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PART I AMINE-BORANES: HYDROLYTIC STABILITY AND STEREOCHEMISTRY OF FORMATION

PART II AMINOBORANES: BARRIER TO ROTATION ABOUT THE BORON-NITROGEN BOND

EVERETT WEST SOUTHWICK

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Keywords
Chemistry, Inorganic

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PART II AMINOBORANES: BARRIER TO ROTATION ABOUT THE BORON-NITROGEN BOND

by

EVERETT WEST SOUTHWICK

B.A., University of Rhode Island, 1963

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This thesis has been examined and approved.

Robert E. Lyle, Prof. of Chemistry
Thesis Director

Colin D. Hubbard, Assoc. Professor of Chemistry

Gloria G. Lyle, Assoc. Professor of Chemistry

Miyoshi Ikawa, Prof. of Biochemistry

James D. Morrison, Prof. of Chemistry

August 22, 1973

Date
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ABSTRACT

PART I AMINE-BORANES: HYDROLYTIC STABILITY AND STEREOCHEMISTRY OF FORMATION

PART II AMINOBORANES: BARRIER TO ROTATION ABOUT THE BORON-NITROGEN BOND

by

EVERETT WEST SOUTHWICK

A method has been developed for the quantitative determination of tertiary amines based upon the hydrogen gas evolution from the decomposition of excess borane (BH₃) in a sample of amine-borane. This method was developed after an intensive study of the hydrolytic stability of amine-boranes.

An investigation of the geometry of coordination of borane and substituted boranes with a number of substituted piperidines is reported. A study of the conformational equilibria of these amine-boranes revealed that the boron-containing substituent has a slightly smaller steric requirement than the analogous carbon-containing substituent. The stereochemistry of borane coordination is shown to be closely analogous to the reported stereochemistry of quaternization reactions.

A dynamic nuclear magnetic resonance study of the hindered rotation of the boron-nitrogen bond in 2-methylpiperidinoboranes is discussed. Analysis of the spectra, using a complete line-shape method, revealed that an aryl
substituent on boron decreases the barrier to rotation relative to a simple unsubstituted aryl ring.
PART I. AMINE-BORANES

INTRODUCTION

The chemistry of boron-nitrogen compounds continues to fascinate organic chemists in part because incorporation of a boron-nitrogen bond in a molecule results in an entity which is isoelectronic with the carbon-carbon bond. In addition, the compounds may be isostructural as a result of the very similar bond distances for boron-nitrogen (1.58 Å) and carbon-carbon (1.54 Å) bonds. These similarities have been exploited, for example, in studies of aromaticity in cyclic boron-nitrogen compounds.\(^1\)

The chemical reactivity of trivalent boron compounds arises exclusively from their electrophilic nature. Boron, as the first member of Group III in the periodic table, has available only three valence electrons for the formation of covalent bonds. Thus tricovalent boron has only six electrons in its valence shell and does not possess a stable octet electron configuration. This lack, in turn, results in the electrophilic character displayed by trivalent boron compounds, for example, the Lewis acid properties of boron trifluoride.\(^2\)

As a first approximation each of the sigma bonds to boron can be regarded as \(sp^2\) hybridized and thus the molecule is planar at boron. The vacant orbital is available for formation of a fourth bond to boron by interaction with an electron pair from a suitable orbital of a Lewis base.
Formation of a fourth bond to boron will necessitate rehybridization of the boron orbitals to a configuration closely resembling the $sp^3$ tetrahedral configuration of quadricovalent carbon. Such would be the case for example in the reaction between trimethylamine and trimethylborane:

$$\begin{align*}
\text{H}_3\text{C}-\text{N} : \text{CH}_3 + \text{B} & \rightleftharpoons \text{H}_3\text{C}-\text{N} - \text{B} - \text{CH}_3 \\
\text{CH}_3 + \text{CH}_3 & \rightleftharpoons \text{CH}_3 - \text{CH}_3
\end{align*}$$

The stability of amine-borane complexes must be considered with respect to two different modes of decomposition, dissociation into the component parts and irreversible decomposition of the complex. The first mode, dissociation, has been investigated in an elegant series of experiments by Brown and resulted in the formulation of the concept of steric strain which has proven so fruitful in subsequent years.

The irreversible decomposition of amine-borane complexes can occur by a number of different methods, of which the principal ones are displacement reactions and hydrolytic decomposition. Displacement reactions should perhaps be described more properly as ligand exchange reactions, as indicated for a general case in Equation 1. Ligand exchange does not imply any particular mechanism for the process and, in fact, in addition to a simple displacement, a preliminary
dissociation of the amine-borane complex followed by recombination may well be the principal process at high temperature."^^

\[
R_3N-BX_3 + BY_3 \rightarrow R_3N-BY_3 + BX_3 \quad \text{(Eq. 1)}
\]

Studies of the hydrolytic decomposition of amine-borane complexes have been concerned principally with elucidating the mechanism of the hydrolysis. Coordination of borane (BH\_3) with an amine enhances the stability of the hydridic bonds towards hydrolytic decomposition and has thereby provided a convenient starting point for studies of the reactivity of boron hydrides. These studies have demonstrated that a broad range of mechanistic interpretation is associated with the hydrolysis reaction, in much the same way as has been found for the solvolysis of organic substrates.

One mechanism that can be envisioned would consist of dissociation of the amine-borane into its component parts as the rate limiting step, followed by rapid hydrolysis of the borane. In obvious reference to carbon chemistry, this has been termed an \( S_{N1-B} \) mechanism.\(^6\) Another likely possibility would be simply reaction of the boron-hydrogen bond with the hydrolytic reagent. Regardless of which mechanism more accurately describes the hydrolysis reaction, the boron hydride must decompose in water to release molecular hydrogen. This fact, and the kinetic stability of certain amine-boranes\(^7\), seemed to offer the possibility of developing an analytical

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method for the quantitative determination of amines by the simple procedure of measuring the volume of hydrogen evolved on hydrolysis of an amine-borane.

The remarkable stability of trialkylamine-boranes to hydrolytic decomposition indicated that the borane adducts of substituted piperidines could be successfully prepared. The introduction of borane as a fourth substituent on nitrogen in substituted piperidines would be similar to the classical quaternization reaction using various alkyl reagents. The quaternization of various saturated nitrogen heterocyclic compounds has been the subject of numerous investigations.⁸ A study of the quaternization reaction using trivalent boron compounds offered a new approach to the problem of the stereochemistry of the quaternization reaction. The similarity of borane (BH₃) to the methyl cation (+CH₃) suggested that the results to be expected from this approach would closely parallel the results obtained using alkyl quaternization reagents. Furthermore, the lower bond strength of the B-N bond relative to the C-N bond promised the possibility that the initial product of the reaction (kinetic product) could be isomerized thermally to the thermodynamically more stable diastereomeric mixture. Formation of trimethylamine-borane from the constituent molecules in solution is calculated⁹ to involve an enthalpy change of -32.7 kcal/mole. This is approximately half the bond energy of a carbon-nitrogen single bond (72.8 kcal/mole).¹⁰
The stereochemistry of quaternization of substituted piperidines has been an area of some intellectual chaos in recent years, in part because it has been difficult to isomerize the kinetic product mixture to a thermodynamic mixture without extensive decomposition of the quaternary salts. Thus piperidine boranes seemed to offer an optimum combination of reactivity and stability which could be exploited to advantage in an investigation of the stereochemistry of coordination. This expectation was fully realized and led in turn to a study of aminoboranes.

The boron-nitrogen bond in aminoboranes is isoelectronic with the carbon-carbon double bond and as such exhibits similar properties. The behavior of particular interest was the hindered rotation around the boron-nitrogen bond which provided a means to study the effect of various substituents on the bond properties of aminoboranes using dynamic nuclear magnetic resonance techniques.
DISCUSSION

Quantitative Determination of Amines

The investigation of the use of the complexation of borane by amines as an analytical technique for the determination of amines was conducted in two stages. First, it was necessary to demonstrate that the amine-borane complex, if formed, was stable to reagents required to decompose any excess borane. Once this criterion was satisfied, it was then necessary to determine under what conditions the amine-borane could be decomposed. It is known that amine-boranes decompose in mineral acid on heating on a steam bath; it was desirable to develop a means of decomposition which could be carried out at room temperature and within a brief period of time.

Although the formation of an amine-borane from the direct reaction of an amine with borane is well documented\textsuperscript{11}, preparation of the complex was carried out under conditions closely resembling those to be used in the analytical scheme contemplated. Thus, addition of a solution of borane in tetrahydrofuran (BH\textsubscript{3}/THF) to the amine in ether followed by removal of the solvent and distillation at reduced pressure gave the amine-borane in nearly quantitative yield. The amine-borane was identified by the characteristic B-H stretching frequency (2300-2500 cm\textsuperscript{-1}) in the infrared spectrum.\textsuperscript{12}
Preliminary evaluations of methods of decomposition were carried out in test tubes and a qualitative estimate of the rate of decomposition was made based on the observed rate of gas evolution. Promising reagents and conditions were then investigated quantitatively by collecting and measuring the volume of gas evolved. A small quantity of amine-borane in a test tube was treated with various hydrolysis reagents with the results shown in Table 1. The qualitative results suggested that the amine-boranes were relatively stable to alcohols; methanol was selected for evaluation as a reagent to decompose excess borane without significant decomposition of the amine-borane.

The amine-borane was generated by the addition of a known excess of standardized BH$_3$/THF solution to a measured quantity of the amine in tetrahydrofuran. After stirring for one half hour to assure complete reaction, a large excess of methanol was added and the gas evolved was measured. The volume of hydrogen evolved agreed quite well with that predicted for the excess borane calculated to be present. From the data presented in Table 1, it can be seen that decomposition of the excess free borane by methanol is nearly 100 times faster than decomposition of the amine-borane. Methanol was therefore selected as the reagent to effect selective decomposition of uncomplexed borane.

Having thus determined that the amine-borane was stable to reaction conditions necessary for the decomposition of any excess borane, investigation of methods of hydrolysis of amine-boranes was initiated. The stoichiometry of the
Table 1

Decomposition of Excess Borane at Room Temperature

<table>
<thead>
<tr>
<th>Amine-borane</th>
<th>Reaction with:</th>
<th>Rate of gas evolution from excess BH₃ (CH₃OH)</th>
<th>Rate of gas evolution from amine-borane (CH₃OH)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CH₃OH</td>
<td>C₂H₅OH</td>
<td>i-C₃H₇OH</td>
</tr>
<tr>
<td>Piperidine-BH₃</td>
<td>slight</td>
<td>slight</td>
<td>-</td>
</tr>
<tr>
<td>1-methylpiperidine-BH₃</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1-ethylpiperidine-BH₃</td>
<td>slight</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>triethylamine-BH₃</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>N,N-diisopropylethylamine-BH₃</td>
<td>moderate</td>
<td>moderate</td>
<td>slow</td>
</tr>
</tbody>
</table>
hydrolysis of amine-boranes\textsuperscript{13} is that shown in equation 2. The hydrolysis of trimethylamine-borane has been reported to be acid catalyzed\textsuperscript{14} and, in general, acid catalysis seems to be operative in all cases studied to date.\textsuperscript{15} The initial investigation was therefore directed toward developing an acidic medium that would completely hydrolyze a tertiary amine-borane at room temperature within a brief period of time, ideally one half hour or less. The borane adduct (1) of 1-methylpiperidine was selected as a standard substrate for this investigation since, as the data in Table 1 show, this amine-borane seemed most resistant to hydrolysis. To ensure a homogeneous medium for the reaction of aqueous acid with the amine-borane, tetrahydrofuran was selected as the solvent for the preparation of the amine-borane \textit{in situ} as well as its subsequent decomposition. Decomposition of the excess borane was accomplished by treatment with methanol prior to treatment with the acidic reagent. In this way it was possible to differentiate between hydrolysis of excess borane and hydrolysis of amine-borane.

\[
R_3N\cdot BH_3 + 3H_2O \rightarrow R_3N + B(OH)_3 + 3H_2 \quad \text{(Eq. 2)}
\]

In consonance with expectations based on mechanistic considerations, acid concentration is an important variable in the rate of hydrolysis. A preliminary investigation was carried out in test tubes using previously prepared 1-methylpiperidine borane (1) dissolved in tetrahydrofuran. To this was added an acidic solution and a qualitative estimate of the rate of hydrolysis was made visually. The results of
this preliminary screening of representative acidic reagents are compiled in Table 2. Further investigation of both sulfuric acid and perchloric acid showed that these particular acids were both equally effective for the hydrolysis of amine-boranes. However, the potential hazard associated with treating a well-known reducing agent (borane) with a powerful oxidizing agent (perchloric acid) was an influential factor in the decision to use sulfuric acid as the acidic reagent of choice for the hydrolysis of amine-boranes. A quantitative comparison of aqueous sulfuric acid with 20% sulfuric acid in acetic acid established that the latter effected hydrolysis to the extent of about 30% reaction in one half hour while the former gave less than 25% reaction in the same time period. Thus, a 20% solution of sulfuric acid in acetic acid emerged as the best candidate of those studied to effect the hydrolysis of amine-boranes.

In a study of the propanolysis of pyridine boranes, it is reported that the rate of reaction was increased on addition of dioxane to the solvolysis medium. This rate enhancement is explicable on the basis of the decreased polarity of the medium. A polar reaction medium would be expected to stabilize the polarized bond of an amine-borane and decrease the reactivity of the amine-borane. This rationalization is supported by the results reported by Kelly showing that a decrease in the dielectric constant of the solvent medium causes an increase in the rate of the acid-independent hydrolysis of amine-boranes. This reaction is considered to be the dissociation of the amine-borane into
Table 2

**Qualitative Test of Acidic Reagents**

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. dilute HCl</td>
<td>very slow</td>
</tr>
<tr>
<td>2. dilute CH(_3)COOH</td>
<td>very slow</td>
</tr>
<tr>
<td>3. aq. p-toluenesulfonic acid</td>
<td>negligible</td>
</tr>
<tr>
<td>4. methanolic HCl</td>
<td>negligible</td>
</tr>
<tr>
<td>5. 50% aqueous H(_2)SO(_4)</td>
<td>vigorous</td>
</tr>
<tr>
<td>6. 30% aqueous HClO(_4)</td>
<td>vigorous</td>
</tr>
<tr>
<td>7. 20% H(_2)SO(_4) in CH(_3)COOH</td>
<td>vigorous</td>
</tr>
</tbody>
</table>
its constituent parts prior to hydrolysis of the hydridic bonds.

