# Chemical transformations of solvent-derived ozonolysis products: acid-catalysed reactions of α-alkoxy α′-hydroperoxy isochromans with aldehydes

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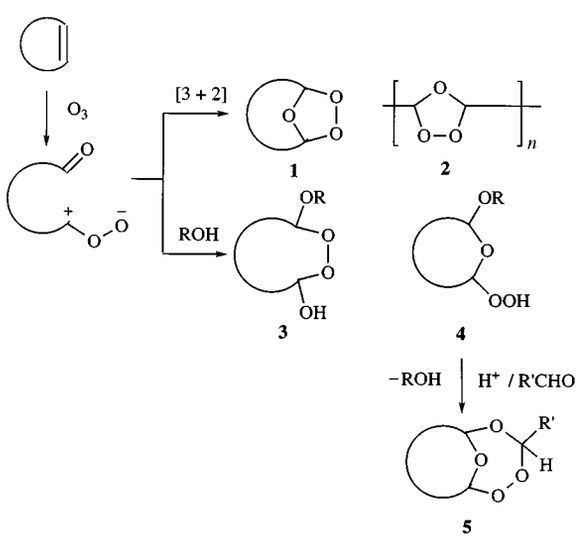
***Received (in Cambridge) 17th June 1998, Accepted 17th July 1998***

α-(2,2,2-Trifluoroethoxy) α′-hydroperoxy cyclic ethers **6**, derived from the ozonolysis of 1-substituted indenes in 2,2,2-trifluoroethanol, undergo acid-catalysed cyclocondensations with aliphatic aldehydes to yield 1,2,4,6-tetroxepanes **8**. With formaldehyde, hydroperoxides **6** afford the structurally novel 1,2,4,6,8-pentoxonane derivatives **9** in addition to 1,2,4,6-tetroxepanes. In contrast, the analogous acid-catalysed cyclocondensations involving the isomeric hydroperoxides **7** result in extensive degradation, though acidolysis of hydroperoxides **7** gives rise to the symmetrical 1,2-dialkyl peroxides **16**.

Ozonolysis of cyclic alkenes may produce a variety of peroxidic products depending on the nature of the substrate and the reaction conditions.[1] In addition to bicyclic and polymeric ozonides **1** and **2** respectively, solvent-derived products such as **3** and **4** may also be formed when the ozonolysis is carried out in the presence of participating solvents such as alcohols (Scheme 1).[2]

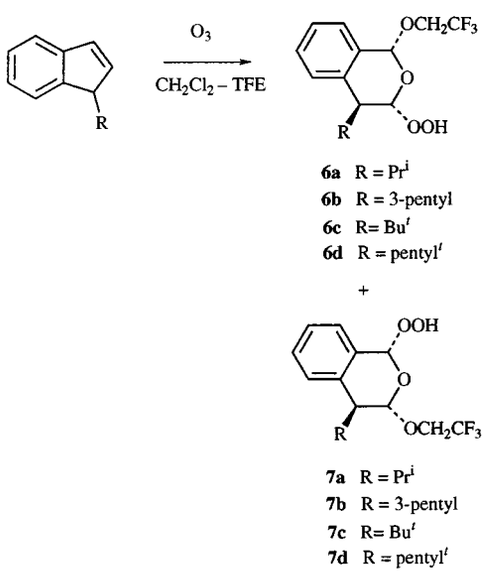



**Scheme 1**

In developing synthetic routes to novel cyclic peroxide systems which are structurally analogous to peroxidic natural products,[3] we have shown (see preceding paper) that α-alkoxy α′-hydroperoxy cyclic ethers **4** undergo acid-catalysed cyclocondensations with aliphatic aldehydes to produce the corresponding bicyclic 1,2,4,6-tetroxepane derivatives **5** (Scheme 1).[4] We now report some results obtained from a further series of acid-catalysed transformations involving solvent-derived products obtained from the ozonolysis of 1-substituted indenes.

## Results and discussion

Ozonolysis of the appropriate 1-substituted indenes in $CH_2Cl_2$–2,2,2-trifluoroethanol (TFE) afforded the isomeric isochroman




**Scheme 2**

derivatives **6** and **7** in varying relative ratios (Scheme 2).[5] The relative stereochemistries of the hydroperoxides **6** and **7** were established by either X-ray crystallography (for compound **6c**) or $^1$H NOE experiments.[5]

### Acid-catalysed condensation reactions between the alkoxy hydroperoxides 6a–d and carbonyl compounds

Acid-catalysed condensation reactions between the alkoxy hydroperoxides **6a–d** and simple aliphatic aldehydes produced the corresponding 1,2,4,6-tetroxepane derivatives **8a–j** in moderate to good yields as summarized in Table 1. Although the tetroxepanes **8b**, **8d**, **8f–h** and **8i** could have been formed as stereoisomers, only one isomer was actually obtained in each case. $^1$H NOE experiments on the isopropyl-substituted tetroxepane **8h** suggested that it was the *exo*-isomer (Fig. 1). X-Ray crystallographic analysis of the crystalline tetroxepane derivative **8j** showed that this was also the *exo* isomer (*vide infra*).

