) *1,2-Dioxacyclopentanes.* The conformations of several 1,2-dioxacyclopentanes with differing degrees of methyl substitution at C(3) and C(5) have been studied and will be discussed in a separate publication.[22] The ring has a half-chair or envelope shape with the methyl groups in pseudo-equatorial or -axial positions, as illustrated by the conformers (9) of *trans*-(2a). This

(9a)   (9b)

results in the *cis*- and *trans*-isomers of compound (2a) being easily identified by their methylene signals in the ^{1}H n.m.r. spectrum (Table 2). Thus it was easy to establish that the major product obtained by reducing compound (3a) [equation (16)] was the *cis*-isomer and so this configuration was correlated with the stronger set of ^{13}C n.m.r. lines (Table 3).

The configurations of the remaining 1,2-dioxacyclo-pentanes are assigned on the assumption that each *trans*-isomer will have the upfield ^{13}C n.m.r. signal for the

[22] A. J. Bloodworth and J. A. Khan, in preparation.

EXPERIMENTAL

Commercial penta-1,4-diene and hexa-1,5-diene (high grade), deuterium oxide (99.5 atom%), and $Hg(NO_3)_2 \cdot H_2O$ and $NaBH_4$ (reagent grade) were used without further purification. Other reagents and solvents were as described in Part 10.[1]

Spectra were recorded as described previously.[1] When obtaining n.m.r. spectra at low temperatures the solvent for compound (2b) was $(CD_3)_2CO–CDCl_3$ (to -90 °C) or $CF_2Cl_2–CH_2Cl_2$ (below -90 °C), and for compound (3b) was $(CD_3)_2CO$ (^{1}H) or $PhMe–CH_2Cl_2–C_6D_6$ (^{13}C).

General procedures for peroxymercuration, hydrogeno-demercuration, and bromodemercuration are described below and details of individual compounds are presented in Tables 1—3.

Peroxymercuration.—To a vigorously stirred suspension of mercury(II) nitrate monohydrate (10 mmol) in dichloro-methane (25 cm³) was added 80—85% hydrogen peroxide 5—9 mmol) followed *immediately* by a solution of diene (5 mmol) in dichloromethane (5 cm³). The mixture was stirred for 10 min; a heavy oil separated. The super-natant liquid was decanted. The oil was washed with dichloromethane (15 cm³) and then treated as follows.

(a) *To prepare a solution for* ^{13}C *n.m.r. spectroscopy.* The oil was evacuated (12 mmHg, 5 min) and dissolved in D_2O (5 cm³), and a few drops of 1,4-dioxacyclohexane were added as an internal standard. For the product from hexa-1,5-diene it was necessary to add four drops of 4M-HNO_3 to get all the oil into solution.

(b) *To isolate the organomercury chloride* (1). The oil was dissolved in water (5 cm³, plus a few drops of 4M-HNO_3 for the product from hexa-1,5-diene), an aqueous solution of potassium chloride (10 mmol in 15 cm³) was added, and the mixture was stirred vigorously for 45 min. The white precipitate of bis(chloromercuriomethyl)-1,2-dioxacyclo-alkane was filtered off and dried *in vacuo*.

Hydrogenodemercuration.—An ice-cold solution of sodium borohydride (15—40 mmol) in 3M-sodium hydroxide (20—

40 cm³) was added to a stirred suspension of the organomercury chloride (1) (7—9.5 mmol) in dichloromethane (40 cm³) at −10 °C at such a rate that the temperature remained below 0 °C. The mixture was kept at −5 °C for 30 min, and then allowed to warm slowly to room temperature; two colourless layers and a bead of mercury were obtained. The organic layer was separated and the aqueous layer extracted with more dichloromethane (40 cm³). The combined dichloromethane solution was dried (MgSO₄) and concentrated at ⩾12 mmHg. The volatile fraction was collected in a trap at −80 °C and each 10 cm³ portion was examined by ¹H n.m.r. spectroscopy to confirm that it contained no peroxide. Crude (2a) was distilled (b.p. 32 °C at 19 mmHg) to remove the last trace of dichloromethane.