Dioxane, like tetrahydrofuran, is miscible with water as well as most organic solvents, and in addition it presented the promise of enhanced rates of hydrolysis relative to the more polar tetrahydrofuran. In fact, the use of dioxane for the preparation of 1-methylpiperidine borane \( (1) \) \textit{in situ} resulted in a dramatic increase in the rate of the subsequent hydrolysis. Whereas with tetrahydrofuran, the reaction was only 30% complete in one half hour, with dioxane the hydrolysis proceeded to the extent of 60% in the same time period. However, even upon prolonged reaction at room temperature, the theoretical quantity of hydrogen was not collected. As a consequence, further attempts to hasten the decomposition of amine-boranes were initiated.

It was reported that diethylamine borane could be used for the reduction of nickel ions in a nickel-plating process.\textsuperscript{17} As described, the nickel-plating process was accompanied by the evolution of hydrogen gas. Although it was not clear whether the hydrogen was formed as part of the reduction of nickel ions or was merely the result of an undesirable side reaction, the possibility that metal salts would catalyze the hydrolysis of amine-boranes could not be ignored. Accordingly a qualitative evaluation of several metal salts in aqueous solution was carried out by observing signs of gas evolution on addition to the amine-borane in a test tube. Those salts which appeared promising were sub-
jected to study under conditions where an accurate measure of the gas evolved could be made. Although in some cases reduction to the metal did occur, as evidenced by the deposition of a mirror on the walls of the flask, the evolution of hydrogen was sluggish and incomplete. These results are compiled in Table 3. Thus, the reduction of metal ions, for example nickel ions, by borane can be described accurately by equation 3, and the observed hydrogen gas evolution probably was derived from a competing hydrolysis of the amine-borane.

$$3\text{Ni}^{2+} + \text{BH}_3 + 3\text{H}_2\text{O} \rightarrow 3\text{Ni}^0 + \text{B(OH)}_3 + 6\text{H}^+ \quad (\text{Eq. 3})$$

In a study of the cleavage of the boron-carbon bonds of triethylborane, Toporcer reported\textsuperscript{18} that, whereas hydrochloric acid is a poor reagent for effecting such cleavage, carboxylic acids can easily accomplish bond scission. This difference in reactivity was attributed to coordination of the non-bonding electrons of the carbonyl group with the electron-deficient boron and thereby a weakening of the boron-carbon bonds. The boron atom in an amine-borane is not electron-deficient and therefore it was not expected that a carboxylic acid alone would be effective in causing the decomposition of an amine-borane. A suitable reagent would be one that contained a carboxylic acid functional group and another functional group capable of coordination with an electron-deficient center. A preliminary investigation using anthranilic acid and salicylic acid as the reagents to effect decomposition of the amine-borane was carried out.
### Table 3

**Hydrolysis of 1-Methylpiperidine Borane (1) by Metal Salts**

<table>
<thead>
<tr>
<th>Metal Salt</th>
<th>Gas Evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromium (III) chloride</td>
<td>none</td>
</tr>
<tr>
<td>Ferric chloride</td>
<td>none</td>
</tr>
<tr>
<td>Cobalt (III) chloride</td>
<td>none</td>
</tr>
<tr>
<td>Nickel (II) chloride</td>
<td>yes*</td>
</tr>
<tr>
<td>Zinc chloride</td>
<td>yes*</td>
</tr>
<tr>
<td>Copper (II) chloride</td>
<td>none</td>
</tr>
<tr>
<td>Lithium chloride</td>
<td>none</td>
</tr>
<tr>
<td>Silver nitrate</td>
<td>yes*</td>
</tr>
<tr>
<td>Platinum (II) chloride</td>
<td>yes*</td>
</tr>
<tr>
<td>Lead (II) acetate</td>
<td>none</td>
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</table>

*Quantitative measurement showed negligible gas evolution.*
There was no enhancement in the rate of hydrolysis of the amine-borane. In retrospect this finding is not surprising since neither reagent possessed a functional group that was sufficiently basic to displace the amine from the amine-borane. This approach to the hydrolysis of amine-boranes was abandoned because a reagent that could displace the amine would seemingly result in the formation of a more stable borane adduct.

A more fruitful approach to increasing the rate of decomposition of the amine-boranes was suggested by a report\textsuperscript{19} of the halogen exchange between boron tribromide and amine-boranes (eq. 4). It was conceivable that in addition to this exchange, a simple displacement of borane by the boron trihalide could occur (ligand exchange).\textsuperscript{20} In either event, the net result would be the release of borane into the solvolysis medium. The decomposition of 1-methylpiperidine borane (1) was attempted using boron trifluoride etherate in dioxane and boron tribromide in benzene. After forming the amine-borane in situ and decomposing the excess borane with methanol in the usual way, the boron trihalide reagent was introduced into the reaction mixture. This was stirred for one half-hour and then the acidic reagent was added. Using a large excess of boron tribromide, the rate of hydrolysis was nearly equal to that obtained using 10% H\textsubscript{2}SO\textsubscript{4} in acetic acid. An enormous excess of boron trifluoride etherate was comparable to using 20% H\textsubscript{2}SO\textsubscript{4} in acetic acid. Lesser quantities of these reagents were not effective in increasing the rate of gas evolution.
R₃N-BH₃ + BBr₃ → R₃N-BH₂Br + BHBr₂
R₃N-BH₂Br + BHBr₂ → R₃N-BHBr₂ + BH₂Br (Eq. 4)
R₃N-BHBr₂ + BH₂Br → R₃N-BBr₃ + BH₃

The unsuccessful attempts to complete the hydrolysis of amine-boranes at room temperature under any reaction conditions described above led to the conclusion that the amine-boranes of tertiary amines were too stable for the proposed analytical scheme to be successful. However, the clear difference in the rate of hydrolysis of uncomplexed and complexed borane suggested a quantitative analytical method for the determination of amines.

The treatment of a solution of amine with an excess volume of standard borane solution followed by decomposition of the excess borane with methanol and measurement of the gas evolved permits an accurate measurement of the amine present. This method is attractive because from each mole of unreacted borane is obtained three moles of hydrogen gas on hydrolysis. A report of this work has been published and is included in the Appendix in its entirety.

Stereochemistry of Borane Coordination

With a new respect for the hydrolytic stability of the amine-boranes of saturated heterocyclic amines, investigations of the stereochemistry of piperidine boranes were initiated. The stereochemistry of the quaternization of substituted nitrogen heterocycles has, since the advent of NMR spectroscopy, received considerable attention. The
results of these studies are the subject of several recent review articles\(^9\); the general conclusions and some aspects of the experimental techniques are included here for the purpose of placing in perspective the research to be discussed.

Reaction of a substituted piperidine with an alkylating agent results in the formation of two diastereomeric quaternary salts (Figure 1). Two related aspects of this reaction have been closely scrutinized during the past decade:

1. the stereoselectivity\(^8a\), as measured by the composition of the diastereomeric mixture, and
2. the stereospecificity\(^8a\), or the preferred direction of the quaternization reaction.

The use of proton magnetic resonance techniques has been instrumental in these studies and requires therefore a brief discussion. To be successful, the nuclear magnetic resonance technique requires that an unequivocal assignment of the resonance signals of the spectrum can be made for at least one of the diastereomers. Here the stratagem usually employed is the study of diastereomeric mixtures of N-methyl piperidines so that one can then analyze the relatively simple singlets arising from the magnetically non-equivalent methyl protons of the two diastereomers. Integration of the areas of each of the signals then permits a determination of the stereoselectivity of the reaction. It is not necessary to assign the signals to a particular diastereomer; it is
Figure 1. Formation of Diastereomers.
sufficient that the signals being measured be separated and be attributable to each member of the diastereomeric mixture.

To determine the degree of stereospecificity of the reaction it is necessary that an unambiguous assignment of the nuclear magnetic resonance spectrum be made. Much of the confusion in the literature has arisen as a result of the inability to make definitive assignments of the spectra of diastereomeric mixtures. In practice it is not yet possible to calculate a priori the nuclear magnetic resonance spectrum of a compound by summing the bond anisotropies because reliable values for the latter are not available. Thus interpretations of spectra are, of necessity, of an empirical nature, occasionally requiring application of chemical intuition.

The principal empirical approach to the interpretation of the spectra of N-methyl quaternary salts has been to correlate the chemical shifts of the respective proton and quaternary salts. The assignment of signals in the spectrum of the proton salt makes the reasonable assumption that the more intense N-methyl signal arises from the diastereomer with the methyl group equatorial, as would be expected from consideration of thermodynamic properties. From this one obtains the relative chemical shifts of the axial and equatorial N-methyl groups in the proton salts. The relative chemical shifts are then used for structural assignments of the N-methyl quaternary salts. This method is not always successful because there may be undetected
solvent and concentration dependencies of the chemical shifts or drastic conformational changes in going from the proton salt to the quaternary salt.

The introduction of a second alkyl group on nitrogen would be expected to change the chemical shift of the methyl group already present. The simplifying assumption is made that the change in chemical shift will be in the same direction for both diastereomers and therefore their relative chemical shifts will be unchanged. As can easily be imagined, these various factors have conspired on occasion to complicate an otherwise straightforward analysis of the stereochemistry of the quaternization reaction.23-24

From sets of internally consistent data obtained as described above, the simplified generalization that the signal for an axial N-methyl group usually occurs at a higher field than that for an equatorial N-methyl group has been made.25 Neither of these methods can be considered to be infallible for structural assignments, but both are useful for preliminary assignments pending corroboration by other data.

Ideally, confirmatory evidence can be obtained by separation of the diastereomeric mixture followed by an X-ray structure determination. This method has had limited success owing to the difficulty of achieving separations. A more general approach has been the thermal equilibration of the diastereomeric mixture with the assignment of the more intense signal to the thermodynamically more stable...
diastereomer. Unfortunately, the thermal equilibration has been accompanied by varying degrees of decomposition and therefore the results must be interpreted with some caution until the extent of decomposition is established. In cases where the equilibration has been successful it has been possible to formulate an internally consistent assignment of structures and thereby arrive at a detailed description of the quaternization process.

In general, it has been found that the introduction of the quaternary alkyl group occurs preferentially from an axial direction in piperidines. The stereospecificity decreases as the alkylating group increases in steric bulk and/or upon introduction of a substituent at the 2-position or at the 3-axial position of the piperidine ring.

It was of interest therefore to investigate the reaction of borane with various substituted piperidines in order to accumulate a body of data which would corroborate the conclusions summarized above regarding the stereochemistry of the quaternization reaction. This would provide an independent determination of the stereochemistry of the reaction and, in addition, serve to dispel some of the confusion in the literature.

Exploratory experiments were carried out using 1-methyl-2-n-propylpiperidine (2); use of a sterically hindered amine would permit a clear delineation of the limitations on the scope of the investigation which would be imposed by the instability of the amine-borane. The source of borane was a molar solution of borane in tetrahydrofuran (BH$_3$/THF).
Reaction of the amine with borane at room temperature gave a product which could be distilled at reduced pressure without significant decomposition. Comparison of the infrared spectrum of the product with that of the amine (Figure 2) showed the disappearance of the Bohlmann bands due to the free amine and the appearance of strong absorptions in the region 2200-2400 cm\(^{-1}\), attributed to B-H stretching vibrations.\(^{12}\) The proton magnetic resonance (PMR) spectrum of the neat liquid (Figure 3) showed two singlets at a chemical shift consistent with a methyl group on a quaternary nitrogen. The characteristically disagreeable smell of a volatile tertiary amine had changed to a pleasant odor similar to that of camphor.

This experiment confirmed the expectation that the preparation and isolation of amine-boranes would present no unusual difficulties. The presence of two singlets in the N-methyl region of the PMR spectrum (2.0-3.0 ppm) established the feasibility of studying the stereochemistry of the coordination by PMR methods and thereby maintaining a close analogy to the previous studies of the quaternization. Accordingly an investigation of the stereochemistry of piperidine boranes was initiated.

Reaction of borane with 1-methyl-2-n-propylpiperidine (2) at \(-75^\circ\) and PMR analysis of the reaction product prior to purification showed that the two diastereomers were present in unequal amounts (Figure 4). Integration of the areas of the N-methyl proton resonances showed the signal at higher field, assigned to an axial methyl group by analogy.
Figure 2. Infrared Spectrum of 1-Methyl-2-n-propylpiperidine (2) and Its Amineborane Adduct (2A and 2B).
Figure 3. PMR Spectrum of 1-Methyl-2-n-propylpiperidine Borane (2A and 2E).
Figure 4. N-Methyl Proton Resonance Signals of a Diastereomeric Mixture of 1-Methyl-2-n-propylpiperidine Borane (2A and 2E): A - before distillation; B - after distillation.
to previous work on the quaternization reaction, to represent 29% of the diastereomeric mixture. Thus, the predominant diastereomer (71%) in the mixture was the one in which the N-methyl group was equatorial and the borane was axial. From this result, it was argued that, like the quaternization of tertiary piperidines, the coordination of borane occurred predominantly by an axial approach of the reagent. After distillation at reduced pressure, the integrated area (Figure 4) had changed from a ratio of 71:29 to a ratio of 43:57, indicating that thermal isomerization had occurred during distillation. From the nearly quantitative isolation of amine-borane it was established that the thermal isomerization took place with little, if any, irreversible decomposition of the amine-borane. Prolonged heating at 77° failed to change the observed ratio of 43:57 and this was taken to be the thermodynamic composition at that temperature. The PMR spectra of all these samples showed that they underwent no significant changes over a period of two days standing at room temperature.

This series of experiments established that PMR analysis of the crude reaction mixture would permit a determination of the stereospecificity of the reaction. In conjunction with empirical methods for assigning structures, the facile thermal isomerization would permit the acquisition of corroborative thermodynamic data in support of the structural assignments. Further evidence in support of these structural assignments was provided by the carbon-13 magnetic resonance spectra, obtained through the coopera-
tion of Professor Ernest Wenkert.

Preparation of the borane adducts of 1,4-dimethylpiperidine (3) and 1,3-dimethylpiperidine (4) gave kinetic products whose NMR spectra showed only a single N-methyl signal. Attempts to resolve the signal by using different solvents were unsuccessful. As a consequence it was not possible to evaluate the stereospecificity of the coordination reaction. Following purification by distillation at reduced pressure the amine-boranes were converted to a thermodynamic mixture by heating at 77° and 140°, respectively. The equilibrium composition was determined by integration of the two overlapping N-methyl signals measured in bromobenzene solution by means of a Dupont Curve Resolver with the results shown in Table 4. From these data it can be seen that the steric requirement for borane bonded to nitrogen is very nearly the same as that for a methyl group bonded to nitrogen. Included in Table 4 are the data for the thermal equilibration of 1-methyl-4-t-butylpiperidine borane (5) from which it was possible to calculate a value of 1.6 kcal/mole for the conformational free energy of borane. This value is only 100 cal/mole less than the accepted value for the methyl group (1.7 kcal/mole).

