# Oxymetallation. Part 13.[1] Synthesis of Bicyclic Peroxides *via* Peroxymercuriation of Cyclic Dienes

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The bis-mercuriated derivative (12) of 9,10-dioxabicyclo[3.3.2]decane has been prepared by peroxymercuriation of *cis,cis*-cyclo-octa-1,5-diene, but substantial amounts of bicyclic ethers are also formed in the reaction. The bicyclic peroxides (4) and (5) have been obtained from (12) by reduction and brominolysis respectively. 8,9-Dioxabicyclo[5.2.1]decane (6) and the dibromo-derivative (7) have similarly been prepared by peroxymercuriation and demercuriation of cyclo-octa-1,4-diene. It is suggested that the isomeric purity of the peroxides and the concurrent formation of bicyclic ethers both result from equilibrium control of reversible (per)oxymercuriation–de(per)oxymercuriation. A low yield of the [3.2.1]-peroxide (8) has been obtained by peroxymercuriation and brominolysis of cyclohexa-1,4-diene, but attempts to prepare [2.2.1]-compounds from 5,5-disubstituted cyclopentadienes have been unsuccessful.

DIHYDROASCARIDOLE [2] (1) has been known since 1938, yet until quite recently it remained the only reported example of a saturated bicyclic peroxide. Interest in such compounds was stimulated by the discovery that derivatives of 2,3-dioxabicyclo[2.2.1]heptane, the so-called prostaglandin endoperoxides [*e.g.* (2)] are intermediates in the biosynthesis of prostaglandins and other hormones from polyunsaturated fatty acids.[3] Chemical models of the prostaglandin endoperoxides were required to enable the peroxide chemistry associated with prostaglandin biosynthesis to be put on a firm basis, and considerable effort was directed towards preparing 2,3-dioxabicyclo[2.2.1]heptane (3).


(1)   (2)   (3)
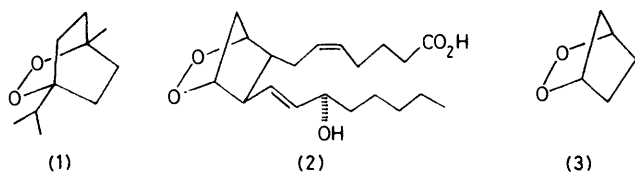
Four independent syntheses of compound (3) have now been reported, each employing a different approach.[4] One route involved photo-oxygenation of cyclopentadiene followed by reduction of the resultant singlet oxygen adduct with di-imide. The combination of singlet oxygenation of a cyclic conjugated diene and di-imide reduction has also provided several substituted 2,3-dioxabicyclo[2.2.1]heptanes [4] and a homologous series of dioxabicyclo[*n*.2.2]alkanes [equation (E1); *n* = 1—4].[5] It is thus a proven method for the synthesis of bicyclic peroxides that contain the 1,2-dioxacyclohexane ring.
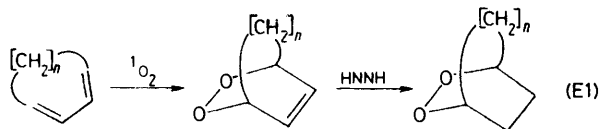

Concurrently with this work we have been developing a synthesis of bicyclic peroxides based on peroxymercuriation. We have shown that the reaction of acyclic dienes with mercury(II) nitrate and hydrogen peroxide coupled with demercuriation affords good yield of 1,2-dioxacyclo-pentanes and -hexanes [equation (E2); *n* = 1 or 2, X = H or Br].[1,6] It therefore appeared
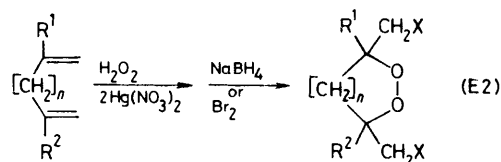
likely that similar reactions with cyclic dienes could provide a route to dioxabicycloalkanes. We now give full details of the application of this approach to the synthesis from cyclo-octadienes of 9,10-dioxabicyclo[3.3.2]decane (4) [7] and of 8,9-dioxabicyclo[5.2.1]decane (6) [8] together with their dibromo-derivatives (5) and (7).[8] We also describe attempts to apply this strategy to the preparation of dioxabicyclo-octanes and -heptanes, which has resulted in the isolation of a low yield of compound (8).


(4)   (5)   (6)   (7)   (8)
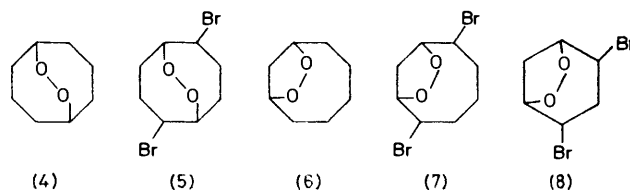
RESULTS

cis,cis-*Cyclo-octa-*1,5-*diene.*—— *cis,cis*-Cyclo-octa-1,5-diene (1,5-COD) was an obvious substrate to choose for the first attempt to prepare bicyclic peroxides *via* peroxymercuriation. It is commercially available, has one of the double-bond arrangements that proved successful in monocyclic peroxide synthesis, and has been shown to undergo oxymercuriation [9–12] and aminomercuriation [13,14] to afford bicyclic ethers and amines respectively [equation (E3); Y = O or NPh].

(a) *Peroxymercuriation; choice of mercury(II) salt.* Since mercury(II) nitrate gave the best yields of monocyclic peroxides in the peroxymercuriation of acyclic dienes,[1,6] it was used in the initial work with 1,5-COD. An exothermic

reaction took place when 1,5-COD (5 mmol) was added to a well stirred mixture of $Hg(NO_3)_2 \cdot H_2O$ (10 mmol) and 80—85% H_2O_2 (5—8 mmol) in CH_2Cl_2 (25 cm³). The oil thus formed (ca. 90% of total starting materials) was dissolved in D_2O and the ¹H-decoupled ¹³C n.m.r. spectrum was

(E3)
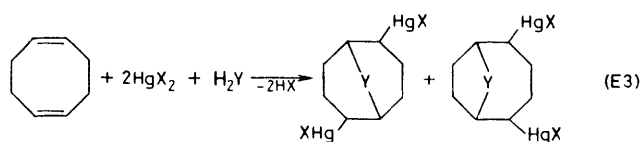
recorded. This showed that 2,6-bisnitratomercuria-9-oxabicyclo[3.3.1]nonane (9a) was essentially the only organic product present; no bicyclic peroxide was detected. Product identification was by spectral identity with the authentic material prepared by a modification of Bordwell and Douglass's method [9] in which 1,5-COD (1.2 mmol) was treated with $Hg(NO_3)_2 \cdot H_2O$ (2.4 mmol) in D_2O (5 cm³). Confirmation of the structure of (9a) was provided by conversion into the corresponding organomercury chloride (9b) and subsequent demercuration to afford 9-oxabicyclo[3.3.1]nonane 10 [9] and its 2,6-dibromo-derivative (11).

(E4)

(9a)   (9b)   (10) X = H
   (11) X = Br
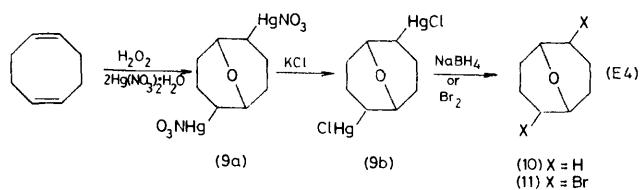
The peroxymercuration was carried out under similar conditions but using anhydrous mercury(II) trifluoroacetate [equation (E5)]. The resulting dichloromethane solution was washed with water to remove trifluoroacetic acid and excess hydrogen peroxide, dried, and the solvent removed to afford the crude product in 75—90% yield. The ¹³C n.m.r. spectrum of this showed the presence of (12), (9c), and (13) in a molar ratio of 1 : 1.2 : 0.5, respectively; no significant amounts of any other organic products were detected. The

(E5)

(12)   (9c)   (13)
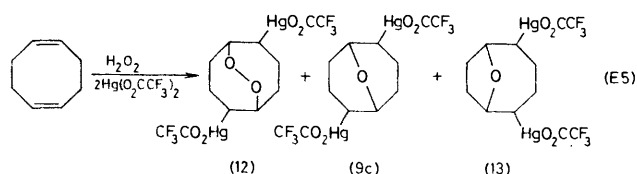
bicyclic ethers (9c) and (13) were identified by comparison with authentic samples prepared by reaction of the corresponding organomercury chlorides [from oxymercuriation of 1,5-COD using mercury(II) acetate 10—12] with silver trifluoroacetate. The main evidence for the identity of the peroxide (12) came from its isolation and subsequent reduction to 9,10-dioxabicyclo[3.3.2]decane (see later). It proved possible to isolate peroxide (12) free of ethers (9c) and (13) by dissolving the crude mixture of organomercury trifluoroacetates in benzene. Within seconds a crystalline precipitate (m.p. 118—119 °C decomp.) of (12) solvated with benzene was formed; no peroxide remained in solution.

The peroxymercuriation was carried out under similar conditions but using mercury(II) acetate, and the resulting organomercurial was reduced in situ with basic sodium

borohydride. No peroxide was detected in the product and the major component (70%) present was cyclo-oct-4-enyl acetate (14), which was identified by comparison with an authentic sample. The peroxymercuriation was again carried out with mercury(II) acetate, but using a large excess of 30% H_2O_2 at -10 °C. The resulting product was precipitated as the organomercury chloride and then reduced with basic sodium borohydride to afford a crude product in 65% yield. The ¹³C n.m.r. spectrum of this indicated the presence of six components [equation (E7)] with the following approximate mol fractions: (4) (7%), (15) (6%), (16) (14%), (10) (9%), (17) (41%), and (18) (23%). The components were identified by comparison with the ¹³C n.m.r.

