trobenzene resulted in a temperature rise of 0.03°. This increase was independent of the concentration. It therefore was concluded that the increase in temperature must not be due to any heat of dilution, but rather to a reaction of the carrier with trace amounts of a basic impurity present in the nitrobenzene. Since the carrier always was used in excess, a correction of −0.03° always was applied to the observed temperature rise.

A detailed study was made of the heat equivalent of the calorimeter filled with 100 ml. of nitrobenzene and filled with nitrobenzene containing the typical reaction products pyridine–boron trifluoride, tetrahydropyran and excess carrier. A total of 24 determinations with pure nitrobenzene gave the value for the electrical equivalent of the calorimeters of 74.7 ± 0.5 cal./deg. With the reaction products present, a total of 9 determinations gave the value of 74.8 ± 0.5 cal./deg. Moreover, there was evident no dependence on the concentration of the reagents (0.096–0.29 *M*). It therefore was concluded that the heat capacity of the solutions must be very similar to the heat capacity of the nitrobenzene.

Typical data illustrating the precision attained are presented in Table II.

To further test the reliability of the procedure, the heat capacity of nitrobenzene and the heat of reaction of sodium hydroxide and hydrochloric acid were determined. Three determinations gave for the heat capacity of nitrobenzene at 24° the value 0.355 ± 0.003 cal./deg. g., as compared to values of 0.347,[9] 0.362,[10] 0.352[11] reported in the literature. For the heat of reaction of sodium hydroxide with hydrochloric acid at 23.88°, five determinations gave the value 13.70 ± 0.07 kcal./mole as compared to the literature value of 13.62.[12]

These results support the conclusion that the calorimetric procedure should be capable of giving data on the heats of formation of molecular addition compounds in solution with a precision of 1%.

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[9] G. Schulze, *Verhandlungen der Physikalischen Gesellschaft zu Berlin*, **14**, 189, 258, 244 (1912).

[10] G. S. Parks and S. S. Todd, *J. Chem. Phys.*, **2**, 440 (1934).

[11] J. Mazur, *Nature*, **143**, 28 (1939).

[12] T. W. Richards and A. W. Rowe, THIS JOURNAL, **44**, 684 (1922).

LAFAYETTE, INDIANA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF PURDUE UNIVERSITY]

Steric Effects in Displacement Reactions. VI. The Heats of Formation of the Addition Compounds of Boron Trifluoride with the Monoalkylpyridines. A Linear Relationship Involving Sterically Hindered Reactants[1]

BY HERBERT C. BROWN AND RAYMOND H. HOROWITZ[2]

RECEIVED JULY 8, 1954

The heats of reaction of the monoalkylpyridine bases with tetrahydropyran–boron trifluoride have been measured in nitrobenzene solution. The presence of a methyl group in the 3- or 4-position increases the heat of reaction from 12.2 kcal./mole observed for pyridine to 12.5 for 3-picoline and 12.7 for 4-picoline. Changes in the structure of the alkyl group (alkyl = methyl, ethyl, isopropyl, *t*-butyl) in the 3- or 4-position has little further effect on the stability of the addition compounds. These heats of reactions therefore parallel the pK_a values of the bases—the stronger the base the larger the heat of reaction with tetrahydropyran–boron trifluoride. In the 2-position the opposite effect is observed. Whereas the methyl group in 2-picoline results in an increase in the strength of the base, there is observed with this base a decreased heat of reaction with tetrahydropyran–boron trifluoride ($-\Delta H = 10.5$ kcal./mole). The effect becomes increasingly important with 2-ethyl ($-\Delta H = 9.9$), 2-isopropyl ($-\Delta H = 8.9$), and 2-*t*-butyl ($-\Delta H = 2.0$). The decrease is attributed to steric strains in the addition compounds arising from the conflicting steric requirements of the 2-alkyl groups and the boron trifluoride group. A plot of the heat of reaction data for these pyridine bases *vs.* the activation energy data for the reaction of the bases with methyl iodide reveals a reasonably good linear relationship. It is concluded that to obtain such linear relationships with sterically hindered reactants it is necessary to compare reactions with similar steric requirements.

