Conformational Analysis of Saturated Heterocycles. Part 91.[1] Synthesis and Conformational Equilibria of 1-Oxa-2,5-diazacyclohexanes [2]

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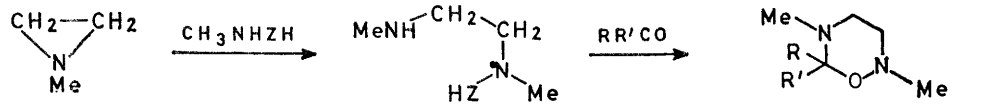
Three examples of the novel 1-oxa-2,5-diazacyclohexane ring system were synthesised. Each shows two conformational barriers: (i) of 13.5—14.00 kcal mol^{-1} corresponding to the slowing of ring reversal *or* N(2)—CH_3 inversion and (ii) of 7.5—8.2 kcal mol^{-1} corresponding to slowing N(5)—CH_3 inversion. The proton and ^{13}C n.m.r. spectra, and conformational equilibria of these compounds are discussed and compared with those for analogous saturated six-membered rings containing two heteroatoms.

COMPARED with the extensive work devoted to the conformational analysis of saturated six-membered heterocyclic rings containing one or two heteroatoms,[3] far less attention has been paid to their analogues with three or four heteroatoms; many of which were until recently unknown. Thus six isomeric oxadiazacyclohexanes could exist: we have recently studied the 1,3,4-[4] and 1,3,5-isomers,[5] and the unknown 1,2,3- and 1,2,6-isomers are expected to be unstable containing as they do three adjacent heteroatoms. The 1,2,4-isomer had also apparently never been prepared.† The present paper deals with the 1-oxa-2,5-diazacyclohexanes recording the synthesis and elucidation of the conformational equilibria of these previously unknown compounds.

Synthesis.—We have previously shown[6] that *N*-methylaziridine (1) is opened by 1,2-dimethylhydrazine

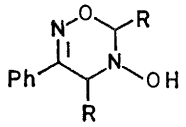


(1)

(2) Z = NMe
(3) Z = O

(4) R = R' = H
(5) R = H, R' = Me
(6) R = R' = Me

to yield a β-aminoethylhydrazine derivative (2) which is ring-closed by carbonyl compounds to 1,2,4-triazanes. Our 1-oxa-2,5-diazacyclohexane synthesis involves the analogous ring opening of (1) to the β-aminoethylhydroxylamine (3) which smoothly condensed with formaldehyde, acetaldehyde, and acetone to yield the



(7)

derivatives (4)—(6) respectively. These 1-oxa-2,5-diazacyclohexanes are colourless oils which distil unchanged: compound (4) is stable for several weeks at room temperature but the derivatives (5) and (6) show some decomposition upon exposure to air. There are no previous reports on the fully saturated 1-oxa-2,5-diazacyclohexane ring system, although the dihydro-derivative (7) has been prepared by Russian workers,[7] who employed a reaction scheme similar to ours.

Spectra of Equilibrating Systems.—At higher temperature, both ^1H and ^{13}C n.m.r. spectra for each of (4), (5), and (6) are as expected for completely equilibrating systems. Chemical shifts and assignments are shown in Table 1. The N(2)-CH_3 (δ 2.55—2.61) occurs to lower field of the N(5)-CH_3 (δ 2.25—2.35), *cf.* N(2)-CH_3 of 2-methyl-1-oxa-2-azacyclohexane at δ 2.46,[8] and N(3)-CH_3 of 3-methyl-1-oxa-3-azacyclohexane at δ 2.29.[9,‡] The four N-CH_2CH_2N protons form a complex multiplet near 2.8 p.p.m. and the OC*RR'*N signals are as expected.

The proton-noise-decoupled ^{13}C n.m.r. spectra at high temperatures of (4), (5), and (6) consist of 5, 6, and 6 single well-resolved lines respectively, consistent with 'fast' conformational equilibration. Assignments (Table 1) employed off-resonance decoupling data and chemical shifts. Thus, N(2)-CH_3 absorbs at lower field (47 p.p.m.) than N(5)-CH_3 (at *ca.* 38 p.p.m.), and this assignment is confirmed by the behaviour at low temperatures (*vide infra*). Similarly C-3, which is β to the ring oxygen absorbs at lower field than C-4 which is γ to the ring oxygen (as found in other systems):[11] in agreement, C-4 for compound (6) shows the significant upfield shift caused by the axial C-Me at C-6 (*γ-gauche*-effect).[12] These assignments for C-3 and C-4 are again confirmed by the lower temperature spectrum.

