The Conformational Analysis of Saturated Heterocycles. Part 87.[1] Carbon-13 Nuclear Magnetic Resonance Studies of 1,3-Diazacyclohexanes and Some Bi- and Tri-cyclic Analogues

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Variable temperature ^{13}C n.m.r. studies elucidate the conformational equilibria and energetics of 1,3-dimethyl- and 1,2,3-trimethyl-1,3-diazacyclohexane, *cis*-1,3,4,7,8-pentamethyl-1,3,7-triazabicyclo[3.3.1]nonane, and 1,2,4,5,7,8-hexamethylperhydro-1,4,7,9*b*-tetra-azaphenalene. ^{13}C N.m.r. shifts of the *N*-methyl carbon atoms in these compounds are correlated using the *γ-gauche* upfield shift criterion.

THE present paper describes the results of variable temperature ^{13}C n.m.r. experiments on a series of mono-, di-, and tri-cyclic 1,3-diazacyclohexanes which confirm and extend our knowledge of the conformational equilibria of these compounds.

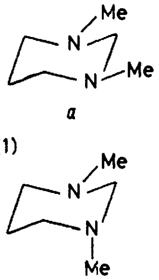
TABLE 1

^{13}C (25.16 MHz) N.m.r. data [a] for 1,3-dimethyl-1,3-diazacyclohexane (1)

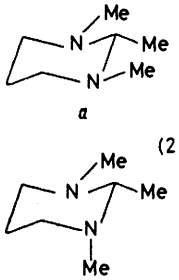
Temp. (°C)	Conformers	N–*C*–N	N–*C*H$_2$–C	N–*C*H$_3$	C–*C*H$_2$–C
5	(1*ee*) $\rightleftharpoons$ (1*ae*)	80.4	55.0	43.2	24.1
	b	t	t	AB$_3$q	t
–150	(1*ee*)	80.0	54.2	43.6	25.1
	(1*ae*)	77.1	*eq.* 56.2 *ax.* 50.4	*eq.* 43.6 *ax.* 40.6	19.4
	Coalescence data				
	t_c/°C	–120	–120	–123	–123
–150	$\Delta\nu$/Hz	72.9			143.4
–150	Population (%) [c] (1*ee*)	88		90	91
	$\Delta G^{\ddagger}_c$ ($\pm$0.3 kcal mol^{-1})	7.2			6.8
–150	ΔG^0_c ($\pm$0.05 kcal mol^{-1})	0.61		0.65	0.69

[a] Solvent: CF_2Cl_2–$(CD_3)_2CO$(2 : 1): δ downfield from Me_4Si. [b] Obtained from off resonance spectra; solvent: $CDCl_3$ (t = triplet; d = doublet; q = quartet). [c] Obtained from n.O.e. suppressed gated decoupling, relative peak weight (%).

Monocyclic 1,3-Diazacyclohexanes.—The conformational equilibria of 1,3-dimethyl-1,3-diazacyclohexane (1) and its 2-methyl derivative (2) have recently [2] been investigated by ^1H n.m.r. For (2) ΔG^0_{298} 0.85 kcal mol^{-1} in favour of the *ae* conformer was obtained; the same paper applied dipole moments to give 0.62 kcal mol^{-1}, in fair agreement. However, nitrogen inversion in 1,3-dimethyl-1,3-diazacyclohexane (1) remained fast at the lowest temperature attained,[2] although much earlier work had [3] given ΔG^0_{298} 0.54 kcal mol^{-1} from dipole moments. More recently Eliel had found 0.65 kcal mol^{-1} for (1) from n.m.r. chemical shift interpolations,[4] and Riddell [5] ΔG^0_{298} 0.4 kcal mol^{-1} from anancomeric systems. Other work on these compounds has been qualitative rather than quantitative: thus p.e.s. data [6] show merely that both (1) and (2) form conformationally biased equilibrium mixtures.



(1)



(2)

We now find that at 36 °C the ^{13}C spectrum of the dimethyl compound (1) displays four sharp lines as expected for the equilibrating system. An n.O.e. suppressed gated decoupled spectrum demonstrated the intensity ratio 1 : 2 : 2 : 1 which, together with an off resonance decoupled spectrum, allowed assignment of the signals (Table 1).

On lowering the temperature these signals first broaden and then resharpen. Maximum broadening occurs at –120 °C and at low temperatures additional small peaks appear to higher field of the main signals (Figure 1). The four-line set of intense signals must correspond to the diequatorial conformer (1*ee*) while the minor set of five lines is assigned to (1*ae*) (*cf.* Scheme 1). Conformer (1*ae*) should show six lines: the assignments (Table 1) are based on the fact that an axial substituent causes upfield shifts [7] for the ring carbons owing to steric effects. Thus the axial N–*C*H$_3$ signal resonates at higher field (δ 40.6) than the corresponding equatorial N–*C*H$_3$ signal, which is presumably under the intense equatorial N–*C*H$_3$ signal (δ 43.6) of (1*ee*).

$$\Delta G^{\ddagger}_c = 4.57\, T_c\, [9.97 + \log(T_c/\Delta\nu)] \qquad (1)$$

Application of the Eyring equation [8] [equation (1)] gives $\Delta G^{\ddagger}_{153}$ 7.0 $\pm$ 0.3 kcal mol^{-1} † for the conformational process slowed, and integration of the n.O.e. suppressed gated decoupled peaks at –150 °C gives ΔG^0_{123} 0.65

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† The Eyring approximation [8] applies to the case for equal populations. Treatment of this value to obtain *eq*→TS and *ax*→TS $\Delta G_c^{\ddagger}$ components following the method adopted for the analysis of the n.m.r. spectrum of cyclohexyl fluoride by F. A. Bovey, E. W. Anderson, F. P. Hood, and R. L. Kornegay, *J. Chem. Phys.*, 1964, **40**, 3099, gives $\Delta G_c^{\ddagger}$ 6.9 kcal mol^{-1} for *ax*→TS (minor →major).

