Experimental Section

Pmr spectra were measured with Varian A-60, A-60A, and HA-100 spectrometers equipped with variable temperature probes and accessories. Chloroform-*d* ($CDCl_3$) and chlorobenzene (C_6H_5Cl) were used as solvents and tetramethylsilane was included as an internal standard and field lock.

A computer program, written in Fortran IV for an IBM 1800 computer, which utilized the Gutowsky–Holm line equation, was used to generate line shapes for a given relaxation time. The experimental line widths less T_2 of methylene chloride were computed to give the rate constant at a given temperature. Plots of log k *vs.* $1/T$°K (see Discussion) were used to obtain the activation energies.

For all compounds, whether previously reported or not, microanalyses were obtained from Schwartzkopf Microanalytical Laboratory, Woodside, N. Y., and Micro-Analysis, Inc., Wilmington, Del. Melting points were obtained on a Fisher-Johns block or a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra were obtained on a Beckman IR-5A spectrophotometer.

1-Benzyl-2-acetyl-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline (1) was prepared as previously noted.[1b]

1-*t*-Butyl-2-acetyl-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline (2) was prepared by a modification of the procedure of Craig, *et al.*[18] The amine, prepared as noted,[18] was acetylated with acetyl chloride in pyridine and recrystallized from benzene–heptane (1:1).

Anal. Calcd for $C_{17}H_{25}NO_3 \cdot 0.5H_2O$: C, 67.97; H, 8.72; N, 4.66. Found: C, 68.14; H, 8.92; N, 4.65.

1-Methyl-2-acetyl-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline (3), mp 100–101° (lit.[19] mp 100–101°), was prepared according to Hromatka, *et al.*,[19] and recrystallized from hexane.

2-Acetyl-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline (4) was prepared as previously noted.[1b]

1-(2′-Aminobenzyl)-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline (5) was prepared according to the procedure of Weisbach and Douglas,[20] mp (hydrochloride) 257–258° dec (lit.[20] mp 256–257° dec).

1-(2′-Ambinobenzyl)-2-methyl-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline (6) was prepared according to the procedure of Gulland and Haworth,[21] mp 95–96°, hydrochloride mp 240° dec (lit.[21] mp 243–244° dec).

1-(2′-Aminobenzyl)-2-benzyl-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline (7) was prepared according to the procedure of Weisbach and Douglas,[20] mp 120° (lit.[20] mp 112–114°).

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Nuclear Magnetic Resonance Spectroscopy. Slow Nitrogen Inversion in an Acyclic Substituted Hydrazine[1a]

J. Edgar Anderson,[1b] Dean L. Griffith, and John D. Roberts

Contribution Number 3815, Gates and Crellin Laboratories of Chemistry, California Institute of Technology, Pasadena, California 91109.
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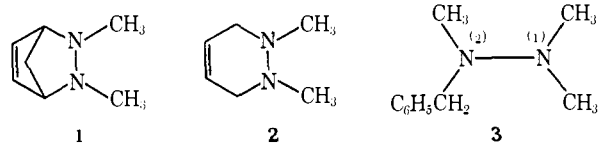
Abstract: Changes which were found to occur in the proton nmr spectrum of benzyltrimethylhydrazine at low temperatures are discussed in terms of hindered rotation about the nitrogen–nitrogen bond and slow nitrogen inversion. It is concluded that, below −130°, inversion of the nitrogen atom bearing the benzyl group is slow on the nmr time scale. The barrier to inversion is calculated to be 6.8 kcal/mol, which is substantially lower than the barriers found for cyclic and bicyclic hydrazines or for group V analogs of hydrazine.

Recently, there have been several studies of nitrogen inversion in cyclic and bicyclic hydrazine derivatives.[2-9] At about −60°, nitrogen inversion is slow on the nmr time scale for compounds of types **1**[3] and **2**.[9]

The barriers to nitrogen inversion in these substances are substantial, and it is perhaps surprising that there has been no report of barriers to nitrogen inversion of acyclic alkylhydrazines. Clearly, knowledge of such barriers is important for an understanding of those found in the cyclic compounds.

Some time ago we reported studies of the inversion rates of nitrogen atoms bearing electronegative substituents,[10] among which was benzyltrimethylhydrazine (**3**). No significant change in the proton nmr spectrum of **3** was observed on cooling to −70°. We have now extended our examination to much lower temperatures, and report here the changes observed.



