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Conformational Dynamics of Triple Rotors: Tris(dimethylamino)methane, Triisopropylamine, and Related Molecules[1]

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NMR spectra and their temperature-dependence are reported for tris(dimethylamino)methane (**1**), for tris(diethylamino)methane (**2**), for triisopropylamine (**3**), and for *N*,*N*-diisopropyl-3-pentylamine (**4**) and are discussed in terms of the conformations adopted and interconversion of these conformations, as indicated by molecular mechanics calculations. Solid state NMR spectra, obtained by freezing the neat liquids at low temperatures, were also used to support the conclusions of the conformational analysis. Proton NMR spectra of protonated forms of **3** and **4** were similarly analyzed. Less crowded triple rotors prefer a *gauche*, *gauche*, *gauche* conformation while more crowded ones adopt an *anti*, *gauche*, *gauche* arrangement.

Introduction

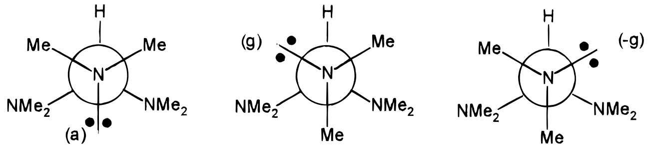
The conformational analysis of a simple organic molecule which has a single center (CH, or CR, or N) with three identical unsymmetrical substituents attached to it is intriguingly complex. To be suitable for a dynamic NMR investigation substituents would ideally be CH_2X or CHX_2 or NX_2. Substituents of the first type are encountered in published studies of tris(chloromethyl)ethane,[3a] triethylamine,[3b] and tribenzylamine.[3c] With the latter two substituent types there is more congestion round the central atom, and examples already reported are triisopropylmethane,[4] triisopropylethane,[5] tricyclohexylmethane,[6] and triisopropylamine.[7] As an addition to this class we now report an analysis of triple rotors tris(dimethylamino)methane (**1**) and tris(diethylamino)methane (**2**) based on dynamic NMR measurements and molecular mechanics calculations, and we comment on studies of triisopropylamine[7] (**3**) and *N*,*N*-diisopropyl-3-pentylamine[8] (**4**), with some further results. The protonated forms **5** and **6** of these last two amines, likewise triple rotors, are also reported.

$HC(NMe_2)_3$ **1** $HC(NEt_2)_3$ **2** $N(Pr^i)_3$ **3**

$N(Pr^i)_2CHEt_2$ **4** $^+HN(Pr^i)_3$ **5** $^+HN(Pr^i)_2CHEt_2$ **6**

The complexities can be illustrated by considering compound **1**. The conformation of each dimethylamino group can be defined by the torsion angle of the nitrogen lone-pair with the central C−H bond. There are three likely staggered arrangements labeled a, +g, and −g, as shown in Scheme 1 (**7, 7′,7″** respectively**)**. The terms +g (or −g) indicate that the *gauche* lone pair orbital has to be rotated clockwise (or anticlockwise) to eclipse the C−H bond. Actual torsion angles may be quite different from the 60° and 180° values suggested by **7**−**7″**, to reduce interactions between dimethylamino groups.

Scheme 1



7 **7'** **7"**

There are 3 × 3 × 3 = 27 conformational minima for the compound **1**, arising from the three HC−N bonds, but since the three dimethylamino groups are identical, these possibilities reduce to seven, the remaining twenty being either degenerate or enantiomeric versions. There are two limiting ways by which interconversions between such conformations may take place, i.e. by rotation of about 120° (or 240°) around the HC−N bonds in either direction, or by inversion of the configuration at the nitrogen atoms. Many examples exist in the literature[9] where distinct inversion/rotation and C−N bond-rotation processes have been demonstrated in the same molecule. Both will be considered in more detail.

Two sets of molecular mechanics calculations have been carried out on these seven conformations for com-

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(9) Bushweller, C. H. In *Acyclic Organonitrogen Stereodynamics;* Lambert, J. B.,Takeuchi, Y., Eds.; VCH: New York, 1992; Chapt. 1, p 1. Nitrogen inversion is almost inevitably accompanied by a net measure of rotation about the C−N bonds to achieve a new local conformational minimum, thus the interconversion of **7′** and **7″** implies that one methyl group has rotated past a C−H bond during inversion. There are high-barrier rotation processes which are likely to be distinct from this nitrogen inversion/rotation, such as the **7′** to **7** interconversion when one *N*-methyl bond has to rotate past a C−Me bond. When, because of the molecular structure, both processes have to be slow before a dynamic effect is seen in the NMR, careful arguments have to be adduced to assign the experimental barrier to one or another process. To the extent that a transition state conformation with a flat nitrogen and simultaneous eclipsing along the significant C−N bond is implausible, one or another process is rate-determining and may in principle be assigned the experimentally measured barrier.

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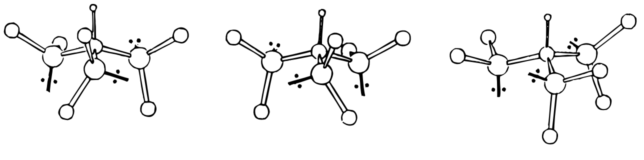
Table 1. MM3-Calculated Parameters for Conformations of HC(NMe$_2$)$_3$ (1)

conformation and label	dihedral angles (H−C−N−lp)[a]	final steric energy[b]	relative enthalpy:[b] MM3 (MMX)[c]
8 a,−g,−g	−167, −102, −70	21.86[d]	0.00 (0.00)
9 a,+g,−g	−175, 58, −75	22.33	0.47 (2.51)
10 a,a,−g	−128, −151, −103	24.89	3.03 (−)[e]
11 −g,−g,−g	−96, −97, −95	25.61	3.75 (3.22)
12 a,−g,+g	−164, −106, 72	27.15	6.29 (7.76)
13 −g,−g,+g	−92, −96, 55	27.60	6.74 (7.36)

[a] The term lp indicates the orbital containing the lone pair electrons of the nitrogen atom. [b] kcal mol^{-1}. [c] The values in parentheses refer to the MMX calculations. [d] Calculated heat of formation = 10.35 kcal mol^{-1}. [e] Conformer **10** is not a minimum according to MMX calculations (see ref 12).

