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CONFORMATIONAL STUDIES BY DYNAMIC NMR—28[1]

STEREOMUTATIONS IN SOME DI-, TRI- AND TETRAALKYLHYDRAZINES

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Abstract—Low temperature NMR spectra allowed us to "freeze" some of the internal motions in a number of di-, tri- and tetraalkylhydrazines and to measure the corresponding free energies of activation. In particular, tetramethylhydrazine ($Me_2N—NMe_2$) was found to have, at −150°, two pairs of diastereotopic methyls: this is due to the fact that both N-inversion and N,N-rotation are slow at this temperature and that a *gauche* conformation is adopted. The observed barrier (6.0 kcal mol^{-1}) has been attributed to N,N-rotation, the barrier due to N-inversion being higher and not measurable via NMR in the presence of a concomitant fast rotation. In other cases, notably $Pr^iMeN—NH_2$, $Me_2N—NPr^i_2$ and $Pr^i_2N—NHMe$, two different motions (inversion and rotation) were detected. In the case of $Me_2N—NHMe$ it was also possible to observe the first example of anisochronous behaviour of nitrogen-bonded methyls (Me_2N) induced by an aminic nitrogen that becomes chiral at low temperature.

The stereomutations occurring in alkyl hydrazines have been studied and discussed, amongst others, by Dewar and Jennings,[2,3] and Fletcher and Sutherland[4] by proton NMR. On the basis of the evidence collected on the conformation of various hydrazines Dewar and Jennings were able to predict that tetramethyl hydrazine ($Me_2N—NMe_2$, **1**) should adopt a *gauche* conformation (see Scheme 1) where the two pairs of methyls would be diastereotopic.[3] Unfortunately, not even at −150° could they see the two different Me signals they expected in the NMR spectrum. More recently we were able to show that ^{13}C-NMR does allow us to detect[5] the restricted motion of 2,3-dimethylbutane ($Me_2CH—CHMe_2$) which is isoelectronic with Me_2NNMe_2. Research was thus undertaken to study, via ^{13}C-NMR, the dynamic behaviour of Me_2NNMe_2 as well as of other alkyl hydrazines not yet investigated. ^{13}C-NMR has been shown to be quite a powerful tool in the investigation of motions involving both rotation and N-inversion.[6] In order to detect N-inversion in alkyl hydrazines by low temperature ^{13}C-NMR, either of the following conditions has to be fulfilled.

(i) The molecule must contain a "probe" (e.g. isopropyl) where two nuclei become anisochronous when a nitrogen is "frozen" in a pyramidal situation.[3,6–8]
(ii) When such a probe is lacking, the N,N-rotation, in addition to N-inversion, has also to be "frozen".

Furthermore, both cases require that the hydrazine has some kind of asymmetry. In case (i) no plane of symmetry bisecting the two nuclei of the "probe" must be present, this means that the nitrogen atom must behave as a prochiral centre.[8] In case (ii) the hydrazine must also adopt a conformation that does not have two planes of symmetry.

It has also to be stressed that these are only necessary but not sufficient conditions to detect N-inversion in hydrazines.

RESULTS AND DISCUSSION

At −150° the ^{13}C-NMR spectrum of tetramethyl hydrazine (1) shows (Fig. 1) two signals of equal intensity separated by 1.2 ppm (280 Hz). The failure[3] of detecting the corresponding effect at ^{1}H-NMR was

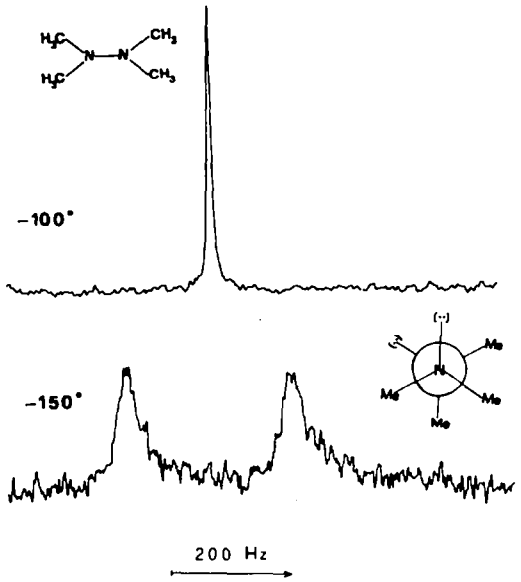


Fig. 1. ^{13}C-NMR spectrum (25.16 MHz) of Me_2NNMe_2 (1) in $CHF_2Cl—CHFCl_2$ at −100° (upper), displaying one line for four equivalent methyls and at −150°, where the *gauche* conformation renders the two pairs of methyls diastereotopic.

Scheme 1. Newman projection along the NN axis of Me_2NNMe_2 (1).

therefore due only to the insufficient chemical shift difference of the protons. As predicted in Dewar and Jennings,[3] two lines of equal intensity require the existence of a *gauche* rather than a *trans* conformation (Scheme 1).