1 2 3

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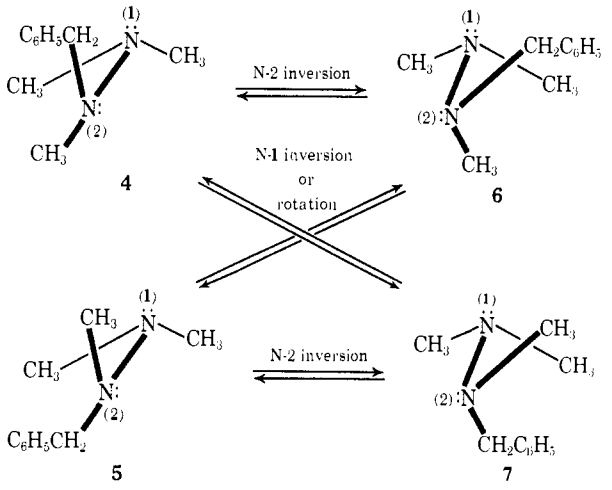

Figure 1. Conformational equilibration of benzyltrimethylhydrazine showing possible interconversions by rotation about the N–N bond and inversion of the nitrogen atoms.

Results

The nmr spectrum of **3** taken as previously described[10] in dichlorodifluoromethane solution at the ambient probe temperature shows three singlets of relative intensities 2:3:6 with chemical shifts of 3.20, 2.17, and 2.32 ppm from tetramethylsilane (internal reference), respectively. These absorptions can be assigned to the benzylic hydrogens, the hydrogens of the N-2 methyl group, and the hydrogens of the two N-1 methyl groups, respectively.

As the temperature of the sample is lowered below −60°, at a spectrometer frequency of 60 MHz, these signals begin to broaden, but this is, in our experience, a general feature of the spectra of compounds of this type. It may be that this broadening is associated with incomplete quadrupole-induced relaxation involving the nitrogen-14 atoms. Below about −115°, the signal of the benzylic hydrogens begins to broaden much more markedly than that of the methyl hydrogens, and at about −130° it is almost undetectable in the base-line noise. At still lower temperatures, the signal reappears as two absorptions separated by about 50 Hz, and at −137° each of these absorptions shows a suggestion of splitting. At lower temperatures, further broadening associated with viscosity changes tends to obscure the spectrum, which at −150° appears as a single very broad peak spanning the N-methyl and N-benzyl region. The N-methyl peaks show no broadening which could not be accounted for by either viscous or quadrupole broadening. Below about −135°, this broadening is sufficiently great that only one unsymmetrical N-methyl peak is observed.

The benzylic hydrogen signal at −137° has the form then of an AB quartet with a chemical-shift difference of about 0.83 ppm and J_{AB} of about 14 Hz. Thence, at the coalescence temperature −130°, the rate of the process causing the spectral line-shape changes is about 135 sec^{-1} which corresponds to a free energy of activation ($\Delta G^{\ddagger}$) of 6.8 ± 0.3 kcal/mol for the process.[11,11a]

(11) The method of determination of the kinetic parameters is described by M. Oki, H. Iwamura, and N. Hayakawa, *Bull. Chem. Soc. Jap.*, **37**, 1865 (1964). The transmission coefficient is taken here as unity.

(11a) NOTE ADDED IN PROOF. The recent communication of M. J. S. Dewar and B. Jennings, *J. Am. Chem. Soc.*, **91**, 3655 (1969), gives an inversion barrier $\Delta G^{\ddagger}$ for N,N-dibenzylhydrazine of ~8.5 kcal/mol which is reasonably compatible with that reported here for **3**, considering the differences in structures. The conclusions of Dewar and Jennings about the nature of the shift-averaging process(es) in compounds of this type are similar to ours.

Discussion

It seems generally accepted on the basis of theoretical[12] and experimental[13] evidence that the preferred conformation of hydrazine itself has a dihedral angle of about 90° as in **4** or **5** or their mirror images **6** and **7** (see Figure 1). For substituted hydrazines, the preferred dihedral angle will depend on the particular interactions associated with each alkyl group but could well be close to 90° as shown in the figure.

There are three possible processes in terms of which the experimental results should be discussed. These are rotation about the nitrogen–nitrogen bond and inversion of either N-1 or N-2. These possibilities are reflected in Figure 1, and we can make the following predictions about the effect of having one or more of these three processes become slow on the nmr time scale. (1) If rotation is slow, and both nitrogen inversions are fast, there should be no change in the nmr spectrum. A molecule can interconvert between any of the conformations **4**–**7** by the correct series of nitrogen inversions. (2) If inversion of N-2 is slow and the other processes are fast, then molecules are separated into two groups, those which adopt **4** or **7** and those which adopt **5** or **6**. Because the possible pairs are enantiomers the populations of the groups will be equal. The configuration at N-2 is *R* for **4** and **7**, and *S* for **5** and **6**. The methylene hydrogens in either group are now diastereotopic and should appear as an AB quartet, both groups giving the same AB quartet. As long as inversion of N-1 is fast, the methyl groups of the dimethylamino fragment are not diastereotopic with respect to N-2 and should show only one singlet absorption. (3) If inversion of N-1 is slow, and the other two processes are fast, complete interconversion of **4**–**7** is possible by the two allowed processes, so that no change is seen in the nmr spectrum.