Scheme 2. Schematic Representation of the Two More Stable Conformers (enantiomers 8, and 8′, and 9) of HC(NMe$_2$)$_3$ (1) (for simplicity only the methine hydrogen is displayed)



8 **8'** **9**

pound **1** using the MM3[10] and MMX[11] programs. The results are shown in Table 1 and will be further discussed: for the time being we use them here to limit the number of conformations that need to be brought forward and considered. Of the seven conformations, one [i.e. (a,a,a)] is not a minimum for MM3, and two [i.e. (a,a,a) and (a,a,−g)] are not minima for MMX,[12] while of the others **8**−**13** (see Table 1) only **8** and **9**, both much more stable than the rest, need be considered as likely ground states.

The (a,−g,−g) conformation **8** has an enantiomeric conformation (a,+g,+g) **8′**, each of them being triply degenerate since any one of the three NMe$_2$ groups may be the *anti* one (Scheme 2). These, accordingly, make up a set of six of the twenty-seven "versions" mentioned above. The three dimethylamino groups in any (a,−g,−g) conformation are distinct, even though two of them are labeled "−g", since one "−g" group has its lone pair pointing at the *anti* NMe$_2$ group, while in the other "−g" group the lone pair points at the first "−g" group (see **8** in Scheme 2). As a result there are six different methyl groups in this conformation.

In the (a,+g,−g) conformation **9**, there is a plane of symmetry because both *gauche* NMe$_2$ groups have their lone-pair pointing toward the *anti*-NMe$_2$ group (Scheme 2). In **9** there are two kinds of dimethylamino groups and there are three versions of **9**. The minimum energy conformation is probably not as symmetrical as shown in Scheme 2, but oscillates with high frequency on the NMR timescale about this symmetrical arrangement, so there are two each of three kinds of methyl groups. Each of compounds **1**−**6** can be analyzed in a comparable way as an aid to interpreting experimental observations.

Results and Discussion

Tris(dimethylamino)methane (1). Since the lone pairs of the three nitrogen atoms are not located in MM3 calculations, they were taken to be on the external bisector of the angle Me−N−Me. Thus, conformations of the three dimethylamino groups in each of the six minima **8**−**13** are best defined by the torsion angle of the central methine hydrogen and the lone pair. Table 1 shows the relative enthalpy of the various conformational minima that were located by calculation and, as in earlier compounds,[4−6] the arrangement **8** of Scheme 2 (i.e. that with one lone pair *anti* to CH and the other two *gauche* to CH and pointing in the same sense) is the minimum both in MM3 and MMX calculations. MM3 suggests that a second conformation [i.e. (a,+g,−g), **9** in Scheme 2] might also be populated, whereas this is not the case for MMX. Table 2 shows some other details of the MM3 calculations of the two most stable conformations **8** and **9**. It is noticeable that the *gauche* dimethylamino groups are considerably flattened in both conformations (C−N−C bond angle sums are between 338° and 349°) while dimethylamino groups in the *anti*-conformation are less flattened, having bond angle sums smaller than 334° (for a planar nitrogen the bond angle sum would be 360°).[13] The nitrogen atoms of the flattened *gauche* dimethylamino groups are expected to invert rapidly on the NMR timescale at all temperatures, which means that conformations **8**, **8′**, and **9** should merge their NMR identities. This set of three conformations, where the high energy conformation **9** may be only a minor component,[14] can be represented by a single structure **14** (Scheme 3), where the dimethylamino groups are displayed as planar in order to describe the fast N-inversion process and to indicate the dynamic symmetry achieved.[15]

In **14** (as we will henceforth call the equilibrating set of conformations **8**, **8′**, **9** which form the ground state) there are three kinds of methyl groups, which we labeled *a*, *b* and *c* (Scheme 3). Importantly the *anti* dimethylamino group retains its identity, and to exchange *anti* and *gauche* conformations requires visiting a conformation other than **8** or **9**. Both sets of calculations agree that conformations **12** and **13** are much higher in energy than the others. They are certainly local minima but in both, methyls in adjacent groups appear to crowd each other quite severely. Conformation **10** is only a shallow minimum for MM3 calculations and is not an MMX minimum, so it is not discussed further. More interesting is the (−g,−g,−g) conformation **11** calculated to be too high in energy to be significantly populated but energetically accessible and, importantly, of higher symmetry than **8** or **9**.

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(11) MMX forcefield as in PCMODEL, Serena Software, Bloomington, IN. See also Gajewski, J. J.; Gilbert, K. K.; and McKelvey, J. *Advances in Molecular Modelling*; JAI Press: Greenwich, CT, 1992; Vol. 2.

(12) An arrangement with two or more groups *anti*, [i.e. (a,a,−g) or (a,a,a)] is of relatively high energy and no minimum of this type was found in the MMX calculations. MM3 calculations too do not have the (a,a,a) arrangement as a minimum but located a shallow minimum **10** with H−C−N−lp torsion angles −128°, −151°, −103° which thus bears the description (a,a,−g) and is included in Table 1 for completeness sake, although all three groups are far removed from the 180° and 60° torsion angles expected for a "perfect" (a,a,−g) situation.

