Preference for Eclipsed Conformations in Acyclic Neopentylidalkylamines and the Stereodynamical Consequences: An NMR and Molecular Mechanics Investigation

J. Edgar Anderson,*1 Daniele Casarini,‡ Anthony I. Ijieh, and Lodovico Lunazzi*4

Contribution from the Chemistry Department, University College, Gower Street, London WC1 E6BT, U.K., and Department of Organic Chemistry “A. Mangini”, University of Bologna, Viale Risorgimento 4, Bologna 40136, Italy

Received April 1, 1997

Abstract: A dynamic NMR study of a number of acyclic N,N-dialkynopentylamines, supported by molecular mechanics calculations, is reported. With simple alkyl groups, eclipsed conformations are encountered for the NCH2—Bu1 bond, which has a high 1-fold rotational barrier. The N-inversion/rotation process for Me2NCH2Bu1 was rendered detectable by desymmetrizing the molecule as Me2NCHDBu1. Here the decoalescence of separate 13C signals for the diastereotopic NMe groups allowed the measurement of the corresponding free energy of activation (ΔG‡ = 9.4 kcal mol−1). With significantly more branched alkyl groups, the N—CH3Bu1 bond adopts a conformation intermediate between staggered and eclipsed. Trineopentylamine and an analogue undergo a novel concerted back and forward 60° rotation through eclipsed conformations about the N—CH3Bu1 bonds, with a barrier which dynamic NMR indicates must be at least 8.3 kcal mol−1.

Introduction

There has been much recent interest in molecules having a saturated bond which prefers to adopt an eclipsed conformation.2–4 Particularly notable are simply substituted compounds such as N-neopentylpiperidine 4a and N-neopentyl-1,2-ethylenediamine 4b where the exocyclic N—CH2 and C—O bonds, respectively, are eclipsed. This paper reports an investigation of the conformations of a number of acyclic neopentylidalkylamines R1R2NCH2Bu1 (1–10) and shows that, while eclipsing results from the interaction of substituents, the likelihood of eclipsed conformations does not necessarily increases with the increasing bulk of the substituents. It was early recognized that eclipsed bonds are generally to be associated with relatively high rotational barriers,3a,b for these two features are a consequence of the same

©1997 American Chemical Society

R1, R2 = Me
1 R1, R2 = Mep
4 R1, R2 = Ph
7 R1 = Me, R2 = CH2Bu1
2 R1 = Me, R2 = Et
5 R1 = Et, R2 = Bu1
8 R1 = CH2Ph, R2 = CH2Bu1
3 R1, R2 = Et
6 R1 = CH2Ph, R2 = Bu1
9 R1, R2 = CH3Bu1
10 R1 = CH3Bu1, R2 = CH3-(1-adamantyl)

1 University College.
2 University of Bologna.
3a,b Published in Advance ACS Abstracts, August 1, 1997.
measurements. An appropriate example of how much higher can become the barrier of a rotation-dominated process is that reported by Nelsen and Cunkle, who determined a $\Delta G^\circ = 12.0$ kcal mol$^{-1}$ in a N-neopentyl-substituted azabicyclo derivative. Three additional studies of crowded acyclic neopentylamines are also worth noting. In compounds 4–6, it is calculated that the most stable conformation for the molecule has the nitrogen lone pair to neopentyl group bond about 20° from eclipsed, with nitrogen inversion/rotation barriers of 8.8, 8.2, and 9.2 kcal mol$^{-1}$, respectively, which are relatively large for such highly substituted amines. In the case of 6, the conformation is confirmed by a crystal structure determination. For each of these molecules, other conformations of quite low relative energy, having the neopentyl group more or less perfectly eclipsed, are calculated to exist. In the case of 5, a signal is seen in the NMR at $-141°$ for this conformation, which is calculated to be over 20% populated at room temperature.