Variable-temperature Spectra for 2,5-Dimethyl-1-oxa-2,5-diazacyclohexane (4).—The conformational cube § is

† Dr. F. G. Riddell has informed us that his group has recently prepared this compound (F. G. Riddell and E. S. Turner, *Heterocycles*, 1978, **9**, 267).

‡ Ref. 9 reports this figure to be δ 2.48; however, the recent proton n.m.r. spectrum of 3-methyl-1-oxa-3-azacyclohexanes[10] gives the value for the N—CH_3 resonance at ambient temperatures.

§ Analogous to the one proposed for 1,2-dimethyl-1,2-diazacyclohexane by Nelsen and Weisman,[13] which is topographically the same but easier to understand than our earlier representation (R. A. Y. Jones, A. R. Katritzky, and R. Scattergood, *Chem. Comm.*, 1971, 644).

TABLE 1

N.m.r. spectra of equilibrating systems of compounds (4), (5), and (6)

Proton spectra [a] at 31 °C (100 MHz)					¹³C Spectra [b] at +25 °C (25.05 MHz)				
Signal	type	(4)	(5)	(6)	Signal	type [c]	(4)	(5)	(6) [d]
N(2)–C*H*$_3$	s, 3 H	2.55	2.61	2.55	N(2)–*C*H$_3$	q	47.0	47.0	47.0
C(3)–*H*$_2$ / C(4)–*H*$_2$	m, 4 H	2.81	2.84	2.83	*C*(3)	t	54.6	55.5	57.1
					C(4)	t	52.4	54.9	50.1
N(5)-C*H*$_3$	s, 3 H	2.35	2.25	2.29	N(5)-*C*H$_3$	q	39.6	36.9	38.4
C(6)–*H*$_2$	s, 2 H	4.32			*C*(6)	t,d,s [f]	87.9	91.8	90.8
C(6)–*H*	q, 1 H		4.12, 4.26 [e]						
C(6)–*R*$_2$	s, 6 H		1.35						
C(6)–C*H*$_3$	d, 3 H		1.00, 1.06		C(6)–*C*H$_3$	q		18.4	22.1

[a] Solvent: $CDCl_3$; δ downfield from $SiMe_4$. [b] Solvent: CF_2Cl_2/[$^2H_6$]acetone; δ downfield from $SiMe_4$. [c] Multiplicity obtained from off-resonance decoupling. [d] Solvent: [$^2H_6$]acetone–[$^2H_4$]methanol (1 : 1), measured at 40 °C. [e] $^3J_{HH}$ = 6 Hz. [f] Respectively for (4), (5), (6).

TABLE 2

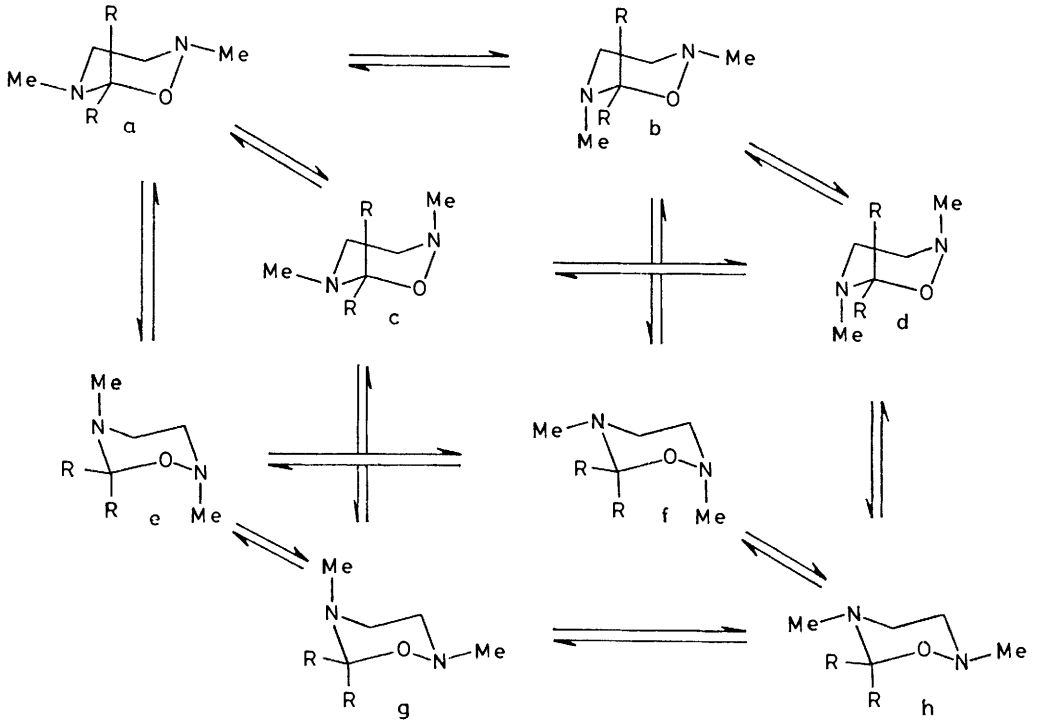
Proton n.m.r. coalescence data [a] for the 1-oxa-2,5-diazacyclohexanes (4) and (6)

