NMR Parameters for 1,3-Dioxanes: Evidence for a Homoanomeric Interaction

Jiaqiang Cai,[a] **Alwyn G. Davies**[*,a] **and Carl H. Schiesser**[*,b]
[a] *Chemistry Department, University College London, 20 Gordon Street, London, UK WC1H OAJ*
[b] *Department of Chemical Sciences, Deakin University, Geelong, Victoria 3217, Australia*

^{1}H and ^{13}C NMR spectra have been recorded for a series of 1,3-dioxanes, 2-oxo-1,3,2-dioxathianes, 1,3,2-dioxaphosphorinanes and 2-thioxo-1,3,2-dioxaphosphorinanes, which are held in a chair conformation. In all of them, the spectral parameters are compatible with the equatorial C(5)–H bond being weaker and longer than the axial C(5)–H bond [*e.g.* $^1J_{C(5)H(5eq)} < {}^1J_{C(5)H(5ax)}$ (a reversed Perlin Effect), and $^3J_{H(4)H(5eq)} < {}^3J_{H(4eq)H(5ax)}$]. This is the reverse of what is usually observed in cyclohexanes, or at the 2-position in tetrahydropyrans, where the sequence is ascribed to an n→σ* (anomeric) interaction between the α-oxygen and the axial C(5)–H bond. It is suggested that this reversal may be due to an n→σ* (homoanomeric) interaction between the β-oxygen and the equatorial C(5)–H bond, through a W-arrangement of orbitals.

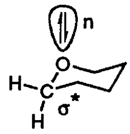
This interpretation is supported by *ab initio* 6-31G* calculations on the 1,3-dioxane molecule, which show that the equatorial C(5)–H bond is weaker and longer than the axial C(5)–H bond.

Chemical shifts and coupling constants in ^{1}H and ^{13}C NMR spectra have been used extensively for determining the axial/equatorial location of protons and substituents in cyclohexane and heterocyclohexanes.[1] In cyclohexanes, an equatorial proton shows a chemical shift 0.1–0.7 ppm downfield of an axial proton. Values of $^3J_{H(ax)H(ax)}$ are typically 8–10 Hz, and of $^3J_{H(ax)H(eq)}$ and $^3J_{H(eq)H(eq)}$ are 2–3 Hz, and in cyclohexane, $^1J_{CH(ax)}$ is 122.4 Hz, less than $^1J_{CH(eq)}$ which is 126.4 Hz.[2] In methylcyclohexanes, an axial methyl group (δ_C 17.5–18.9) is always upfield of an equatorial one (δ_C 23).[3]

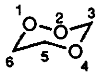
Similar rules are accepted to apply to heterocyclohexanes containing first row atoms.[4–7] Thus in β-D-glucopyranose, the axial proton at C(1) shows $^1J_{CH(ax)}$ 160 Hz, and in α-D-glucopyranose the corresponding equatorial proton shows $^1J_{CH(eq)}$ 169 Hz.[8] This order of the one-bond coupling constants ($^1J_{CH(ax)} < {}^1J_{CH(eq)}$) which was first described by Perlin and Casu in 1969,[8] has been referred to by Wolfe[9] as the Perlin effect. At the 1-position in pyranoses, it has been ascribed to the anomeric interaction[10] between the axially directed non-bonding electron pair on oxygen and the σ* orbital associated with the axial C(1)–H bond **1**.[9] This lengthens and weakens the bond and attenuates the Fermi coupling. This model is supported by *ab initio* calculations.[9] Different rules may apply with heterocycles containing atoms below the first row,[9] and in 1,3-dithianes $^1J_{CH(ax)} > {}^1J_{CH(eq)}$ at all positions around the ring; this has been suggested to result from a dominant $\sigma_{C-S} \rightarrow \sigma^*_{C-H}$ interaction which weakens the equatorial C–H bonds.[11] In three 1,3-oxathianes it was found that $^1J_{C(5)H(5ax)} \sim {}^1J_{C(5)H(5eq)}$.[12]

We became involved in this problem when we needed to determine the axial and equatorial placement of protons at the 3-position in 1,2,4-trioxanes **2**.[13] We found a reversal of the Perlin effect, *i.e.* $^1J_{CH(eq)} < {}^1J_{CH(ax)}$, and a similar effect was also found at the 6-position.[12] These appear to be the first examples of this anomalous effect in heterocycles containing first row atoms.

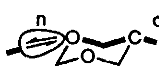
It appeared that this reversal of the Perlin effect might be associated with the presence of one or more oxygen atoms in the β-position to the methylene group. This would place an equatorial non-bonding electron pair on oxygen in a W-conformation with respect to the C–H(eq) bond. This might give rise to a homoanomeric interaction **3** between the equatorially oriented n-electrons and the σ* CH orbital, with the same consequences as that of the anomeric interaction in reducing $^1J_{CH}$.



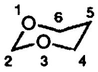
1



2



3



4

We report here a study of the ^{1}H and ^{13}C NMR spectra of some 1,3-dioxanes **4** and related compounds, in a search for further evidence for this interaction. Bock and Wiebe[4] reported the NMR spectra of a series of 1,3-dioxanes. They showed that at the 2-position, $^1J_{CH(ax)} < {}^1J_{CH(eq)}$, *i.e.* that there was a normal Perlin effect. When the 5-position carried a *tert*-butyl group, $^1J_{C(5)H(5ax)}$ was 127.5 Hz. When the *tert*-butyl substituent was absent, an averaged value of $^1J_{C(5)H(5ax)}$ and $^1J_{C(5)H(5eq)}$ of 166–167.5 Hz was observed, but in *cis,cis*-2,4,6-trimethyl-1,3-dioxane two coupling constants of 123.5 and 127.5 Hz were recorded; no comment was made on this observation.

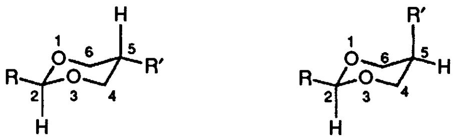
Results

The 1,3-dioxanes listed in Table 1 were chosen for study because the 5-methylene group is symmetrically placed with respect to the two oxygen atoms. A configuration-holding *tert*-butyl or aryl group was provided at the 2-position, and a methyl group at the 5-position in order to facilitate the identification of $^1J_{C(5)H}$.