TABLE 2

^{13}C (25.16 MHz) N.m.r. data [a] for 1,2,3-trimethyl-1,3-diazacyclohexane (2)

		Signals				
Temp. (°C)	Conformer(s)	N–*C*–N	N–*C*H$_2$–C	N–*C*H$_3$	C–*C*H$_2$–C	C–*C*H$_3$
10	(2*ee*) $\rightleftharpoons$ (2*ae*)	80.0	55.9	37.7	22.5	17.8
	b	d	t	AB$_3$q	t	AB$_3$q
−130	(2*ae*)	78.1	*eq.* 57.7 *ax.* 54.3	*eq.* 42.7 *ax.* 33.3	20.4	19.3
Broadening data [c]						
t_c/°C		−110	−40		−110	−40
$\Delta w_{\frac{1}{2}}$/Hz		5	12		8	17
$\Delta\nu$/Hz [d]		72.9	125.8		143.4	151.0
Population (%)	(2*ee*)	6.6			5.2	
	C-methyl *ax*		9.5			11.2
ΔG^0_c ($\pm$0.05 kcal mol^{-1})		0.86	1.04		0.94	1.02
$\Delta G^\ddagger_c$ ($\pm$0.2 kcal mol^{-1})		7.3	10.4		7.1	10.3
Coalescence data						
t_c/°C			−103	−97		
$\Delta\nu$/Hz			87.3	236.3		
$\Delta G^\ddagger_c$ ($\pm$0.2 kcal mol^{-1})			8.0	7.9		

[a] Solvent: CF_2Cl_2–$(CD_3)_2CO$ (2 : 1): δ, downfield from Me_4Si. [b] Obtained from off resonance decoupled spectra. [c] Two broadening phenomena observed (at −110 and −40 °C). [d] Obtained from corresponding values in (1) and methylcyclohexane, as explained in text.

$\pm$ 0.05 kcal mol^{-1} in favour of the (1*ee*) conformer. Compound (1) exists in eight conformers (Scheme 1): the diaxial conformers are expected to be of high energy and the low temperature spectrum can only reasonably be attributed to (1*ee*) and (1*ea*/*ae*). Extrapolation gives ΔG^0_{298} 0.4 $\pm$ 0.1 kcal mol^{-1} in favour of the *ee* conformer which is in fair agreement with the dipole moment result [3] (0.54 kcal mol^{-1}). The process slowed can only reasonably be ascribed to *N*-inversion: signal splitting on ^{13}C n.m.r. cannot occur by stopping ring-inversion alone (*cf.* Scheme 1) and ring inversion is expected to have $\Delta G^\ddagger$ *ca.* 11.3 kcal mol^{-1} [$f\,\frac{1}{2}$].[9]

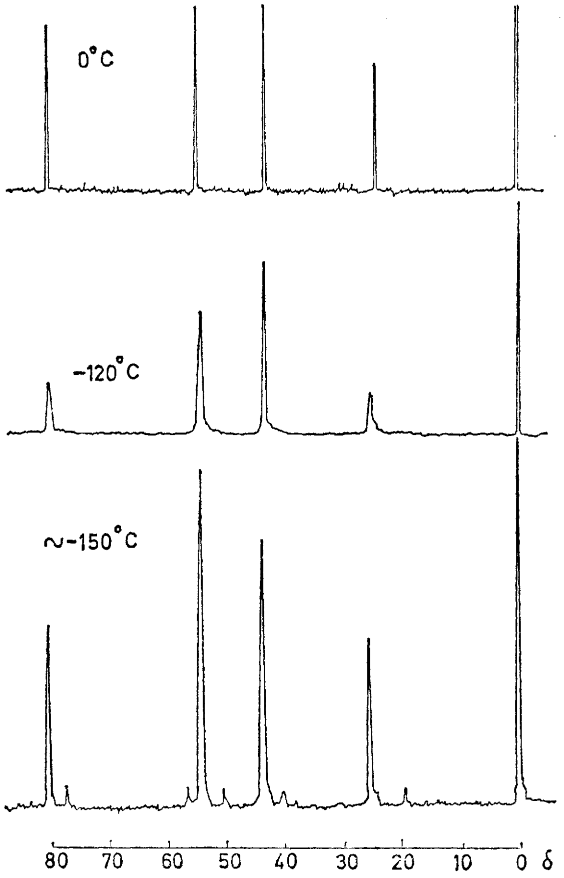

FIGURE 1 ^{13}C Dynamic n.m.r. spectra of 1,3-dimethyl-1,3-diazacyclohexane (1)

The trimethyl compound (2) shows the expected five lines in the ^{13}C spectrum at 36 °C; assignments (Table 2) follow from Overhauser suppressed gated decoupling and off resonance decoupling. The behaviour on lowering the temperature was considerably more complex than that found for (1): two successive broadening and resharpening phenomena occurred (Figure 2).

The first dynamic process slowed is observed as the broadening and resharpening (Figure 2a) of the N–*C*H$_2$–C (δ 55.9) and C–*C*H$_3$ (δ 17.8) signals (Table 2). Although no peaks assignable to minor conformers could be detected, application of the Anet equations [equations (2) and (3)] [10,*] gave for the first coalescence (observed at −40 °C) ΔG^0_{233} 1.03 $\pm$ 0.05 and $\Delta G^\ddagger_{233}$ 10.3 $\pm$ 0.3 kcal mol^{-1}. The chemical shift difference Δν needed for equation (2) was taken as 6 for C–*C*H$_3$[11] and 5 p.p.m. for N–*C*H$_2$–C,[10] as for methylcyclohexane.