**Table 1** Reaction of the solvent-derived ozonolysis products with aldehydes in the presence of trifluoroacetic acid.[a]

| Substrate | Aldehyde | Reaction time/h | Tetroxepanes (yield, %) | Others (yield, %) |
|---|---|---|---|---|
| **6a** | HCHO | 2 | **8a** (32) | **9a** (24) |
| **6a** | MeCHO | 1 | **8b** (61) | |
| **6b** | HCHO | 4 | **8c** (11) | **9b** (34), **10b** (39) |
| **6b** | MeCHO | 1.5 | **8d** (74) | |
| **6c** | HCHO | 2 | **8e** (31) | **9c** (27) |
| **6c** | MeCHO | 2 | **8f** (61) | |
| **6c** | EtCHO | 2 | **8g** (74) | |
| **6c** | $Me_2CHCHO$ | 18 | **8h** (49) | |
| **6c** | $Me_3CCHO$ | 2 | | **14c** (32) |
| **6c** | *o*-$CF_3C_6H_4CHO$ | 2 | | **10c** (39), **14c** (22) |
| **6c** | $PhCOCF_3$ | 2 | | **10c** (60), **14c** (34) |
| **6d** | HCHO | 17 | **8i** (30) | **9d** (23) |
| **6d** | MeCHO | 17 | **8j** (74) | |
| **7a** | | 2 | **16a** (27) | |
| **7b** | | 2 | **16b** (33) | |
| **7c** | | 2 | **16c** (29) | |
| **7d** | | 2 | **16d** (34) | |
| **17** | MeCHO | 2 | **18** (30)[b] | **20** (11), **21** (44) |
| **17** | PhCHO | 2 | | **20** (37) |

[a] Treatment of a *ca.* 1 : 10 mixture of the hydroperoxide **6** with an aldehyde in the presence of 1 equiv. of trifluoroacetic acid. [b] A *ca.* 1 : 1 mixture of two stereoisomers.

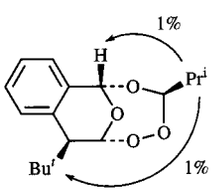
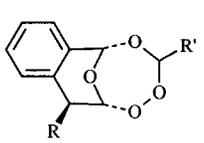
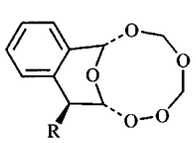


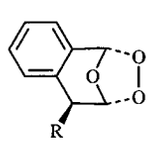

**Fig. 1** NOE in the tetroxepane **8h**.



**8a** R = $Pr^i$, R' = H
**8b** R = $Pr^i$, R = Me
**8c** R = 3-pentyl, R' = H
**8d** R = 3-pentyl, R' = Me
**8e** R = $Bu^t$, R = H
**8f** R = $Bu^t$, R = Me
**8g** R = $Bu^t$, R = Et
**8h** R = $Bu^t$, R = $Pr^i$
**8i** R = pentyl$^t$, R' = H
**8j** R = pentyl$^t$, R' = Me



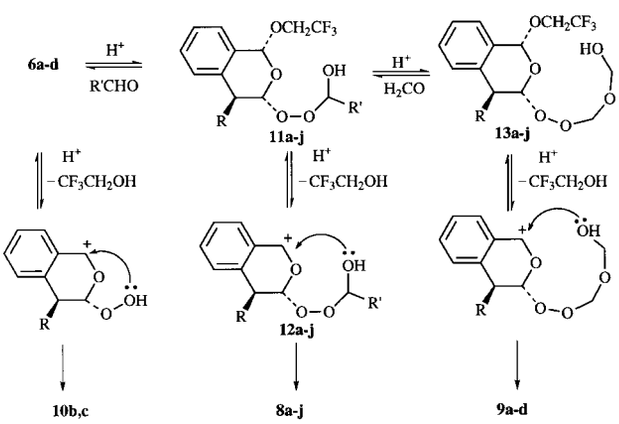
**9a** R = $Pr^i$
**9b** R = 3-pentyl
**9c** R = $Bu^t$
**9d** R = pentyl$^t$



**10b** R = 3-pentyl
**10c** R = $Bu^t$

With formaldehyde, additional peroxidic products, subsequently shown to be the structurally novel 1,2,4,6,8-pentoxonane derivatives **9a**–**d** (*vide infra*),[6] were also obtained in each case. Ozonide **10b** was also obtained from the reaction of compound **6b** and formaldehyde.

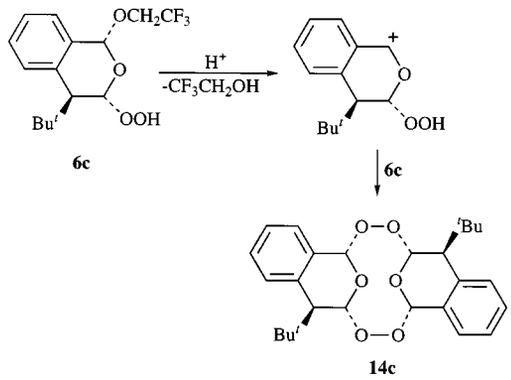
The formation of the bicyclic peroxidic compounds **8**–**10** can be rationalized by the sequence outlined in Scheme 3. Since the hydroperoxy and trifluoroethoxy groups are *cis*, cyclization of the adducts, derived from hemiperacetals **6a**–**d** and the indicated aldehydes, **11a**–**j** can only take place *via* the corresponding stabilized carbocations **12a**–**j** to give the tetroxepanes **8a**–**j** (*cf.* the formation of 1,2,4-trioxanes from




**Scheme 3**

allylic hemiperacetals[7]). Given the propensity of formaldehyde to oligomerize in solution,[8] it is not surprising that the addition of second molecule of formaldehyde to the intermediates **11** (R′ = H) to give the extended hemiperacetals **13a**–**d**, the most likely precursors of the pentoxonanes **9a**–**d**, could compete effectively under acidic conditions with the aforementioned pathway to the tetroxepanes. Although recognized as being disfavoured for carbocyclic systems, cyclization reactions producing 9-membered ring heterocycles are, however, more common, *e.g.* the formation of hexoxonanes from the peroxidation of ketones.[9] This may be attributed to a comparative reduction in destabilizing factors such as Pitzer strain in the conformations of intermediates leading to the heterocyclic systems.