The condensation of 2-methylpropane-1,3-diol with pivalaldehyde or 4-nitro-, 2-methoxy-, 4-methyl-, or 3-chlorobenzaldehyde in the presence of anhydrous copper(II) sulfate as a dehydrating agent[14] gave in each case a pair of isomeric (*cis* and *trans*) 1,3-dioxanes (Table 1, **7**–**16**). The 1,3-dioxanes **5** and **6** with a C(5)H$_2$ group were examined in order to confirm that the presence of a methyl group at C(5) did not perturb the values of $^1J_{C(5)H(5)}$.

The ^{1}H NMR spectra confirm that all the dioxanes exist in

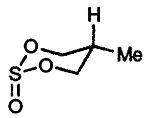
Table 1 Structures of 1,3-dioxanes



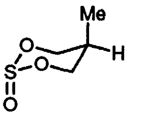
Compound	Config.	R	R'	Compound	Config.	R	R'
5	—	Bu^t	H	**6**	—	$p\text{-}NO_2C_6H_4$	H
7	*trans*	Bu^t	Me	**8**	*cis*	Bu^t	Me
9	*trans*	$p\text{-}NO_2C_6H_4$	Me	**10**	*cis*	$p\text{-}NO_2C_6H_4$	Me
11	*trans*	$o\text{-}MeOC_6H_4$	Me	**12**	*cis*	$o\text{-}MeOC_6H_4$	Me
13	*trans*	$p\text{-}MeC_6H_4$	Me	**14**	*cis*	$p\text{-}MeC_6H_4$	Me
15	*trans*	$m\text{-}ClC_6H_4$	Me	**16**	*cis*	$m\text{-}ClC_6H_4$	Me

the chair conformation, in agreement with the results of molecular mechanics calculations. The spectra showed that the isomer which was formed in higher yield in each reaction had the Me(5) group equatorial, with ${}^3J_{H(4ax)(5ax)}$ 11.3–11.5 Hz (*i.e.* R and Me *trans*) and the minor isomer had Me(5) axial with ${}^3J_{H(4ax)(5eq)}$ 1.2–1.3 Hz (*i.e.* R and Me *cis*). In all the compounds, ${}^1J_{C(2)H(2)}$ was 158.5–161.9 Hz, which is consistent with the hydrogen lying in the axial position, again in agreement with molecular mechanics calculations.[15]

The 5-methyl-2-oxo-1,3,2-dioxathianes **17** and **18** were prepared from 5-methylpropane-1,3-diol and thionyl chloride. The ${}^1H$ NMR spectra showed a similar pattern of coupling constants to those of the 1,3-dioxanes, confirming that these compounds exist in a chair conformation as has been established previously by ${}^1H$,[16] ${}^{13}C$,[17,18] and ${}^{17}O$[19,20] NMR spectroscopy. They had a strong IR absorption band for the SO group at 1189 cm^{-1} showing that the oxygen is in the axial position as shown in structures **17** and **18**.

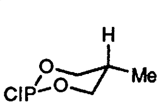


17

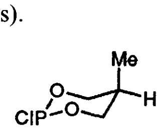


18

The 2-chloro-5-methyl-1,3,2-dioxaphosphorinanes **19** and **20** were prepared from the 1,3-diol and phosphorus trichloride. The proton–proton coupling constants show that both exist in a chair conformation, and according to Nifantiev's results,[22] the chlorine probably lies in the axial position (though this is not crucial to our discussion which follows).

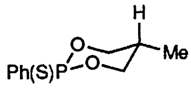


19

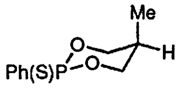


20

The 2-phenyl-2-thioxo-1,3,2-dioxaphosphorinanes **21** and **22** were obtained from the reaction between the diol and phenylphosphonothioic dichloride. There appears to be no evidence regarding the configuration at the phosphorus centre.



21



22

The ${}^1H$ and ${}^{13}C$ NMR parameters for the 1,3-dioxanes, 1,3-dioxathianes and 1,3-dioxaphosphorinanes are given in the Experimental section. 1-Bond ${}^{13}C$–${}^1H$ coupling constants were obtained from the undecoupled ${}^{13}C$ spectra, or from the ${}^{13}C$ satellites to the signals in the ${}^1H$ spectra.

Discussion

The regularities which differentiate the isomeric 1,3-dioxanes are shown in Table 2, and those for the hetero-1,3-dioxanes in Table 3; we have ignored differences smaller than 0.1 ppm in chemical shift, or of 1 Hz in coupling constant. Within the limited family of compounds which we have studied, there are no exceptions to the rules which are given in Tables 2 and 3.

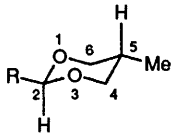
Trends in coupling constants can usually be interpreted with more confidence than trends in chemical shifts. Tables 2 and 3 show that in both the dioxanes **5–16** and the heterodioxanes **17–22**, ${}^1J_{C(5)(H5eq)}$ is consistently less than ${}^1J_{C(5)(H5ax)}$, by an average of about 6.3 Hz. This is opposite to the order which is observed (the Perlin effect) in the cyclohexanes or at the 2- or 6-position in tetrahydropyrans; the relevant data do not appear to be available for the 3-, 4-, or 5-positions in tetrahydropyrans. These results however are in line with those which we obtained for the 2- and 6-positions in the trioxanes, where each of these positions has one or two oxygens at the β-position.

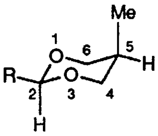
This is compatible with our suggestion that a doubly occupied equatorially-directed sp^3-like orbital on oxygen shows a special (homoanomeric) interaction with the equatorially directed C(5)–H(5eq) σ* orbital as shown in **3**. This weakens the C–H bond and attenuates the coupling. A similar type of argument is commonly used in both NMR[23] and EPR[24] spectroscopy to account for the long-range spin–spin interactions between two nuclei, or an electron and a nucleus, which lie in a W-configuration.

Other coupling constants involving the C(5)–H(5eq) bond might be expected to show a similar effect, and this is apparent in the values of the vicinal coupling constants ${}^3J_{H(4eq)H(5ax)}$ being greater than ${}^3J_{H(4ax)H(5eq)}$ (by *ca.* 4.6 and 1.2 Hz respectively in the 1,3-dioxanes **5–16**), although the corresponding dihedral angles, by molecular mechanics calculations, are about 121° and 131°, respectively. Of course, the same effect is observed involving the 6-position. Indeed, this effect has been noted previously by Anteunis, Tavernier and Borremans[25] who similarly tentatively ascribed it to a special interaction between the equatorial doubly-occupied non-bonding orbital on oxygen and the W-oriented equatorial C–H bond. The substantial size of the effect can be ascribed to the fact that whereas the C(5)–H(eq) bond is homoanomerically weakened by two β-oxygen atoms, the C(4)–H(ax) and C(6)–H(ax) bonds are also anomerically weakened by one α-oxygen atom.