Compound	Signal	δ [b]	t_c (°C)	*J* (Hz) [b]	Δν (Hz) [b]	$\Delta G_c^{\ddagger}$ (kcal mol^{-1})
(4)	O–C*H*$_2$–N	4.39, 4.26	0	10.2	13.0	13.7 ± 0.3 [c]
(6)	O–C*Me*$_2$–N	1.09, 0.98	−5		11.0	13.9 ± 0.4

[a] Eyring equation employed, $f = 1$.[15] [b] Taken from low (*ca.* −50 °C) temperature ^1H n.m.r. spectra. [c] See footnote *.

shown in Scheme 1 (R = H). Previous results on 2-methyl-1-oxa-2-azacyclohexane derivatives ($\Delta G^\circ \geqslant 1.9$ kcal mol^{-1}) [14] indicate that all those conformers (4c, d, e, f) with N(2)-CH$_3$ axial should be sparsely populated, whereas ^{13}C n.m.r. work on 3-methyl-1-oxa-3-azacyclohexane ($\Delta G^\circ = 0.10$ kcal mol^{-1} favouring NMe axial) [10] leads us to expect appreciable quantities of the N(5)-CH$_3$ axial forms (4b, g) together with the diequatorial conformers (4a, h).

Changes are expected in the proton spectrum when *either* N(2)–CH$_3$ inversion *or* ring reversal becomes 'slow', for this separates (4a)⇌(4b) from (4g)⇌(4h). Indeed lowering the temperature splits the O–C*H*$_2$–N signal into an AB quartet (Table 2) and complex changes also occur in the N–C*H*$_2$–C*H*$_2$–N multiplet. Applying the Eyring equation [15] gives $\Delta G_c^{\ddagger}$ 13.7 ± 0.3 kcal mol^{-1}.* No further changes were observed in the ^1H spectrum down to −100 °C, the lowest temperature studied.



SCHEME 1 Conformational cube for 2,5-dimethyl- (4; R = H), and 2,5,6,6-tetramethyl-1-oxa-2,5-diazacyclohexane (6; R = Me)

Neither slowing of N(2)–CH$_3$ inversion nor ring rever-

* This value is unreliable because of the rapidly changing and small chemical shift difference. Dr. F. G. Riddell (University of Stirling, Scotland) kindly informs us that he finds values of 14.6 ± 0.2 and 15.2 ± 0.2 kcal mol^{-1} for this barrier in toluene and D_2O respectively in which solvents this chemical-shift difference, although highly temperature-variable, is sufficiently large to give reliable values (see F. G. Riddell and E. S. Turner, *Heterocycles*, 1978, **9**, 267).

sal should affect the ^{13}C spectrum: in agreement, changes are only found below *ca.* −90 °C (Table 3) when N(5)–CH_3 inversion becomes 'slow' and each peak coalesces and re-emerges as two singlets of unequal size, corresponding to a superposition of the spectra for the individual conformers (4a) [and its mirror image (4h)] and (4b) [with (4g)]. The high temperature ^{13}C assignments are confirmed by the chemical shift difference between the peaks for the individual conformers which is very small for N(2)–CH_3 but significantly larger for N(5)–CH_3 which is the seat of the conformational change slowed; again it is larger for C-3 (where the steric compression *γ-gauche*-effect applies [16]) than for C-4.

TABLE 3 [a]

^{13}C N.m.r. spectra [b] for individual conformers at −136 °C of compounds (4), (5), and (6)

Compound	(4)		(5)		(6)	
Conformers	b, g	a, h [c]	b [c]	a	b, g [c]	a, h
N(2)–CH_3	46.6	46.9 [d]	46.5 [d]	46.7	46.7	46.7
C(3)	51.9	57.0 (0.31)	51.1 (0.84)	57.6	50.2 (0.13)	57.7
C(4)	50.3	53.4 (0.36)	53.1 (0.88)	54.4	48.9	48.9
N(5)–CH_3	38.9	39.8 (0.22)	32.4 (0.74)	40.1	36.3 (0.10)	38.8
C(6)	86.6	87.9 (0.38)	89.2 (0.80)	92.9	90.6	90.6
C(6)–CH_3			18.2 [d]	18.4	26.5 [e]	26.5 [e]
					25.1 [f] (0.15)	14.7 [f]

