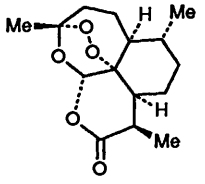
# An Improved Route to 1,2,4-Trioxanes Using Tin(IV) as a Hydrogen Equivalent

**Jiaqiang Cai and Alwyn G. Davies***
*Chemistry Department, University College London, 20 Gordon Street, London WC1H 0AJ, UK*

Bloodworth's route to the 1,2,4-trioxanes has been duplicated using tin(IV) as a hydrogen equivalent throughout. Thus a tetraallyltin compound is treated with singlet oxygen to give a tetraallylperoxytin compound; this adds to an aldehyde to give the tin derivative of a peroxyhemiacetal, and this tin alkoxide undergoes ring-closing intramolecular addition to the olefinic group in the presence of mercury(II) acetate to give the 1,2,4-trioxane.

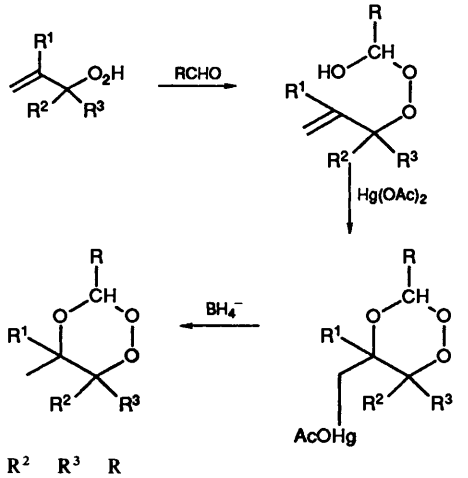
The antimalarial activity of the plant extract *Qinghaosu* **1** is associated with the presence of the 1,2,4-trioxane ring **2**,[1] and a substantial effort has been devoted to developing new synthetic routes to these cyclic peroxides.[2,3]



**1**

**2**

Bloodworth and his colleagues[3] have formed the ring by preparing a peroxyhemiacetal from an allylic hydroperoxide and an aldehyde, followed by intramolecular oxymercuration to close the ring, then reductive demercuration (Scheme 1).



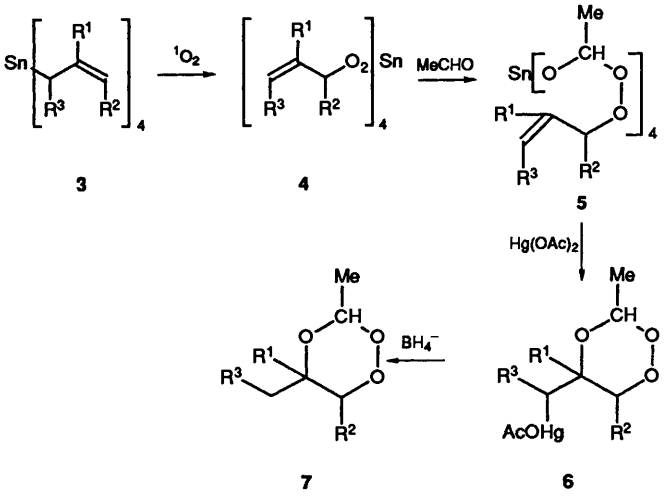
| $R^1$ | $R^2$ | $R^3$ | R |
|---|---|---|---|
| Me | Me | Me | Me, Et, Pr, $Pr^i$, $Bu^t$, 2-$NO_2C_6H_4$, 4-$ClC_6H_4$ |
| H | Ph | H | Me, $Pr^i$, $Bu^t$, $Cl_3C$ |

**Scheme 1**

The two key steps in building the ring involve reactions of OH nucleophiles. We have been interested in the principle that metal substituents often simulate the behaviour of the hydrogen which they replace,[4] and that by a judicious choice of the metal and its ligands, metals may with advantage be used as hydrogen equivalents.[5] We report here such a modification of Bloodworth's methodology as shown in Scheme 2.

## Results

Tetrapropenyltin **3a** and tetra(2-methylprop-2-enyl)tin **3b** were prepared in greater than 80% yield from tin tetrachloride and



**3**–**7a** $R^1$ = H, $R^2$ = H, $R^3$ = H
**b** $R^1$ = Me, $R^2$ = H, $R^3$ = H
**c** $R^1$ = H, $R^2$ = Me, $R^3$ = H
**3**–**5d** $R^1$ = H, $R^2$, $R^3$ = $-(CH_2)_3-$

**Scheme 2**

the appropriate Grignard reagent. The compound **3c**,[6] which was derived from the Grignard reagent from crotyl chloride, might be expected to contain a mixture of *E*- and *Z*-but-2-enyl, and 1-methylprop-2-enyl groups, but the NMR spectra showed that it contained only but-2-enyl groups, and this was confirmed by the spectra of the derived peroxides **4c**, **5c** and **6c** (see below). Tetra(cyclohex-2-enyl)tin **3d** was obtained in 80% yield by metallation of cyclohexene with butyllithium and potassium *tert*-butoxide in the presence of tetramethylethylenediamine,[5b,7] then reaction with $SnCl_4$.

