

# Nuclear Magnetic Resonance Spectroscopy. Magnetic Nonequivalence Due to Slow Inversion in Amines<sup>1</sup>

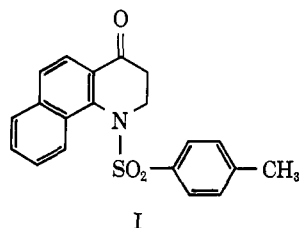
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Contribution No. 3250 from the Gates and Crellin Laboratories of Chemistry, California Institute of Technology, Pasadena, California. Received May 20, 1965

Investigation of the low-temperature n.m.r. spectrum of *N*-benzyl-*O,N*-dimethylhydroxylamine has permitted a determination of the rate and activation energy for nitrogen inversion. The energy barrier to inversion has been found to be inversely proportional to the solvent dielectric constant in four rather nonpolar solvents. In *n*-hexane,  $E_a$  was found to be  $12.9 \pm 0.3$  kcal. while in methylene chloride a value of  $9.4 \pm 0.4$  kcal. was obtained.

The use of n.m.r. spectroscopy is potentially a very powerful method for investigating inversion rates of amines. When a methylene group is bonded to a nitrogen carrying two dissimilar groups, it is expected that the methylene protons will experience differing chemical shifts as a result of the asymmetric environment. The nonequivalence so produced should be similar to that produced by an asymmetric carbon.<sup>3,4</sup> However, if inversion at the nitrogen occurs rapidly, the two methylene protons will interchange environments, and the resulting spectrum will show a single, sharp line at the average of the two chemical shifts.

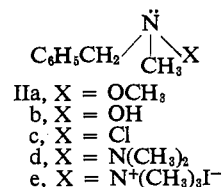
Nitrogen inversion rates have been successfully determined by changes of n.m.r. spectra with temperature for ethylenimines<sup>5-7</sup> and the *N*-tosylbenzquinolone I,<sup>8</sup> where the rate of inversion is believed to be unusually



slow as a result of steric restrictions.<sup>5,8,9</sup> Unfortunately, the very high inversion rates of simple aliphatic tertiary amines preclude general use of the n.m.r. method. However, Saunders and Yamada<sup>10</sup> have employed an elegant modification of the method which involves

protonation of the amine and observing the rate of loss of nonequivalence of methylene groups in the amine salt. By this means, it was possible to show that the rate constant  $k$  for the inversion of dibenzylmethylamine is  $2 \pm 1 \times 10^5$  sec.<sup>-1</sup> at 25°. The procedure encounters some difficulties in accurate measurement of energy barriers, and it is more or less limited in application to aqueous solutions.

In the present investigation we have set out to determine whether one could find a substituent, X, for simple amines of structure II which would give sufficiently slow rates of inversion to allow convenient, direct measurement of rates and activation energies by the n.m.r. method.



Investigation of the low-temperature n.m.r. spectra of several derivatives of structure II revealed that only *N*-benzyl-*O,N*-dimethylhydroxylamine (IIa, X = OCH<sub>3</sub>) appeared to undergo inversion at a moderately slow rate in the temperature range studied. When X was OH, Cl, N(CH<sub>3</sub>)<sub>2</sub>, or N<sup>+</sup>(CH<sub>3</sub>)<sub>3</sub>I<sup>-</sup>, inversion seemed to be fast down to -70°. From experience with other types of systems,<sup>3d,e</sup> it is reasonable to argue that the failure to observe slow inversion may be due to accidental rather than real equivalence of the benzyl methylene groups. However, insofar as possible, more than one solvent was used for each compound: with IIb, CHCl<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>, and (CH<sub>3</sub>)<sub>2</sub>CO; with IIc, CS<sub>2</sub>; with II d, CS<sub>2</sub> and CH<sub>2</sub>Cl<sub>2</sub>; and with II e, CHCl<sub>3</sub>-CH<sub>3</sub>CN. All of these solvents and *n*-hexane as well were successful with IIa (X = OCH<sub>3</sub>). However, in neither methanol or acetone as solvent could slow inversion be detected with IIa above -70°.