Tables 2 and 3 show that a variety of anomalous effects are apparent also in the ${}^1H$ and ${}^{13}C$ chemical shifts, not only at the 5-position, but also at the 2-position. The ${}^1H$ and ${}^{13}C$ NMR spectra show that an equatorial proton or equatorial methyl group at the 5-position is more shielded than the equivalent group in the axial position, the reverse of what is usually observed in cyclohexanes. This unusually high ${}^{13}C$ shift of an equatorial methyl group at C(5) has been noted previously by

Table 2 Systematics of the NMR spectra of 1,3-dioxanes

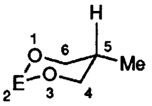


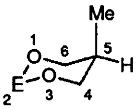


Parameter	Me equatorial range	Relation	Me axial range	Av. difference[a]
δ(C-2)	—[b]	<	—[b]	0.55
δ(4-H_{ax})	3.23–3.52	<	3.72–3.96	0.50
δ(C-4)	73.28–73.59	>	71.83–72.29	1.33
δ(5-H)	1.94–2.32	>	1.43–1.72	0.59
δ(C-5)	29.16–29.36	>	28.81–29.15	0.31
δ[H(5-Me)]	0.66–0.78	<	1.23–1.39	0.59
δ[C(5-Me)]	12.09–12.27	<	15.76–15.84	3.57
$^1J_{C(5)H}$	131.2–132.3	>	125.0–126.0	6.2
$^3J_{H(4eq)H(5ax)}$ or $^3J_{H(4ax)H(5eq)}$	4.5–4.8	>	1.2–1.3	3.4

[a] Average difference in ppm or Hz. [b] The chemical shift is strongly dependent on the nature of the group R.

Table 3 Systematics of the NMR spectra of 2-oxo-1,3,2-dioxathianes, 2-chloro-1,3,2-dioxaphosphorinanes and 2-phenyl-2-thioxo-1,3,2-dioxaphosphorinanes





Parameter	Me equatorial range	Relation	Me axial range	Av. difference[a]
δ(H-4_{ax})	4.17–4.46	<	4.61–4.98	0.43
δ(4-H_{eq})	3.73–4.14	<	3.58–3.86	0.54
δ(5-H)	2.43–2.47	>	1.87–2.27	0.42
δ(C-5)	29.86–31.71	>	29.51–30.98	0.71
δ[H(5-Me)]	0.79–0.89	>	1.02–1.37	0.38
δ[C(5-Me)]	11.86–13.04	<	13.36–15.10	1.84
$^1J_{C(5)H}$	131.7–132.1	>	123.0–128.3	6.5
$^3J_{H(4eq)H(5ax)}$ or $^3J_{H(4ax)H(5eq)}$	4.5–4.6	>	2.2–3.7	1.7

[a] Average difference in ppm or Hz.

Eliel *et al.* who associated it with the presence of two antiperiplanar O–C bonds in the ring.[26,27] The C(5) atom is more shielded when H rather than Me is equatorial. This would be compatible with a homoanomeric interaction occurring not only with the C(5)–H(eq) bond, but also, perhaps less effectively, with the C(5)–Me(eq) bond.

Ab initio Calculations

The above model is crude and is open to the criticism that we have assumed that the non-bonding electron pairs on oxygen to occupy tetrahedrally-directed sp^3 orbitals. This model is often adequate in considering stereoelectronic interactions, but a more realistic model should take account of the fact that the 'axially' directed pair of electrons occupy an orbital of increased p character, and the 'equatorially' directed pair have more s character.[9,10]

To supplement this pictorial approach, we have carried out *ab initio* calculations on 1,3-dioxane **4** (C_s symmetry) in order to examine the effect of β-oxygen atoms on the C(5) methylene group. Similar calculations have been carried out by David on tetrahydropyrans using the STO-3G basis set,[28] and by Wolfe *et al.* on open-chain model compounds at the RHF/6-31G* level,[9] in order to probe the effect of oxygen in the α-position (the anomeric effect).

Ab initio calculations were performed using the Gaussian 92 system of programs.[29] The structure of 1,3-dioxane was optimised at the RHF/6-31G* level of theory and with the inclusion of electron correlation (MP2/6-31G*) using standard gradient-optimisation techniques.[30] At the lower level the structure of **4** was proven to correspond to an energy minimum on the $C_4H_8O_2$ potential energy surface by the evaluation of the complete set of harmonic force constants.[30] The results of these calculations are displayed in Fig. 1. Inspection of this reveals that at the 2-, 4-, and 6-positions, which have α-oxygens, the axial CH bonds are longer than the equatorial CH bonds; MP2/6-31G* calculations predict that C(2)–H(ax) = 1.106 Å; C(2)–H(eq) = 1.090 Å; C(4)–H(ax) = 1.103 Å; C(4)–H(eq) = 1.092 Å. Force constant analysis at the lower level also reveals that the axial CH bonds are weaker than the corresponding equatorial bonds [C(2)–H(ax) = 6.26 mD $Å^{-1}$; C(2)–H(eq) = 7.21 mD $Å^{-1}$; C(4)–H(ax) = 6.39 mD $Å^{-1}$; C(4)–H(eq) = 7.02 mD $Å^{-1}$]. This endorses the result which Wolfe obtained for calculations on acyclic model compounds and is compatible with the Perlin effect on one-bond couplings and the other manifestations of the anomeric effect. With respect to the present work, these calculations also show that the equatorial C(5)–H bond, with the two oxygen atoms in the β-position, is longer and weaker than the axial C(5)–H bond. MP2/6-31G* calculations predict that C(5)–H(ax) = 1.094 Å, C(5)–H(eq) = 1.097 Å, with RHF/6-31G*-calculated force constants of 6.94 mD $Å^{-1}$ and 6.49 mD $Å^{-1}$ for the axial and equatorial CH bonds respectively. The difference in bond lengths is smaller (*ca.* 0.003 Å) than that calculated when oxygen is in the α-position, and while being too small to be conclusive, is consistent with the reversal of the order of the NMR coupling constants which we