The reaction of tetra(prop-2-enyl)tin **3a** with singlet oxygen, generated from triplet oxygen and tetraphenylporphine in the presence of sodium light, to give tetra(prop-2-enylperoxy)tin(IV) **4a**, has already been reported.[5c] Compounds **3b**–**d** reacted in the same way to give the corresponding peroxides **4b**–**d** in quantitative yield (NMR).

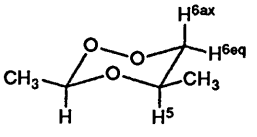
The tetra(allylperoxy)tin compounds **4a**–**d** reacted with acetaldehyde immediately on mixing at room temperature to give the corresponding stannylated peroxyhemiacetals **5a**–**d**, again in quantitative yield. The NMR spectrum showed that **5c** consisted of two diastereoisomers in approximately equal amount, but **5d** showed the presence of only one isomer.

The peroxyhemiacetals **5a**–**c** were then stirred with mercuric acetate in dichloromethane for 5–8 hours, when the $Hg(OAc)_2$ dissolved to give the mercurated trioxanes **6a**–**c**; no reaction occurred with the cyclohexene derivative **5d** under these conditions.

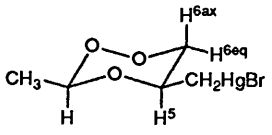
The mercurated trioxanes **6a**–**c** were demercurated by

Bloodworth's method of reduction with sodium borohydride in sodium hydroxide solution,[3a] and the trioxanes **7a–c** were isolated by bulb-to-bulb distillation followed by column chromatography to remove the allylic alcohol which was also formed. The overall yields of the trioxanes **7a–c** were 25–30% based on the allylic tin compounds **3a–c**. As Bloodworth showed,[3a] the carbonyl addition, ring closure, and reduction can be carried out in a one-pot procedure.

The trioxane **7a** contains two chiral centres, and the proton NMR spectrum showed the presence of two diastereoisomers in the relative concentrations 5:1. The major isomer shows $^3J_{5\text{-H}-6\text{-H}}$ 10.2 Hz and thus has 5-Me equatorial. To confirm this, the organomercury precursor, which was normally reduced *in situ*, was isolated as its bromide, **6a′**. Again two isomers were present in the ratio *ca.* 5:1, with $^3J_{5_{ax}\text{-H}-6_{ax}\text{-H}}$ 9.58 Hz.




**7a**

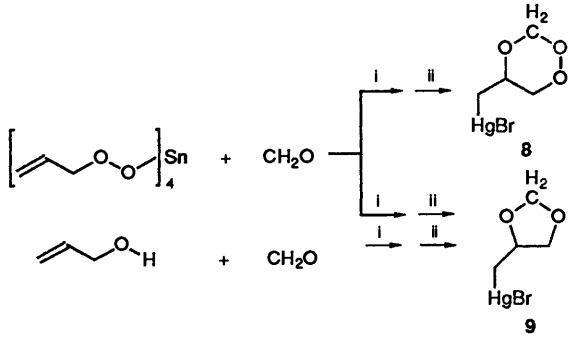



**6a′**

The trioxane **7c** contains three chiral centres, and showed the presence of two, rather than four, isomers, in the ratios 42:58. The minor isomer has 5-Me, 6-Me and 3-Me (see below) equatorial, with $^3J_{5_{ax}\text{-H}-6_{ax}\text{-H}}$ 8.8 Hz, and the major isomer has 5-Me axial, with $^3J_{5_{eq}\text{-H}-6_{ax}\text{-H}}$ 3.1 Hz.

The configuration of the trioxanes at C-3 was determined by $^{13}$C NMR spectroscopy in a separate study in collaboration with Drs. J. E. Anderson and A. J. Bloodworth, and included further trioxanes prepared in Dr. Bloodworth's research group.[3] By NOE experiments, we showed that the value of $^1J_{C-H}$ at the C-3 position in trioxanes lies in the range 166.8–169.3 Hz for axial protons, and 163.5–164.8 Hz for equatorial protons. These compounds therefore show a reversal of the usual Perlin effect.[8] By this criterion, all the trioxanes prepared here from acetaldehyde have the methyl group at C-3 in the equatorial position, as indicated in the formulae. This work has been published separately.[9]

For this ancillary study we needed to obtain a trioxane with both axial and equatorial protons on C-3, and to this end, tetra(allylperoxy)tin was added to formaldehyde, then the ring-closing oxymercuration was carried out in the usual way. By chromatography, both 5-bromomercurimethyl-1,2,4-trioxane **8** and 4-bromomercurimethyl-1,3-dioxolane **9** were isolated each in about 10% yield (Scheme 3). This partial reduction of the peroxide is not observed with acetaldehyde. To confirm the identity of **9**, it was also prepared by acetoxymercurative ring closure of the hemiacetal formed between allyl alcohol and formaldehyde (Scheme 3).