**Energy Barriers to Inversion of *N*-Benzyl-*O,N*-dimethylhydroxylamine (IIa).** N.m.r. spectra were taken for 20% (w./v.) solutions of IIa in several solvents from +30 to -60°. In each case, the single, sharp line of the methylene protons broadened as the temperature was decreased. The coalescence temperature  $T_c$  was taken as the temperature at which maximum broadening occurred. Below  $T_c$ , two peaks became apparent, and finally near the lowest temperatures the spectra were clearly of the AB type. The lowest temperature spectra permitted measurement of  $\nu_A - \nu_B$ ,  $J_{AB}$ , and  $T_2$ .<sup>11</sup> The inversion rates were determined with the aid of theoretical spectra having various values of the mean half-life ( $\tau$ ) calculated by means of a

(11) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 119 ff.

(1) Supported in part by the National Science Foundation.  
(2) National Science Foundation Postdoctoral Fellow, 1964-1965.  
(3) (a) P. R. Shafer, D. R. Davis, M. Vogel, K. Nagarajan, and J. D. Roberts, *Proc. Natl. Acad. Sci., U.S.A.*, **47**, 49 (1961); (b) F. Kaplan and J. D. Roberts, *J. Am. Chem. Soc.*, **83**, 4666 (1961); (c) G. M. Whitesides, F. Kaplan, K. Nagarajan, and J. D. Roberts, *Proc. Natl. Acad. Sci. U.S.A.*, **48**, 1112 (1962); (d) G. M. Whitesides, D. Holtz, and J. D. Roberts, *J. Am. Chem. Soc.*, **86**, 2628 (1964); (e) G. M. Whitesides, J. J. Grocki, D. Holtz, H. Steinbert, and J. D. Roberts, *ibid.*, **87**, 1058 (1965).  
(4) H. S. Gutowsky, *J. Chem. Phys.*, **37**, 2196 (1962).  
(5) A. T. Bottini and J. D. Roberts, *J. Am. Chem. Soc.*, **80**, 5203 (1958).  
(6) A. Lowenstein, J. F. Neumer, and J. D. Roberts, *ibid.*, **82**, 3599 (1960).  
(7) A. L. Logothetis, *J. Org. Chem.*, **29**, 3049 (1964).  
(8) W. N. Speckamp, U. K. Pandit, and H. O. Huisman, *Tetrahedron Letters*, No. 44, 3279 (1964).  
(9) J. F. Kincaid and F. C. Henriques, *J. Am. Chem. Soc.*, **62**, 1474 (1940).  
(10) M. Saunders and F. Yamada, *ibid.*, **85**, 1882 (1963).

**Table I.** Solvent Dependence of Activation Energies and Chemical-Shift Differences for IIa

Solvent <sup>a</sup>	$\epsilon^b$	$(\nu_A - \nu_B)$ , c.p.s.	$J_{AB}$ , c.p.s.	$T_c$ , °C.	$E_a$ , kcal.	$\log A$
<i>n</i> -Hexane	1.89	16.0	-12.7	-16	$12.9 \pm 0.3^c$	$12.8 \pm 0.3^c$
Carbon disulfide	2.64	12.3	-13.2	-27	$12.4 \pm 0.5$	$12.7 \pm 0.4$
Chloroform	4.81	9.3	-12.9	-26	$11.7 \pm 0.4$	$11.8 \pm 0.4$
Methylene chloride	9.08	8.3	-13.2	-34	$9.4 \pm 0.4$	$10.0 \pm 0.4$
Acetone	20.7	...	...	... <sup>d</sup>	...	...
Methanol	32.6	...	...	... <sup>d</sup>	...	...

<sup>a</sup> Solutions were  $20 \pm 2\%$  (w/v.) in IIa. <sup>b</sup> Handbook of Chemistry and Physics,<sup>12</sup> 42nd Ed., Chemical Rubber Publishing Co., Cleveland, Ohio. <sup>c</sup> Errors are reported as the root-mean-squared error from the least-squares line. <sup>d</sup> The coalescence point was not reached above  $-70^\circ$ .