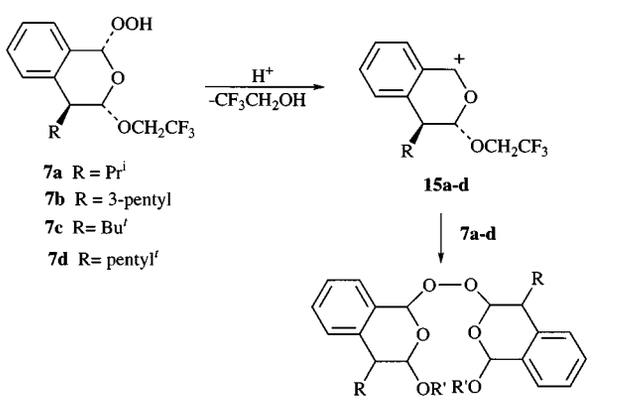
Contrary to the above observations, attempted condensation of **6c** with pivaldehyde afforded the symmetrical hexoxecane derivative **14c**, resulting from the cyclocondensation of two molecules of the hydroperoxide **6c**, in 32% yield (Scheme 4) instead of the expected tetroxepane derivative.[10] Similarly, the reactions of **6c** with *o*-trifluoromethylbenzaldehyde and trifluoroacetophenone yielded only the ozonide **10c** and the dimeric hexoxecane **14c** (Table 1, entries 10 and 11). These latter observations were surprising because the analogous mercurinium ion-mediated cyclisation reactions involving electron-deficient aldehydes such as 4-chlorobenzaldehyde and allylic hydroperoxides provide an effective synthetic route to 1,2,4-trioxanes.[7]




Scheme 4

### Acid-catalysed condensation reactions between the alkoxy hydroperoxides 7a–d and carbonyl compounds

The analogous acid-catalysed reactions between the isomeric hydroperoxides **7a–d** and aldehydes such as formaldehyde and acetaldehyde did not produce the expected cyclocondensation products; complex product mixtures were obtained instead. Acidolysis of the hydroperoxides **7a–d**, on the other hand, gave the corresponding dialkyl peroxides **16a–d** in moderate yield (*cf.* acidolysis of **6c** which gives **14c**[10]) (Scheme 5). There is,



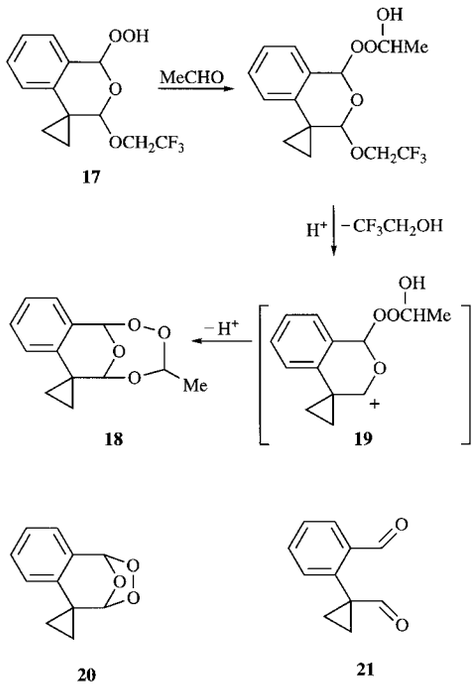

**16a** R = $Pr^i$, R' = $OCH_2CF_3$ (27%)
**16b** R = 3-pentyl, R' = $OCH_2CF_3$ (33%)
**16c** R= $Bu^t$, R' = $OCH_2CF_3$ (29%)
**16d** R= $pentyl^t$, R' = $OCH_2CF_3$ (34%)

Scheme 5

however, some precedent for the acid-catalyzed condensation of alkyl hydroperoxides leading to dialkyl peroxides.[11]

These results are generally consistent with the selective elimination of the hydroperoxy group from hydroperoxides **7a–d** to generate the corresponding carbocation intermediates **15a–d** which are subsequently captured by a second molecule of **7a–d** as appropriate. Thus, the remarkable contrast in behaviour between the isomeric isochromans, **6** and **7**, would imply that the relative stability of the intermediate carbocation rather than the nature of the leaving group determines which group should leave in the acidolysis process.

With the above in mind, the acid-catalyzed condensation reaction between hydroperoxide **17** and acetaldehyde was carried out. Certainly, the tetroxepane **18** was isolated in 30% yield along with ozonide **20** and dialdehyde **21**, suggesting that the presence of the cyclopropyl group accelerated the formation of the key carbocation intermediate **19** leading to the tetroxepane derivative **18** (a 1 : 1 mixture of two isomers) (Scheme 6). Only the bicyclic ozonide **20** was isolated from the attempted cyclocondensation of **17** with benzaldehyde.




Scheme 6

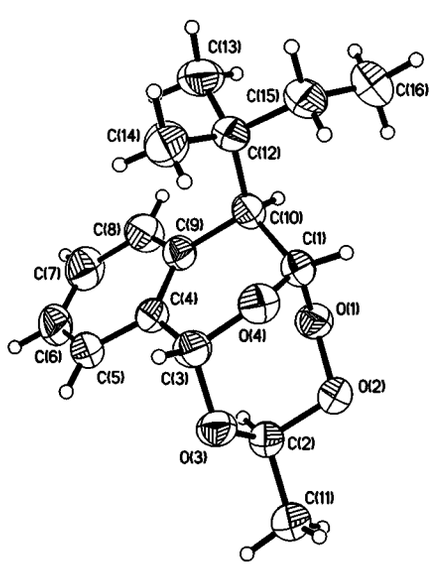



**Fig. 2** The solid state structure of one molecule of 1,2,4,6-tetroxepane **8j** (ORTEP,[17] the non-hydrogen atoms are represented by 50% probability ellipsoids and hydrogen atoms by spheres of arbitrary radius).