**Scheme 3** *Reagents:* i, $Hg(OAc)_2$; ii, NaBr

## Discussion

A number of aspects of these syntheses illustrate the potential advantages of using metals as hydrogen equivalents.

Bloodworth prepared the 1,1,2-trimethylprop-2-enyl hydroperoxide for Scheme 1 by treating 2,3-dimethylbut-2-ene with singlet oxygen,[3a] but this process would not be convenient for the oxygenation of propene, 2-methylpropene, or but-2-ene which are gases. The allyltin compounds **3a–d** on the other hand are easy to handle, are much more reactive than the hydrocarbons towards singlet oxygen,[5] and the allylperoxytin compounds which are formed appear to be safer to handle than the allyl hydroperoxides themselves, the lower members of which can be dangerously explosive.

It is important that these tetraallyl compounds **3a–d** react with singlet oxygen to show only the metalloene reaction, whereas tri(butylallyl)tin compounds give also the products of the hydrogen-ene reaction, and of cycloaddition with shift of the metal. We have suggested[5c] that this chemoselectivity may be the result of π–σ conjugation between the C=C double bonds and the $CH_2$–Sn bonds, which enhances the electropositivity of the tin, and this is conducive towards the metalloene reaction. After the reaction of the first of the allyl groups, the electronegative allylperoxy ligand will further enhance the electropositivity of the tin, and favour the metalloene process.

Tin alkoxides are known to simulate the behaviour of alcohols in adding to carbonyl groups.[10] Nothing appears to have been published on the comparison between the behaviour of tin peroxides and hydroperoxides towards carbonyl compounds, but from the little we have done here, the analogy appears to be close.

The ring closure is the most interesting step in our synthesis, as it establishes that alkoxytin(IV) compounds simulate the behaviour of alcohols[11] in the oxymercuration of alkenes. But whereas the addition of alcohols often needs an acid catalyst,[3a] our reactions proceed smoothly in the absence of a catalyst. This suggests that the scope of the hydroxy-,[12] alkoxy-,[11] hydroperoxy-[13] and alkylperoxy-mercuration[14] reactions, which are used in organic synthesis[15] should be widened considerably by the judicious use of a metallic derivative.

## Experimental

$^1$H and $^{13}$C NMR spectra were recorded on $CDCl_3$ solutions on a Varian VXR-400 spectrometer unless otherwise stated; a Varian XL-200 instrument was used for those compounds which were thermally unstable and for which the spectra had to be recorded immediately. Chemical shifts were measured relative to the solvent using $\delta_H$ 7.24 and $\delta_C$ 77.00. Complete analysis of the $^1$H NMR spectra of the tin(IV) compounds was sometimes not possible, because the four ligands each contained a number of chiral centres, giving rise to a number of diastereoisomers with overlapping spectra. Coupling constants are in Hz. IR spectra were recorded on a Perkin-Elmer PE983 instruments, and mass spectra on a VG7070H spectrometer at 70 eV. Column chromatography was carried out on Merck silica gel 60 (70–230 mesh).

*Allylic Tin Compounds* **3a–c**. *General Procecure.*—A solution of allyl chloride or bromide, methallyl chloride, or crotyl bromide (20 mmol) in THF (20 $cm^3$) was added dropwise to magnesium (20 mmol) in THF (100 $cm^3$) under nitrogen, with stirring and ice-cooling to keep the temperature below the b.p. of THF. After all the allylic halide had been added, the solution was stirred for a further 2 h. A solution of $SnCl_4$ (3 mmol) in hexane (10 $cm^3$) was then added dropwise at room temperature. After work-up, the crude product was chromatographed on silica gel using light petroleum (b.p. 30–40 °C) as eluent. The yields and characteristics of the products were as follows.

*Tetraprop-2-enyltin* **3a**.[5c] Yield 85–95%.

