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1-METHYLARSENANE

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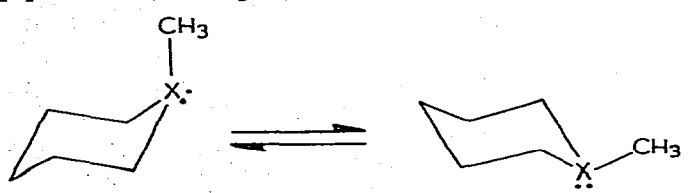
Summary

The barrier (E_a) to ring reversal in 1-methylarsenane is 7.8 kcal mol^{-1} (log A = 14.1). At the coalescence temperature (—128°C), the free energy of activation is 6.8 kcal mol^{-1}. The axial and equatorial conformations have essentially equal populations at —140°C. Identical R values of 2.7 for the α,β and the β,γ portions of the ring indicate a small but uniform puckering with respect to the shape of the cyclohexane chair.

Introduction

The conformational preference of a substituent on a six-membered ring is determined by the steric and polar properties of the system. When the substituent is a nonpolar group such as methyl, it is usually assumed that only steric considerations are necessary. Thus the large preference of methyl for the equatorial position in cyclohexane is attributed to unfavorable steric interactions of the axial substituent with the ring atoms. We have been engaged in a study of the effect of ring heteroatoms on conformational properties [1]. The ideal method for determination of the free energy difference between conformations is to observe and integrate separate nuclear magnetic resonances below the temperature of coalescence for ring reversal. Because of rapid inversion of nitrogen in an extremely biased equilibrium, this method has not been applied to 1-methylpiperidine (I in eq. 1). As a result, indirect methods have had to be used. Dipole



(1)

(I) X = N
(II) X = P
(III) X = As

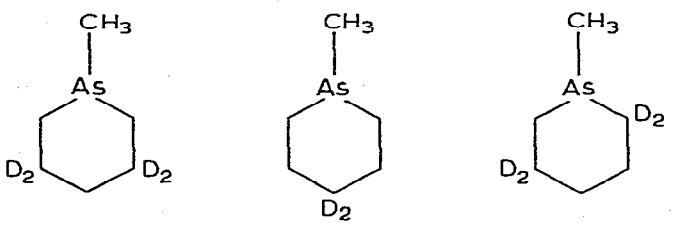
moment studies [2] that gave a relatively small free energy difference for the methyl group (0.6 kcal mol^{-1}) have been superceded by ^{13}C NMR methods [3] that indicate an equatorial preference of at least 1.35 kcal mol^{-1}.

The repulsive interactions that destabilize the axial conformation in 1-methylpiperidine (I) should be reduced in its phosphorus analogue, 1-methylphosphorinane (II). Quin and Featherman [4] were able to observe separate resonances for the axial and equatorial conformers, because inversion about phosphorus is slow on the NMR time scale. These authors found a preference of only 0.12 kcal mol^{-1} for the equatorial position at −110°C, corresponding to an equatorial : axial ratio of about 2 : 1. The considerable decrease in the equatorial preference in phosphorinane, compared to that in piperidine, is most likely due to the reduced steric interactions that result from the longer C—P bond lengths.

The next member in the Group V series, 1-methylarsenane (III), offers bond lengths that are still longer. The question arises as to whether the equatorial preference continues to decrease, so that the axial conformation ultimately becomes favored. The present study involves a complete conformational examination of the 1-methylarsenane system. In addition to the question of the conformational preference of the methyl group, we examine the barrier to ring reversal, the shape of the ring, and conformational effects on the proton chemical shifts.

Results

Three different deuterated modifications of 1-methylarsenane have been synthesized in order to carry out the various NMR analyses (IIIa—c). The β-deuterated form (IIIa) is used for the low temperature kinetic studies. β-Deute-

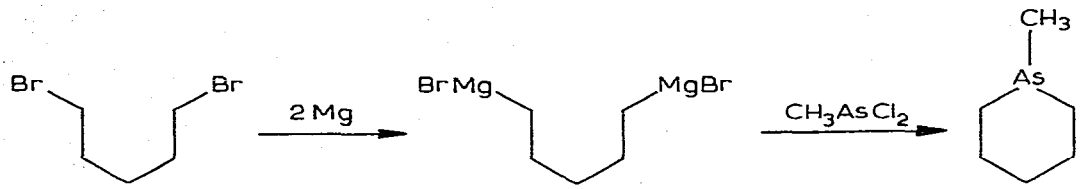


(IIIa) (IIIb) (IIIc)

ration isolates the α and γ spin systems and brings about an appreciable simplification of the spectrum by elimination of coupling to the β protons. The γ-deuterated (IIIb) and α,β′-deuterated (IIIc) forms are used for derivation of the vicinal proton—proton coupling constants. The four-spin system of the α and β protons can be analyzed from IIIb, and the four-spin system of the β and γ protons can be analyzed from IIIc. The geometry of the entire ring can then be determined from these vicinal coupling constants.