(a) *Chromatography.* The dimethyl-1,2-dioxacycloalkanes were purified by g.l.c. using a Varian Aerograph 712 instrument fitted with a column (10 ft × 3/8 in o.d.) of silicone oil on Supasorb (40—60 mesh); 100—200 μl were injected for each run and the carrier gas was nitrogen. For an oven temperature of 50 °C and carrier-gas pressure of 14 lb in⁻², the product from penta-1,4-diene had fractions with retention times 9.8 (pent-4-en-2-ol) and 22.4 min [compound (2a)]. For an oven temperature of 75 °C and carrier gas pressure of 11 lb in⁻², the product from hexa-1,5-diene had fractions with retention times 2.0 (unknown), 13.0 (perhaps hex-5-en-2-ol), 20.5 (major) plus 23.0 (minor) [compound (2b)], and 33.0 min (unknown) (Found for fraction 2: C, 69.6; H, 11.35. Calc. for C₆H₁₂O: C, 72.05; H, 12.1%).

(b) *Mass spectra.* The following values of *m/e* (% of base peak) were observed. (*i*) For compound (2a): 102 (22), 87 (9), 84 (8), 69 (22), 58 (18), and 43 (100). (*ii*) For compound (2b): 116 (6.5), 101 (7.5), 98 (11), 83 (35), 72 (7), 55 (100), and 43 (100+; this peak was off-scale for the lowest sensitivity galvanometer).

Bromodemercuration.—Bromine (9 mmol) in dichloromethane (5 cm³) was added to a suspension of compound (1a) (4.5 mmol) in dichloromethane (25 cm³) and the mixture stirred for 25 h. The solution was then filtered and the dichloromethane removed from the filtrate (12 mmHg). The residue was extracted with a mixture of pentane (90 cm³) and dichloromethane (10 cm³) and the solvent removed from the extract (12 mmHg) to yield compound

(3a). Compound (3b) was similarly prepared on half the scale using a mixture of pentane (95 cm³) and dichloromethane (5 cm³) for the extraction.

Mass spectra. The following values of *m/e* (% of base peak) were observed. (*i*) For compound (3a): 262 (12), 260 (24), 258 (12), 179 (5), 177 (10), 175 (7), 169 (24), 167 (100), 165 (100), 151 (10), 149 (10), 125 (20), 123 (52), 121 (36), 95 (60), and 93 (64). (*ii*) For compound (3b): 276 (6), 274 (12), 272 (6), 181 (100), 179 (100), 125 (5), 123 (10), 121 (9), 100 (25), 99 (18), 96 (13), 95 (32), 94 (13), and 93 (32).

Reaction of Hexa-1,5-diene with Hydrogen Peroxide and Mercury(II) Trifluoroacetate.—To a stirred solution of mercury(II) trifluoroacetate (10 mmol) in dichloromethane (25 cm³) was added 80—85% hydrogen peroxide (5—9 mmol) followed *immediately* by a solution of hexa-1,5-diene (5 mmol) in dichloromethane (5 cm³). After 15 min the solution was washed with water (15 cm³), dried (MgSO₄), and evaporated (12, then 0.05 mmHg) to afford crude organomercury trifluoroacetate. The proton-decoupled ¹³C n.m.r. spectrum (CDCl₃) showed strong lines at δ 79.59 (CH), 32.95 (ring CH₂), and 28.30 (CH₂Hg) plus six lines δ 27.2—29.5 and 33.75) three or four times less intense, of which two may belong to the second isomer of the 1,2-dioxacyclohexane.

The organomercury trifluoroacetate was redissolved in dichloromethane (15 cm³), aqueous potassium chloride (10 mmol in 10 cm³) was added, and the mixture was stirred for 35 min. The dichloromethane layer was separated, dried (MgSO₄), and evaporated (12 mmHg). The resultant crude organomercury chloride was washed with dichloromethane (3 cm³) to leave a residue of analytically pure 3,6-*bis(chloromercuriomethyl)*-1,2-dioxacyclohexane (1b).

Reduction of 3,5-Bis(bromomethyl)-1,2-dioxacyclopentane.—A mixture of compound (3a) (0.9 mmol) and tributylstannane (10.5 mmol) was stirred at room temperature for 60 min. Trap-to-trap distillation at 0.05 mmHg then yielded compound (2a) (0.034 g, 37%).