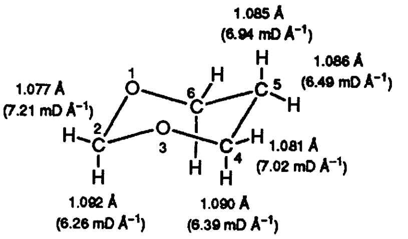


Fig. 1 RHF/6-31G* optimised structure of 1,3-dioxane

observe, and with the contrasting results for cyclohexane, where $^{1}J_{\text{C-(eq)}} > {}^{1}J_{\text{C-H(ax)}}$.[8]

Conclusion.—Our NMR studies on the 1,3-dioxanes, -dioxathianes, -dioxaphosphorinanes and 2-thioxo-1,3,2-dioxaphosphorinanes, show that the presence of the β-oxygen atoms in the ring has a special effect on the methylene group at C(5), which reverses the relative magnitude of NMR parameters of the axial and equatorial C–H bonds (*e.g.* $^{1}J_{\text{CH(eq)}} < {}^{1}J_{\text{CH(ax)}}$, the reversed Perlin effect). This is the same as the effect which we observed previously with the 1,2,4-trioxanes. The MO calculations support the suggestion that the effect of the β-oxygen atoms is to weaken and lengthen the equatorial C–H bond, and we suggest that this is caused by an n→σ* interaction operating through a W-configuration of orbitals. This is analogous to the anomeric interaction of oxygen in the α-position with an axial C–H bond, which weakens and lengthens the axial C–H bond.

If this picture of a homoanomeric interaction is correct, further evidence should be available from other sources, as it is for the anomeric interaction.[10] The calculated differences in C–H bond lengths are too small to be detected by X-ray crystallography but should be measurable by microwave spectroscopy, and the differences in bond strengths should be detectable by IR spectroscopy.[31] The interaction of the n electrons should show up in electron spectroscopy, and if C–Cl bonds interact in the same way, this should be detectable by NQR spectroscopy.[28] The differential interaction with the equatorial and axial C–H bonds should also show up in a difference in homolytic[32–34] and heterolytic[35] reactivities, as has been demonstrated for anomeric interactions.

Similar effects should be detectable in other 6-ring heterocycles containing first row atoms, and the tetrahydropyrans, 1,2-dioxanes, 1,4-dioxanes and 1,2,4,5-tetraoxanes, and their nitrogen analogues are obvious candidates for further studies. It would be particularly important to design molecules which could show whether an antiperiplanar disposition of the X–C–C–H bonds is a sufficient condition for reversing the usual order of the NMR parameters, or whether a W-arrangement, which includes a non-bonding electron pair on X, is necessary.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on $CDCl_3$ solutions on a Varian VXR-400 spectrometer unless otherwise stated; chemical shifts were measured relative to the solvent (δ_H 7.24 and δ_C 77.00). Coupling constants are in Hz. IR spectra were recorded on a Perkin-Elmer PE 983 instrument. Column chromatography was carried out on Merck silica gel 60 (70–230 mesh).

1,3-*Dioxanes* **5**–**16**.—*General method.* A solution of anhydrous copper sulfate (15 g), the appropriate aldehyde (10 mmol), propane-1,3-diol (or 2-methylpropane-1,3-diol) (11 mmol) and toluene-*p*-sulfonic acid (0.3–0.5 g; catalyst) in dichloromethane (30 cm^3) was heated under reflux for 3 h. The copper sulfate was filtered off, and the solvent was removed by rotary evaporation. The residue was distilled or recrystallised to give the appropriate 1,3-dioxanes in 65–95% yield. The properties of the products were as follows.

2-tert-*Butyl*-1,3-*dioxane* **5**. B.p. 43–44 °C/16 mmHg (lit.,[36] 147–149 °C); δ_H 0.85 (9 H, s, Bu^t), 1.25 (1 H, dm, *J* 13.3, 5-H$_{eq}$), 1.99 (1 H, m, 5-H$_{ax}$), 3.68 (2 H, m, 4,6-H$_{ax}$), 4.05 (1 H, s, 2-H$_{ax}$) and 4.07 (2 H, m, 4,6-H$_{eq}$); δ_C 24.70 (Me$_3$), 25.95 (C-5, $^{1}J_{CH}$ 125 and 131), 34.82 (Me$_3$*C*), 67.04 (C-4,6) and 107.97 (C-2).

2-(p-*Nitrophenyl*)-1,3-*dioxane* **6**. M.p. 110–111 °C (lit.,[37] 111.5 °C). δ_H 1.51 (1 H, m, 5-H$_{eq}$), 2.23 (1 H, dtt, *J* 13.5, 5.1 and 12.4, 5-H$_{ax}$), 4.00 (2 H, ddd, *J* 2.5, 11.3 and 12.4, 4,6-H$_{ax}$), 4.28 (2 H, ddd, *J* 5.1, 11.3 and 1.0, 4,6-H$_{eq}$), 5.56 (1 H, s, $^{1}J_{CH}$ 160.3, 2-H$_{ax}$), 7.65 (2 H, d, *J* 8.4, Ar) and 8.21 (2 H, d, *J* 8.9, Ar); δ_C 25.59 (C-5), 67.24 (C-4,6), 99.80 (C-2), 123.33, 127.14, 145.23 and 148.04 (Ar).

trans-2-tert-*Butyl*-5-*methyl*-1,3-*dioxane* **7**. B.p. (**7** + **8**, 4:1) 55–56 °C/18 mmHg (lit.,[13] 162–166 °C and 44–46 °C/14 mmHg); δ_H 0.66 (3 H, d, *J* 6.6, 5-Me$_{eq}$), 0.88 (9 H, s, Me$_3$), 1.94 (1 H, ttq, 5-H$_{ax}$), 3.23 (2 H, dd, *J* 11.3 and 11.3, 4,6-H$_{ax}$), 3.99 (1 H, s, 2-H$_{ax}$) and 4.01 (2 H, dd, *J* 4.6 and 11.6, 4,6-H$_{eq}$); δ_C 12.23 (5-Me), 24.75 (*Me*$_3$C), 29.36 (C-5, *J* 131.2), 34.63 (Me$_3$*C*), 73.32 (C-4,6, $^{1}J_{CH}$ 143.2) and 107.46 (C-2, $^{1}J_{CH}$ 158.5).