Dynamic NMR spectroscopy is suitable for studying unsymmetrical amines $R_1 R_2 NCH_2 Bu^t$ ($R_1 \neq R_2$) since, when interconversion of forms I and IV of Scheme 1 is slow on the NMR time scale, protons $H_1$ and $H_4$ are diastereotopic and there may be also changes in the spectrum of groups $R_1$ and $R_2$, if they are suitable. When $R_1$ and $R_2$ are identical, there are no changes in the signals of the neopentyl group, but the interconversion may be studied from changes in the spectrum of the substituent $R_1$ if it comprises a prochiral group.

The evidence for eclipsing of the $NCH_2$–$R$ bond is usually indirect. Molecular mechanics calculations (programs MMX and MM3 have been used) suggest whether the bond is eclipsed, and in at least one case, this conclusion was confirmed by direct X-ray crystallographic evidence. Forsyth has suggested that, in $R_2 NCH_2 Bu^t$ derivatives, which have been desymmetrized by deuterium substitution (i.e., $R_2 NCDH_{Bu^t}$), the temperature-dependent separation of the $^{13}$C NMR signals for groups $R_2$ (which are enantiotopic in the absence of labeling) “is diagnostic of isotopic perturbation of a degenerate equilibrium”. On this basis he concluded that in compounds such as $4$-tert-butyl-$N$-benzyl-$d_1$-piperidine or $Me_2 NCHD(CH_2)_3 Me$ a substantial amount of gauche $N$–$CD$ bond conformation had to be present. On the contrary, the 4-tert-butyl-$N$-neopentyl-$d_1$-piperidine is likely to adopt essentially a single (eclipsed)

| Table 1. Calculated Conformations (Torsion Angles) for Dialkynopenylamines $R_1 R_2 NCH_2 Bu^t$ (1–10) as Obtained by MM3 Calculations$^a$ |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| compd | $R_1$ | $R_2$ | group $R_1$ | group $R_2$ | relative energy |
| 1 | Me | Me | $lp$-$N$–$CH_2 Bu^t$ | $lp$-$N$–$C$–$X$ | $lp$-$N$–$C$–$X$ | 13 | 56 | 62 | 0.00 |
| 2 | Et | Me | $lp$-$N$–$CH_2 Bu^t$ | $lp$-$N$–$C$–$X$ | $lp$-$N$–$C$–$X$ | 13 | 48 | 64 | 0.00 |
| 3 | Et | Et | $lp$-$N$–$CH_2 Bu^t$ | $lp$-$N$–$C$–$X$ | $lp$-$N$–$C$–$X$ | 19 | 42 | 64 | 0.00 |
| 4 | Pr$^a$ | Pr$^a$ | $lp$-$N$–$CH_2 Bu^t$ | $lp$-$N$–$C$–$X$ | $lp$-$N$–$C$–$X$ | 22 | 73 | 80 | 0.00 |
| 5 | Et | Bu$^a$ | $lp$-$N$–$CH_2 Bu^t$ | $lp$-$N$–$C$–$X$ | $lp$-$N$–$C$–$X$ | 26 | 22 | 176 | 0.00 |
| 6 | CH$_2$Bu$^a$ | $lp$-$N$–$CH_2 Bu^t$ | $lp$-$N$–$C$–$X$ | $lp$-$N$–$C$–$X$ | 24 | 33 | 176 | 0.00 |
| 7 | CH$_2$Bu$^a$ | Me | $lp$-$N$–$CH_2 Bu^t$ | $lp$-$N$–$C$–$X$ | $lp$-$N$–$C$–$X$ | 23 | 37 | 61 | 0.00 |
| 8 | CH$_2$Bu$^a$ | CH$_2$Ph | $lp$-$N$–$CH_2 Bu^t$ | $lp$-$N$–$C$–$X$ | $lp$-$N$–$C$–$X$ | 27 | 32 | 47 | 0.00 |
| 9 | CH$_2$Bu$^a$ | $lp$-$N$–$CH_2 Bu^t$ | $lp$-$N$–$C$–$X$ | $lp$-$N$–$C$–$X$ | 24 | 35 | 167 | 0.00 |
| 10 | CH$_2$Bu$^a$ | CH$_2$Ad | $lp$-$N$–$CH_2 Bu^t$ | $lp$-$N$–$C$–$X$ | $lp$-$N$–$C$–$X$ | 31 | 32 | 32 | 0.00 |

$^a$ The relative energies are given in kcal mol$^{-1}$.

conformation$^a$ since the $^{13}$C shift separation of its carbons C2 and C6 appeared to be independent of temperature.