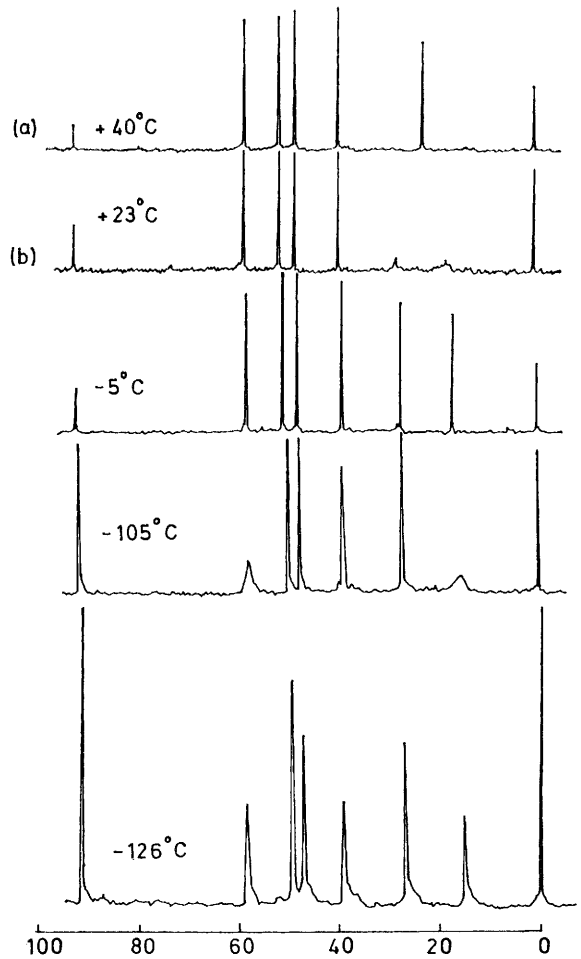
[a] These assignments, based on N–CH_3 axial predominance in 3-methyl-1-oxa-3-azacyclohexane from recent ^{13}C n.m.r. correlations,[10] are the reverse of the assignments in the preliminary communication [2] which were based on the previous ^1H n.m.r. result [9] of N–CH_3 equatorial predominance in 3-methyl-1-oxa-3-azacyclohexane. [b] Solvent: CF_2Cl_2–[$^2H_6$]acetone, δ p.p.m. downfield from $SiMe_4$. [c] Fractional integration relative to major signal. [d] Overlap precludes assessment of fractional integration. [e] Equatorial C(6)–CH_3. [f] Axial C(6)–CH_3.

The assignments for the individual conformers in Table 3 are based on the model compound 3-methyl-1-oxa-3-azacyclohexane,[10] where the axial N–CH_3 is favoured by *ca.* 0.10 kcal mol^{-1} over the equatorial conformation. The N(5)–CH_3 signals at δ 39.8 and 38.9 are assigned to equatorial (a, h) and axial (b, g) environments respectively *cf.* the corresponding signals [10] for N(3)–CH_3 in 3-methyl-1-oxa-3-azacyclohexane at δ 40.7 and 38.8. The rest of the signals are assigned by reference to the gated decoupled (Overhauser suppressed) spectrum.

From the gated decoupled (with n.O.e. suppression) spectrum of (4) at *ca.* −136 °C, signal integration (Table 3) led to $\Delta G^\circ_{147} = 0.31 \pm 0.05$ kcal mol^{-1} in favour of the N(5)-CH_3 axial conformer (b, g). The activation energy ($\Delta G_c^\ddagger$) for the process 'slowed' on ^{13}C n.m.r. at *ca.* −90 °C, *i.e.* N(5)–CH_3 inversion, is determined to be 7.7 ± 0.2 kcal mol^{-1} in excellent agreement with recent ^{13}C n.m.r. results [10] for the N(3)–CH_3 inversion in 3-methyl-1-oxa-3-azacyclohexane: previously reported ^1H n.m.r. results [9] for this compound are now thought to have been in error because of temperature discrepancies.[10]

Variable-temperature Spectra for 2,5,6,6-*Tetramethyl*-1-*oxa*-2,5-*diazacyclohexane*.—The situation is very similar to that for the dimethyl analogue (4). Again we expect the mirror-image pairs of conformers (6b, g) and (6a, h) to coexist. For the proton spectrum, lowering the temperature splits the *gem*-dimethyl group into an equal doublet. Precise measurement of t_c was difficult accounting for the large error in $\Delta G_c^\ddagger$ 13.9 ± 0.4 kcal mol^{-1} (Table 2) which could be due to slowing of either N(2)–CH_3 inversion or ring reversal.