No signals belonging to the *trans* conformation could be observed, contrary to the isoelectronic hydrocarbon case ($Me_2CH—CHMe_2$) where the *trans* and *gauche* conformers were present according to their statistical distribution.[5,9] *Trans* conformation has only been observed in extremely crowded bicyclic hydrazines.[10] In order to explain the spectrum of 1 at $-150°$ both internal motions (N-inversion and N,N-rotation) have to be slow in the NMR time scale. In other words situation (ii) is obeyed. The barrier measured at the coalescence point ($\Delta G^{\neq} = 6.0$ kcal mol^{-1}, Table 1) is thus the lowest between N,N-rotation and N-inversion.

In order to have some indication about the motions corresponding to this barrier, the spectra of other substituted hydrazines were investigated for comparison. The following alkyl hydrazines were thus examined in this work:

Me_2NNMe_2 (1) Pr^iMeNNH_2 (2)

$Pr^i_2NNH_2$(3) $Pr^iBu^tNNH_2$ (4)

Et_2NNEt_2 (5) Me_2NNEt_2 (6)

$Me_2NNPr^i_2$ (7)

Me_2NNHMe (8) Pr^i_2NNHMe (9)

It has been recognised that in a homogeneous series the rotational barrier about a sp^3—sp^3 bond increases with the bulkiness of the substituents[6,11–15] (steric deceleration) whereas the barrier to N-inversion seems to decrease (steric acceleration).[4,6,16] This trend could then be used, albeit with extreme caution, to help in deciding which type of motion is observed in hydrazines.

Dialkylhydrazines

To check the above mentioned trend in hydrazines, at least with regard to N-inversion, a number of 1,1-disubstituted hydrazines ($R_1R_2N—NH_2$) were investigated.

Owing to the small dimension of NH_2, the N,N-rotation is expected to be faster with respect to the rate of inversion at R_1R_2N and the interaction between these two motions is likely to be small. Accordingly, the inversion barrier at the alkyl substituted nitrogen in $R_1R_2N—NH_2$ will essentially depend upon the dimensions of R_1 and R_2.

As a probe to detect N-inversion in 1,1-dialkylhydrazines we selected the isopropyl group ($R_1 = Me_2CH$) that displays two ^{13}C signals (anisochronous methyls) when Pr^iN inversion is slow in the NMR time scale. The values of the free energies of activation for N-inversion when R_2 = Me (2), = Pr^i (3) = Bu^t (4) are collected in Table 1 and the ^{13}C shifts in Table 2. It is obvious that, within this series, the larger the R_2 dimension, the lower is the inversion barrier. It should also be noted that in $Pr^iBu^tN—NH_2$(4) the methyls of the t-butyl become anisochronous at low temperatures (Table 2, two are accidentally coincident and the third clearly separated). This additional motion is due to the restricted Bu^t—N rotation that is invisible in the presence of fast N-inversion, but becomes observable when the latter is "frozen". This phenomenon has been observed and discussed in detail in the case of amines;[6,7,17] it has been shown that $\Delta G^{\neq}$ values for t-butyl rotations higher than for N-inversion, cannot be measured by dynamic NMR, even when its effects on the NMR spectra are detected at low temperature.

In the case of $Pr^iMeN—NH_2$ (3) a second motion, in addition to N-inversion, was observed. Below $-150°$, most of the signals further split into a pair of lines, with a relative intensity 2.5 : 1 (Table 2). Thus we observed two such signals for CH, NCH_3 and for one of the two

Table 1. Free energies of activation (kcal mol^{-1}) for internal motions measured (^{13}C-NMR) at the temperatures indicated for the hydrazines **1**, **3**, **7** and **8** in CHF_2Cl–$CHFCl_2$ (4 : 1) and for **2**, **4**, **5**, **6** and **9** in CHF_2Cl

Compound		$\Delta G^{\neq}$	Temperature	$\Delta G^{\neq}$	Temperature
Me_2NNMe_2	(1)	6.0 ± 0.1 (N,N-rotation)	$-137°$		
Pr^iMeNNH_2	(2)	9.3 ± 0.1 (Pr^iMeN inversion)	$-78°$	5.7 ± 0.3 (N—Pr^i rotation)	$-153°$
$Pr^i_2NNH_2$	(3)	7.8 ± 0.1 (Pr^i_2N inversion)	$-104°$		
$Pr^iBu^tNNH_2$	(4)	7.0 ± 0.1 (Pr^iBu^tN inversion)	$-125°$		
Et_2NNEt_2	(5)	6.75 ± 0.15 (N,N-rotation)	$-127°$		
Me_2NNEt_2	(6)	6.75 ± 0.2	$-118°$; $-131°$		
$Me_2NNPr^i_2$	(7)	7.5 ± 0.1 (Me_2N inversion)	$-112°$	5.1 ± 0.3 (Pr^i_2N inversion)	$-160°$
Me_2NNHMe	(8)	7.5 ± 0.1 (Me_2N or NHMe inversion)	$-111°$		
Pr^i_2NNHMe	(9)	9.85 ± 0.1 (N,N-rotation)	$-63°$	5.6 ± 0.15 (NHMe inversion)	$-148°$

