Nuclear Magnetic Resonance Studies on some Cyclic Esters Containing the *t*-Butyl Group

Desmond G. Hellier* and Frederick J. Webb Department of Chemistry, Westfield College, London NW3 7ST, England

The high resolution proton magnetic resonance spectra of a series of cyclic inorganic esters and analogous 1,3-dioxans have been analysed. The coupling constants and chemical shifts involved indicate that most of the compounds exist preferentially in a chair form.

N.m.r. studies show that trimethylene sulphite¹⁻³ exists predominantly in a biased (anancomeric) chair conformation whereas trimethylene sulphate,¹ trimethylene carbonate⁴ and 1,3-dioxan⁵ invert at ordinary temperatures between equivalent conformations, as shown for the sulphate. ¹H n.m.r. spectroscopy has been



extensively used to investigate the conformational analysis of substituted trimethylene sulphites⁶⁻⁸ and 1,3-dioxans.^{5,9,10} From the n.m.r. analysis it is apparent that increased alkylation normally leads to preferred chair forms. Furthermore, data obtained from dipole moment measurements,⁷ i.r. spectroscopy¹ as well as ¹H n.m.r. spectroscopy indicate that the presence of a bulky substituent such as *t*-butyl, in isomeric 1,3-dioxans⁹ and trimethylene sulphites,¹ usually results in one isomer with a stable chair form and the *t*-butyl group in an equatorial position, the other isomer having a chair form with the bulky group axial, in equilibria with non-chair forms. The present work analyses ¹H n.m.r. data for a series of *t*-butylated cyclic inorganic esters and 1,3-dioxans to predict conformational preferences.

Compounds 1-8 are all six-membered ring cyclic esters formed from inorganic acids with a *t*-butyl group on C-5; the numbering of the ring is as shown. In 3, 4, 6, 8 and 10 a methyl group is also a substituent on C-5. The heteroatom in the X group has a pyramidal environment except for 7 and 8 where it is planar.



Analysis of the 100 MHz ¹H spectra of all the * Author to whom correspondence should be addressed. © Heyden & Son Ltd, 1977 compounds was possible, either directly or by interpretation of 220 MHz spectra. The 100 MHz ¹H spectra of 1, 7, 9 and the 220 MHz spectrum of 5 were analysed directly as $AA'XX'(R \rightarrow Y)$ spin systems.¹¹ The results are summarized in Table 1.

The stereochemistry of 5-t-butyltrimethylene sulphite, isomer 1 (1) and isomer 2 (2), has been investigated by a number of techniques.^{1,12-14} All results suggest the liquid phase form for 1 to be either anancomeric⁵ or a single chair form with the S=O bond axial. In contrast, 2 apparently exists in conformational equilibrium between a chair form (t-butyl group and S=O bond axial) and non-chair forms.

If we assume an anancomeric equilibrium for 1 the data summarized in Table 1 can be used to calculate chemical shifts for ring protons by consideration of shielding or deshielding effects, and provide a unique basis for the assignment of structures for these compounds.

Maroni and coworkers^{15,16} have shown that a chemical shift additivity relationship is valid between simple methyltrimethylene sulphites and 1,3-dioxans when considering the chemical shifts of the axial C-4, C-6 protons. The equation $\delta = \delta_o + \sum \Delta$ gave the chemical shift of the axial protons in the sulphite, where δ_0 is the chemical shift of these protons in a 1,3-dioxan with the same trimethylene structure. $\sum \Delta$ represents the combined effects of substituents on the chemical shifts.

It can be shown that this linear equation is valid for the *t*-butyl esters in calculating the chemical shifts of BOTH axial and equatorial C-4, C-6 protons if the following assumptions are made.

- An axial S=O bond deshields axial protons by c. 1.28 ppm but shields the equatorial protons by c. 0.20 ppm compared to 9.
- (2) An axial C-5 methyl group deshields axial protons by c. 0.17 ppm but shields the equatorial protons by c. 0.47 ppm.
- (3) The equatorial S=O bond in **5** and **6** has little effect on the axial protons but deshields the equatorial protons by c. 0.80 ppm compared to **1**.
- (4) The C=O bond deshields axial protons by 0.78 ppm and equatorial protons by 0.36 ppm compared to 9.

