

# NMR Studies on Cyclic Arsenites. Spectral Analyses of the High-resolution Proton-coupled Carbon-13 NMR Spectra of Five 1,3,2-Dioxarsenanes

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The high-resolution proton-coupled  $^{13}\text{C}$  NMR spectra of five six-membered arsenites have been obtained and completely analyzed. The analysis of these spectra has provided all the  $^{13}\text{C}$ – $^1\text{H}$  coupling constants including their relative signs. Our results clearly demonstrate that the  $^{13}\text{C}$ – $^1\text{H}$  coupling constants are very sensitive to stereochemical effects. Since the observed one-bond coupling constants vary with the axial-equatorial orientation of the C–H bond (with a significantly larger coupling to the equatorial proton) it can be used as a conformational probe.

The observed variation in the geminal  $^{13}\text{C}$ – $^1\text{H}$  coupling constants reflects a stereospecific inductive effect of the oxygen heteroatoms.

The measured vicinal  $^{13}\text{C}$ – $^1\text{H}$  coupling constants are considerably larger than all the geminal ones. It has also been found that the vicinal *trans*-coupling is significantly larger than the corresponding *gauche*-coupling.

The 4-methyl substituent produces an increase of about 1–2 Hz in the one-bond couplings at carbons 4 and 6. A positive contribution of 1–1.3 Hz is observed for the geminal couplings involving the axial  $\text{H}_{4a}$  and  $\text{H}_{5a}$  protons and carbons 5 and 4, respectively.

In recent years increasing attention has been paid to studies of  $^{13}\text{C}$ – $^1\text{H}$  coupling constants.<sup>1</sup> Previous studies have, however, largely concentrated on one-bond  $^1J_{\text{C-H}}$  couplings since these are the most easily available from natural abundance  $^{13}\text{C}$  NMR spectra or  $^{13}\text{C}$  satellites in proton spectra. The geminal and vicinal  $^2J_{\text{C-H}}$  and  $^3J_{\text{C-H}}$  couplings are generally small and usually obtainable only after analysis of complex second-order  $^{13}\text{C}$  spectra. These coupling constants have, therefore, in spite

of their potential usefulness, received rather limited attention in the past.<sup>1</sup> In particular, the data on  $^{13}\text{C}$ – $^1\text{H}$  coupling constants in saturated ring systems are scarce due to the complexity of their proton-coupled  $^{13}\text{C}$  NMR spectra.

This paper reports experimental values of the  $^{13}\text{C}$ – $^1\text{H}$  coupling constants in four 2-substituted 1,3,2-dioxarsenanes and one 4-methyl substituted derivative. The latter compound was included in order to study the effect of a methyl substituent on the  $^{13}\text{C}$ – $^1\text{H}$  coupling constants. The present data constitute a very useful and complementary extension to our previous  $^1\text{H}$  NMR investigations.<sup>2</sup>

## RESULTS AND DISCUSSION

The proton-coupled  $^{13}\text{C}$  spectra of the  $\text{C}_4$ ,  $\text{C}_5$  and  $\text{C}_6$  ring carbons were analyzed as AA'BB'CDX and ABC<sub>3</sub>KLMX (X= $^{13}\text{C}$ ) spin systems. The proton chemical shifts and coupling constants, except for compound I, were taken from two previous papers.<sup>2</sup> The  $^1\text{H}$  NMR spectrum of I in benzene-*d*<sub>6</sub> solution (20 % v/v) was rerun at 90.02 MHz. However, due to rapid exchange of the nuclear magnetic environments of the axial and equatorial methylene protons<sup>2</sup> only averaged spectral parameters were observed. The calculated  $^{13}\text{C}$  spectra were not particularly sensitive to small changes in these parameters. This is reasonable since the  $^{13}\text{C}$  spectra are nearly first-order with almost identical low- and highfield spectral patterns. It was thus possible to obtain good trial values for the  $^{13}\text{C}$ – $^1\text{H}$  coupling constants from first-order analysis. The assignment of these coupling constants