Fortran IV coded program based on equations of Alexander.<sup>12</sup> In each case,  $\tau$  was adjusted until the theoretical spectra were superimposable on the observed spectra. Samples of the calculated and experimental spectra are shown in Figure 1. A typical Arrhenius plot for the inversion rates (equal to  $\tau^{-1}$ ) is shown in Figure 2.

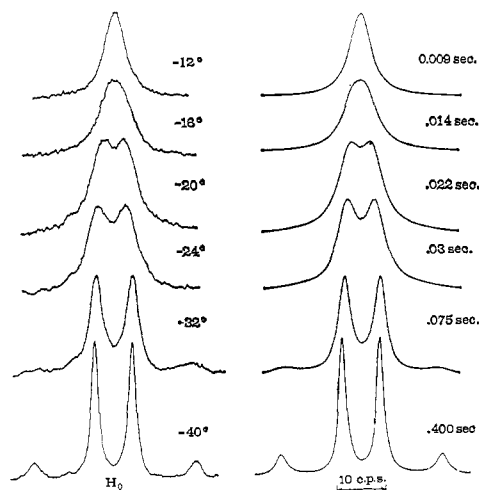


Figure 1. Calculated and experimental spectra in *n*-hexane ( $\nu_A - \nu_B = 16.0$  c.p.s.,  $J_{AB} = -12.7$  c.p.s.,  $T_2 = 0.212$  sec./radian).

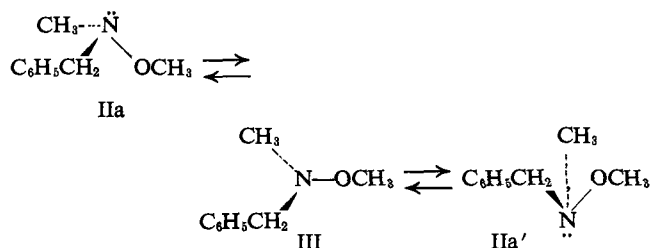
Both the activation energies and the chemical-shift differences ( $\nu_A - \nu_B$ ) appear to be sensitive to the solvent. Table I summarizes the data for six solvents.

## Discussion

Although inversion of aliphatic tertiary amines is normally extremely rapid, the rate of inversion of *N*-benzyl-*O,N*-dimethylhydroxylamine is easily measured by the n.m.r. method. The decreased rate with methoxy substitution must reflect either some destabilization of the transition state (III) in the inversion process  $\text{IIa} \rightleftharpoons$

(12) S. Alexander, *J. Chem. Phys.*, **37**, 967, 974 (1962); **38**, 1787 (1963); **40**, 2741 (1964); the program is described in the undergraduate thesis of J. L. Beauchamp, California Institute of Technology, 1964.

IIa', or else extensive stabilization of the pyramidal forms relative to the transition state.



The methoxyl group differs from alkyl groups in two important ways. First, methoxyl groups are strongly electron attracting by the inductive effect and, second, the oxygens of the methoxyl groups have two pairs of nonbonding electrons.

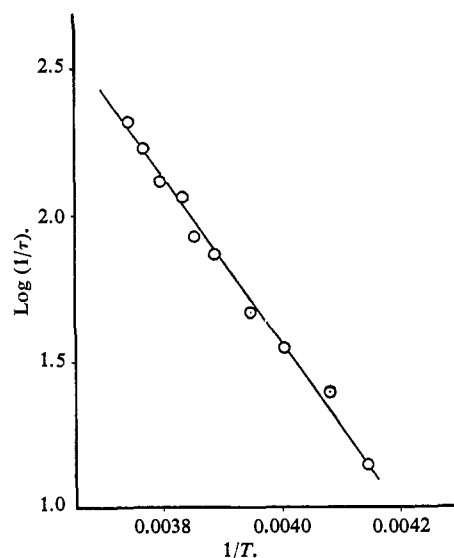
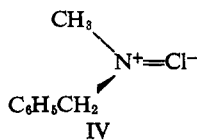


Figure 2. Arrhenius plot for IIa in *n*-hexane.

