NMR Studies on Cyclic Arsenites. ^{13}C NMR Spectra of Twenty-one 1,3,2-Dioxarsenanes. Substituent Effects of Alkyl and Phenyl Groups on the Chemical Shifts of the Ring Carbons

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[13]C chemical shifts have been measured for twenty-one alkyl- and phenyl-substituted 1,3,2-dioxarsenanes. By comparing compounds differing only in the 2-substituent it is seen that the axial substituent at arsenic has a marked influence on the shielding of the ring carbons. For all substituents, except phenyl, the shift effect on C(5) is smaller and in the opposite direction to that suffered by C(4) and C(6).

Alkyl and phenyl ring-substituents have large and stereospecific effects on the ^{13}C chemical shifts of the ring carbons. The α, β, and γ substituent effects of methyl groups have been calculated by means of a least-squares analysis. The chemical shifts of the ring carbons can be predicted fairly accurately by using the obtained substituent parameters. The general trend in the substituent effects of methyl groups in arsenites and related heterocyclic systems, is that α and β carbons are strongly deshielded whereas γ carbons in gauche positions are shielded.

The ^{13}C nucleus of a single equatorial methyl group at C(4,6) and C(5) resonates near 24 and 13.5 ppm from TMS, respectively. Furthermore, the ^{13}C signal of an axial methyl group appears downfield from the signal of its equatorial counterpart.

In recent years considerable effort has been expended in ^{13}C NMR studies of various six-membered heterocycles,[1] in particular dioxanes,[1-3] sulfites[4,5] and phosphites.[6-8] The ^{13}C NMR parameters are extremely sensitive to molecular geometry, and relations between chemical shifts and structural and conformational properties of the heterocyclic rings have been established.

Extensive studies of substituent effects have given rise to empirical correlations[9] that offer valuable assistance in ^{13}C signal identification and, hence, may lead to definitive stereochemical assignments. In this context it is worth mentioning that substituent parameters for ^{13}C chemical shifts in the chair forms of methyl-substituted cyclohexanes,[10] 1,3-dioxanes[2] and 1,3-dithianes[11] have been derived. These substituent effects enable one to make remarkably good predictions for the ^{13}C chemical shifts in similar compounds. Substantial discrepancies between observed and predicted chemical shifts may then be ascribed to the presence of non-chair conformations. It is thus clear that ^{13}C NMR studies on six-membered rings constitute a very useful and complementary extention to previous proton investigations.

In a previous paper in this series[12] ^{13}C NMR data for some methyl-substituted 1,3,2-dioxarsenanes and their unsubstituted analogues, were reported. The introduction of methyl groups in the cyclic system was found to produce significant incremental shift effects on the ring carbons. In order to gain more information about ring-substituted dioxarsenanes we have investigated the ^{13}C NMR spectra of the twenty-one compounds listed in Table 1. The present and previously reported data[12] make it possible to perform a least-squares regressional analysis to obtain more precise values for the substituent effects of methyl groups.

EXPERIMENTAL

The syntheses of the investigated 1,3,2-dioxarsenanes have been described in two previous papers.[13,14]