As an example, the chemical shifts of the C-4, C-6 axial protons of 1, 3, 5, 6, 7, 8 and 10 may be

Table 1. Chemical shifts	(ppm) an	d spin–spin	coupling	constants ^a	(Hz)	for 1	-10
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						H,Me,t-Bu H,Me,t-Bu H H H H					
	5a	5e	4a/6a	4e/6e	² J(4ae)/ ² J(6ae)	³ J(4a5a)	^з J(4е5а)	 ³ J(4а5е)	³ J(4e5e)	⁴ J(4e6e)	⁴ J(5 Me4a)
5-t-butyltrimethylene											
sulphite, isomer 1 (1)	2.13	0.97	4.71	3.82	-11.5	11.5	4.2			1.2	
5-t-butyltrimethylene								. –			
sulphite, isomer 2 (2)	1.07	1.66	4.76	3.96	-12.0			4.7	4.2		
5-t-butyl-5-methyltrimethylene			4 00								
sulphite, isomer 1 (3)	1.25	0.92	4.88	3.39	-11.3					1.3	0.7
5-t-butyl-5-methyltrimethylene											
sulphite, isomer 2 (4)	1.04	0.92	4.17	3.90	-12.1						
5-t-butyltrimethylene			4 70	4 00							
sulphate (5)	2.21	1.02	4.72	4.62	-11.4	10.6	5.1			1.1	
5-t-butyl-5-methyltrimethylene			4 07	4.00							~ ~
sulphate (6)	1.29	0.98	4.87	4.20	-11.3					1.5	0.6
5-t-butyltrimethylene	<u> </u>			4.07		40.0					
carbonate (7)	2.05	1.00	4.21	4.37	-11.2	10.3	5.2			1.2	
5-t-butyl-5-metnyltrimetnylene		0.00	4 20	2.00						10	
carbonate (8)	1.13	0.96	4.39	3.90	-11.1	40.0				1.3	0.5
5-t-Dutyi-1,3-dioxan (9)	1.70	0.92	3.43	4.01	-10.4	10.2	4.5			1.3	
5-t-butyl-5-methyl-		0.00	0.05	0.40							
1,3-dioxan (10)	1.12	0.89	3.05	3.46	-11.0					1.5	0.4

* Values are quoted to the nearest 0.1 Hz.

calculated using the δ_0 value of 9. Thus for

1 $\delta(\text{ppm}) = \delta_0 + \Delta(\text{S=O axial})$ = 3.43 + 1.28 = 4.71 (4.71 obs.)**3** $\delta(\text{ppm}) = \delta_0 + \Delta(\text{S==O axial})$ $+\Delta$ (C-5 methyl axial) = 3.43 + 1.28 + 0.17=4.88 (4.88 obs.) 5 $\delta(\text{ppm}) = \delta_0 + \Delta(\text{S==O axial})$ $+\Delta$ (S=O equatorial) = 3.43 + 1.28 + 0 = 4.71 (4.72 obs.) 6 $\delta(\text{ppm}) = \delta_0 + \Delta(\text{S=O axial})$ $+\Delta$ (S=O equatorial) $+\Delta$ (C-5 methyl axial) = 3.43 + 1.28 + 0 + 0.17=4.88 (4.87 obs.) 7 $\delta(\text{ppm}) = \delta_0 + \Delta(\text{C==O})$ = 3.43 + 0.78 = 4.21 (4.21 obs.) 8 $\delta(\text{ppm}) = \delta_0 + \Delta(\text{C=O}) + \Delta(\text{C-5 methyl axial})$ = 3.43 + 0.78 + 0.17= 4.38 (4.39 obs.)10 $\delta(\text{ppm}) = \delta_0 + \Delta(\text{C-5 methyl axial})$ = 3.43 + 0.17 = 3.60 (3.65 obs.)