We here discuss dialkynopenylamines 1–10, compounds 7–10 having two or more neopentyl groups. The results for 4–6 have been taken from the literature.$^6$

Results and Discussion

Calculations of Conformations and Their Energies. Table 1 shows selected information on the MM3-calculated minimum energy conformations of compounds 1–10. For each of these compounds, all conformational minima having more than 2.5 kcal mol$^{-1}$ excess relative energy have been excluded. For convenience the torsion angle between the lone pair and the group X (when R is of the form CH$_2$X) is shown unless otherwise stated. Except for 7, conformations with the tert-butyl of a neopentyl group anti to the lone pair are always at least 4 kcal mol$^{-1}$ higher in energy so will not be further discussed. It is important however that this justifies our talking of nitrogen inversion/rotation as a single process. In other systems,$^3$ nitrogen inversion and bond rotation in neopentyl compounds can be distinguished clearly and given separate barriers.

NMR Observations. (a) N,N-Dimethylneopentylamine (1). MM3 calculations (Table 1) indicate that along the NCH$_2$ bond there is a significant predominance of the eclipsed conformation over the gauche-staggered one. MMX suggests a less marked preference, eclipsed being more stable by only 0.2 kcal mol$^{-1}$ compared with 0.68 kcal mol$^{-1}$ (MM3). Experimental support for an eclipsed form might come from a barrier for the N-inversion/rotation process close to or higher than 9 kcal mol$^{-1}$.

This suggests that the interconversion is rotation dominated, a feature associated with an eclipsed ground state conformation (Scheme 1). Because of its symmetry, compound 1 is unsuitable for dynamic NMR study, so we used Forsyth’s stratagem of isotopic desymmetrization of 1 as Me$_2 NCDH_{Bu^t}$ (1-$d_1$). Here the N-methyl groups become diastereotopic when the N-inversion/rotation is slow on the NMR time scale. Furthermore, as explained in the Introduction, their observed chemical shift separation, by being dependent on (or independent of) the temperature, shows whether a significant amount of the two gauche conformers (i.e., 1B, C of Scheme 2) is present (or not) in the equilibrium.
In a CCl₃F/CHF₂Cl/CD₂Cl₂ solution, the NMe signal of 1-1d₁, which appears as a single line (¹³C, 75.5 MHz) at ambient temperature, broadens below −80 °C, decoalesces at about −104 °C and splits (at −110 °C) into a doublet, with a chemical shift separation (0.029 ± 0.001 ppm) which remains constant down to −130 °C. Nitrogen inversion/rotation is now slow on the NMR time scale, and the methyl groups are diastereotopic due to the chirality, created by the deuterium labeling, of the tert-buty1 bonded carbon atom (intrinsic isotope effect). A complete line-shape fit of the signal leads to a free energy of activation (∆G₁) of 9.4 ± 0.2 kcal mol⁻¹, corresponding to the interconversion of I and IV in Scheme 1.

It seems therefore appropriate to conclude that the quite high (9.4 kcal mol⁻¹) interconversion barrier, as well as the temperature-independent shift separation of the two NMe lines is indicative of a single, eclipsed conformer (1A in Scheme 2). This agrees with MM3 calculations mentioned above which correspond to a population of almost 90% eclipsed (at −110 °C). Furthermore, the observed chemical shift difference of 0.029 ppm agrees exactly with that found in the corresponding deuterated N-neopentylpiperidine derivative which is eclipsed at the N=CHD bond. This suggests that there is no conformational equilibrium contributing to the difference in chemical shifts but, in both cases, merely an intrinsic isotope-induced asymmetry.