Table 1. ^{13}C NMR chemical shifts (in ppm form TMS) of 1,3,2-dioxarsenanes measured in deuteriochloroform solution.
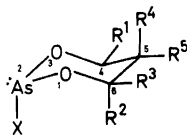
Compound	X	Substituents $R^{i\ a}$	C(4)	C(5)	C(6)	4-Me (eq)	5-Alkyl ^{b} (ax)	(eq)	6-Me (ax)	(eq)
I	Cl	R^5 = Me	68.16	33.21	68.16			13.56		
II	OMe		67.33	34.22	67.33			13.73		
III	OPh		67.29	33.58	67.29			13.41		
IV	Ph		69.64	34.56	69.64			13.58		
V	Cl	R^5 = Ph	66.58	44.49	66.58					
VI	OPh		64.63	49.06	64.63					
VII	Ph		68.25	46.46	68.25					
VIII	Cl	R^5 = Bu^t	64.52	46.93	64.52			27.10		
								31.17		
IX	Ph		64.64	44.70	64.64			26.30		
								30.28		
X	Ph	R^4 = R^5 = Me	73.16	33.59	73.16		22.74	21.83		
XI ^{c}	Cl	R^4 = R^5 = Et	69.72	37.62	69.72		6.69	6.69		
							23.33	23.33		
XII	OMe		68.18	37.85	68.18		7.41	6.33		
							25.18	21.70		
XIII	OPh		68.61	37.59	68.61		7.58	6.29		
							25.40	21.99		
XIV	Ph		70.98	38.46	70.98		7.24	6.24		
							24.66	22.03		
XV	Ph	R^1 = Me	68.64	38.17	63.87	24.50				
XVI	OMe	R^1 = Ph	73.80	40.91	61.14					
XVII	OPh		74.08	40.83	61.33					
XVIII	Ph		78.42	33.79	66.63					
XIX	OPh	R^1 = R^2 = R^3 = Me	64.00	47.69	76.08	24.04			33.66	29.04
XX	Ph		67.90	48.05	74.56	24.72			33.40	28.33
XXI	Ph	R^1 = R^3 = Me	65.23	45.94	65.23	23.72				23.72

^{a} R^i = H unless otherwise stated. ^{b} In cases where two chemical shifts are reported the upper refers to the methyl carbon and the lower to the secondary or quaternary carbon. ^{c} The observed chemical shifts are the result of rapid exchange of chlorine.

The samples were prepared in 10 mm o.d. tubes as 30 % solutions in deuteriochloroform. A small amount of TMS was added to the samples and used as internal standard whereas deuteriochloroform served as internal ^{2}H lock signal source.

The ^{13}C spectra were recorded at ambient probe temperature on JEOL FX 60 and BRUKER CXP 100 spectrometers operating at 15.04 and 22.63 MHz, respectively. The broad band proton decoupled ^{13}C spectra were run at a spectral width of about 4 kHz and a data memory size of 8 or 16 K depending on the required resolution. Off-resonance proton decoupling was used for some of the compounds for the purpose of signal identification.

RESULTS AND DISCUSSION

The studied compounds and the measured ^{13}C chemical shifts are listed in Table 1. The resonance signals of the proton decoupled ^{13}C NMR spectra were assigned on the basis of empirically established trends of alkyl and phenyl substituents,[9,12] off-resonance decoupling and intensity considerations.

A variety of systematic trends can be observed in the ^{13}C chemical shift data of Table 1. Since the carbon nuclei are buried in the molecular framework medium-induced shifts are expected to be small, in particular since all compounds were studied at

similar concentrations in the same solvent. In the subsequent discussion emphasis will therefore be on intramolecular shielding effects. The empirical approach used in this paper to rationalize the experimental data has become a widely accepted practice.[9]

Previous ¹H NMR investigations[13-15] and other evidence,[16] have shown that the 1,3,2-dioxarsenane ring adopts a chair conformation usually with an axial substituent at arsenic.