(13) Anderson, J. E.; Casarini, D.; Lunazzi, L. *J. Org.Chem.* **1993**, *58*, 714.

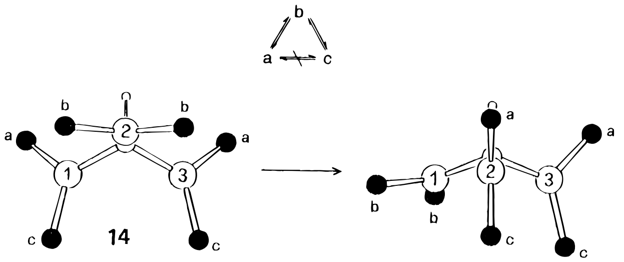
(14) Even in the unfavorable case of MM3 calculations, that predict (Table 1) an energy difference of 0.47 kcal mol^{-1} between **8** and **9**, the proportion of the latter would be as low as 14% at −142°, if ΔS° is reasonably assumed to be negligible.

(15) Even though in **8** (or **9**) N-inversion for the NMe$_2$ *anti* to CH is not necessarily fast as for its *gauche* companions, the conclusions concerning the stereodynamics are not altered. For the invertomer one might obtain by N-inversion of the *anti* NMe$_2$ group is not a minimum (as indicated by both MM3 and MMX calculations) and therefore cannot be populated. As a consequence it is immaterial whether the latter group is represented as planar or as locked into a unique pyramidal invertomer.

Table 2. Additional Calculated Parameters for Conformations 8 and 9 of $HC(NMe_2)_3$

geometric feature	conformer **8**	conformer **9**
C−N bond lengths (pm)	147.46	147.17
	147.73	147.14
	147.20	147.17
N−C−N bond angles (deg)	113.7, 110.1, 111.8	110.6, 115.6, 110.7
C−N−C bond angles (deg) and sum of these, in parentheses	a: 112.1, 112.4, 108.0, (332.6)	a: 112.4, 111.9, 109.4, (333.8)
	+g: 117.7, 112.7, 114.6, (345.0)	+g: 118.7, 116.7, 112.4, (347.8)
	+g: 110.7, 112.4, 115.3, (338.4)	−g: 116.7, 118.8, 113.1, (348.6)

Scheme 3



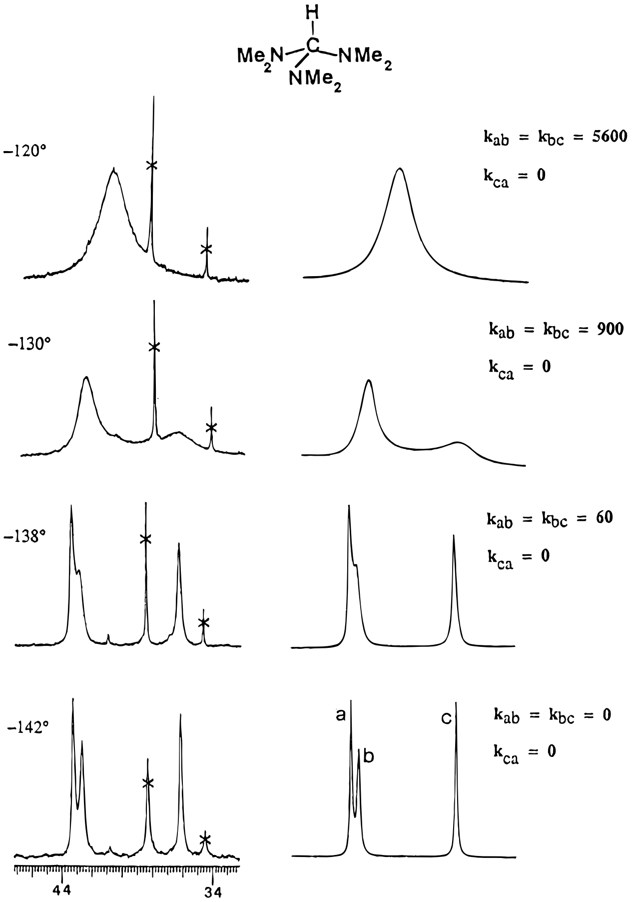


Figure 1. Methyl region of the ^{13}C spectrum (100.7 MHz) of **1** (in Me_2O) at various temperatures (left). The line shape simulations (right) required equal values (s^{-1}) for the rate constants k_{ab} and k_{bc} as well as null values for the rate constant k_{ca}. The lines marked with an x are due to impurities.

If a molecule represented as **14** visits conformation **11**, it can then return to a new conformation **14** in which a different dimethylamino group is in the *anti* conformation. There is a 2 in 3 chance that reversal to **14** will lead to a new *anti* dimethylamino group and if **11** is visited a second time, there is a one in three chance that the third dimethylamino ends up returning to an *anti* conformation. The NMR observed rate in this case is 2/9 of the rate of interconverting **14** and **11,** and a transmission coefficient of 0.22 should be used to convert the NMR observed *k*-values into the rate constants for the interconversion.

The ^1H NMR spectrum of **1** (at room temperature in CHF_2Cl) shows the expected two singlets of relative intensity 1:18 at δ 2.95 and 2.17. Only the latter is temperature-dependent, broadening below about −110 °C and splitting at −152 °C into a 1:1:1 triplet at δ 2.02, 2.08, and 2.20. It is not possible to distinguish whether two successive sets of changes or a single set of changes give rise to this final spectrum.