(E6)

(14)
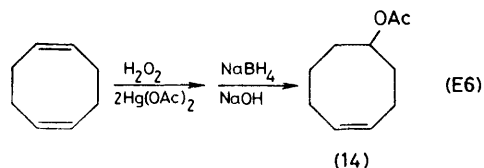
data for authentic samples of compounds (4) (see later), (15),[7] (16),[15] (10),[9] (17), [11] and (18).[16]

Thus mercury(II) trifluoroacetate and high-strength H_2O_2 are the reagents of choice for the peroxymercuriation of 1,5-COD. When the reaction was carried out using $Hg(O_2CCF_3)_2 \cdot H_2O$, the ratio of peroxide to ethers was 1 : 3.6 compared with the 1 : 1.7 ratio obtained using the anhydrous salt. This suggests that it is important to minimise the amount of water present in the reaction mixture in order to optimise the yield of peroxide. The best results (mol fraction of peroxide isolated as benzene solvate = 40—50%) were obtained when the mercury(II) trifluoroacetate was dried over P_2O_5 at 40 °C and 0.1 mmHg

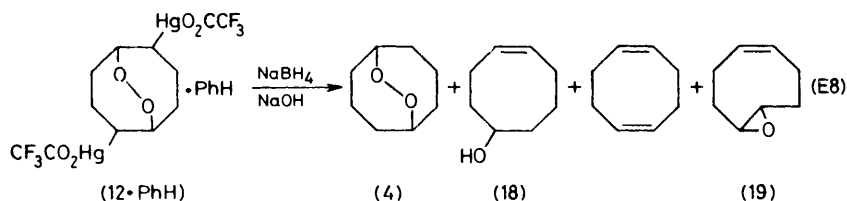
(E7)

(4)   (15)   (16)

(10)   (17)   (18)
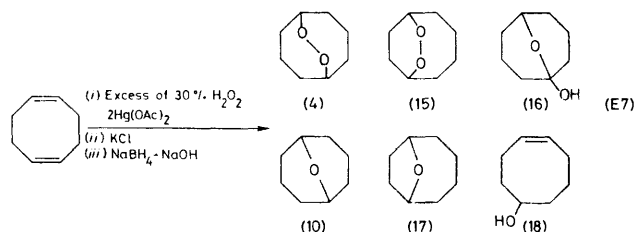
immediately before use. However, the yield of peroxide was not improved by adding anhydrous $MgSO_4$, K_2CO_3, or 2,3-dimethylpyridine to the reaction mixture, or by using 98% H_2O_2 or $DABCO-(H_2O_2)_2$ [17] in place of the 80—85% H_2O_2 routinely employed.

(b) Reduction; isolation of 9,10-dioxabicyclo[3.3.2]decane, (4). Reduction [equation (E8)] of the solvated organomercury peroxide (12·PhH) by alkaline sodium borohydride under conditions similar to those used to prepare monocyclic peroxides [1,6] afforded, in 76% yield, a mixture containing the following components with the approximate mol fractions indicated: (4) (40%), (18) (40%), 1,5-COD (11%), and (19) (9%). These products were separated by chromatography but, under the conditions used (SiO_2/CH_2Cl_2), (19) had only a slightly longer retention time than (4) and about 60% of the peroxide (75%) that was recovered from the column was contaminated with it.

Pure (4) is a white crystalline solid, m.p. 116—118 °C, with a strong 'sharp' smell that is characteristic of bicyclic peroxides. The material instantly oxidises acidified iron(II)

thiocyanate, contains no hydroxy-group (i.r.), shows a parent-ion $(C_8H_{12}O_2^+)$ peak in the mass spectrum, and has the correct C and H analyses. Non-identity with authentic 7,8-dioxabicyclo[4.2.2]decane (15), prepared by di-imide reduction of the singlet oxygen adduct of cyclo-octa-1,3-diene [equation (E9)],[7] suggested the [3.3.2]-structure for (4). This was confirmed by the presence of only three

Cyclo-octa-1,4-*diene*.—The successful synthesis of the [3.3.2]-peroxides from 1,5-COD encouraged us to try similar reactions with cyclo-octa-1,4-diene (1,4-COD). Initial experiments were carried out using a mixture of 1,4-COD (70%) and 1,5-COD since this is readily accessible *via* hydrobromination–dehydrobromination of 1,5-COD [equation (E12)].[21,22a]

(12·PhH)   (4)   (18)   (19)

resonances in the ^{13}C n.m.r. spectrum and by catalytic hydrogenation [equation (E10)] which led to the known[18] *cis*-cyclo-octane-1,5-diol. The main by-product of reduc-

(4)
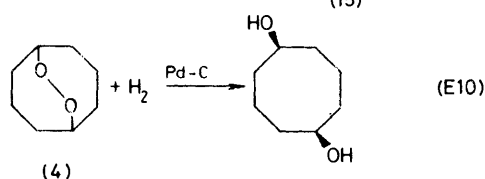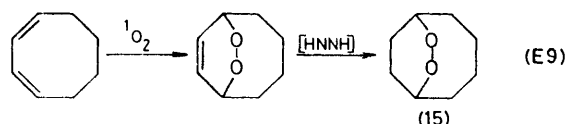
tion was isolated and identified as cyclo-oct-4-en-1-ol (18) by comparison with an authentic sample.[16] The identification of (19) is based primarily on a good agreement between its ^{13}C n.m.r. spectrum (δ 130.28, 58.74, 28.89, 25.31) and that reported[19] for authentic *trans*-1,2-epoxy-*cis*-cyclo-oct-5-ene. We found no evidence for the presence of any other epoxides in the reduction mixture.

(c) *Brominolysis; isolation of 2,6-dibromo-9,10-dioxabicyclo*[3.3.2]*decane*, (5). Brominolysis [equation (E11)] of the solvated organomercury peroxide (12·PhH) in dichloromethane afforded (5). Although the ^{13}C n.m.r. spectrum of


(12 · PhH)   (5)
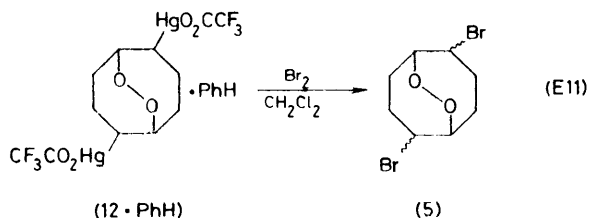
the crude product indicated that, as expected under these conditions,[20] all three diastereoisomers were formed (e.g. observation of signals in the CO_2 region at δ 88.19, 87.63, 85.88, and 85.19), only one of them was isolated by h.p.l.c. in sufficient yield for full characterisation. This was identified as the *trans,trans*- or *cis,cis*-isomer * since it showed only four lines in the ^{13}C n.m.r. spectrum.

* In describing the stereoisomers of brominated bicyclic per-oxides and ethers we use *cis* and *trans* to define the disposition of each bromine on the hydrocarbon ring with respect to the oxygen bridge.

(a) *Peroxymercuriation and reduction.* Peroxymercuriation with mercury(ii) trifluoroacetate followed by reduction of the resultant mercurial with basic sodium borohydride afforded a crude product (70%) shown by t.l.c. to contain 9,10-dioxabicyclo[3.3.2]decane (4) and a second peroxide with an R_F value similar to, but not identical with, that of 7,8-dioxabicyclo[4.2.2]decane (15). The ^{13}C n.m.r. spectrum of the mixture confirmed the presence of (4) and absence of (15), and indicated that the main component was the previously unknown peroxide 8,9-dioxabicyclo[5.2.1]-decane (6). Pure (6) was isolated by silica chromato-

70%   30%
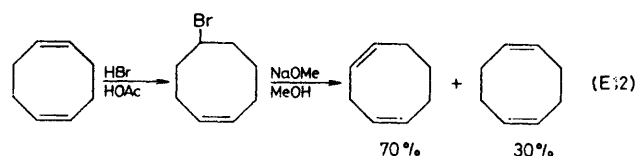
graphy. It is a white crystalline solid, m.p. 63—64 °C, with an appearance and smell similar to that of its isomers (4) (m.p. 116—118 °C) and (15) (m.p. 96—98 °C). The origin of (6) and its similarity to (4) and (15) points firmly to the [5.2.1]-structure. Elemental analysis, mass spectrum, i.r. spectrum, and ^1H n.m.r. spectrum are all consistent with this but the five-line ^{13}C n.m.r. spectrum with resonances at δ 77.61 (bridgehead) and 45.18 (methylene bridge) places the identity beyond doubt.