### Structural studies of bicyclic peroxides 8j and 9c

The structure of the crystalline tetroxepane derivative **8j** was determined by X-ray crystallographic analysis. The molecular structure of **8j** in the solid state is shown in Fig. 2 along with the numbering system used in the structural study. The observed bond distances and angles all lie within expected ranges [*e.g.* the bond distance O(1)–O(2) 1.462(2) Å is within the normal range].[12,13] Since the magnitudes of torsion angles around ring are substantially greater than zero, the conformation of the 1,2,4,6-tetroxepane ring corresponds more closely to a twist-chair than a chair [smallest torsion angle O(3)–C(1)–O(1)–O(2) 37.0(2)°]. In the isochroman ring system, C(1) lies significantly out of plane with respect to the other atoms [r.m.s. deviation for atoms C(3)–C(10) and O(4) 0.032 Å; C(1) −0.621 Å] and the *t*-pentyl group is in an axial position. The methyl group at C(2) occupies a sterically favoured pseudo-equatorial position,

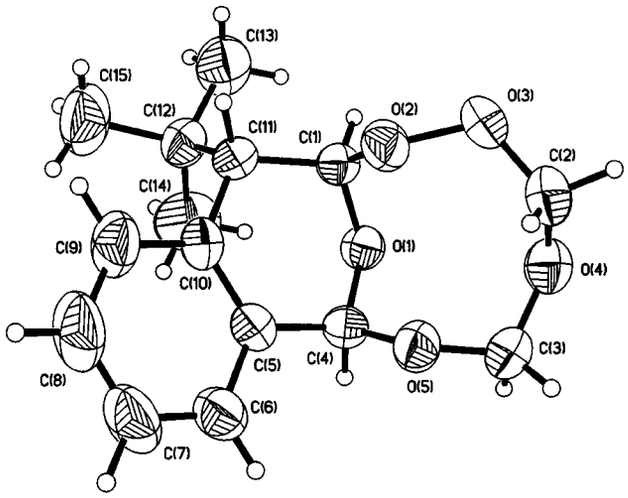



**Fig. 3** The solid state structure of one molecule of 1,2,4,6,8-pentoxonane **9c** (ORTEP,[17] the non-hydrogen atoms are represented by 50% probability ellipsoids and hydrogen atoms by spheres of arbitrary radius).

*exo* with respect to the bridging oxygen atom O(4) as observed previously.[4]

From the complexity of its $^{13}C$ NMR spectrum, pentoxonane derivative **9c** appeared to exist in solution as a mixture of conformers. Even at −80 °C (in $CD_3COCD_3$), eight signals attributable to the carbons bound in each case to two oxygen atoms (93–102 ppm) were observed, suggesting that there were at least two conformers in equilibrium even at this low temperature.

By X-ray crystallographic analysis, compound **9c** was unambiguously shown to be a novel 1,2,4,6,8-pentoxonane derivative as illustrated in Fig. 3 along with the associated numbering scheme. The calculated bond lengths and angles all lie within expected ranges [*e.g.* the peroxide bond distance O(2)–O(3) 1.469(2) Å is not significantly different from that in **8j**].[12,13] Given the geometrical constraints on atoms C(1), O(1) and C(4), which are an integral part of the isochroman ring, the central pentoxonane ring of **9c** adopts a twist-boat conformation. This is less well defined than the conformations observed for more symmetrical nine-membered ring systems such as the cyclononanes[14] or the trimeric ketone peroxides.[15] Atom C(1) lies significantly out of plane with respect to the other atoms of the isochroman ring system [r.m.s. deviation for atoms C(4)–C(11) and O(4) 0.032 Å; C(1) −0.621 Å] and the *t*-butyl group at C(11) is in an axial position, anti to O(2) [torsion angle O(2)–C(1)–C(11)–C(12) 159.8(2)°].

In the solid state, the pentoxonane ring of **9c** is not disordered although the principal thermal parameters for the ring atoms C(2) and C(3) are slightly larger than those for C(1) and C(4) which would be consistent with a degree of conformational flexibility in that portion of the ring. It is likely that in the pentoxonane ring systems, even when constrained as in **9c**, conformational interconversions may take place *via* low energy barrier pseudo rotation processes.

In summary, acid-catalyzed reactions of α-alkoxy α′-hydroperoxy cyclic ethers such as **6a–d**, **7a–d** and **17** proceed *via* the more highly stabilized carbocation intermediates. Thus, acid-catalysed cyclocondensations between hydroperoxides **6** and aldehydes provide a convenient synthetic route to 1,2,4,6-tetroxepanes **8** whereas the isomeric compounds **7** generally undergo degradation under the similar reaction conditions. With formaldehyde, hydroperoxides **6** afford the structurally novel 1,2,4,6,8-pentoxonane derivatives **9** in addition to the expected 1,2,4,6-tetroxepanes. Acidolysis of hydroperoxides **7** results in the formation of symmetrical 1,2-dialkyl peroxides **16**.

## Experimental

### General

$^1H$ (270 MHz) and $^{13}C$ NMR (67.5 MHz) spectra were obtained in $CDCl_3$ solution with $SiMe_4$ as standard.