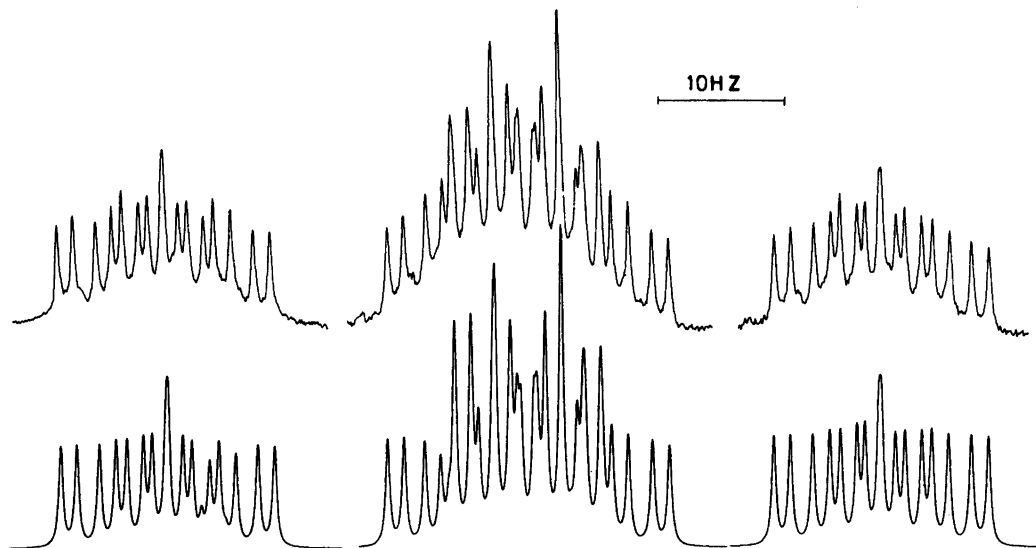


Fig. 1. Experimental (upper) and calculated (lower) 22.63 MHz proton-coupled  $^{13}\text{C}$  NMR spectrum of the three multiplets of carbon 4 (6) in 2-methoxy-1,3,2-dioxarsenane (increasing field from left to right).

does not, however, follow from the direct analysis. However, since the calculated spectra were very sensitive to a particular choice of assignment a unique solution was readily obtained. Furthermore, the relative signs of the  $^{13}\text{C}-^1\text{H}$  coupling constants were determined by using several sets of starting parameters with different likely sign combinations, and observing changes in intensities. The obtained relative signs are in agreement with literature data on saturated systems.<sup>1</sup>

The final parameters, number of assigned lines and RMS errors resulting from the computer analysis, are summarized in Tables 1–3. Good fits between the observed and calculated  $^{13}\text{C}$  spectra were obtained as demonstrated in Figs. 1 and 2 for carbon 4 in 2-methoxy-1,3,2-dioxarsenane and 2-chloro-4-methyl-1,3,2-dioxarsenane, respectively.

Our results clearly demonstrate that the  $^{13}\text{C}-^1\text{H}$  coupling constants are very sensitive to stereochemical effects. Another important factor affecting the magnitude of these coupling constants is substituent electronegativity. Generally, there is little effect on  $^1J_{\text{C-H}}$  of electronegative  $\beta$ -substituents but an appreciable positive contribution from directly bonded electronegative oxygen or nitrogen atoms.<sup>1</sup> In the present compounds the  $\alpha$ -effect of the ring oxygen atoms produces an increase of about 20 Hz in  $^1J_{\text{C-H}}$ .

It is interesting to note that  $^1J_{\text{C-H}}$  always has a significantly higher value for the equatorial C–H bond than for the axial C–H bond. Similar observations have also been made for cyclohexanones<sup>3</sup> and cyclohexane (at  $-104^\circ\text{C}$ ).<sup>4</sup> The  $^1J_{\text{C-H}}$  (equatorial)  $>$   $^1J_{\text{C-H}}$  (axial) inequality has also been found to hold in 2-amino-sugars<sup>1,5</sup> and for half-chair conformations of unsaturated pyranose derivatives,<sup>6</sup> and has been used for determining anomeric configuration in polysaccharides.<sup>7</sup> Since the direct coupling constant is a function of the axial–

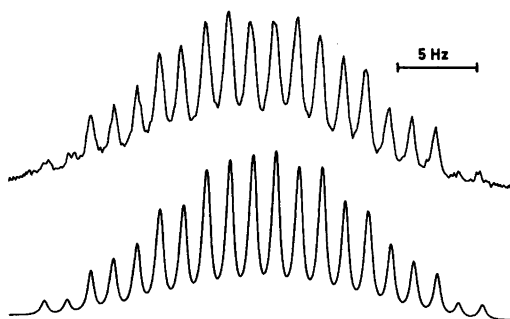
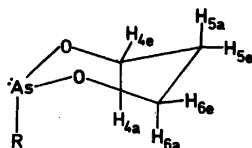


Fig. 2. Experimental (upper) and calculated (lower) 22.63 MHz proton-coupled  $^{13}\text{C}$  NMR spectrum of the downfield multiplet of carbon 4 in 2-chloro-4-methyl-1,3,2-dioxarsenane.

Table 1. One-bond and geminal <sup>13</sup>C–<sup>1</sup>H coupling constants<sup>a</sup> and chemical shifts<sup>b</sup> of carbon 5 in four 1,3,2-dioxarsenanes.