The amount of (4) present in the mixture can be accounted for by it being formed solely from 1,5-COD [equations (E5) and (E8)]. That the peroxymercuriation–reduction of 1,4-COD gives (6) regiospecifically was confirmed by carrying out the reaction [equation (E13)] with a sample of 1,4-COD that had been separated from the 1,5-isomer by preparative

(6)   (20)
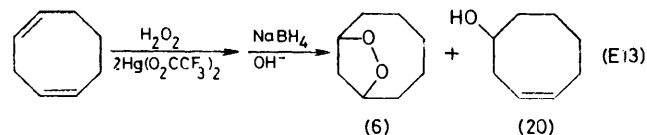
g.l.c. T.l.c. and ^{13}C n.m.r. analyses of this product showed the absence of (4). ^{13}C N.m.r. analysis further indicated the presence of cyclo-oct-3-en-1-ol (20) as a major by-product. Compound (20) was identified by comparison with an authentic sample prepared[22b] by reduction of 3,4-epoxycyclo-octene.[22c]

(b) *Peroxymercuriation and brominolysis.* The peroxy-

mercuriation of 1,4-COD, conversion into organomercury bromide, and bromodemercuriation under free-radical conditions [20] gave a high yield of the three diastereoisomers of (7) [equation (E14)]. [13]C N.m.r. spectroscopy indicated

(7)
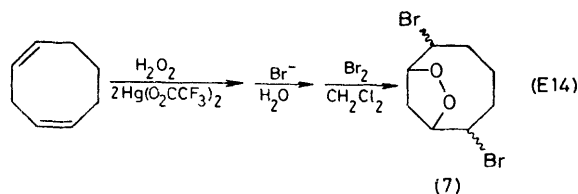
that the ratio of stereoisomers in the crude product was *ca.* 1 : 2 : 1, but only two of them were separately isolated by h.p.l.c. The most abundant isomer, which had the longer retention time of those isolated, was unambiguously assigned the *cis-trans*-configuration since it showed eight lines in the [13]C n.m.r. spectrum. The elemental analysis and [13]C n.m.r. spectrum of the crude product showed that the reaction is very clean, only a minor amount of a nonperoxidic component, possibly a bicyclic ether, being detected.

Cyclo-octa-1,3-diene.—Peroxymercuriation and reduction of cyclo-octa-1,3-diene gave primarily 9-oxabicyclo[4.2.1]-non-7-ene (21), which was identified by its characteristic [1]H n.m.r. spectrum.[10] [13]C N.m.r. spectroscopic studies showed that (21) is formed, at least in part, in the peroxymercuriation step [equation (E15)]. There was no conclusive

(21)
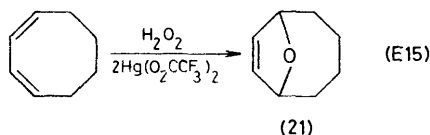
evidence for the presence of any bicyclic peroxides in the products.

In view of the vital role played by [13]C n.m.r. spectroscopy in identifying products obtained *via* peroxymercuriation and demercuriation of cyclo-octadienes, we summarise the relevant data in the Table.

Cyclohexa-1,4-diene.—The peroxymercuriation and brominolysis of cyclohexa-1,4-diene gave a mixture containing peroxides (t.l.c.) and alkyl trifluoroacetates (i.r.). A bicyclic peroxide, m.p. 91—93 °C, was isolated by h.p.l.c. in low yield (*ca.* 2% based on diene) and was assigned structure (8) on the strength of its mass spectrum, which showed the appropriate molecular ions, and its ^{1}H and [13]C n.m.r. spectra. The four-line [13]C n.m.r. spectrum with charac-

(8a)   (8b)
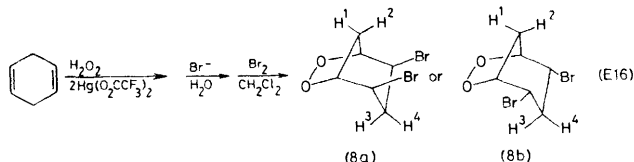
teristic resonances at δ 76.48 (bridgehead) and 43.04 (methylene bridge) provides compelling evidence for a [3.2.1]-skeleton with *cis, cis* (8b) or *trans, trans* (8a) bromines. This is strongly supported by the [1]H n.m.r. spectrum which shows striking similarities to that of the corresponding [5.2.1]-bromoperoxide (7a), particularly the appearance of two doublets of triplets for H[1] and H[2]. A

choice between (8a) and (8b) cannot be made with certainty by analysis of the multiplets for H[3] and H[4] because they overlap partially with the signal for H[2].

Small quantities of other peroxide materials with similar h.p.l.c. characteristics were obtained, but none were positively identified.

5,5-Disubstituted Cyclopentadienes (with B. P. Leddy).—In an attempt to extend peroxymercuriation-demercuriation to the synthesis of [2.2.1]-peroxides, reactions with spiro-[4.4]nona-1,3-diene,[23] spiro[4.2]hepta-1,3-diene,[23] and 6,6-dimethylfulvene [24] were carried out. Trifluoroacetate incorporation appeared (i.r.) to be a major reaction pathway and although peroxides were detected (t.l.c.) in some products, none could be isolated or identified.

DISCUSSION

This discussion aims to assess the scope of peroxymercuriation and demercuriation of cyclic dienes as a route to bicyclic peroxides, paying particular attention to the aspects of regiospecificity and formation of by-products which respectively enhance and detract from the synthetic value of the method. In discussing these last two topics we concentrate mainly on 1,5-COD since its reactions have been studied in greatest detail.

A major problem in the peroxymercuriation of 1,5-COD is the competing generation of bicyclic ethers. In a mixture that contains 1,5-COD, mercury(II) salt, hydrogen peroxide, and water, the formation of bicyclic peroxides (12) and (22), and bicyclic ethers (9) and (13), can be envisaged. We believe that all four compounds participate in a series of linked equilibria [equation (E17)] so that interconversions may take place under conditions of thermodynamic control.
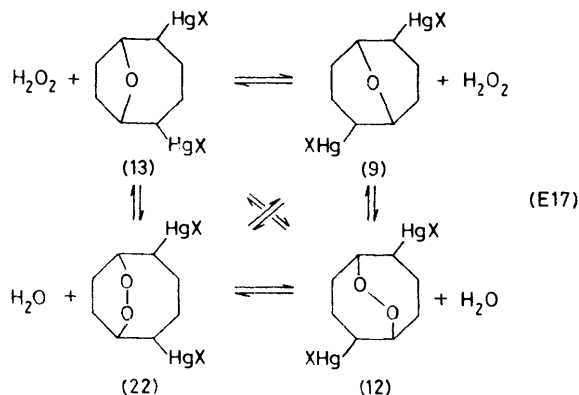

We believe that this accounts for both the regiospecificity of peroxymercuriation and the formation of ethers, and after discussing the evidence which supports this view, we address ourselves to the possible mechanisms of equilibration.

Scope.—The peroxymercuriation of cyclic dienes provides the basis of a convenient synthesis of hitherto unknown bicyclic peroxides that contain the [3.3.2]- and [5.2.1]-skeletons. The dioxabicyclo[3.3.2]decanes obtained from 1,5-COD are the first and only bicyclic peroxides to be prepared that do not contain either a five- or six-membered peroxide ring. The [5.2.1]-system can

TABLE

^{13}C N.m.r. spectra of peroxides, ethers, and alcohols containing a cyclo-octane or cyclo-octene ring (δ) [a]

Formula	Carbon				Formula	Carbon			
	1	2	3	4		1	2	3	4
	5	6	7	8		5	6	7	8
(6)	45.18	77.61	33.12	25.13	b,n	32.48	81.99	53.38	27.98
	26.14								
(7a)	40.00	80.66	52.17	34.60	(21)	130.86	83.11	33.88	24.29
	16.39								
(7b)	42.61	81.26	53.79	34.60	(10) b,f	67.02	29.75	19.17	
	21.59	37.32	53.55	83.30					
(7c) b	45.45	83.58	54.79	37.29	(16)	72.45	28.37	20.64	36.28
	17.12					93.98			
c	58.76	93.34	52.50	37.69	(9a) i,j	72.79	50.76	36.20	27.58
	26.33	25.33	30.66	88.88					
c	62.04	88.59	33.28	25.31	(9b) g,h	72.23	54.23	37.23	28.57
	25.83								
(15)	34.60	76.02	24.45	20.68	(9c) b,e	70.84	52.49	36.19	27.29
d	128.24	76.58	33.25	24.08	(11a) b,n	69.74	50.30	31.17	26.09
(4)	83.96	31.38	23.82		(11b)	72.18	51.87	30.15	28.88
						69.96	50.02	29.88	19.56
(12) b,e	85.27	48.42	34.06	29.09	k	71.81	36.43	20.07	
(5a)	86.15	48.18	32.75	26.23	l	33.34	71.78	30.52	22.31
(17) b,f	31.58	77.75	36.16	24.44	(18)	72.70	37.60	25.69	130.14
						129.49	24.94	22.84	36.31
(13) b,e	31.81	80.44	56.56	36.12	(20) m	71.92	34.95	131.93	126.51
(13) b,g,h	31.11	81.70	58.07	36.37		28.42	25.75	21.45	34.08

[a] Solution in $CDCl_3$ unless otherwise stated; assignments are uncertain where chemical shifts of carbons in equal abundance are very similar. [b] Spectrum of component in mixture. [c] Reference 25. [d] Sample provided by W. Adam. [e] X = O_2CCF_3. [f] Mixture of (10) and (17) prepared by Brown's method;[11] in our hands the product also contained small amounts of cyclo-oct-4-enol (18) and 1,5-COD. [g] X = Cl. [h] In pyridine (80%) and C_6D_6. [i] In D_2O. [j] X = NO_3. [k] Aldrich Chemical Co. Ltd. [l] Prepared from cis-cyclo-octene oxide and trifluoroacetic acid (J. C. Traynham and J. Schneller, *J. Amer. Chem. Soc.*, 1965, 87, 2398. [m] Prepared by reduction of 3,4-epoxycyclo-octene.[22c] [n] Prepared independently from 1,5-COD, NBS, and H_2O (for conditions see reference 39).