By comparing compounds differing only in the 2-substituent it is seen that the substituent at arsenic
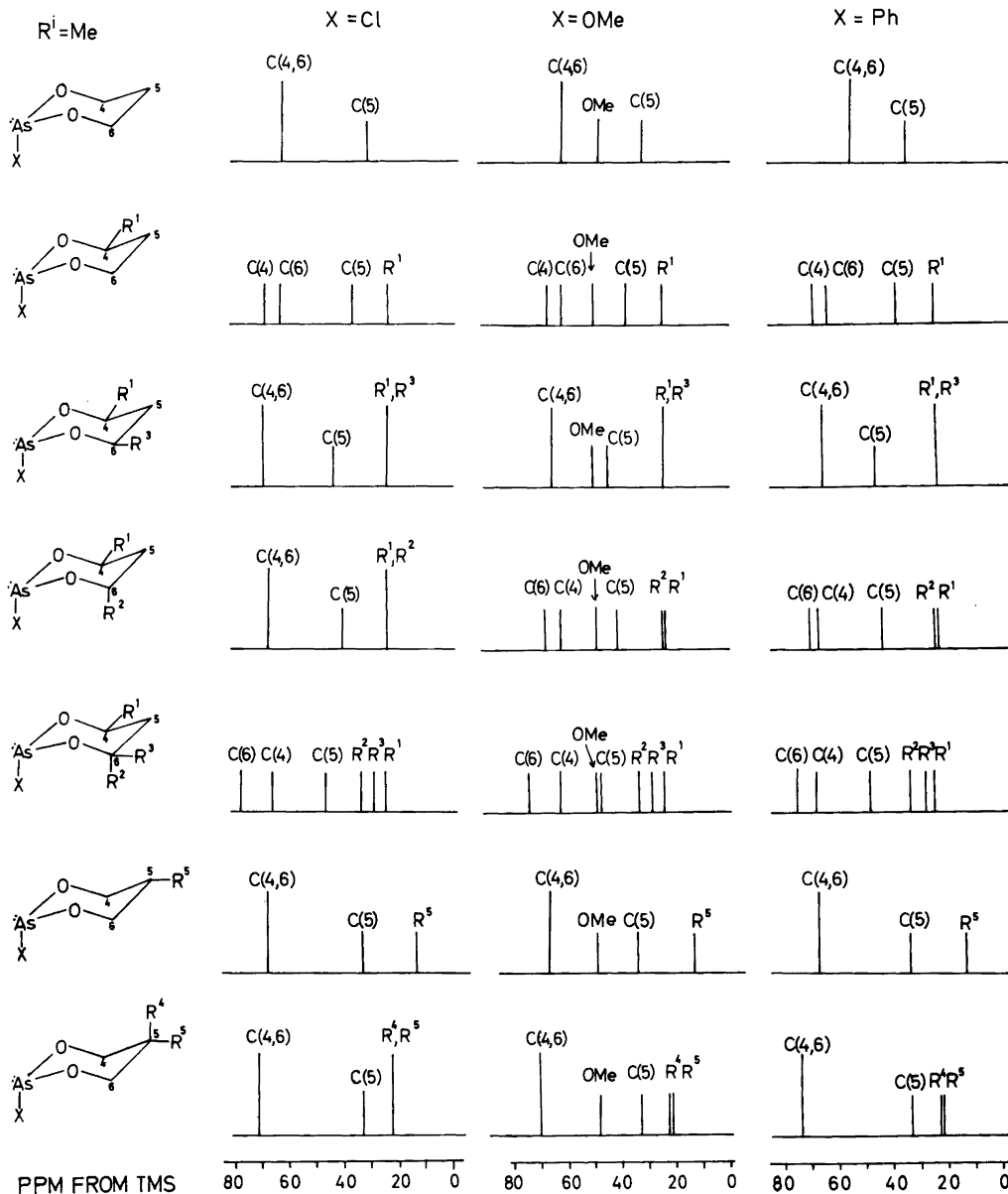

Fig. 1. Carbon-13 chemical shift correlation chart for methyl-substituted 2-X-1,3,2-dioxarsenanes.

has a marked influence on the ring carbon shield-ings. For all substituents, except phenyl, the shift effect on C(5) is smaller and in the opposite direction to that suffered by C(4) and C(6). These incremental shifts can be rationalized on the basis of sterically induced γ and δ effects of opposite sign. An axially oriented substituent at arsenic is *gauche* related to the C(4,6) carbon atoms and should give rise to an upfield γ-*gauche* effect [9,10,17] as observed. In con-trast, substituents δ to the observed carbon are reported to produce small but measurable deshield-ing effects ($\sim 1-2$ ppm).[4,7] The relatively large downfield shifts observed for all ring carbons in the 2-phenyl compounds are apparently caused by the ring current effect of the phenyl group.

The effect of ring-substituted alkyl and phenyl groups on the chemical shifts of the ring carbons will now be discussed. A correlation shart for the methyl-substituted 2-X-1,3,2-dioxarsenanes (X = Cl, OMe and Ph) is shown in Fig. 1.

The empirical additivity approach relies on the selection of suitable model compounds and on the availability of a minimum number of appro-priately substituted compounds for regressional analysis. In this respect the methyl-substituted dioxarsenanes constitute a very suitable system. In these compounds the chemical shift $\delta_C(k)$ of carbon k can be predicted by means of eqn. (1).[9]

$$\delta_C(k) = C_k + \sum_i A_{ik}(R^i) \tag{1}$$

where C_k is the corresponding chemical shift of the parent compound and A_{ik} is the shift increment (α,

β and γ effects) predicted for carbon k upon introduction of substituent R^i at carbon i.