$$\Delta w_{\frac{1}{2}} = P\Delta\nu \qquad (2)$$

$$k = 2\pi\Delta\nu = (k_B f T_c/h)\exp(-\Delta G_c^\ddagger/RT_c) \qquad (3)$$

The second more dramatic dynamic process comprises the collapse of the signals for N–*C*H$_3$ and N–*C*H$_2$–C (Figure 2b) and their reappearance as equal doublets (t_c −100 °C). At −120 °C, the spectrum consists of seven lines of equal intensity just as expected for the *ae*-conformer (Scheme 1). The assignment (Table 2) follows as discussed for (1). Application of the Eyring equation for equal populations gives $\Delta G^\ddagger_{173}$ 8.0 $\pm$ 0.2 kcal mol^{-1}. In this temperature region broadening is also observed

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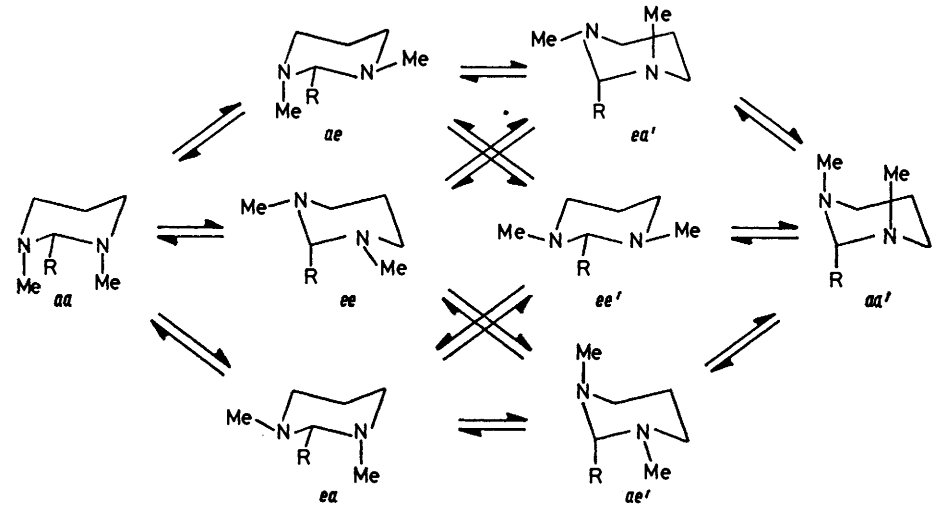
[*] Δν is the chemical shift difference in Hz. $\Delta w_{\frac{1}{2}}$ is the broadening of signals (Hz) in the coalescence region, and corrected for natural line width at half height. P is the fractional population of the minor form. T_c is the temperature (K) of coalescence [for equation (1)] or temperature of maximum broadening of line widths [for equation (3)].



SCHEME 1 Conformational cube for (1; R = H) and (2; R = Me)

of the N-C-N (δ 80.0) and C-CH_2-C (δ 22.5) signals (Figure 2c). From the data collected in Table 2 and using Anet's equations we find ΔG^0_{163} 0.90 ± 0.05 and $\Delta G^{\ddagger}_{163}$ 7.2 ± 0.2 kcal mol^{-1} (minor→TS).

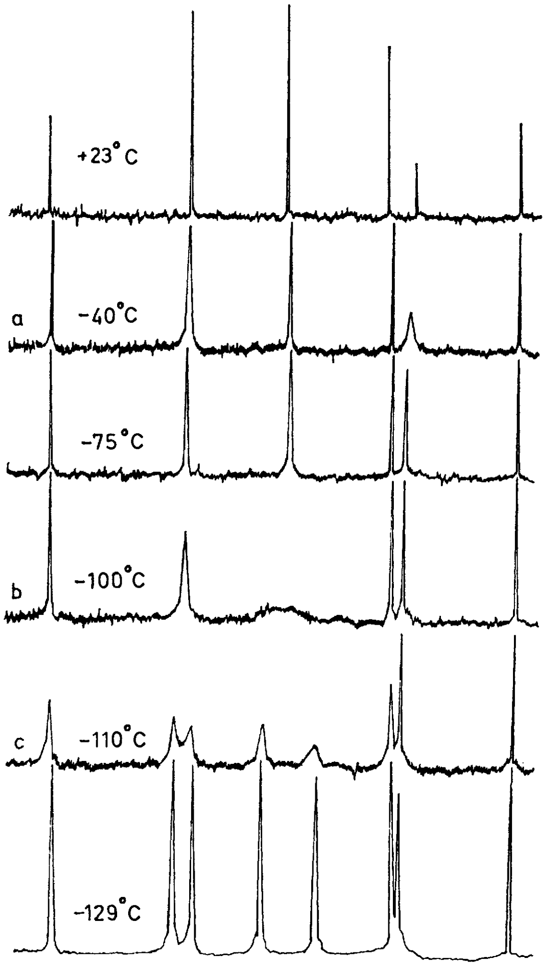
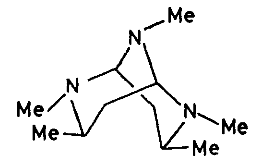


FIGURE 2 ^{13}C Dynamic n.m.r. spectra of 1,2,3-trimethyl-1,3-diazacyclohexane (2) in CF_2Cl_2-$(CD_3)_2CO$: a, first broadening; b, total coalescence; c, second broadening

We interpret the higher temperature coalescence as the slowing of the lowest energy of the three possible ring inversions * and believe that the ΔG^0_{233} value measured refers to the C-methyl group conformational equilibrium. The rather low value of ΔG^0_{233}, 1.03 ± 0.05 kcal mol^{-1}, is ascribed to the influence of the two N-methyl groups adjacent to C-methyl, and to the general reluctance of three adjacent methyl groups to be all equatorial: *cf.* ΔG^0_{172} 1.74 kcal mol^{-1} for methylcyclohexane.[11]