For 1,5-COD: δ 128.70, 28.22; for 1,4-COD: δ 130.46, 128.42, 29.59, 24.81, and 23.11.

also be entered *via* cyclopcroxymercuriation of cyclo-oct-2-enyl hydroperoxide [equation (E18)],[25] but the yield of bicyclic peroxide is much lower than that obtained from 1,4-COD [equation (E14)]; both reagents afford dibromo-peroxides but the substitution patterns are different.

(E18)
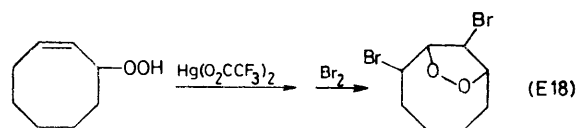
As expected from model systems,[26] the peroxymercuriation of 1,5-COD is stereospecific (and presumably involves *trans*-addition). More significant from a synthetic viewpoint is the fact that both it and the corresponding reaction with 1,4-COD are also regiospecific. Furthermore these peroxymercuriations when coupled with borohydride reduction [equations (E19) and (E20)] provide dioxabicyclodecanes isomeric with the [4.2.2]-compound available from 1,3-COD [equation (E21)] *via* the recently developed [5] technique of singlet oxygenation and di-imide reduction.

(E19)

(4)

(E20)

(6)

(E21)

(15)
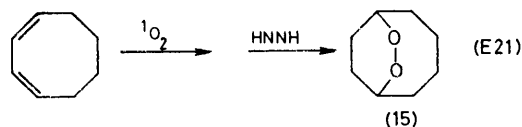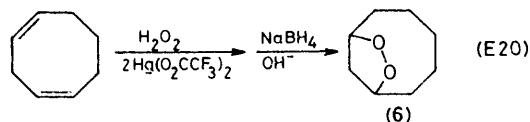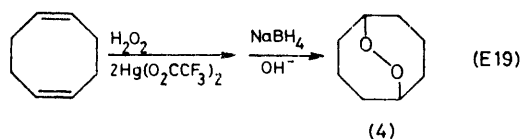
Preliminary attempts to extend the strategy to smaller cyclic dienes have not been encouraging. A dioxabicyclo[3.2.1]octane was obtained from cyclohexa-1,4-diene, but the yield was <2% and the concurrent formation of [2.2.2]-peroxides cannot be ruled out. We failed to isolate any [2.2.1]-peroxides from reactions with three 5,5-disubstituted cyclopentadienes; the substituents were incorporated to avoid 5-mercuriation [27] and the dienes used were chosen on the basis of preparative convenience. Our hopes for this reaction were based on our previous work with penta-1,3-diene where an acceptable yield of a 1,2-dioxacyclopentane was obtained *via* peroxymercuriation.[1] The failure to obtain any [5.2.1]-peroxide from 1,3-COD was discouraging, but we felt that the type of bicyclic ether formation observed in that system would not occur with the cyclopentadienes. In the light of recent studies [28] of the reactivity of 2,3-dioxabicyclo[2.2.1]heptane, it seems unlikely that any

[2.2.1]-systems would survive long under our reaction and work-up conditions.

Regiospecificity.—Oxymercuriations with mercury(II) acetate are kinetically controlled, but the presence of a mineral acid leads to equilibrium control by catalysing both back (deoxymercuriation) and forward reactions. Thus in the oxymercuriation–reduction of 1,5-COD,[9–11] use of mercury(II) acetate affords a mixture of (10) and (17) whereas *only* (10) is obtained with mercury(II) nitrate [equation (E22)].

	(17)	(10)
X = OAc	75 %	25 %
X = NO₃	0 %	100 %
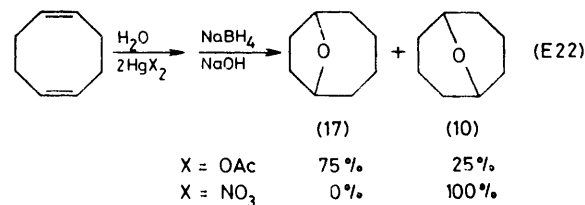
A similar result was obtained for the peroxides. Thus whereas *both* (4) and (15) were detected among the products from a peroxymercuriation–reduction with mercury(II) acetate, *only* (4) was obtained when mercury(II) trifluoroacetate was used. It appears that trifluoroacetic acid can induce deperoxymercuriation to occur at a sufficient rate for equilibration of (22) to (12) to take place *via* (23) or the corresponding mercurinium ion [equation (E23); X = CF₃CO₂].

Peroxymercuriation of 1,5-COD differs from oxymercuriation in that the thermodynamically favoured product is also formed the faster. Thus assuming that (16) is derived from (12) (see later), the product distribution in the mercury(II) acetate reaction [equation (E7)] suggests that (12) is formed about three times faster than (22). [This also assumes that (18) is not formed

(E23)
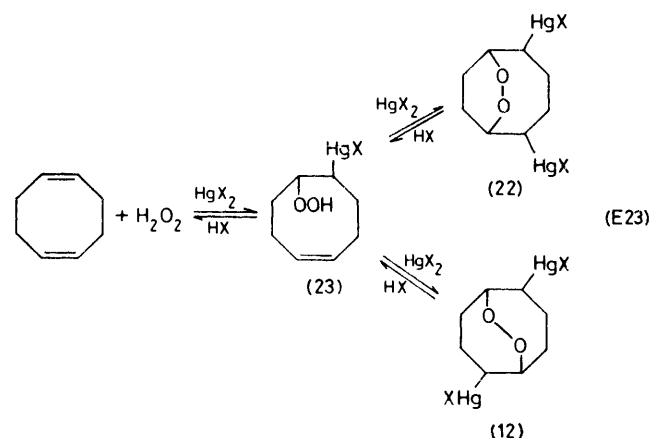
from (12) and (22) at markedly different rates.] Considering the similarity of the two reactions this difference between peroxy- and oxy-mercuriation is curious.

The peroxymercuriation of 1,4-COD is potentially more complicated in that the initial hydroperoxymercuriation could also take place with two orientations so that

three bicyclic peroxides could be formed [equation (E24)]. The observed regiospecificity for (25) when mercury(II) trifluoroacetate is used can again be explained in terms of equilibrium control. In fact the homoallylic hydroperoxide (24) which leads to (25) is probably favoured kinetically over the alternative hydroperoxymercurial, for it has been reported [10] that

(E24)
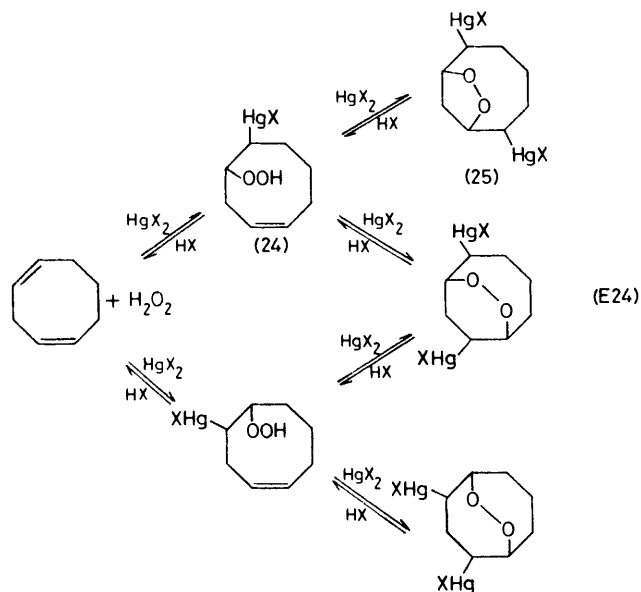
oxymercuriation of 1,4-COD using mercury(II) acetate followed by reduction gives mainly cyclo-oct-3-enol.

Origin of Bicyclic Ethers in Peroxymercuriation.— Ether formation in the peroxymercuriation of 1,5-COD using 80—85% H_2O_2 and mercury(II) nitrate or trifluoroacetate can be explained in terms of the intervention of water under conditions of thermodynamic control [equation (E17)]. Water is present to the extent of 30—40 mol% in the hydrogen peroxide and an equimolar amount is associated with the mercury(II) nitrate. The *complete* absence of bicyclic peroxide in the nitrate system can be explained by the fact that the product is dissolved in water prior to observation (by n.m.r. spectroscopy or by precipitation as the organomercury chloride) and nitric acid is *still present*. The high concentration of water in the aqueous solution and the presence of the powerful equilibrating catalyst (HNO_3) will ensure complete conversion to the ether (9).