It should also be reported that the ¹³C tert-buty1 methyl signal in both 1-1d₁ and in the unlabeled 1 broadens below −140 °C and eventually splits (−155 °C at 75.5 MHz) into a 1:2 doublet (Figure 1), whereas the other signals of the spectrum are not affected. Such a feature is clearly the consequence of a restricted H₂C=CMMe₃ bond rotation, which yields a staggered rotamer where two equivalent methyl groups of the tert-buty1 moiety are gauche to the dimethylamino group and the third one is anti. The corresponding interconversion barrier (∆G = 5.9 ± 0.15 kcal mol⁻¹) fits the expectation for this type of rotational process.

Quite surprisingly, in an acetone-δ₂/CCl₃F solution of 1-1d₁, the separation of the two ¹³C NMe signals (detected below −100 °C at 100.6 MHz) increases remarkably on further lowering the temperature (i.e., 0.045, 0.062, 0.078, and 0.090 ppm at −105, −110, −115, and −120 °C, respectively), whereas the interconversion barrier was unaffected by the change of the solvent. As mentioned above, such a change in relative shifts indicates a temperature-dependent equilibrium, the most obvious possibility being one involving eclipsed and gauche conformations. This implies that in the highly polar acetone solution there is now a significant population of the asymmetric (thus probably more polar) gauche conformer in contrast to the situation encountered in a solvent of lower polarity such a CCl₃F/CHF₂Cl/CD₂Cl₂. Indeed MM3 (and even more so MMX) calculations yield an energy difference between the two conformers which is relatively small (Table 1), so it is not implausible that there be a noticeable change of their relative proportions in solvents of quite different polarity. Any significant equilibrium, however, might be responsible for the temperature dependence of chemical shifts.

(b) N,N-Diethylneopentlamine (3). This compound is considered before N-ethyl-N-methylneopentlamine (2) since knowledge of the conformations of the former helps an understanding of the latter. Both the ¹H and ¹³C NMR spectra of 3 are temperature dependent, and some of the changes of ¹H spectra have been reported previously by Forsyth. Thus, the protons of the ethyl groups become diastereotopic at low temperatures (see Table 2), showing that the nitrogen inversion/
The doubling of the signals for the lone neopentyl group (lines a and c of Figure 2) indicates that two different sets of conformations, fortuitously of about equal population, are present. The very low temperature range at which these conformers become detectable strongly suggests that they result from restricted rotation of the N ethyl groups. Indeed both MM3 and MMX calculations (see Table 1, first two entries for 3) suggest that two such forms, differing by the arrangement at the two ethyl moieties, have quite similar energies (the computed difference being respectively 0.36 and 0.1 kcal mol$^{-1}$). The same calculations suggest that the neopentyl group eclipses the N lone pair in both cases.

The three signals (lines b of Figure 2) observed for the NCH$_2$ ethyl carbons at $-151^\circ$C, and the 3:1 intensity ratio observed for the two signals of the methyl ethyl carbons (lines e of Figure 2), indicate that in one of the two exchanging sets the two ethyl groups are different, whereas in the other they are equivalent. Since neither of the two most stable computed structures of 3 has a symmetry which would account for two equivalent ethyl groups, the observed equivalence must be the result of a fast (in the NMR time scale) dynamic exchange. The stereodynamics of such a process can be understood on the basis of Scheme 3.

Structure 3A corresponds to the first entry for 3 in Table 1, calculated to be most stable, and has both the methyl groups of the ethyl moiety in a gauche relationship to the nitrogen lone pair. The methyl (starred) of one of the two ethyl groups can rotate past the nitrogen lone pair in a low-energy process leading to the symmetrical conformer 3B (where the two ethyl groups are equivalent).

The energy of 3B is computed to be more than 2 kcal mol$^{-1}$ higher than 3A, so that this conformer is not appreciably populated (thus not observed experimentally). From 3B, however, an analogous rotation of the methyl of the other ethyl group (unstarred) leads equally easily to the enantiomeric conformer (3A’, not shown) of 3A. The rapidly interconverting conformational set comprising 3A, 3B, and 3A’ thus yields only one set of signals for the two ethyl groups even at the lowest temperatures.