Likewise, the chemical shifts of the C-4, C-6 equatorial protons may be calculated using the δ_0 value of **9** leading to

1 $\delta(\text{ppm}) = 4.01 - 0.20 = 3.81 (3.82 \text{ obs.})$ **3** $\delta(\text{ppm}) = 4.01 - 0.20 - 0.47 = 3.34 (3.39 \text{ obs.})$ **5** $\delta(\text{ppm}) = 4.01 - 0.20 + 0.80 = 4.61 (4.62 \text{ obs.})$ **6** $\delta(\text{ppm}) = 4.01 - 0.20 + 0.80 - 0.47$ = 4.14 (4.20 obs.) **7** $\delta(\text{ppm}) = 4.01 + 0.36 = 4.37 (4.37 \text{ obs.})$ **8** $\delta(\text{ppm}) = 4.01 + 0.36 - 0.47 = 3.90 (3.90 \text{ obs.})$ **9** $\delta(\text{cpm}) = 4.01 + 0.47 = 2.54 (2.46 \text{ obs.})$

10 δ (ppm) = 4.01 - 0.47 = 3.54 (3.46 obs.)

The close agreement in results for both sets of calculations strongly suggests a similar geometry in solution for these compounds. For **3**, further evidence is provided from $\nu_{S=O}$ values in a number of solvents together with the Raman spectra of the neat liquid. Apart from the $\nu_{S=O}$ band in the 1200 cm⁻¹ region there are additional bands which may be assigned to skeletal vibrations of the *t*-butyl group¹⁷ and/or $-CH_2$ - twist vibrations.² It is possible to identify the $\nu_{S=O}$ band by measuring its changing value from nonpolar to polar solvents. An average value $\nu_{S=O}$ of *c*. 1190 cm⁻¹ supports the assignment of an axial S=O bond.

The anancomeric structures suggested for the sulphates, **5** and **6**, are highly probable since ultrasonic measurements for 4-methyltrimethylene sulphate¹⁸ and 5,5-dimethyltrimethylene sulphate¹⁹ suggest a heavily biased conformational equilibrium.

It should be noted that the assignment of chemical shifts for 7 shows some differences to that of 1. Since the anisotropy of the C=O bond in the planar $-CO_3$ -



group is in an opposite direction to that of the S=O bond² the positions of the axial and equatorial C-4, C-6 protons are reversed compared to trimethylene sulphites. Compound 9 is similarly assigned but 8 and

10 have the usual sulphite pattern due to the inductive effects of the axial C-5 methyl group.

It is not possible to obtain simple chemical shift additivity relationships for sulphites 2 and 4. Since 2 has been shown to be conformationally unstable it is probable that 4 undergoes a similar conformational equilibrium involving a chair form with an axial tbutyl/equatorial methyl group. Also, two solvent dependent $\nu_{S==0}$ bands are observed for 2 and 4 which is consistent with this assumption.

Finally, the data summarized in Table 1 allow some comparison of J values. Thus, the C-4, C-6 geminal couplings in the 5-t-butyl series show a similar trend to those of the 5-t-butyl-5-methyl series with the ${}^{2}J(4ae)/{}^{2}J(6ae)$ value of sulphite, isomer 2>sulphite, isomer 1>sulphate>carbonate>dioxan. This trend usually indicates a gradual rise in geminal angle since the coupling constant decreases with increasing angle.²⁰ The same trend is observed in the monosubstituted series for ${}^{3}J(4a5a)$ axial-axial couplings which, from Karplus,²¹ suggest a gradual narrowing of the dihedral angle. This is commensurate with the conclusion that the C-4, C-5, C-6 region of the 1,3-dioxan ring is flattened relative to cyclohexane^{5,9} whereas the sulphite ring appears to be slightly puckered.²² The other ring systems, 4-8, are apparently intermediate.

Long-range ${}^{4}J$ coupling between an axial C-5 methyl group and axial C-4, C-6 protons is observed for **3**, **6**, **8** and **10** with ${}^{4}J(MeH)$ c. 0.6 Hz. The cross-ring coupling ${}^{4}J(4e6e)$ observed in trimethylene sulphite^{2,3} is apparent for all compounds except **2** and **4** with values c. 1.3 Hz. This type of cross-ring coupling is invariably a characteristic feature of rigid chair structures and is expected from the stable structures predicted for these compounds.

EXPERIMENTAL

The ¹H n.m.r. and i.r. spectra were recorded under conditions identical to those previously described.^{1,23} All new compounds gave satisfactory elemental analysis and purity was in all cases greater than 99% by preparative g.l.c.