Each of the deuterated modifications (IIIa—c) was prepared from the correspondingly labeled 1,5-dibromopentane according to eq. 2 [5]. The labeled dibromopentanes have been prepared previously [6]. Useful modifications to these preparations have been described more recently [7]. Methyldichloroarsine was prepared by the method of Banks et al. [8].

1-Methylarsenane-3,3,5,5-d_4 (IIIa) was examined at low temperature in a 5%(v/v) solution of $CBrF_3$ (Freon 13B1) containing 5%(v/v) CHF_2Cl (Freon 22)



for an internal lock. Spectra were recorded at 270 MHz in order to obtain sufficient spectral separations. Fig. 1 illustrates the proton NMR spectrum as a function of temperature (the observed spectra are on the left). At the stage of fast ring reversal (top spectrum), the spectrum contains six peaks: a singlet for the methyl group at high field, a singlet for the γ protons, and an *AB* quartet for the α protons. The α protons are diastereotopic even under conditions of rapid ring reversal because slow inversion about arsenic maintains the configuration at the 1-position at all temperatures. The accidental coincidence of the γ resonances is explained below. Coalescence is reached at about —128° C, and the slow exchange spectrum is achieved at —144° C (bottom spectrum). The methyl resonance is clearly split into a doublet, corresponding to resonances from the axial-methyl and equatorial-methyl conformations. The less intense peak has a larger linewidth. The α protons give two *AB* spectra, one for each conformer, for a total of 8 peaks. The analogous 8 peaks from the γ protons overlap with the α resonances, so that only 12 of the 16 possible peaks are resolved. The only set of parameters that fitted both the fast and the slow exchange spectra are given in Table 1.

Above —100° C, the protons with a common subscript (a or b in Table 1) are averaged to give the fast exchange spectrum. In each case the low field resonance (presumably the equatorial) of conformer A averages with the high field resonance (presumably the axial) of conformer B. This cross-over averaging leads to an accidental collapse of the γ resonances to a singlet at the fast exchange limit, since $\Delta\nu = 0.46$ ppm for both conformers. The equality of J, $\Delta\nu$, and the population renders it impossible to assign specific *AB* quartets to isomers for the γ protons. The α protons offer a more favorable case. The conformer labeled A in Table 1 clearly has a larger $\Delta\nu$ (0.58 ppm) than does conformer B (0.10 ppm). The larger value of $\Delta\nu$ has been found to be characteristic of the equatorial isomer (axial lone pair) in piperidines and thiane oxides or imides [1,6]. Furthermore, conformer A has the smaller J (—13 Hz) that is also characteristic of the equatorial form [1]. Although the assignment is by no

TABLE 1

CHEMICAL SHIFTS AND GEMINAL COUPLING CONSTANTS FOR 1-METHYLARSENANE

α Protons			γ Protons	
	Conformer A	Conformer B	Conformer A (or B)	Conformer B (or A)
δ_a (ppm)	1.14	1.48	1.38	1.67
δ_b (ppm)	1.72	1.38	1.84	1.21
$\Delta\nu$ (ppm)	0.58	0.10	0.46	0.46
J (Hz)	—13.0	—14.0	—12.0	—12.0

