

5. The replacement of the bromine atom in 2-amino-3-bromo-5,6-dimethylpyrazine and some of its derivatives with chlorine on treatment with

aqueous hydrochloric acid in ethanol was unexpected.

EVANSVILLE, IND.

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Strains in Methyl Amines and Hydrocarbons¹

BY RALPH SPITZER AND KENNETH S. PITZER

H. C. Brown and co-workers have written a series of interesting articles on the anomalous basic strength of the methyl amines.² In order to eliminate complicating effects due to hydration, they worked in the gas phase and used trimethylboron as reference acid. They concluded that trimethylamine was weakened, in comparison with ammonia or mono- or dimethylamine, by a type of steric effect to which they referred as B-strain and which resulted from spreading of the methyl groups. We propose to show, by a semi-quantitative calculation, that the magnitude of the B-strain is far too small to account for the observed anomaly and that the anomaly is probably due to ordinary steric effects of the type referred to by Brown as F-strain.

Perhaps a brief description of our understanding of Brown's use of the term F-strain is in order at this time. Under this heading are lumped all types of steric strain resulting from the interference of groups attached to two adjacent atoms, including van der Waals repulsion, increase in the bonded distance, and interference with the preferred rotational configuration about the bond. It is our opinion that strains of this type are primarily responsible for the weakness of trimethylamine.

Let us quote from Dr. Brown's paper his definition of B-strain: "There are theoretical reasons for believing that the three bonds of a trivalent nitrogen atom should be directed in space at angles of 90° to each other. In all cases which have been investigated, however, the angles are considerably greater, probably because they must be increased to accommodate the attached groups. An electron diffraction investigation of trimethylamine led Brockway and Jenkins to the conclusion that the C-N-C angle in this molecule is $108 \pm 4^\circ$.^{3a} In the explanation here proposed, it is assumed that the bond angle in trimethylamine is

somewhat greater than the normal tetrahedral angle, probably close to the upper limit set by Brockway and Jenkins. In other words, the three rather bulky methyl groups spread the bonds of the nitrogen atom from their preferred configuration (90°) to a value greater than the tetrahedral angle.

"In the trivalent nitrogen derivative, such spreading of the bond angles is relatively easy since the fourth position in the valence shell is not occupied. However, the addition of a fourth group to the vacant position, be it a proton or a trimethylboron molecule, forces the nitrogen atom toward a tetrahedral configuration and results in a reduction of the expanded angles. The methyl groups are, therefore, crowded toward each other, setting up a strain which reduces the stability of the addition compound.

"The term B-strain is proposed for this effect. (The letter B is used to indicate that the interference which causes the strain is localized at the "back" of the molecule—trimethylamine in the case under discussion—away from the entering group; it is thus contrasted to F-strain which results from interference at the front of the molecule, at the interface between the two components of the addition compound."

Our problem is thus to calculate the energy needed to crowd the methyl groups together to tetrahedral angles. This will be accomplished by calculating the energy needed to bend trimethylamine into the tetrahedral configuration. As long as the C-N-C bond angles remain the same, the actual addition of the acid can introduce only F, not B strain. Also any B strain already in the free base at its expanded angles is not significant since it is the change in B-strain on addition of the acid which would affect the energy or equilibrium in that reaction.^{3b}

Total Strain in Amines.—In order to discuss this concept, it is necessary to estimate the amount of the B-strain. Brown estimates that the total strain is about 9000 kcal. per mole in the free energy of the trimethylamine-trimethylboron complex. Although he does not divide this into B-strain and ordinary steric strain (F-strains), he implies that the B strain is of considerable im-

(3b) We have discussed this matter at considerable length because Dr. Brown does not agree that our calculation is in accord with his definition quoted above.

(1) Presented in part at the Northwest Regional Meeting, American Chemical Society, May, 1947. Published with the approval of the Monographs Publication Committee, Oregon State College, as Research Paper No. 118, School of Science.

(2) (a) H. C. Brown, M. D. Taylor and M. Gerstein, *THIS JOURNAL*, **66**, 431 (1944). (b) H. C. Brown, H. Bartholomay, Jr., and M. D. Taylor, *ibid.*, p. 435. (c) H. C. Brown and M. D. Taylor, *ibid.*, **69**, 1332 (1947).