In contrast, the product from mercury(II) trifluoroacetate is soluble in dichloromethane and aqueous washing serves only to remove the trifluoroacetic acid and thus inhibit further equilibration. The presence of some [4.2.1]-ether (13) suggests that equilibration is incomplete at the stage of aqueous washing, *i.e.* 10—15 min after mixing the reagents. Indeed for longer reaction times the fraction of [3.3.1]-ether (9) increased at the expense of both (12) and (13). We do not believe that the aqueous washing procedure itself generates any appreciable amount of ether, for replacing it by rapid neutralisation with aqueous sodium hydroxide, which

should quench equilibration, did not affect the product balance as monitored by reduction with sodium borohydride.[29]

Consistent with this picture of equilibrium-controlled ether formation was the observation that the ratio of peroxide to ethers in the product changed from 1 : 1.7, when anhydrous $Hg(O_2CCF_3)_2$ was used to 1 : 3.6 when the reaction was carried out with $Hg(O_2CCF_3)_2 \cdot H_2O$. Attempts were made to improve the yield of peroxide by eliminating water from the trifluoroacetate system. However, use of 98% H_2O_2 or 85% H_2O_2 with added anhydrous $MgSO_4$ failed to raise the molar fraction of peroxide above 50%. It may be that water is generated *in the course of the peroxymercuriation* by the rapid reaction of hydrogen peroxide with liberated trifluoroacetic acid [equation (E25)].[30] In effect this provides a

$$H_2O_2 + CF_3CO_2H \rightleftharpoons CF_3CO_3H + H_2O \quad \text{(E25)}$$
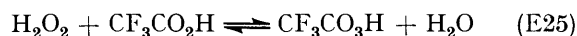
mechanism whereby bicyclic ether can be generated from hydrogen peroxide according to the stoicheiometry in equation (E26). Attempts were made to intercept
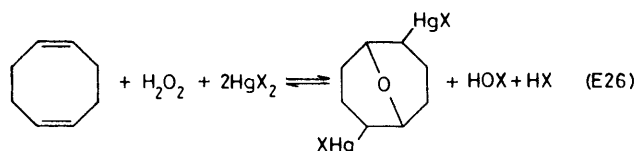
the trifluoroacetic acid by carrying out the peroxymercuriation in the presence of anhydrous K_2CO_3 or 2,6-dimethylpyridine and with DABCO-$(H_2O_2)_2$, but no improvement in peroxide yield resulted.

The mechanism by which bicyclic peroxymercurials are converted into bicyclic oxymercurials presumably involves deperoxymercuriation to (23) [equation (E23)] followed by β-oxy-exchange [31] [equation (E27)] to afford
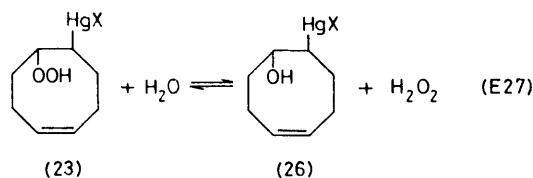
(26) which can proceed to ethers (9) and (13). All steps are favoured by the use of mercury(II) salts of strong acids, especially the nitrate but also the trifluoroacetate. The presence of (13) but not (22) in the mercury(II) trifluoroacetate system indicates that peroxide equilibration is faster than ether equilibration, a reasonable result in view of the fact that (13) is the kinetically favoured ether whereas (12) is the faster-formed peroxide. The success of the mercury(II) trifluoroacetate reaction as a regiospecific synthesis of bicyclic peroxide further depends on peroxide equilibration being faster than peroxide–ether interconversion.

In view of the conclusion that the bicyclic ethers (9) and (13) arise through equilibrium control [equation (E17)], we attempted to improve the yield of peroxide by carrying out kinetically controlled peroxymercuri-

ation with mercury(II) acetate. However, under conditions comparable to those used with nitrate and trifluoroacetate, *i.e.* 2 mol HgX_2 and 1 mol 80—85% H_2O_2, the major product obtained was that of acetoxymercuriation. This result is not surprising when it is remembered that extensive acetoxymercuriation occurred during the t-butyl peroxymercuriation of medial alkenes, even when a one-fold excess of hydroperoxide was used.[32]

We decided to use a large excess of hydrogen peroxide to suppress acetoxymercuriation. Model studies [33] showed that only mono-methoxymercuriation of 1,5-COD takes place with 2 equiv. of $Hg(OAc)_2$ in solvent methanol, and so we felt that dihydroperoxymercuriation would not compete with the desired dioxabicyclization. For safety reasons we wished to avoid using a large quantity of high-strength H_2O_2, and model studies [22b] showed that peroxymercuriation of styrene using 30% H_2O_2 affords $PhCH(OOH)CH_2HgOAc$ but *none* of the corresponding hydroxymercurial. Thus the peroxymercuriation of 1,5-COD was carried out with $Hg(OAc)_2$ using 30% H_2O_2 as solvent, and the product was analysed by precipitation as the organomercury chloride followed by reduction with alkaline $NaBH_4$. We were surprised to find that ethers (17) (4 parts) and (10) (1 part) accounted for 50% of the product mixture.

The presence of [4.2.2]-peroxide (15) and the predominance of [4.2.1]-ether (17) indicates that kinetic control has been achieved in the reaction. It therefore appears that β-oxy-exchange to convert hydroperoxymercurial (23) into hydroxymercurial (26) [equation (E27); X = OAc] takes place in the *absence* of strong acid catalysis. Previous work [31] has indicated that such a process in 2-oxy-cyclo-octylmercury(II) acetates is very slow. However it was shown in the same study [31] that β-oxy-exchange can be catalysed by *alkenes*, and we tentatively suggest that the double bond remaining in (23) might fulfil this role.

It appears that the rate of β-oxy-exchange and subsequent intramolecular alkoxymercuriation to afford bicyclic ethers (9) and (13) is competitive with that of intramolecular peroxymercuriation to yield bicyclic peroxides (12) and (22) [equation (E28)]. The normal

$$(12) + (22) \xleftarrow{HgX_2} \underset{(23)}{\overset{HgX}{\boxed{\quad OOH \quad}}} \xrightleftharpoons[H_2O_2]{H_2O} \underset{(26)}{\overset{HgX}{\boxed{\quad OH \quad}}} \xrightarrow{HgX_2} (9) + (13) \quad (E28)$$

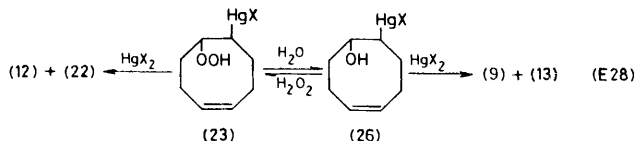expectation that peroxymercuriations will be faster than alkoxymercuriations may be unjustified for the intramolecular processes of (23) and (26) because the bicyclic peroxides (12) and (22) are strained by comparison with the bicyclic ethers (9) and (13).

We have considered the possibility that the bicyclic ethers (9) and (13) arise directly from (23) *via* a process that involves O–O cleavage, but we have no evidence to support such a mechanism and we currently favour the

explanation given above based on conventional oxymercuriation chemistry [equation(E28)].

The results with 1,4- and 1,3-COD are consistent with the idea that bicylic ethers arise through the intervention of water. Thus much less bicyclic ether was obtained in the peroxymercuriation of 1,4-COD, as judged by the products of subsequent brominolysis [equation (E14)], and it is known [10] that bicyclic ethers are not the main products from the oxymercuriation of 1,4-COD. On the other hand, 9-oxabicyclo[4.2.1]non-7-ene (21) is formed in the oxymercuriation of 1,3-COD [10,11] and was also the main product obtained under peroxymercuriation conditions. The mechanism previously suggested [10] for the formation of (21) involves an initial 1,4-addition to the conjugated system followed by intramolecular oxydemercuriation of the resultant allylic mercurial [equation (E29)]. An analogous process with hydrogen peroxide

$$(E29)$$
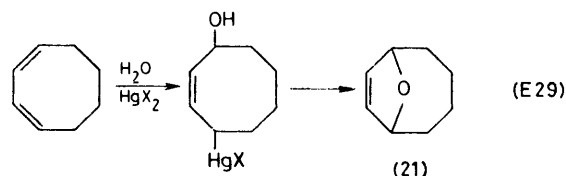
would be expected to afford 7,8-dioxabicyclo[4.2.2]-dec-9-ene, which can be obtained by singlet oxygenation of 1,3-COD [equation (E9)], but this was not detected.

In view of the results with these cyclo-octadienes, the absence of ether formation in the peroxymercuriation of acyclic dienes with $Hg(NO_3)_2 \cdot H_2O$ [1,6] deserves comment. This is to be expected with penta-1,4-dienes since oxacyclobutanes would have to result and there is no precedent for this in oxymercuriation. In the case of hexa-1,5-diene it appears that formation of the six-membered peroxide ring is favoured over that of the five-membered ether, a choice that is not self-apparent but equally is not surprising.

Origin of Non-peroxide Products in Reduction.— The major by-product in the reduction [equation (E8)] of 2,6-bistrifluoroacetoxymercuria-9,10-dioxabicyclo-[3.3.2]decane (12) was cyclo-oct-4-enol (18). This result parallels that for the monocyclic peroxymercurials derived from penta-1,4-dienes and hexa-1,5-dienes [1,6] and the same explanation of partial deoxymercuriation can be offered. The formation of an appreciable amount (11%) of 1,5-COD from (12) indicates that double deoxymercuriation also takes place.

Our results [22b] and those of others [34] indicates that deoxymercuriation during reduction can be suppressed by pre-treating the oxymercurial with aqueous sodium hydroxide before mixing it with the alkaline sodium borohydride. When we carried out this procedure with (12), (18) was indeed not formed, but neither was the demercuriated peroxide (4), and the only product detected was 1-hydroxy-9-oxabicyclo[3.3.1]nonane (16).[29] We assume that (16) arises from base-induced isomerisation of (12) to an oxo-alcohol (a similar reaction was previously observed with a bis-mercuriated 1,2-di-

oxacyclopentane),[6] followed by rearrangement to the hemi-acetal and reduction [equation (E31)]. The mercuriated peroxide (12) must be more susceptible to base-induced isomerisation than the parent compound

(E30)

(12)　　　(16)
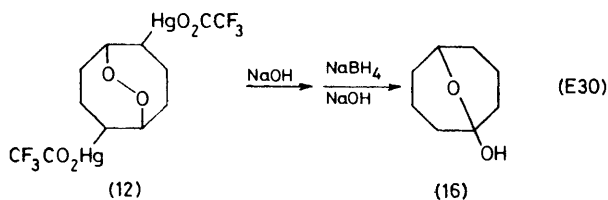
(4), presumably as the result of a higher solubility in the basic aqueous medium.