A least-squares analysis of the ring carbon chemical shifts was undertaken to determine more precise values for the α, β, and γ substituent effects of methyl groups in dioxarsenanes. Thirty chemical shift differences derived from twelve methyl-substituted 2-X-1,3,2-dioxarsenanes (X = Cl, OMe and OPh) and their unsubstituted analogues, where included in the regressional analysis. The 2-phenyl compounds were omitted from the anal-ysis since their incremental carbon shifts were considerably smaller than in the above series. The deviation was particularly large for the 4- and 6-substituted compounds. This observation indicates that the downfield shifts produced by the methyl groups are partly compensated by sterically induced upfield shifts involving the bulky phenyl sub-stituent.

The calculated α, β, and γ substituent parameters are listed in Table 2 together with their probable errors. It is seen from Table 3 that the chemical shifts of the ring carbons can be predicted fairly accurately by using the substituent parameters in Table 2.

The substituent parameters listed in Table 2 are quite close to those reported for the analogous 1,3-dioxanes[2,9] with the exception of the α_a effects. Similar substituent effects of 4- and 6-methyl groups have also been observed in the related trimethylene sulfites ($\alpha_e \approx \beta_e \approx 7$, $\alpha_a \approx 6$ to 14, $\beta_a \approx 5$, $\gamma_a \approx -2$ to -4, and $\gamma_e \approx 0.3$ ppm).[4] A few substituent parameters have also been estimated on the basis

Table 2. Substituent effects on ^{13}C chemical shifts of methyl-substituted 2-chloro-, 2-methoxy- and 2-phenoxy-1,3,2-dioxarsenanes determined by least-squares analysis of 30 incremental shifts.

Substituent	Affected carbon	Parameter A_{ik}	Value[a]	
5eq-Me	C(5)	α_e	2.95 ± 0.05	(2.7)
	C(4,6)	β_e	5.54 ± 0.29	(5.8)
5ax-Me[c]	C(5)	α_a	-0.60 ± 0.25[b]	(2.7)
	C(4,6)	β_a	3.66 ± 0.29[b]	(4.5)
4eq-Me	C(4)	α_e	5.85 ± 0.22	(5.6)
	C(5)	β_e	6.56 ± 0.05	(7.2)
	C(6)	γ_e	0.37 ± 0.12	(0.1)
4ax-Me[c]	C(4)	α_a	7.81 ± 0.42[b]	(0.4)
	C(5)	β_a	3.45 ± 0.40[b]	(3.5)
	C(6)	γ_a	-4.02 ± 0.39[b]	(-5.1)

[a] In ppm $\pm$ probable error. For comparison the corresponding values for 1,3-dioxanes are given in parentheses. [b] These values include possible contributions from geminal dimethyl substitution. [c] Substituent effects for 6-methyl groups are obtained by interchanging position numbers 4 and 6.

of the reported ^{13}C NMR data for 2-methoxy-5-methyl-1,3,2-dioxaphosphorinanes[7] viz., $\alpha_a \approx 2.8$, $\alpha_e \approx 3.4$, $\beta_a \approx 5.1$, and $\beta_e \approx 5.6$ ppm.

The general trend in the substituent effect of methyl groups in these four related heterocyclic systems is that α and β carbons are strongly deshielded whereas γ carbons in *gauche* positions are shielded. The main difference between these systems is found in the large variation of the α_a effect from a negligible contribution in 1,3-dioxanes[2] to a 14 ppm downfield shift in *trans*-4,6-dimethyltrimethylene sulfite.[4] In the arsenites, phosphites and sulfites (axial S=O) there will be strong non-bonded interactions between the axial 2-substituent and the *syn*-axial methyl group at C(4,6). This interaction which might vary considerably from one system to another, would be expected to have a strong influence on the α_a effect by affecting the shielding at C(4,6). The significantly smaller α effect at C(5) as compared with C(4,6) may be a reflection of the much less hindered environment of the former carbon. In contrast, the β effect is seen to be roughly independent of the point of substitution.