(3a) L. O. Brockway and Jenkins, *ibid.*, **58**, 2036 (1936). More recently V. Schomaker (private communication) has obtained for the C-N-C angle, $109 \pm 2^\circ$ for trimethylamine, $111 \pm 3^\circ$ for dimethylamine, $112 \pm 3^\circ$ for diethylamine and $113 \pm 3^\circ$ for triethylamine.

portance. We shall use energy rather than free energy in our discussion in order to eliminate the complicating effects of entropy changes, and it is therefore necessary to re-estimate the strain.

Table I shows the energy of dissociation of the trimethylboronamine complexes. The addition of one methyl group increases dissociation energy by 3.9 kilocalories per mole. If we assume, with Brown, that the effect of adding more methyl groups is linear in the number of methyl groups, we may derive the third column in Table I, which shows expected dissociation energy. The last column then gives the difference between expected and observed dissociation energies, and this difference may be attributed to a steric strain of some sort. Actually, these estimates are probably high. If we accept Brown's hypothesis that methylamine is a stronger base than ammonia because of the positive inductive effect, we really should not expect the strength of the amines to increase linearly with number of methyl groups added. Whereas the dipole moment of ethyl chloride is about 10% higher than that of methyl chloride—presumably because of the positive inductive effect of the added methyl group—we find little or no additional increase in the dipole moments of isopropyl and *t*-butyl chlorides. This fact would indicate that the positive inductive effect of methyl groups falls off beyond the first. If we arbitrarily assume that the second methyl may have as little as one-half the effect of the first and that the third one-third the effect, we would obtain 0.35 and 3.3 kcal./mole for the strain energies of the last two compounds in the table. These values are used as lower limits to the strain energies in Table III.

TABLE I
SUMMARY OF DISSOCIATION ENERGIES

Compound	ΔH of dissociation	Kcal. per mole Expected dissociation	Strain energy
$\text{NH}_3\text{—B}(\text{CH}_3)_3$	13.7	13.7	(0)
$\text{CH}_3\text{NH}_2\text{—B}(\text{CH}_3)_3$	17.6	17.6	(0)
$(\text{CH}_3)_2\text{NH—B}(\text{CH}_3)_3$	19.3	21.5	2.2
$(\text{CH}_3)_3\text{N—B}(\text{CH}_3)_3$	17.6	25.4	7.8

Calculation of B-Strain.—We are now ready for an approximate calculation of B-strain in the trimethylamine complex. Inasmuch as the C–N–C angle changes only a few degrees when boron trimethyl is added to trimethylamine, the energy increment due to the change in this angle should be calculable to good approximation by use of the angle bending constant for trimethylamine. It should be noted that the use of an empirical potential constant accounts for energy of methyl group compression as well as pure angle bending. If we make the extreme assumptions that the C–N–C angles in the trimethylamine and the trimethylamine–boron trimethyl complex are, respectively, 112° and $109\frac{1}{2}^\circ$, the angle change is $2\frac{1}{2}^\circ$.

Although the bending potential constants for

similar molecules are known to range near 1×10^{-11} erg./radian², there seemed to be no good literature value for trimethylamine. We calculated the C–N–C bending constant from the Raman frequencies⁴ 368, 827 and 1179 cm.^{-1} which are to be identified as primarily C–N–C bending, C–N stretching and CH_3 wagging, respectively, all in the symmetry class A_1 . We set up the exact equations for the A_1 class and then reduced them by making the CH_3 groups rigid and of the generally accepted dimensions. Then assuming a valence force potential, we obtained the constants 1.17×10^{-11} erg./radian² for C–N–C bending, 4.77×10^5 dynes/cm. for C–N stretching, and 0.70×10^{-11} erg./radian² for the C–C–H angles in CH_3 wagging. This result may be compared, *e. g.*, with Sutherland's^{5a} estimate of the stretching and bending constants for isobutane of 4.5×10^5 dynes/cm. and 0.95×10^{-11} erg./radian².

With the bending constant 1.17×10^{-11} erg./radian², we find that the energy of trimethylamine increases by $25(\Delta\theta)^2$ calories per mole per C–N–C angle where $(\Delta\theta)$ is the change in degrees from the equilibrium value of the C–N–C angle. Taking the upper limit $\Delta\theta = 2\frac{1}{2}^\circ$, we obtain a destabilization of 156 calories per angle or a total destabilization for the molecule of three times this amount. The resulting maximum value of about 0.5 kcal. per mole is certainly small compared with the 3–8 kcal. per mole estimated in Table III. This calculation indicates that B-strain is not primarily responsible for the anomalous weakness of trimethylamine.

