

# NMR Studies on Cyclic Arsenites. $^1\text{H}$ NMR Spectral Analysis and Conformational Studies of 1,3,2-Diazarsolanes, 1,3,2-Oxazarsolanes and 1,3,2-Dioxarsolanes

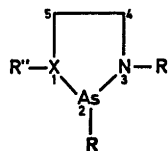
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This paper reports preparation and  $^1\text{H}$  NMR studies of ten arsolanones of which seven have been fully analyzed in terms of chemical shifts and coupling constants. Approximate values of the ring torsional angles have been obtained by means of the  $R$ -value method. The NMR data are adequately explained on the basis of rapidly interconverting twist-envelope conformations which, however, show several features of specific steric interactions and favoured conformations.

$^1\text{H}$  NMR investigations on a series of arsolanones have been reported in preceding papers.<sup>1-3</sup> The NMR data of these five-membered rings were adequately explained on the basis of rapidly interconverting non-planar conformations. Although the precise conformation adopted by a five-membered ring compound is dependent on the number and nature of substituents,<sup>4</sup> we have observed that the steric requirements of the arsolanone ring are as important as those of the substituents. Our previous results<sup>2,3</sup> also demonstrated the tendency of a sulfur atom, as compared to oxygen, to increase the puckering of the ring. Similar observations have also been reported for 1,3,2-dithiaphospholanes,<sup>5</sup> 1,3-dithiolanes,<sup>6,7</sup> and 1,3-oxathiolanes.<sup>8</sup>

Although the  $^1\text{H}$  NMR spectra of a series of 1,3,2-diazaphospholanes<sup>9</sup> and 1,3,2-oxazaphospholanes<sup>10,11</sup> have been analyzed, no NMR analyses of the analogous arsolanones have been



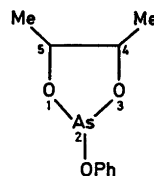
X = N; 1,3,2-diazarsolanes.  
 I; R' = R'' = CH<sub>3</sub>, R = OCH<sub>3</sub>  
 II; R' = R'' = CH<sub>3</sub>, R = OPh

X = O, R'' = lone pair; 1,3,2-oxazarsolanes.  
 III; R' = Ph, R = OCH<sub>3</sub>  
 IV; R' = Ph, R = OPh  
 V; R' = CH<sub>3</sub>, R = OCH<sub>3</sub>

reported. In order to investigate the effect of nitrogen as hetero-atom in arsolanones we have prepared compounds I–V and investigated their  $^1\text{H}$  spectra.

Trigonal inversion about the nitrogen atom and a possible preference of the substituent at nitrogen for either the one or other side of the ring,<sup>12</sup> complicate the conformational assignment of these systems.

The chloro-compounds (see experimental) have also been prepared. However, only exchange-averaged NMR spectra resulting from rapid exchange of chlorine were observed.



VI; *cis* (4,5-dimethyl)  
 VII; *trans* (4,5-dimethyl)

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We have also extended our previous studies on 4,5-dimethyl-1,3,2-dioxarsolanes<sup>1</sup> by analyzing the <sup>1</sup>H NMR spectra of VI and VII.

## EXPERIMENTAL

The general procedure for the preparation of 2-chloro-1,3-dimethyl-1,3,2-diazarsolane, 2-chloro-3-phenyl-1,3,2-oxazarsolane, and 2-chloro-3-methyl-1,3,2-oxazarsolane as starting materials for the syntheses of I–V is given:<sup>13</sup> A solution of *N,N*-dimethyl-ethylenediamine, *N*-phenyl-ethanolamine or *N*-methylaminoethanol in dried diethyl ether was added dropwise, while stirring, to a solution of trichloroarsine and triethylamine in dried diethyl ether. The triethylamine hydrochloride was filtered off and the diethyl ether was removed by rotary evaporation. The oily residue was distilled at reduced pressure in a heated jacket column.