This same process can be followed in the ^{13}C spectrum where the C(6)–CH_3 peak also splits into two singlets of equal magnitude (δ 27.0; 16.9) with $t_c = +25$ °C yielding $\Delta G_c^\ddagger$ 13.7 ± 0.2 kcal mol^{-1}. Further changes occur in the ^{13}C spectrum below −90 °C (Table 3; Figure) due to 'slowing' of N(5)–CH_3 inversion and at



Carbon-13 variable temperature n.m.r. of 2,5,6,6-tetramethyl-1-oxa-2,5-diazacyclohexane: (a) $CDCl_3$ and (b) CF_2Cl_2

TABLE 4

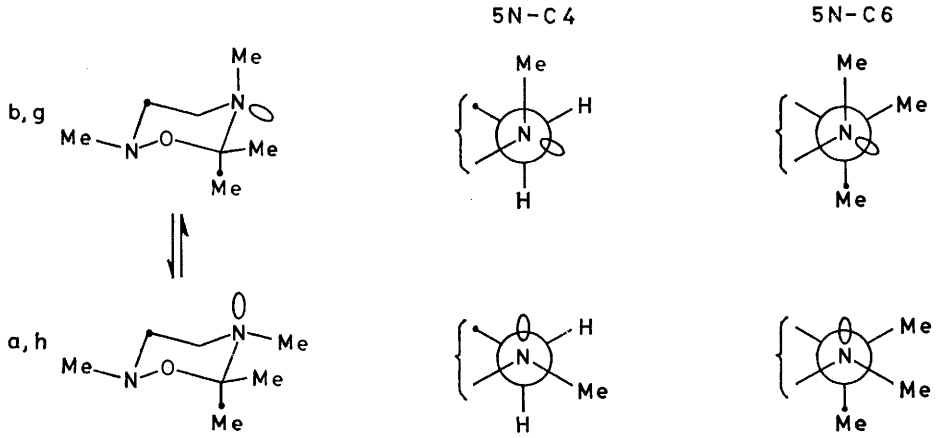
^{13}C D.n.m.r. coalescence data [a] for some 1-oxa-2,5-diazacyclohexanes at −137 °C

	(4)			(5)			(6)		
	t_c (°C)	$\Delta\nu$ (p.p.m.)	$\Delta G_c^{\ddagger}$ (kcal mol^{-1})	t_c (°C)	$\Delta\nu$ (p.p.m.)	$\Delta G_c^{\ddagger}$ (kcal mol^{-1})	t_c (°C)	$\Delta\nu$ (p.p.m.)	$\Delta G_c^{\ddagger}$ (kcal mol^{-1})
N(2)–CH_3	−127	0.2		−119	0.2	8.09	*b*		
C(3)	−106	5.2	7.69	−93	6.6	8.26	−103	7.5	7.71
C(4)	−110	3.1	7.69	−108	1.3	8.05	*b*		
N(5)–CH_3	−119	1.0	7.58	−93	7.7	8.20	−111	2.5	7.69
C(6)	−114	1.3	7.74	−98	3.7	8.19	*b*		
C(6)–CH_3				−115	0.3	8.24	−103 [c]	10.3	7.60

[a] Solvent: CF_2Cl_2–$(CD_3)_2CO$; Eyring equation, $f = 1.^{15}$ [b] No dynamic change observed. [c] Axial C–CH_3 shows this dynamic change.

low-temperature spectra of the individual conformers are found, substantially biased to the conformer with N(5)–CH_3 equatorial (6a, 6h) with $\Delta G_c^{\circ} = 0.5 \pm 0.1$ kcal mol^{-1}. Comparison of the C-3 shift in (4a) and (6a) (δ 57.0 and 57.7) provides convincing evidence that (6a) is the preferred conformation [*cf.* C-3 shift in (4b) at δ 51.9]. Noteworthy is the fact that the signals for axial *C*-methyl group in (6) destabilises the ground state by *ca.* 0.4 kcal mol^{-1}, consequently little difference is observed in $\Delta G_c^{\ddagger}$ for (4) and (6).

2,5,6-*Trimethyl*-1-*oxa*-2,5-*diazacyclohexane* (5).—The conformational cube (Scheme 3) represents one set of stereoisomers because, even when all kinetic processes are fast, (5) is chiral. Again the four N(2)–CH_3 axial



SCHEME 2 *γ-Gauche* effect at *C*–3 and C(6)–CH_3 (axial)

C-3 and axial C(6)–CH_3 carbon atoms display similar 'dynamic' behaviour upon 'slowing' of N(5)–CH_3 inversion because spatially they display a similar *γ-gauche* [12] relationship with the N(5)–CH_3 group (see Scheme 2): whatever the conformation, C(6)–CH_3 axial is *anti* to N(5)–CH_3 in (6b, g) and *gauche* to N(5)–CH_3 group in (6a, h). This relationship, albeit in an opposite sense, is also present at the C-3 carbon atom (Scheme 2).