Compound	R	$\delta$	$^1J_{C_5-H_{5a}}$	$^1J_{C_5-H_{5e}}$	$^2J_{C_5-H_{4a}}$	$^2J_{C_5-H_{4e}}$	Assigned transitions	RMS error
I <sup>c</sup>	Cl	30.45	127.53		-2.26		64	0.050
II	OMe	31.31	124.04	128.97	-1.80	-2.79	64	0.038
III	OPh	30.83	125.26	128.78	-1.84	-2.74	39	0.052
IV	Ph	32.10	124.30	128.59	-1.59	-2.67	63	0.071

<sup>a</sup> In Hz. <sup>b</sup> In  $\delta$ -values relative to internal C<sub>6</sub>D<sub>6</sub> at 128.00 ppm. <sup>c</sup> The observed spectral parameters are the result of rapid exchange of chlorine. The following averaged proton parameters were used:  $\delta_{4a} = \delta_{4e} = 4.724$  ppm,  $\delta_{5a} = \delta_{5e} = 2.053$  ppm,  $J_{4a(4e)5a(5e)} = 5.180$  Hz, and  $J_{4a(4e)6a(6e)} = 0.090$  Hz.

Table 2. One-bond, geminal and vicinal <sup>13</sup>C–<sup>1</sup>H coupling constants<sup>a</sup> and chemical shifts<sup>b</sup> of carbon 4 in compounds I–IV.

Compound	$\delta$	$^1J_{C_4-H_{4a}}$	$^1J_{C_4-H_{4e}}$	$^2J_{C_4-H_{5a}}$	$^2J_{C_4-H_{5e}}$	$^3J_{C_4-H_{6a}}$	$^3J_{C_4-H_{6e}}$	Assigned transitions	RMS error
I <sup>c</sup>	63.10	146.98		-3.38		5.14		64	0.039
II	61.45	142.99	148.33	-3.41	-1.33	5.34	7.37	60	0.033
III	62.10	143.82	149.29	-3.34	-1.30	5.39	7.28	61	0.053
IV	63.93	141.09	146.97	-3.74	-1.61	5.09	7.10	64	0.057

<sup>a</sup> In Hz. <sup>b</sup> In  $\delta$ -values relative to internal C<sub>6</sub>D<sub>6</sub> at 128.00 ppm. <sup>c</sup> The observed spectral parameters are the result of rapid exchange of chlorine.

Table 3. <sup>13</sup>C–<sup>1</sup>H coupling constants<sup>a</sup> and chemical shifts<sup>b</sup> of the ring carbons in 2-chloro-4-methyl-1,3,2-dioxarsenane.<sup>c</sup>

Carbon	$\delta_{C_i}$	$^k J_{C_i-H_{4a}}$	$^k J_{C_i-CH_3}$	$^k J_{C_i-H_{5a}}$	$^k J_{C_i-H_{5e}}$	$^k J_{C_i-H_{6a}}$	$^k J_{C_i-H_{6e}}$	Assigned transitions	RMS error
C <sub>4</sub>	69.28	145.28	-2.94	-4.43	-1.41	5.90	7.36	170	0.053
C <sub>5</sub>	37.23	-0.49	4.73	124.44	129.08	-2.03	-2.86	103	0.047
C <sub>6</sub>	63.71	5.61	-0.67	-2.70	-0.87	144.05	150.29	141	0.065

<sup>a</sup> Coupling constants in Hz. <sup>b</sup> In  $\delta$ -values relative to internal C<sub>6</sub>D<sub>6</sub> at 128.00 ppm. <sup>c</sup> The indices i=4, 5, or 6 and k=1, 2, or 3 as appropriate.

equatorial orientation of the C–H bond, it can thus be used as a conformational probe. In this connection it should be pointed out that the axial proton signals in six-membered arsenites appear downfield for the corresponding equatorial proton signals<sup>2</sup> opposite the situation in cyclohexanes.<sup>8,9</sup> Appar-

ently, the stereospecific coupling and chemical shift effects are not correlated.

In aliphatic systems typical values of  $^2J_{C-H}$  range from about -6 to -4 Hz.<sup>1</sup> They increase upon introduction of electronegative substituents and move into the region between -5 and +2 Hz.<sup>1</sup> The