2-Chloro-1,3-dimethyl-1,3,2-diazarsolane, b.p.<sub>0.5</sub> 65 °C, yield 55 %.

2-Chloro-3-phenyl-1,3,2-oxazarsolane, b.p.<sub>0.5</sub> 132 °C, yield 40 %.

2-Chloro-3-methyl-1,3,2-oxazarsolane, b.p.<sub>0.1</sub> 50 °C, yield 45 %.

The 2-methoxy and 2-phenoxy compounds were prepared from the appropriate chloro-compounds and methanol or phenol, respectively, in diethyl ether using triethylamine as base. The yield varied and was at most 40 %. The boiling points (°C) at 0.1 mmHg pressure of compounds I through VII are as follows: 37, 97, 105, 154, 27, 48–50, and 48–50, respectively.

The <sup>1</sup>H NMR spectra were examined in benzene, deuteriochloroform, and deuteriochloroform/benzene solutions (ca. 50 % v/v). A small amount of TMS was added to the samples and used as internal standard and lock signal source. The 100 MHz spectra were run at ambient probe temperature (ca. 30 °C) on a VARIAN HA-100 spectrometer. Line positions were obtained by averaging the results of two frequency-calibrated spectra recorded at 100 Hz sweep width (2 Hz/cm).

The <sup>1</sup>H NMR spectra were analyzed by means of the computer programs LAOCN3,<sup>14</sup> UEAITR,<sup>15</sup> and KOMBIP.<sup>16</sup> The computations were performed on a UNIVAC 1110 computer. The graphical output was obtained using a Calcomp Plotter.

## SPECTRAL ANALYSIS

The largest chemical shift difference between geminal methylene protons in compounds I and II was achieved by using benzene as solvent. The <sup>1</sup>H NMR spectra for the CH<sub>2</sub>–CH<sub>2</sub> fragment in I and II show a close resemblance and are symmetrical about their mid-points. The detailed spectral analyses were carried out

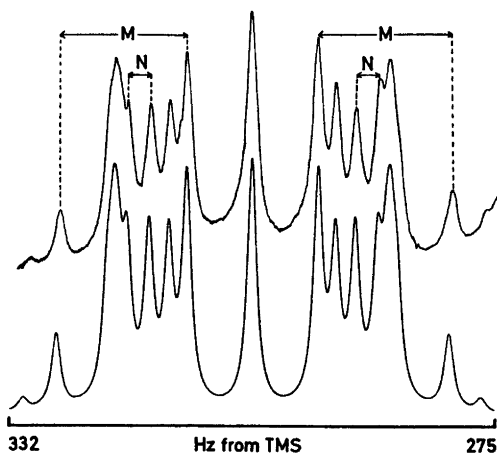


Fig. 1. Experimental (upper trace) and calculated (lower trace) 100 MHz spectrum of the methylene protons in compound I.  $N = J_{AB} + J_{AB'}$  and  $M = J_{AB} - J_{AB'}$  are directly obtainable from the spectrum when  $J_{AA'} = J_{BB'}$ .

successfully on the basis of an AA'BB' spin system. The spectrum is most conveniently characterized by linear combinations  $K$ ,  $L$ ,  $M$ , and  $N$  of the four coupling constants.<sup>17</sup> Explicit equations may be given for twelve lines in AA'BB' spectra.<sup>17</sup> If these lines can be recognized  $|v_A - v_B|$ ,  $|L|$ ,  $|M|$ , and  $|N|$  are directly obtainable from the spectrum. We approached the problem using a mixture of computations and direct assignment. We estimated values of the coupling constants from the literature and assumed that  $L = J_{AA'}$

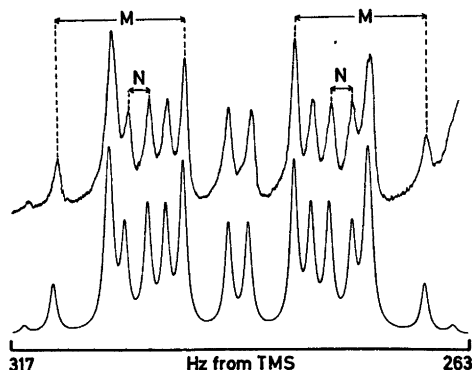


Fig. 2. Experimental (upper trace) and calculated (lower trace) 100 MHz spectrum of the methylene protons in compound II.  $N$  and  $M$  are defined in Fig. 1.