The second kind of conformational minimum 3C (or its enantiomer 3C’) corresponds to the second entry for 3 in Table 1 and has one methyl group anti to the lone pair while the other is gauche. Contrary to the previous case, a low barrier rotation of a methyl group past a lone pair is not a means of interconverting 3C and 3C’ so a single molecule in conformation 3C (or 3C’) gives two ethyl signals, one each for the anti and...
gauche ethyl groups. The interconversion of 3C (and 3C') into the first conformational set (3A, 3B, 3A') involves a methyl group rotating past an ethyl or neopentyl group, and it is such rotation processes which are slow on the NMR time scale at −151 °C. A complete line-shape analysis yielded the corresponding barrier, i.e., $\Delta G^\ddagger = 6.0 \pm 0.2 \text{ kcal mol}^{-1}$.

(c) N-Ethyl-N-methylneopentylamine (2). Two dynamic processes appear in the NMR of this compound. The first is visible only in the $^1$H NMR spectra (300 MHz) of the CH$_2$-N groups, where the two protons of the CH$_2$Bu$_t$ and of the CH$_2$-Me groups become diastereotopic, below −80 and −100 °C, respectively. These changes, summarized in Table 2, correspond to nitrogen inversion/rotation becoming slow on the NMR time scale with barriers (derived again by total line-shape analysis) equal to 8.95 and 8.75 kcal mol$^{-1}$, respectively, yielding an average value of 8.85 ± 0.15 kcal mol$^{-1}$.

Below about −120 °C, further changes are seen in the $^{13}$C spectra (75.5 MHz). Different degrees of broadening, followed by sharpening on further cooling, are observed for a number of the signals, behavior typical of a dynamic NMR process between two conformers of very different intensity. The effect is most evident for the methyl signal of the ethyl group, which reaches its maximum broadening at −129 °C. A separate minor signal could not be observed, however, when the line sharpened again at the lowest attainable temperature (−145 °C), which suggests an intensity for this second conformer lower than about 5%. It seems reasonable to conclude, by comparison with 3, that an ethyl-group rotation process is taking place, and the method of Anet and Basus$^{11}$ allowed us to determine a free energy of activation of 6.6 ± 0.3 kcal mol$^{-1}$ for the N−CH$_2$ bond rotation.

Calculations suggest (see Table 1) that the neopentyl group is always eclipsed but that the three staggered conformations for the ethyl group are of similar energy. The first two of these, where the methyl of the ethyl group is gauche to the lone pair, interconvert by that methyl group rotating past the lone pair in a low-barrier process. The process producing the observed line broadening (at −129 °C) is plausibly the interconversion of the gauche pair of conformations with the anti conformation, in which the methyl of the ethyl group rotates past a methyl or a neopentyl group. Within the experimental errors the barrier measured for 2 (6.6 kcal mol$^{-1}$) is of a size comparable to that found for ethyl group rotation in 3 (6.0 kcal mol$^{-1}$).

(d) Trineopentylamine (9) and N-[(1-Adamantyl)methyl]dineopentylamine (10) are calculated to have similar conformational behaviors, with one conformer (and its enantiomer) being more stable than all others. The preferred conformation is calculated (Table 1) to be the one in which each tertiary alkyl group is gauche to the lone pair in the same sense with a torsion angle just over 30°, almost exactly halfway between staggered and eclipsed.

---


Structure V in Scheme 4 represents this conformation for 10 (R = 1-adamantyl) with each N−CH₂ bond rotated anticlockwise from eclipsed by 32°. This is accompanied by anticlockwise rotation of 11° about each CH₂−C_quat bond away from its normal staggered conformation and rotation of about 2° in a similar sense for each Me−C_quat bond.