To determine whether one or the other or both of these structural features are important in reducing the inversion rate of IIa, the low-temperature spectra of *N*-benzyl-*N*-methylchloramine (IIc) and 1-benzyl-1,2,2,2-tetramethylhydrazinium iodide (IIe) were examined. The chloramine IIc appears to undergo inversion at a rate too fast to be measured above  $-70^\circ$ . However, this may be due to a new factor, namely, a significant contribution from IV toward stabilization of the transition state for inversion by d-orbital resonance. The

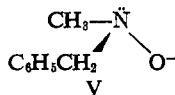


failure of the hydrazinium salt (IIe) to undergo slow inversion above  $-70^\circ$  seems to indicate that electron-attracting effects do not play a major role in decreasing the inversion rate, unless in the particular case the bulky  $(\text{CH}_3)_3\text{N}^+$  group provides an overriding steric effect which destabilizes the pyramidal ground state (when the substituents are relatively close together) with respect to the transition state (where the substituents are farther apart).<sup>5</sup>

It is difficult to test the second possibility, that electronic repulsion from the unshared electron pairs of the oxygen may cause destabilization of the transition state (III). It was not possible to observe slow inversion above  $-70^\circ$  for 1-benzyl-1,2,2-trimethylhydrazine (IIId), but in this case the lone-pair electrons of the two nitrogens reside in mutually perpendicular orbitals<sup>18</sup> which presumably decreases repulsion between them.

It seems reasonable that N-benzyl-N-methylhydroxylamine (IIb) would exhibit a rate of inversion similar to that of IIa. Although considerable line broadening is observed at  $-70^\circ$ , the coalescence point must be below this temperature. However, below  $-70^\circ$ , the solutions crystallized, making further studies impossible. The lower solubility of IIb as compared with IIa prevented the use of the less polar solvents where both the energy barrier and chemical-shift differences would be expected to be greatest, and the failure to observe slow inversion may be partly attributed to unfavorable solvent effects (*vide supra*).

A possible reason for rapid inversion of the hydroxylamine might be that hydrogen bonding involving hydroxyl groups could destabilize the pyramidal ground states relative to the transition state for inversion. Another possibility is that reversible ionization of the OH group occurs and the conjugate base (V) undergoes rapid inversion because it is electron donating by the inductive effect.



Although it appears likely that the unusually slow inversion of IIa is the result of electronic repulsion in the transition state, the present data do not permit a very definite conclusion to this effect.

**Solvent Effects.** Among the four solvents where  $E_a$  could be determined for IIa, the barrier appeared to be linearly related to the solvent dielectric constant (see Figure 3), the larger values of  $E_a$  being associated with solvents having low dielectric constants.

Unlike the simple alkyl-substituted amines, the change between the tetrahedral ground state (IIa) and the planar transition state (III) of N-benzyl-O,N-dimethylhydroxylamine is expected to involve an increase in the dipole moment. This is because in the planar state the C-N dipoles tend to reinforce the N-O dipole more than in the pyramidal state. As a result,

(13) W. G. Penney and G. B. B. M. Sutherland, *Trans. Faraday Soc.*, 30, 898 (1934); *J. Chem. Phys.*, 2, 492 (1934).

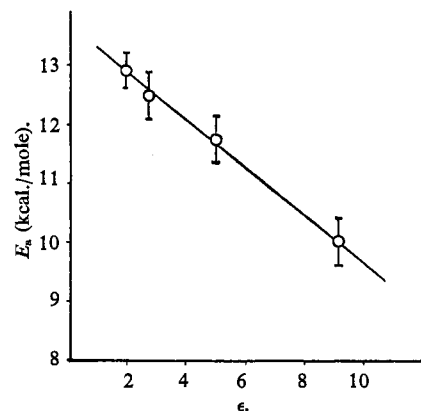


Figure 3. Variation of  $E_a$  for N-benzyl-O,N-dimethylhydroxylamine with solvent dielectric constant  $\epsilon$ .

the transition state for inversion is expected to be (and is) more stabilized by solvents having higher dielectric constants, thereby decreasing the energy barrier to inversion. Indeed, in acetone and methanol, inversion of IIa was too fast to be measured above  $-70^\circ$ .

### Experimental

The n.m.r. spectra were taken with a Varian A-60 instrument equipped with a variable-temperature probe.<sup>14</sup> Microanalyses were performed by Spang Laboratory, Ann Arbor, Mich.