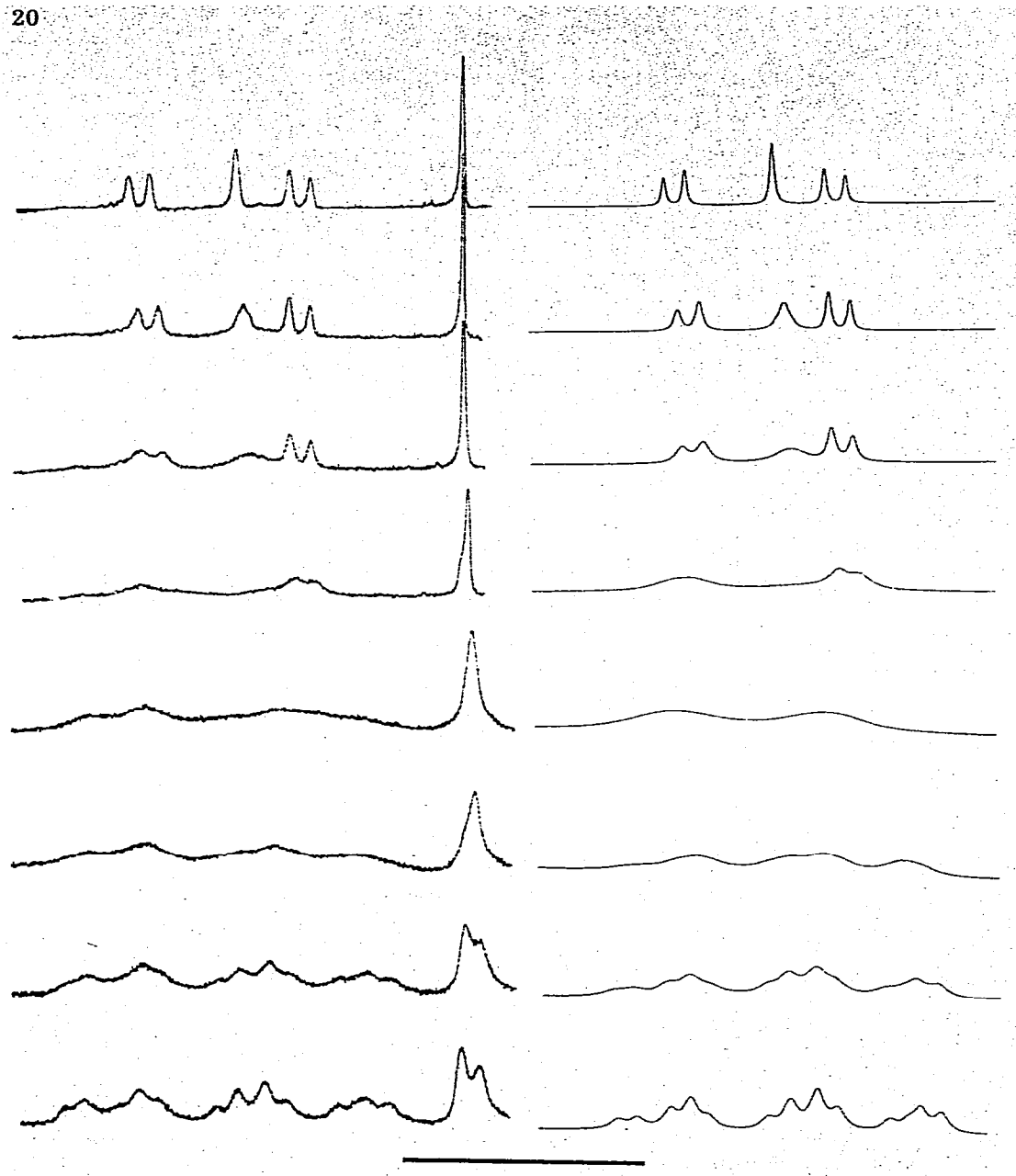


Fig. 1. The observed (left) and calculated 270-MHz proton spectrum of 1-methylarsenane-3,3,5,5-d_4 (IIIa) in $CBrF_3$ as a function of temperature. The calibration bar represents 150 Hz. The temperatures (and mean lifetimes in sec) are (top to bottom): —100.5 (0.000066), —110 (0.00024), —120 (0.00115), —123.5 (0.0020), —128 (0.0045), —134 (0.016), —138 (0.032), and —141 (0.074).

means certain, these observations suggest that conformer A of Table 1 is the equatorial-methyl form.

Rate constants were obtained by complete lineshape analysis, and the calculated spectra are given on the right of Fig. 1. The mean lifetimes (reciprocal rate constants) are given in the caption to Fig. 1. The best fit to all spectra was

obtained with equal populations of the two conformers, i.e., $\Delta G^{\circ} \cong 0.0$ kcal mol^{-1}. The activation parameters from the Arrhenius plot for all eight points were $E_a = 7.8$ kcal mol^{-1}, $\log A = 14.1$, $\Delta G_c^{\ddagger} = 6.7$ kcal mol^{-1}, $\Delta H_{25}^{\ddagger} = 7.2$ kcal mol^{-1}, and $\Delta S_{25}^{\ddagger} = 3.9$ eu (correlation coefficient = 1.000). Deletion of the —100.5 and —141°C points made no significant change. The coalescence temperature (—128°C) method gave $\Delta G_c^{\ddagger} = 6.8$ kcal mol^{-1}, in excellent agreement with the complete lineshape method.