Table 1. 100 MHz NMR parameters (in Hz) and ring torsional angles of compounds I–VII.<sup>a</sup>

Compound Solvent	I C <sub>6</sub> H <sub>6</sub>	II	III C <sub>6</sub> H <sub>6</sub> /CDCl <sub>3</sub> , 1:1	IV	V	VI CDCl <sub>3</sub>	VII
$\nu_A$	316.93	301.49	310.22	282.93	318.56	453.97	389.94
$\nu_B$	290.30	277.66	298.95	280.16	291.64		390.93
$\nu_K$			417.18	400.71	448.59	113.86	128.76
$\nu_L$			406.44	393.55	417.73		128.91
$J_{AA'}$	6.00	6.29				5.29	
$J_{BB'}$	5.91	6.21					
$J_{AB}$	-8.94	-8.97	-9.27	-9.26	-8.72		8.81
$J_{AB'}$	6.35	6.29					
$J_{AK}$			6.46	6.57	6.17	6.31	5.98
$J_{AK'}$						-0.19	
$J_{AL}$			2.91	3.07	4.89		-0.17
$J_{BK}$			5.77	6.23	6.10		-0.19
$J_{BL}$			9.62	9.53	7.65		5.97
$J_{KL}$			-9.24	-9.67	-8.88		
Assigned transitions	15	21	28	20	32	151	122
RMS error	0.098	0.096	0.053	0.078	0.061	0.068	0.044
R-value	1.07	1.01	1.85	1.73	1.26		
$\psi$ (deg.)	47	45	55	54	49		

<sup>a</sup> Chemical shifts downfield from TMS. K and L represent the O-CH<sub>2</sub> or CH<sub>2</sub> protons, as appropriate.

- $J_{BB'}$ =0 thereby reducing the number of explicit lines to eight (with degeneracy). We were able to pick out these eight lines after some trial and error analyses, thus providing good values of  $|M|$  and  $|N|$  directly from the spectrum as shown in Figs. 1 and 2. Once  $|N|$  is known  $|\nu_A - \nu_B|$  is obtained indirectly from the two  $N$ -"doublets". Computations with variation of  $K$  then enabled a complete assignment to be made. Computer iteration gave the refined parameters listed in Table 1. Good fits between the observed and calculated spectra were obtained as demonstrated in Figs. 1 and 2.

The <sup>1</sup>H NMR spectra of compounds III–V were broad and showed little fine structure when pure benzene or deuteriochloroform were used as solvents. A considerable improvement in the resolution was achieved, however, by using a 1:1 mixture of benzene and deuteriochloroform as solvent.

The methylene protons of compounds III–V give rise to NMR spectra of the ABKL type owing to the relatively large chemical shift differences between the two signal groups. Since the AB region of the spectrum is almost a mirror image of the KL region (Figs. 3 and 4) it follows that  $J_{AB} \approx J_{KL}$ .