Table 2. Chemical shifts (ppm from TMS) of the ^{13}C signals (25.16 MHz) of hydrazines **1–9**, in the solvents of Table 1, at temperatures where there is a single line for a given carbon and at temperatures were some of the lines are split

Compound		Temperature	NMe	NCH_2	NCH	Me (isopropyls)	Me (others)
Me_2NNMe_2	1	−130°	38.8				
		−150°	44.6; 33.4				
Pr^iMeNNH_2	2	−40°	45.2		59.4	18.1	
		−100°	45.0		59.2	19.4; 17.0	
		−155°	47.7; 44.5		64.4; 58.1	20.2; 22.6, 10.8	
$Pr^i_2NNH_2$	3	−40°			53.7	18.9	
		−124°			53.6	21.5; 16.25	
$Pr^iBu^tNNH_2$	4[a]	−80°			49.1	20.1	22.9 (3 Me)
		−140°			48.5	23.3; 16.95	28.8 (2 Me); 19.7 (1 Me)
Et_2NNEt_2	5	−80°		43.2			14.4
		−150°		44.1; 40.4			13.2
Me_2NNEt_2	6	−112°	38.6	42.6			13.5
		−151°	44.0; 32.9	44.4; 40.3			13.4
$Me_2NNPr^i_2$	7	−107°	45.1		48.3	22.4	
		−127°	44.9		50.3; 47.0	24.0; 20.5	
Me_2NNHMe	8	−40°	35.9[b] and 47.4[c]				
		−140°	35.9[b] and 49.3[c]; 45.2[c]				
Pr^i_2NNHMe	9	−25°	41.7		53.7	19.8 (4 Me)	
		−90°	41.7		53.7	21.8 (2 Me); 17.3 (2 Me)	
		−151°	41.6		55.2; 51.0	22.3 (2 Me); 22.3 (1 Me), 12.4 (1 Me)	

[a] Signal of quaternary carbon at 59.0 ppm.
[b] Signal of NHMe.
[c] Signals of NMe_2.

anisochronous isopropyl methyls that had been previously split (below −80°) into pairs of lines of equal intensity. There are two possible explanations to account for this second dynamic behaviour, whose barrier has been estimated (line shape simulation) as 5.7 ± 0.3 kcal mol^{-1}.

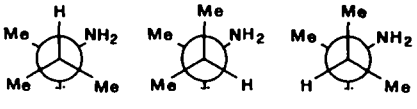
(1) The rotation about the Me_2CH—N bond has been "frozen": three different conformers (Scheme 2) can thus be generated, two of which are populated appreciably according to the observed ratio, the third being negligible.

(2) Both NH_2 inversion and NN rotation are "frozen"; again three conformers can be obtained, two of which (most likely to be those with the lone pair electrons in the *gauche* position) could be populated appreciably according to the observed ratio (Scheme 3).

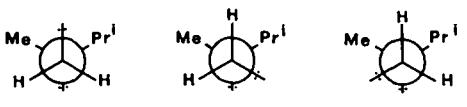
We cannot discriminate unambiguously between the two cases: however it has to be remembered that N—Pr^i rotation has been observed in a molecule (Pr^iMeNEt) of similar bulkiness[7c] with a barrier (5.6 kcal mol^{-1}) very close to that we measured in **2**. However, no report of NH_2 inversion observable by NMR in solution has yet appeared: it is likely that this motion is too fast to be detected by this technique. We wish to point out that we did not find evidence of restricted N—Pr^i rotation in the other hydrazines containing the Pr^i moiety investigated in the present study. Although this fact might cast some doubt on the interpretation of this internal motion in **2**, it could still be explained either with an equilibrium totally biased toward a single rotamer or with a lower (< 5.5 kcal mol^{-1}) rotational barrier that would prevent detection in the other hydrazines of the exchange phenomenon.

Tetraalkylhydrazines

Even though we have verified in 1,1-dialkylhydrazines that the bulkier the substituent the lower is the barrier to N-inversion, such a trend should not be assumed to be the case for every hydrazine. In the tetraalkylhydrazines R_2N—NR'_2, where the two barriers for N-inversion (NR_2 and NR'_2) are likely to couple with each other and with N,N-rotation as well, the "rule" is probably more questionable. In other words the effect of the "bulkiness" of NR'_2 on both N,N-rotation and NR_2 inversion will be different when the NR'_2 inversion is fast (the system will be dynamically planar) with respect to the case when NR'_2 inversion and N,N-rotation are slow (pyramidal conformation). Therefore, although the trend can still hold when one compares hydrazines with major differences in the bulkiness of their substituent, it cannot be used with



Scheme 2. Newman projection along the CH—N axis of Pr^iMeN—NH_2 (**2**), showing the conformers arising from the restricted rotation of isopropyl and the slow inversion of the alkyl substituted nitrogen.