The most intriguing by-product from the reduction of (12) was *trans*-1,2-epoxy-*cis*-cyclo-oct-5-ene (19). Epoxides are formed in the reduction of acyclic peroxymercurials,[35] particularly those derived from medial

(E31)

(12)
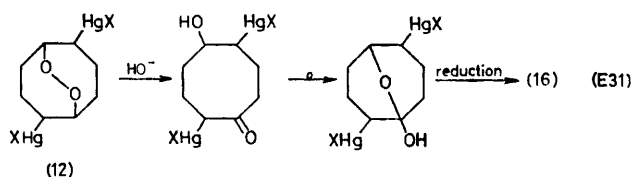
alkenes,[22b] and epoxy-alcohols have been obtained in the reduction of monocyclic peroxymercurials.[36] In each case it was suggested that the epoxide arose *via* γ-scission of a β-peroxyalkyl radical [equation (E32)]. The

(E32)
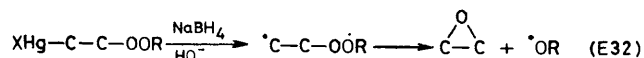
formation of (19) requires both a γ-scission of this type and a deoxymercuration, but the sequence of these events is unknown.

EXPERIMENTAL

Commercial 1,5-COD, 1,3-COD, and cyclohexa-1,4-diene were used without further purification. A mixture of 1,4-COD (*ca.* 70%) and 1,5-COD [δ_C (CDCl$_3$) 128.70 and 28.22] was prepared by dehydrobromination [22a] of 5-bromocyclo-octene [δ_C (CDCl$_3$) 129.44, 129.19, 55.07, 39.78, 37.05, 27.05, 25.27, and 25.27] which was obtained by hydrobromination [21] of 1,5-COD. A pure sample of 1,4-COD was obtained by g.l.c. using multiple injections (200 µl) of the mixture on a column (10 ft × ⅜ in outside diameter) of triscyanoethoxypropane (20% on Supasorb 40—60 mesh) at 60 °C with nitrogen carrier gas (150 cm³ min⁻¹); the ¹H n.m.r. spectrum was in agreement with that previously reported; [22a] δ_C (CDCl$_3$) 130.46, 128.42, 29.59, 24.81, and 23.11.

Mercury(II) trifluoroacetate was prepared by Brown and Rei's method [37] and was stored in a desiccator; samples were dried for several hours over P$_2$O$_5$ at 40 °C and 0.1 mmHg immediately before use. Mercury(II) nitrate monohydrate and mercury(II) acetate were commercial samples (reagent grade) which were stored in a desiccator. Hydrogen peroxide was a gift from Laporte Industries Ltd., and was stored at 0 °C; required amounts ($\pm$5%) were measured

out by glass pipette assuming the density to be 1.33 g cm⁻³.

Commercial sodium borohydride (reagent grade), potassium bromide, potassium chloride, and bromine (AnalaR), deuteriochloroform (99.8 atom %), deuterium oxide (99.5 atom %), and hexadeuteriobenzene (99.5 atom %) were used without further purification. Reagent-grade solvents were redistilled for h.p.l.c. work but otherwise were used without purification, except that for some peroxymercuriations the dichloromethane was distilled from P$_2$O$_5$. Silica gel for chromatography was 70—230 mesh.

¹H N.m.r. spectra were recorded with a Perkin-Elmer R12 or Varian HA 100 instrument, and ¹³C n.m.r. spectra with a Varian CFT 20 spectrometer. Mass spectra were recorded with an A.E.I. MS12 (inlet temperature 40—60 °C).

Peroxide test: peroxides were detected (*e.g.* on t.l.c.) by their ability to oxidise acidified iron(II) thiocyanate [38] to give a blood-red colour.

cis,cis-*Cyclo-octa*-1,5-*diene* (1,5-*COD*).—(a) *Peroxymercuriation using* Hg(NO$_3$)$_2$·H$_2$O. To a vigorously stirred suspension of mercury(II) nitrate monohydrate (3.50 g, 10.3 mmol) in dichloromethane (25 cm³) was added 80% hydrogen peroxide (0.25 cm³, 7.8 mmol) followed *immediately* by a solution of 1,5-COD (0.56 g, 5.2 mmol) in dichloromethane (5 cm³). The mixture was stirred for 10 min and a heavy oil separated. The supernatant liquid was decanted off. The oil was washed with dichloromethane (10 cm³) and evacuated at a water pump for 5 min (yield 3.81 g, 88% of starting materials).

(i) *Analysis by* ¹³C *n.m.r. spectroscopy.* The oil was dissolved in D$_2$O (4.0 cm³) and a few drops of 1,4-dioxan were added as an internal standard. The spectrum showed four strong peaks at δ 72.79, 50.76, 36.20, and 27.58, together with several relatively weak peaks in the range δ 36—22.

(ii) *Isolation of the organomercury chloride* (9b). The oil was dissolved in H$_2$O (5 cm³) containing a few drops of nitric acid and this solution was stirred vigorously with aqueous potassium chloride (10 mmol in 15 cm³) for 45 min. The white precipitate thus formed (59%) was filtered off and dried *in vacuo* (Found: C, 12.65; H, 1.55. Calc. for C$_8$H$_{12}$Cl$_2$Hg$_2$O: C, 16.1; H, 2.05%); δ_C (C$_5$H$_5$N–C$_6$D$_6$) 72.23, 54.23, 37.23, and 28.57; no other peaks. Thus the precipitate is probably a mixture of (9b) (80%) and HgCl$_2$.

(iii) *Isolation of the product of bromodemercuriation* (11). Bromine (1.87 g, 11.7 mmol) in dichloromethane (5 cm³) was added to a suspension of crude (9b) (3.59 g, 5.8 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 pentane (100 cm³) and the solvent removed from the extract (12 mmHg) to yield crude (11) (43%). The ¹³C n.m.r. spectrum showed 16 major lines with chemical shifts virtually the same as those found for the purified fractions (below). About one-third of the product was purified by h.p.l.c. using Porasil A (8 ft × ⅜ in) and a mixture of heptane (74%) and dichloromethane as eluant (flow rate 5 cm³ s⁻¹). Three fractions were obtained: fraction 1 (31 mg) was unidentified; fraction 2 contained 72 mg of a 1 : 1.2 mixture of the *trans,trans*-isomers of 2,5-dibromo-9-oxabicyclo[4.2.1]nonane [δ_C (CDCl$_3$) 81.99, 53.38, 32.48, and 27.98] and 2,6-dibromo-9-oxabicyclo[3.3.1]nonane (11a) [δ_C (CDCl$_3$) 69.74, 50.30, 31.17, and 26.09]; fraction 3 contained 148 mg of (11b) (*cis,trans*-isomer) [δ_C (CDCl$_3$) 72.18, 69.96, 51.87, 50.02, 30.15, 29.88, 28.88, and 19.56]. Mass spectra of fractions 2 and 3 were identical, showing parent ion (C$_8$H$_{12}$Br$_2$O⁺) peaks at *m/z* 282, 284, and 286 with

intensities in the ratio 1 : 2 : 1, and base peaks at m/z 203 and 205 with intensities 1 : 1.

A 10 : 1 mixture of *trans,trans*-2,5-dibromo-9-oxabicyclo-[4.2.1]nonane and (11a) was prepared independently from 1,5-COD by reaction with *N*-bromo-succinimide and aqueous acetone under conditions similar to those used previously [39] to obtain (11a).

(b) *Peroxymercuriation using* $Hg(O_2CCF_3)_2$. To a well-stirred solution of mercury(II) trifluoroacetate (4.27 g, 10.0 mmol) in dichloromethane (25 cm³) was added 80% hydrogen peroxide (0.25 cm³, 7.8 mmol) followed *immediately* by a solution of 1,5-COD (0.54 g, 5.0 mmol) in dichloromethane (5 cm³). The mixture was stirred for 10 min, then washed with water (15 cm³), dried ($MgSO_4$), and the solvent removed at a water-pump and finally at 0.1 mmHg to yield a white solid (2.83 g; 74%) [Found: C, 21.1; H, 1.85. Calc. for $C_{12}H_{12}F_6Hg_2O_6$ (peroxide): C, 18.8; H, 1.6%; and for $C_{12}H_{12}F_6Hg_2O_5$ (ether): C, 19.2; H, 1.6%].

(i) *Analysis by* ^{13}C *n.m.r. spectroscopy.* A solution of the crude product in $CDCl_3$ showed major resonances at δ 85.27, 48.42, 34.06, and 29.09 [assigned to (12)], 70.84, 52.49, 36.19, and 27.29 [assigned to (9c)], and 80.44, 56.56, 36.12, and 31.81 [assigned to (13)]; the molar ratio was calculated from the averages of the intensities of the peaks assigned to each compound and was found to be 1 : 1.2 : 0.5. Additional small peaks were present in the range δ 37—24.

The spectrum of a similar product obtained in 81% yield by using 5.0 mmol of 80% H_2O_2 showed the same components present in molar ratio 1 : 1.3 : 0.5, whereas the spectrum of the product obtained in 92% yield by using 10 mmol of 85% H_2O_2 + 10 mmol H_2O showed a molar ratio of 1 : 2.5 : 1.1. The number of accumulations (5—6 × 10⁴) was similar for each spectrum and the chemical shift of each of the 12 lines varied by no more than 0.15 p.p.m. from the value quoted above.