The α-alkoxy α′-hydroperoxy cyclic ethers **6a–d** and **17** were prepared according to literature procedures.[5] The physical properties of the products **8a–f**,[10] **9a–c**,[10] **10b**,**c**,[5] **20**[5] and **14c**[5] have been described previously.

**CAUTION**: Since organic peroxides are potentially hazardous compounds, they must be handled with due care; avoid exposure to strong heat or light, or mechanical shock, or oxidizable organic materials, or transition metal ions. No particular difficulties were experienced in handling any of the new peroxides synthesized in this work using the reaction scales and procedures described below together with the safeguard mentioned above.

Ozonolysis reactions must be carried out in a well ventilated fume cupboard.

### Acid catalysed condensation of α-alkoxy α′-hydroperoxy cyclic ethers 6a–d with aldehydes

The reaction of the hydroperoxide **6d** with formaldehyde is representative. Anhydrous sodium sulfate (500 mg) was added to a solution of the hydroperoxide **6d** (541 mg, 1.6 mmol) and formaldehyde (1315 mg of 37 wt% aqueous solution) in $CH_2Cl_2$ (10 $cm^3$) and the resulting mixture stirred at 0 °C for 2 h. After the addition of a solution of trifluoroacetic acid (182 mg, 1.6 mol) in $CH_2Cl_2$ (10 $cm^3$), the reaction was continued at room temperature for 19 h. Subsequently, the reaction mixture was poured into ice-cold aqueous $NaHCO_3$ and was extracted with diethyl ether (2 × 25 $cm^3$). The organic extracts were combined, dried over anhydrous sodium sulfate, and the solvent removed under reduced pressure. The products were isolated by column chromatography on silica gel (column, 2 × 50 cm; 20 g silica gel; elution with diethyl ether–hexane; the ratio was changed from 5 : 95 to 15 : 85) to give the tetroxepane **8i** (130 mg, 30%) and the pentoxonane **9d** (110 mg, 23%).

**6,7-Dihydro-7-*tert*-pentyl-1,6-epoxy-1*H*-2,4,5-benzotrioxonine 8i.** Oil (Found: C, 68.4; H, 7.7. $C_{15}H_{20}O_4$ requires: C, 68.2; H, 7.6%); $\delta_H$ 0.7–1.7 (11 H, m), 2.54 (1 H, s), 4.81 (1 H, d, *J* 9.5), 5.07 (1 H, d, *J* 9.5), 5.83 (1 H, s), 6.09 (1 H, s) and 7.1–7.4 (4 H, m); $\delta_C$ 8.18, 24.96, 25.89, 33.15, 36.85, 45.55, 94.63, 95.27, 100.82, 125.88, 126.70, 128.21, 130.66, 131.65 and 135.17.

**9-*tert*-Pentyl-8,9-dihydro-1,8-epoxy-1*H*-2,4,6,7-benzotetroxacycloundecine 9d.** Mp 66 °C (from diethyl ether–hexane) (Found: C, 65.5; H, 7.6. $C_{16}H_{22}O_5$ requires: C, 65.3; H, 7.5%); $\delta_H$ 0.8–1.6 (11 H, m), 2.66 (1 H, s), 4.77 (1 H, d, *J* 6.5), 5.00 (2 H, s), 5.15 (1 H, d, *J* 6.5), 5.66 (1 H, s), 5.96 (1 H, s) and 7.0–7.4 (4 H, m); $\delta_C$ 8.25, 24.45, 25.15, 32.69, 37.28, 45.69–45.82 (1C), 92.93–100.45 (4C), 126.18, 127.12, 127.95, 128.30, 130.53 and 130.60.

**3-Methyl-6,7-dihydro-7-*tert*-pentyl-1,6-epoxy-1*H*-2,4,5-benzotrioxonine 8j.** Mp 79 °C (from diethyl ether–hexane) (Found: C, 68.8; H, 8.05. $C_{16}H_{22}O_4$ requires: C, 69.0; H, 8.0%); $\delta_H$ 0.7–1.7 (14 H, m), 2.48 (1 H, s), 4.94 (1 H, q, *J* 6), 5.76 (1 H, s), 5.95 (1 H, s) and 7.1–7.4 (4 H, m); $\delta_C$ 8.20, 17.36, 24.98, 25.90, 33.20, 36.79, 45.56, 93.88, 100.90, 101.36, 125.86, 126.63, 127.96, 130.60, 132.49 and 135.00.

**7-*tert*-Butyl-6,7-dihydro-3-ethyl-1,6-epoxy-1*H*-2,4,5-benzotrioxonine 8g.** Mp 67.5–68.5 °C (from hexane) (Found: C, 69.01; H, 8.0. $C_{16}H_{22}O_4$ requires: C, 69.0; H, 8.0%); $\delta_H$ 0.89 (3 H, t, *J* 7), 0.98 (9 H, s), 1.2–1.8 (2 H, m), 2.37 (1 H, s), 4.71 (1 H, t, *J* 5), 5.81 (1 H, s), 5.98 (1 H, s) and 7.1–8.4 (4 H, m); $\delta_C$ 8.59, 24.84, 28.60, 34.22, 48.41, 93.82, 100.91, 105.17, 125.79, 126.73, 127.90, 130.85, 132.36 and 134.87.