Scheme 3. Newman projection along the NN axis of Pr^iMeN—NH_2 (**2**), showing the conformers arising from the restricted N,N-rotation and the slow inversion of both nitrogens.

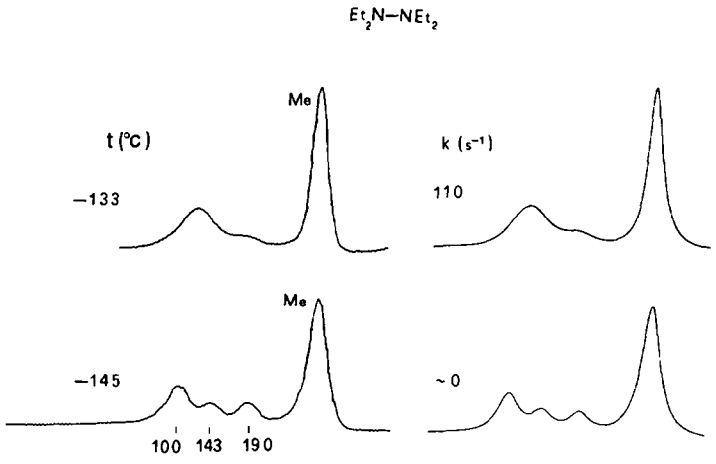


Fig. 2. ^{1}H-NMR spectrum (100 MHz) of Et_2NNEt_2 (5) in CHF_2Cl (left). At $-145°$ the internal motions are slow ($k \cong 0\ s^{-1}$); at $-133°$ exchange occurs between CH_2 signals at 100 Hz with those at 143 and 190, as shown by the computer simulated (right) spectrum ($k = 110\ s^{-1}$). This corresponds to N,N-rotation rather than N-inversion. The chemical shifts are arbitrary.

certainty as a precise guideline to explain the barriers observed in every single case.

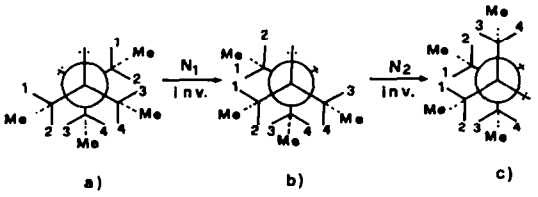
At low temperatures Me_2NNMe_2 (1) and Et_2NNEt_2 (5) give a ^{13}C spectrum with two different signals for the carbons bonded to nitrogen. Below $-127°$ the line of methylenic carbons of (5) splits into two whereas that of the methyls remains as a singlet. We attribute this fact to too small a shift difference of the CH_3 lines in (5).

The barrier measured at the coalescence (6.75 kcal mol^{-1}) is higher than that measured for 1 and, as in tetramethylhydrazine, represents the barrier of the faster process between inversion and rotation. However the 100 MHz proton spectrum (that has invisible J_{HH} values, below $-120°$ owing to the viscosity) displays, at $-145°$, three different lines for the CH_2 hydrogens (Fig. 2). As proved by the corresponding ^{13}C spectrum they are originated by a *gauche* conformation where both N-inversion and N,N-rotation are "frozen".

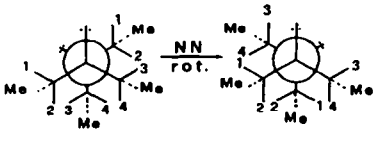
Two of the four diastereotopic hydrogens give overlapping lines, owing to a shift difference smaller than line width. Accordingly in Fig. 2 the three lines have a 2:1:1 relative intensity. Let us assign the two coincident lines (whose shift is arbitrarily taken as 100 Hz) to H1 and H2 in Scheme 4(a) and the other two lines (relative shifts 143 and 190 Hz respectively) to H3 and H4.

If N-inversion occurs at both nitrogens (N_1 and N_2) even in the presence of a "frozen" N,N-rotation (i.e. $\Delta G^{\neq}_{rot} > \Delta G^{\neq}_{inv}$) the "outer" CH_2 hydrogens (labelled 1 and 2 in Scheme 4(a)) will take the place of the "inner" (i.e. of H3 and H4)[4] as shown in Scheme 4(c). Accordingly the line corresponding to H1 will exchange with the line of H4 (or H3) and that of H2 with that of H3 (or H4). At the same time the N-inversion will cancel the prochirality of the nitrogens so that hydrogens *within* each methylic group (1,2 and 3,4 respectively) will become isochronous. In other words, N-inversion will also make H1 exchange with H2, and H3 with H4. This means that nitrogen inversion, even in the absence of N,N-rotation, will make all the hydrogens exchange with each other. However, if N-inversion is "frozen" and N,N-rotation occurs (i.e. $\Delta G^{\neq}_{rot} < \Delta G^{\neq}_{inv}$), then H1 will exchange with H3 (or H4) and H2 with H4 (or H3), but the prochiral nitrogen will keep H1 and H2 anisochronous (the same will hold for H3 and H4), thus avoiding H1 exchanging with H2 and H3 exchanging with H4 (Scheme 5).