The room temperature proton spectra (except the methyl resonance) for the γ-deuterated (IIIb) and the α,β′-deuterated (IIIc) modifications of 1-methylarsenane are given in Figs. 2 and 3. The spectrum of IIIb was taken at 270 MHz without deuterium decoupling; that of IIIc was taken at 60 MHz with broadband deuterium decoupling. The calculated spectra given at the bottom of the figures were obtained by the iterative Swalen—Reilly procedure [9]. The spectrum of IIIb (Fig. 2) is an *ABCM* pattern, and that of IIIc (Fig. 3) is an *AA′BC* pattern superimposed on an *AB* quartet. The α protons of IIIb (*B* and *M*) are identified by their sharpness in Fig. 2, since the β protons (*A* and *C*) are broadened by coupling with the γ deuteriums. The *AB* quartet in IIIc, designated by the letter a in Fig. 3, is from the unlabeled α′ protons and is ignored in the anal-

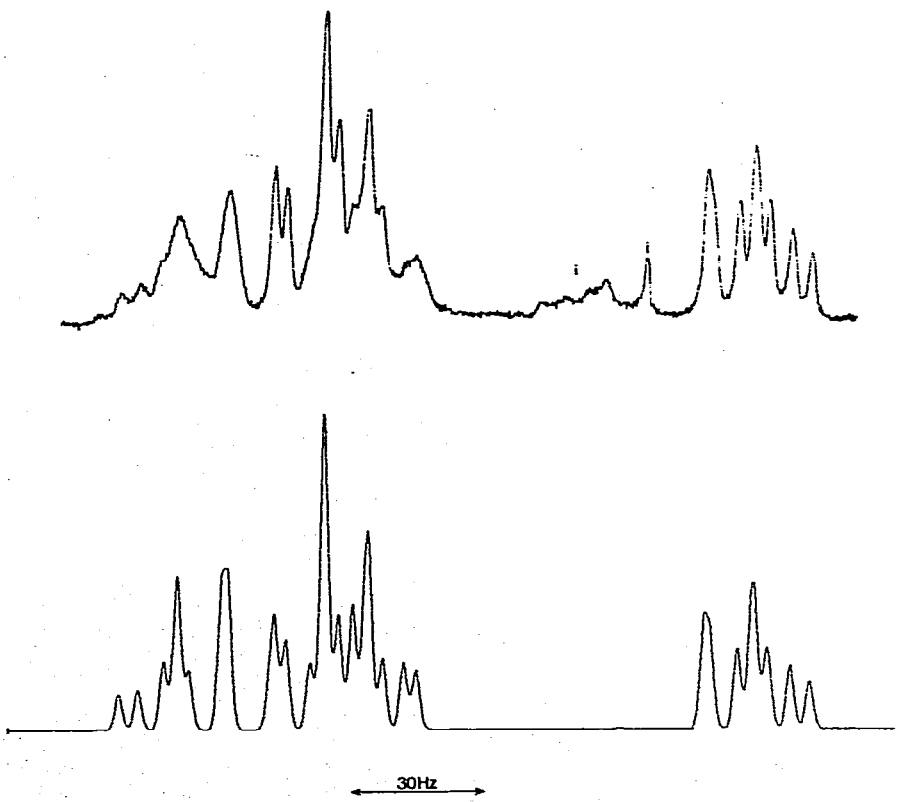


Fig. 2. The observed (top) and calculated 270-MHz proton spectrum of 1-methylarsenane-4,4-d_2 (IIIb) with the methyl resonance omitted. Impurities are labeled i.