Comparison with Related Hydrocarbons.—Having indicated that the effect of B-strain is small in the methylamines, we shall now show that hydrocarbons with structures related^{5b} to the structures of the compounds discussed here show a corresponding increase in strain energy as the complexity of the structures increases. This strain must be a manifestation of F-strain, because, even if B-strain is present in the hydrocarbons which we shall discuss, it must not vary greatly from one to another because the number and nature of bonds attached to carbon is essentially constant. As we have seen in the preceding discussion, B-strain becomes manifest in such a situation as the change from trivalent to tetravalent nitrogen in which the methyl groups attached to nitrogen are forced back toward the tetrahedral angle. Table II shows the heats of formation of some hydrocarbons in the gas phase at 25° .⁶ Column 3 gives the difference between the heat of formation of the given hydrocarbon and the normal hydrocarbon with the same num-

(4) K. W. F. Kohlrausch and J. Wagner, *Z. physik. Chem.*, **B52**, 185 (1942).

(5a) G. B. B. M. Sutherland and D. M. Simpson, *J. Chem. Phys.*, **15**, 153 (1947).

(5b) This relationship has been mentioned by H. C. Brown, H. I. Schlesinger and S. Z. Cardon, *THIS JOURNAL*, **64**, 325 (1942).

(6) E. J. Prosen, K. S. Pitzer and F. D. Rossini, *J. Research Natl. Bur. Stds.*, **54**, 403 (1945).

ber of carbon atoms. We observe that the iso hydrocarbons are about 1.7 and the neo hydrocarbons about 4.6 kcal. per mole more stable than the related normal hydrocarbon. If we assume that the effects of branching would be additive in more complex molecules, we obtain the results in column 4 of Table II for the expected difference from the heat of formation of the normal hydrocarbon. For example, 2,2,3-trimethylbutane contains both iso and neo type configuration, and so should be more stable than *n*-heptane by $1.7 + 4.6 = 6.3$ kcal. per mole. The difference between columns 4 and 3 represents destabilization which we shall attribute to steric strain of the F type. The assumption of additivity is no doubt an oversimplification. Some justification for the assumption may be derived from a consideration of 2,5-dimethylhexane. In this compound, where two iso groups are widely separated, additivity is strict. We were unable to test the assumption with regard to combinations with neo groups due to lack of data on compounds in which these groups are separated sufficiently.

TABLE II
HEATS OF FORMATION OF HYDROCARBONS IN THE GAS PHASE AT 25° AND RELATED DATA

Hydrocarbon	-ΔH _f	Kcal. per mole		Steric strain
		Difference from normal hydrocarbon	Expected difference from normal hydrocarbon	
<i>n</i> -Butane	29.8	0.0	0.0	0.0
Isobutane	31.5	-1.7	-1.7	.0
<i>n</i> -Pentane	35.0	0.0	0.0	.0
Isopentane	36.9	-1.9	1.7	-.2
Neopentane	39.7	-4.7	-4.6	-.1
<i>n</i> -Hexane	40.0	0.0	0.0	.0
2-Methylpentane	41.7	-1.7	-1.7	.0
2,2-Dimethylbutane	44.4	-4.4	-4.6	.2
<i>n</i> -Heptane	44.9	0.0	0.0	.0
2-Methylhexane	46.6	-1.7	-1.8	.0
2,2,3-Trimethylbutane	49.0	-4.1	-6.3	2.2
<i>n</i> -Octane	49.8	0.0	0.0	0.0
2,2,3,3-Trimethylbutane	54.0	-4.2	-9.2	5.0
2-Methylheptane	51.5	-1.7	-1.7	0.0
2,5-Dimethylhexane	53.2	-3.4	-3.4	.0

The skeletons of the hydrocarbons 2,2-dimethylpropane, 2,2-dimethylbutane, 2,2,3-trimethylbutane and 2,2,3,3-tetramethylbutane are identical, respectively, with those of the addition compounds of trimethylboron with ammonia, mono-, di-, and trimethylamines if we consider B + N atoms as equivalent to C atoms, as the first two columns of Table III show. Columns 3 and 4 of the same table summarize the steric strains of the hydrocarbons and of the amine-boron compounds. This agreement as to order of magnitude makes it probable that this steric effect in the hydrocarbons, in which B-strain should be substantially

eliminated, is of the same nature as that in the amine complexes.