cis-2-tert-*Butyl*-5-*methyl*-1,3-*dioxane* **8**. δ_H 0.89 (9 H, s, *Me*$_3$C), 1.23 (3 H, dd, *J* 1.0 and 7.0, 5-Me$_{ax}$), 1.43 (1 H, ttq, 5-H$_{eq}$), 3.72 (2 H, dd, *J* 1.2 and 11.2, 4,6-H$_{ax}$), 3.80 (2 H, dd, *J* 10.6, 4,6-H$_{eq}$) and 4.08 (1 H, s, 2-H$_{ax}$); δ_C 15.73 (5-Me), 24.54 (*Me*$_3$C), 29.15 (C-5, $^{1}J_{CH}$ 125.7), 34.84 (Me$_3$*C*), 71.83 (C-4,6, ^{1}J 144.4) and 107.86 (C-2, $^{1}J_{CH}$ 158.7).

trans-5-*Methyl*-2-(p-*nitrophenyl*)-1,3-*dioxane* **9**. M.p. 85–87 °C (lit.[3] 55 °C); δ_H 0.78 (3 H, d, *J* 6.7, 5-Me$_{eq}$), 2.22 (1 H, ttq, 5-H$_{ax}$), 3.53 (2 H, dd, *J* 11.5 and 11.5, 4,6-H$_{ax}$, $^{1}J_{CH}$ 139.5), 4.20 (2 H, dd, *J* 4.6 and 11.7, 4,6-*H*$_{eq}$), 5.47 (1 H, s, 2-H$_{ax}$), 7.65 (2 H, d, *J* 8.4, Ar) and 8.20 (2 H, d, *J* 8.9, Ar); δ_C 12.23 (Me), 29.25 ($^{1}J_{CH}$ 131.2, C-5), 73.59 ($^{1}J_{CH}$ 142.5, C-4,6), 99.46 ($^{1}J_{CH}$ 160.7, C-2), 123.35 (Ar), 127.17 (Ar), 144.92 (Ar) and 148.03 (Ar); ν_{max}(Nujol)/cm^{-1} 2919.9, 2854.1, 2722.5, 1607.7, 1518.0, 1458.2, 1374.5, 1347.6, 1278.8, 1233.9, 1210.0, 1162.2, 1111.3, 1072.5, 1027.6, 994.7, 970.8, 893.0, 851.2, 827.3, 743.5, 722.6, 707.6, 680.7 and 638.9.

cis-5-*Methyl*-2-(p-*nitrophenyl*)-1,3-*dioxane* **10**. δ_H 1.33 (3 H, d, *J* 7.1, 5-Me$_{ax}$), 1.72 (1 H, ttq, 5-H$_{eq}$), 3.96 (2 H, dd, *J* 1.3 and 11.5, 4,6-H$_{ax}$), 4.15 (2 H, dd, *J* 2.1 and 12.1, 4,6-H$_{eq}$), 5.56 (1 H, s, 2-H$_{ax}$), 7.66 (2 H, d, *J* 9.0, Ar) and 8.21 (2 H, d, *J* 8.9, Ar); δ_C 15.81 (Me), 28.88 ($^{1}J_{CH}$ 125.1, C-5), 72.29 ($^{1}J_{CH}$ 141.0, C-4,6), 100.01 ($^{1}J_{CH}$ 158.7, C-2), 123.40 (Ar), 127.18 (Ar), 145.18 (Ar) and 148.03 (Ar).

trans-2-(o-*Methoxyphenyl*)-5-*methyl*-1,3-*dioxane* **11**. B.p. (**11** + **12**, 5:1) 110–111 °C/0.6 mmHg; m.p. 60–62 °C; δ_H 0.73 (3 H, d, *J* 6.7, 5-Me$_{eq}$), 2.23 (1 H, ttq, 5-H$_{ax}$), 3.52 (2 H, dd, *J* 11.5 and 11.5, 4,6-H$_{ax}$), 3.79 (3 H, s, OMe), 4.15 (2 H, dd, *J* 4.8 and 11.7, 4,6-H$_{eq}$), 5.81 (1 H, s, 2-H$_{ax}$), 6.85 (1 H, d, *J* 8.4, Ar), 6.98 (1 H, dd, *J* 8.2 and 7.52, Ar), 7.28 (1 H, ddd, *J* 1.8, 7.5 and 8.3, Ar) and 7.64 (1 H, dd, *J* 1.9 and 7.6, Ar); δ_C 12.09 (5-Me), 29.16 ($^{1}J_{CH}$ 132.2, C-5), 55.26 (OMe), 73.58 ($^{1}J_{CH}$ 142.0, C-4,6), 96.19 ($^{1}J_{CH}$ 161.8, C-2), 110.3 (Ar), 120.37 (Ar), 126.78 (Ar), 129.72 (Ar), 135.68 (Ar) and 156.13 (Ar); ν_{max}(Nujol; **11** + **12**, 5:1)/cm^{-1} 2836.2, 1601.7, 1586.8, 1494.1, 1458.2, 1374.5, 1308.7, 1281.8, 1245.9, 1198.1, 1159.2, 1117.3, 1105.4, 1069.5, 1048.5, 1024.6, 991.7, 943.9, 925.9, 893.0, 848.2, 782.4, 758.5, 734.6, 656.8 and 635.9 (Found: C, 69.3; H, 8.0. $C_{12}H_{16}O_3$ requires C, 69.21; H, 7.74%).

cis-2-(o-*Methoxyphenyl*)-5-*methyl*-1,3-*dioxane* **12**. δ_H 1.39 (3 H, d, *J* 7.0, 5-H$_{ax}$), 1.59 (1 H, ttq, 5-H$_{eq}$), 3.84 (3 H, s, OMe), 3.94 (2 H, dd, *J* 1.2 and 10.0, 4,6-*H*$_{ax}$), 5.87 (1 H, s, 2-H$_{ax}$), all aromatic and 4,6-H$_{eq}$ protons overlap with 7-H of the main isomer. δ_C 15.76 (Me), 28.82 ($^{1}J_{CH}$ 126.0, C-5), 55.26 (OMe), 72.26 ($^{1}J_{CH}$ 144.0, C-4,6), 96.72 ($^{1}J_{CH}$ 161.9, C-2), 111.35 (Ar), 120.33 (Ar), 126.38 (Ar), 128.13 (Ar), 142.00 (Ar) and 156.02 (Ar).