Although the reaction of borane with trimethylamine in the gas phase has been shown to be very fast ($k_2=10^9$ l/mol sec.) the kinetics of amine-borane formation in solution have not been studied. Since rapid mixing techniques were not employed in this study, it was possible that during
Table 4

Thermodynamic Compositions of Substituted Piperidine Boranes

\[
\begin{array}{cccc}
\text{R} & \text{T (°C)} & \%A & \%E \\
4\text{-t-Butyl (5)} & 77 & 53 & 47 \\
2\text{-n-Propyl (2)} & 77 & 43 & 57 \\
3\text{-Methyl (4)}^a & 140 & 52 & 48 \\
4\text{-Methyl (3)}^a & 77 & 48 & 52 \\
\end{array}
\]

\(^a\)Compositions determined by integration of three spectra using a Dupont Curve Resolver agreed within +2%. 

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the addition of the borane to the amine, the unreacted amine, which would be present until complete reaction had occurred, was causing the isomerization of the amine-borane. If this were the case, the composition of the crude diastereomeric mixture would not represent the kinetic mixture and thus statements concerning the stereospecificity of the reaction would be invalid.

Treatment of the crude reaction mixture from the preparation of 1-methyl-2-n-propylpiperidine borane (2A and 2E) in dichloromethane with approximately 10% by volume of 1-methyl-2-n-propylpiperidine (2) in an NMR tube showed that, at 28° for a period of nearly two hours, no appreciable isomerization occurred. As this experiment was performed at a temperature of 100° higher and for a time period nearly four times longer than the experiments for the preparation of the amine-boranes, it was concluded that no isomerization was likely and the crude product did actually represent a kinetically-controlled diastereomeric mixture.

Treatment of another portion of the same crude reaction mixture in dichloromethane with approximately 30% by volume of 1-methyl-2-n-propylpiperidine (2) at 46° gave the results summarized in graphical form in Figure 5. The total area of the proton resonance signals of all methyl groups bonded to nitrogen was measured; the proportions of the two diastereomeric amine-boranes and the free amine were then calculated as a percentage of this total area. From this presentation of the data it was readily apparent that the diastereomer with the axial borane disappeared at a faster
Figure 5. Disappearance of 1-Methyl-2-n-propylpiperidine Borane (2A and 2E) During Equilibration.
rate than the diastereomer with an equatorial borane appeared. During the course of the study the evolution of a gas was observed, presumably hydrogen formed from the hydrolysis of the amine-borane by moisture from the warm water bath in which the sample was heated. If the only pathway for the disappearance of axial borane were simply isomerization to the equatorial borane, one would expect that the rate of disappearance of axial borane would match the rate of appearance of equatorial borane. That these rates were not equal and further, that the population of free amine increased during the course of the experiment and a gas was evolved, demonstrated that isomerization occurred concurrently with decomposition under these more severe conditions.

Apparently the hydrolytic decomposition occurs preferentially with the diastereomer with an axial borane. A similar preference has been reported by McKenna et al.\textsuperscript{32} for the nucleophilic displacement of an alkyl group by thiophenoxide ion in the decomposition of quaternary piperidinium salts. These authors state that "nucleophilic displacement removes an alkyl group more readily when this is in the orientation it preferentially adopts during introduction". Since preferential attack of a quaternizing reagent and borane is from an axial approach to the piperidine ring, the conclusion from this statement is that an axial group will preferentially undergo reaction.
From the study of the stereospecificity of the reaction of borane with 1-methyl-2-n-propylpiperidine (2) and other substituted piperidines\textsuperscript{29}, it is now firmly established that, like the quaternization reaction, preferential coordination occurs from an axial approach to the piperidine. Furthermore, the expectation that the isoelectronic boron-nitrogen and carbon-carbon bonds would also be isostructural is confirmed by the finding that the steric requirement of borane in 1-methylpiperidine boranes is very nearly the same as the steric requirement for a methyl group in cyclohexanes.

With the successful development of the use of borane as a mechanistic probe into the subtleties of the stereochemistry of the quaternization of heterocyclic amines, it was of interest to extend the investigation to organoboranes. Interest in studying the stereochemistry of N-benzyl amines suggested that phenylborane, isoelectronic and probably isostructural with the benzyl group, would be an appropriate organoborane. Here, the interest was not directed toward using phenylborane as a probe for conformational analysis in the same sense that the benzyl group has been used.\textsuperscript{33} Rather, the intent was to determine whether the parallel behavior of borane and methyl, which became evident in the previous study, would also apply to phenylborane and the benzyl group. As was true for the methyl group, there already existed in the literature a substantial body of information describing benzyl quaternary salts.\textsuperscript{34}
The phenylborane was conveniently handled as its pyridine adduct. Pyridine was selected as the amine to stabilize phenylborane because it was a weaker base than the tertiary piperidines, thereby insuring that formation of the phenylborane-piperidine adduct would occur. For studies by PMR, pyridine was preferred to aliphatic amines because there were no proton signals from pyridine which appeared in the region of interest (2.0–3.0 ppm) of the spectrum.

The preparation of pyridine phenylborane (6) was accomplished according to literature methods\textsuperscript{35} as summarized in Figure 6. The study of coordination of phenylborane with substituted piperidines was carried out in an NMR tube and no attempt was made to isolate the piperidine phenylborane adducts. A weighed quantity of pyridine phenylborane (6) was placed in an NMR tube and dissolved in 1 ml of dichloromethane. The proton spectrum of this solution was then recorded to insure that there was no absorption in the aliphatic region. A slight molar excess of the appropriate amine was then added from a syringe; in all cases, the amine, as calculated from its density and the volume added, was present in approximately 10% excess. This excess of free amine was not considered as a complication in the analysis of the stereochemical results since, in the reaction with the pyridine phenylborane (6), pyridine is displaced. Furthermore, from earlier studies of the effect of free amine on the diastereomeric mixture of 1-methyl-2-\textit{n}-propyl-piperidine borane (2A and 2E), it was known that the
\[
\text{PhMgBr} + B(\text{OCH}_3)_3 \rightarrow [\text{Ph-B(OCH}_3)_2] \xrightarrow{\text{H}_3\text{O}^+} \text{Ph-B(OH)}_2
\]

\[
\text{Ph-B(OH)}_2 + 2 \text{CH}_3\text{CH}_2\text{OH} \rightarrow \text{Ph-B(OCH}_2\text{CH}_3)_2
\]

\[
\text{Ph-B(OCH}_2\text{CH}_3)_2 + \text{LiAlH}_4 + \text{C}_5\text{H}_5\text{N} \rightarrow \text{PhBH}_2\cdot\text{C}_5\text{H}_5\text{N}
\]

Figure 6. Preparation of Pyridine Phenylborane.
presence of amine would catalyze the equilibration to a thermodynamic mixture but would not otherwise affect the experiment. Following the addition of the substituted piperidine (3,4,7-10), the NMR tube was inverted once to insure adequate mixing. The progress of the reaction was then followed by repeated scans of the PMR spectrum.

Formation of the piperidine phenylborane was evident within five minutes of mixing of the reagents and was complete after fifteen minutes. Isomerization of the kinetic product occurred concurrently with the formation but at a slower rate; thus it was not possible to determine quantitatively the isomer distribution of the kinetic product. Generally, after about two hours, no further change in the isomer distribution could be detected. The thermodynamic composition of the diastereomeric mixture was determined by integration of the resonance signals arising from the axial and equatorial N-methyl protons.

The assignment of configuration for the products of the addition of phenylborane to substituted 1-methylpiperidines (3,4,7,8,9) was based on thermodynamic considerations. It was expected that in the reaction shown in Figure 7, the predominant isomer after thermal equilibration would be that with the phenylborane occupying an equatorial position. Previous work\textsuperscript{29} has established that the steric requirement of borane and the methyl group were essentially equal. It follows logically that phenylborane and the benzyl group also would have a similar steric requirement, both larger
Figure 7. Formation of Diastereomers in the Reaction of Pyridine Phenylborane with Substituted Piperidines.
than methyl. The data compiled in Table 5 are in full accord with this expectation. The kinetic product was that whose N-methyl resonance signal first appeared; as can be seen in Figure 8, within a short period of time of the initial appearance of the amine-borane the diastereomer present in greater amount was that dictated by thermodynamics. Thus the kinetic product was that with an equatorial N-methyl group. This was in full agreement with earlier investigations which demonstrated that the preferred direction of quaternization was an axial approach.

As the success of this method for determining configuration is heavily dependent on the criterion that no extensive decomposition of the amine-borane adducts occurs during the equilibration, it was important to determine that no decomposition did occur. This was accomplished by determining that the sum of the areas of the N-methyl signals for the coordinated amine-borane did not decrease significantly during the experiment. Further, the ratio of this sum to the area of the free amine signal did not vary significantly during the equilibration. This ensures that the data reflect an isomerization and not the selective decomposition of one of the isomers.

Although the above arguments establish the configuration of the phenylborane adducts, further evidence was sought from the chemical shifts of the N-methyl signals. By an application of the empirical method discussed by House, it was anticipated that the resonance for the axial N-methyl
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Table 5. (cont.)

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</tr>
<tr>
<td></td>
<td>no evidence of coordination</td>
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ᵃoverlap of high field signals precluded quantitative measurement.
Figure 8. Concurrent Formation and Isomerization of 1-Methyl-4-t-butylpiperidine-phenylborane (7a and 7e).
group would appear at higher field than that of the equatorial N-methyl. As may be seen in Table 5, this is not the case; the equatorial N-methyl signal is at higher field by more than 0.1 ppm.

However, the assignment of configuration based on thermodynamic arguments is corroborated by a comparison of the chemical shifts of the t-butyl protons of the phenylborane adduct with those of similar compounds as depicted in Figure 9. This comparison clearly shows the structural assignment to be consistent with previous studies.

The chemical shifts of the N-methyl protons compiled in Table 5 are all at higher field by about 0.5 ppm than was observed for the piperidine borane adducts. A study of the aromatic solvent-induced shift (ASIS) behavior of borane adducts resulted from some earlier confusion in the interpretation of the data for the exchange reactions between amine-boranes and free amines. For trimethylamine borane the methyl proton resonance shifts upfield in perdeuteriobenzene by 0.57 ppm relative to the resonance in CCl$_4$. Both the magnitude and direction of the observed chemical shifts reported in Table 5 are similar to the ASIS effect for trimethylamine borane. In the present study there are two possible sources of an ASIS effect, the phenyl ring of the phenylborane and pyridine displaced during the coordination reaction. A tentative choice can be made between these two possibilities by comparing the N-methyl chemical shifts for 1-methyl-4-t-butyl piperidine borane (5) prepared from
Figure 9. Proton Chemical Shifts (in ppm) of 1-Methyl-4-t-butylpiperidine Phenylborane (7a and 7e) and Related Compounds; the t-Butyl Group.
BH$_3$/THF and pyridine borane.$^{29}$ When prepared from pyridine borane, the N-methyl resonances shift upfield by 0.17 ppm and maintain their relative positions. There is no reversal in position (see Figure 10). It seems unlikely that the presence of pyridine is the cause for the upfield shift and the reversal of the resonance signals in the phenylborane adducts.

The effect of the phenylborane group on the chemical shifts of the N-methyl protons is more difficult to assess because of the number of possible rotameric orientations for the group. Comparison with benzyl quaternary salts (cf Figure 9), which seem to follow the general tendency for an axial N-methyl to appear at higher field, may be invalid because the quaternary salts have a counterion associated with them which may bias the rotameric distribution. The absence of a counterion in the phenylborane adducts may permit the aromatic ring to assume an orientation which exerts a strong shielding effect on the N-methyl protons. For an axial phenylborane one possible orientation would place the aromatic ring in close association with the N-methyl protons and induce a large upfield shift. The equatorial phenylborane, which is more stable, would have a less severe interaction and therefore the induced shift would be smaller. Thus the observed reversal of the N-methyl resonance positions may be the result of a different degree of interaction between the aromatic ring and the N-methyl protons in the two epimers.
Figure 10. Proton Chemical Shifts (in ppm) of N-methyl Protons in Amine-boranes.
From the equilibrium compositions presented in Table 5 a value for the equilibrium constant for the two diastereomers can be calculated. The equilibrium constant can then be used to calculate the conformational free energy value for phenylborane using the value of 1.7 kcal/mole for the conformational free energy value of the methyl group. As is shown in Figure 11 the calculated value is 2.1 kcal/mole which is identical to the value (2.1 kcal/mole) determined for the benzyl group by the equilibration of 1-benzyl-4-t-butylcyclohexane.

In conjunction with studies of borane adducts of tertiary piperidines, the preparation of trifluoroborane adducts was of interest. The initial experiment was conducted using cis-1,2,6-trimethylpiperidine (11); in this way the limitations on the reaction as a result of severe steric interactions would be readily apparent if no trifluoroborane adduct were isolated.

Reaction of boron trifluoride etherate with cis-1,2,6-trimethylpiperidine (11) gave a product which could be distilled without decomposition. The infrared spectrum of the distillate suggested that it was the desired trifluoroborane adduct. The NMR spectrum showed the expected resonance signals for epimeric N-methyl groups at a chemical shift consistent with those observed for borane adducts. However, the C-methyl region of the NMR spectrum showed an unexpectedly complex resonance signal consisting of ten peaks. This was in sharp contrast to cis-1,2,6-trimethylpiperidine borane.
\[ K = \frac{68}{32} = 2.12 \]

\[ \Delta G = -RT \ln K \]
\[ \Delta G = -(1.98)(2.303)(300) \log 2.12 \text{ cal/mole} \]
\[ \Delta G = -448.6 \text{ cal/mole} \]
\[ -\Delta G = 0.4 \text{ kcal/mole} \]

\[ -\Delta G_{BH_2Ph} = G_{CH_3} + 0.4 \]
\[ = -(-1.7) + 0.4 \]
\[ = 2.1 \text{ kcal/mole} \]

Figure 11. Conformational Free Energy of Phenylborane.
(12) which showed the pair of doublets expected for a diastereomeric mixture of compounds having equivalent methyl groups coupled to only one other proton.

The observed complexity could arise if, in the presence of boron trifluoride etherate, the cis-1,2,6-trimethylpiperidine (11) had undergone isomerization to the trans isomer. If this were the case, the distillate would consist of two diastereomeric pairs of compounds. Hydrolysis of a portion of the distillate gave cis-1,2,6-trimethylpiperidine (11) in nearly quantitative yield as the only organic product. Thus the complex resonance signals were not the result of the presence of isomeric compounds. Comparison of the spectra obtained at 60 MHz and 100 MHz showed that while the coupling constants remained the same the chemical shift difference between the diastereomers differed by the predicted amount. These two pieces of evidence eliminated isomeric compounds from further consideration. The data obtained at 60 MHz and 100 MHz strongly suggested that the cause of the observed complexity was long-range coupling.