*Tetra(2-methylprop-2-enyl)tin* **3b**.[16] Yield 85–95%; $\delta_H$ 1.69 (12 H, t, *J* 1.1, $J_{Sn}$ 11.7, Me), 1.9 (8 H, s, $J_{^{117}Sn}$ 60.7, $J_{^{119}Sn}$ 63.2, $CH_2$), 4.5 (4 H, s, $J_{Sn}$ 21.5, olefinic) and 4.5 (4 H, s, $J_{Sn}$ 21.5, olefinic); $\delta_C$ 21.70 ($J_{Sn}$ 254.8, C-1), 25.02 ($J_{Sn}$ 10.0, C-4), 107.66 ($J_{Sn}$ 45.6, C-3) and 144.53 ($J_{Sn}$ 43.1, C-2). $\nu_{max}$(neat)/cm$^{-1}$ 3069.4, 2967.7, 2925.9, 1622.7, 1437.3, 1371.5, 1275.8, 1111.3, 991.7, 973.8, 863.1, 824.3, 755.5 and 707.6; *m/z* 285 (M − methylpropenyl, 27%), 230 (M − 2 × methylpropenyl, 5), 175 (M − 3 × methylpropenyl, 100), 120 (Sn, 20) and 55 (methylpropenyl, 32); this pattern of fragmentation has been observed before for allylic tin compounds.[17]

*Tetra(3-methylprop-2-enyl)tin* **3c**.[18] Yield 35%; $\delta_H$ 1.57–1.65 (12 H, Me), 1.75–1.84 (8 H, $CH_2$), 5.15–5.32 (4 H, olefinic) and 5.47–5.65 (4 H, olefinic); $\delta_C$ 10.79, 11.03, 11.24, 12.47 (Me); 14.70, 14.95, 15.16, 17.87 ($CH_2$); 118.84, 118.99, 119.14, 119.29 (olefinic); 121.07, 121.19, 121.31, 121.43 (olefinic); 127.97, 128.03, 128.10 (olefinic); and 128.83, 128.90, 128.97 (olefinic); $\nu_{max}$(neat)/cm$^{-1}$ 3009.6, 2949.8, 2919.9, 1652.6w, 1637.6, 1449.2, 1392.4, 1356.5, 1156.2, 1093.4, 1066.5, 991.7, 958.8 and 719.6; *m/z* 285 (M − methylpropenyl, 25%), 230 (M − 2 × methylpropenyl, 5) and 175 (M − 3 × methylpropenyl, 100).

*Tetrahex-2-enyltin* **3d**.—Cyclohexene was metallated as described previously,[5b] then $SnCl_4$ (3 mmol) in hexane (10 cm$^3$) was added dropwise with stirring. After work-up, the crude product was chromatographed on silica gel using light petroleum as eluent; yield 80%; $\delta_H$ 1.27–2.22 (24 H, m), 2.46 (4 H, m, CHSn), 5.46 (4 H, m, olefinic) and 5.84 (4 H, m, olefinic); $\delta_C$ 23.67, 25.00, 26.85, 28.63 and 28.47 (CHSn) and 122.72, 130.97 and 131.05 (olefinic); *m/z* 363 (M − cyclohexenyl, 5%), 282 (M − 2 × cyclohexenyl, 2), 201 (M − 3 × cyclohexenyl, 90) and 81 (cyclohexenyl, 100).

*Tetra(allylperoxy)stannanes* **4a–d**.—The photoxidations were carried out in $CH_2Cl_2$ or $CHCl_3$ in a temperature-controlled cell, using a 400 W sodium lamp, and tetraphenylporphine as the photosensitizer, on 2.5 mmol of the stannane, as describe previously.[3] Reactions were also carried out on an analytical scale in $CDCl_3$ in an NMR tube (200 MHz). The yields of the peroxides **4a–d** were quantitative (NMR).

*Tetra(prop-2-enylperoxy)tin* **4a**. $\delta_H$ 4.49 (8 H, d, *J* 6.2, $CH_2$), 5.30 (4 H, dd, *J* 1.4 and 5.6, 3-H), 5.37 (4 H, dd, *J* 1.4 and 12.8, 3′-H) and 5.97 (4 H, ddt, *J* 5.6, 12.8 and 6.2, 2-H).

*Tetra(2-methylprop-2-enylperoxy)tin* **4b**. $\delta_H$ 1.81 (12 H, s, Me), 4.42 (8 H, s, $CH_2$), 5.03 (4 H, s, 3-H) and 5.04 (4 H, s, 3′-H).

*Tetra(1-methylprop-2-enylperoxy)tin* **4c**. $\delta_H$ 1.25 and 1.26 (12 H, 2 d, *J* 6.5, Me), 4.30 and 4.48 (4 H, 2 q, *J* 6.5, 1-H), 5.02–5.34 (8 H, m, 3-H and 3′-H) and 5.75–5.90 (4 H, m, 2-H).