The lower temperature coalescence is ascribed to the 'slowing' of nitrogen inversion. The results compare well with $\Delta G_c^{\ddagger}$ 8.0 kcal mol^{-1} from ^{1}H dynamic n.m.r.[2] and the increase from $\Delta G^{\ddagger}_{153}$ 7.0 kcal mol^{-1} for (1) reflects the buttressing effect of the adjacent C-methyl group which also constrains one of the N-methyl groups to the axial conformation. $\Delta G^{\ddagger}_{163}$ 7.2 ± 0.2 kcal mol^{-1} obtained from Anet's equations (2) and (3)[10] is of course $\Delta G^{\ddagger}_{eq\rightarrow TS}$, whereas $\Delta G^{\ddagger}_{173}$ 8.0 ± 0.2 from the Eyring equation (1) may be assigned to *ax*→TS transition in the interconversion (2*ae*) $\rightleftharpoons$ (2*ea*) *via* the intermediate (2*ee*) (see Figure 3). Thus Anet's equation (3) is confirmed as the limiting form of Eyring's coalescence approximation equation (1). The difference matches quite well with ΔG^0_{163} 0.90 kcal mol^{-1}, which affords support for the reasonable value of $\Delta\nu$ 3 for the N-C-N and 6 p.p.m. for C-CH_2-C, taken from the low temperature spectrum of (1) (Table 1).



(3)

1,3,4,7,8-*Pentamethyl*-1,3,7-*triazabicyclo*[3.3.1]*nonane*.—The bicyclononane (3) was prepared from methylamine

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* It is only after the lowest energy ring inversion is slowed that all conformers no longer invert.

and crotonaldehyde. Primary amines and crotonaldehyde have previously given 1,3-diaminopropenes which are easily reduced to 1,3-diaminopropanes.[12] However, we have now found that under the appropriate conditions (see Experimental section), the reaction with methylamine yields (3). The simple (100 MHz) ^{1}H n.m.r. spectrum (Table 3, Figure 4) immediately suggests a single configuration. The *C*-methyl doublet (δ 0.98) shows that the *C*-methyl groups must be either both axial (4) or both equatorial (3); the axial equatorial isomer (5) would show two doublets. Bicyclo[3.3.1]nonane itself and various heteroanalogues[13] exist in the dichair conformation with the nonbonded 'flagpole' interactions alleviated by some flattening of the chairs.[14] The highly strained diaxial product (4) can thus be excluded. Hence, the isomer formed must be (3) with diequatorial *cis*-*C*-methyl groups: such a product is not unlikely considering the Robinson tropinone synthesis.[15] Specific decoupling and integration allowed assignment of the other ^{1}H n.m.r. signals (Figure 4).

TABLE 3

^{1}H N.m.r.[a] data for some 1,3-diazacyclohexanes

Proton(s)	Compound (δ[a]) (3)[b]	 (6)[b]	 (7)[c]
N–C*H*–N	3.35 (dd, 2 H)	2.72 (dd, 1 H)	3.05 (dd, 1 H)
N–C*H*–CH$_3$	2.75 (m, 2 H)	2.60 (m, 1 H)	2.84 (m, 1 H)
N–C*H*$_3$	2.52 (s, 3 H) 2.20 (s, 6 H)	2.17 (s, 3 H)	
C–C*H*$_2$–C	1.70 (m, 4 H)	1.70 (m, 1 H$_{ax}$) 1.42 (dt, 1 H$_{eq}$)	1.91 (dt, 1 H$_{eq}$) 1.02 (m, 1 H$_{ax}$)
C–C*H*$_3$	0.98 (d, 6 H, $^2J_{H,H}$ 6.3 Hz)	1.09 (d, 3 H, $^2J_{H,H}$ 6.5 Hz)	1.10 (d, 3 H, $^2J_{H,H}$ 6.4 Hz)

[a] Downfield from Me$_4$Si, in p.p.m. [b] In CDCl$_3$. [c] In (CD$_3$)$_2$CO.

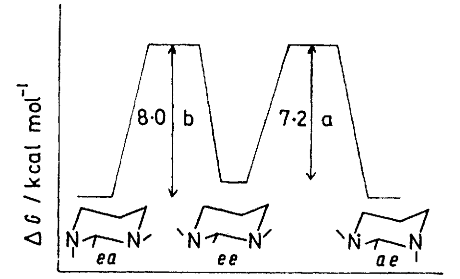
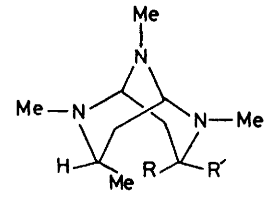


FIGURE 3 Energy level diagram for *N*-inversions in (2): a, obtained from broadening phenomenon [Anet's equations (2) and (3) (ref. 10)]; b, obtained from total coalescence data



(4) R = Me, R′ = H
(5) R = H, R′ = Me

The room temperature decoupled ^{13}C spectrum (Table 4) consists of six lines only, confirming the ^{1}H n.m.r. evidence of the stereospecific symmetric structure (3). Gated decoupling (n.O.e. suppressed mode) shows that one of the signals (δ 40.3) is half as intense as the others. With off resonance decoupling this signal is a quartet, hence it corresponds to the bridge N–*C*H$_3$. The rest of the signals are assigned from the data in Table 4. On lowering the temperature, a dynamic change is observed below −90 °C. The C–*C*H$_2$–C (δ 30.4) signal broadens and resharpens, with maximum broadening ($\Delta w_{\frac{1}{2}}$ 8 Hz) observed at −105 °C. No unambiguous further changes are seen; apparent broadening of the N–*C*H$_3$ (δ 39.2) signal at *ca.* −110 °C is observed, but the compound freezes out at −120 °C.