The ABKL spin system can be partially broken down into two ab sub-spectra and two kl sub-spectra.<sup>18</sup> These sub-spectra are characterized by the coupling constants of the full system, that is,  $J_{AB}$  and  $J_{KL}$ , but by effective chemical shifts:

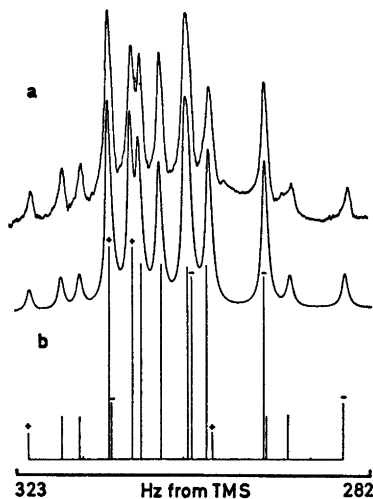


Fig. 3. Experimental (a) and calculated (b) 100 MHz spectrum of the O-CH<sub>2</sub> protons (KL region) in compound III. The two kl sub-spectra are indicated in the stick-plot.

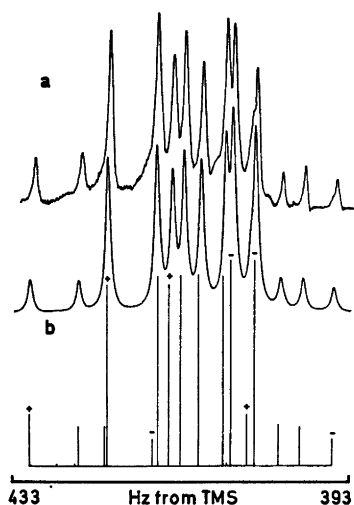


Fig. 4. Experimental (a) and calculated (b) 100 MHz spectrum of the N-CH<sub>3</sub> protons (AB region) in compound III. The two ab sub-spectra are indicated in the stick-plot.

$$\nu_{a\pm} = \nu_A \pm \frac{1}{2}(J_{AK} + J_{AL})$$

$$\nu_{b\pm} = \nu_B \pm \frac{1}{2}(J_{BK} + J_{BL})$$

$$\nu_{k\pm} = \nu_K \pm \frac{1}{2}(J_{AK} + J_{BK})$$

$$\nu_{l\pm} = \nu_L \pm \frac{1}{2}(J_{AL} + J_{BL})$$

The extreme lines in the AB and KL spectra must originate from the ab and kl sub-spectra since the weak coupling constants have the same sign (Figs. 3 and 4). Furthermore, since  $J_{AB} \approx J_{KL} \approx -9$  Hz two more lines originating from the ab and kl sub-spectra are readily picked out. By manipulating these lines acceptable trial values of the parameters were obtained. A fresh computation then allowed the remaining lines to be assigned. The final computer iteration gave the refined parameters for the 1,3,2-oxazarsolanes listed in Table 1. Figs. 3 and 4 show excellent fit between the experimental and calculated spectra of III.

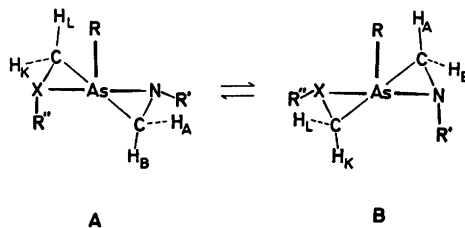
The NMR signals originating from the CHCH<sub>3</sub>-CHCH<sub>3</sub> protons in compounds VI and VII were analyzed on the basis of AA'K<sub>3</sub>K<sub>3</sub>' and ABK<sub>3</sub>L<sub>3</sub> spin systems, respectively. When  $J_{KK'} = 0$  all the spectral parameters of the AA'K<sub>3</sub>K<sub>3</sub>' system may be obtained directly from the experimental spectrum with the limitation that  $|J_{AK} + J_{AK'}|$  is found instead of the two individual coupling constants.<sup>19</sup> Reasonable trial parameter of the *trans* molecule (VII)

were obtained directly from the experimental spectrum or by comparison with related systems.<sup>1</sup> The refined parameters of VI and VII obtained from the iterative computer analysis are listed in Table 1.