From the above we conclude that the only single process which can produce the observed spectral changes is slow inversion of N-2, and the barrier to inversion is 6.8 kcal/mol. The arguments here depend rather importantly on the preferred conformation of **3** being one of **4**–**7**, that is, with the dihedral angle between the lone pairs being 90°. This is not in agreement with the conclusions of Colburn, Johnson, and Haney[14] for tetrafluorohydrazine, nor those of Imbery and Friebolin[15] for substituted aminophosphines. For these substances, the stable conformation appears to have a dihedral angle of 180°.

However, we have recently shown[9] that in a six-membered cyclic tetrahydropyridazine such as **2**, where steric strain in the ring plays only a small role, the preferred conformation of the hydrazine moiety is as in **8** rather than **9**. We consider that this is likely to be a better analogy for **3** than tetrafluorohydrazine or aminophosphines.

Because the changes in spectra were observed near the lower temperature limit attainable with our nmr equip-

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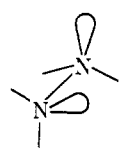

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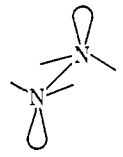


9

ment, we feel we can draw no definite conclusions as to the barriers to hindered rotation and to inversion of N-1. These may in fact be almost as great as the barrier measured, especially because there is little difference between the substituents on the nitrogens and one would expect that at the lowest temperatures attained inversion of N-1 should also be slow. There is no spectral evidence of this, but the doubling of the signal of the dimethylamino fragment expected when inversion of N-1 is also slow may have been obscured by the considerable line widths of the signals at the low temperatures of observation.

Of the pair of conformations **4** and **5** (and **6** and **7**), one is expected to be slightly more stable than the other because of different steric interactions. If **5** (and **7**), with the benzyl group *gauche* with respect to the two N-methyl groups, is more stable, then inversion of N-2 involves the interconversion between equal energy conformers; thus, there is no consequent driving force for for a second inversion to follow the first. Inversion of N-1 converts a stable conformation to an unstable one, but inversion of the second nitrogen does not return the molecule to the stable conformation, whereas rotation about the nitrogen–nitrogen bond does. Thus, in either case, there is no reason for the two nitrogen inversions to be energetically dependent on or connected to each other.

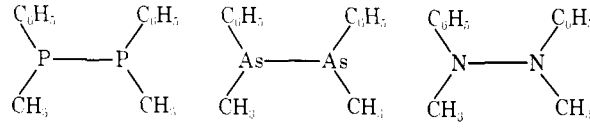
This situation is in marked contrast to that which obtains in compounds of type **1** discussed by Anderson and Lehn.[3] For these substances, inversion of one nitrogen atom leads to a rather strained intermediate form, and there is an energetic incenti' e for a second nitrogen inversion to take place to return the molecule to a stable conformation. However, there is no alternative process equivalent to rotation about the nitrogen–nitrogen bond in **3** for achieving this.

Barriers to nitrogen inversion in compounds of the series **1** and **2** are, in all cases, greater than 11 kcal/mol, and have been found as high as 14.5 kcal/mol.[3,9] The present work suggests that the contribution to these barriers from distortion of the configuration at one nitrogen atom is about 7 kcal/mol. The remaining 4.0–7.5 kcal/mol must then be associated with the cyclic character of these compounds.

The effect of an adjacent nitrogen atom on the inversion of a nitrogen is difficult to evaluate because there is as yet no experimental knowledge of the barrier to inversion of a simple trialkylamine in similar circumstances. The most recent theoretical calculation of the barrier to inversion of trimethylamine is 7.5 kcal/mol;[16] clearly an adjacent dimethylamino group does less to enhance the barrier to inversion than does an adjacent methoxyl function.[17]

The barrier to inversion found for **3** is much lower than that of corresponding diphosphines and diarsines. For compounds **10** and **11** barriers of 26.0[18] and 27.0[19] kcal/mole have been determined.

It would be expected that the barrier to inversion of



10 11 12

12, the exact analog of **7** and **11**, should be even lower than that of **3**[20] because the configuration at the nitrogen atoms in **12** is likely to be considerably flattened by delocalization of the nitrogen lone pair over the aromatic ring.

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(17) The barrier to inversion of N,O-dimethyl-N-benzylhydroxylamine is 12.7 kcal/mol at −16° in *n*-hexane solution.[10] It has been suggested by A. H. Cowley, M. J. S. Dewar, and W. R. Jackson, *ibid.*, **90**, 4185 (1968), that for this particular case hindered rotation about the nitrogen–oxygen bond could be the source of changes in the nmr spectrum. However, this possibility does not seem likely because, even if rotation about this bond were slow and configurational inversion at the nitrogen atom were fast, fast configurational inversion at the oxygen atom should render the benzylic hydrogens magnetically identical; see J. B. Lambert and D. H. Johnson, *ibid.*, **90**, 1349 (1968). The opposite view has been supported by M. Raban and G. W. J. Kenney, Jr., *Tetrahedron Lett.*, 1295 (1969), on the basis of substituent effects on conformational changes in trialkylhydroxylamines.

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