From the 100 MHz spectrum it could be seen that each signal from the predicted pair of doublets was further split into a quartet of relative intensity 1:3:3:1 (Figure 12). The relative intensities were those predicted for coupling with three equivalent fluorine nuclei \( I = \frac{1}{2} \) and were inconsistent with those predicted for either boron \( I = \frac{3}{2} \) or nitrogen \( I = 1 \). The latter two nuclei would also cause splitting of each peak in the pair of doublets, but they would all be of equal intensity. Thus the observed complexity in the C-methyl region of the PMR spectrum of cis-1,2,6-
Figure 12. The C-methyl Region of the PMR Spectrum (at 100 MHz) of cis-1,2,6-Trimethylpiperidine Trifluoroborane (13).

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trimethylpiperidine trifluoroborane (13) was attributed to long-range coupling with fluorine. This is the first example to be reported of long-range coupling over five bonds in trifluoroborane amine adducts.

The structural assignments and pertinent nuclear magnetic resonance data are shown in Figure 13. These data did not allow an unequivocal assignment because the diastereomers were present in nearly equal amounts. Thus it was not possible to interrelate the N-methyl and C-methyl signals. The PMR spectrum of 1,2-dimethylpiperidine trifluoroborane (14) showed similar spectral characteristics and, in addition, the diastereomeric composition was sufficiently different to permit an unequivocal assignment of structures.\textsuperscript{29} These data are reproduced in Figure 14. As the data in Figures 13 and 14 show, the long-range coupling $J_{\text{HF}}^5$ in the diastereomer in which the BF$_3$ and C-CH$_3$ groups are trans is approximately half the value of when they are oriented in a cis relationship.

Long-range fluorine coupling has been the subject of numerous investigations, principally aimed at elucidating the mechanism by which this coupling occurs. The two extreme mechanistic possibilities are considered\textsuperscript{39} to be direct, i.e., transmission of spin information through sigma bonds, and indirect, transmission through space. Early work by Cross and Landis\textsuperscript{40} indicated that long-range coupling would be observable only if a vector drawn from C to F intersected a similar vector originating at the carbon atom and passing through the hydrogen under consideration. This
Figure 13. Nuclear Magnetic Resonance Data for cis-1,2,6-Trimethylpiperidine Trifluoroborane (13).
Figure 14. Nuclear Magnetic Resonance Data for 1,2-Dimethylpiperidine Trifluoroborane (I).\textsuperscript{29}
"converging vector" rule was formulated from studies utilizing the rigid steroid nucleus; the formulation of such a rule and its validity imply that spin-spin coupling is transmitted through space. Later work by P. C. Myhre led to the conclusion that a necessary condition for long-range coupling is proximate orientation of the nuclei. Several more recent reports of long-range coupling have been equally unsuccessful in establishing unequivocally which mechanism is operative.

Transmission of spin information by a direct mechanism implies that the electrons of the intervening sigma bonds actually transmit this information. The data shown in Figures 13 and 14 support the prediction that the N-CH₃ protons would be weakly coupled and the C-CH₃ protons strongly coupled if the coupling is electron-mediated. This prediction is based on the theory proposed by Koide and Duval. The observation of different coupling constants for the two diastereomers is not readily explicable in terms of their theory. Furthermore, unlike carbocyclic compounds, the amine-trifluoroboranes contain nuclei with substantial quadrupole moments.

Long-range coupling between boron and hydrogen has been observed in the bonding arrangement H-C-N-B-X. Significantly no coupling was observed when either hydrogen or fluorine was bonded to boron, although the coupling was easily detected when boron was bonded directly to bromine or chlorine. For molecules in which a nearly spherical charge distribution exists at the nucleus in question, a negligible
electric field gradient will be present and coupling will be observed. Distortion of the charge distribution around the nucleus will be severe when the electronegativity of the atom differs greatly from that for its substituent. In this case, the relatively large electric field gradient will interact strongly with the nuclear quadrupole and long-range coupling will not be observed. The amine-trifluoroboranes and the amine-boranes fall in the latter category and as predicted, do not show any long-range coupling with boron. Furthermore the strong interaction of the electric field gradient with the boron quadrupole should interrupt the transmission of spin information from fluorine to other nuclei in the molecule. This suggests that the predominant mechanism for the observed long-range coupling in these amine-trifluoroboranes is an indirect mechanism.

Spin-spin coupling by an indirect mechanism requires that there be a non-negligible orbital overlap between the atoms in question. This spatial requirement was deduced earlier by Myhre.41 Two lines of evidence may be adduced to demonstrate that in the present case the atoms in question are indeed in close proximity.

In 1,2-dimethylpiperidine trifluoroborane (14) the BF3 group can bend away from the C-methyl group, although this requires some distortion of the ring. However, in 1,2,6-trimethylpiperidine trifluoroborane (13), the BF3 group is flanked by C-methyl groups and cannot therefore increase the separation to the same extent. This is reflected in the
values for the long-range coupling which are larger for 1,2,6-trimethylpiperidine trifluoroborane (13).

More direct evidence for the proximity of the BF₃ and C-methyl groups is available from the ¹⁹F-NMR chemical shifts. It is known⁴⁵ that fluorine nuclei are deshielded when internal van der Waal's forces between atoms are large. As the data in Table 6 show, the fluorine nuclei are most strongly deshielded (furthest downfield) in 1,2,6-trimethylpiperidine trifluoroborane (13) in agreement with the expectation of close proximity of the BF₃ and C-methyl groups.

As discussed by Barfield and Karplus⁴⁹, long-range spin-spin coupling is probably the result of contributions from both mechanistic possibilities. The direct mechanism cannot be eliminated entirely from consideration on the basis of the presence of strong quadrupolar interactions in the molecule. Each of the amine-trifluoroborane adducts showed substantial coupling between boron and fluorine (Table 6) which must occur by the direct mechanism. However, the weight of the evidence suggests that the predominant mechanism of the observed long-range spin-spin coupling is the indirect (through-space) mechanism.
Table 6

Fluorine Chemical Shifts (in ppm)

![Diagram showing BF₃ and CH₃ groups with R = axial BF₃ and equatorial BF₃]

<table>
<thead>
<tr>
<th>R =</th>
<th>axial BF₃</th>
<th>equatorial BF₃</th>
<th>J_BF</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-methyl (15)</td>
<td>164.28</td>
<td>152.92</td>
<td>15-16 Hz</td>
</tr>
<tr>
<td>2-methyl (14)</td>
<td>147.07</td>
<td>157.18</td>
<td>16-18 Hz</td>
</tr>
<tr>
<td>2,6-dimethyl (13)</td>
<td>137.77</td>
<td>148.43</td>
<td>18-19 Hz</td>
</tr>
</tbody>
</table>
PART II. AMINOBORANES

INTRODUCTION

The early postulate\textsuperscript{46} that the formal sigma bond between boron and nitrogen in aminoboranes would also possess some pi-bond character as a result of electron delocalization of the non-bonding pair of electrons on nitrogen into the vacant p-orbital of boron has been the subject of several investigations in the past decade. On the basis of studies of the boron-nitrogen stretching frequency of aminoboranes and their physical properties, Niedenzu and Dawson\textsuperscript{47} reported experimental evidence for the presence of a pi-bond between boron and nitrogen in aminoboranes and suggested the existence of cis-trans isomers. The general availability of nuclear magnetic resonance spectrometers occasioned further study of aminoboranes. The existence of cis-trans isomers in aminoboranes was made readily apparent by the detection of magnetically non-equivalent protons in the PMR spectra of aminoboranes.\textsuperscript{48} Following the detection of such isomers, variable temperature PMR studies showed that the barrier to rotation about the B-N bond lay within the range of energies (10-20 kcal/mole\textsuperscript{-1}) amenable to NMR analysis.

The evidence available from nuclear magnetic resonance experiments has justified a description of the bonding in aminoboranes which ascribes some pi-bond character to the boron-nitrogen bond. In valence terms, the bonding in aminoboranes may be described as:
Although this representation is useful for depicting the interaction of the non-bonding pair of electrons on nitrogen with the vacant orbital on boron, the negligible dipole moment of dimethylaminodimethylborane\(^{49}\) (16) indicates that charge separation of this type does not make a significant contribution to the bonding between boron and nitrogen in aminoboranes. Furthermore, molecular orbital calculations using an extended Hückel LCAO-MO method\(^{50}\) reveal that, although in the pi-molecular orbital there is some electron density transfer to boron, in the sigma framework there is a larger shift in electron density from boron to nitrogen as a result of the greater electronegativity of the latter. The result is a slight polarization which is opposite in sign to that predicted from valence bond theory.

A more detailed study\(^{51}\) using essentially the same calculational approach (Hückel LCAO-MO) investigated the influence of a phenyl group on bonding in aminoboranes. A phenyl group on boron was found to decrease the calculated B-N bond order but to a lesser degree than when phenyl substitution was on nitrogen. A considerable bond order for the boron-phenyl bond was found, indicating a resonance interaction between boron and phenyl.

The classical method for investigating resonance interactions\(^{52}\) is to measure how the introduction of various substituents into the aromatic ring affects one or more molecular properties, either physical or chemical. The low
barrier to rotation about the B-N bond of aminoboranes suggested that dynamic nuclear magnetic resonance studies of B-aryl substituted aminoboranes would reveal the extent of the resonance interaction between boron and phenyl.

The application of dynamic nuclear magnetic resonance (DNMR) techniques to the study of bonding in aminoboranes has allowed evaluation of the change in the barrier to rotation about the B-N bond with varying structural parameters. None of the investigations reported to date have employed complete line shape analysis and the results are plagued by the same uncertainties as those described for amides.\(^53\) For example, the replacement of a methyl group on boron by a chlorine has been reported to increase the barrier to rotation.\(^54\) Later work\(^55\) reported that chlorine substitution lowered the barrier by about 2 kcal/mole. Substitution of a methyl group on nitrogen by an alkyl group with greater steric requirements lowered the barrier to rotation.\(^55\) Similarly, replacement of a methyl group on boron by a phenyl group also decreased the barrier\(^56\), although this may not be the result solely of steric interactions. Interestingly, it has been found that on replacement of a methyl group on boron by a vinyl, the barrier to rotation is raised.

The most complete study\(^57\) of the effect of boron substituents on the barrier to rotation in aminoboranes employed several methods of approximation for the derivation of Arrhenius parameters and as a result the values reported show considerable scatter. From these data a lower barrier
to rotation was found when the boron substituent was -OCH$_3$ rather than chlorine; this is consistent with other work$^{58}$ which indicated that oxygen is a better pi-donor towards boron than chlorine. Similar values for the Arrhenius parameters for rotation about the boron-nitrogen bond in aminoboranes were found when boron was substituted with either a phenyl or p-anisyl group. On this basis the authors concluded "that the substituent had little effect on pi-bonding between aryl and boron or between nitrogen and boron".

**Preparation of Piperidinoboranes**

Investigation of substituent effects on bonding in aminoboranes has been severely hampered by the lack of simple, reliable synthetic procedures for the preparation of unsymmetrically substituted compounds. It has been especially tedious to prepare aminoboranes with two different substituents on boron. Most synthetic approaches are based on the reaction of a secondary amine with a chloroborane, followed by dehydrohalogenation with triethylamine$^{59}$ (Figure 15, Scheme A). The aminodichloroborane is then added to a Grignard reagent and a symmetrically substituted boron results.$^{60}$ By using alkyl- or aryl-dichloroboranes it has been possible to prepare aminoboranes with different substituents on boron.$^{47}$ This method is tedious and lacks versatility because the preparation of the dichloroborane limits the functional groups which may be introduced. Consequently an investigation of alternative routes to the
Figure 15. Synthetic Approaches to Aminoboranes.
preparation of unsymmetrically substituted aminoboranes was initiated.

The initial approach utilized the sequence of reactions depicted in Figure 15, Scheme B. This sequence was essentially that used by Niedenzu and Dawson except that the aryldichloroborane was prepared from a Grignard reagent rather than by exchange between a tetra-aryltin and boron trichloride. Although the aminoborane was obtained in acceptable yields (20-30% overall) the sequence was not considered sufficiently versatile to be attractive.

A second approach proved to be more satisfactory. This sequence involved the initial preparation of the aminodichloroborane; substituents on boron were then introduced by sequential inverse additions of the appropriate Grignard reagents (Figure 15, Scheme C). The order of introduction of the substituents on boron had little effect on the yield from the reaction; it was possible in this way to prepare quantities of the aminochloromethylborane and then introduce a variety of aryl substituents. Inverse addition of the Grignard reagents was employed because in this way monosubstitution could be assured and a reagent free of unreacted magnesium was obtained. It was found that whenever there was unreacted magnesium metal in the reaction mixture, a highly pyrophoric volatile material was formed. The experimental inconvenience of an inverse addition of Grignard reagent was small in comparison to the hazards associated with volatile pyrophoric byproducts.
The aminoboranes were isolated by distillation at reduced pressure as colorless liquids which froze to glasses at -78°. They were stored at -78° under a nitrogen atmosphere without significant decomposition for several months. At room temperature they discolored in a few hours, even when under nitrogen. Satisfactory analytical data were obtained for all the aminoboranes. The infrared spectra were characterized by a strong absorption at 1450 cm⁻¹ which has been attributed to the B-N stretching vibration.47

The PMR spectra showed two singlets of approximately equal intensities at 0.4 ppm downfield from external TMS for the B-methyl protons. The C-methyl region (~1.1 ppm) showed two overlapping doublets (J=7.0 Hz). Thus the expectation that rotation about the B-N bond of the aminoboranes would be slow at room temperature was confirmed.

The aminoboranes prepared for this study along with their pertinent physical data are listed in Table 7.

A discussion of the geometry of aminoboranes can be separated into two principal divisions; the existence of monomeric species and the planarity of the B-N bond and its attached ligands.

The Existence of Monomeric Species

In addition to the aforementioned double bond character of aminoboranes there is the possibility that interaction of the non-bonding pairs of electrons on nitrogen with the electron deficient center at boron can occur in an
Table 7
**Arylmethyli-(2-methylpiperidino)boranes**

<table>
<thead>
<tr>
<th>Ar</th>
<th>b.p. (mm Hg)</th>
<th>B-CH$_3$ (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Structure" /></td>
<td>60° (0.4mm) - 75° (0.2mm)</td>
<td>0.32</td>
</tr>
<tr>
<td><img src="image2" alt="Structure" /></td>
<td>81-82° (0.35mm)</td>
<td>0.41</td>
</tr>
<tr>
<td><img src="image3" alt="Structure" /></td>
<td>78-79° (0.2mm)</td>
<td>0.38</td>
</tr>
<tr>
<td><img src="image4" alt="Structure" /></td>
<td></td>
<td>0.41</td>
</tr>
<tr>
<td>Ar=</td>
<td>B-CH&lt;sub&gt;3&lt;/sub&gt; (ppm)</td>
<td>b.p. (mm Hg)</td>
</tr>
<tr>
<td>------------</td>
<td>-------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(20)</td>
</tr>
<tr>
<td></td>
<td>0.40</td>
<td>0.43</td>
</tr>
</tbody>
</table>

**Table 7. (cont.)**

![Chemical Structures](image)
intermolecular fashion. This would result in formation of dimers or higher oligomers.

\[ \text{B-N} \quad \text{2}\text{B-N} \rightarrow \text{N-B} \]

Gyroscopic molecular weight determinations were used by Niedenzu and Dawson\(^47\) to establish the presence of monomeric species in the series of compounds investigated. They did find that on standing for short periods of time, monochlorophenylaminoboranes showed a tendency to dimerize; tetra-alkyl aminoboranes showed no tendency to dimerize. A more detailed investigation\(^61\) of the monomer-dimer equilibrium has been reported in which \(B^{11}\) magnetic resonance spectroscopy was employed. The results of this study corroborated those reported by Niedenzu and Dawson\(^47\); tetra-alkyl aminoboranes were found to exist as monomeric species.