**7-*tert*-Butyl-6,7-dihydro-3-isopropyl-1,6-epoxy-1*H*-2,4,5-benzotrioxonine 8h.** Mp 42–45 °C (from hexane) (Found: C, 69.8; H, 8.4. $C_{17}H_{24}O_4$ requires: C, 69.8; H, 8.3%); $\delta_H$ 0.92 (3 H,

d, *J* 6.9), 0.95 (3 H, d, *J* 6.9), 0.98 (9 H, s), 1.8–2.0 (1 H, m), 2.44 (1 H, s), 4.60 (1 H, d, *J* 5.3), 5.93 (1 H, s), 6.11 (1 H, s) and 7.1–7.4 (4 H, m); $\delta_C$ 13.64, 13.77, 25.00, 27.06, 30.62, 44.82, 90.15, 91.25, 103.74, 122.14, 123.12, 125.27, 127.26, 128.81 and 131.25.

### Treatment of the hydroperoxides 7a–d with trifluoroacetic acid

The acidolysis of the hydroperoxide **7b** is representative of the general procedure. To a solution of the hydroperoxide **7b** (752 mg, 2.25 mmol) in $CH_2Cl_2$ (20 $cm^3$), was added a solution of trifluoroacetic acid (256 mg, 2.25 mmol) in $CH_2Cl_2$ (5 $cm^3$) at 0 °C and the resulting reaction mixture was stirred at room temperature for 2 h. After the workup as described above, the products were isolated by column chromatography on silica gel. Elution with benzene–hexane (3 : 7) gave the dialkyl peroxide **16b** (242 mg, 33%).

**Bis[4-isopropyl-3,4-dihydro-3-(2,2,2-trifluoroethoxy)-1*H*-2-benzopyran-1-yl] peroxide 16a.** Mp 188–190 °C (from diethyl ether–hexane) (Found: C, 58.1; H, 5.6. $C_{28}H_{32}F_6O_6$ requires: C, 58.1; H, 5.6%); $\delta_H$ 0.94 (6 H, d, *J* 6), 1.01 (6 H, d, *J* 6), 1.7–2.2 (2 H, m), 2.78 (2 H, d, *J* 6), 4.18 (4 H, q, *J* 9), 5.38 (2 H, s), 6.40 (2 H, s) and 7.1–7.6 (8 H, m).

**Bis[4-(3-pentyl)-3,4-dihydro-3-(2,2,2-trifluoroethoxy)-1*H*-2-benzopyran-1-yl] peroxide 16b.** Mp 132–134 °C (from diethyl ether–hexane) (Found: C, 60.2; H, 6.4. $C_{32}H_{40}F_6O_6$ requires: C, 60.6; H, 6.4%); $\delta_H$ 0.83 (6 H, t, *J* 7), 0.94 (6 H, t, *J* 7), 1.3–1.6 (10 H, m), 3.05 (2 H, d, *J* 5), 4.0–4.2 (4 H, m), 5.30 (2 H, s), 6.36 (2 H, s) and 7.2–7.5 (8 H, m); $\delta_C$ 11.54, 11.75, 22.41, 22.88, 42.81, 45.66, 63.99 (q, *J* 34), 97.43, 97.77, 124.21 (q, *J* 279), 126.60, 127.26, 128.18, 129.24, 129.42 and 135.54.

**Bis[4-*tert*-butyl-3,4-dihydro-3-(2,2,2-trifluoroethoxy)-1*H*-2-benzopyran-1-yl] peroxide 16c.** Mp 191–193 °C (from diethyl ether–hexane) (Found: C, 59.3; H, 6.1. $C_{30}H_{36}F_6O_6$ requires: C, 59.4; H, 6.0%); $\delta_H$ 0.99 (18 H, s), 2.76 (2 H, s), 4.12 (2 H, q, *J* 9), 4.18 (2 H, q, *J* 9), 5.52 (2 H, s), 6.36 (1 H, s), 6.46 (1 H, s) and 7.1–7.6 (8 H, m); $\delta_C$ 28.14, 34.01, 51.21, 64.01 (q, *J* 34), 96.82, 97.35, 97.68, 98.74, 124.26 (q, *J* 275), 126.68, 126.84, 127.00, 128.33, 128.42, 129.07, 129.31, 131.29, 133.06 and 133.43.

**Bis[4-*tert*-pentyl-3,4-dihydro-3-(2,2,2-trifluoroethoxy)-1*H*-2-benzopyran-1-yl] peroxide 16d.** Mp 154–156 °C (from diethyl ether–hexane) (Found: C, 60.3; H, 6.4. $C_{32}H_{40}F_6O_6$ requires: C, 60.6; H, 6.35%); $\delta_H$ 0.8–1.3 (18 H, m), 1.3–1.8 (4 H, m), 2.86 (2 H, s), 4.10 (2 H, q, *J* 7), 4.18 (2 H, q, *J* 7), 5.50 (2 H, s), 6.37 (1 H, s), 6.48 (1 H, s) and 7.4–7.7 (8 H, m); $\delta_C$ 8.15, 8.17, 24.49, 25.39, 32.87, 32.90, 36.58, 48.47, 64.02 (q, *J* 34), 64.03 (q, *J* 34), 96.75, 97.26, 97.80, 98.86, 125.69 (q, *J* 278), 125.73 (q, *J* 278), 126.69, 126.78, 127.02, 128.35, 128.45, 129.36, 129.62, 131.10, 133.15 and 133.53.

### Acid catalysed reaction of the solvent-derived ozonolysis product 17 and aldehydes

A mixture of the hydroperoxide **17** (330 mg, 1.14 mmol) and acetaldehyde (502 mg) in $CH_2Cl_2$ (10 $cm^3$) was stirred at 0 °C for 2 h. Then, a solution of trifluoroacetic acid (131 mg, 1.14 mmol) in $CH_2Cl_2$ (10 $cm^3$) was added and the reaction was continued at room temperature for 19 h. After work-up as described above, the products were separated by column chromatography on silica gel (column, 2 × 50 cm; 20 g silica gel). Elution with diethyl ether–hexane (5 : 95) gave the ozonide **20** (23 mg, 11%). Subsequent elution gave first the minor isomer of the tetroxepane **18** (38 mg, 14%) and then the major **18** (43 mg, 16%). Further elution with ether–hexane (10 : 90) gave the dialdehyde **21** (87 mg, 44%).