The energies of activation of the reactions of 2-alkylpyridines with methyl iodide increase with the increasing bulk of the 2-substituent. These increases are attributed to steric strains in the activated complex arising from the conflicting steric requirements of the 2-substituent and the methyl group of the iodide.[3]

The bulk of the 2-substituent has but a small effect upon the pK_a value[4] and upon the heat of reaction of methanesulfonic acid with these bases.[5] It is considered that in these reactions the steric requirements of the proton are so small that there is no significant steric interaction with the bulky 2-substituents.

As a test of this interpretation it appeared desirable to examine the effect of the steric requirements of the 2-substituents on the reaction of these pyridine bases with a reference acid of moderate steric requirements. Boron trifluoride offered a number of advantages for such a study. Accordingly, it was decided to measure the heat of reaction of this acid with the monoalkylpyridines.

Results

In the previous paper there was described a calorimeter which was developed for the determination of the heat of reaction of pyridine with boron trifluoride and with tetrahydropyran–boron trifluoride, both in nitrobenzene solution.[6] In this study, the use of the carrier resulted in much better precision.

We were interested primarily in differences in the heats of reaction of the pyridine bases with boron trifluoride. These differences are as easily determined from the data for the reaction of the pyridine bases with tetrahydropyran–boron trifluoride as from data for the direct reaction of these bases with boron trifluoride. In view of the greater precision attainable by the use of a carrier, it was decided to measure the heats of reaction of the pyridine bases with tetrahydropyran–boron trifluoride.

Typical data are summarized in Table I.

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[1] Based upon a thesis submitted by Raymond H. Horowitz in January, 1951, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[2] Research Fellow at Purdue University, 1948–1951, under a contract with the Office of Naval Research for the study of "Steric Strains in Chemical Reactions."

[3] H. C. Brown and A. Cahn, THIS JOURNAL, **77**, 1715 (1955).

[4] H. C. Brown and X. R. Mihm, *ibid.*, **77**, 1723 (1955).

[5] H. C. Brown and R. R. Holmes, *ibid.*, **77**, 1727 (1955).

[6] H. C. Brown and R. H. Horowitz, *ibid.*, **77**, 1730 (1955).

TABLE I

HEAT OF REACTION OF TETRAHYDROPYRAN–BORON TRIFLUORIDE WITH THE 2-MONOALKYLPYRIDINES

Base	Concentration, M Base	Concentration, M THP:BF$_3$	Temp. rise,[a] °C.	Heat of reaction $-\Delta H$ (kcal./mole)
2-Picoline	0.200	0.300	1.410	10.55
	.200	.300	1.433	10.72
	.200	.300	1.410	10.55
	.200	.300	1.370	10.25
	.200	.300	1.414	10.58
			Mean	10.53 ± 0.11
2-Ethylpyridine	.200	.300	1.307	9.78
	.200	.300	1.337	10.00
	.200	.300	1.338	10.01
			Mean	9.93 ± 0.10
2-Isopropylpyridine	.200	.300	1.210	9.05
	.200	.300	1.165	8.71
	.200	.300	1.185	8.86
			Mean	8.88 ± 0.12
2-*t*-Butylpyridine	.200	.230	0.265	1.98
	.200	.230	.310	2.32
	.200	.230	.270	2.02
	.200	.350	.250	1.87
	.200	.350	.260	1.94
	.200	.350	.260	1.94
			Mean	2.01 ± 0.11

[a] Corrected by −0.03° as in ref. 6.

The heat of reaction of 2-*t*-butylpyridine with tetrahydropyran–boron trifluoride was only 2.0 kcal., and we were concerned with the possibility that the reaction might not be going to completion. However, repetition of the experiments with the carrier at two different concentrations, 0.230 and 0.350 M, revealed no significant effect of the concentration on the heat evolved. It was therefore concluded that in spite of the low heat, the reaction must be proceeding essentially to completion.

The experimental data for the heats of reaction, rounded off to the nearest 0.1 kcal., are summarized in Table II.