Preparation of sulphites

All sulphites were prepared by the method and techniques previously described.¹

5-t-Butyltrimethylene sulphite

Diethyl t-butylmalonate⁹ was reduced with LiAlH₄ to give 2-t-butylpropane-1,3-diol, m.p. 57.5-58.5 °C (lit.¹⁷ 58-59 °C). Using the standard procedure, 0.10 mol of diol in ether gave 0.062 mol (62%) of sulphite which was collected 95% pure, b.p. 120-130 °C/25 mm. The isomers, **1** and **2** (5.3:1), were separated by preparative g.l.c. using a 7 ft column of 20% Apiezon L on Chromosorb P (60-85) at 184 °C, gas flow 75 ml min⁻¹ with injection samples of 15 μ l. Retention times were 21.2 min for isomer **1** and 23.7 min for isomer **2**. Even under optimum conditions the two isomers could not be completely resolved, requiring 'topping and tailing' of the peaks to obtain a separation. Both isomers were obtained at least 99% pure: **1**, m.p. 47-48 °C (lit.¹⁷ 47.5-48.5 °C); **2**, m.p. 36.5-37.5 °C (lit.¹⁷ 37.5-38.5 °C).

5-t-Butyl-5-methyltrimethylene sulphite

Diethyl t-butylmethylmalonate was prepared as follows: 0.15 mol of diethyl t-butylmalonate¹⁷ was added dropwise, with stirring, to 0.17 mol of sodium hydride dispersed in toluene followed by 0.18 mol of methyl iodide. The mixture was refluxed for 1.5 h and, on cooling, precipitated sodium iodide. After filtering, distillation gave 0.11 mol (73%) of diethyl tbutylmethylmalonate; b.p. 118-125 °C/20 mm, lit.²⁴ 104 °C/10 mm. 0.125 mol of the ester was reduced with 0.265 mol of LiAlH₄. After workup the solvent (ether) was removed over a water bath to give crude diol. 0.085 mol (68%) of diol was obtained by recrystallization of the residue with ether, m.p. 184-185 °C. 0.062 mol of diol in ether gave 0.044 mol (71%) of sulphite (b.p. 115-118 °C/20 mm). The isomers (3/4, 6.6:1) were separated and purified by preparative g.l.c. using a 3 ft column of 20% Apiezon L on Chromosorb P (60-85) at 152 °C, gas flow 72 ml min⁻¹ with injection samples of 25 μ l. Retention times were 14.1 min for 3 and 16.8 min for 4. 'Topping and tailing' of the peaks was required to effect separation giving >99% purity for both isomers; 3, m.p. 34 °C and 4, n_D^{20} = 1.4707.

5-t-Butyltrimethylene sulphate (5)

The sulphate was prepared by oxidation of the corresponding sulphite with acidic barium permanganate.²⁵ Recrystallization of the crude sulphate from ether gave a 17% yield of pure *t*-butyltrimethylene sulphate, m.p. 134-135 °C.

5-t-Butyl-5-methyltrimethylene sulphate (6)

Similarly, oxidation of the sulphite gave a c. 40% yield of crude sulphate. Two recrystallizations from ether gave the pure sulphate (15%), m.p. 132–133 °C.

5-t-Butyltrimethylene carbonate (7)

Following a described procedure, 26 0.039 mol of 2-*t*butylpropane-1,3-diol, 0.047 mol of diethyl carbonate and a catalytic amount of sodium were heated under reflux for 3 h, the temperature being allowed to rise to 180 °C as the ethanol formed distilled off. Recrystallization of the residue from ether gave 0.015 mol (39%) of pure carbonate, m.p. 134–135 °C.

5-t-Butyl-5-methyltrimethylene carbonate (8)

Following the procedure described for 7, 0.039 mol of 2-*t*-butyl-2-methylpropane-1,3-diol and 0.047 mol of diethyl carbonate gave 0.011 mol (28%) of pure carbonate, m.p. 182-184 °C.

5-t-Butyl-1,3-dioxan (9)

Prepared according to the method of Ayras and Pihlaja,²⁷ $n_{\rm D}^{19} = 1.4408$ (lit,⁹, $n_{\rm D}^{20} = 1.4381$).

5-t-Butyl-5-methyl 1,3-dioxan (10)

Similarly,²⁷ the diol gave a 45% yield of the dioxan,

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b.p. $85-90 \degree C/20 \text{ mm}$ (lit.²⁴ $72 \degree C/10 \text{ mm}$), $n_D^{19} =$ 1.4476.

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