TABLE III
COMPARISON OF STERIC STRAINS OF AMINE-TRIMETHYLBORON COMPLEXES AND RELATED HYDROCARBONS

Amine-boron complex	Hydrocarbons	Estimated strain of amine, kcal.	Estimated steric strain of hydrocarbon
$\begin{array}{c} \text{H} \quad \text{CH}_3 \\ \quad \\ \text{H}-\text{N}-\text{B}-\text{CH}_3 \\ \quad \\ \text{H} \quad \text{CH}_3 \end{array}$	$\begin{array}{c} \text{H} \quad \text{CH}_3 \\ \quad \\ \text{H}-\text{C}-\text{C}-\text{CH}_3 \\ \quad \\ \text{H} \quad \text{CH}_3 \end{array}$	0.0	-0
$\begin{array}{c} \text{H} \quad \text{CH}_3 \\ \quad \\ \text{CH}_3-\text{N}-\text{B}-\text{CH}_3 \\ \quad \\ \text{H} \quad \text{CH}_3 \end{array}$	$\begin{array}{c} \text{H} \quad \text{CH}_3 \\ \quad \\ \text{CH}_3-\text{C}-\text{C}-\text{CH}_3 \\ \quad \\ \text{H} \quad \text{CH}_3 \end{array}$	0.0	0.2
$\begin{array}{c} \text{CH}_3 \quad \text{CH}_3 \\ \quad \\ \text{CH}_3-\text{N}-\text{B}-\text{CH}_3 \\ \quad \\ \text{H} \quad \text{CH}_3 \end{array}$	$\begin{array}{c} \text{CH}_3 \quad \text{CH}_3 \\ \quad \\ \text{CH}_3-\text{C}-\text{C}-\text{CH}_3 \\ \quad \\ \text{H} \quad \text{CH}_3 \end{array}$	0.3-2.2	2.2
$\begin{array}{c} \text{CH}_3 \quad \text{CH}_3 \\ \quad \\ \text{CH}_3-\text{N}-\text{B}-\text{CH}_3 \\ \quad \\ \text{CH}_3 \quad \text{CH}_3 \end{array}$	$\begin{array}{c} \text{CH}_3 \quad \text{CH}_3 \\ \quad \\ \text{CH}_3-\text{C}-\text{C}-\text{CH}_3 \\ \quad \\ \text{CH}_3 \quad \text{CH}_3 \end{array}$	3.3-7.8	5.0

Discussion.—The comparison with the hydrocarbons does not apply to the formation of ammonium salts in water solution, in which a parallel trend has been found.^{2b} Inasmuch as the situation in water is much more complex, as was recognized by Brown, it is probable that the parallelism is to some extent fortuitous. Indeed correction⁷ for symmetry number changes on proton addition spoils the exact parallelism by making methylamine the strongest base. Possibly hydration energy effects are responsible for the effect in water solution.

It is clear, then, as was pointed out by Lewis (and also by Brown in his later experiments on F-strain) that the reference acid is very important in determination of the order of basic strengths.

With hydrochloric as a reference acid, Brown⁸ found a regular order of base strength for the methylphosphines. His conclusion that this result supports his theory is not necessarily correct. It is quite possible that if experiments could be performed in the gas phase, the alkylamines would show the normal order of basic strength against hydrochloric acid. In any event, the structure of the hydrochlorides is so different from that of the trimethyl boron complexes that any comparison between the two must be made with caution. Also, it should be pointed out that in compounds such as the phosphines, in which the bond angles are less than tetrahedral, B-strain should have a base-strengthening effect. The change from p to sp³ bonds caused by the addition of the acid and consequent expansion of the bond angles should relieve the B-strain, thereby making the salt or addition complex more stable compared with the free base.

(7) We are indebted to Prof. V. Schomaker for suggesting this point.

(8) H. C. BROWN, THIS JOURNAL, 67, 503 (1945).