The aminoboranes reported in Table 7 were therefore assumed to be monomeric compounds. Support for this assumption was provided by the analysis of the mass spectrum of each compound. The mass spectrum obtained at low ionizing voltage gave no indication of the presence of dimeric species. The absence of peaks corresponding to a dimer in the mass spectrum of these compounds could be the result of dissociation of the dimer at the ionizing voltage used or the fact that the dimeric species was not volatile and did not enter the ionizing chamber. However, the consistency between the results from the analysis of the mass spectra and the find-
ings of other investigators indicate that the aminoboranes reported in Table 7 are monomeric compounds.

Planarity of B-N Bond

An X-ray diffraction study of dimethylaminodimethylborane (16) showed the molecule to be of approximate \( C_{2v} \) symmetry with a slight twisting about the B-N bond of 6-7°. The B-N bond length was determined to be 1.43 Å, which indicated a pi-bond order of 0.57. The Bovey-Johnson relationship allows one to determine the disposition in space of a proton with respect to a phenyl ring on the basis of the chemical shift displacement of the proton resonance signal. This technique has been applied to the analysis of the geometry of phenyl- and methyl-substituted aminoboranes. The authors concluded that for dimethylaminomethylphenylborane (22) among other compounds studied, the plane of the phenyl ring is twisted out of the plane of the B-N bond by as much as 50° and that the B-N bond itself is twisted 10-40° out of a coplanar arrangement.

Lack of evidence to the contrary suggests that the assumption of a planar arrangement of ligands around boron is valid. The arrangement of ligands on nitrogen can be either planar or pyramidal. It has been shown that conjugation of the non-bonding electrons on nitrogen with an adjacent unsaturated system does not of itself dictate a planar, \( sp^2 \) hybridized geometry at nitrogen. It was suggested that the geometry at nitrogen would always be non-planar unless the degree of resonance stability to be obtained by a planar con-
configuration is large. Since in a neutral molecule such resonance interactions lead to charge separation, the required amount of resonance stabilization would probably seldom be attained. Support for this argument is found in studies of barriers to inversion and rotation in amides. The NMR investigation of benzyl-substituted aminoboranes did not show any observable magnetic non-equivalence of the benzyl protons, thereby eliminating a rigid pyramidal configuration for either boron or nitrogen. From these data it was not possible to distinguish between a planar arrangement or a rapidly inverting pyramidal configuration at nitrogen. If the latter were the case, however, the conclusions based on dynamic nuclear magnetic resonance studies would remain unchanged because nitrogen inversion would simply transfer the alkyl group to an electronically equivalent environment in an enantiomorphic structure.

Geometry of the Piperidine Moiety

The geometry of the 2-methylpiperidine moiety of these aminoboranes, although not intimately involved in the interpretations of the results of this study, was of some interest. Two reports in the literature announced the surprising conclusion that amides of 2-methylpiperidine and 2,6-dimethylpiperidine existed in chair conformations in which the methyl substituent occupied an axial position. Since these initial reports, several other examples have been disclosed in which similar behavior was observed. In all cases reported, the exocyclic substituent on nitrogen is
capable of forming a planar conjugated system involving the non-bonding electrons on nitrogen. This results in a planar, exocyclic substituent on nitrogen which exhibits restricted rotation about the carbon-nitrogen bond, which effects acting in concert force the the 2-substituent into an axial position. Similar observations in carbocyclic compounds led F. Johnson to propose\textsuperscript{70} and defend\textsuperscript{71} the concept of allylic (1,3) strain in six-membered rings.

The restricted rotations observed for the 2-methylpiperidinoboranes suggested that they would show analogous behavior. Unfortunately the resonance signals for the ring protons at positions 2 and 6 of the piperidine ring appeared as a broad absorption from 2.9 to 4.1 ppm; as such it was not possible to extract coupling constants or any other distinguishing features from these signals. Thus the analysis which was applied so effectively to the interpretation of the spectra of the amides of 2-methylpiperidine\textsuperscript{68} was not applicable in this case. As a result, conformational assignments were based on circumstantial evidence as summarized below.

It is reported that, for methylcyclohexanes\textsuperscript{72}, the methyl-methine proton-proton coupling varies with the disposition of the methyl group. For an equatorial methyl group, the reported values are close to 6.3 Hz whereas for an axial methyl the coupling constant is generally greater than 7 Hz. Similar variations have been reported for 2-methylpiperidines.\textsuperscript{69} These values are of course dependent...
to a large extent on the position of the conformational equilibrium and deviations from these values are to be expected. It was, therefore, desirable to determine the equilibrium population of the conformer with an axial methyl group for comparison with the methyl-methylene coupling constant.

Carbon-13 nuclear magnetic resonance spectroscopy (CMR) provided an independent method for determining the position of the equilibrium. Direct measurements of the aminoboranes were not suitable because the influence of the boron nucleus on the carbon chemical shifts was unknown. Furthermore the samples were not stable over the time period required to obtain spectra. The benzoamides of substituted piperidines were selected as model compounds to correlate the position of the conformational equilibrium with the methyl-methylene coupling constants. The chemical shift data are presented in total in the appendix; chemical shifts pertinent to the determination of the position of the equilibrium are presented in Table 8.

The method of analysis of the chemical shift data is based on results reported by Dalling and Grant from their comprehensive study of C-13 chemical shifts of various methyl-cyclohexanes. From their analysis of the changes of chemical shifts of the ring carbons as a function of the conformational preferences of methyl substituents, they were able to elucidate numerical factors which would permit the determination of the position of a mobile equilibrium. In the piperidines, the chemical shift of the C-4 carbon is of paramount interest.
<table>
<thead>
<tr>
<th>C-4 Chemical Shift (in ppm)</th>
<th>Substituent Parameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>167.0</td>
<td>+1.8</td>
</tr>
<tr>
<td>168.8</td>
<td></td>
</tr>
</tbody>
</table>

**Table 8**

$^{13}C$ Chemical Shifts of Piperidine Benzamides

- CH$_3$ (axial) $+5.4$
- (23)
- (24)
Table 8 (continued)

<table>
<thead>
<tr>
<th>Chemical Shift (in ppm)</th>
<th>Substituent Parameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>167.0</td>
<td>+6.8</td>
</tr>
<tr>
<td>173.8</td>
<td></td>
</tr>
<tr>
<td>167.3</td>
<td>+11.1</td>
</tr>
<tr>
<td>178.4</td>
<td></td>
</tr>
</tbody>
</table>
The introduction of an axial methyl substituent in cyclohexane causes an upfield shift of 5.4 ppm for the resonance signal of the C-3 carbon; this structural relationship is indicated in Table 8 by a solid circle at the ring position in question. This value (5.4 ppm) represents the chemical shift change for a conformational equilibrium in which the sole conformer is one with an axial methyl substituent. The successful application of this technique requires that one be able, by use of suitable model compounds, to isolate the chemical shift change due to the conformational preference of the methyl substituent. In the present case, the chemical shift change as a result of the benzamide function can be determined by comparing entries 1 and 2 of Table 8; likewise the effect of the introduction of a methyl substituent at the 2-position can be determined by comparing entries 1 and 3. It is reassuring to note that in the latter comparison there is virtually no effect on the chemical shift of C-4. This is precisely the same result obtained by Dalling and Grant for an equatorial methyl substituent on a cyclohexane ring.

Comparison of the chemical shifts for C-4 in 2-methylpiperidine (25) and its benzamide (26) shows that for the latter, the resonance position of the C-4 carbon has shifted upfield 6.8 ppm. When this shift is corrected for the effect of the benzoyl group (6.8-1.8), the net chemical shift difference is 5.0 ppm, all of which may be attributed to the presence of an axial 2-methyl substituent. This leads to the
conclusion that for the conformational equilibrium shown,

\[
\begin{align*}
\text{Ph-C-N} & \hspace{1cm} \text{CH}_3 \\
\text{Ph-C-N} & \hspace{1cm} \text{H}_3\text{C}
\end{align*}
\]

the conformer with an axial methyl group predominates to the extent of 93% \(\frac{5.0}{5.4} = 0.93\).

A similar analysis for the benzamide (28) of cis-2,6-dimethylpiperidine (27) shows the conformer with diaxial methyl substituents to predominate to the extent of 83% \(\frac{9.0}{10.8} = 0.83\).

In agreement with the analysis of the proton spectra\(^{67,68}\), the position of the conformational equilibrium as determined by C-13 NMR heavily favors the conformer with an axial methyl substituent. A summary of methyl-methine coupling constants is presented in Table 9. From these data strong support for the structural assignments of the aminoboranes is evident.

Furthermore, it must be noted that the aminoborane functional group is isoelectronic with a carbon-carbon double bond and may be isostructural as well. It is not surprising then that considerations of allylic (1,3) strain\(^{70}\) would lead similarly to the conclusion that the 2-methyl substituent occupies an axial position.
Table 9

Values of Methyl-Methine Coupling Constants

\begin{align*}
\text{H} & \quad \text{CH}_3 \quad 6.3 \text{ Hz} \\
\text{CH}_3 & \quad \text{H} \quad \text{ref. 72} \\
\text{CH}_3 & \quad \text{Ph-C-N} \quad 7 \text{ Hz} \\
\text{Ph-C-N} & \quad 7 \text{ Hz} \\
\text{Ar} & \quad \text{CH}_3 \quad 7 \text{ Hz}
\end{align*}

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Dynamic Nuclear Magnetic Resonance Study

The geometry of the aminoboranes was assumed to be as shown below:

\[
\begin{array}{c}
\text{Ar} \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \Quad
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<th></th>
<th>Phenyl</th>
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<th>m-tolyl</th>
<th>p-chloro</th>
<th>p-anisyl</th>
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</thead>
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<tr>
<td>chemical shift (Hz) A</td>
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<td>3.60</td>
<td>3.00</td>
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</tr>
<tr>
<td>chemical shift (Hz) B</td>
<td>5.20</td>
<td>5.55</td>
<td>4.95</td>
<td>5.80</td>
<td>5.90</td>
</tr>
<tr>
<td>relaxation time (sec) A</td>
<td>0.225</td>
<td>0.22</td>
<td>0.22</td>
<td>0.245</td>
<td>0.240</td>
</tr>
<tr>
<td>relaxation time (sec) B</td>
<td>0.300</td>
<td>0.29</td>
<td>0.255</td>
<td>0.354</td>
<td>0.265</td>
</tr>
<tr>
<td>population A</td>
<td>51.0</td>
<td>51.0</td>
<td>51.0</td>
<td>53.0</td>
<td>48.0</td>
</tr>
<tr>
<td>population B</td>
<td>49.0</td>
<td>49.0</td>
<td>49.0</td>
<td>47.0</td>
<td>52.0</td>
</tr>
</tbody>
</table>
height and thus included all factors contributing to the width of the peak. These approximations were refined by visually matching the peak width and height. In the same manner the populations, approximated by integration, were also adjusted. It was assumed without verification, that none of these parameters possess a significant temperature dependence over the range of temperatures studied.

The theoretical curves were then visually matched with the experimental curves to determine a value for $\tau$, the lifetime of each isomer. From these values the rate constants were calculated using the simplifying assumption of equal populations.

Activation parameters for rotation about the B-N bond were calculated using a least squares analysis applied to the appropriate linear equations. It was necessary to restrict the range of rate constants because the spectral changes are greatest at rates close to the rate at coalescence. In either the fast or slow exchange limits, rate constants determined by this method are subject to the greatest uncertainty because changes in the curve shapes are very small. Thus in order to make valid comparisons among the members of this series of compounds, the activation parameters were determined for each compound from the same range of rate constants and temperatures. Furthermore it was imperative that very careful measurements of sample temperature be available for this comparison; the precautions taken to obtain the sample temperature are presented in the experimental
section. The temperature values reported here are very likely within the limits accessible by the present instrumentation (+ 2°C).

The activation parameters were calculated using two similar treatments, the Arrhenius equation (Eq. 5) and the Eyring relation (Eq. 6). The data are summarized in Table 11.

\[
\log k_r = \log A - \frac{E_a}{2.3 RT}
\]

(Eq. 5)

\[
\log \frac{k_r}{T} = -\frac{\Delta H^\ddagger}{2.3 RT} + \frac{\Delta S^\ddagger}{2.3 R} + \log C
\]

(Eq. 6)

From the data in Table 11, it can be seen that there is a dependence of the barrier to rotation about the B-N bond on the aryl substituent; a substituted phenyl ring lowers the energy of activation. Surprisingly the type of substituent makes little difference. At the outset of this investigation, it was anticipated that electron-donating substituents would decrease the barrier to rotation (lower \( E_a \)) by increasing the electron density on boron, and thereby decreasing the pi-bond order of the B-N bond. Such a resonance interaction had been predicted\(^{51} \) on the basis of theoretical calculations.

All attempts to establish a linear relationship between the energy of activation and known values for substituent constants were unsuccessful. Values for the substituent constants that were investigated are presented in Table 12.
Table II
Activation Parameters

<table>
<thead>
<tr>
<th>Ar =</th>
<th>$T_c (^\circ K)$</th>
<th>$\tau$ range (sec)</th>
<th>$E_a$ (kcal/mole)</th>
<th>log $A$</th>
<th>$\Delta H^#$ (kcal/mole)</th>
<th>$\Delta S^#$ (cal/deg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$\sim 346^\circ$</td>
<td>65-10</td>
<td>18.2</td>
<td>10.1</td>
<td>17.5</td>
<td>-38.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$\sim 366^\circ$</td>
<td>75-12</td>
<td>20.0</td>
<td>10.5</td>
<td>18.0</td>
<td>-39.1</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$\sim 357^\circ$</td>
<td>60-11</td>
<td>21.1</td>
<td>11.5</td>
<td>20.4</td>
<td>-38.3</td>
</tr>
</tbody>
</table>
Table 11. (cont.)