observed geminal  $^{13}\text{C}-^1\text{H}$  coupling constants in the dioxarsenanes fall well within the latter range. The marked variation in the  $^2J_{\text{C}-\text{H}}$  values compared with low-temperature cyclohexane<sup>4</sup> reflects a stereospecific inductive effect of the oxygen heteroatoms. It has been found that the substituent effect depends on the substituent orientation and is maximal when the substituent is in the plane of the  $^{13}\text{C}-\text{C}-^1\text{H}$  coupling path.<sup>10</sup> Inspection of molecular models shows that the  $\text{O}-\text{C}_4-\text{C}_5-\text{H}_{5e}$  segment of the 1,3,2-dioxarsenane ring is roughly *trans*-coplanar. In accordance with this observation  $^2J_{\text{C}_4-\text{H}_{5e}}$  is about 2 Hz more positive than  $^2J_{\text{C}_4-\text{H}_{5a}}$ . A similar stereospecific variation in the geminal  $^{13}\text{C}-^1\text{H}$  coupling constant has been observed in sugar rings. For example, in  $\alpha$ - and  $\beta$ -D-glucose with *cis* and *trans* configuration of the hydroxyl groups at  $\text{C}_1$  and  $\text{C}_2$ , the geminal coupling constants between  $\text{C}_1$  and the equatorial or axial proton at  $\text{C}_2$  are about 1 and 6 Hz, respectively.<sup>11</sup>

The measured  $^3J_{\text{C}-\text{H}}$  coupling constants in the arsenanes are considerably larger than all  $^2J_{\text{C}-\text{H}}$ 's in agreement with the normal situation in aliphatic and aromatic systems.<sup>1</sup> We believe that the assignment of geminal and vicinal  $^{13}\text{C}-^1\text{H}$  coupling constants in some trimethylene sulfites<sup>12</sup> is partly wrong ( $|^2J_{\text{C}-\text{H}}| \approx |^3J_{\text{C}-\text{H}}|$ ). This is not surprising in view of the poor experimental data on which the spectral analyses were based. The  $^3J_{\text{C}-\text{H}}$  coupling constants depend on the dihedral angle in a manner similar to that found for the corresponding  $^1\text{H}-^1\text{H}$  coupling constants.<sup>1,13</sup> It is thus seen that the *trans*-coupling  $^3J_{\text{C}_4-\text{H}_{6e}}$  is significantly larger than the corresponding *gauche*-coupling,  $^3J_{\text{C}_4-\text{H}_{6a}}$  in the present compounds in agreement with similar observations in other six-membered rings of fixed chair conformation.<sup>1,3,4</sup>

On comparing the  $^3J_{\text{C}-\text{H}}$  coupling constants in low-temperature cyclohexane<sup>4</sup> and 1,3,2-dioxarsenanes it is seen that the electron-withdrawing ring oxygen atoms have opposing effects on the two vicinal coupling constants, *i.e.*, the *trans*-coupling decreases whereas the *gauche*-coupling increases. This observation is consistent with theoretical calculations on propanes<sup>13,14</sup> which have shown that electronegative substituents on the coupled carbon ( $\alpha$ -carbon) lead to an increase in the appropriate vicinal coupling constants whereas a similar substitution on the  $\gamma$ -carbon causes a significant decrease in the *trans*-coupling.

The 4-methyl substituent produces an increase of about 1–2 Hz in the one-bond coupling con-

stants at carbons 4 and 6 whereas a positive contribution of 0.7–1 Hz in the geminal coupling constants involving proton  $\text{H}_{5a}$  is observed. The methyl substituent appears to have a negligible influence on the  $^{13}\text{C}-^1\text{H}$  vicinal coupling constants. This is consistent with the observation that methyl substitution at carbons along the coupling path has very little effect on the calculated values of  $^3J_{\text{C}-\text{H}}$ .<sup>13</sup>

The 4-methyl substituent has a small effect (<0.5 Hz) on all  $^{13}\text{C}-^1\text{H}$  coupling constants involving carbon 5 except for an increase of 1.3 Hz in  $^2J_{\text{C}_5-4a}$ .

## EXPERIMENTAL

The syntheses of the cyclic arsenites have been described in previous papers.<sup>2</sup> The five freshly distilled compounds were examined in benzene- $d_6$  (20 % v/v, as deuterium lock) in 10 mm o.d. sample tubes.  $\text{O}_2$  was removed from the solutions by bubbling dry  $\text{N}_2$  gas into the NMR tubes for about 30 s followed by immediate capping and taping of the tubes.

The proton-coupled  $^{13}\text{C}$  NMR spectra were obtained at 22.63 MHz at ambient probe temperature (*ca.* 30 °C) on a Bruker CXP 100 Spectrometer. Gated decoupling with a duty cycle of 6 s, was used to retain the increase in the signal-to-noise produced by the NOE while at the same time giving a fully coupled spectrum. The spectral windows were carefully chosen to avoid that folding obscured the spectral region of interest. About 15000 transients, obtained using an acquisition time of about 10 s, were stored for the ring carbon resonances of each compound. Exponential weighting with a line-broadening factor of 0.02 Hz was applied to the free induction decays.

The  $^{13}\text{C}$  NMR spectra were analyzed by means of the LAOCN3,<sup>15</sup> KOMBIP<sup>16</sup> and UEAITR<sup>17</sup> computer programs. The computations were performed on a Univac 1100/32 computer. The graphical output was obtained using a Calcomp plotter.

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