trans-5-*Methyl*-2-(p-*tolyl*)-1,3-*dioxane* **13**. M.p. (**13** + **14**, 4:1) 71–75 °C; $\delta_{\rm H}$ 0.76 (3 H, d, J 6.8, 5-Me$_{\rm eq}$), 2.23 (1 H, ttq, 5-H$_{\rm ax}$), 2.35 (3 H, s, Ar*Me*), 3.50 (2 H, dd, J 11.5 and 11.5, 4,6-H$_{\rm ax}$), 4.18 (2 H, dd, J 4.7 and 11.8, 4,6-H$_{\rm eq}$), 5.40 (1 H, s, 2-H$_{\rm ax}$), 7.18 (2 H, d, J 7.92, Ar) and 7.39 (2 H, d, J 7.92, Ar); $\delta_{\rm C}$ 12.26 (5-Me), 21.14 (Ar*Me*), 29.21 ($^1J_{\rm CH}$ 132.2, C-5), 73.52 ($^1J_{\rm CH}$ 142.4, C-4,6), 101.23 ($^1J_{\rm CH}$ 159.1, C-2), 125.83 (Ar), 128.77 (Ar), 135.52 (Ar) and 138.36 (Ar); $\nu_{\rm max}$ (Nujol; **13** + **14**, 4:1)/cm^{-1} 2925.9, 2848.1, 1607.7, 1512.0, 1458.2, 1380.5, 1278.8, 1230.9, 1165.2, 1111.3, 1072.5, 1033.6, 1018.6, 1003.7, 982.8, 967.8, 949.9, 893.0, 803.3, 779.4 and 644.9 (Found: C, 74.6; H, 8.7. $C_{12}H_{16}O_2$ requires C, 74.97; H, 8.39%).

cis-5-*Methyl*-2-(p-*tolyl*)-1,3-*dioxane* **14**. $\delta_{\rm H}$ 1.36 (3 H, d, J 7.0, 5-Me$_{\rm ax}$), 1.57 (1 H, ttq, 5-H$_{\rm eq}$), 2.35 (3 H, s, Ar*Me*), 3.94 (2 H, dd, J 1.3 and 11.3, 4,6-H$_{\rm ax}$), 4.11 (2 H, dd, J 1.8 and 2.4, 4,6-H$_{\rm eq}$), 5.48 (1 H, s, 2-H$_{\rm ax}$), aromatic protons overlap with the main isomer; $\delta_{\rm C}$ 15.80 (5-Me), 21.14 (Ar-Me), 28.94 ($^1J_{\rm CH}$ 125.0, C-5), 72.06 ($^1J_{\rm CH}$ 141, C-4,6), 101.61 ($^1J_{\rm CH}$ 159, C-2), 125.83 (Ar), 128.77 (Ar), 135.82 (Ar) and 138.36 (Ar).

trans-2-(m-*Chlorophenyl*)-5-*methyl*-1,3-*dioxane* **15**. M.p. (**15** + **16**, 5:1) 64–68 °C; $\delta_{\rm H}$ 0.75 (3 H, d, J 6.8, 5-Me$_{\rm eq}$), 2.02 (1 H, ttq, 5-H$_{\rm ax}$), 3.48 (2 H, dd, J 11.5 and 11.5, 4,6-H$_{\rm ax}$), 4.17 (2 H, dd, J 4.6 and 11.6, 4,6-H$_{\rm eq}$), 5.37 (1 H, s, 2-H$_{\rm ax}$), 7.25–7.36 (3 H, m, Ar) and 7.50 (1 H, s, Ar); $\delta_{\rm C}$ 12.27 (Me), 29.25 ($^1J_{\rm CH}$ 132.3, C-5), 73.56 ($^1J_{\rm CH}$ 140.9, C-4,6), 100.15 ($^1J_{\rm CH}$ 160.2, C-2), 124.25 (Ar), 126.38 (Ar), 128.83 (Ar), 129.49 (Ar), 134.12 (Ar) and 140.27 (Ar); $\nu_{\rm max}$(Nujol; **15** + **16**, 5:1)/cm^{-1} 2919.9, 2854.1, 1595.8, 1568.8, 1458.2, 1374.5, 1281.8, 1230.9, 1207.0, 1165.2, 1114.3, 1093.4, 1072.5, 1027.6, 1000.7, 970.8, 917.0, 875.1, 851.2, 782.4, 734.6 and 680.7 (Found: C, 61.9; H, 6.3. $C_{11}H_{13}ClO_2$ requires C, 62.12; H, 6.16%).

cis-2-(m-*Chlorophenyl*)-5-*methyl*-1,3-*dioxane* **16**. $\delta_{\rm H}$ 1.33 (3 H, d, J 7.0, 5-Me$_{\rm ax}$), 1.67 (1 H, ttq, 5-H$_{\rm eq}$), 3.92 (2 H, d, J 10.5, 4,6-H$_{\rm ax}$), 4.10 (2 H, d, J 10.1, 4,6-H$_{\rm eq}$), 5.45 (1 H, s, 2-H$_{\rm ax}$), aromatic protons overlap with the main isomer; $\delta_{\rm C}$ 15.84 (Me), 28.92 ($^1J_{\rm CH}$ 125.4, C-5), 72.18 ($^1J_{\rm CH}$ 141.3, C-4,6), 100.68 ($^1J_{\rm CH}$ 160, C-2), 124.25 (Ar), 126.38 (Ar), 128.83 (Ar), 129.49 (Ar), 134.12 (Ar) and 140.52 (Ar).

5-*Methyl*-2-*oxo*-1,3,2-*dioxathianes* **17** *and* **18**.—At 0 °C, $SOCl_2$ (1.2 mol) was added dropwise to 2-methylpropane-1,3-diol (1 mol) in CH_2Cl_2 (100 cm^3) over about 1 h, then the mixture was warmed to room temperature and heated under reflux for 0.5 h. After hydrolysis and extraction with CH_2Cl_2, the organic layer was dried over $MgSO_4$ and gave, by distillation, the title product (50 g, 38%), with the two isomers, **17** and **18**, in the ratio of 8:1; b.p. 30 °C/0.5 mmHg (lit.[20] *cis*-isomer, 58–60 °C/8 mmHg, *trans*-isomer, 65–69 °C/8 mmHg).

Main isomer, **17** (5-methyl equatorial) $\delta_{\rm H}$ 0.79 (3 H, d, J 6.9, 5-Me$_{\rm eq}$), 2.47 (1 H, ttq, 5-H$_{\rm ax}$), 3.73 (2 H, dd, J 4.6 and 11.7, 4,6-H$_{\rm eq}$) and 4.46 (2 H, dd, J 11.7 and 11.7, 4,6-H$_{\rm ax}$); $\delta_{\rm C}$ 13.04 (5-Me), 29.86 ($^1J_{\rm CH}$ 132.1, C-5) and 62.19 ($^1J_{\rm CH}$ 148.5 and 155.7, C-4,6); $\nu_{\rm max}$(neat; mixture of **17** and **18**)/cm^{-1} 2949.8, 2919.9, 2884.0, 1458.2, 1386.4, 1222.0, 1189.1, 1087.4, 1057.5, 982.8, 955.8, 902.0, 887.1, 857.2, 776.4, 743.5, 667.7 and 641.9 [Found (mixture of isomers): C, 35.4; H, 5.7. $C_4H_8O_2S$ requires C, 35.29; H, 5.92%].