Compound (3) possesses eight conformers, the 'conformational cube' is shown in Scheme 2. Four of the conformers (3*aa*, *aa*′, *ae*, and *ae*′) possess axial methyl groups and are expected to be of high energy. The six signals observed at −110 °C suggest that the major conformation is (3*ee*), with the *N*-inversion at the bridge nitrogen (3*ee*) $\rightleftharpoons$ (3*ee*′) (Scheme 2) remaining fast at this temperature. Thus the dynamic change near −100 °C is attributed to the 'slowing' of *N*-inversions at the non-bridgehead nitrogen atoms [(3*ee*) $\rightleftharpoons$ (3*ea*) and

TABLE 4

^{13}C N.m.r data[a] for 1,3,4,7,8-pentamethyl-1,3,7-triazabicyclo[3.3.1]nonane (3)

Temp. (°C)	Conformer(s)	Signals N–*C*–N	 N–*C*H–C	 N–*C*H$_3$ (bridge)	 N–*C*H$_3$ (ring)	 C–*C*H$_2$–C	 C–*C*H$_3$
ca. 20	All	75.4	54.8	40.3	39.2	30.4	22.7
	b	d	d	AB$_3$q	AB$_3$q	t	AB$_3$q
−130	(3*ee*) $\rightleftharpoons$ (3*ee*′)	75.0	55.6	40.9		30.7	23.4
Broadening data							
t_c/°C	(3*ae*)/(3*ee*)					−105	
$\Delta w_{\frac{1}{2}}$/Hz[c]						8	
$\Delta\nu^d$/Hz						150	
Population (%)	(3*ae*)					5.3	
ΔG^0_c ($\pm$0.05 kcal mol^{-1})[e]						0.96	
$\Delta G^{\ddagger}_c$ ($\pm$0.2 kcal mol^{-1})[e]						7.3	

[a] Solvent: CF$_2$Cl$_2$–(CD$_3$)$_2$CO (2 : 1); chemical shifts quoted as δ (p.p.m. downfield from Me$_4$Si). [b] Obtained from off resonance spectra. [c] $\Delta w_{\frac{1}{2}}$ is the maximum broadening observed; the width at half height is corrected for the natural line width (2.9 Hz). [d] $\Delta\nu$ obtained from corresponding $\Delta\nu$ from low temperature spectrum of (1): see Table 1. [e] Error limits cover the temperature range $\pm$3°.

(3*ee'*) $\rightleftharpoons$ (3*ea'*)].* The broadening is most dramatic at the C–*C*H$_2$–C carbon, because it is γ to all three *N*-methyl groups. Using Anet's equations (2) and (3), $\Delta G^{\ddagger}_{ax\rightarrow eq} = 7.3 \pm 0.2$ and $\Delta G^{0}_{c} = 0.96 \pm 0.05$ kcal mol^{-1} in favour of the diequatorial conformer (3*ee*) (see Table 4).

trans-*Perhydro*-1,2,4,5,7,8-*hexamethyl*-1,4,7,9b-*tetra-azaphenalene* (6).—The corresponding trisde-*N*-methyl analogue (7) is obtained readily from reaction of crotonaldehyde and ammonia.[16] The recently reported[17] ¹H n.m.r. spectrum of (7) has demonstrated the *trans*-ring fusions in (7) and that the three *C*-methyl groups are all equatorial (see Figure 5a). The ^{13}C n.m.r. spectrum (Table 5) confirms the symmetrical *trans*-structure: only four signals are observed in the ^{1}H noise decoupled spectrum and assignments follow from the off resonance spectrum.

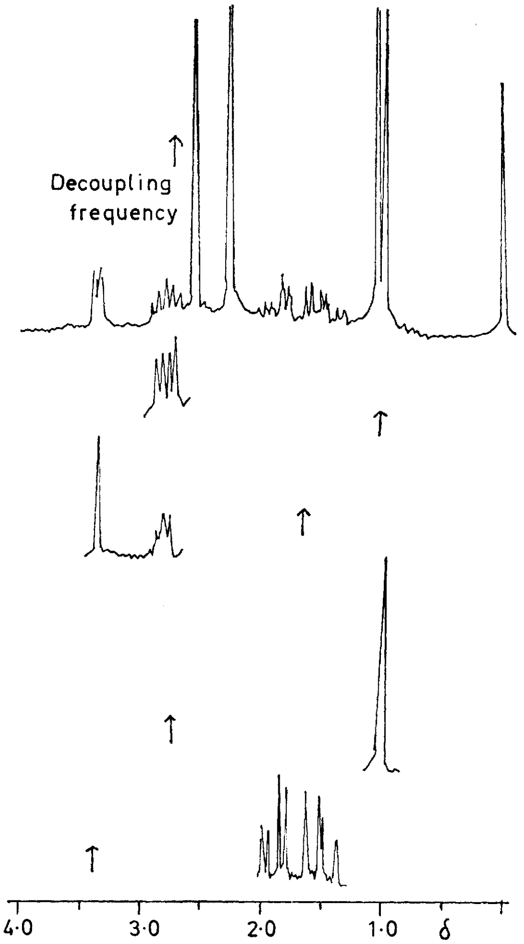
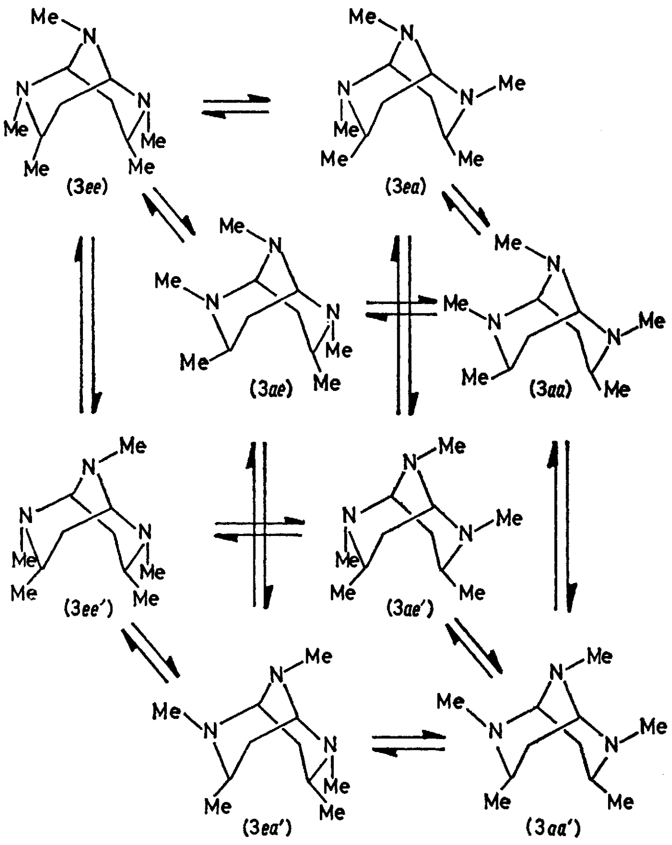


