Tetrahedron Letters No. 8, pp 503 - 506, 1975. Pergamon Press. Printed in Great Britain.

STEREODYNAMICS OF N-ISOPROPYL-N,N-DIALKYLAMINES. DIRECT NMR OBSERVATION OF DIASTEREOTOPIC ISOPROPYL METHYL GROUPS AND SLOW NITROGEN INVERSION

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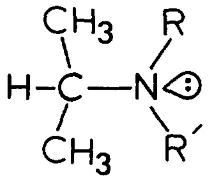
(Received in USA 21 November 1974; received in UK for publication 14 January 1975)

A considerable effort has been expended to determine the relative rates of nitrogen inversion and carbon-nitrogen single bond rotation in simple amines,[2] more hindered N-tert-butyl-N,N-dialkylamines,[3] and cyclic amines.[4] Although evidence exists to support concerted tert-butyl rotation and nitrogen inversion in N-tert-butyl-N,N-dialkylamines,[3] there have been no reports concerning the stereodynamics of the less hindered and more unsymmetrical N-isopropyl-N,N-dialkylamines.

Examination of the ^1H dnmr spectrum (60MHz)[5] of **1** (7% v/v in $CBrF_3$) revealed



1: R = CH_3; R′= CD_2CD_3

2: R = R′= CH_3

5: R = R′= $CH(CH_3)_2$

6: R = R′= $CH_2C_6H_5$

7: R = CD_2CD_3; R′= $CH(CH_3)_2$

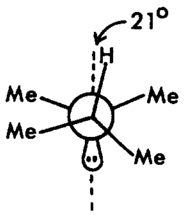
8: R = CH_3; R′= $CH_2C_6H_5$; isopropyl deuteriated at the methine position

9: R = CH_3; R′= $CH(CH_3)_2$

10: R = R′= CH_2CD_3

a typical isopropyl doublet (δ1.00) at -61.8° (Figure) resulting from spin-spin coupling to the methine hydrogen (^3J = 6.3 Hz). At lower temperatures (Figure), the isopropyl resonance broadens and then sharpens into an apparent triplet consistent with slowing a rate process on the dnmr time scale. Indeed, a complete dnmr line shape analysis at -141.7° (Figure) using computer program DNMR3[5] revealed the apparent triplet to be two overlapping doublets (δ0.95, ^3J = 6.3 Hz; δ1.05, ^3J = 6.3 Hz) of equal area consistent with the diastereotopic isopropyl methyl groups being rendered nonequivalent due to slowing the nitrogen inversion rate process.[3] The accompanying observation that the N-methyl resonance of **1** remains a singlet from -61.8° to -141.7° in addition to the observation of equal areas under the two isopropyl methyl signals at -141.7° (Figure) are consistent with slow nitrogen inversion and either fast N-isopropyl C-N rotation between different rotamers at -141.7° or a strong rotamer conformational preference with fast or slow N-isopropyl rotation.

Theoretical calculations performed in this laboratory using the intermediate neglect of differential overlap (INDO) method[3] reveal interesting conformational preferences relevant to the above discussion. Using a geometry optimization approach,[3] the minimum potential energy conformation for pyramidal **2** occurs with all CNC bond angles equal to 113.1° and a dihedral angle between the lone pair and the methine C-H bond of 159° (**3**). Conformation **3** is calculated to be 1.6 kcal/mole more stable than the distorted gauche form **4** in which optimum CNC bond angles are also 113.1° and the dihedral angle between the lone pair and the methine C-H bond is 90°. At -140° assuming $\Delta S°$ is equal to zero, the calculated equilibrium constant (K_{eq}=[**3**]/[**4**]) is approximately 400 rendering the two equivalent gauche forms essentially invisible to the nmr method which is consistent with two of the dynamical models described above. In fact, no changes were observed in the ^{1}H dnmr spectra of **2** and **5** to -178° consistent with the strong conformational preference calculated above and with fast or slow N-isopropyl



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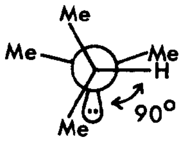