TABLE II

MOLAR HEATS OF REACTION OF THE MONOALKYLPYRIDINES WITH TETRAHYDROPYRAN–BORON TRIFLUORIDE IN NITROBENZENE SOLUTION

Pyridine base RC$_5$H$_4$N, R–	Heats of reaction, $-\Delta H$ (kcal./mole) THP:BF$_3$[a]	BF$_3$[b]	$\Delta H_{Py} - \Delta H_B$
Hydrogen	12.2	25.0	0.0
2-Methyl	10.5	23.3	− 1.7
2-Ethyl	9.9	22.7	− 2.3
2-Isopropyl	8.9	21.7	− 3.3
2-*t*-Butyl	2.0	14.8	−10.2
3-Methyl	12.5	25.3	0.3
3-Ethyl	12.4	25.2	0.2
3-Isopropyl	12.5	25.3	0.3
3-*t*-Butyl	12.8	25.6	0.6
4-Methyl	12.7	25.5	0.5
4-Ethyl	12.5	25.3	0.3
4-Isopropyl	12.6	25.4	0.4
4-*t*-Butyl	12.5	25.3	0.3

[a] $RC_5H_4N(soln.) + (CH_2)_5O:BF_3(soln.) = RC_5H_4N:BF_3(soln.) + (CH_2)_5O(soln.)$. [b] $RC_5H_4N(soln.) + BF_3(soln.) = RC_5H_4N:BF_3(soln.)$. Calculated on basis that the heat of reaction for pyridine is 25.0 kcal. (See ref. 6.)

Discussion

Steric Strains in the Reactions of the 2-Alkylpyridines.—For convenience in following the discussion the available data for the pK_a values of the alkylpyridines,[4] the heats of reaction with methanesulfonic acid[5] and with boron trifluoride, and the rate constants and activation energies for the reaction with methyl iodide[3] are summarized in Table III.

TABLE III

SUMMARY OF RATE AND EQUILIBRIUM DATA FOR REACTIONS INVOLVING THE MONOALKYLPYRIDINES

Pyridine base RC$_6$H$_4$N, R–	pKa[a]	Heat of reaction ($-\Delta H$) CH$_3$SO$_3$H[b]	BF$_3$[c]	Rate data for CH$_3$I[d] $k_2^{25°} \times 10^5$	E_{act}
Hydrogen	5.17	17.1	25.0	34.3	13.9
2-Methyl	5.97	18.3	23.3	16.2	14.0
2-Ethyl	5.97	18.2	22.7	7.64	14.2
2-Isopropyl	5.83	18.1	21.7	2.45	14.8
2-*t*-Butyl	5.76	18.0	14.8	0.0080	17.5
3-Methyl	5.68	17.8	25.3	71.2	13.6
3-Ethyl	5.70	18.1	25.2	76.1	
3-Isopropyl	5.72	18.0	25.3	81.0	
3-*t*-Butyl	5.82	18.2	25.6	95.0	
4-Methyl	6.02	18.4	25.5	76.0	13.6
4-Ethyl	6.02	18.3	25.3	77.7	
4-Isopropyl	6.02	18.4	25.4	76.7	
4-*t*-Butyl	5.99	18.3	25.3	75.7	13.7

[a] Water, 25°. [b] Nitrobenzene, 25°, kcal./mole. [c] Nitrobenzene, 25°, kcal./mole. [d] Nitrobenzene, E_{act} in kcal./mole. Values of $k_2^{25°}$ calculated from rate constants at other temperatures. See Table VI, ref. 3.

The introduction of a methyl group in the 3-position results in an increase in the heat of reaction of 0.3 kcal./mole. In the 4-position a methyl group causes a somewhat larger increase, 0.5 kcal./mole. Within the limits of the experimental error of the measurements, changes of the structure of the alkyl group from methyl to ethyl to isopropyl to *t*-butyl have no significant effect upon the heat of reaction. In the case of the 3- and 4-alkyl derivatives the results therefore parallel closely the pK_a data[4] and the data obtained in the corresponding reactions of the pyridine bases with methanesulfonic acid.[5]

In the 2-position alkyl groups cause major changes in the heats of reaction. In 2-picoline, instead of an increase in the heat of reaction similar to that observed with methanesulfonic acid,[5] there occurs a decrease of −1.7 kcal./mole. With increasing steric requirements of the alkyl group in the 2-position there is observed an increasing drop in the heat of reaction: 2-ethyl-, −2.3; 2-isopropyl-, −3.3; 2-*t*-butyl-, −10.2.