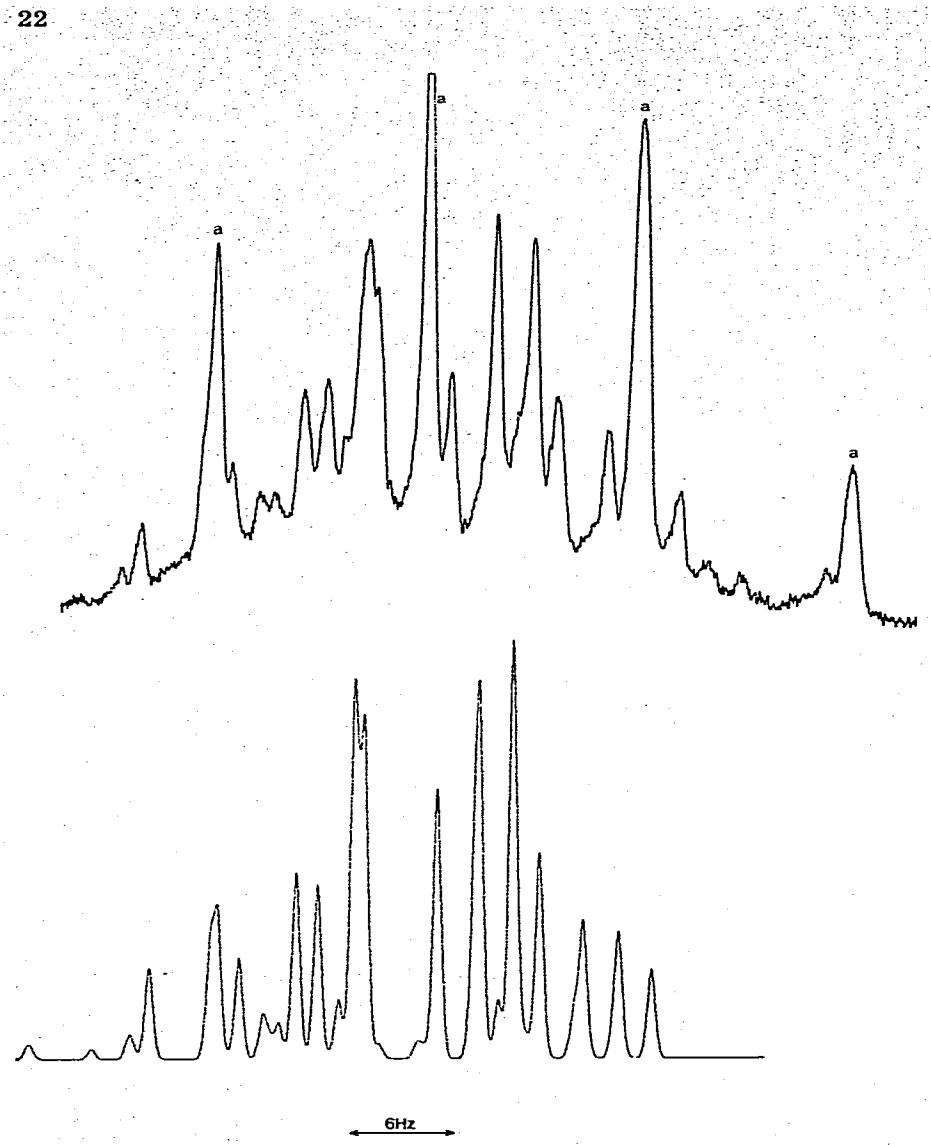


Fig. 3. The observed (top) and calculated 60-MHz proton spectrum of 1-methylarsenane-2,2,5,5-d_4 (IIIc) (methyl resonance ommitted) with deuterium decoupling. The letter a designates the *AB* quartet of the 6 protons (α').

ysis of the β,γ resonances. The γ protons of IIIc are accidentally degenerate (AA') at room temperature for the reasons given above, so the *B* and *C* resonances are assigned to the β protons. Each spectrum gives two *trans* and two *cis* vicinal couplings. The spectra are not sensitive to the sum of the geminal couplings, so only the difference (ΔJ_{gem}) is obtained. The derived parameters are given in Table 2. The ratio of coupling constants, *R*, is given by eq. 3, and the internal dihedral angle (the X—CH_2—CH_2—Y torsional angle for a given bismethylene fragment) is obtained from eq. 4 [10].

$$R = \frac{J_{trans} + J'_{trans}}{J_{cis} + J'_{cis}} \qquad (3)$$

TABLE 2

VICINAL COUPLING CONSTANTS AND STRUCTURAL PARAMETERS FOR 1-METHYLARSENANE

	α,β Protons	β,γ Protons
J_{trans} (Hz)	10.0	8.0
	8.6	7.6
J_{cis} (Hz)	3.3	3.1
	3.5	2.7
R	2.7	2.7
Ψ (°)	61	61
ΔJ_{gem} (Hz)	0.7	0.9