**4′-Methyl-6′,7′-dihydro-1′,6′-epoxyspiro[cyclopropane-1,7′-1*H*-2,3,5-benzotrioxonine] 18 (minor isomer).** Mp 115 °C (from diethyl ether–hexane) (Found: C, 66.5; H, 5.9. $C_{13}H_{14}O_4$ requires: C, 66.7; H, 6.0%); $\delta_H$ 0.9–1.5 (4 H, m), 1.19 (3 H, d, *J* 5), 4.70 (1 H, s), 5.74 (1 H, q, *J* 5), 6.18 (1 H, s) and 6.6–7.6 (4 H, m); $\delta_C$ 9.31, 16.94, 18.22, 22.92, 100.95, 101.75, 102.35, 121.70, 125.88, 126.35, 129.36, 130.77 and 136.88.

**1,2,4,6-Tetroxepane 18 (major isomer).** Oil (Found: C, 66.4; H, 5.9%); $\delta_H$ 0.7–1.6 (4 H, m), 1.24 (3 H, d, *J* 5), 4.78 (1 H, s), 5.14 (1 H, q, *J* 5), 6.01 (1 H, s) and 6.5–7.6 (4 H, m); $\delta_C$ 10.42, 16.61, 17.81, 22.73, 97.08, 102.04, 106.02, 121.77, 125.75, 126.30, 128.34, 129.20 and 134.71.

**1-(*o*-Formylphenyl)cyclopropanecarbaldehyde 21.** Oil (Found: C, 75.9; H, 5.5. $C_{11}H_{10}O_2$ requires: C, 75.86; H, 5.75%); $\delta_H$ 1.31 (2 H, t, *J* 3), 1.58 (2 H, t, *J* 3), 7.1–8.0 (4 H, m), 8.97 (1 H, s) and 9.10 (1 H, s); $\nu_{max}/cm^{-1}$ 1700, 1595, 1490, 1270, 1190, 1095, 1010, 960, 895, 820, 755 and 590.

### Acid catalysed reaction of the solvent-derived ozonolysis product 6c and aldehydes

A mixture of the hydroperoxide **6c** (640 mg, 2.20 mmol) and α,α,α-trifluoro-*o*-tolualdehyde (1777 mg) in $CH_2Cl_2$ (10 $cm^3$) was stirred at 0 °C for 2 h. Then, a solution of trifluoroacetic acid (230 mg, 2.00 mmol) in $CH_2Cl_2$ (10 $cm^3$) was added and the reaction was continued at room temperature for 19 h. After work-up as described above, the products were separated by column chromatography on silica gel (column, 2 × 50 cm; 20 g silica gel). Elution with benzene–hexane (1 : 1) gave the ozonide **10c**[5] (172 mg, 39%). Subsequent elution with benzene gave the acyclic peroxide **16c**[10] (96 mg, 22%).

### Structure determination of 1,2,4,6-tetroxepane 8j

The crystal of **8j** used for X-ray data collection (approx. dimensions 0.50 × 0.65 × 0.65 mm) was grown by slow evaporation from a dichloromethane–hexane (1 : 1) solution and mounted in a sealed Lindemann capillary tube.

**Crystal data.** $C_{16}H_{22}O_4$, $M = 278.3$, colourless block, monoclinic, space group $P2_1/c$ (No. 14), $a = 7.6667(5)$, $b = 7.7101(5)$, $c = 25.182(2)$ Å, $\beta = 93.031(6)°$, $U = 1465.5(2)$ Å$^3$, $Z = 4$, $D_c = 1.244$ g cm$^{-3}$, $F(000)$ 600, $\mu$(Mo-Kα) 0.088 mm$^{-1}$.

**Data collection.** The intensity data were collected on a Siemens P4 diffractometer ($-1 \leqslant h \leqslant 9$, $-1 \leqslant k \leqslant 9$, $-29 \leqslant l \leqslant 29$; temperature 293 (2) K; $\theta$ range: 1.62 to 24.99°; Mo-Kα X-radiation ($\lambda$ 0.710 73 Å) and $\omega$-scanning). Of the 2592 unique data [$R$(int) = 0.025] measured, 1953 had $I > 2\sigma(I)$. The structure was solved by direct methods (SHELXS-86[16]) and was refined by full-matrix least-squares methods on $F^2$ (SHELXTL/PC[17]) using all $F^2$ data and anisotropic temperature factors for all the non-hydrogen atoms. At convergence, the discrepancy factors $R$ [$F > 4\sigma(F)$] and $wR^2$ were 0.045 and 0.108 respectively. The weighting scheme, $w = 1/[\sigma^2(F_o^2) + (0.0404\ P)^2 + 0.3733\ P]$ where $P = (F_o^2 + 2F_c^2)/3$ was found to give satisfactory analyses of variance. The final difference Fourier map was essentially featureless (general noise level less than ±0.10 e Å$^{-3}$) with largest difference peak and hole of 0.17 and −0.13 e Å$^{-3}$ respectively.

### Structure determination of 1,2,4,6,8-pentoxonane 9c

The crystal of **9c** used for X-ray data collection (approx. dimensions 0.7 × 0.4 × 0.3 mm) was grown by slow evaporation from a dichloromethane–hexane (1 : 1) solution and mounted in a sealed Lindemann capillary tube.