FIGURE 4 ^{1}H N.m.r. spectrum of *cis*-1,3,4,7,8-pentamethyl-1,3,7-triazabicyclo[3.3.1]nonane (3) and some decoupling results for (3)

Recently, the perhydroazatrioxaphenalene (8) has been synthesised[18] in two forms, *cis*- and *trans*-isomers, analogous to the tetra-azaphenalene configurations: the



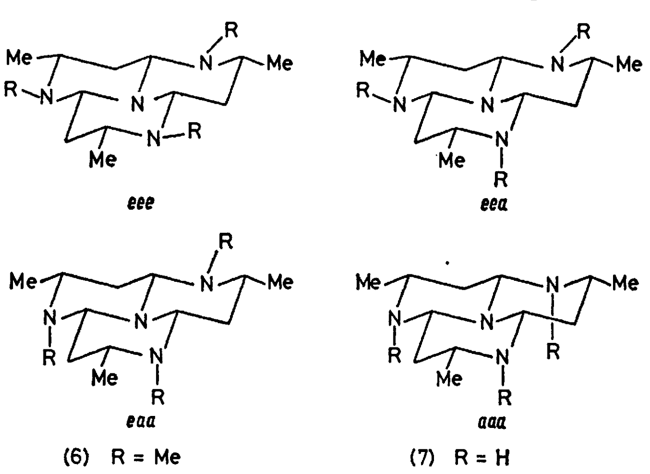
SCHEME 2 Conformational cube for (3)

TABLE 5

^{13}C N.m.r. data[a] for *trans*-perhydro-2,5,8-trimethyl-1,4,7,9b-tetra-azaphenalene (7)

	Temp. (°C)	Signal assignment N–*C*–N	N–*C*H–C	C–*C*H$_2$–C	C–*C*H$_3$
Chemical shift δ (p.p.m.)[b]	*ca.* 36	72.7	49.6	42.1	22.2
Multiplicity[c]		d	d	t	AB$_3$q

[a] Solvent: (CD$_3$)$_2$CO; JEOL FX-100 (25.05 MHz). [b] Downfield from Me$_4$Si. [c] Obtained from off resonance spectra.



SCHEME 3

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* This implies that the bridge nitrogen inverts much more rapidly than that observed for 9-methyl-9-azabicyclo[3.3.1]nonane (S. F. Nelsen, G. R. Weisman, E. L. Clennan, and V. E. Peacock, *J. Amer. Chem. Soc.*, 1976, **98**, 6893). This may be perhaps due to flattening of the six-membered rings expanding the C(2)N(1)C(6) angle.

major isomer was confirmed by ^{13}C n.m.r. to be *trans*-fused.[18]

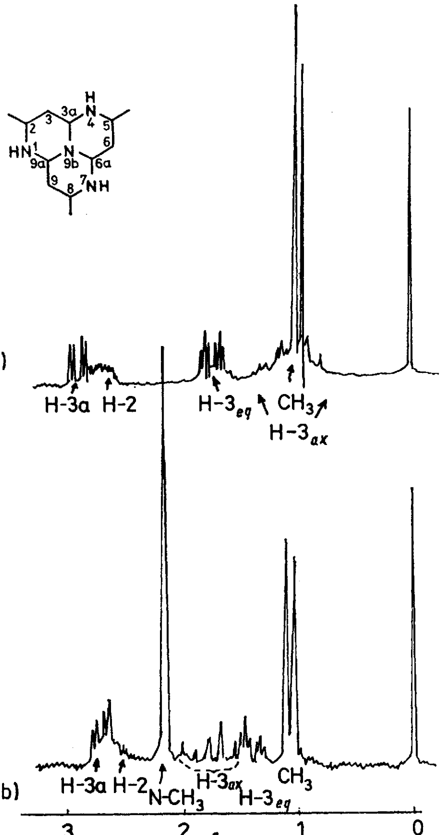
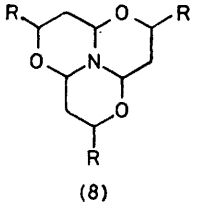


FIGURE 5 ^{1}H N.m.r. spectra at *ca.* 36 °C, (a) of *trans*-perhydro-2,5,8-trimethyl-1,4,7,9b-tetra-azaphenalene (7) in $(CD_3)_2CO$ at 100 MHz; (b) of *trans*-perhydro-1,2,4,5,7,8-hexamethyl-1,4,7,9b-tetra-azaphenalene (6) in $CDCl_3$ at 100 MHz

Methylation of (7) to the desired tri-*N*-methyl compound (6) was finally achieved (after many attempts [19]) with HCHO and $NaBH_3CN$ in acetonitrile.[20] ^{1}H N.m.r. shows the retention of all the signals of the parent (7), together with the *N*-methyl signal (δ 2.17) in correct integration. The tricycle (6) can exist in four conformations (Scheme 3) *eee*, *eea* (triply degenerate), *eaa* (triply degenerate), and *aaa*. The ^{1}H n.m.r. spectrum does not show any dramatic conformational change down to −130 °C, indicating a conformationally biased system, either *eee* or *aaa*.



(8)

At 0 °C, a simple five line decoupled ^{13}C n.m.r. spectrum was observed (Figure 6) and assignments were made using off resonance decoupling (Table 6). The appearance of only five signals confirmed the rigid *trans*-symmetric structure for (6). This spectrum persists down to −90 °C when the N-CH_3 (δ 33.5) and C-CH_2-C (δ 29.7) signals dramatically collapse into unequal doublets (Figure 6). This coalescence is shown to a lesser degree by the other signals as well. Viscosity broadening and sample freezing prevent well resolved spectra at temperatures below −130 °C. From the temperature of coalescence, $\Delta G^{\ddagger}_c = 8.0 \pm 0.2$ and $\Delta G^0_c = 0.4 \pm 0.1$ kcal mol^{-1} (Table 6) were measured using equation (1).