B-strain may become important when groups much larger than methyl are attached to the central atom because both the angles of distortion and the angle force constant will increase.

Summary

1. It is shown, by a semi-quantitative calculation, that the B-strain postulated by H. C. Brown is too small to account for the observed weakness of trimethylamine as an acid.

2. A comparison of ordinary steric forces (F-

strain) in hydrocarbons of related structure shows that the steric strains in trimethylboron-alkyl amine compounds are probably of the same nature as those in the hydrocarbons.

3. The importance of the reference acid in establishing basic strengths is re-emphasized.

4. It is pointed out that B-strain will be base-strengthening rather than base-weakening when the angles are less than tetrahedral.

CORVALLIS, OREGON
BERKELEY, CALIFORNIA

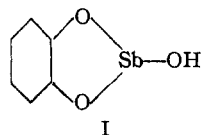
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Antimonycatechol. I. Coördination of Simple Amines and Alcohols

BY L. M. WHEELER AND C. K. BANKS

The combination of inorganic, trivalent antimony with phenols and α -hydroxyacids has long been known, but only a few derivatives with alcohols have been reported¹ and these compounds are unstable in the presence of water. Since antimonycatechol² (I) appeared to be of interest in the treatment of filariasis,³ efforts were made to solubilize this compound. It is insoluble in water, aqueous ammonia, alcohol, ether, chloroform and other solvents and dissolves only in strong sodium hydroxide and concentrated hydrochloric acid. However, it was noted that in the presence of both an alcohol and an amine, antimonycatechol readily formed solutions from which crystalline products could be isolated. Both the alcohol and the amine were combined, in some fashion, with the antimonycatechol in the isolated products. That such combinations were not fortuitous was readily demonstrated. The ratios of combination were always the same regardless of the reactants and experiments showed that no combination occurred in aqueous solution when only the alcohol or the amine was present.



The atomic ratio of antimony to nitrogen was always one within experimental limits. The products dissolved readily in water to give nearly neutral solutions which could be decomposed with strong acids to yield antimonycatechol, the alcohol and the amine salt. When both the alcohol and amine were low-boiling, prolonged heating at 100° in a high vacuum resulted in the loss of these fragments, leaving antimonycatechol. Preparations containing ammonia or other volatile amines would lose the nitrogenous constituent during pro-

longed shelf storage, resulting in decreased solubility and altered crystalline properties. If the amines were relatively non-volatile, the products were stable to heat and storage.

Solutions of these compounds in water appeared to undergo hydrolysis on standing and a hydrated form of antimonycatechol was separated. An excess of any amine would stabilize the solutions indefinitely. Aqueous solutions appeared to have all the properties of salt solutions, particularly in that they were excellent conductors of electricity, showing about forty per cent. the conductance of equimolar sodium chloride solutions.

Determinations of carbon and hydrogen in the presence of antimony were extremely variable, but both antimony and nitrogen were readily determined. To further elucidate the structures, inductive postulations were necessary.

The alcohols used were methanol, propanol, glycols, glycerol, sorbitol, mannitol, dextrose, galactose and levulose. The amines studied consisted of ammonia, diethyl- and triethylamine. The properties of the resulting products are given in Table I.

The reaction product of antimonycatechol and tartaric acid⁴ was also investigated. When equimolar amounts of the two substances were heated in water containing a four-fold excess of sodium bicarbonate, a product similar in every respect to the alcohol-amine complexes was formed.

Experimental

Alcohol-Amine-Antimonycatechol Complexes.—Antimonycatechol (0.2 mole) was suspended in 100 ml. of water in which had been dissolved 0.2 mole of the alcohol and 0.5 mole of amine in a 500-ml. round-bottomed flask equipped with stirrer and condenser. The temperature of the vigorously stirred solution was raised to 80–90° and was maintained at this temperature for fifteen minutes after complete solution occurred. The hot solutions were filtered rapidly and cooled. The products crystallized on cooling or on adding acetone to the cold solution. They were recrystallized from hot water, methanol or

(1) Meerwein, *Ann.*, **476**, 113 (1929).

(2) Causse, *Bull. soc. chim.* [3] **8**, 245 (1892).

(3) Feinberg, U. S. Patent 2,330,962, Oct., 1943.

(4) U. S. Patent 1,688,964.