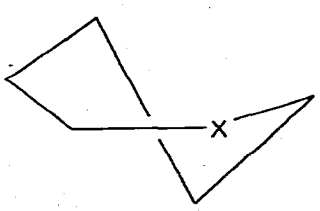
$$\cos \Psi = \left(\frac{3}{2 + 4R}\right)^{1/2} \tag{4}$$

The ^{13}C spectrum of 1-methylarsenane contained peaks at 5.1, 22.4, 23.9, and 29.3 ppm below the TMS standard (neat solution). The 5.1 ppm peak was assigned to the methyl carbon, the 22.4 peak to the α carbon, the 23.9 to the β carbon, and the 29.4 to the γ carbon. These chemical shifts [11] and the relaxation times as well [12] have been discussed elsewhere and will not be examined further here.

Discussion

The free energy of activation for ring reversal in 1-methylarsenane (6.8 kcal mol^{-1}) follows the trend established by 1-methylpiperidine (11.8 kcal mol^{-1}) [1,13] and 1-methylphosphorinane (8.7 kcal mol^{-1}) [4]. These values are very approximately a linear function of the covalent radii of the heteroatoms (Fig. 4) [14]. A similar trend is apparent in the Group VI heterocycles (Fig. 4), data for which we have already reported [15]. No other series (Group IV 1,1-dimethyl, Group V unsubstituted, and Group VI 1-oxides and 1,1-dioxides) contains more than two points, so that meaningful plots cannot be made.

The transition state to ring reversal is a half chair such as IV, in which four



(IV)

atoms are coplanar. It is generally thought that torsional (eclipsing) interactions are most important in determining the barrier to ring reversal [1]. The half chair IV tends to minimize torsional interactions, in comparison with those in other half chairs with the X group or atom elsewhere in the ring. The apparent relationship between the ring reversal barrier and the covalent radius (Fig. 4) may result simply from the fact that the C—X torsional barrier decreases monoton-

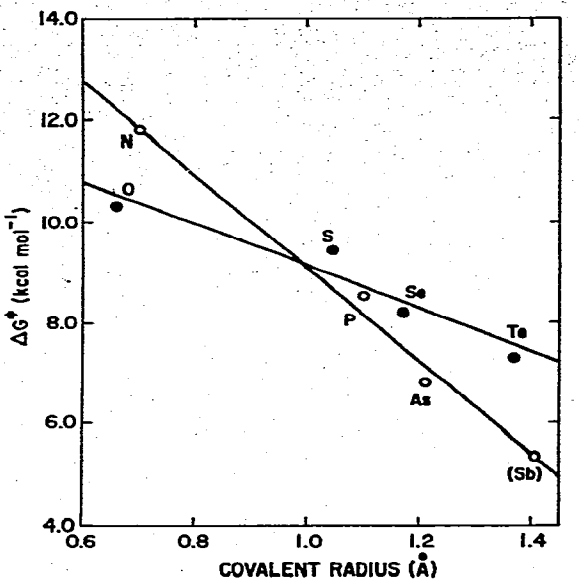


Fig. 4. The barrier ($\Delta G^{\ddagger}$) to ring reversal of pentamethylene heterocycles as a function of the covalent radius of the heteroatom [14].

ically within a vertical series of X in the periodic table [1]. Although the linear relationship of Fig. 4 sheds no real light on the mechanism of ring reversal, it may prove useful in a predictive sense. Extrapolation of the Group V barriers leads to the prediction of a barrier of 5.0 kcal mol^{-1} for 1-methylantimonane. The two point correlation from 1,1-dimethylcyclohexane and 1,1-dimethylsilinane [16] predicts a barrier of 4.9 kcal mol^{-1} for 1,1-dimethylgerminane, and from thiane 1-oxide and selenane 1-oxide gives a barrier of 6.0 kcal mol^{-1} for tellurane 1-oxide [7].

In 1-methylarsenane, there is an essentially equal preference by methyl for the axial and equatorial positions at —144° C. In contrast, the equatorial preference in 1-methylpiperidine is at least 1.35 kcal mol^{-1} (and probably much larger) at room temperature [3], and that in 1-methylphosphorinane is 0.12 kcal mol^{-1} at —110° C. The shorter C—N bonds bring about repulsive interactions between the axial methyl group and various atoms in the ring, such as the *syn*-axial protons at the 3 and 5 positions. The longer C—P bonds decrease these interactions, and the C—As bonds bring it essentially to null. At least in this series, there is no evidence that net attractive interactions develop, as would have been inferred from a strong axial preference in 1-methylarsenane.