From the effect of the alkyl groups in the 3- and 4-positions of the pyridine bases upon the heats of reaction with boron trifluoride, we may estimate that these alkyl groups should increase the stability of the addition compounds of boron trifluoride with the 2-alkylpyridines by approximately 0.4 kcal./mole. Consequently we may estimate the steric strains in the addition compounds of boron trifluoride to be: 2-picoline, 2.1; 2-ethylpyridine, 2.7; 2-isopropylpyridine, 3.7; and 2-*t*-butylpyridine, 10.6 kcal./mole.

The same assumptions may be utilized to estimate the strains present in the reactions of the 2-alkylpyridine bases with methyl iodide and with methanesulfonic acid. The results are summarized in Table IV.

TABLE IV

ESTIMATED STERIC STRAINS FOR THE REACTIONS OF THE 2-ALKYLPYRIDINES

Pyridine base RC_5H_4N, R-	Steric strains Methane-sulfonic acid[a]	 Methyl iodide[b]	 Boron trifluoride[c]
2-Methyl	0.0	0.4	2.1
2-Ethyl	.1	0.6	2.7
2-Isopropyl	.2	1.2	3.7
2-*t*-Butyl	.3	3.9	10.6

[a] Estimated assuming $-\Delta H$ to be 18.3 kcal./mole in absence of steric strains (ref. 5). [b] Estimated assuming E_{act} to be 13.6 kcal./mole in absence of steric strains (ref. 3). [c] Estimated assuming $-\Delta H$ to be 25.4 kcal./mole in absence of steric strains.

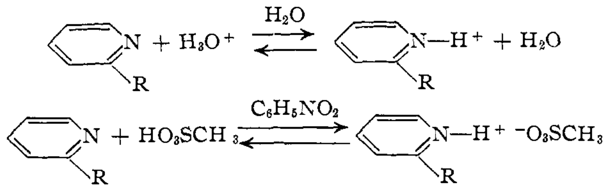
It is evident that in each case the steric strains increase both with the increasing steric requirements of the 2-substituent and with the increasing steric requirements of the second reactant: methanesulfonic acid < methyl iodide < boron trifluoride.

Linear Relationships Involving Sterically Hindered Reactants.—The failure of the *ortho* substituted aromatic systems to obey the Hammett $\rho\sigma$-relationship[7] is generally recognized. For example, in an earlier paper of this group it was shown that a Hammett-type plot of the rate data for the reaction of methyl iodide with the pyridine bases *versus* their pK_a values did not yield a linear relationship for the 2-alkyl derivatives.[4]

It is apparent that similar plots of the heats of reaction of the pyridine bases *versus* their pK_a values (Fig. 1) or *versus* their heats of reaction with methanesulfonic acid (Fig. 2) yield linear relationships only for pyridine and the 3- and 4-alkylpyridines. The 2-alkylpyridines deviate from this linear relationship, and the magnitude of the deviation increases with the bulk of the 2-alkyl substituent.

It appears reasonable that the failure of *ortho* substituted aromatics to obey the Hammett relationship might be due to the effect of the steric requirements of these substituents on the reaction rate or equilibrium.[8] This factor presumably would not be significant in the case of the corresponding *meta* and *para* derivatives where the substituent is relatively remote from the reaction center.

The fact that a linear relationship is observed between the heats of reaction of the pyridine bases with methanesulfonic acid and their pK_a values[5] is attributed to the similarity in the steric requirements of both reactions.