**Crystal data.** $C_{15}H_{20}O_5$, $M = 280.3$, colourless block, monoclinic, space group $P2_1/n$ (non-standard setting of No. 14), $a = 6.3115(14)$, $b = 30.689(9)$, $c = 7.536(3)$ Å, $\beta = 95.48(2)°$, $U = 1453.0(8)$ Å$^3$, $Z = 4$, $D_c = 1.281$ g cm$^{-3}$, $F(000)$ 600, $\mu$(Mo-Kα) 0.096 mm$^{-1}$.

**Data collection.** The intensity data were collected on an Enraf-Nonius CAD4 diffractometer [$-7 \leqslant h \leqslant 7$, $0 \leqslant k \leqslant 36$, $0 \leqslant l \leqslant 8$; temperature 293 (2) K; $\theta$ range: 1.33 to 24.96°; Mo-Kα X-radiation ($\lambda$ 0.710 73 Å) and $\omega$–2$\theta$-scanning]. Of the 2544 unique data [$R$(int) = 0.016] measured, 1761 had $I > 2\sigma(I)$. The structure was solved by direct methods (SHELXS-86[16]) and was refined by full-matrix least-squares methods on $F^2$ (SHELXTL/PC[17]) using all $F^2$ data and anisotropic temperature factors for all the non-hydrogen atoms. At

convergence, the discrepancy factors $R$ [$F > 4\sigma(F)$] and $wR^2$ were 0.049 and 0.116 respectively. The weighting scheme, $w = 1/[\sigma^2(F_o^2) + (0.0439\ P)^2 + 0.6579\ P]$ where $P = (F_o^2 + 2F_c^2)/3$ was found to give satisfactory analyses of variance. The final difference Fourier map was essentially featureless (general noise level less than ±0.10 e Å$^{-3}$) with largest difference peak and hole of 0.14 and −0.14 e Å$^{-3}$ respectively.

Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, available *via* the RSC Web page (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 207/247.

## Acknowledgements

This work was supported in part by a Grant-in Aid for Scientific Research on Priority Areas (10153238 and 10166211) from Ministry of Education, Science, Culture and Sports of Japan. We thank British Council (Tokyo) for the award of travel grants to M. N., A. M. and K. J. M.

## References

1 (*a*) *Ozonation in Organic Chemistry*, ed. P. S. Bailey, Academic Press, New York, 1978, vol. 1; 1982, vol. 2; (*b*) *The Chemistry of Peroxides*, ed. S. Patai, Wiley, New York, 1983.
2 K. J. McCullough and M. Nojima, in *Organic Peroxides*, ed. W. Ando, Wiley, New York, 1992, pp. 661–728.
3 D. A. Casteel, *Nat. Prod. Rep.*, 1992, **9**, 290; K. J. McCullough, *Contemp. Org. Synth.*, 1995, **2**, 225.
4 K. J. McCullough, Y. Ushigoe, S. Tanaka, A. Masuyama and M. Nojima, *J. Chem. Soc., Perkin Trans. 1*, 1998, 3053.
5 K. Teshima, S. Kawamura, Y. Ushigoe, M. Nojima and K. J. McCullough, *J. Org. Chem.*, 1995, **60**, 4755.
6 Y. Ushigoe, S. Tanaka, M. Nojima and K. J. McCullough, *Tetrahedron Lett.*, 1994, **35**, 9741.
7 (*a*) A. J. Bloodworth and A. Shah, *J. Chem. Soc., Chem. Commun.*, 1991, 947; (*b*) A. J. Bloodworth and N. A. Tallant, *J. Chem. Soc., Chem. Commun.*, 1992, 428.1.
8 J. C. Bevington, *Quart. Rev. Chem. Soc.*, 1952, **6**, 141.
9 M. Schulz and K. Kirschke, '*Organic Peroxides*' Vol III, ed. D. Swern, Wiley, New York, 1972, pp. 67–140.
10 Y. Ushigoe, S. Kawamura, K Teshima, M. Nojima and K. J. McCullough, *Tetrahedron Lett.*, 1996, **37**, 2093.
11 (*a*) A. Rieche and E. Schmitz, *Chem. Ber.*, 1957, **90**, 1082; (*b*) A. Rieche and M. Schulz, *Justus Liebigs Ann. Chem.*, 1962, **653**, 32.
12 (*a*) T. Sugimoto, M. Nojima, S. Kusabayashi and K. J. McCullough, *J. Am. Chem. Soc.*, 1990, **112**, 3690; (*b*) K. J. McCullough, T. Sugimoto, S. Tanaka, S. Kusabayashi and M. Nojima, *J. Chem. Soc., Perkin Trans. 1*, 1994, 643.
13 (*a*) F. H. Allen, S. A. Bellard and O. Kennard, *Acta Crystallogr., Sect. C*, 1986, **42**, 829; (*b*) G. Bernardelli, C. W. Jefford, J. Boukouvalas, D. Jaggi and S. Kohmoto, *Acta Crystallogr., Sect. C*, 1987, **43**, 701.
14 E. L. Eliel and S. H. Wilen, *Stereochemistry of Organic Compounds*, Wiley, New York, 1994, pp. 766–767.
15 See J. Z. Gougoutas, in *The Chemistry of Peroxides*, ed. S. Patai, Wiley, New York, 1983, pp. 375–415.
16 SHELXS-86, G. M. Sheldrick, *Acta Crystallogr.*, 1990, **A46**, 467.
17 SHELXTL/PC (Vers. 5.03), G. M. Sheldrick, University of Göttingen, 1994.

*Paper 8/04605K*