Analysis of the vicinal coupling constants provides information about the overall conformation of the ring. The shape of the α,β portion comes from analysis of IIIb (Fig. 2). Slow inversion about arsenic ensures that the configurational relationship between any two protons is not altered when ring reversal is fast. As a result, there are two *trans* and *cis* vicinal couplings within any CH_2—CH_2 group. The ratio R utilizes the average *trans* and average *cis* couplings (eq. 3). The vicinal couplings are larger between the α and β protons than between the β and γ protons because of the polar effect of the electropositive arsenic

atom. The R value is 2.7 for both fragments of the molecule, corresponding to a slightly puckered chair, very similar to the shape of thiane and selenane in Group VI [6c]. There is an important difference between the R value analysis of monoconformational systems such as thiane or selenane and biconformational systems such as 1-methylarsenane. The measured R values represent the weighted average for both forms (eq. 1). Thus the torsional angle of 61° derived from eq. 4 for the As—C_α—C_β—C_γ and the C_α—C_β—C_γ—C_β, represents the average for the two conformations of eq. 1.

Experimental

Proton NMR spectra were recorded at 60 MHz on Varian T-60 and Perkin—Elmer R-20B spectrometers and at 270 MHz on a Bruker HX-270 spectrometer (University of Chicago). The R-20B was equipped with a heteronuclear broadband decoupling unit, and the HX-270 and R-20B were equipped with variable temperature accessories. ^{13}C spectra were obtained on a Bruker HFX-90 operating at 22.628232 MHz in a single-coil pulse mode. Hexafluorobenzene provided the ^{19}F signal for the heteronuclear lock. A Bruker B-SV2 power amplifier was used for broadband decoupling of protons. A Control Data Corporation 6400 digital computer equipped with Calcomp 565 and 1136 plotters was used for spectral and kinetic analyses. Programs ENIT, NMRPLOT, ABAB, and ARRP were used for the analyses. All reactions were carried out under dry N_2. Solvents were distilled from appropriate drying agents and stored over molecular sieves.

1,5-Dibromopentane-2,2,4,4-d_4 (IIIa)

This material was prepared by the reported procedure [6a], with some modifications [7].

1,5-Dibromopentane-3,3-d_2 (IIIb)

This material was also prepared by a literature procedure [6b].

1,5-Dibromopentane-1,1,4,4-d_4 (IIIc)

This material as well was prepared by a literature procedure [6c].

Methyldichloroarsine

Sodium methylarsenate, $CH_3AsO_3Na_2 \cdot 6H_2O$ (29.2 g, 0.1 mol), and 0.5 g KI were dissolved in 35 ml of H_2O. Concentrated HCl (200 ml) was then added, and any precipitate (primarily NaCl) was filtered off. A gentle stream of SO_2 was bubbled through the solution for 6 h. Two layers were formed, and the bottom layer was separated, dried ($CaCl_2$), and distilled to give 12.5 g (80%) of the desired product, b.p. 130—132° (lit. [8] 129—130°C).

Pentamethylenemagnesium bromide

To a solution containing 4.8 g (0.2 mol) of Mg turnings and 50 ml of dry ether was added dropwise with vigorous stirring a solution of 23 g (0.1 mol) of 1,5-dibromopentane (appropriately labeled with deuterium) in 100 ml of dry ether. After the dibromide solution had been added, the reaction was allowed

to stir at room temperature overnight. The bottom layer containing the desired di-Grignard reagent was separated and filtered under N_2.

1-Methylarsenane (III)

The di-Grignard solution generated from 0.1 mol of the labeled 1,5-dibromopentane was added dropwise to an ice-cooled solution of 0.06 mol of methyldichloroarsine in 125 ml of dry ether. After the di-Grignard solution had been added, the mixture was stirred overnight. Saturated NH_4Cl solution (100 ml) was then added to destroy any excess Grignard reagent, and the ether layer was separated. The water layer was extracted with 3 × 50 ml of ether. The combined organics were dried ($MgSO_4$) and distilled to give the desired product in 40% yield, b.p. 153—155° (lit. [5] 156° C).

Acknowledgments

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