*N-Benzyl-O,N-dimethylhydroxylamine (IIa)* was obtained as a colorless oil, b.p.  $94-96^\circ$  (35 mm.), by alkylation of O,N-dimethylhydroxylamine (Aldrich Chemical Co.) with benzyl chloride. The material was analyzed as its methiodide salt, m.p.  $110.5-111.5^\circ$ .

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_{16}\text{INO}$ : C, 40.97; H, 5.50; N, 4.78. Found: C, 41.10; H, 5.52; N, 4.92.

*1,2,2-Trimethylhydrazine* was obtained as a colorless oil, b.p.  $59-60^\circ$  (lit.<sup>15</sup>  $58.8-60^\circ$ ), by the procedure of Aston and Oakwood.<sup>15</sup>

*1-Benzoyl-1,2,2-trimethylhydrazide.* Benzoyl chloride was allowed to react with 1,2,2-trimethylhydrazine under Schotten-Baumann conditions; colorless needles were obtained, m.p.  $87-88^\circ$ , after recrystallization from ether.

*1-Benzyl-1,2,2-trimethylhydrazine (IIId)* was obtained by the lithium aluminum hydride reduction of 1-benzoyl-1,2,2-trimethylhydrazide in tetrahydrofuran. The product was a colorless liquid, b.p.  $114-116^\circ$  (30 mm.). The n.m.r. spectrum of the material in carbon disulfide showed two N-methyl resonances at 2.18 and 2.34 p.p.m. which gave integrals corresponding to 3.04 and 5.96 protons, respectively.

*1-Benzyl-1,2,2,2-tetramethylhydrazinium iodide (IIe)* was obtained as colorless crystals, m.p.  $166-167^\circ$ , through reaction of IIb with methyl iodide. The n.m.r. spectrum in chloroform showed two N-methyl resonances at 224 and 287 c.p.s. upfield from chloroform with integrated intensities of 9.00 and 3.04 protons, respectively.

*Anal.* Calcd. for  $\text{C}_{11}\text{H}_{19}\text{IN}_2$ : C, 43.15; H, 6.25; N, 9.15. Found: C, 43.27; H, 6.18; N, 9.22.

(14) The authors wish to thank Dr. S. L. Manatt of the Jet Propulsion Laboratories, Pasadena, Calif., for the use of this instrument.

(15) J. G. Aston and T. S. Oakwood, *J. Am. Chem. Soc.*, 75, 2937 (1953).

*N*-Benzyl-*N*-methylchloramine (Iic) was prepared by the method of Coleman.<sup>16</sup> The product was a pale yellow oil which had an n.m.r. spectrum consistent with the pure chloramine.

(16) G. H. Coleman, *J. Am. Chem. Soc.*, **55**, 3001 (1933).

*N*-Benzyl-*N*-methylhydroxylamine (Iib) was obtained as colorless crystals, m.p. 39.5–40.5° (lit.<sup>17</sup> m.p. 41–42°), by alkylation of *N*-methylhydroxylamine (Aldrich Chemical Co.) with benzyl chloride.

(17) J. Meisenheimer and H. Denner, *Ber.*, **65**, 1799 (1932).

## Spin-Echo Nuclear Magnetic Resonance Studies of Chemical Exchange. VI. Rearrangement of Bullvalene and of Its Silver Nitrate Complex<sup>1</sup>

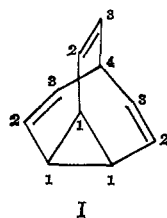
Adam Allerhand and H. S. Gutowsky<sup>2</sup>

Contribution from Noyes Chemical Laboratory, University of Illinois, Urbana, Illinois. Received May 17, 1965