The simulation of the experimental spectrum in the range $-145°$ to $-133°$ (Fig. 2) could be obtained by exchanging the line at 100 Hz with those at 143 and 190 Hz; this corresponds to the exchange of H1 with H3 and H2 with H4 (since the shifts assigned to H1 and H2 are coincident, this is the same as exchanging H1 with H4 and H2 with H3). This process corresponds to the exchange due to N,N-rotation and the measured $\Delta G^{\neq}$ (6.75 ± 0.15 kcal mol^{-1}) is therefore that of a rotational barrier. On the contrary, simulation with a model where all the four hydrogens exchange with each other (i.e. N-inversion) failed to reproduce the experimental



Scheme 4. Newman projection of Et_2NNEt_2 along the NN axis showing the stereomutations due to the inversion of the first and second nitrogen. The nitrogen labelled N_2 is indicated by the circle.



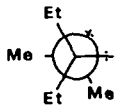
Scheme 5. Newman projection of Et_2NNEt_2 (5) along the NN axis showing the stereomutations due to rotation along the NN bond.

patterns in the mentioned range, whatever the rate constant employed. We also checked that the arbitrary assignment of the shift to the hydrogens of Scheme 1 did not affect the conclusion. In fact, if the two coincident signals (at 100 Hz) are assigned to H1 and H3, rather than to H1 and H2, and the upfield signals (at 143 and 190 Hz) to H2 and H4, the theoretical line shape will not be modified in the case of an N-inversion model. For, all the hydrogens have to exchange with each other with the same rate constant and the shift assignment is thus immaterial; consequently inversion cannot be the faster of the two dynamic processes, whatever assignment is assumed. On the other hand, the model of an N,N-rotation predicts different line shapes, depending on the assignment; we found that the experimental spectrum at $-133°$ could not be reproduced if the assignment of Scheme 4 is reversed. It seems therefore that the only way of reproducing the spectra is the use of a rotational model and of the shift assignment as in Scheme 5. The $\Delta G^{\neq}$ measured at the proton is equal to that measured at ^{13}C.

Having found that rotation is faster than N-inversion in Et_2NNEt_2, one could, in principle, detect at higher temperature the effects due to N-inversion on the proton line shape.[18] However, this could be accomplished, in practice, only if the difference between the two $\Delta G^{\neq}$s is sufficiently high,[7c,18] but this does not seem to be the case for hydrazine **5**. For, at temperatures higher than $-130°$ the spectral simulation could no longer be achieved with the rotational model (this corresponds to rate constants for rotations higher than $150\,s^{-1}$). The signals, in fact, merge into a unique broad line (the J_{HH} is still obscured by the linewidth). If rotation is a process with a much lower barrier than inversion, the spectrum will become a doublet (a signal at 122.5 Hz, average of those of H1, H3, and a signal at 145 Hz, average of those of H2, H4) before merging into a singlet. Since this does not happen it means that, when the rotation is not yet fast, the rate of N-inversion begins to affect the line shape. Accordingly, both processes, albeit with different rate constants, are effective at $-130°$ and at higher temperatures. The line shape has not sufficient detail to allow the determination of the rate constants for N-inversion. We estimated however that the corresponding $\Delta G^{\neq}$ is within 7 to 8 kcal mol^{-1}.

The conclusion that N,N-rotation seems to be faster than N-inversion in Et_2NNEt_2 is the reverse of that reached for tetrabenzylhydrazine[2] ($\Delta G^{\neq}_{rot} > \Delta G^{\neq}_{inv} \cong 8.2$ kcal mol^{-1}). This is not surprising since the latter molecule has four substituents (benzyls) bulkier than the four ethyls of Et_2NNEt_2. In fact tetraalkylhydrazines with substituents bulkier than ethyl have rotational barriers[4,19] larger than 10 kcal mol^{-1}. However benzyltrimethylhydrazine ($PhCH_2NMe—NMe_2$) was found[20] to have an inversion barrier (at $PhCH_2N$) equal to 6.8 kcal mol^{-1}, whereas the effect of the N,N-rotation was not detected since the corresponding barrier is either equal to or lower than this value.[20] Tetraethylhydrazine has slightly bulkier substituents (three ethyls rather than three methyls) and, accordingly, the rotational barrier we measured is equal to or (slightly) higher than the rotational barrier of $PhCH_2NMe—NMe_2$.