*Tetra(cyclohex-2-enylperoxy)tin* **4d**. $\delta_H$ 1.10–2.20 (24 H, m), 4.46 (4 H, m, 1-H), 5.73 (4 H, m, olefinic) and 5.98 (4 H, m, olefinic).

*Peroxyhemiacetals* **5a–d**.—The peroxyhemiacetals were formed in quantitative yield (200 MHz NMR) when acetaldehyde (3 equiv.) was added to the allylperoxytin compound.

*Tetrakis[1-(prop-2-enylperoxy)ethoxy]tin* **5a**. $\delta_H$ 1.24 (12 H, d, *J* 5.4, Me), 4.49 (8 H, dm, *J* 6.1, $CH_2$), 5.22 (4 H, m, olefinic), 5.27 (4 H, m, olefinic), 5.36 (4 H, q, *J* 5.5, MeCH) and 5.93 (4 H, m, olefinic).

*Tetrakis[1-(2-methylprop-2-enylperoxy)ethoxy]tin* **5b**. $\delta_H$ 1.14 (12 H, d, *J* 5.5, *Me*CH), 1.66 (12 H, s, Me), 4.32 (8 H, s, $CH_2$), 4.82 (4 H, s, olefinic), 4.86 (4 H, s, olefinic) and 5.28 (4 H, q, *J* 5.5, MeC*H*).

*Tetrakis[1-(1-methylallylperoxy)ethoxy]tin* **5c**. $\delta_H$ 1.18–1.29 (24 H, m, Me) 4.56 (4 H, m, $CH_3CH$), 4.99–5.42 (12 H, m, olefinic and MeC*H*) and 5.73–5.97 (4 H, m, olefinic).

*Tetrakis[1-(cyclohex-2-enylperoxy)ethoxy]tin* **5d**. $\delta_H$ 1.21 (12 H, d, *J* 5.4, $CH_3CH$) 1.10–2.20 (24 H, m), 4.50 (4 H, m, $CHO_2$) 5.34 (4 H, q, *J* 5.4, $CH_3CH$), 5.69 (4 H, m, olefinic) and 5.90 (4 H, m, olefinic).

1,2,4-*Trioxanes* **6a–c** *and* **7a–c**. *General Procedure*.—A mixture of mercury(II) acetate (10 mmol) and a solution of the tetrakis(1-allylperoxyethyoxy)tin compound **5** (2.5 mmol) in $CH_2Cl_2$ was stirred at room temperature. Dissolution of the mercury acetate was complete in 5–8 h. The solvent and the excess of acetaldehyde was removed under reduced pressure. The residue was treated with $CH_2Cl_2$ then with 2 mol dm$^{-3}$ NaOH solution (10 cm$^3$) and with $NaBH_4$ in 2 mol dm$^{-3}$ NaOH (30 cm$^3$) at 0 °C. After work-up, the crude product subjected to bulb-to-bulb distillation, then was chromatographed on silica gel with pentane–$CH_2Cl_2$ (2:1) as eluent. The following trioxanes were obtained.

3,5-*Dimethyl*-1,2,4-*trioxane* **7a**. Yield 25–30% ($CH_2Cl_2$ solvent), 35–40% ($CHCl_3$ solvent). Major (*cis*) isomer: $\delta_H$ 1.16 (3 H, d, *J* 6.2, 5-Me$_{eq}$), 1.26 (3 H, d, *J* 5.4, 3-Me$_{eq}$), 3.85 (1 H, dd, *J* 2.5 and 11.9, 6-H$_{eq}$), 3.98 (1 H, ddq, *J* 10.2, 2.5, and 6.2, 5-H$_{ax}$), 4.07 (1 H, dd, *J* 10.2 and 11.9, 6-H$_{ax}$) and 5.37 (1 H, q, *J* 5.4, 3-H$_{ax}$); $\delta_C$ 16.47 (5-Me), 18.13 (3-Me), 69.96 (C-5), 76.46 (C-6) and 101.55 ($^1J_{C-H}$ 169.0, C-3); $\nu_{max}$(neat)/cm$^{-1}$ 2973.7, 2901.9, 1446.2, 1398.4, 1377.5, 1335.6, 1296.7, 1254.9, 1174.1, 1150.2, 1117.3, 1087.4, 994.7, 949.9, 893.0, 869.1, 842.2, 806.3 and 665.8 (Found: C, 50.1; H, 8.6. $C_5H_{10}O_3$ requires C, 50.84; H, 8.53%).