## DISCUSSION

It may be confidently concluded, on the basis of the coupling constants, that the molecular conformations of I and II are very similar. The 2-substituted 1,3-dimethyl-1,3,2-diazarsolanes may, in principle, exist in *trans* and *cis* forms with respect to the *N,N*-dimethyl groups. The *trans* form is unique whereas the *cis* form may exist as *anti* and *syn* conformers. All these forms are, however, readily interconverted by inversion at nitrogen. Inspection of molecular models suggests, however, that the *anti* form predominates strongly over the *syn* form.

The type of spin system observed for I and II implies that the heterocyclic ring is planar or, more likely, undergoes rapid interconversions between equivalent nonplanar forms, like A and B below with X=N, at rates that are large on the NMR time scale. At any rate, only the *cis* form can explain the observed symmetrical spin system. The NMR data for I and II are thus consistent with a strong predominance of the *anti* form possessing *cis* *N,N*-dimethyl groups. Moreover, the similarity of the *cis* and *trans* vicinal coupling constants together with the steric requirements of the heterocyclic ring (*cf.* rabbit-ear effect<sup>13</sup>), suggest firmly that the ring is non-planar. It follows that the NMR results are adequately explained only in terms of rapidly interconverting twist-envelope conformations, A and B, possessing one pseudo-axial and one pseudo-equatorial *N*-methyl group. This conclusion is supported by earlier results on analogous systems.<sup>1-3,5,20</sup> Furthermore, the preferred conformation of the related 2-alkyl-*N,N*-dimethyl-1,3-diazanes con-



A

B

tains one axial and one equatorial *N*-methyl group.<sup>12</sup>

Our NMR data for compounds III–V can also be satisfactorily explained on the basis of the A and B pseudo-rotamers above. However, comparable contributions of the A and B pseudo-rotamers would result in similar values of  $J_{AK}$  and  $J_{BL}$ , contrary to experiment. The large value of  $J_{BL}$  in III and IV indicates a strong predominance of one particular conformation. Dreiding stereomodels readily showed that the A pseudo-rotamer possessing a pseudo-equatorial phenyl group at nitrogen, is the most probable conformation. However, replacement of the bulky phenyl substituent at nitrogen by a methyl group reduces significantly the diaxial interactions between the pseudo-axial hydrogen at carbon 5 and the pseudo-axial substituent at nitrogen. In accordance with this observation the reduced difference between  $J_{AK}$  and  $J_{BL}$  indicates that the A and B pseudo-rotamers are more equally populated.

It can be anticipated from Dreiding stereomodels and the Karplus relationship,<sup>21</sup> that the largest vicinal coupling constant in compounds III–V involves the pseudo-axial protons of the predominating conformation (A). From this assumption it follows that the resonance signals of the pseudo-axial protons appear at higher field than the geminal pseudo-equatorial protons in agreement with previous results on 1,3,2-oxathiarsolan<sup>2</sup> and 1,3-oxathiolanes.<sup>22</sup>

The chemical shift assignments of I and II, made by analogy with the 1,3,2-oxazarsolan<sup>2</sup>, are consistent with the reported downfield shifts of protons *cis* rather than *trans*, to a pseudo-axial substituent at arsenic or phosphorus in arsolan<sup>1–3</sup> and phospholan<sup>20,23</sup>. The validity of this rule has been disputed, however.<sup>5,23</sup> At any rate, the reverse assignment of *cis* and *trans* O–CH<sub>2</sub> protons in 1,3,2-oxazarsolan<sup>2</sup> and 1,3,2-oxathiarsolan<sup>2</sup> has been made.

It is seen that replacement of the *N*-methyl group by phenyl produces a substantial decrease in the internal shift difference  $|\nu_A - \nu_B|$  on the adjacent methylene protons. The reduced shift is presumably caused by a combination of conformational effects and the anisotropy of the equatorial *N*-phenyl group.