The γ-gauche effect, a ^{13}C spectral characteristic [12] which is used extensively to make stereochemical assignments,[13] has been found to be *ca.* 5 p.p.m. for the γ-carbon in methylcyclohexane,[17] *ca.* 6.4 p.p.m. in *trans*-decahydro-*N*-methylquinoline,[16] and *ca.* 10.2 and 5.4 p.p.m. for the, γ N-CH_2–C and C–CH_2–C in 1,2-dimethyl-1,2-diazacyclohexane.[13] We now find 7.5 and 10.3 p.p.m. for C-3 and C(6)–CH_3 (axial) carbon resonances respectively.

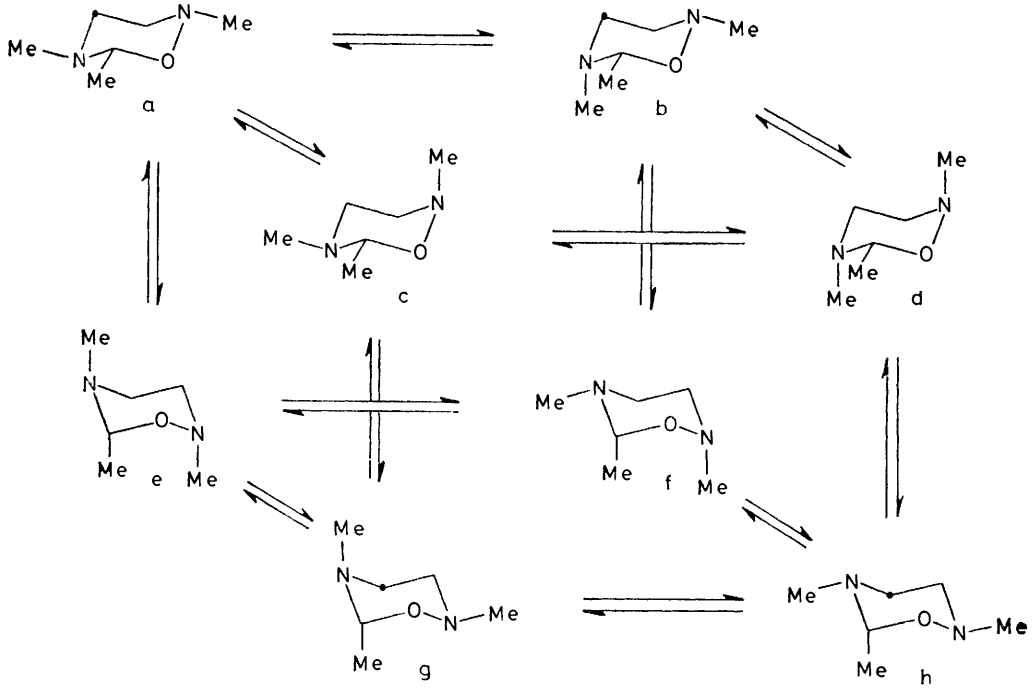
The barrier ($\Delta G_c^{\ddagger}$) to this second process (Table 4) is *ca.* 7.65 ± 0.20 kcal mol^{-1} using the Eyring equation. 'Passing' *C*-methyl interactions [9,13] in (6) should have raised $\Delta G_c^{\ddagger}$ by *ca.* 0.4 kcal mol^{-1} compared with the barrier to N(5)–CH_3 inversion in (4). It is clear that the conformers (5c, d, e, f) will be sparsely populated. A higher-energy barrier will again separate (5a, b) from (5g, h) but these are now no longer mirror images and (5a, b) should predominate considerably over (5g, h).

Near +10 °C in the proton spectrum the C(6)–*H* quartet broadens and resharpens. In the ^{13}C spectrum a dynamic process also occurs particularly in the C-4 signal which is γ to both N(2)–CH_3 and C(6)–CH_3 groups. This dynamic broadening represents the 'freezing' out of minor conformations (5g, h).