The ^{13}C NMR shows much clearer changes. At room temperature (in Me_2O) the proton-coupled spectrum comprises two signals at δ 100.3 (a doublet $^1J = 132.9$ Hz of presumably nineteen-line multiplets with $^3J = 3.9$ Hz) and at δ 41.2 (a quartet $^1J = 147.3$ Hz, of quartets $^3J = 4.9_5$ Hz of doublets $^3J = 3.9_5$ Hz). The proton-decoupled spectrum comprises two singlets, and the more intense upfield one broadens below about −70 °C and splits below about −117 °C to a broad 2:1 doublet which sharpens up on further cooling to show a 1:1:1 triplet at δ 36.5, 43.0, and 43.6 at −142 °C. We call these peaks *a*, *b*, and *c* respectively, see Figure 1.

Since the singlet for the central carbon of the molecule is temperature-invariant, this spectral behavior fits well with the rapid equilibrium involving **8**, **9**, and **8′** which is implied by the averaged structure **14**, with the interconversion shown in Scheme 3 becoming slow at low temperatures. One of the methyl carbon signals *b* is broader at lower temperatures (e.g. at −138 °C in Figure 1) than the other, *a*. This can be understood in terms of a process where *b* interchanges with both *c* and *a* but there is no direct exchange of *c* and *a*. Complete line shape simulation was successfully achieved only on the basis of this exchanging pattern (for *any* $k_{ac} \neq 0$ the results become unacceptable) and leads to a barrier (ΔG^*) of 6.1−6.6 kcal mol^{-1}, depending on the temperature. A plot using rates at eight temperatures gave an enthalpy of activation $\Delta H^* = 10.1_5$ kcal mol^{-1} and an entropy of activation $\Delta S^* = +27 \pm 16$ eu. With the mentioned transmission coefficient of 0.22 the free energy of activation is reduced by about 0.4 kcal mol^{-1} (i.e. $\Delta G^* = 5.7-6.2$ kcal mol^{-1}) and the entropy of activation is increased by 3 eu, becoming $\Delta S^* = +30 \pm 16$ eu (see Experimental Section), with ΔH^* remaining unchanged.

Signal *b* is assigned to the methyls of the *anti* dimethylamino group while each *gauche* dimethylamino group has one *a* and one *c* methyl group (Scheme 3). The *gauche* dimethylamino groups do not undergo 180° rotation (i.e. *a* does not interchange with *c* directly) but one *gauche* dimethylamino group may exchange with an *anti*-one by the means described above (i.e. one *a* and one *c* together exchange with *b*). This is the process which is slow on the NMR timescale at −142 °C (and which is effected by multiple visits to conformations **11**) and involves substantial rotation (approximately 90°) of two dimethylamino groups (one *anti* and one *gauche*) and small (or null) rotations of the third one (*gauche*).[16] The preferred conformation set (described by **14)** is then re-established with a different dimethylamino group in the

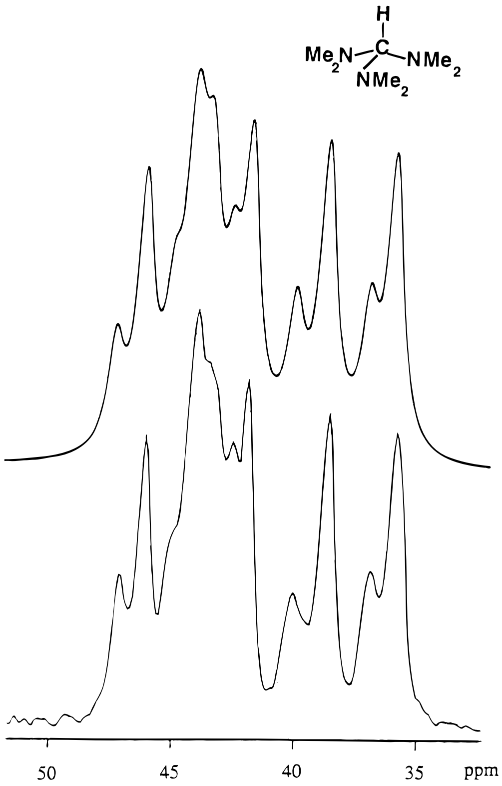


Figure 2. Lower trace: ^{13}C CP-MAS spectrum (75.5 MHz) of the methyl region of **1** at −73 °C The computer simulation (upper trace) was obtained using six different shifts for the six methyl groups (see text).

anti conformation (see Scheme 3 where the labels 1, 2, and 3 indicate the fate of the dimethylamino group after a visit to conformations **11**). Such a complex exchange pathway requires a combinations of various transition states much less ordered than the ground state, and this is reflected in the unusually large (and positive) value for ΔS^*.

The solid state proton decoupled ^{13}C NMR spectrum (CP-MAS) was observed by cooling a neat liquid sample of the compound **1** to −73 °C and allowing the solidified sample to equilibrate. Six separate signals of equal intensity are seen for the *N*-methyl carbons at δ 36.12, 39.02, 42.31, 42.92, 43.20, 44.44, and 46.45 (Figure 2). Each signal is a 1:2 doublet of a type quite expected for a carbon directly attached to a ^{14}N nucleus.[17] The signal of the central carbon atom of the molecule appears as a broad singlet. In contrast to solution, conformational interconversions are slow on the NMR timescale at −73 °C, so the barrier to the processes must be higher in the solid phase, as previously observed for various internal motions.[18−20]

The difference between the low temperature ^{13}C NMR of the solid state, showing six *N*-methyl signals, and that of the solution, showing only three, requires explanation. Since there is no doubling of the central carbon signal, it seems unlikely that the lattice creates two different kinds of molecular sites. If indeed only a single conformation (*viz*. **8**, the most stable by calculation) is present, the crystal lattice, as often occurs, has destabilized the conformation **9** which is intermediate between **8** and **8′**.[21] Then not only bond rotation but also nitrogen inversion must now be slow and there are six different sites for a methyl group, as shown in the picture of conformer **8** in Scheme2.