<table>
<thead>
<tr>
<th>Ar =</th>
<th>$T_C(°K)$</th>
<th>t_range (sec)</th>
<th>$E_a$ (kcal/mole)</th>
<th>log A</th>
<th>$\Delta H$ (kcal/mole)</th>
<th>$\Delta S$ (cal/deg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Cl" /></td>
<td>$\sim 365°$</td>
<td>60-10</td>
<td>22.3</td>
<td>11.9</td>
<td>21.5</td>
<td>-38.4</td>
</tr>
<tr>
<td><img src="image" alt="Cl" /></td>
<td>$\sim 365°$</td>
<td>65-10</td>
<td>23.5</td>
<td>12.7</td>
<td>22.7</td>
<td>-38.2</td>
</tr>
</tbody>
</table>
Table 12
Values for Substituent Constants

<table>
<thead>
<tr>
<th></th>
<th>m-CH₃</th>
<th>p-CH₃</th>
<th>p-OCH₃</th>
<th>p-Cl</th>
</tr>
</thead>
<tbody>
<tr>
<td>σⁿ</td>
<td>-0.13</td>
<td>-0.11</td>
<td></td>
<td>+0.24</td>
</tr>
<tr>
<td>σₒ</td>
<td>-0.07</td>
<td>-0.15</td>
<td>+0.16</td>
<td>-0.27</td>
</tr>
<tr>
<td>σ₊</td>
<td>-0.31</td>
<td>-0.78</td>
<td></td>
<td>+0.11</td>
</tr>
<tr>
<td>σ₋</td>
<td>-0.07</td>
<td>-0.17</td>
<td>-0.27</td>
<td>+0.23</td>
</tr>
<tr>
<td>σ_I</td>
<td>-0.05</td>
<td>+0.03</td>
<td></td>
<td>+0.47</td>
</tr>
<tr>
<td>σ_R</td>
<td>-0.12</td>
<td>-0.57</td>
<td></td>
<td>-0.24</td>
</tr>
</tbody>
</table>

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As is readily apparent from inspection of these data, the para-chloro substituent seems to exert an anomalous effect on the energy of activation for rotation about the B-N bond. Disregarding the para-chloro substituent did not significantly improve the correlation although there was agreement with the general nature of the effect as predicted. The failure to find a simple correlation between the energy of activation and the various substituent constants aroused the suspicion that a Hammett-type correlation was not applicable to this series of compounds. This would be the case, for example, if the interaction of the aryl ring with the B-N bond changed significantly as rotation about the B-N bond occurred.

Application of the Bovey-Johnson relation\textsuperscript{63} to the observed chemical shifts of phenyl-substituted dimethylaminoboranes led Baecher and Baechle\textsuperscript{64} to the conclusion that the phenyl ring is substantially twisted out of the plane of the B-N bond. The aromatic pi-system would then be independent of the pi-bond in the B-N bond. This separation of pi-systems is presumably the result of severe steric interactions present in a coplanar pi-system of this type. Support for the independence of the pi-bonds in phenyl substituted aminoboranes can be inferred from the mass spectral data reported for the piperidinoboranes. The relatively high abundance of doubly-charged ions is suggestive of independent pi-systems each of which may be separately ionized.

The inability to correlate the energies of activation with any of the known substituent constants becomes explicable in terms of a significant change in the interactions of
the aryl ring with the B-N bond in the ground state and the activated complex for rotation. From the available evidence, in the ground state the aryl ring is not co-planar with the B-N bond and cannot interact with that bond by a resonance interaction. Therefore, regardless of the substituent on the aryl ring, the ground state energies of all members of the series are probably very nearly identical. However, in the activated complex the geometric constraints on the aryl ring are removed and it can assume a geometry in which it interacts with the vacant orbital on boron, in effect lowering the energy of the activated complex. This results in a lowering of the barrier to rotation as is observed.

This inability to correlate substituent parameters as a result of substantial changes in resonance interactions in going from the ground state to the activated complex provides strong evidence in support of the presence of allylic (1,3) strain\textsuperscript{70} in these aminoboranes. As mentioned above, the aminoboranes are isoelectronic and probably isostructural with the corresponding alkene, as shown below.

\[
\begin{align*}
\text{N} & \quad \text{CH}_3 \\
\text{B} & \quad \text{CH}_3 \\
\text{Ar} & \\
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3 & \\
\text{Ar} & \quad \text{CH}_3
\end{align*}
\]
The theory of allylic strain has been applied to elucidating the geometry of stable cyclohexylidene derivatives; even for allylic substituents as large as phenyl, the preferred conformation is that with an axial allylic substituent. It must be that the substituents directly bonded to the pi-system are equally crowded; as no conformational release is available, these must reduce the severe interaction as much as possible by rotational motions. In the case of a phenyl group, the rotation to alleviate steric interactions takes place at the expense of the stabilizing resonance interactions with the adjacent pi-system. This behavior is a necessary consequence of the allylic strain arguments and has been referred to as "steric inhibition of resonance" in the literature.

Analysis of Mass Spectra of Aminoboranes

As mentioned above, the presence of doubly-charged ions in the mass spectra of the aminoboranes first suggested that the pi-systems were independent in the ground state. Low resolution mass spectral analysis was employed principally to establish the monomeric nature of each of the aminoboranes. At low ionizing voltage (11 ev), each gave a peak at the mass-to-charge ratio (m/e) corresponding to the molecular ion of the monomeric aminoborane. At higher ionizing voltage (70 ev) peaks assigned to doubly-charged molecular ions appeared.
The analysis of the fragmentation sequence of phenylmethyl-2-methylpiperidinoborane (17) is shown in Figure 16. This is the parent compound in the series; however, important differences between the members of the series were found. Thus, Figure 16 may not represent typical fragmentation for this type of compound; however, it is the most fully interpreted spectrum as a result of the presence of several metastable ions. In Figure 16 metastable ions are indicated by the abbreviation ms above the transition arrow and the observed mass-to-charge ratio is enclosed in parentheses below the arrow.

A metastable ion\(^7\) appears in the mass spectrum as a broad diffuse peak. Such a peak is useful in elucidating a mechanistic pathway because it relates the decomposition of a parent ion to a daughter ion. The parent ion is accelerated to a velocity determined by its mass and then enters a field-free region where it decomposes to a daughter ion and a neutral fragment. The daughter ion is deflected by a magnetic field by an amount appropriate to its mass but its excessive kinetic energy causes it to impinge on the recorder at a lower mass-to-charge ratio. Since the kinetic energy will be approximately Gaussian in distribution, the observed peak will be Gaussian in shape. For a conventional magnetic mass spectrometer, this process permits a direct mathematical relation to be formulated between the observed mass-to-charge ratio of a metastable ion and the mass-to-charge ratio of the parent and daughter ion. This relation is shown in equation 7.
Figure 16. Postulated Fragmentation Sequence of Phenylmethyl-(2-methylpiperidino)borane (17).
where \( ms \) is the metastable, \( m_2 \) is the mass-to-charge ratio of the daughter ion and \( m_1 \) is that for the parent ion. Thus from the observed mass-to-charge ratio for a metastable ion it is possible to calculate the parent and daughter ions involved in the process. Mathematically there is no unique solution to this equation but frequently chemical intuition allows a choice of reasonable values. Usually the parent and daughter ions will produce intense peaks at a mass-to-charge ratio for which a plausible structure may be assigned.

The mass spectral data for the aminoboranes are summarized in graphical form in Figures 17-21 in which each peak is represented as a percentage of the most intense peak observed in the spectrum. This presentation shows the general characteristics of the spectrum of each of the aminoboranes. Examination of these figures reveals, for example, that the loss of a methyl group, probably from the piperidine ring, is a common decomposition route of the molecular ion. Not unexpectedly, the fragmentation sequence of the 2-methylpiperidine moiety of these aminoboranes was the same regardless of the aromatic substituent. Furthermore it was identical to that reported for such heterocyclic amines.75

The fragmentation sequence shown in Figure 16 proposes that the ion of m/e 89 has the boratropylium structure
Figure 18. Mass Spectrum of p-Tolylmethy(2-methylpiperidino)borane (18).
Figure 19. Mass Spectrum of m-Tolylmethyl-(2-methylpiperidino)borane (19).
Figure 20. Mass Spectrum of p-Chlorophenylmethyl-(2-methylpiperidino)borane (20).
and that of m/e 63 the boracyclopentadienylium structure. The boratropylium ion has been the subject of several recent reports\textsuperscript{76,77} in which circumstantial evidence is adduced for its existence in the mass spectra of various boron-containing compounds.\textsuperscript{78} Unlike the tropylium ion, whose structure was elegantly established by Meyerson\textsuperscript{79}, the boratropylium ion is not symmetrical and therefore can lead to monosubstituted isomers. This promises to introduce some complexity in the search for this ion.

According to the Hückel rule of aromaticity, a monocyclic pi-electron system will exhibit some degree of aromatic stabilization if that system contains \((4n + 2)\) pi-electrons where \(n\) is an integer. The boratropylium ion, with 6 pi-electrons, represents such an aromatic system. This requires that the stabilization of the ion be sufficient to force the unpaired electron to occupy an orbital that is in the plane of the ring and not in the pi-electron system. As yet there are no theoretical calculations available which permit an assessment of the stability of this ion. The parent compound has not been reported in the literature although there are reports\textsuperscript{80} of derivatives with a benzene ring fused to the boracycloheptatriene ring which indicates some stability.

\[
\begin{align*}
\text{H} & \quad \text{\large +} \\
\text{\large +} & \quad \text{\large B} \\
\end{align*}
\]
The boracyclopentadienylium structure at m/e 63 does not satisfy the requirement for aromatic stabilization; to the contrary it would be expected to be destabilized relative to an acyclic structure. It is depicted only by analogy to a report\textsuperscript{78} in which the existence of the boratropylium ion was postulated on the basis of a metastable ion at m/e 44.5. The observation of a metastable ion does not, of course, provide any evidence for the structure of an ion.

Interest in the possible occurrence of the boratropylium ion prompted a closer examination of the mass spectra of the aryl boranes. In order to compare the various spectra it is necessary to know to what extent each of the peaks of interest contributes to the total ion intensity. For this purpose the total ion intensity\textsuperscript{81} has been calculated as the sum of the intensities of all integral peaks from m/e 80 to the molecular ion ($M^+$). The intensities of the peaks of interest are then expressed as a percentage of this summation ($\Sigma 80$). These results are compiled in Table 13.

With the data expressed in this manner it becomes possible to make comparisons among the members of the series. The intensity of the peak arising from the molecular ion is a measure of the stability of that ion to further decomposition. The aminoborane molecular ions seem to exhibit different degrees of stability depending on the substituent on the aromatic ring. The presence of an aromatic substituent with non-bonding electrons decreases markedly the stability of the molecular ion. This dichotomy appears with other ions in the spectra as well and suggests a fundamental difference in the
Table 13
Total Ionization Values

<table>
<thead>
<tr>
<th></th>
<th>(17)</th>
<th>(18)</th>
<th>(19)</th>
<th>(20)</th>
<th>(21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M⁺</td>
<td>4.3</td>
<td>6.0</td>
<td>5.4</td>
<td>0.6</td>
<td>0.3</td>
</tr>
<tr>
<td>(M-1)⁺</td>
<td>2.4</td>
<td>2.4</td>
<td>2.6</td>
<td>2.2</td>
<td>0.9</td>
</tr>
<tr>
<td>(M-15)⁺</td>
<td>5.3</td>
<td>22.5</td>
<td>12.5</td>
<td>3.9</td>
<td>1.5</td>
</tr>
<tr>
<td>m/e 91</td>
<td>5.2</td>
<td>1.6</td>
<td>1.1</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>m/e 89</td>
<td>2.9</td>
<td>1.0</td>
<td>2.8</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>m/e 99</td>
<td>2.8</td>
<td>0.3</td>
<td>1.4</td>
<td>0.7</td>
<td>4.0</td>
</tr>
<tr>
<td>m/e 98</td>
<td>2.6</td>
<td>0.4</td>
<td>1.25</td>
<td>1.7</td>
<td>3.4</td>
</tr>
<tr>
<td>m/e 84</td>
<td>3.8</td>
<td>1.6</td>
<td>9.5</td>
<td>1.5</td>
<td>31.2</td>
</tr>
<tr>
<td>m/e 83⁺</td>
<td>0.4</td>
<td>0.1</td>
<td>3.5</td>
<td>3.0</td>
<td>0.5</td>
</tr>
<tr>
<td>(M-99)⁺</td>
<td>2.6</td>
<td>1.2</td>
<td>1.1</td>
<td>4.2</td>
<td>0.2</td>
</tr>
<tr>
<td>(M-98)⁺</td>
<td>5.1</td>
<td>3.8</td>
<td>3.4</td>
<td>2.0</td>
<td>0.6</td>
</tr>
</tbody>
</table>
series.

For convenience the first three aminoboranes in Table 13 are designated as Group 1 and the remaining two members are Group 2. Comparisons between the two groups reveal that generally the presence of a positive charge on a boron-containing ion in Group 2 is considerably less likely than for Group 1. In an extensive study of the mass spectra of aminoboranes related to aromatic hydrocarbons, Dougherty found that the positive charge was associated preferentially with the boron-containing fragment. That this generalization does not hold for the aminoboranes reported here may be seen by examining the intensity data in Table 13. For those ions which contain boron, for example $M^+$, $(M-15)^+$ and $(M-98)^+$, there is a clear differentiation in intensity. A similar differentiation is possible for those ions which probably do not contain boron. These are ions arising from the piperidine moiety such as $m/e$ 99, 98, 84 and 83. This suggests that in addition to a fragmentation similar to that shown in Figure 16, there is a significant cleavage of the boron-nitrogen bond following the formation of the molecular ion for the compounds in Group 2. Significantly, the spectra of both of these compounds show a metastable ion at $m/e$ 71.5 ($98 + 83$), which corresponds to the loss of a methyl group from the 2-methylpiperidino moiety of the aminoborane. The common method of fragmentation of alkylbenzenes is cleavage of the $\beta$-bond to form a benzyl cation. It may be that the partial double bond character of the aminoborane inhibits
β-cleavage and results in degradation of the piperidine ring system.

Both members of Group 2 also gave a metastable ion at m/e 44.3 (89 + 63) corresponding to the loss of acetylene from the postulated boratropylium ion. However, as the data in Table 13 clearly show, the intensity of the peak assigned to the boratropylium ion is much less for Group 2.

The aminoboranes (18 and 19) in which the aryl group on boron is tolyl showed a metastable ion at m/e 67.6 which was not observed in any other spectra. The appearance of the same metastable ion in the spectra of isomeric compounds suggested that the metastable ion had a symmetrical structure. From the expression used to calculate the mass-to-charge ratios involved, a reasonable structure for this ion emerged. As shown in Figure 22, ring expansion of the meta and para isomers to a tropylium ion leads to only one structure. Loss of the neutral molecule, methylborane, results in an ion of mass 89, whose structure most likely is acyclic. Without high resolution mass spectral data it is not possible to determine whether boron-containing species make a contribution to the intensity of this peak. This analysis suggests that the boratropylium ion is less stable than the tropylium ion.
Figure 22. Formation of Tropylium Ion.
EXPERIMENTAL

General

Methods

Melting Points. All melting points were determined on a Thomas Hoover Capillary Melting Point apparatus and are corrected.