The *γ gauche* effect is 5 p.p.m. in methylcyclohexane [17] and 6.4 p.p.m. in *trans*-decahydro-*N*-methylquinoline: [16] thus we take Δν for the Anet equations [17] as 5.5 ± 0.5 p.p.m. This gives 13.3 ± 0.3 kcal mol^{-1} for $\Delta G_c^{\ddagger}$ (minor to major conversion; $t_c = 11$ °C) and, in conjunction with the broadening in the line width at half height ($\Delta\omega_{\frac{1}{2}} = 5$ Hz), a free-energy difference (ΔG_c°) of 1.9 ± 0.2 kcal mol^{-1} in favour of (5a, b) over (5g, h). This process cannot be unequivocally assigned: either 'slowing' of *N*(2)-methyl (*cf.* 2-methyl-1-oxa-2-aza-cyclohexane; [8] $\Delta G_c^{\ddagger} = 13.7$ kcal mol^{-1}) or *C*(6)-methyl ring inversion can lead to this dynamic broadening in the C-4 signal.

Compound (5) shows a second more dramatic dynamic change in its ^{13}C n.m.r. spectrum at *ca.* −90 °C. All signals collapse into doublets: the set of minor signals (Table 3) is upfield relative to the corresponding signals of the major conformation. This pattern is opposite to that observed for (4), thus providing good evidence that the major conformer for (5) is likely to be (5a) with N(5)–CH_3 equatorial ($\Delta G_c^\circ = 0.10 \pm 0.05$ kcal mol^{-1}). The energy of activation ($\Delta G_c^\ddagger$) for the *N*(5)-inversion in (5) is determined by the Eyring equation [15] to be 8.2 ± 0.2 kcal mol^{-1} (Table 4) and provides confirmatory evidence that an adjacent equatorial *C*-methyl group raises $\Delta G_c^\ddagger$ for *N*-inversion by *ca.* 0.4 kcal mol^{-1}.[9,13]

This anomalous effect has recently been observed in 1-oxa-3-aza-cyclohexanes [10] and 1,4-dioxa-2-azacyclohexanes.[20] In the latter system, 2-methyl-1,4-dioxa-2-azacyclohexane (8a) prefers the N–CH_3 equatorial form by 0.93 kcal mol^{-1}: this preference is enhanced in 2-methyl-3-*p*-nitrophenyl-1,4-dioxa-2-azacyclohexane (8b) (*cf.* $\Delta G^\circ = 1.17$ kcal mol^{-1} in favour of the N–CH_3 equatorial form). Slightly different *gauche* torsional interactions about the N–C–O bonds [20] in the axial and equatorial conformations are considered responsible, upon insertion of α-*C*-methyl groups, for the increased predominance of equatorial conformations in heterocycles containing the 1-oxa-3-aza-fragment.

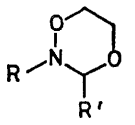


SCHEME 3 Conformational cube for 2,5,6-trimethyl-1-oxa-2,5-diazacyclohexane

Conformational Populations in Compounds (4), (5), *and* (6).—Assignment of the more intense δ 38.9 signal to N–CH_3 axial in 3-methyl-1-oxa-3-azacyclohexane [10] implies that (i) the N(5)–CH_3 axial form (b, g) is predominant for 2,5-dimethyl-1-oxa-3,5-diazacyclohexane (4) and (ii) that, surprisingly, the N(5)–CH_3 equatorial conformer (a) is the predominant one in (5) and even more so in (6).

In previous examples, *e.g.* 1,2-[13,18] and 1,3-diazacyclohexanes [19] it has been convincingly shown that insertion of an α-*C*-methyl group, to give *three* adjacent methyl groups, has shifted the equilibrium of *N*-methyl groups towards *N*-methyl axial conformations. In contrast, we now conclude in the present paper that insertion of an α-*C*-methyl group into heterocycles containing the 1-oxa-3-aza unit leads to greater difficulty in placing *N*-methyl groups axial [*cf.* ΔG°, in favour of N(5)–CH_3 equatorial for (4), (5), and (6), by −0.31, 0.10, and 0.50 kcal mol^{-1} respectively].

Conclusion.—All three compounds show high-energy barriers of *ca.* 14 kcal mol^{-1} which may be assigned to either *N*(2)-atomic inversion or to ring reversal.



(8a) R = Me, R′ = H
(8b) R = Me, R′ = *p*-NO_2·C_6H_4

SCHEME 4

The 1-oxa-2,5-diazacyclohexanes (4), (5), and (6) also display *N*(5)-methyl inversion barriers of *ca.* 7.7 kcal mol^{-1} [for (4) and (6)] and *ca.* 8.2 kcal mol^{-1} [for (5)]. These values are consistent with currently accepted *N*-methyl inversion barriers in 3-methyl-1-oxa-3-aza-cyclohexane.[10] The slight differences in ΔG_c° [*cf.*

$\Delta G_c^\circ = 0.10$ kcal mol^{-1} in favour of the axial *N*-methyl conformer in 3-methyl-1-oxa-3-azacyclohexane and $\Delta G_c^\circ = 0.31$ kcal mol^{-1} in (4)] are probably due to slight differences in ground-state energies.