In the enantiomeric conformation VI, all of these rotations are in a clockwise sense. Minimum energy conformations have thus been reached by rotation of all bonds, concertedly in the same sense, away from the ideal, taking this to mean the eclipsed conformation reported earlier for simpler molecules, for the N−CH₂ bonds.

As for NMR evidence, considering the more symmetrical compound 9 first, the ¹³C NMR spectrum shows no changes down to −150 °C, while in the ¹H NMR (Figure 3), the singlet for the methylene group broadens and splits to a symmetric AB-spectrum below −95 °C, with a barrier of 8.4 kcal mol⁻¹ for the dynamic process responsible. In contrast, the CH₂ signals of triethylamine⁵⁶ and tribenzylamine,⁵⁸ which have the same 3-fold symmetry formally, were found to split into more complex, asymmetric groups of lines.

Additional information was afforded by the less symmetric close analogue 10, in which the adamantyl moiety, although a different substituent, has steric requirements similar to those of the tert-butyl group. In the ¹³C NMR at −120 °C (Figure 4), the signals of the neopentyl group are split into equal doublets, except for the methyl carbon signal which is, however, broadened. There is no significant change in the adamantyl carbon signals compared with room temperature.

The low temperature appearance of the ¹H signals of the three N−CH₂ groups could be clearly interpreted only at much higher field (600 MHz). Down to −75 °C, this region appears as two singlets of relative intensity 4:2, but splits into three AB-type quartets of equal intensity at −125 °C (Figure 5 and Table 2). From the spectral parameters and the temperature of maximum broadening of these quartets, the barrier at the coalescence temperature was evaluated as 8.3 kcal mol⁻¹, which is not different, within the experimental error, from that (8.6 kcal mol⁻¹, as in Table 3) determined by ¹³C NMR.

Figure 3. ¹H signal (300 MHz) of the methylene hydrogens of trineopentylamine (9) as function of temperature.

Figure 4. ¹³C NMR spectrum (75.5 MHz) of 10 at −35 °C (top) and −120 °C (bottom). At the latter temperature, the line of the neopentyl NCH₂ carbons and that of the quaternary tert-butyl carbons are split.

There are two sets of processes that can interconvert enantiomeric conformations, and in Scheme 4, which shows Newman projections along CH₂−N bonds, some protons and carbons are labeled A, B, X, and Y to indicate their fate when this happens. The first process is a rotation of about 60° by each CH₂R group which interconverts conformers V and VI. According to the calculations, there is no conformational minimum with one CH₂R group rotated in the sense opposite to the other two, so this suggests that the three groups must rotate together in a single process in which each N−CH₂ bond is eclipsed in turn.

The second enantiomerization route is formally inversion of the nitrogen atom plus rotation of about 180° about N−CH₂ bonds leading to structures VII and VIII, which correspond to V and VI but with groups X and Y interchanged. If N−CH₂ bond rotation and N-inversion occur independently of each other, a very unstable intermediate structure like IX would be involved. It is more likely that as nitrogen inversion progresses some degree of rotation of one or more of the CH₂R groups takes place, so that interconversion takes place with a smaller barrier by not involving IX.

Consideration of Scheme 4 shows that for the more symmetrical compound 9, neither the slowing of 60° rotation alone nor the slowing of nitrogen inversion/rotation alone produces a change in the spectrum. H₈ becomes different from H₉ only when both processes are slow on the NMR time scale, and even then, groups X and Y remain equivalent. Thus, of the two enantiomerization processes for 9, one has a barrier of 8.4 kcal mol⁻¹ while the other has a barrier greater than this, but how much greater cannot be determined, nor is there any indication which barrier is which.

Considering the less symmetrical compound 10 in the light of Scheme 4, slowing of 60° rotation on the NMR time scale does not make H₈ different from H₉, nor group X different from group Y. Slowing of nitrogen inversion/rotation alone does make H₈ different from H₉ but does not make X and Y different. Differentiation of X and Y requires both processes...
to be slow. Since, in the dynamic NMR experiment, A becoming different from B and X becoming different from Y are associated with barriers which are the same within experimental error, the barrier to 60° rotation must be at least as high as that for nitrogen inversion/rotation.