Infrared Absorption Spectra (IR). All IR spectra were obtained using a Perkin-Elmer Model 337 grating spectrophotometer. The spectra of liquids were obtained as films between salt (NaCl) plates. The spectra of solids were obtained as KBr pellets.

Proton Magnetic Resonance (PMR) Spectra. All PMR spectra were obtained using a Varian Model A-60 or HA-100 spectrometer. Chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane (TMS). The cooperation of Dr. Robert Stolow, Tufts University, in measuring spectra at 100 Mz is gratefully acknowledged.

Fluorine Magnetic Resonance Spectra ($^{19}$F-NMR). All $^{19}$F-NMR spectra were obtained on dichloromethane solutions using a Varian Model HA-60/DA-60 spectrometer. The fluorine chemical shifts are reported in parts per million (ppm) relative to internal Freon 11 (CFC$_3$). The cooperation of Dr. David Lemal, Dartmouth College, in measuring the fluorine spectra is gratefully acknowledged.
**Carbon Magnetic Resonance Spectra (CMR).** The CMR spectra were obtained on chloroform solutions. The CMR chemical shifts are reported in parts per million (ppm) relative to carbon disulfide ($^{13}\text{CS}_2$). The cooperation of Dr. Ernest Wenkert, Indiana University, in obtaining the carbon spectra is gratefully acknowledged.

**Elemental Analyses.** Elemental analyses were determined with an F and M Model 180 carbon, hydrogen and nitrogen analyzer. Hydride analyses were determined by the volumetric evolution of hydrogen gas.

**Low Resolution Mass Spectra.** Low resolution mass spectra were obtained using an Hitachi Model RMU-6 mass spectrometer. Samples were introduced using a liquid-solid introducer with the oven heated at 60°C. The sample pressure was in the range $1.3\times10^{-6}$ mm. Fragment ions were recorded on photosensitive paper in a strip chart recorder using four galvanometers.

**Preparation of Amines**

**General**

The following amines were prepared by the methylation of the corresponding piperidine by the Eschweiler-Clark procedure. The amines were distilled from barium oxide (BaO) prior to use.
1,3-Dimethylpiperidine (4). Methylation of 29.7 g of 3-methylpiperidine gave 23.8 g (80%) of 1,3-dimethylpiperidine (4): bp 124-126° [lit. 85 bp 124-126°; PMR (CDCl₃) δ 2.9 (s, 3H), 2.0-1.0 (7H) and 0.83 (d, 3H, J=6 Hz).

1,4-Dimethylpiperidine (3). Methylation of 29.7 g of 4-methylpiperidine gave 17.8 g (60%) of 1,4-dimethylpiperidine (3): bp 124-126° [lit. 86 bp 125°]; PMR (CDCl₃) δ 2.9 (m, 2H), 2.2 (s, 3H), 2.1-1.0 (7H) and 0.90 (d, 3H).

cis-1,2,6-Trimethylpiperidine (11). Methylation of 33.9 g of cis-2,6-dimethylpiperidine gave 23.7 g (70%) of cis-1,2,6-trimethylpiperidine (11): bp 143-146° [lit. 87 bp 149°]; PMR (CDCl₃) δ 2.2 (s, 3H), 2.1-1.2 (8H) and 1.1 (d, 6H, J=6 Hz).

1-Methyl-2-n-propylpiperidine (2). Methylation of 38.1 g of 2-n-propylpiperidine gave 29.2 g (75%) of 1-methyl-2-n-propylpiperidine (2): bp 60-62° (10 mm); [lit. 88 bp 61-63° (13 mm)]; PMR (CDCl₃) δ 2.9 (m, 2H), 2.2 (s, 3H), 2.0-1.1 (11 H) and 0.90 (t, 3H).

General

1-Methyl-4-t-butylpiperidine (7); 1-benzyl-4-t-butylpiperidine (10); 1-methyl-4-phenylpiperidine (8), and 1,2-dimethylpiperidine (9) were obtained from James J. Kaminski. Their preparation is described in his thesis. 29 The major portion of this thesis is devoted to the stereochemistry of amine-borane formation. Further details of the chemistry of amine-borane formation can be found in this thesis.
Preparation of Amine-Boranes

1,3-Dimethylpiperidine Borane (4A and 4E). To 2.1 g of 1,3-dimethylpiperidine (4) in 35 ml of dichloromethane cooled to -78° was added 17 ml of a 1 M solution of borane in tetrahydrofuran (BH\textsubscript{3}/THF). The solution was stirred at -78° for 1 hour, and the excess borane was decomposed by the drop-wise addition of methanol. The solution was concentrated at reduced pressure at 0°, leaving a white solid. A portion of the solid was dissolved in dichloromethane and filtered through glass wool into an NMR tube for analysis of the kinetically-formed mixture. The remainder of the solid was sublimed at room temperature (0.05 mm) to give a quantitative yield of 1,3-dimethylpiperidine borane (4A and 4E), mp 56-56.5°. IR (KBr) 2370 and 2280 cm\textsuperscript{-1} (B-H); PMR (CDCl\textsubscript{3}) δ 2.97 (m, 2H), 2.60 (s, 3H), 2.5-1.2 (7H) and 0.85 (d, 3H, J=6 Hz).

Anal. Calcd for C\textsubscript{7}H\textsubscript{18}BN: C, 66.18; H, 14.28; N, 11.03; hydride, 2.38. Found: C, 64.18; H, 14.12; N, 10.52; hydride, 2.34.

The elemental microanalysis of this compound presented some difficulty because of its physical behavior. At room temperature the compound exists as a highly volatile solid which could not be introduced into the combustion furnace without losses due to volatilization. Attempts to introduce the sample as a liquid were not successful.
1-Methylpiperidine Borane (1). The conversion of 5.0 g of 1-methylpiperidine following the preparation of 4a and 4E gave a quantitative yield of 1-methylpiperidine borane (1): bp 48-49° (0.15 mm); [lit.89 bp 105-107° (14 mm)].

1,4-Dimethylpiperidine Borane (3A and 3E). The reaction of BH$_3$ with 2.05 g of 1,4-dimethylpiperidine (3) following the preparation of 4A-4E, gave a quantitative yield of 1,4-dimethylpiperidine borane (3A and 3E): bp 64-66° (0.3 mm); IR (neat) 2360 and 2270 cm$^{-1}$ (B-H); PMR (CDCl$_3$) $\delta$ 2.87 (m, 2H), 2.57 and 2.50 (s, 3H), 2.3-1.0 (7H) and 0.97 (d, 3H, J=6 Hz).

Anal. Calcd for C$_7$H$_{18}$BN: C, 66.18; H, 14.28; N, 11.03; hydride, 2.38. Found: C, 66.18; H, 14.59; N, 11.29; hydride, 2.36.

1-Methyl-2-n-propylpiperidine Borane (2A and 2E). The conversion of 1.21 g of 1-methyl-2-n-propylpiperidine (2) following the procedures for the preparation of 4A-4E, gave a quantitative yield of 1-methyl-2-n-propylpiperidine borane (2A and 2E): bp 82-85° (0.4 mm); IR (neat) 2370 and 2270 cm$^{-1}$ (B-H); PMR (CDCl$_3$) $\delta$ 2.92 (m, 2H), 2.52 and 2.37 (s, 3H), 2.13-1.9 (11H) and 0.97 (t, 3H).

Anal. Calcd for C$_9$H$_{22}$BN: C, 69.69; H, 14.30; N, 9.03; hydride, 1.95. Found: C, 69.46; H, 14.63; N, 8.96; hydride, 1.88.

cis-1,2,6-Trimethylpiperidine Borane (12). To 1.27 g of cis-1,2,6-trimethylpiperidine (11) were added 11 ml of 1 M BH$_3$/THF solution at room temperature. The resulting
solution was stirred for 2 hr. The solvent was removed in a stream of dry nitrogen leaving a white waxy solid which was distilled. The product was collected as the fraction, bp 76-80° (0.4 mm). Attempts to obtain analytical data were unsuccessful because the amine-borane seemed to decompose during analysis. The PMR spectrum is reproduced in Appendix B.

1,2,6-Trimethylpiperidine Trifluoroborane (13). To 3.11 g of cis-1,2,6-trimethylpiperidine (11) in 40 ml of ether were added 3.5 g of boron trifluoride in a stream of nitrogen. Distillation of the residue gave a quantitative yield of 1,2,6-trimethylpiperidine trifluoroborane (13); bp 94.96° (0.4 mm). The PMR spectrum is reproduced in Appendix B.


Diethyl Phenylboronate (24). A solution of phenylmagnesium bromide prepared from 12.0 g of Mg and 78 g of bromobenzene in 250 ml anhydrous ether was added dropwise with stirring to a solution of 52 g of trimethylborate in 250 ml anhydrous ether at -78°. After the addition was complete, the reaction mixture was allowed to warm to room temperature by standing overnight. The mixture was cooled in an ice bath and 3N HCl was added until the magnesium salts dissolved. The ether layer was separated, dried over magnesium sulfate, and filtered; the ether was removed at reduced pressure. This left approximately 40 g of a brown solid which, without further purification, was heated under reflux with 200 ml of
anhydrous benzene and 80 ml of absolute ethanol. After heating 4 hr, the solution was concentrated at reduced pressure and the residue was distilled to afford 30 g (30% based on trimethylborate) of diethyl phenylboronate (29), bp 38-41°/0.08 mm (lit. bp 70°/0.08 mm).

Pyridine Phenylborane (6). Lithium aluminum hydride (2.5 g) was dissolved in 500 ml anhydrous ether by heating under reflux under nitrogen. The resulting solution was cooled in a Dry Ice-acetone bath and 10 ml of pyridine were added in one portion.

Diethyl phenylboronate (29) (17.7 g), dissolved in 70 ml anhydrous ether, was added slowly with stirring to the lithium aluminum hydride solution. After the addition was complete, the reaction mixture was allowed to warm to 0°, and a solution of 5 ml of pyridine and 12 ml of water was added slowly. The ethereal solution was filtered through a medium glass frit, and the filtrate was concentrated at reduced pressure to 20% of the original volume. Pentane was added to the concentrate and the solution was placed in an ice bath to crystallize. The white crystalline amine-borane (5.0 g, 30%) was collected by filtration and dried in a vacuum desiccator over potassium hydroxide. This solid, mp 78-82° (lit. 83-85°), was used without further purification. The proton spectrum showed only aromatic protons; the infrared spectrum showed no aliphatic hydrogens and had strong absorptions at 2350, 1155 and 1138 cm⁻¹ characteristic of amine-boranes.
Reaction of Pyridine Phenylborane (6) with Tertiary Amines. A sample of pyridine phenylborane (6) in an NMR tube was dissolved in dichloromethane and the spectrum recorded. An excess of the tertiary amine was then added and the spectrum scanned periodically. The progress of the reaction was monitored by scanning the N-methyl region (2.0-3.0 ppm) of the spectrum. The appearance of the amine-phenylborane usually occurred within 5 min. of mixing and the formation was generally complete within 15 min, although isomerization continued. After about 1 hr, no further change in isomer distribution could be detected.

Preparation of Aminoboranes

General

As a result of the extreme sensitivity of these compounds to the atmosphere, all operations were performed under an atmosphere of nitrogen. The highly reactive intermediates were distilled directly into a reaction flask immersed in a Dry-acetone bath or were transferred from the receiver as very dilute solutions in order to minimize losses. No attempts were made to characterize the intermediates other than by PMR spectroscopy.

Phenyldichloroborane (30). To 14.8 g of the boronate ester (31) prepared from phenylboronic acid90 (32) and ethylene glycol was added 20.8 g of solid phosphorous pentachloride (PCl5). The solution was stirred at 40° for 1 hr and a second portion of 20.8 g of PCl5 was added. The
mixture was then heated at 90° for 6 hr at which time most of the PCl₅ had dissolved. The solution was decanted into a distilling flask and distilled at atmospheric pressure to remove most of the low-boiling materials. Distillation at reduced pressure gave 5.05 g (30%) of phenyldichloroborane (30), bp 68° (10 mm).

Phenylchloro-(2-methylpiperidino)borane (33). To a solution of 5.05 g of phenyldichloroborane (30) in 25 ml of benzene immersed in an ice bath was added a solution of 3.0 g of 2-methylpiperidine (25) in 10 ml of benzene. The addition required 0.5 hr during which time a white solid began to appear. The ice bath was removed and a solution of 3.0 g of triethylamine in 10 ml of benzene was added. The mixture was heated under reflux for 2 hr and then cooled and filtered rapidly through a glass wool plug into a distilling flask. The filtrate was concentrated in a stream of nitrogen and the residue distilled to give 4.0 g (60%) of phenylchloro-(2-methylpiperidino)borane (33), bp 100-105° (0.3 mm).

Phenylmethyl-(2-methylpiperidino)borane (17). The Grignard reagent, prepared from 0.48 g of magnesium and 2.84 g of methyl iodide in 60 ml of anhydrous ether, was filtered and transferred to a three-necked reaction flask cooled in an ice bath. A solution of 4.0 g phenylchloro-(2-methylpiperidino)borane (33) in 20 ml of benzene was added dropwise with stirring. After addition was complete the reaction mixture was heated under reflux for 2 hr, cooled to room temperature and filtered. The filtrate was concentrated in
a stream of nitrogen and the residue was distilled to give 1.6 g (27% based on phenyldichloroborane) of phenylmethyl-(2-methylpiperidino)borane (17), bp 60° (0.4 mm) -75° (0.2 mm).

Anal. Calcd for C_{13}H_{20}BN: C, 77.63; H, 10.23; N, 6.96. Found: C, 77.75; H, 9.85; N, 6.22.

p-Chlorophenylmethyl-(2-methylpiperidino)borane (20). o-Chlorophenyl dichloroborane (34) was prepared from the boronate ester following the procedure for the synthesis of phenyldichloroborane (30). The reaction gave 26.2 g (73%) of p-chlorophenyldichloroborane (34), bp 76-80° (6 mm). Without characterization p-chlorophenyldichloroborane (34) was treated with 2-methylpiperidine following the procedure for the preparation of phenylchloro-(2-methylpiperidino)borane (33) to give p-chlorophenylchloro-(2-methylpiperidino)borane (35) which was not isolated. The reaction of 35 with methyl magnesium iodide gave 5.05 g (29%) of p-chlorophenylmethyl-(2-methylpiperidino)borane (20), bp 95-105° (0.4 mm).

Anal. Calcd for C_{13}H_{18}BClN: C, 66.25; H, 8.12; N, 5.94. Found: C, 65.03; H, 8.10; N, 5.57.