From classical energy considerations, it is difficult to decide which conformation(s) for (6) will predominate: conformation (6*aaa*) has six 1,3-*syn*-axial interactions whereas (6*eee*) has only three '*peri*' repulsions but considerable 1,3-lone-pair–lone-pair repulsion. However, comparison of (6) with the result obtained for (2) (*i.e.* axial equatorial preferred) it may be concluded that (6*aaa*) is the preferred conformation with (6*eaa*) as the minor form. Further evidence for (6*aaa*) as the major form derives from the chemical shifts. The minor signals for N-*C*-N, N-*C*-CH_3, C-CH_2-C, and C-CH_3 appear at low field: upfield shifts have been observed for carbons adjacent to atoms bearing axial substituents in alkylcyclohexanes and alkylpiperidines.[21] Thus the intense upfield signals indicate a preponderance of (6*aaa*).

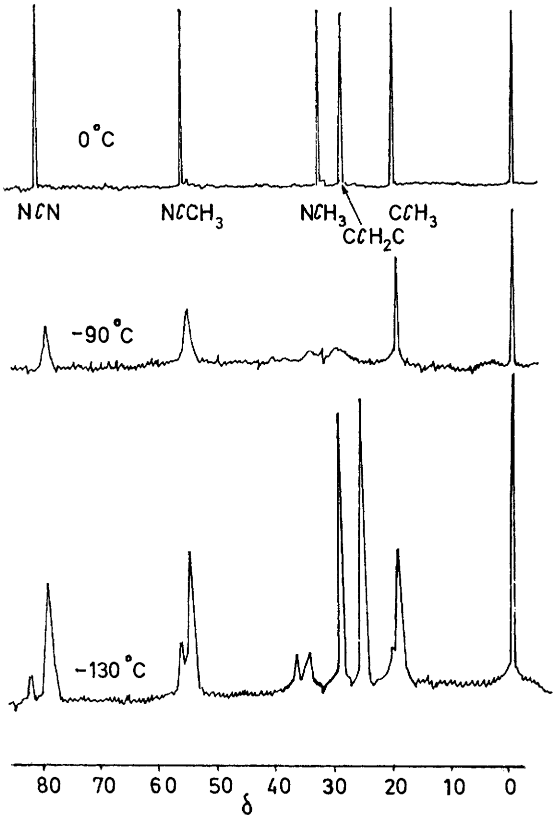


FIGURE 6 ^{13}C Dynamic n.m.r. spectrum of *trans*-perhydro-1,2,4,5,7,8-hexamethyl-1,4,7,9b-tetra-azaphenalene (6)

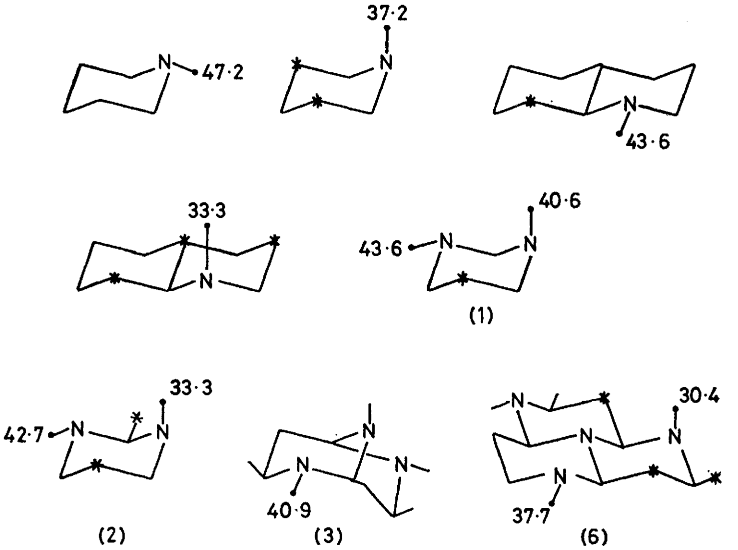
^{13}C *N.m.r. Chemical Shifts.*—The upfield shift of ^{13}C n.m.r. signals, due to steric polarization of γ-C–H bonds

TABLE 6

^{13}C N.m.r. data [a] for 1,2,4,5,7,8-hexamethylperhydro-1,4,7,9b-tetra-azaphenalene (6)

Temp. (°C)	Conformer(s)	Signals				
		N–*C*–N	N–*C*H–C	N–*C*H$_3$	C–*C*H$_2$–C	C–*C*H$_3$
ca. 0	All	82.0	57.0	33.5	29.7	20.9
	b	d	d	AB$_3$q	t	AB$_3$q
−140	(6*aaa*)	80.5	55.9	30.4	26.5	20.3
	(6*aae*) [c]	82.9	57.9	37.7	35.4	21.5
Coalescence data						
t_c/°C		−105	−105	−100	−100	−105
$\Delta\nu$/Hz		60.4	50.3	183.7	223.9	30.2
Population (%) [d]	(6*aaa*)	86	78	81	89	*f*
ΔG^0 ($\pm$0.10 kcal mol^{-1}) [e]		0.48	0.33	0.38	0.55	*f*
$\Delta G^{\ddagger}_c$ ($\pm$0.3 kcal mol^{-1}) [e]		8.0	8.0	7.9	7.8	8.2

[a] Solvent: CF_2Cl_2–CD_3OD (2 : 1): δ downfield from Me_4Si. [b] Obtained from off resonance spectra. [c] Rest of *aae* signals under *aaa* (major) peaks. [d] Obtained from n.O.e. suppressed gated decoupling (pulse delay 4 s) with the major signals corrected for peak weight contribution from the signals of the *aa* part of the *eaa* (minor) conformer. [e] Error limits cover the temperature range ±3°. [f] Signal overlap precludes relative peak ratio determination.