It is difficult to suggest what barrier should be expected for a concerted 60° rotation about N atoms. The nitrogen inversion/rotation process involves a tert-butyl or adamantyl group rotating past a neopentyl or adamantylmethyl group, so it is plausible that the barrier is greater not only than the 8.4 kcal mol⁻¹ experimental value but also than the 9.4 kcal mol⁻¹ value found for compounds 1, 4, and 5. tert-Butyl rotated away from eclipsing by 23° and 36° in the same sense, so that there are two enantiomeric versions of this structure. Almost as stable is the pair of enantiomeric conformations with tert-butyl groups rotated away from eclipsing in opposite directions, i.e., toward the methyl group substituent, one by only 6° (thus eclipsed) and the other by 49° (thus nearly staggered). Interconversion of these four conformations is presumably always fast on the NMR time scale since it is calculated to require an energy as low as 0.9 kcal mol⁻¹.

The additional phenyl substituent of compound 8 compared with 7 makes it more like 9 superficially, and the conformation like V of Scheme 4 is calculated to be the most stable, see Table 1. There is much less crowding than in 9 since the phenyl group rotates to present a face toward the two adjacent tert-butyl groups. The rotation process of about 60° appears to be much easier for 8 than 9 and to follow a stepwise mechanism, since it is calculated that for 8 conformational minima exist with one group skewed in the opposite sense from the other two.

For 7 and 8, interlocking of alkyl groups in the ground state is much less important than in 9 and 10 and in a different way in 6. The high barriers associated with eclipsed neopentyl groups in compounds 1–3 are not found, so 7 and 8 are closest in behavior to compounds 4 and 5.

Conclusions

Eclipsing is expected for a trialkylamine R¹R²NCH₂R³ when R¹, sterically compressed by R² and R³, prefers to distance itself as much as possible from these groups and ends up eclipsing the nitrogen lone pair. Forsyth showed that for neopentylamines, i.e., where R³ is as big as a tert-butyl group, eclipsing is found even when R¹ and R² are quite small, as in N-neopentylpiperidine and diethylneopentylamine (3). Eclipsing has now been demonstrated in even simpler compounds 1 and 2, and the relatively high tert-butyl rotation barrier in 1 suggests that the eclipsed ground state of that molecule is not particularly strained. In 3, substantial barriers have been found for rotation about the N-ethyl bond when it involves a methyl group rotating past another alkyl group. The results reported for 7–10, when considered together with earlier results for 4–6, show that, with additional steric crowding, eclipsing of the neopentyl group is no longer the favored outcome, although sometimes the eclipsed conformation is quite close in energy to the most stable (it is even 20% populated in 5). When R¹ and R² do little more than compress the tert-butyl group laterally, as in 1–3, eclipsing is favored, but when these two groups are branched enough to make significant steric demands on each other, eclipsing of the neopentyl group is not the outcome. It is reasonable to be mindful that eclipsing of bonds other than C–N may become less likely in a similar way as the degree of substitution increases.

(e) N,N-Dineopentylmethyamine (7) and N,N-Dineopentylbenzylamine (8). As the temperature is lowered in both of these compounds, the methylene protons of the neopentyl groups broaden and split to give an AB-quartet (see Table 2) in a way that is quite typical of nitrogen inversion/rotation becoming slow on the NMR time scale. This corresponds in both cases to a barrier of 8.4 kcal mol⁻¹. At lower temperatures, down to −135 °C, in both cases no further changes are observed in the spectra, in particular the benzylmethene protons signal remains a singlet, and no changes are seen in the ¹³C NMR.