(ii) *Treatment with benzene.* The crude product (3.14 g) was dissolved in benzene (50 cm³) and almost immediately a white crystalline precipitate began to form. After 5 min the precipitate was filtered off and dried at 0.1 mmHg for several hours (yield 1.52 g), m.p. 118—119 °C (decomp.) (Found: C, 24.4; H, 2.2. $C_{12}H_{12}F_6Hg_2O_6\cdot0.85C_6H_6$ requires C, 24.6; H, 2.05%); δ_C (CH_2Cl_2–$CDCl_3$) 128.55 (C_6H_6), 85.35, 48.93, 34.28, and 29.48; the i.r. spectrum showed absence of $\nu(OH)$. The ^{13}C n.m.r. spectrum of the benzene-soluble portion showed the usual eight resonances for ethers (9c) and (13), but the complete absence of the lines assigned to peroxide (12).

When 98% H_2O_2 was used for the peroxymercuriation, treatment of 3.47 g (76% yield) of crude product with benzene (25 cm³) gave 1.62 g of (12·PhH) (42 mol%), while adding benzene (75 cm³) to 11.9 g (83% yield) of crude product gave 6.8 g of (12·PhH) (52 mol%).

(iii) *Reduction; isolation and characterisation of 9,10-dioxabicyclo[3.3.2]decane (4).* A pre-cooled solution of sodium borohydride (1.28 g, 33.7 mmol) in aqueous sodium hydroxide (50 cm³ × 0.6M) was added during 15 min to a well-stirred solution/suspension of (12·PhH) (6.1 g, 7.2 mmol) in dichloromethane (75 cm³) cooled in a bath of ice and methanol. Stirring was continued for a further 20 min and then the flask was allowed to come to room temperature. The layers were separated and the aqueous layer was saturated with potassium carbonate and extracted with more dichloromethane (50 and 20 cm³). The dichloromethane portions were combined, dried ($MgSO_4$), and the solvent removed *in vacuo* (finally at 2 mmHg) to afford an

oily solid (774 mg, 76%). The molar fractions of the main components [(4) and (18)] of this product was calculated from its integrated ^1H n.m.r. spectrum. T.l.c. (SiO_2, CH_2Cl_2 or EtOAc) showed the presence of a single peroxide and the absence of 7,8-dioxabicyclo[4.2.2]decane (15) by comparison with an authentic sample; the [4.2.2]-peroxide had a slightly larger R_F value than the [3.3.2]-compound in both solvents.

The crude product (406 mg) was chromatographed on silica gel (12 g) using dichloromethane as eluant and collecting 5-cm³ fractions. The first peroxide fraction contained only (4) (51 mg), the second (53 mg) contained (4) plus 15 mol% of *trans*-1,2-epoxy-*cis*-cyclo-oct-5-ene (19), and the third (41 mg) contained (4) plus 35 mol% of (19) as judged by ^1H n.m.r. spectroscopy; (18) (73 mg) was recovered from later fractions. The solid from the first fraction was sublimed at 45 °C (bath) and 15 mmHg to afford an analytically pure sample of (4), m.p. 116—118 °C (Found: C, 67.3; H, 9.5. $C_8H_{14}O_2$ requires C, 67.55; H, 9.9%); mass spectrum showed a parent-ion peak at m/z 142 with an intensity equal to 7% of the base peak at m/z 55; δ_H (CCl_4) 4.65—4.35 (m, 2 H) and 2.30—1.50 (m, 12 H); δ_C ($CDCl_3$) 83.96, 31.38, and 23.82.

Catalytic hydrogenation was carried out by stirring a solution of (4) (45 mg) in methanol (10 cm³) containing 10% Pd–C (7 mg) and connected to a reservoir of hydrogen for 2.5 h. The mixture was filtered and the methanol removed from the filtrate *in vacuo* to afford a low-melting solid (39 mg) with a ^1H n.m.r. spectrum identical with that of authentic *cis*-cyclo-octane-1,5-diol (Aldrich). Washing the solid with a little cold hexane afforded crystals, m.p. 73—75 °C (lit.,[18] m.p. 73.8—74.8 °C).

(iv) *Brominolysis; isolation and characterisation of 2,6-dibromo-9,10-dioxabicyclo[3.3.2]decane (5).* A solution of bromine (0.5 cm³, 9.8 mmol) in dichloromethane (5 cm³) was added with stirring to a solution/suspension of (12·PhH) 3.74 g, 4.4 mmol) in dichloromethane (30 cm³). The mixture was stirred overnight, filtered, and the filtrate evacuated at a water-pump. The resultant residue was extracted with a mixture of pentane (45 cm³) and dichloromethane (5 cm³) and the solvent removed from the extract (at 12, then 0.1 mmHg) to afford the crude bromoperoxide (67%) (Found: C, 30.65; H, 4.0; Br, 59.65. $C_8H_{12}Br_2O_2$ requires C, 32.05; H, 4.05; Br, 53.25%).

This material was purified by h.p.l.c. using a Waters Associates LC 500 instrument fitted with a column (30 cm × 5.7 cm outside diameter) of silica gel. Elution (250 cm³ min⁻¹) with dichloromethane–pentane (1 : 3) afforded two main fractions. Fraction 1 contained (5a), a white crystalline solid, m.p. 81—83 °C (Found: C, 31.65; H, 3.85%); mass spectrum showed molecular ions at m/z 298, 300, and 302 (relative intensities 1 : 2 : 1); δ_H ($CDCl_3$) 4.71 (m, 2 H, ΣJ *ca.* 12 Hz), 4.17 (m, 2 H, ΣJ *ca.* 25 Hz), and 2.47 (m, 8 H); δ_C ($CDCl_3$) 86.15, 48.18, 32.75, and 26.23. Fraction 2 was still a mixture (t.l.c.). By re-running the sample on h.p.l.c. using a Waters Associates LC100 instrument fitted with three columns (25 cm × 4.5 mm internal diameter) of Partisil 10 and an eluant (2 cm³ min⁻¹) of dichloromethane afforded a very small sample of a second diastereoisomer (5b); δ_H ($CDCl_3$) 4.66 (m, 2 H; ΣJ *ca.* 30 Hz), 4.38 (m, 2 H, ΣJ *ca.* 25 Hz), and 2.61 (m) and 2.32 (m) (8 H).

(c) *Peroxymercuriation using* $Hg(OAc)_2$. (i) *With* 80% H_2O_2. To a well stirred suspension of mercury(II) acetate (12.8 g, 40 mmol) in dichloromethane (70 cm³) cooled in an ice-bath was added 80% H_2O_2 (0.64 cm³, 20 mmol) followed

immediately by a solution of 1,5-COD (2.4 cm³, 20 mmol) in dichloromethane (7 cm³). The orange colouration which resulted had disappeared after 30 min. A pre-cooled solution of 3M NaOH (10 cm³) was added and a yellow precipitate was formed (showing the presence of unreacted Hg^{II} salt). A pre-cooled solution of sodium borohydride (2.3 g, 61 mmol) in 3M NaOH (50 cm³) was added over a period of 30 min, and after stirring for a further 15 min the flask was allowed to come to room temperature. The resulting layers were separated and the aqueous layer extracted with more dichloromethane (20 cm³). The dichloromethane portions were combined, dried (MgSO₄), and the solvent removed at a water-pump and then at 0.1 mmHg to give a colourless, viscous, sweet-smelling oil (56%); a test for peroxide was negative. Column chromatography (SiO₂; CH₂Cl₂) afforded cyclo-oct-4-enyl acetate (14) (Found: C, 72.0; H, 9.6. Calc. for C₁₀H₁₆O₂: C, 71.45; H, 9.5%); mass spectrum showed a strong parent-ion peak at m/z 168; δ_H (CDCl₃) 5.5—5.8 (m, 2 H), 4.5—4.9 (m, 1 H), 2.0 (s, 3 H), and 1.5—2.4 (m, 10 H); δ_C (CDCl₃) 169.95, 129.76, 128.64, 75.49; 33.81, 28.16, 25.67, 24.96, 22.47, and 21.31.

(ii) *With* 30% H₂O₂. (We thank J. L. Courtneidge for carrying out these experiments.) To a well-stirred suspension of mercury(II) acetate (20 mmol) in 30% H₂O₂ (40 cm³) at −10 °C was added 1,5-COD (10 mmol). The mixture was stirred at −15 to −5 °C for 3.5 h and then treated with cold aqueous KCl (30 mmol in 15 cm³). The resultant white precipitate was filtered off, washed with water (2 × 15 cm³), and added to dichloromethane (15 cm³). This suspension was treated with cold 2M NaOH (20 cm³) and the resultant mixture was added to sodium borohydride (40 mmol) in 2.5M NaOH (30 cm³) at 0 °C over 10 min. The dried dichloromethane layer afforded a crude product (65%) which by ¹³C n.m.r. analysis contained the following compounds in the mol fractions indicated: (4) (7%), (15) (6%), (16) (14%), (10) (9%), (17) (41%), and (18) (23%).

A similar experiment in which the base pre-treatment of the organomercury chloride was omitted afforded the following mixture: (4) (10%), (15) (8%), (16) (5%), (10) (10%), (17) (21%), (18) (41%), and 1,5-COD (5%).

(d) *Preparation of authentic 2,6-bistrifluoroacetoxymercuria-9-oxabicyclo[3.3.1]nonane*, (9c), *and 2,5-bistrifluoroacetoxymercuria-9-oxabicyclo[4.2.1]nonane*, (13). A mixture of 2,5-bischloromercuria-9-oxabicyclo[4.2.1]nonane and (9b) was prepared *via* oxymercuration of 1,5-COD using mercury(II) acetate (10 mmol) in a mixture of acetone (30 cm³) and water (5 cm³). This was suspended in dichloromethane (25 cm³), silver trifluoroacetate (10 mmol) was added, and the mixture stirred for 20 h in the dark. Filtration through Kieselguhr and removal of the solvent *in vacuo* afforded (13) and (9c) (34%).