For the minor (*trans*) isomer (15% of crude); $\delta_H$ 1.22 (3 H, d, *J* 5.9, 3-Me), 1.41 (3 H, d, *J* 6.9, 5-Me$_{ax}$), 3.73 (1 H, dd, *J* 1.5 and 12.4, 6-H$_{eq}$), 4.59 (1 H, dd, *J* 3.2 and 12.4, 6-H$_{ax}$) and 5.62 (1 H, q, *J* 5.4, 3-H$_{ax}$).

3,5,5-*Trimethyl*-1,2,4-*trioxane* **7b**. Yield 25–30%; $\delta_H$ 1.20 (3 H, s, 5-Me$_{eq}$), 1.22 (3 H, d, *J* 5.3, 3-Me$_{eq}$), 1.38 (3 H, s, 5-Me$_{ax}$), 3.65 (1 H, d, *J* 12.2, 6-H$_{eq}$), 4.18 (1 H, d, *J* 12.3, 6-H$_{ax}$) and 5.59 (1 H, q, *J* 5.3, 3-H$_{ax}$); $\delta_C$ 18.37 (5-Me$_{aq}$), 20.91 (5-Me$_{ax}$), 25.86 (3-Me), 69.84 (C-5), 78.91 (C-6) and 96.04 ($^1J_{C-H}$ 170, C-3); $\nu_{max}$(neat)/cm$^{-1}$ 2973.7, 2907.9, 1470.2, 1440.3, 1389.4, 1368.5, 1239.9, 1216.0, 1186.1, 1144.2, 1114.3, 1093.4, 1024.6, 997.7, 985.7, 952.9, 908.0, 878.1, 854.2, 806.3, 776.4 and 677.7; *m/z* 117 (M − Me, 22%) 101 (100) and 88 (M − MeCHO, 70) (Found: C, 54.1; H, 8.9. $C_6H_{12}O_3$ requires C, 54.53; H, 9.15%).

3,5,6-*Trimethyl*-1,2,4-*trioxane* **7c**. Yield 25–30%. Minor isomer (40%); $\delta_H$ 1.03 (3 H, d, *J* 6.5, 6-Me$_{eq}$), 1.17 (3 H, d, *J* 6.4, 5-Me$_{eq}$), 1.25 (3 H, d, *J* 5.4, 3-Me$_{eq}$), 3.52 (1 H, dq, *J* 6.4 and 8.8, 5-H$_{ax}$), 4.02 (1 H, dq, *J* 6.4 and 8.8, 6-H$_{ax}$) and 5.34 (1 H, q, *J* 5.4, 3-H$_{ax}$); $\delta_C$ 13.89 (Me), 16.46 (Me), 17.91 (Me), 72.30 (C-5), 80.73 (C-6) and 101.62 ($^1J_{C-H}$ 168.6, C-3).

Major isomer (60%); $\delta_H$ 1.09 (3 H, d, *J* 6.6, 6-Me$_{eq}$), 1.25 (3 H, d, *J* 5.4, 3-Me$_{eq}$), 1.40 (3 H, d, *J* 6.5, 5-Me$_{ax}$), 3.83 (1 H, dq, *J* 6.5 and 3.1, 5-H$_{eq}$), 4.09 (1 H, dq, *J* 6.6 and 3.1, 6-H$_{ax}$) and 5.33 (1 H, q, *J* 5.3, 3-H$_{ax}$); $\delta_C$ 11.87 (Me), 16.75 (Me), 18.03 (Me), 75.83 (C-5), 78.42 (C-6) and 101.59 ($^1J_{C-H}$168.4, C-3); $\nu_{max}$(neat mixture of isomers)/cm$^{-1}$ 2979.7, 2931.8, 2884.0, 1443.3, 1398.4, 1377.5, 1332.6, 1186.1, 1144.2, 1117.3, 1093.4, 1057.5, 1006.7, 988.7, 967.8, 946.9, 884.1, 854.2, 830.3, 809.3, 776.4, 737.6 and 683.7 (Found: C, 53.7; H, 9.6. $C_6H_{12}O_3$ requires C, 54.53; H, 9.15%).

5-*Bromomercurimethyl*-3-*methyl*-1,2,4-*trioxane* **6a′**. After the dissolution of the mercuric acetate, a solution of KBr (20 mmol) in water (15 cm$^3$) was added, and the mixture was stirred for 5 min. After a hydrolytic work-up, the product was chromatographed on silica gel with pentane–$CH_2Cl_2$ as eluent, giving **6a′** as a viscous oil; yield 50%. This was further purified twice by chromatography and recrystallised from the chromatography solvent to give the major isomer as crystals, m.p. 92–93 °C; $\delta_H$ 1.27 (3 H, d, *J* 5.4, 3-Me$_{eq}$), 1.97 (1 H, dd, *J* 8.1 and 12.2, $CH_2Hg$), 2.15 (1 H, dd, *J* 5.0 and 12.2, $CH_2Hg$), 3.96 (1 H, dd, *J* 3.2 and 12.3, 6-H$_{eq}$), 4.03 (1 H, dd, *J* 9.6 and 12.2, 6-H$_{ax}$), 4.25 (1 H, m, 5-H$_{ax}$) and 5.40 (1 H, q, *J* 5.3, 3-H$_{ax}$); $\delta_C$ 18.17 (3-Me), 35.49