Geminal coupling constants in CH<sub>2</sub> groups  $\alpha$  to a nitrogen atom cover a wider range of

values, even in apparently closely related structures, than in any other type of CH<sub>2</sub> groups.<sup>24</sup> On this basis the magnitude of the geminal coupling constants of the N–CH<sub>2</sub> moiety in I–V is remarkably similar and close to the values reported for the analogous 1,3,2-diazaphospholan<sup>9</sup> and 1,3,2-oxazaphospholan<sup>10,11</sup>. The geminal coupling constants of the O–CH<sub>2</sub> protons are within the expected range.<sup>24</sup>

The two *cis* coupling constants,  $J_{AA'}$  and  $J_{BB'}$  in I and II are virtually identical in accordance with the situation in 1,3,2-dithiarsolan<sup>2</sup>, 1,3,2-dioxaphospholan<sup>23,25</sup> and ethylene sulfite.<sup>23</sup> However, the two *cis* coupling constants differ considerably in some 1,3,2-diazaphospholan<sup>9</sup> and 1,3,2-dithiaphospholan<sup>5</sup>.

The near-equality of the *cis* and *trans* coupling constants in I and II is in contrast to the reported situation in the analogous diazaphospholan<sup>9</sup> and dioxaphospholan<sup>23,25</sup> ( $J_{trans} < J_{cis}$ ) as well as in dithiarsolan<sup>2</sup> and dithiaphospholan<sup>5</sup> ( $J_{trans} > J_{cis}$ ). The large variation in the vicinal coupling constant reflects changes in the X–C–C–X torsional angle (X=O, N, S) in these five-membered rings.

The X–C–C–N torsional angle,  $\psi$ , has been calculated from the vicinal coupling constants of the CH<sub>2</sub>–CH<sub>2</sub> moiety using the *R*-value method due to Buys and Lambert<sup>26</sup> (Table 1). It should be emphasized, however, that the obtained torsional angles characterize only the mean geometry of the heterocyclic ring. Similar calculations based on the reported coupling constants for 1,3,2-diazaphospholan<sup>9</sup> and 1,3,2-oxazaphospholan<sup>10</sup> give torsional angles in the ranges 37–43° and 41–43°, respectively. This indicates that the diazarsolan<sup>2</sup> and oxazarsolan<sup>2</sup> rings are more puckered than their phosphorus counterparts. It also seems that the steric requirements of the *N*-phenyl substituent, as compared to an *N*-methyl group, increase the puckering of the oxazarsolan<sup>2</sup> ring by about 5°.

The vicinal coupling constants found in the *cis* and *trans* isomers of 2-phenoxy-4,5-dimethyl-1,3,2-dioxarsolan<sup>2</sup>, VI and VII, respectively, are fairly close to the corresponding parameters in 2-chloro- and 2-phenyl-4,5-dimethyl-1,3,2-dioxarsolan<sup>1</sup>. This observation

indicates that the conformations of corresponding isomers are similar and little affected by the substituent at arsenic.

The large value of  $J_{AB}$  in the *trans* form indicates that this coupling constant mainly involves the pseudo-axial protons, that is, the conformation possessing pseudo-equatorial methyl groups predominates. This conclusion is also reasonable on steric grounds since the 2-phenoxy substituent probably occupies a pseudo-axial position.

The steric requirements of the methyl groups are certainly more important in the *cis* molecule and are expected to produce a highly puckered conformation. The resulting enlarged H-C-C-H angle should produce a fairly small vicinal coupling constant<sup>21,26</sup> contrary to experiment. It seems that a compensating reduction in the electronegativity effect of the adjacent oxygen atoms is operating. This is reasonable since the magnitude of the electronegativity effect depends on the dihedral angle, and empirically it is found that the effect is greatest when the electronegative group (atom) is *trans* to one of the coupled protons.<sup>27</sup>

In accordance with previous assignments, we believe that the methine and methyl signals at lower and higher field arise from protons *cis* and *trans* to the pseudoaxial phenoxy group at arsenic.

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