Molecular mechanics calculations are once again helpful in understanding the conformational possibilities. For 7, two closely related types of minima of very similar energy, interconverting readily with each other, are the most stable. In the slightly more stable, the conformation is reminiscent of the trineopentylamine conformation discussed above, with the tert-butyl rotated away from eclipsing by 23° and 36° in the same sense, so that there are two enantiomeric versions of this structure. Almost as stable is the pair of enantiomeric conformations with tert-butyl groups rotated away from eclipsing in opposite directions, i.e., toward the methyl group substituent, one by only 6° (thus eclipsed) and the other by 49° (thus nearly staggered). Interconversion of these four conformations is presumably always fast on the NMR time scale since it is calculated to require an energy as low as 0.9 kcal mol⁻¹.
and 5 g (0.16 mol) of dimethyamine in 20 mL of dry benzene was added dropwise 2 mL (0.0185 mol) of TiCl₄ in 5 mL of benzene. The mixture was stirred for 3 h until the IR aldehyde band (1729 cm⁻¹) in benzene was replaced by that of the imine (1673 cm⁻¹). The precipitate was filtered off under nitrogen, whereas the solution was slowly added to a mixture of 1.6 g (0.038 mol) of LiAlD₄ in 20 mL of dry ether. After being stirred overnight at room temperature, the reaction was completed. A saturated aqueous NH₄Cl solution (20 mL) was slowly added, and after stirring for 0.5 h, the organic layer was separated, dried, and saturated with dry HCl to yield 4 g of the white chloridate of the deuterate secondary amine. The amine, separated by treating the salt with 5 mL of 10 M KOH, was reflushed 3 h with 8 mL of formic acid and 4.8 mL of formic aldehyde (40% in water). The rough product obtained after the work up was distilled to yield 2 g of a colorless liquid: ¹H NMR (CDCl₃) δ 0.83 (s, 9H, CMe₃), 1.98 (t, J = 9.7 Hz, 1H, NCHD), 2.25 (s, 6H, NMe); ¹³C NMR (CDCl₃) δ 28.0 (CMe₃), 32.60 (CMe₃), 48.76 (NMe), 65.78 (NCHD).

Amines 2–10 were synthesized with a general procedure starting from neopentylamine (Aldrich) that was reacted with the appropriate acyl chloride. The amide was reduced with LiAlH₄ and the secondary amine reacted again with the appropriate acyl chloride. The resulting secondary amide was reduced with LiAlH₄ to give the desired tertiary amine. The compounds were identified as follows.

**N-Ethyl-N-methylenepentamethylamine (2):** ¹H NMR (CDCl₃) δ 0.87 (s, 9H, CMe₃), 1.02 (t, J = 3H, C₂H₂CH₂), 2.07 (s, 2H, NCH₂), 2.28 (s, 3H, NMe), 2.45 (q, 2H, CH₂CH₂); ¹³C NMR (CDCl₃) δ 28.18 (CH₂CH₂), 28.13 (CMe₃), 32.75 (CMe₃), 45.28 (NMe), 54.26 (CH₂CH₂), 69.62 (NCHD).

**N-Diethylpentamethylamine (3):** ¹H NMR (CDCl₃) δ 0.83 (s, 9H, CMe₃), 0.88 (t, J = 3H, C₂H₂CH₂), 2.05 (s, 2H, NCH₂), 2.45 (q, 2H, NCH₂CH₂); ¹³C NMR (CDCl₃) δ 12.43 (CH₂CH₂), 28.26 (CMe₃), 32.70 (CMe₃), 49.58 (NCH₂CH₂), 66.58 (NCHD).

**N,N-Dipentamethylbenzylamine (8):** ¹H NMR (CDCl₃) δ 0.82 (s, 18H, CMe₃), 2.20 (s, 4H, NCH₂), 2.32 (s, 3H, NMe); ¹³C NMR (CH₂Cl/CD₄) δ 28.9 (CMe₃), 33.4 (CMe₃), 48.1 (NMe), 74.6 (NCH₃).

**N,N-Trinemethylpentamethylamine (9):** ¹H NMR (CDCl₃) δ 0.97 (s, 9H, CMe₃), 2.40 (s, 2H, CH₂); ¹³C NMR (CDCl₃) δ 28.67 (CMe₃), 32.79 (CMe₃), 71.44 (NCH₃).