Dichloro-(2-methylpiperidino)borane (36). To a solution of 9.0 g of boron trichloride in 30 ml of benzene was added dropwise 7.62 g of 2-methylpiperidine in 15 ml of benzene. When the addition was complete a solution of 7.75 g of triethylamine in 15 ml of benzene was added. The resulting suspension was stirred overnight and then filtered. The filtrate was concentrated at reduced pressure, filtered into a distillation flask and distilled to give 12.5 g (90%) of dichloro-(2-methylpiperidino)borane (36), bp 67-71° (10 mm).
Chloromethyl-(2-methylpiperidino)borane (37). The Grignard reagent prepared from 14.0 g of methyl iodide and 2.36 g of magnesium in 90 ml of ether was added dropwise with vigorous stirring to a solution of 17.74 g of dichloro-(2-methylpiperidino)borane (36) in 70 ml ether cooled to -70°. When the addition was complete (ca. 1 hr), the reaction mixture was allowed to warm to room temperature and stirred for 3 hr. The suspension was filtered and the filtrate concentrated at reduced pressure. Distillation of the residue gave 7.4 g (47%) of chloromethyl-(2-methylpiperidino)borane (37), bp 60-62° (10 mm).

p-Tolylmethyl-(2-methylpiperidino)borane (18). The Grignard reagent prepared from 8.55 g of p-bromotoluene and 1.2 g of magnesium in 80 ml of ether was added dropwise to 7.4 g of chloromethyl-(2-methylpiperidino)borane (37), in 80 ml of ether cooled to 0°. The reaction mixture was stirred overnight at room temperature and filtered, and the filtrate was concentrated at reduced pressure. The concentrate was filtered into a distillation flask and distilled to give 3.37 g (34%) of p-tolylmethyl-(2-methylpiperidino)borane (18), bp 81-82° (0.35 mm).

Anal. Calcd for C_{14}H_{22}BN: C, 78.15; H, 10.30; N, 6.51. Found: C, 77.71; H, 10.54; N, 6.26.

p-Anisylmethyl-(2-methylpiperidino)borane (21) was prepared by the method above to give 3.0 g of 21, (31%), bp 100-105° (10.15 mm).
Anal. Calcd for C_{14}H_{22}BNO: C, 72.74; H, 9.59; N, 6.06. Found: C, 70.94; H, 9.54; N, 5.86.

m-Tolylmethyl-(2-methylpiperidino)borane (19) was prepared by the method above to give 1.6 g (30%), bp 78-79° (0.2 mm).

Anal. Calcd for C_{14}H_{22}BN: C, 78.15; H, 10.30; N, 6.51. Found: C, 78.61; H, 10.39; N, 6.11.

Variable Temperature NMR Spectra

The variable temperature spectra were obtained on degassed, 30% solutions in 1,1,2,2-tetrachloroethane using a Varian A-60 spectrometer equipped with a Varian V-6040 variable temperature control. Probe temperature was determined by measuring the peak separation of an ethylene glycol sample which was allowed to equilibrate thermally for 10 min before recording; this was done for each temperature change. The sample was also allowed to equilibrate thermally before recording the spectrum. At each temperature the field homogeneity was optimized using the singlet from the solvent; at higher temperatures there was a slight loss of resolution. Variable temperature spectra of the B-methyl region were recorded at a sweep width of 50 Hz; saturation effects were minimized by operation at slow sweep rates and low r.f. power levels. At each temperature the spectrum was recorded twice to detect anomalous behavior; none of the reported data were obtained from spectra recorded only once. Each sample showed only slight decomposition on heating; the spectra before and
after heating were identical with the exception of some peaks of weak intensity which were attributed to decomposition products.

**Calculation of Rate Constants**

The theoretical curves were calculated using the computer program CLATUX \(^{53}\) which treats exchange processes for the classical two-site exchange. The input parameters were determined by fitting the experimental spectra obtained at the slow exchange limit. The relaxation times were approximated by the width of the peak at half-height and thus included all factors contributing to the width of the peak. The relation between the "apparent" relaxation time \(T_2\) and the peak width \(W\) (in cps) is given by

\[
T_2 = \frac{1}{\pi W}
\]

The populations were approximated by integration. Refinement of these parameters was accomplished by matching the experimental spectra obtained at the slow exchange limit. Values for tau, the lifetime of each isomer, were obtained by visually matching the calculated and experimental curves. Values for tau were converted to rate constants with the assumption of equal populations using the relation

\[
k = \frac{1}{2\tau}
\]
The analysis of the mass spectral data indicates that aryl substituents on boron which contain non-bonded electrons exert an influence on the boron-nitrogen bond of aminoboranes. These compounds (20 and 21) show a greater degree of boron-nitrogen bond cleavage to form an ion which is structurally analogous to a benzyl cation. The investigation of the barrier to rotation about the boron-nitrogen of these compounds did not reveal any simple relationship between the energy of activation and values for substituent constants. It was concluded that steric interactions in the ground state minimized the resonance interaction between the aromatic substituent on boron and the boron-nitrogen bond. Among the substituents which were studied the p-chlorophenyl group seemed anomalous in that the energy of activation for rotation was lower than for a simple phenyl substituent. While the p-anisyl substituent did not appear anomalous, it did show the largest reduction in the energy of activation for rotation about the boron-nitrogen bond.

Cleavage of the boron-nitrogen bond and the energy of activation for rotation are both dependent on the strength of the boron-nitrogen bond. The bond strength can be considered as a measure of the electron density in the region between the boron and nitrogen atoms. The resonance interaction between the aromatic ring and the vacant orbital on boron serves to decrease the electron density in the boron-nitrogen bond. Substituents on boron which contain electronegative elements can decrease the electron density in the sigma bond between boron and nitrogen. Thus it is possible that these
two effects, resonance and electronegativity, act in concert to minimize the energy requirements of aminoboranes.
REFERENCES


26. Ref. 8a, p 293; Ref. 8b, p 100.

27. Ref. 8b, p 101.


38. Unpublished results of Dr. Edgar Garbisch, University of Minnesota.
46. E. Wiberg, Naturwissenschaften, 35, 182, 212 (1948).


81. Ref. 74, pp 44-45.
82. R. C. Dougherty, Tetrahedron, 24, 6755 (1968).


APPENDIX A

REPRINT

Quantitative Analysis of Amines via Amine Boranes

Robert E. Lyle and Everett W. Southwick

Department of Chemistry, University of New Hampshire, Durham, N. H. 03824

The boron-hydrogen bond of borane or diborane has been shown to be hydrolyzed quantitatively with many protic solvents (1). The conversion of the borane to a complex with an amine has been shown to stabilize the boron-hydrogen bond to hydrolytic or oxidative reaction conditions (2-6). These observations suggested a feasible analytical procedure for estimating the molar quantities of amine based on formation of amine boranes.

EXPERIMENTAL

Procedure. A weighed sample of the amine was placed in a flask which had been flushed with dry nitrogen. To this was added 20 ml of dry solvent (tetrahydrofuran in most instances) and the flask was attached to a gas buret. A similar apparatus was prepared in which no amine was added. To each flask was added a measured volume of solution of borane in tetrahydrofuran. After being stirred for 0.5 hour, the solution was treated with 2 ml of methanol. The volume of gas evolved from each reaction flask was measured and the volume from the reaction flask containing no amine was used to calculate the molarity of the borane-tetrahydrofuran solution. The evolution of hydrogen was usually complete within 5 to 10 minutes and any reaction after this time probably results from decomposition of the amine borane. Such complications were avoided by changing the solvent to one of higher dielectric constant or by lowering the temperature of the reaction during the analysis.

On the basis of the volume of hydrogen evolved from the flask containing amine, an estimation of the amount of excess borane present was made. The difference between this value and the moles of borane added gave the amount of borane protected as the amine borane and, therefore, indicated the number of equivalents of amine present. Typical results of this analytical procedure are given in Table I.

RESULTS

A procedure for the estimation of amines was developed which involved the treatment of the amine with an excess, but measured volume, of a standardized solution of diborane in tetrahydrofuran. The excess diborane was decomposed by the addition of water or alcohol, and the volume of hydrogen which was liberated was measured. A similar volume of the diborane solution was hydrolyzed to determine the titre of the solution. The difference in the volume of hydrogen evolved in the two experiments indicated the amount of amine borane which was formed and thus the molar equivalents of borane that were stabilized to hydrolytic conditions.

Because the nitrogen-hydrogen bond of amines is not broken by reaction with diborane (1) this analytical technique may be effective for primary, secondary, or tertiary amines. Such an analytical procedure could be used to determine the quantity of amines in a solution, the molecular weight (equivalent weight) of an amine, or the composition of a mixture of two amines of different molecular weights.

The analysis depends on the amine borane being kinetically stable to the hydrolytic conditions used to destroy the excess borane. With the strongly basic, unhindered amines, such as the cyclic amines, there was no difficulty in achieving selective decomposition; however, to increase the rate of hydrogen evolution a solvent of low dielectric constant, such as dioxane, was used. With less stable amine boranes formed with amines of large steric requirements or of weak basicity the selective hydrolysis was more difficult. The amineborane of the large amine, diisopropylethylamine, underwent partial hydrolysis in dioxane; however, a satisfactory analysis was accomplished by using tetrahydrofuran as solvent and a temperature of 0 °C for the methanolysis of the excess borane. With the weakly basic diethylamine the amine borane was too unstable to be compatible with methanol in either solvent. These results are in agreement with hydrolysis rates reported for amine boranes (3-6). Varying the analytical procedure to fit the require-

<table>
<thead>
<tr>
<th>Amine</th>
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<th>Borane mmole</th>
<th>Hydrogen evolved</th>
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</table>

- Volume uncorrected for temperature and pressure.
- Corrected.
- mmole BH₃ = mmole H₂ / 3.
- mmole amine = mmole BH₃ + Added mmole BH₃ excess.

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ments of the amine under analysis permits the estimation of
the molar quantity of aliphatic amines with a deviation of
about 3% which compares favorably with other analytical
procedures for amines (see Table I). Amines which form
borane complexes of low stability, such as aniline derivatives,
may be too easily alcoholized to permit analysis by this
method (3-6).

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1968.
APPENDIX B

AMINE-BORANE SPECTRUM
PMR Spectrum of cis-1,2,6-Trimethylpiperidine Trifluoroborate (13).
APPENDIX C

SPECTRA OF AMINO-BORANES
PMR Spectrum of p-Tolylmethyl-(2-methylpiperidino)borane (18).
PMR Spectrum of p-Anisylmethyl-(2-methylpiperidino)borane (21).
APPENDIX D

Temperature-dependent PMR Spectra of Arylmethyl-(2-methylpiperidino)boranes (17-21)

The spectra which follow are the β-methyl resonances recorded as a function of temperature. Each of these is accompanied by the curve calculated using Program CLATUX. For reference the temperature at which the spectrum was obtained is recorded beside the curve.
Phenylmethyl-(2-methylpiperidino)borane (17).
Experimental vs. calculated spectra for p-Tolylmethyl-(2-methylpiperidino)borane (18).
m-Tolylmethyl-(2-methylpiperidino)borane (19).

Experimental

Calculated
p-Chlorophenylmethyl-(2-methylpiperidino)borane (20).
P-Anisylmethyl-(2-methylpiperidino)borane (21).

calculated

experimental

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PROGRAM CLATUX
ORDERING OF DATA
TECH
NMR LINESHAPES FOR CLASSICAL TWO-SITE EXCHANGE

1. NRUN (13)
2. TEXT (184)
3. NTAU, FR1, FR2, SCALE, HEIGHT (140.0)
    NTAU = NUMBER OF TAU VALUES
    FR1 = LEFT PLOT FREQUENCY (CPS)
    FR2 = RIGHT PLOT FREQUENCY (CPS)
    SCALE = HORIZONTAL SCALE (MH/CPS)
    HEIGHT = HEIGHT OF HIGHEST PEAK (MM)
4. NEXT SET OF CARDS EXCHANGE VARIABLE TAU (FIO.O), ONE PER CARD
5. NEXT PROBLEM FINISHES, REPEAT 3 THRU 5
6. AFTER LAST PROBLEM BLANK CARD

DIMENSION Y(5000), T0(150)
PI = 3.14159
DENS = 200.
COMPLEX IM, AA, AB, FRE7, A
PI = 3.14159
DENS = 200.
IM = COMPLEX(0., 1.)
XX = 1.0DENS
READ (5, 1001) NRUN
1001 FORMAT (13)
      IF (NRUN) 2, 2, 3
2 CALL PLOT(100)
STOP
3 READ (5, 1002) TEXT
1002 FORMAT (19AR)
      READ (5, 1003) NTAU, FR1, FR2, SCALE, HEIGHT
1003 FORMAT (I10, GF10.D)
      READ (5, 1004) FR1, FR2, SCALE, HEIGHT
1004 FORMAT (RF10.O)
WRITE (6, 1005) NRUN, TEXT
1005 FORMAT (11) 113, 20X19AR//)
      WRITE (6, 1006) FR1, FR2, SCALE, HEIGHT
1006 FORMAT (2SH GENERAL INPUT PARAMETERS//10X CHEMICAL SHIFT A//10X CHEMICAL SHIFT B//10X RELAXATION TIME A//10X RELAXATION TIME B//10X POPULATION A//10X POPULATION B//10X LEFT PLOT FREQUENCY//10X RIGHT PLOT FREQUENCY
50XI = FR1, FR2, SCALE, HEIGHT
68.31 MM;//2X TAU VALUES IN SECONDS//)
XMAX = SCALE*(FR2-FR1)/25.A
NPCINT = DENS*(XXMAX)
STEP = (FR2-FR1)/NPCINT
DO 51 K = 1, NTAU
51 READ (5, 1007) TAU
WRITE (6, 1008) TAU .
1008 FORMAT (20XF10.S)
X = -XX
FR = FR1 - STEP
C FOR GENERAL INPUT PARAMETERS//10X CHEMICAL SHIFT A//10X CHEMICAL SHIFT B//10X RELAXATION TIME A//10X RELAXATION TIME B//10X POPULATION A//10X POPULATION B//10X LEFT PLOT FREQUENCY//10X RIGHT PLOT FREQUENCY
50XI = FR1, FR2, SCALE, HEIGHT
68.31 MM;//2X TAU VALUES IN SECONDS//)
XMAX = SCALE*(FR2-FR1)/25.A
NPCINT = DENS*(XXMAX)
STEP = (FR2-FR1)/NPCINT
DO 51 I = 1, NPCINT
51 Y(I) = Y(I) - YMIN*FACTOR
RETURN
END
APPENDIX F

CNMR CHEMICAL SHIFTS OF 2-METHYL PIPERIDINES AND THEIR AMIDES
C-13 Chemical Shifts (in ppm)

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*aValues may be reversed*