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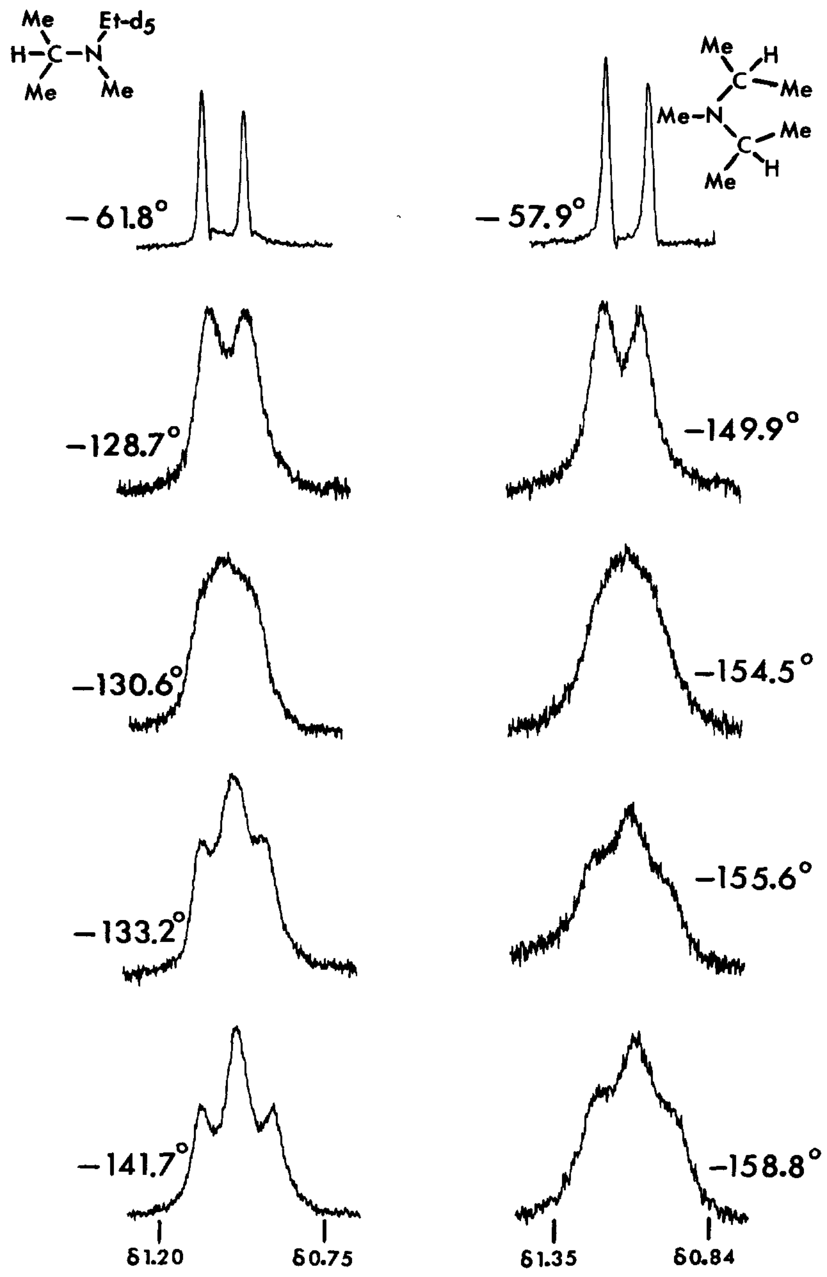
Me
Et-d5
H–C–N
Me
Me
−61.8°
−128.7°
−130.6°
−133.2°
−141.7°
δ1.20
δ0.75
Me
H
C
Me
Me–N
Me
C
H
Me
−57.9°
−149.9°
−154.5°
−155.6°
−158.8°
δ1.35
δ0.84

rotation.

Capitalizing again on the diastereotopic nature of pertinent geminal groups, the ^1H dnmr spectra of compounds **6-10** changed in a manner consistent with slowing at least nitrogen inversion. The N-isopropyl resonance of **9** is illustrated in the Figure. Free energies of activation ($\Delta G^{\ddagger}$) for inversion in this series are compiled in the TABLE. Although the barriers to inversion in this series of isopropyl amines fall within a relatively narrow range (5.9-7.4 kcal/mole), there is a rough direct dependence of the rate of inversion on crowding, e.g., compare **1** and **7**, **9**, or **10**, as well as an apparently strong N-isopropyl conformational preference revealed by the INDO calculations.

TABLE. Inversion Barriers in N-Isopropyl-N,N-Dialkylamines

compd	dynamic resonance	$\Delta G^{\ddagger}$, kcal/mole	compd	dynamic resonance	$\Delta G^{\ddagger}$, kcal/mole
1[a]	$C(CH_3)_2$	7.4±0.2 (-131°)	**8**[a]	CH_2	6.2±0.4 (-138°)
6[b]	CH_2	7.0±0.4 (-138°)	**9**[a]	$C(CH_3)_2$	6.0±0.2 (-155°)
7[a]	$C(CH_3)_2$	6.5±0.2 (-148°)	**10**[a]	CH_2	5.9±0.4 (-155°)

(a) solvent: $CBrF_3$. (b) solvent: CH_2=CHCl.

Acknowledgement: We are grateful to the National Science Foundation (grants GP-18197 and MPS74-17544) for support.

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