Is it reasonable to suggest that nitrogen inversion in **1** is fast in solution, so that the measured barrier corresponds to the rotation of a dimethylamino group? Results for simpler *N*,*N*-dimethylamines suggest that nitrogen inversion should have a fairly high barrier. Nitrogen inversion barriers in *N*-ethyldimethylamine,[22] *N*-*sec*-butyldimethylamine,[22] and *N*-ethyl-*N*-isopropylmethylamine,[23,24] are 8.6, 7.8, and 7.4−7.5 kcal mol^{-1}, respectively, rather larger than the experimental barrier measured here. We believe, however, that these do not offer good analogies for the present case as their nitrogen atoms are essentially tetrahedral and thus display relatively high nitrogen inversion barriers. The MM3 calculations of *N*-ethyldimethylamine (which has a nitrogen inversion barrier[22] of 8.6 kcal mol^{-1}) give a sum of 333.6° for the C−N−C bond angles. In contrast the *gauche* nitrogen atom in **8** which inverts to give **9**, and both *gauche* nitrogen atoms in **9** are much flatter, with sums 345.0, 347.8, and 348.6 respectively (Table 2). This flattening is a plausible justification for our suggesting that the nitrogen inversion among conformations **8**, **9**, and **8′** has a barrier significantly lower than in ethyldimethyl amine and is fast at all temperatures accessible to us. It is striking that the interactions causing this flattening are long-range, between the methyl groups on different nitrogens.

Tris(diethylamino)methane (2). The ^{1}H NMR spectrum of HC(NEt$_2$)$_3$ shows that here too a dynamic process is occurring, for the spectral lines broaden and split at low temperatures but the complexity of the unresolved signals prevents an interpretation of the dynamic processes. The ^{13}C spectrum is more informative since the CH$_2$ and CH$_3$ carbon signals, each a singlet at room temperature, are split, at −135 °C, into a number of relatively sharp lines, apparently five for the former and four for the latter. The simulation of the low temperature static spectrum (Figure 3) clearly indicates that both signals comprise six singlets of the same intensity, with two and three near coincidences, respectively. The molecule, accordingly, must adopt an asymmetric con-

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(16) In practice a 90° rotation about the CH−N(1) bond (see Scheme 3) transforms **14** into **11** (−g,−g,−g of Table 1) and a subsequent rotation about the CH−N(1) bond also re-establish the original situation. Of course the process continues involving also the 90° rotation about the CH−N(3) bond. These motions (which are likely to occur in sequence and not simultaneously) are able to re-establish the same structure **14** having, meanwhile, exchanged *b* with both *a* and *c* without exchanging directly *a* with *c*, as experimentally observed.

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(21) A second explanation is that the equilibrium involving **8**, **9**, and **8′** (as represented by **14** of Scheme 3) is still rapid in the solid but that the plane of symmetry present in **14** is removed by the lattice, as happens if adjacent molecules are not in the plane of symmetry nor on the axis perpendicular to the plane of symmetry through the central carbon atom.

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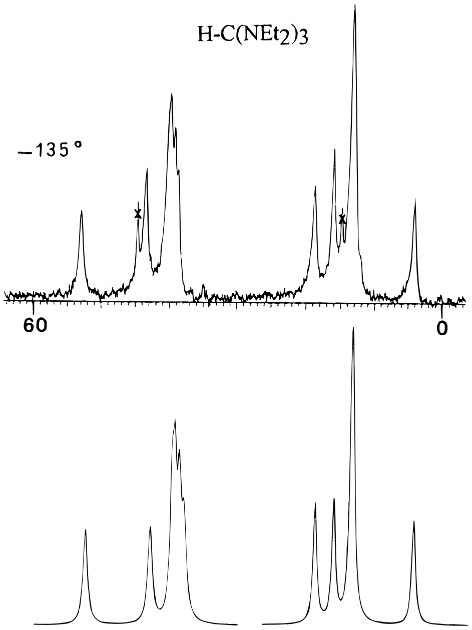
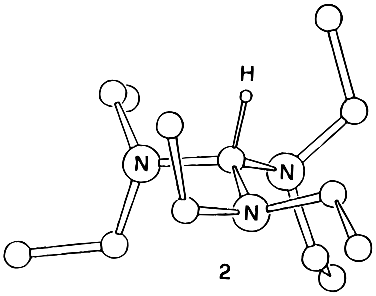


Figure 3. ^{13}C signals (at 50.3 MHz) of the ethyl carbons of **2** in CF_2Cl_2 at −135 °C (above). Underneath is reported the computer simulation obtained with six different lines of equal intensity for both the CH_2 (lines at 35−55 ppm) and the CH_3 carbons (lines at 5−20 ppm). The lines marked with an x are due to impurities.

Scheme 4



2

formation which *is not* dynamically averaged by any motion. The spectrum of **2** should thus correspond to the asymmetric structure (a,−g,−g) shown in Scheme 4 which, according to MMX calculations, is its most stable conformation (it is analogous to conformation **8** of compound **1**, displayed in Scheme 1). The symmetry of **14** has been reduced by the additional methyl groups.

The observation of two sets of six signals in the low temperature spectrum requires that both HC−N and N−CH_2 rotations are slow on the NMR timescale, if so all the CH_2 and CH_3 carbons become anisochronous, whether or not nitrogen inversion is fast. Although we cannot decide this last point experimentally, the fast inversion of **1** should be found in **2** as well, for tris(diethylamino)methane is even more crowded than the tris(dimethylamino)methane, and nitrogen inversion is usually sterically accelerated.