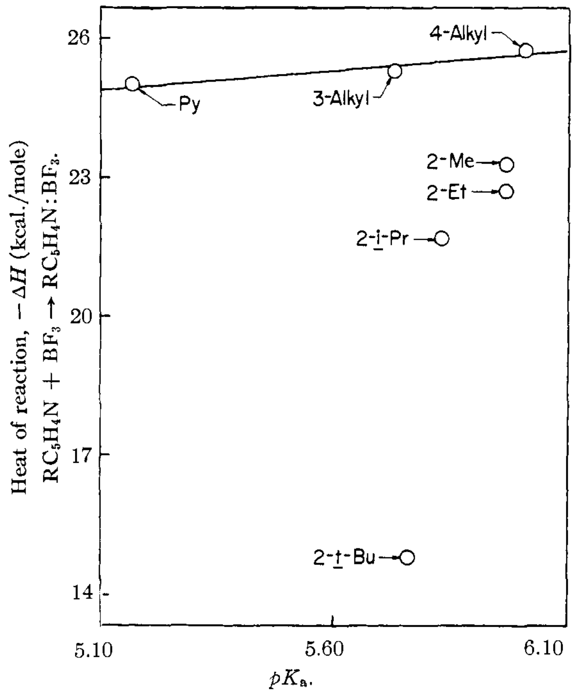


Fig. 1.—Relationship between the heats of reaction of the monoalkylpyridine bases with boron trifluoride and their pK_a values.

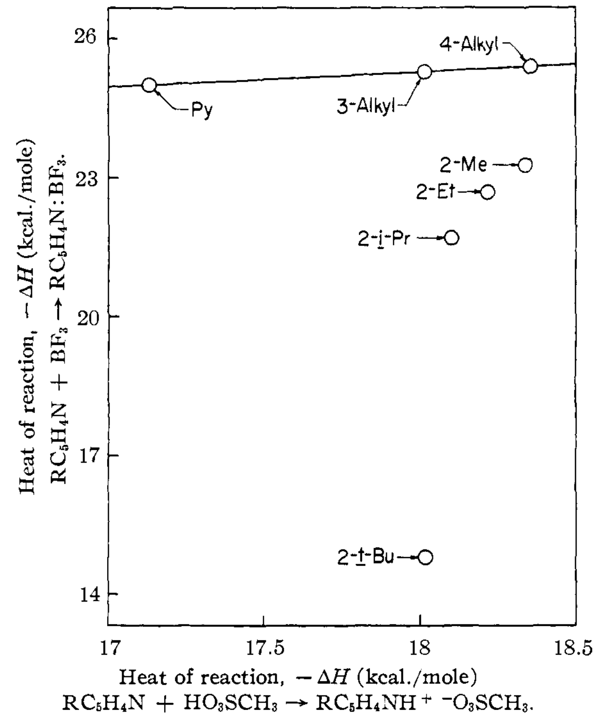


Fig. 2.—Relationship between the heats of reaction of the monopyridine bases with boron trifluoride and with methanesulfonic acid.

The non-linear character of the plots in Figs. 1 and 2 as well as of similar plots involving rate data for the reaction of methyl iodide with these bases[4,5] is attributed to the great difference in the steric requirements of the reactions undergoing comparison.

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(7) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapt. VII.

(8) This conclusion also has been reached by R. Taft, who has proposed an interesting theoretical approach to the problem in a number of publications in THIS JOURNAL. See R. Taft, THIS JOURNAL, **74**, 2729, 3120 (1952); **75**, 4231, 4534, 4538 (1953).

This interpretation might be clarified by an examination of Fig. 3. In the reaction of 2-alkylpyridines with methyl iodide, there are observed decreases in rate and increases in the activation energy with increasing bulk of the 2-alkyl substituent[3] (Table IV). These changes are attributed to steric strains in the activated complexes, arising from the conflicting steric requirements of the 2-alkyl substituents with the methyl group of the methyl iodide.