In hydrazines **1** and **5** the four substituents are equal: however if two kinds of substituents are present, so that the nitrogens are no longer equivalent, three different dynamic processes are, in principle, expected (i.e. two different N-inversions and an N,N-rotation). We thus investigated Me_2NNEt_2 (**6**) and $Me_2NNPr^i_2$ (**7**) with the purpose of detecting some of these processes.



$\Delta G^{\neq} = 6.7_5$

Scheme 6. Newman projection along the NN axis of Me_2NNEt_2 (**6**) showing the conformation responsible for the diastereotopicity of the N-methyl and ethyl groups.

The ^{13}C spectrum of **6** displays, below $-118°$, two different NMe signals and, below $-131°$, two different NCH_2 signals: the absence of a pair of signals for the ethylic methyls is attributed to too small a chemical shift difference. The activation energies measured using the lines of NMe and NCH_2 are, respectively, 6.9 and 6.6 kcal mol^{-1}: within the errors this seems to be the barrier of a unique process with a $\Delta G^{\neq}$ equal to 6.75 ± 0.15 kcal mol^{-1}. Owing to the symmetry of **3**, the mentioned carbons become diastereotopic when all the three possible internal motions are slow in the NMR time scale (Scheme 6). In fact these spectral features cannot be due solely to slow rotation, nor solely to slow inversion. Accordingly, the measured barrier corresponds to the slowest of the three motions: N,N-rotation, NMe_2 inversion and NEt_2 inversion. Unambiguous assignment cannot obviously be achieved, however the rotational barrier of Me_2NNEt_2 (**6**) is expected to be similar (smaller or nearly equal to, but not larger) to that of the slightly bulkier Et_2NNEt_2 (**7**). It seems therefore not unreasonable to tentatively assign the value of 6.75 kcal mol^{-1} to the rotational process of Me_2NNEt_2.

On the other hand, separation of two internal motions is achieved in the ^{13}C spectrum of $Pr^i_2NNMe_2$ (**7**). Below $-111°$ two pairs of signals for CH_3 and for CH of the isopropyl group are detectable (the corresponding barrier has $\Delta G^{\neq} = 7.5 \pm 0.1$ kcal mol^{-1}). At $-160°$ the coalescence of the two different NMe signals is observed, $\Delta G^{\neq} = 5.1 \pm 0.3$ kcal mol^{-1} (although we could not attain a sufficiently low temperature to measure the individual shifts of the two methyls, any value for the difference of these shifts within 50 and 300 Hz would give a $\Delta G^{\neq}$ within the quoted error).

The sequence of the barriers in **7** indicates that the first barrier (7.5 kcal mol^{-1}) is the lower between N,N-rotation and NMe_2 inversion whereas the second barrier (5.1 kcal mol^{-1}) measures the inversion of NPr^i_2 (Scheme 7).

$\Delta G^{\neq} = 7.5$ (NMe inv. or NN rot.) $\Delta G^{\neq} = 5.1$ (NPr^i inv.)

Scheme 7. Newman projection along the NN axis of $Me_2NNPr^i_2$ (**7**) showing the conformation (left) and the barrier responsible for the diastereotopicity of the isopropyls and that (right) responsible for the diastereotopicity of the two N-methyls.

The low value for the latter inversion agrees with the trend predicting the lowest values for N-inversion in the most crowded molecules. On the other hand the value of 7.5 kcal mol^{-1} seems rather low for an N,N-rotation in such a crowded molecule (compare with the values of refs. 2–4 and with that of Pr^i_2NNHMe in the following section); we thus believe that this corresponds to the inversion of NMe_2, and that the N,N-rotation in **7** has the higher, immeasurable barrier.

The trend of the rotational barriers in the tetrasubstituted hydrazines **5**, **6**, **7** would lead to the prediction that the corresponding value in the less hindered Me_2NNMe_2 (**1**) should be the lowest of them all (i.e. $\Delta G^{\neq}_{rot} < 6.75$ kcal mol^{-1}, as measured in **5**). On the other hand the values for NMe_2 inversion in **7** (i.e. 7.5 kcal mol^{-1}) should be lower than that expected for Me_2NNMe_2 (steric acceleration). The experimental barrier measured for **1** (6.0 kcal mol^{-1}) seems therefore a better match for the expectations for N,N-rotation rather than for N-inversion.

Trialkylhydrazines

The simplest of trialkylhydrazines, i.e. trimethylhydrazine **8**, displays, at low temperature, two ^{13}C signals for the two methyls bonded to the tertiary nitrogen. The most striking feature is that the temperature at which this phenomenon becomes observable (−111°) is much higher than in the analogous Me_2NNMe_2 (−137°), despite the much smaller chemical shift difference (Table 2). The corresponding $\Delta G^{\neq}$ in **5** is thus higher than in **1** (7.5 *vs.* 6.0 kcal mol^{-1}). Consequently the simple interpretation that **5** (like **1**) is in a *gauche* conformation with all the three motions "frozen" cannot be accepted. We have shown, in fact, that the barrier of **1** corresponds to N,N-rotation and the less hindered **8** should have a *lower* and not a *higher* barrier to rotation with respect to **1**.