There are at least three precedents for rotation about the N−CH_2 bond of N−ethyl compounds being slow on the NMR timescale (i.e. triethylamine,[3b] *N,N*-diethylmethylamine,[3b] and *N-tert*-butyl-*N*-neopentylethylamine,[25] with barriers of about 6 kcal mol^{-1} in each case) which support our interpretation (which implies a successive rotation about all six N−CH_2 bonds to reach enantiomeric conformations) of the present results.

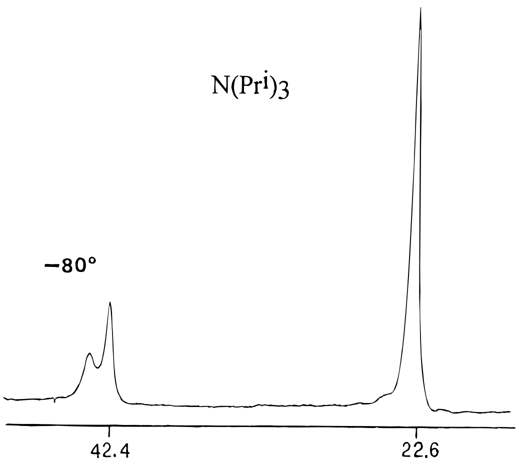


Figure 4. Solid state ^{13}C CP-MAS spectrum (75.5 MHz) of **3** at −80 °C. The single signal (line width 33 Hz) at 22.6 ppm suggests equivalence of the six methyl groups. Such an equivalence is maintained even at the lowest attainable temperature (about −110 °C).

Triisopropylamine (3). These points led us to reconsider triisopropylamine (**3**), which has recently been reported[7] to have a planar structure at the central nitrogen, on the basis of an electron diffraction (ED) study and other observations. There are obvious similarities in the interactions present in **3** and **1**.

Proton NMR investigation of this compound had been previously reported[23] at low temperature and we found that also its ^{13}C NMR spectrum in solution is temperature-independent, with no doubling of signals to suggest that a conformational process has become slow on the NMR timescale. On cooling a neat sample of **3**, solidification takes place and after equilibrating below −80 °C a CP-MAS spectrum was obtained (Figure 4). The 1:2 doublet for the methine carbon reflects coupling with the ^{14}N quadrupole, as found for **1** above. The sharp (line width 33 Hz) singlet at 22.6 ppm, due to the six methyl groups, could be conveniently explained if the molecule had a planar structure at the nitrogen atom, with the three isopropyl groups symmetrically placed around the nitrogen, in such a way as to have three methyl groups above and three below the plane containing the flattened nitrogen [this would correspond to the (−g,−g,−g) conformation]. The recent demonstration,[7] that in **3** bond angles open up so much that in the gas phase the molecule is planar about the central nitrogen atom, is worth considering. This result emerges from an ED study which leads to a series of interatomic distances. The structure best fitting these distances was then derived and, after assuming rotational symmetry for individual methyl groups and isopropyl groups, this led to C−N−C bond angles of 119.2°, which means an almost planar nitrogen.[26,27] Our MM3 calculations predict[28] that

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[25] Anderson, J. E.; Casarini, D.; Lunazzi, L. *J. Chem. Soc. Perkin Trans. 2* **1991**, 1431.

[26] The large deviations from linear relationships involving ^{13}C and ^{15}N chemical shifts of some amines were also attributed to the planarity of the nitrogen atom of triisopropylamine (**3**), see: Wong, T. C.; Collazo, L. R.; Guziec, F. S., Jr. *Tetrahedron* **1995**, *51*, 649.

[27] An analogous ED investigation on $N(CF_2CF_3)_3$ also yielded a C−N−C angle of 119.3°, see: Gaensslen, M.; Gross, U.; Oberhammer, H.; Rüdiger, S. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1467.

[28] Bock *et al.* (ref 7) used for their MM calculations of triisopropylamine (**3**) the MM2 force field, as clearly stated twice in their references 4a and 4b. Thus the MM3 indication, which appears on Table 2 of ref 7, is likely to be a misprint. This would explain why the angle C−N−C of **3**, obtained in ref 7 by means of their MM calculations (i.e. 117.9°), appears to be smaller than ours (i.e. 119.4°, nearly coincident with the experimental value of 119.2°) where MM3 calculations were really employed.

Table 3. MM3-Calculated Parameters for Conformations of Triisopropylamine (3)

conformation and label	dihedral angles (lp−N−C−H)[a]	CNC angle sum	final steric energy[b]	relative enthalpy[b]	protonated amine[c]
3A a,−g,−g	−170, −97, −66	347.0	33.31	3.87	0.00
3B a,+g,−g	−163, 90, −58	350.3	35.97	6.53	1.34
3C a,a,−g	145, 166, −80	345.4	40.52	11.08	5.43
3D −g,−g,−g	**86, 85, 86**	**358.2**	**29.44**	**0.00**	**1.59**
3E a,−g,+g	−175, 93, −81	347.2	37.31	7.87	4.47
3F +g,−g,−g	59, −87, −91	357.3	33.61	4.17	4.72

[a] The term lp indicates the orbital containing the lone pair electrons of the nitrogen atom. [b] kcal mol^{-1}. [c] Relative enthalpies (kcal mol^{-1}) of the conformations of the protonated amine **5.**

Table 4. MM3-Calculated Parameters for the Conformations of *N,N*-Diisopropyl-3-pentylamine (4)