SCHEME 4 ^{13}C N.m.r. shifts of some N–*C*H$_3$(·) groups in different environments. γ-Gauche interactions are represented by *

by axial substituents is well documented as the 'γ-gauche effect.'[21] It is an aid [7] to elucidation of the signals of individual conformers in a 'frozen' ^{13}C n.m.r. spectrum. If the shift of the axial *N*-methyl carbon atom in *N*-methylpiperidine is taken as δ 37.2,[22] the corresponding shift (Scheme 4) in 1,3-dimethyl-1,3-diazacyclohexane (1) is further downfield (δ 40.6) due to substitution of one of the γ-C–H interactions (marked *) by a γ-nitrogen lone pair which has a reduced shielding effect (*ca.* +1.6 p.p.m.). The equatorial *N*-methyl resonance in (1) is itself shifted upfield to δ 43.6, *cf.* the corresponding shift in *N*-methylpiperidine is δ 47.2.[22] This ^{13}C spectral characteristic is an example of the γ-antiperiplanar heteroatom effect.[23]

In 1,2,3-trimethyl-1,3-diazacyclohexane (2), the axial *N*-methyl carbon atom resonates further upfield (δ 33.3) because of an extra γ-gauche interaction experienced from the equatorial *C*-methyl group: *cf.* the axial *N*-methyl group in *trans*-*N*-methyldecahydroquinoline has three γ-gauche C–H interactions and resonates at δ 33.2 Even the equatorial *N*-methyl carbon resonance in (2) is shifted upfield (δ 42.7), albeit to a lesser degree, by steric interaction with the adjacent *C*-methyl group. This latter shift affords good evidence for the *ee* conformation in (3) (N–*C*H$_3$ signal at δ 40.9): axial *N*-methyl groups in (3*ae*) should resonate further upfield.

The C–H bond polarization is accentuated further in hexamethylperhydrotetra-azaphenalene (6) where the axial *N*-methyl shift is influenced by three γ-gauche interactions as well as a 1,3-*syn*-axial nitrogen lone pair polarization. Equatorial N–*C*H$_3$ signals in (6) are also significantly shifted upfield (δ 37.7) due to '*peri*' C–H and adjacent *C*-methyl interactions (*cf.* *N*-methylperhydroquinoline). The use of the γ-gauche effect is admirably demonstrated in this series of 1,3-diazacyclohexanes.

EXPERIMENTAL

The ^{1}H n.m.r. spectra were measured with a Varian HA-100 spectrometer. Temperatures were measured by use of methanol shift [24] down to −90 °C. Below −90 °C, a platinum thermometer set into the low temperature probe was used; this was checked by comparison with a copper–constantan thermocouple mounted in an n.m.r. tube and found to be in agreement, ±1 °C. ^{13}C N.m.r. spectra were obtained on a Varian XL-100 machine operating at 25.16 MHz employing an internal deuterium lock in 12 mm tubes.

Where n.O.e. suppressed gated decoupling was conducted, a pulse delay of 4 s was used. Off resonance spectra were obtained on the JEOL FX-100 spectrometer (^{13}C observed at 25.05 MHz frequency), the irradiation offset was 50.8 KHz and power low: 10 mm tubes were employed.

Preparation of Compounds (1), (2), *and* (7).—1,3-Dimethyl-1,3-diazacyclohexane (1)[25] (70%), b.p. 60 °C at 20 mmHg (lit.,[25] 126 °C at 760 mmHg), 1,2,3-trimethyl-1,3-diazacyclohexane (2)[26] (*ca.* 90%), b.p. 63 °C at 20 mmHg (lit.,[26] 70 °C at 38 mmHg), and *trans*-perhydro-2,5,8-trimethyl-1,4,7,9b-tetra-azaphenalene (7),[16] m.p. 102—103 °C (lit.,[16] 102 °C), were made by literature methods.

cis-1,3,4,7,8-*Pentamethyl*-1,3,7-*triaza*[3.3.1]*bicyclononane* (3).—To a stirred solution of aqueous $MeNH_2$ (50 ml, 37%) was added dropwise freshly distilled crotonaldehyde (10 ml, 8.5 g), the temperature being maintained below 0 °C. The mixture was kept at 0 °C for two days. Water was vacuum distilled and the residue extracted with CH_2Cl_2 (3 × 25 ml). The extract was dried over K_2CO_3 (anhydrous) for 1 h; solvent removal yielded the *triazanonane* (3), a viscous oil, b.p. 55 °C at 0.15 mmHg (Found: C, 67.0; H, 11.8; N, 20.8. $C_{11}H_{23}N_3$ requires C, 67.0; H, 11.7; N, 21.3%); m/e 197 (P^+), 182 ($P^+ - 15$), and 166 ($P^+ - 31$).

trans-*Perhydro*-1,2,4,5,7,8-*hexamethyl*-1,4,7,9b-*tetra-azaphenalene* (6).—Compound (7) (0.5 g, 0.002 mol) was dissolved in MeCN (20 ml). Formaldehyde (37%, 3 ml) was added dropwise to the stirred solution. Sodium cyanoborohydride (0.75 g, 0.01 mol) was added to the reaction mixture which was stirred for 45 min at 25 °C. The pH was maintained as *ca.* 7 with glacial HOAc. After 15 min more at pH 7 the solvent was evaporated off *in vacuo*. Saturated aqueous KOH was added until the solution was basic when it was extracted with CH_2Cl_2 (3 × 25 ml), to yield compound (6) as a pale yellow viscous oil, b.p. 82 °C at 0.1 mmHg, which was characterised by t.l.c., ^1H, and ^{13}C n.m.r. (high hygroscopicity precluded satisfactory analysis); m/e 266 (P^+) and 251 ($P^+ - 15$).

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