Minor isomer **18** (5-methyl axial) $\delta_{\rm H}$ 1.33 (3 H, d, J 7.2, Me$_{\rm ax}$), 1.87 (1 H, ttq, 5-H$_{\rm eq}$), 3.58 (2 H, dd, J 2.4 and 11.5, 4,6-H$_{\rm eq}$) and 4.98 (2 H, dd, J 2.7 and 11.3, 4,6-H$_{\rm ax}$); $\delta_{\rm C}$ 14.88 (C-5Me), 29.51 (C-5, $^1J_{\rm CH}$ 123.0) and 62.71 (C-4,6).

2-*Chloro*-5-*methyl*-1,3,2-*dioxaphosphorinanes* **19** *and* **20**.—At 0 °C, PCl_3 was added dropwise with stirring to 2-methylpropane-1,3-diol (9 g) and *N*,*N*-dimethylaniline (24.3 g), and a trace of its hydrochloride salt as a crystal seed, in 1:1 diethyl ether–1,4-dioxane solvent (300 cm^3). The solid which was precipitated was filtered off and the residue was distilled to give the title products **19** and **20** (5:1) in 60% yield, b.p. 67–68 °C/8 mmHg.

Main isomer **19** (5-Me equatorial) $\delta_{\rm H}$ 0.79 (3 H, d, J 6.7, 5-Me$_{\rm eq}$), 2.43 (1 H, ttq, 5-H$_{\rm ax}$), 3.92 (2 H, ddd, J 4.5, 11.4, and $^3J_{\rm PH}$ 11.4, 4,6-H$_{\rm eq}$) and 4.17 (2 H, ddd, J 11.4, 11.4 and $^3J_{\rm PH}$ 5.71, 4,6-H$_{\rm ax}$). $\delta_{\rm C}$ 12.92 (Me), 31.66 (C-5, $^1J_{\rm CH}$ 131.8) and 66.73 (C-4,6, $^1J_{\rm CH}$ 149.6); $\nu_{\rm max}$(neat; mixture of **19** and **20**, 5:1)/cm^{-1} 2967.7, 2878.0, 1724.3, 1458.2, 1386.4, 1335.6, 1284.8, 1228.0, 1150.2, 1093.4, 1078.4, 1024.6, 982.8, 958.8, 943.9, 908.8, 890.1, 872.1, 833.2, 767.5, 698.7 and 612.0 (Found: C, 30.7; H, 5.1. $C_4H_8ClO_2P$ requires C, 31.10; H, 5.20%).

Minor isomer **20** (with the 5-Me in the axial position) $\delta_{\rm H}$ 1.37 (3 H, d, J 6.98, 5-Me$_{\rm ax}$), 1.92 (1 H, ttq, 5-H$_{\rm eq}$), 3.74 (2 H, ddd, J 1.62, 11.73 and $^3J_{\rm PH}$ 10.16, 4,6-H$_{\rm eq}$) and 4.76 (2 H, J 2.19, 9.21, $^3J_{\rm PH}$ 7.9, 4,6-H$_{\rm ax}$); $\delta_{\rm C}$ 15.10 (Me), 30.98 ($^1J_{\rm CH}$ 124.7, C-5) and 66.32 (C-4,6).

2-*Phenyl*-2-*thioxo*-1,3,2-*dioxaphosphorinanes* **21** *and* **22**.—Phenylphosphonothioic dichloride (42.2 g) was added dropwise at 0 °C to 2-methylpropane-1,3-diol (18 g) and pyridine (32 g) in diethyl ether (350 cm^3). The mixture was stirred for 2 h then the solid was filtered off and the solvent was removed to give a residue which was recrystallised from cyclohexane to give the title product **22** in 20% yield. Distillation of the residue gave **21** which was contaminated with 15% of **22**.

Main isomer **21** (5-Me equatorial) m.p. (**21** + **22**, 6:1) 41–45 °C; $\delta_{\rm H}$ 0.89 (3 H, d, J 6.9, 5-Me$_{\rm eq}$), 2.45 (1 H, ttq, 5-H$_{\rm ax}$), 4.14 (2 H, ddd, J 4.5, 10.3 and $^3J_{\rm PH}$ 22.2, 4,6-H$_{\rm eq}$), 4.44 (2 H, ddd, J 11.4, 10.1 and $^3J_{\rm PH}$ 5.4, 4,6-H$_{\rm ax}$), 7.45–7.53 (2 H, m, Ar), 7.55–7.60 (1 H, m, Ar) and 7.97–8.03 (2 H, m, Ar); $\delta_{\rm C}$ 11.86 (Me), 31.71 ($^1J_{\rm CH}$ 131.7, C-5), 70.05 ($^1J_{\rm CH}$ 149.9, C-4,6), 128.26 (Ar), 131.4 (Ar) and 133.06 (Ar); $\nu_{\rm max}$(Nujol; **21** + **22**, 6:1)/cm^{-1} 2925.9, 2854.1, 1586.8, 1568.8, 1458.2, 1434.3, 1374.5, 1335.6, 1305.7, 1272.8, 1225.0, 1150.2, 1120.3, 1090.4, 1015.6, 943.9, 890.1, 818.3, 803.3, 740.5, 686.7, 626.9 and 603.0 (Found: C, 52.7; H, 5.8. $C_{10}H_{13}O_2PS$ requires C, 52.63; H, 5.74%).

Minor isomer **22** (5-Me axial) m.p. 114–116 °C; $\delta_{\rm H}$ 1.02 (3 H, J 7.0, 5-Me$_{\rm ax}$), 2.27 (1 H, ttq, 5-H$_{\rm eq}$), 3.86 (2 H, ddd, J 6.7, 11.4 and $^3J_{\rm PH}$ 12.6, 4,6-H$_{\rm eq}$), 4.61 (2 H, ddd, J 3.7, 11.3 and $^3J_{\rm PH}$ 13.8, 4,6-H$_{\rm ax}$), 7.46–7.51 (2 H, m, Ar), 7.52–7.57 (1 H, m, Ar) and 7.82–7.88 (2 H, m, Ar); $\delta_{\rm C}$ 13.36 (Me), 30.70 ($^1J_{\rm CH}$ 128.3, C-5), 71.54 ($^1J_{\rm CH}$ 150.5, C-4,6), 128.73 (Ar), 130.45 (Ar) and 132.51 (Ar); $\nu_{\rm max}$(Nujol)/cm^{-1} 2925.9, 2854.1, 1583.8, 1565.9, 1455.2, 1431.3, 1374.5, 1335.6, 1308.7, 1272.8, 1222.0, 1147.2, 1120.3, 1084.4, 1003.7, 967.8, 952.9, 943.9, 887.1, 860.2, 815.3, 749.5, 734.6, 689.7, 650.8 (Found: C, 52.7; H, 5.8. $C_{10}H_{13}O_2PS$ requires C, 52.66; H, 5.76%).