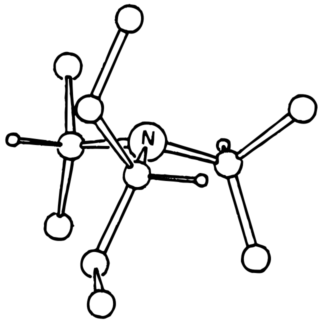
conformation and label (lp-N-C-H)[a]	dihedral angles sum	CNC angle	pentyl group conformation[b]	final steric energy[c]	relative enthalpy[c]	protonated amine[d]
3A a,−g,−g	−173, −93, −67	346.6	gaGg	37.16	3.76	0.06
3A a,−g,−g	−170, −96, −71	346.8	gaGa	37.31	3.91	0.00
3A a,−g,−g	−170, −96, −76	351.0	aaGa	38.81	5.41	3.29
3A a,−g,−g	−165, −100, −64	351.3	aaGg	40.36	6.96	7.80
3A a,−g,−g	−172, −97, −67	346.5	gaA	39.61	6.20	
3D −g,−g,−g	−85, −84, −84	**356.5**	**gaGg**	**33.40**	**0.00**	**7.57**
3D −g,−g,−g	−90, −90, −90	360.0	aaGg	36.03	2.63	
3D −g,−g,−g	−79, −94, −85	358.1	ggGg	36.26	2.86	3.86
			ggA			1.47
			aaA			11.11

[a] The term lp indicates the orbital containing the lone pair electrons of the nitrogen atom. [b] The first two letters describe the conformation of the two central bonds of the pentyl group, the third letter describes the conformation of the pentyl group with the lone pair either A for anti or Ga or Gg for gauche, with the 3-H of the pentyl pointing toward an anti (a) or a gauche (g) isopropyl group. [c] kcal mol^{-1}. [d] Relative enthalpies (kcal mol^{-1}) of the conformations of the protonated amine **6.**

the most stable conformation [which indeed turned out to be the highly symmetrical (−g,−g,−g)] should have a C−N−C angle (119.4°) essentially equal to that derived from the ED experiment. The corresponding sum of the three equivalent C−N−C angles is thus nearly 360° (i.e. 358.2°, Table 3). It is also worth outlining that all the other conformers, which are predicted by MM3 calculations to be much less stable, were computed to have smaller values for the sum of their three C−N−C angles (Table 3), indicating that the most stable structure is also expected to be the most flattened one: this result nicely fits the solid state spectrum of Figure 4, which also agrees with the conclusion of the ED study.

***N,N*-Diisopropyl-3-pentylamine (4).** This compound is a desymmetrized version of **3** whose NMR spectrum has previously been investigated [8] in solution at low temperature. Although we have now repeated that experiment with a higher frequency spectrometer (75.5 rather than 25.16 MHz), the solution-phase ^{13}C spectrum still shows only one set of changes corresponding to a process with a barrier of 9.2 kcal mol^{-1}, as previously reported.[8] All signals for the pentyl group are temperature-independent while all signals for the isopropyl groups split in two in the ^{13}C NMR, showing that the two isopropyl groups have become different on the NMR timescale. The two methyl groups within each isopropyl group remain identical. The process that has become slow on the NMR timescale at low temperatures is interconversion of enantiomeric versions of **4** presumably by rotation of the 3-pentyl group in a molecule with a nitrogen atom that is planar or so flattened as to have a very low nitrogen inversion barrier. This interpretation fits well with the MM3 calculations of Table 4. This table shows only minima of the (a,−g,−g) and (−g,−g,−g) types, with various arrangements of the pentyl group chain. One conformation is much more stable than all others and it exhibits a value for the sum of the three C−N−C angles (356.5°, Table 4) quite close to 360°, strongly suggesting, also on this case, a nearly planar nitrogen atom.

Scheme 5



4

There appear to be two different solid state forms of this compound, as suggested both by differential scanning calorimetry and solid state NMR, one existing between −67.5 °C and −97 °C and a second form below that temperature. The higher temperature form spectrum shows doubling of all signals except the methine of the pentyl group. Assuming that the nitrogen atom continues to be planar in the solid state, this suggests that the lattice makes the two sides of the plane different, and so the two methyl groups or ethyl groups attached to each N−CH fragment give separate signals.

The lower temperature form (<−97 °C) displays a further doubling of the isopropyl methyl signals and, as a whole, the spectrum of the latter phase (in which the low temperature has most likely frozen all the internal motions) agrees well with the MM3-computed conformation having the lowest energy minimum (Table 4). Such a conformation, shown in Scheme 5 (where only the CH hydrogens are represented for simplicity), has indeed four diastereotopic methyl groups for the two isopropyl moieties and two diastereotopic ethyl groups for the 3-pentyl moiety. The failure to detect two different ^{13}C signals for the pair of NCH isopropyl carbons ($\Delta\delta = 1.0$ ppm in isotropic solution[8]) is plausibly due to a near coincidence within the relatively large line width (the NCH carbon signals appear in fact as a broad asymmetric doublet owing to the coupling with ^{14}N, as observed for the other compounds discussed previously).