(e) *Preparation of authentic cyclo-oct-4-enyl acetate* (14) *and cyclo-oct-4-en-1-ol* (18). 5-Acetoxy-6-acetoxymercuria-cyclo-octene was prepared in 83% yield by Barluenga's method;[16] m.p. 91—94 °C (lit., 89—90 °C,[16] 91—92 °C [40]); ¹H n.m.r. spectrum in agreement with that published;[40] δ_C (CDCl₃) 176.95, 169.69, 131.03, 128.89, 77.37, 49.34, 34.96, 30.02, 26.68, 23.24, 22.60, and 21.52.

Reduction of a solution of the acetoxymercurial in dichloromethane with aqueous sodium borohydride (*no* NaOH) followed by column chromatography (SiO₂; CH₂Cl₂) of the crude product (77%) isolated from the dried dichloromethane layer afforded (14) in 60% yield.

As described by Barluenga,[16] treatment of the acetoxy-

mercurial with aqueous sodium hydroxide followed by reduction with basic sodium borohydride gave a mixture of (18) and 1,5-COD. A pure sample of (18) was isolated by column chromatography (SiO₂; CH₂Cl₂); δ_H (CCl₄) 5.2—5.8 (m, 2 H), 3.4—3.85 (m, 1 H), and 1.2—2.4 (m) with strong signals centred at 1.65 and 2.05 (11 H); δ_C (CDCl₃) 130.14, 129.49, 72.70, 37.60, 36.31, 25.69, 24.94, and 22.84.

Cyclo-octa-1,4-diene (1,4-COD).—(a) *Peroxymercuriation and reduction; isolation and characterisation of 8,9-dioxabicyclo[5.2.1]decane* (6). To a well-stirred solution of mercury(II) trifluoroacetate (8.40 g, 19.7 mmol) in dichloromethane (40 cm³) cooled in a bath of ice was added 80% hydrogen peroxide (0.8 cm³, 25 mmol) followed *immediately* by a solution of 1,4-COD containing 30% of 1,5-COD (1.20 cm³, 9.73 mmol, diene) in dichloromethane (5 cm³). The mixture was stirred for 30 min and then the bath of ice was replaced by a bath of ice and salt. Pre-cooled aqueous sodium hydroxide (10 cm³, 3M) was added carefully and then a pre-cooled solution of sodium borohydride (1.0 g, 26.3 mmol) in aqueous sodium hydroxide (40 cm³, 3M) was added slowly. Stirring was continued while the flask was allowed to come to room temperature. The layers were separated and the aqueous layer was extracted with more dichloromethane (15 cm³). The dichloromethane portions were combined, dried (MgSO₄), and the solvent removed *in vacuo* (finally at 0.1 mmHg) to afford a viscous oil (970 mg, 70%).

The crude product was chromatographed on silica gel (12 g) using dichloromethane as eluant. All fractions giving a positive peroxide test were combined and the solvent removed under reduced pressure to yield a white solid (574 mg). ¹³C N.m.r. analysis of this material indicated that it contained the following compounds in the mol fractions indicated: (6) (60%), (4) (20%), (17) (10%), and (10) (10%). This material was re-chromatographed on silica gel (25 g) using pentane (66%) and dichloromethane as eluant. Removal of the solvent *in vacuo* from the peroxide fractions first eluted which did not contain (4) (t.l.c.) yielded pure (6) (261 mg, 19%), m.p. 63—64 °C (Found: C, 67.55; H, 9.8. C₈H₁₄O₂ requires C, 67.55; H, 9.9%); mass spectrum showed a molecular ion peak at m/z 142; δ_H (CCl₄) 4.37 (m, 2 H), 2.79 (dt, ²J 12.0, ³J 9.7 Hz, 1 H), 2.35 (dt, ³J 2.5 Hz, 1 H), and 1.30—2.15 (m, 10 H); δ_C (CDCl₃) 77.61, 45.18, 33.12, 26.14, and 25.13.

The yield of (6) was improved by doubling the scale of the peroxymercuriation, washing the resultant dichloromethane solution, and then adding it over 30 min to basic sodium borohydride (160 mmol in 70 cm³ of 3M NaOH); silica chromatography using pentane (90%) and dichloromethane afforded pure (t.l.c.) (6) (28%).

(b) *Peroxymercuriation and brominolysis; isolation and characterisation of 2,6-dibromo-8,9-dioxabicyclo[5.2.1]decane* (7). To a well-stirred solution of mercury(II) trifluoroacetate (22.9 g, 53.7 mmol) in dichloromethane (50 cm³) cooled in a bath of ice was added 80% hydrogen peroxide (3.0 cm³, 93.9 mmol) followed *immediately* by a solution of 1,4-COD containing 30% of 1,5-COD (2.8 cm³, 22.7 mmol) in dichloromethane (5 cm³). After 15 min an aqueous solution of potassium bromide (5.6 g, in 50 cm³) was added and the mixture shaken vigorously. The white precipitate thus obtained was filtered off, washed with water, dried under suction, and then added to the dried (MgSO₄) dichloromethane layer. To this was added slowly with stirring a solution of bromine (5.6 g, 35 mmol) in dichloromethane (10 cm³) and stirring was continued overnight.

The mixture was filtered and the filtrate concentrated at 12 mmHg, then passed through a short column (5—10 g) of silica gel to yield, after removal of the solvent *in vacuo*, a pale yellow viscous oil (5.2 g, 76%). The ^{13}C n.m.r. spectrum of this material showed strong absorptions at δ 80.52, 52.38, 39.94, 34.54, and 16.35; 83.25, 81.15, 53.79, 53.65, 42.50, 37.29, 34.54, and 21.51; and 83.58, 54.79, 45.45, 37.29, and 17.12, assigned to the three diastereoisomers of (7), and much weaker lines at δ 72.40, 46.07, 34.04, 29.82, 27.48, 26.74, and 23.63 from an unidentified component; very weak peaks in the correct region for (5) were also discernible.

In a separate experiment a product isolated similarly in 38% yield and having an identical ^{13}C n.m.r. spectrum was analytically pure (Found: C, 32.25; H, 3.75. $C_8H_{12}Br_2O_2$ requires C, 32.05; H, 4.05%).

Separation of the diastereoisomers by h.p.l.c. using the same conditions as for (5) afforded, in order of elution, (7a) (7%), and (7b) (14%). Compound (7a) was obtained as transparent needles, m.p. 62—63 °C (Found: C, 31.55; H, 3.8%); mass spectrum showed molecular ions at m/z 298, 300, and 302 with relative intensities of 1 : 2 : 1; δ_H (CDCl$_3$) 4.66 (ddd, $^3J_{CHBr}$ 5.0 Hz, CHO), 4.42 (m, CHBr), 3.50 (dt, ^2J 14.0, $^3J_{CHO}$ 2.75 Hz, CH$_2$ bridge), 2.90 (dt, $^3J_{CHO}$ 9.75 Hz, CH$_2$ bridge), 2.34 (m, 4 H), and 1.98 (m, 2 H); δ_C (CDCl$_3$) 80.88, 52.17, 40.00, 34.60, and 16.39. Compound 7b was obtained as a waxy solid; mass spectrum identical with that of (7a); δ_H (CDCl$_3$) 4.20—5.02 (m, 4 H), 2.96 (t, ^3J 7.0 Hz, 1 H), 2.94 (t, ^3J 6.5 Hz, 1 H), 2.42 (m, 4 H), and 1.83 (m, 2 H); δ_C (CDCl$_3$) 83.30, 81.26, 53.79, 53.55, 42.61, 37.32, 34.60, and 21.59.

Cyclo-octa-1,3-diene.—Peroxymercuriation and reduction was carried out as for 1,4-COD and yielded a colourless viscous oil (65%). Preparative g.l.c. (10 ft × $\frac{3}{8}$ in outside diameter silicone oil on Supasorb; 70 °C; 10 lb in^{-2} N$_2$) afforded a pure sample of (21); δ_H (CDCl$_3$) 5.8 (s, 2 H), 4.9 (d, 2 H), and 1.7 (m, 8 H), in agreement with the published data; [10] δ_C (CDCl$_3$) 130.86, 83.11, 33.88, and 24.29.

Cyclohexa-1,4-diene.—Peroxymercuriation and brominolysis were carried out as for 1,4-COD but on half the scale. Column chromatography [SiO$_2$; pentane–dichloromethane (66 : 34)] on the crude product (26%) followed by h.p.l.c. under the conditions used to isolate (5b) but with pentane–dichloromethane (7 : 3) as eluant afforded (8) (35 mg, 1.8%) as a white solid, m.p. 91—93 °C; mass spectrum showed molecular ions at m/z 270, 272, and 274 with relative intensities 1 : 2 : 1; δ_H (CDCl$_3$ 4.80 (m, ΣJ ca. 12 Hz, CHO), 4.21 (m, ΣJ ca. 14 Hz, CHBr), 3.20 (dt, ^2J 17.5, ^3J 6.0 Hz, CH^{1}H^2 CHO), 2.50 (m, CH$_2$CHBr), and 2.40 (dt, ^3J 2 Hz, CH^{1}H^{2}CHO); δ_C (CDCl$_3$) 76.48, 43.04, 38.14, and 20.91.

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