The degenerate Cope rearrangement of bullvalene has been studied from 25 to 123°, in a tetrachloroethylene solution, by means of a spin-echo n.m.r. method, at 26.85 Mc./sec. In effect, the inhomogeneity broadening of the n.m.r. absorption is avoided in the spin-echo experiments so that exchange rates could be measured which were faster by a tenfold factor than the upper limit in previous high-resolution work. More precise values were obtained for the frequency factor,  $0.8 \times 10^{13}$  sec.<sup>-1</sup>, and for the activation energy,  $12.8 \pm 0.1$  kcal./mole. Bullvalene was found to form several complexes with AgNO<sub>3</sub> in D<sub>2</sub>O and in CH<sub>3</sub>CN solution and with AgBF<sub>4</sub> in CH<sub>2</sub>ClCH<sub>2</sub>Cl. The rearrangement rates were reduced in these solutions. A 3:1 Ag<sup>+</sup> to bullvalene system, 0.32 g. in 7.15 M AgNO<sub>3</sub> in D<sub>2</sub>O, was studied in some detail. For it, the apparent activation energy for the rearrangement is  $15.1 \pm 0.8$  kcal./mole.

### I. Introduction

Since the discovery by Doering and Roth<sup>3</sup> of a rapid degenerate Cope rearrangement in bicyclo[5.1.0]octa-2,5-diene, by means of n.m.r. spectroscopy, the generality of the phenomenon has been confirmed.<sup>4,5</sup> The case of bullvalene (I) is particularly interesting, since all of the four types of protons eventually par-



ticipate in the exchange, so that at elevated temperatures the compound should show a single proton n.m.r. line, as was predicted by Doering and Roth.<sup>3</sup> This

(1) This research was supported in part by the U. S. Office of Naval Research, by the National Science Foundation, and by the National Institutes of Health.

(2) Author to whom inquiries should be addressed.

(3) W. von E. Doering and W. R. Roth, *Tetrahedron*, **19**, 715 (1963).

(4) M. Saunders, *Tetrahedron Letters*, 1699 (1963).

(5) J. B. Lambert, *ibid.*, 1901 (1963).

has been confirmed by Saunders, who investigated the rate of rearrangement as a function of temperature.<sup>4</sup>

Our interest in this compound is twofold. It affords a means of extending the spin-echo methods for n.m.r. rate determinations<sup>6-9</sup> to chemical exchange which is more complex than in the two-site systems studied previously. In addition, the preparation and n.m.r. study of transition metal complexes of bullvalene could throw light on the nature of such olefinic complexes in general.<sup>10</sup> The transition metal-olefin bond can be studied indirectly through its effect on the rate of the degenerate Cope rearrangement in bullvalene and perhaps something can be learned about the nature of the rearrangement as well. Indeed, we have found that bullvalene readily forms complexes with silver nitrate and silver fluoroborate,<sup>11</sup> and that the rate of the degenerate Cope rearrangement is slowed down considerably (in solution) by the presence of the silver cation. The data available at present are insufficient to characterize both the mechanism for the "slowdown" and the equilibrium constant for the complex formation. However, the results obtained thus far and the prospects are sufficiently promising to report at this time.

### II. Chemistry of Bullvalene. Silver Cation Complex Formation

When a solution of bullvalene in CH<sub>2</sub>ClCH<sub>2</sub>Cl was added to a solution of anhydrous AgBF<sub>4</sub> in the same solvent, a white precipitate formed immediately and was collected by filtration. However, upon recrystallization of this precipitate, two different bullvalene complexes were isolated, depending on the solvent and method of recrystallization (see Section IV). One of these was 2C<sub>10</sub>H<sub>10</sub>·AgBF<sub>4</sub>. Silver fluoroborate complexes of simple olefins with this 2:1 stoichiometric ratio have been reported recently.<sup>12</sup> Our 2:1 com-

(6) Part I: A. Allerhand and H. S. Gutowsky, *J. Chem. Phys.*, **41**, 2115 (1964), and prior work cited therein.

(7) Part II: A. Allerhand and H. S. Gutowsky, *ibid.*, **42**, 1587 (1965).

(8) Part III: A. Allerhand, Fu-ming Chen, and H. S. Gutowsky, *ibid.*, **42**, 3040 (1965).

(9) Part IV: A. Allerhand and H. S. Gutowsky, *ibid.*, **43**, 4203 (1965).

(10) For a review of olefin-transition metal complexes see M. A. Bennett, *Chem. Rev.*, **62**, 611 (1962).

(11) We wish to thank Professor J. C. Martin for suggesting the preparation and n.m.r. study of bullvalene-AgBF<sub>4</sub> complexes.