Triisopropylammonium Ion 5. Protonation of triisopropylamine leads to an additional triple rotor with a tetrahedral nitrogen center. The proton NMR spectrum shows, among other spectral changes, a new doublet splitting $^3J = 3.8$ Hz in the isopropyl methine protons multiplet, due to the coupling with the ^+NH proton. The relative energies of the salt conformations, calculated by molecular mechanics, are shown in the last column of Table 3. In contrast to **3** the (a,−g,−g) conformation is by far the most stable, with the (−g,−g,−g) conformation being somewhat less stable than the (a,+g,−g) conformation. The tetrasubstituted nitrogen is clearly tetrahedral, as indicated by the three C−N−C bond angles sum which is now computed to be 333° for its preferred conformer (a,−g,−g).[29] The observed H−N$^+$−C−H coupling constant of 3.8 Hz for **5** can be compared with that for some salts of substituted ethylamines[30] where conventional staggered conformations are adopted. In *N*-ethylpiperidinium ion the exocyclic H−N$^+$−C−H torsion angles are calculated to be close to 60° and 180° and the coupling constant is 5.2 Hz. Thus $^3J_{60} + {}^3J_{180} = 10.4$ Hz. In the triisopropylammonium ion **5** the three-bond coupling of the ^+NH proton to the three methine protons averages to 3.8 Hz, so the sum of the three coupling constants is 11.4 Hz. By calculation the (a,−g,−g) conformation has torsion angles of 174°, 61°, and 90°. If the first two torsion angles contribute 10.4 Hz to the coupling constant sum, as the ethylpiperidinium model suggests, the remaining 90° torsion angle contributes 1.0 Hz. Insofar as this is a reasonable coupling constant for such a torsion angle, the experimentally observed coupling constant agrees with a predominance of the (a,−g,−g) conformation.

***N*,*N*-Diisopropyl-3-pentylammonium Ion 6.** In the NMR spectrum of **6** (i.e. the protonated form of **4**) the three coupling constants of the ^+NH with the methines of the three adjacent alkyl groups are 4.7, 4.7, and 1.6 Hz so the sum is 11.0 Hz, close to the 11.4 Hz sum found for the triisopropylammonium **5**. This agrees with the similarity of the calculated conformations of **5** and **6** both as to the relative energy and the arrangement of the individual alkyl groups. The three isopropyl groups in **5** spend one-third of their time equally in conformations with H−$^+$N−C−H torsion angles of 174°, 90°, and 61°. For **6** similar torsion angles are calculated, but since the observed coupling for the 3-pentyl group is 1.6 Hz, compared with the 4.7 Hz for the isopropyl groups, pentyl and isopropyl groups have very different conformations. The pentyl group is mainly in the perpendicular 90° conformation, while the isopropyl groups equilibrate between *gauche* and *anti* 60 and 180° conformations. In this conformation the pentyl group locates its extra methyl groups out of the crowded mean plane of the *i*-Pr−N−*i*-Pr system.

Conclusions

Both calculations and spectral observations suggest that for triple rotors with diisopropyl or dimethylamino types of substituents, the less crowded examples adopt (g,g,g) conformations while (a,g,g) conformations are increasingly preferred in more crowded molecules. Thus compounds which minimize crowding by being essentially planar at the central atom adopt a (g,g,g) conformation while tetrahedral triisopropylmethane[4] and tricyclohexylmethane[6] adopt (g,g,g) and (a,g,g) conformations in comparable amounts. 1,1,1-Triisopropylethane,[5] more crowded because of the central methyl group, prefers (a,−g,−g) and even (a,+g,−g) conformations. The same two conformations are favored by compounds **1** and **2** which are more crowded than triisopropylmethane since six shorter C−N bonds replace six C−C bonds. Shorter bonds and thus crowding also hold for the trialkylammonium ions **5** and **6** which also adopt (a,−g,−g) conformations.

Experimental Section

Materials. Tris(dimethyl)aminomethane (**1**) and *N*,*N*-diisopropyl-3-aminopentane (**4**) were commercially available and were purified before use. Tris(diethylamino)methane (**2**) was prepared following ref 31 and triisopropylamine (**3**) following ref 7.

NMR Measurements. The samples for the low temperature spectra were prepared by connecting the NMR tubes, containing C_6D_6 or CD_2Cl_2 solutions of the compounds, to a vacuum line and condensing the gaseous solvents (CHF_2Cl, CF_2Cl_2, or Me_2O) by means of liquid nitrogen. The tubes were subsequently sealed *in vacuo* and introduced in the precooled probes of the spectrometers equipped with standard variable temperature devices. The measured temperatures[32] are believed to have errors not exceeding ±3 °C. In the case of **1** eight points were considered for simulation in the range −120 to −140 °C, the corresponding *k*-values covering the range 5600 to 30 s^{-1}: the line relating $\log(k/T)$ to $1/T$ had a correlation coefficient of 0.986. Even allowing for a most unfavorable distribution of the temperature errors at the two extremes of the line, the ΔS^* still remains positive, its possible minimum value being reduced to +14 eu. Thus an error of ± 16 eu (i.e. the difference between the "best" value +30 eu and the minimum value +14 eu) has been quoted in the text, an uncertainty analogous to the one (±13 eu) reported[33] for a similar case of not negligible ΔS^*. The line shape analysis has been carried out by means of a program based upon the Bloch equations.[34] The ammonium salts **5** and **6** were obtained by adding a few drops of trifluoroacetic acid to diluted $CDCl_3$ solutions of the corresponding amines **3** and **4**, respectively. The ^{13}C CP-MAS spectra were run at 75.5 MHz by fitting the liquid compounds into ZrO_2 rotors which were slowly spun while lowering the temperature. When the compounds became solid the spinning speed was accelerated to 3.5−4 kHz, and the spectra were acquired with a standard cross polarization sequence (contact times of 2−5 ms and recycling times of 5 s were employed). The cooling of the samples for the solid state spectra was obtained by a flow of dry nitrogen precooled in a heat exchanger immersed in liquid nitrogen whose temperature was controlled by a resistance. The temperatures were calibrated using the shifts of samarium acetate.[35]

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(29) The ^{13}C and ^{15}N shifts, as well as the J_{NH} coupling constants, also agree in indicating a tetrahedral structure for the ion **5**. (see: Wong *et al.* in ref 26).

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