($J_{^{199}Hg}$ 1557, $CH_2Hg$), 72.47 (C-5), 77.32 (C-6) and 101.51 ($^1J_{C-H}$ 169.6, C-3); $\nu_{max}$(Nujol)/cm$^{-1}$ 2919.9, 2854.1, 1455.2, 1407.4, 1389.4, 1374.5, 1329.6, 1305.7, 1117.3, 1090.4, 1045.5, 979.8, 920.0, 869.1, 857.2, 800.3 and 740.5 (Found: C, 14.85; H, 2.05. $C_5H_9BrHgO_3$ requires C, 15.10; H, 2.28%). For the minor isomer (in mixture), $\delta_H$ 1.31 (3 H, d, $J$ 5.4, 3-$Me_{eq}$), 2.25 (1 H, dd, $J$ 5.9 and 12.3, $CH_2Hg_{ax}$), 2.59 (1 H, dd, $J$ 9.8 and 12.3, $CH_2Hg_{ax}$), 3.81 (1 H, dd, $J$ 2.4 and 12.6, 6-$H_{eq}$), 4.31 (1 H, m, 5-$H_{eq}$), 4.57 (1 H, dd, $J$ 3.2 and 12.6, 6-H) and 5.68 (1 H, q, $J$ 5.4, 3-$H_{ax}$); $\delta_C$ 18.10 (3-Me), 36.30 ($CH_2Hg$), 68.35 (C-5), 75.42 (C-6) and 96.07 ($J_{C-H}$ 167.8, C-3).

*5-Bromomercurimethyl-1,2,4-trioxane* **8** *and 4-Bromomercurimethyl-1,3-dioxolane* **9**.—Formaldehyde (from 5 g paraformaldehyde) was passed through a solution of tetra(allylperoxy)tin **4a** (2 mmol) in dichloromethane at room temperature. This solution was treated with mercury(II) acetate, and worked up as described above for **6a'**, yielding the trioxane **8** and the dioxolane **9** with the following properties.

**8**: Yield 10%. M.p. 90–93 °C; $\delta_H$ 1.95 (1 H, dd, $J$ 7.7 and 12.2, $J_{Hg}$ 202, $CH_2Hg$), 2.16 (1 H, dd, $J$ 4.8 and 12.1, $J$ 216, $CH_2Hg$), 3.97 (1 H, dd, $J$ 3.1 and 9.5, 6-$H_{eq}$), 4.18 (1 H, t, $J$ 9.7, 6-$H_{ax}$), 4.21 (1 H, m, 5-$H_{ax}$), 5.21 (1 H, dd, $J$ 2.9 and 8.7, $^1J_{C-H}$ 164.8, 3-$H_{eq}$) and 5.45 (1 H, d, $J$ 8.7, $^1J_{C-H}$ 168.6, 3-$H_{ax}$); $\delta_C$ 35.42 (CHg), 71.97 (C-5), 78.84 (C-6) and 96.30 ($^1J_{C-H}$ 168.6 and 164.8, C-3); $\nu_{max}$(Nujol)/cm$^{-1}$ 2918.5, 2845.1, 1454.5, 1374.4, 1130.7, 1104.0, 1054.0, 973.9, 953.8, 847.0, 766.9, 736.9 and 720.2 (Found: C, 12.5; H, 1.75. $C_4H_7BrHgO_3$ requires C, 12.52; H, 1.84%).

**9**: Yield 10%. Viscous oil; $\delta_H$ 2.13 (1 H, dd, $J$ 6.0 and 11.9, $J_{Hg}$ 204, $CH_2Hg$), 2.27 (1 H, dd, $J$ 5.6 and 11.9, $J_{Hg}$ 205, $CH_2Hg$), 3.39 (1 H, dd, $J$ 6.1 and 8.1, 5-H), 3.98 (1 H, dd, $J$ 6.3 and 8.1, 5-H), 4.47 (1 H, quin, $J$ 6.0, $J_{Hg}$ 232, 4-H), 4.80 (1 H, s, 2-H) and 5.07 (1 H, s, 2-H); $\delta_C$ 38.59 ($J_{Hg}$ 1553, $CH_2Hg$), 71.93 ($J_{Hg}$ 158, C-4), 74.80 ($J_{Hg}$ 108, C-5) and 94.83 (C-2); $\nu_{max}$(neat)/cm$^{-1}$ 2925.2, 2854.4, 1464.5, 1147.4, 1080.7, 1000.6, 930.5, 860.4 and 756.9 (Found: C, 13.1; H, 2.0. $C_4H_7BrHgO_2$ requires C, 13.07; H, 1.92%). The same product was obtained in 70% yield when the reaction was carried out in the same way but with allyl alcohol in place of the allylperoxytin compound.