However, if inversion at both nitrogens is "frozen" we can have anisochronous methyls even in the presence of fast N,N-rotation. Owing to the molecular asymmetry, the NHMe group in **8** will be a chiral centre and the two methyls bonded to the tertiary nitrogen will be anisochronous as are those of an isopropyl group. In other words $MeNH–NMe_2$ will display, at low temperature, two CH_3 lines, as do (at room temperature) the molecules of general formula $MeCHX–CHMe_2$ ($X \neq H$, Me).

To the best of our knowledge this is the first example of NMR detection of N-inversion at a secondary nitrogen in a non-cyclic derivative. Usually such an inversion is too fast to be observed by NMR[6] (owing to H-exchange?); the examples so far collected concern cyclic amines.[21-23]

For this reason we are inclined to assign the measured values of $\Delta G^{\neq}$ (7.5 kcal mol^{-1}), corresponding to the lower of the two inversion barriers, to NH inversion. Consequently, inversion at the tertiary nitrogen should be even higher, although not detectable in the presence of rapid NH inversion; a value larger than 7.5 kcal mol^{-1} also agrees with the expectation, since we have found that a hydrazine of similar dimension, $MeNPr^i–NH_2$ (**2**), has an inversion barrier for a tertiary nitrogen equal to 9.3 kcal mol^{-1}.

When we increase the dimension of trialkyl hydrazines we expect to detect the N,N-rotational barrier that was too low to be observed in **8**. Actually in

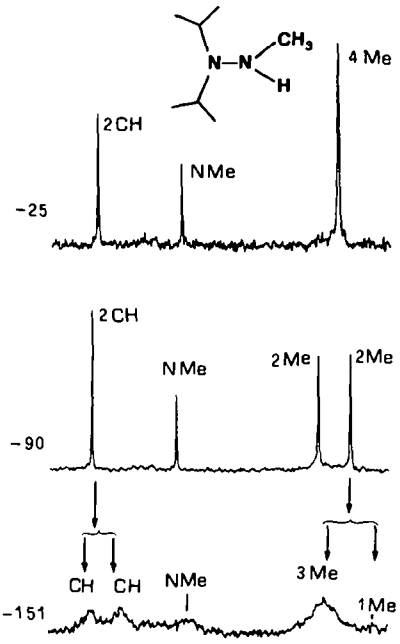
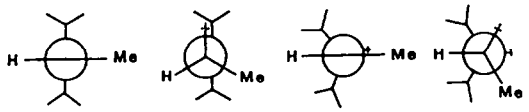


Fig. 3. ^{13}C-NMR spectrum (25.16 MHz) of Pr^i_2NNHMe (**9**) in CHF_2Cl. At −25° a single signal is observed for all the chemically equivalent carbons. At −90° the signal of the methyls of the isopropyl groups are split into two owing to the N,N-restricted rotation: the molecule adopts a conformation (Scheme 8(a)) where there is no plane of symmetry bisecting the Me—CH—Me moiety. At −151° the signals of CH and of one of the isopropyl methyls are further split since N-inversion is slow and a completely asymmetric conformation (Scheme 8(b) or (d)) is adopted.

$Pr^i_2NNHCH_3$ (**9**) we observe, below −90°, two diastereotopic methyls in the isopropyl group whereas all the other carbons remain homotopic (Fig. 3). These effects, as well as the relatively large value of $\Delta G^{\neq}$ (9.85 kcal mol^{-1}) are analogous to those reported[3,4] for similarly hindered hydrazines and should be thus attributed to restricted N,N-rotation. In fact, in the presence of rapid inversion at both nitrogens the conformational preference of hydrazines is that with the lone pair electrons perpendicular to each other. In an asymmetric hydrazine like **9** such an arrangement does not have a plane of symmetry bisecting the Me—CH—Me angle of the isopropyl (see Scheme 8(a)), consequently these methyls are anisochronous. On further lowering the temperature (Fig. 3) the CH signal split and, at the same time, one of the two anisochronous methyl pairs split further.[24] Now a motion that makes the two isopropyl groups diastereotopic has been "frozen". Such a motion ($\Delta G^{\neq}$ = 5.6 kcal mol^{-1}) corresponds to a restricted inversion to secondary nitrogen (Scheme 8(b)); a restricted inversion solely to tertiary nitrogen would not make the two isopropyl groups diastereotopic (Scheme 8(c)).