The power of ^{13}C dynamic n.m.r. spectroscopy is illustrated by the fact that coalescence of the N(2)–CH_3 signal is observed in the spectra of (4) and (5) as the N(5)–CH_3 inversion becomes 'slow', although the chemical-shift difference of the N(2)–CH_3 signal in conformations with N(5)–CH_3 axial/equatorial is only *ca.* 0.2 p.p.m.

EXPERIMENTAL

Physical Methods.—Proton n.m.r. spectra were run employing a Varian HA-100 spectrometer; samples were housed in 5-mm tubes. Temperatures were measured by reference to the methanol shift using an improved Varian calibration graph and are accurate to ±2 °C.

Carbon-13 n.m.r. spectra were obtained using a JEOL FX-100 spectrometer, incorporating a JEOL JEF-980B computer. Spectra were normally run using an internal ^2H lock and employing a sweep width of 3005 Hz, giving a digital resolution of 0.375 Hz. Off-resonance decoupling (OFR; IRSET = 50.8 kHz, power low) and gated decoupling with Overhauser suppression (NNE; pulse delay 8 s) experiments were conducted using normal JEOL settings. Temperatures are accurate to ±2 °C and control units were checked with a copper–constantan thermocouple inserted in a standard 10-mm JEOL FX-100 n.m.r. tube.

2(N-*Methylamino*)*ethylmethylhydroxylamine.*— *N*-methylhydroxylamine (10 g, 0.21 mol) was heated with ammonium chloride (*ca.* 0.5 mol %) to *ca.* 30 °C. Freshly distilled *N*-methylaziridine (5 g, 0.09 mol) was added dropwise. The mixture was kept at 30 °C for 3 h under nitrogen. On cooling, excess of hydroxylamine was distilled off (62 °C at 20 mmHg), the residual 2-(N-*methylamino*)*ethylmethylhydroxylamine* was distilled, b.p. 62 °C at 0.5 mmHg (5.4 g, 58%) (Found, C, 46.0; H, 11.5; N, 26.5). $C_4H_{12}N_2O$ requires C, 46.1; H, 11.6; N, 26.9%); *m/e* 104 $(P)^+$, 89 $(P^+ - 15)$, and 74 $(P^+ - 30)$.

2,5-*Dimethyl*-1-*oxa*-2,5-*diazacyclohexane.*— 2-(*N*-Methylamino)ethylmethylhydroxylamine (1 g, 9.6 mmol) and *p*-formaldehyde (0.3 g, 10 mmol) in dry benzene (25 ml) were stirred for 0.25 h (25 °C) and then refluxed for 0.5 h and water azeotroped out. Distillation gave 2,5-*dimethyl*-1-*oxa*-2,5-*diazacyclohexane* (1.0 g, 90%), b.p. 40 °C at 20 mmHg, which was characterised by ^{13}C and ^1H n.m.r. spectra; *m/e* 116 (P^+), 101 $(P^+ - 15)$.

2,5,6-*Trimethyl*-1-*oxa*-2,5-*diazacyclohexane.*—Freshly distilled acetaldehyde (2 g, 45 mmol) was added dropwise at −5—0 °C to 2-(*N*-methylamino)ethylmethylhydroxylamine (1 g, 9.6 mmol) in sodium-dried ether, under nitrogen. Anhydrous K_2CO_3 (2 g) was added and the mixture stirred for 2 h. K_2CO_3 was filtered off; distillation then gave 2,5,6-*trimethyl*-1-*oxa*-2,5-*diazacyclohexane* (1 g, 80%) as an oil, b.p. 56 °C at 20 mmHg, which was characterised by ^{13}C and ^1H n.m.r. spectroscopy; *m/e* 130 (P^+), 115 $(P^+ - 15)$, 100 $(P^+ - 30)$, 85, 71, and 57.

2,5,6,6-*Tetramethyl*-1-*oxa*-2,5-*diazacyclohexane.*— 2-(*N*-Methylamino)ethylmethylhydroxylamine (1 g, 9.6 mmol), dry AnalaR acetone (1 g, 17 mmol), toluene-*p*-sulphonic acid (*ca.* 0.5 mol %), and dry benzene (25 ml) were kept at 30 °C for 1 h and then at reflux for a further 2 h. Water was azeotroped off, and the whole distilled to give 2,5,6,6-*tetramethyl*-1-*oxa*-2,5-*diazacyclohexane* (0.6 g, 43%) as an oil, b.p. 70 °C at 20 mmHg, which was characterised by ^{13}C and ^1H n.m.r. spectroscopy; *m/e* 144 (P^+), 129 $(P^+ - 15)$, and 114 $(P^+ - 30)$.

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