Acknowledgements

We are grateful to Drs. J. E. Anderson and A. J. Bloodworth for many useful discussions. This work was carried out during the tenure by J. C. of a Royal Fellowship awarded by the Royal Society and the Chinese Academy of Sciences.

References

1 R. K. Harris, *Nuclear Magnetic Resonance Spectroscopy*, Pitman, London, 1983.
2 V. A. Chertkov and N. M. Sergeyev, *J. Am. Chem. Soc.*, 1977, **99**, 6750.
3 F. W. Vierhapper and R. L. Willer, *Org. Magn. Reson.*, 1977, **9**, 13.
4 K. Bock and L. Wiebe, *Acta Chem. Scand.*, 1973, **27**, 2676.
5 K. Bock, I. Lundt and C. Pedersen, *Tetrahedron Lett.*, 1973, 1037.
6 K. Bock and C. Pedersen, *J. Chem. Soc., Perkin Trans. 2*, 1974, 293.
7 R. D. McKelvey, T. Sugawara and H. Iwamura, *Magn. Reson. Chem.*, 1985, **23**, 330.
8 A. S. Perlin and B. Casu, *Tetrahedron Lett.*, 1969, 2921.
9 S. Wolfe, B. M. Pinto, V. Varma and R. Y. N. Leung, *Can. J. Chem.*, 1990, **68**, 1051.
10 A. J. Kirby, *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*, Springer-Verlag, Berlin, 1983, pp. 1–150.

11 E. Juaristi and G. Cuevas, *Tetrahedron Lett.*, 1992, **33**, 1847.
12 E. Jauristi, *Tetrahedron Lett.*, 1992, **33**, 6927.
13 J. E. Anderson, A. J. Bloodworth, J. Cai, A. G. Davies and N. A. Tallant, *J. Chem. Soc., Chem. Commun.*, 1992, 1689.
14 F. G. Riddell and M. J. T. Robinson, *Tetrahedron*, 1967, **23**, 3417.
15 J. E. Anderson, K. Heki, M. Hirota and F. S. Jorgensen, *J. Chem. Soc., Chem. Commun.*, 1987, 554.
16 K. Pihlaja, T. Virtanen, H. Nikander and E. Rahkamaa, *Tetrahedron*, 1982, **38**, 2821.
17 K. Pihlaja, K. Rossi and H. Nikander, *J. Org. Chem.*, 1985, **50**, 644.
18 D. G. Hellier and A. M. Phillips, *Org. Magn. Reson.*, 1982, **18**, 178.
19 D. G. Hellier, *Magn. Reson. Chem.*, 1986, **24**, 163.
20 J. Mattinen and K. Pihlaja, *Magn. Reson. Chem.*, 1987, **25**, 569.
21 T. Virtanen, K. Pihlaja and H. Nikander, *Acta Chem. Scand.*, 1982, **B36**, 117.
22 E. E. Nifantiev, S. F. Sorokina, A. A. Borisenko, A. I. Zavalishina and L. A. Vorobjeva, *Tetrahedron*, 1981, **37**, 3183.
23 L. M. Jackman and S. Sternhell, *Applications of Nuclear Magnetic Resonance in Organic Chemistry*, Pergamon Press, Oxford, 1969.
24 G. A. Russell and K.-Y. Chang, *J. Am. Chem. Soc.*, 1965, **87**, 4381.
25 M. Anteunis, D. Tavernier and F. Borremans, *Bull. Soc. Chim. Belg.*, 1966, **75**, 396.
26 E. L. Eliel and K. M. Pietrusiewicz, *Topics in Carbon-13 NMR Spectroscopy*, 1979, **3**, 171.
27 A. J. Jones, E. L. Eliel, D. M. Grant, M. C. Knoeber and W. F. Bailey, *J. Am. Chem. Soc.*, 1971, **93**, 4772.
28 S. David in *Anomeric Effect, Origin, Consequences*, A.C.S. Symposium Series, 1979, 1.
29 M. J. Frisch, G. W. Trucks, M. Head-Gordon, M. W. Gill, M. W. Wong, J. B. Foresman, B. G. Johnson, H. B. Schlegel, M. A. Robb, E. S. Replogle, R. Gomperts, J. L. Andres, K. Raghavachari, J. S. Binkley, C. Gonzales, R. L. Martin, D. J. Fox, D. J. Defrees, J. Baker, J. J. P. Stewart and J. A. Pople, *Gaussian 92*, Revision F, Gaussian Inc., Pittsburgh, PA, 1992. Calculations were performed on a SUN SparcStation 2 or SparcServer 10/512 Computer.
30 W. J. Hehre, L. Radom, P. v. R. Schleyer and J. A. Pople, *Ab Initio Molecular Orital Theory*, Wiley, New York, 1986.
31 F. Bohlmann, *Chem. Ber.*, 1958, **91**, 2157.
32 V. Malatesta and K. U. Ingold, *J. Am. Chem. Soc.*, 1981, **103**, 609.
33 A. L. J. Beckwith and C. J. Easton, *J. Am. Chem. Soc.*, 1981, **103**, 615.
34 D. Griller, J. A. Howard, P. R. Marriott and J. C. Scaiano, *J. Am. Chem. Soc.*, 1981, **103**, 619.
35 P. Deslongchamps, *Tetrahedron*, 1975, **31**, 2463.
36 E. L. Eliel and M. C. Knoeber, *J. Am. Chem. Soc.*, 1968, **90**, 3444.
37 G. Schneider, O. Kovacs and M. Chinorai, *Acta Univ. Szeged, Acta Phys. Chem.*, 1964, **10**, 95 (*Chem. Abs.*, 1965, **62**, 7747d).

Paper 4/00163J
Received 11*th January* 1994
Accepted 15*th February* 1994