Of course one cannot exclude the possibility that the barriers to inversion at both nitrogens are sufficiently similar as to be indistinguishable: in this event the conformation would be **8d** rather than **8b**. Although this condition is not strictly required to explain the experimental spectrum of Fig. 3, it is not an unreasonable hypothesis since inversion at a tertiary



a) $\Delta G^{\neq}=9.8_5$ (NN-rotation) b) $\Delta G^{\neq}5.6$ (NHMe inversion) c) d)

Scheme 8. Newman projections along the NN axis of Pr^i_2NNHMe corresponding (a) to a restricted NN-rotation, (b) to restricted rotation and restricted NHMe inversion, (c) to restricted rotation and restricted NPr^i inversion and (d) to restricted rotation and restricted inversion at both nitrogens.

nitrogen in the analogous $Pr^i_2NNMe_2$ (7) has a very similar barrier.

EXPERIMENTAL

Materials

1,1-Dialkylhydrazines. Me_2NNH_2 was commercially avaiable. Et_2NNH_2 and $Pr^i_2NNH_2$ (3) were prepared as reported in Lemmal *et al.*[25] $MePr^iNNH_2$ (2) and $Bu^tPr^iNNH_2$ (4) were also prepared according to this general method[25] using ether as solvent; in the case of 4, however, the reaction was carried out for 48 hr. Derivative 2 (b.p. 98°) was identified by ^{13}C-NMR (Table 2) and ^{1}H-NMR in $CDCl_3$: 6H(d) 1.05 ppm; 3H (s) 2.5 ppm; 1H (hept) 2.65 ppm; 2H (s, broad) 2.9 ppm. Derivative 4 (b.p. 135°) was identified by ^{13}C-NMR (Table 2) and ^{1}H-NMR in $CDCl_3$: 6H(d) 1.0 ppm; 9H (s) 1.1 ppm; 2H (s, broad) 3.0 ppm; 1H (hept) 3.3 ppm.

Trialkylhydrazines. Compound 8 was prepared as reported by Beltrami and Bisset,[26] and 9 was prepared with the same general method[26] according to the following procedure. A mixture of 2.9 g (0.025 mol) of 1,1-diisopropylhydrazine (3) and 1.5 g (0.025 mol) of methyl formate was left for 60 days at room temp. Raising the temp above 30° yielded unwanted products. A solid compound (1,1-diisopropyl-2-formylhydrazine) was obtained (additional ppt was obtained at 0°) and purified by distillation (b.p. 120° at 8 mm Hg). The formyl derivative recovered (2.5 g, 0.017 mol) was subsequently dissolved in anhydrous ether (15 ml) and slowly added to a stirred slurry of $LiAlH_4$ (0.76 g, 0.02 mol) in ether (20 ml) in a N_2 atmosphere. After 5 hr at room temp the mixture was carefully decomposed with ice water and subsequently with NaOH aq (30%) until the ppt coagulated. The organic layer was separated and dried; after vacuum elimination of the solvent the residue was distilled (b.p. 68–70° at 8 mm Hg). In addition to the ^{13}C spectrum (Table 2) 1,1-diisopropyl-2-methylhydrazine (9) gave the following ^{1}H-NMR signals in $CDCl_3$: 12H (d) 1.05 ppm; 3H (s) 2.45 ppm; 1H (s) 2.6 ppm; 2H (hept) 3.05 ppm.

Tetraalkylhydrazines. Compound 1 was commercially available. Hydrazines 6 and 7 were obtained by respectively reacting, Me_2NNH_2 with MeCHO and $Pr^i_2NNH_2$ with HCHO according to Nelsen *et al.*[27] Compound 5, that had been previously obtained[28] in a different way, was also prepared with the same general method,[27] according to the following procedure. To a solution containing 2 g (0.023 mol) of Et_2NNH_2 in 60 ml of MeCN were added, at 15 min intervals, 6.1 g (0.138 mol) of MeCHO in a N_2 atmosphere. After a further 15 min, 5.7 g (0.01 mol) of $NaCNBH_3$ were added, keeping the mixture cooled with water. To the stirred mixture were then added dropwise (over 1 hr) 5.5 g (0.09 mol) of acetic acid and the system was left standing at room temp for a further 2 hr. Concentrated HCl (10 mol) was added dropwise, the solvent eliminated *in vacuo* and the residue, washed twice with ether, was basified with solid NaOH.

The oil obtained in this way was collected and distilled (b.p. 98–100° at 185 mmHg): 1.2 g of 5 were recovered. In addition to the ^{13}C spectrum (Table 2) compound 5 was identified by ^{1}H-NMR in $CDCl_3$: 12H (t) 1.0 ppm, 8H (q), 2.4 ppm.

NMR spectra

The samples were prepared condensing with liquid N_2 the gaseous solvents into the NMR tubes containing the products. They were then sealed in vacuum and introduced in the precooled probe of the spectrometer. The spectra were run at 25.16 MHz in the FT mode for ^{13}C and at 100 MHz CW mode for ^{1}H. The temp was monitored with a thermocouple inserted in an empty tube before or after each determination. Line shape simulation was carried out either with a program[1,6] written for a personal computer (Apple II) connected to a plotter or with the DNMR program[29] run on a CDC 7600.

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