The observed long-range shift effect of methyl groups on the γ carbon in the dioxarsenanes and the corresponding dioxanes, sulfites and phosphites is in accord with the well-documented sterically induced γ-effect.[9,10,17] In rigid, cyclic systems of the present type, the effect is roughly zero for a *trans* arrangement (equatorial Me) and maximal when the substituent and the γ carbon are in a *gauche* position (axial Me).

On introducing a *gem*-diethyl group at C(5) the α and β carbon signals are shifted downfield and upfield by about 5 and 2 ppm, respectively, with respect to the corresponding 5,5-dimethyl derivatives. A similar trend is also seen in the substituent effect of 5-*tert*-butyl in comparison with methyl, in 1,3,2-dioxarsenanes,[12] 1,3,2-dioxaphosphorinanes[6,7] and trimethylene sulfite.[4]

Replacement of hydrogen at C(4) or C(5) by an equatorial phenyl group in dioxarsenanes and the analogous sulfites,[5] produces significant downfield shifts of the ring carbons. The downfield shift which is believed to be caused by the ring current effect

Table 3. Observed and predicted chemical shifts (in ppm from TMS) for the set of compounds used in the least-squares analysis.[a]

Substituents		C(4,6)[b] Obs.	Pred.	C(5) Obs.	Pred.
2-Cl		62.85		30.32	
2-OMe		61.30		31.19	
2-OPh		62.02		30.65	
2-Cl		69.07	68.70	36.84	36.88
		63.28	63.22		
2-OMe	4eq-Me	67.01	67.15	37.73	37.75
		61.81	61.67		
2-OPh		67.64	67.86	37.29	37.21
		62.18	62.38		
2-Cl		65.85	65.05	46.20	46.90
		77.58	76.90		
2-OMe	4eq-6,6-triMe	62.94	63.50	48.01	47.77
		74.59	75.35		
2-OPh		64.00	64.21	47.69	47.23
		76.08	76.06		
2-Cl		68.16	68.39	33.21	33.27
2-OMe	5eq-Me	67.33	66.84	34.22	34.14
2-OPh		67.29	67.55	33.58	33.60
2-Cl		71.99	72.05	32.94	32.67
2-OMe	5,5-diMe	70.63	70.50	33.27	33.54
2-OPh		71.15	71.21	33.01	33.00

[a] The experimental data are taken from the present work and Ref. 12. [b] In cases where two shifts are reported the upper refers to C(4) and the lower to C(6).

of the phenyl group, is largest at the α carbon and decreases rapidly with the distance from the point of substitution.

The ^{13}C nucleus of a single equatorial methyl group at C(4,6) and C(5) resonates near 24 and 13.5 ppm, respectively, regardless of the substituent at arsenic. However, on *gem*-dimethyl substitution the axial methyl group produces a significant downfield shift of the resonance of its equatorial counterpart (*ca.* 4 − 8 ppm).

In the 4- and 6-methyl substituted 1,3,2-dioxarsenanes,[12-14] trimethylene sulfites[4,5,18] and 1,3,2-dioxaphosphorinanes[7,19] the relative ^{1}H and ^{13}C chemical shifts of the methyl groups are the same, that is, the axial signal appears downfield to the equatorial one. This observation suggests that local anisotropy contributions which are independent of the nature of the observed nucleus, contribute to the ^{1}H and ^{13}C shieldings. However, a deshielding δ *syn*-axial effect[4,7,20] induced by the axial substituent at arsenic is probably responsible for the much larger difference between axial and equatorial ^{13}C methyl shifts.

Similarly, the ^{1}H and ^{13}C signals of an axial methyl or *tert*-butyl group at C(5) appear at lower field than their equatorial counterparts in appropriately substituted arsenites,[12-14] phosphites,[7,19] sulfites[4,21] and dioxanes.[3,22] This chemical shift order is the reverse of what is observed in methyl cyclohexanes[10] where an upfield γ effect is operating. However, in the four series of heterocyclic compounds the axial 5-methyl group has no *syn*-axial hydrogen atoms with which to interact but rather appears to be deshielded by the 1,3 ring oxygen atoms.

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