## Acknowledgements

We thank the Royal Society and the Chinese Academy of Sciences for the award of a Royal Fellowship to J. Cai, and Dr. A. J. Bloodworth for many helpful discussions.

## References

1 D. Klayman, *Science*, 1985, **228**, 1049; A. R. Butler and Y.-L. Wu, *Chem. Soc. Rev.*, 1992, **21**, 85.
2 G. Schmid and W. Hofheinz, *J. Am. Chem. Soc.*, 1983, **105**, 624; X.-X. Xu, J. Zhu, D.-Z. Huang and W. Zhou, *Tetrahedron*, 1986, **42**, 819; W. Zhou, *Pure Appl. Chem.*, 1986, **58**, 817; M. A. Avery, C. Jennings-White and W. K. M. Chong, *Tetrahedron Lett.*, 1987, **28**, 4629; Y. Imakura, T. Yokoi, T. Yamagishi, J. Koyama, H. Hu, D. R. McPhail, A. T. McPhail and K.-H. Lee, *J. Chem. Soc., Chem. Commun.*, 1988, 372; C. W. Jefford, E. C. McGoran, J. Boukouvalas, G. Richardson, B. L. Robinson and W. Peters, *Helv. Chim. Acta*, 1988, **71**, 1805; M. A. Avery, C. Jennings-White and W. K. M. Chong, *J. Org. Chem.*, 1989, **54**, 1792; M. Jung, X. Li, D. A. Bustos, H. N. ElSohly, J. D. McChesney and W. K. Milhous, *J. Med. Chem.*, 1990, **33**, 1516; P. T. Lansbury and D. M. Nowak, *Tetrahedron Lett.*, 1992, **33**, 1029; A. J. Lin, L. Li, S. L. Andersen and D. L. Klayman, *J. Med. Chem.*, 1992, **35**, 1639.
3 (*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.
4 A. G. Davies, *J. Organomet. Chem.*, 1982, **239**, 87.
5 (*a*) H.-S. Dang and A. G. Davies, *Tetrahedron Lett.*, 1991, **32**, 1745; (*b*) H.-S. Dang and A. G. Davies, *J. Chem. Soc., Perkin Trans. 2*, 1991, 2011; (*c*) H.-S. Dang and A. G. Davies, *J. Organomet. Chem.*, 1992, **430**, 287.
6 H. Kuivila, J. L. Considine, R. H. Sarma and R. J. Mynott, *J. Organomet. Chem.*, 1973, **55**, C11.
7 J. Hartmann and M. Schlosser, *Synthesis*, 1975, 328; L. Bradsma, H. D. Verkruijsse, C. Schade and P. von R. Schleyer, *J. Chem. Soc., Chem. Commun.*, 1986, 260.
8 S. Wolfe, B. M. Pinto, V. Varma and R. Y. N. Leung, *Can. J. Chem.*, 1990, **68**, 1051.
9 J. E. Anderson, A. J. Bloodworth, J. Cai, A. G. Davies and N. A. Tallant, *J. Chem. Soc., Chem. Commun.*, 1992, 1689.
10 A. G. Davies and W. R. Symes, *J. Chem. Soc. C*, 1967, 1009.
11 H. C. Brown and M.-H. Rei, *J. Am. Chem. Soc.*, 1969, **91**, 5646.
12 H. C. Brown and G. J. Lynch, *J. Org. Chem.*, 1981, **46**, 531, 930.
13 A. J. Bloodworth and N. D. Spencer, *J. Organomet. Chem.*, 1990, **386**, 299.
14 A. J. Bloodworth and I. M. Griffin, *J. Chem. Soc., Perkin Trans. 2*, 1975, 195.
15 R. C. Larock, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 27.
16 G. Fraenkel and W. R. Winchester, *J. Am. Chem. Soc.*, 1989, **111**, 3794.
17 C. A. Dooley and J. P. Testa, *Org. Mass. Spec.*, 1989, **24**, 343.
18 D. Seyferth and T. F. Julia, *J. Organomet. Chem.*, 1974, **66**, 195.

*Paper* 2/04721G
*Received* 2nd *September* 1992
*Accepted* 30th *September* 1992