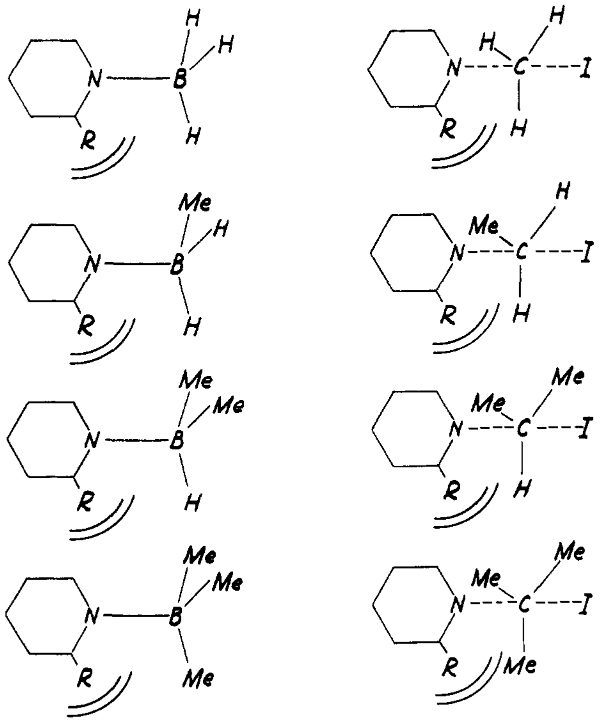

Fig. 3.—Steric relationship between the activated complex and the borine addition compounds.

In reactions involving the transfer of the proton,[4,5] such strains are either quite small or completely absent. Consequently two such reactions with markedly different steric requirements would not be expected to give a simple linear relationship. Instead deviations should be observed, the magnitude of which should correspond to the strains present in the particular reaction under consideration for the compound in question.

This interpretation suggests that it should be possible to realize a linear plot for the rate data of the reaction of methyl iodide with the monoalkylpyridines. Such a linear plot should be obtained by utilizing for the reference reaction one which involves steric strains of the same order of magnitude.

From the atomic dimensions it appears that the steric requirements of a borine group should be quite similar to those of a methyl group. Consequently it appears reasonable that the strains present in the borine addition compounds should be related to the strains present in the activated complex of the pyridine–methyl iodide reaction (Fig. 3). Similarly the strains present in the ethyl and isopropyl iodide reactions should be mirrored in the corresponding pyridine–methylborine and pyridine–dimethylborine addition compounds, respectively (Fig. 3).

It is true that in the addition compound the N–B–H bonds will be approximately tetrahedral in direction, whereas in the activated complex the angle of the corresponding N–C–H bonds will presumably be 90°. This difference in the angles would tend to increase the steric interactions in the activated complexes over those present in the corresponding addition compounds. On the other hand, the half-formed N–C bond in the activated complex would be expected to be longer than the corresponding B–N bond in the addition compound. This difference in length would tend to lessen the strains in the activated complex. In view of these opposing factors, it is not unreasonable to expect that the strains present in the borine addition compounds should be simply related to those present in the transition state of the displacement reaction.

If this argument is valid, a Hammett plot of the rate data *versus* equilibrium data for the pyridine-borine addition compounds should result in a linear relationship which would include even pyridine bases containing bulky alkyl substituents in the 2-position. Unfortunately, the chemical and physical characteristics of diborane are such as to make it particularly difficult to obtain the necessary data on the stability of the alkylpyridine–borine addition compounds.[9]

The steric requirements of boron trifluoride are considerably greater than those of either borine or methyl. Consequently strains involving this group should be considerably larger. This appears to be the case (Table IV). Nevertheless, in the absence of data for borine itself, it is of interest to examine the possible existence of a linear relationship between the heats of formation of the addition compounds of boron trifluoride and the rate data for the methyl iodide reactions.

It is gratifying to observe that in spite of the considerable differences in the steric requirements of the BH_3 and BF_3 groups, the data yield plots of reasonable linearity (Figs. 4 and 5). It is important to observe that only two of the various plots permitted by the data are linear. The two ($-\Delta H$ CH_3SO_3H *vs.* pK_a^5, and $-\Delta H$ BF_3 *vs.* E_{act} CH_3I) involve pairs of reactions of roughly the same steric requirements.

These results establish a linear strain energy relationship between the methyl iodide and the boron trifluoride reaction series, namely

$$(\Delta E_s \pm)_{MeI} = 0.33(\Delta E_s)_{BF_3}$$

where ΔE_s is the strain energy accompanying reaction.[10] Similar linear strain energy relations recently have been reported and discussed by Taft.[8]

It is now generally recognized that *ortho* substituents may affect chemical reactivity through a variety of interactions which are not important in the corresponding *meta* and *para* derivatives.

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(9) We recently have developed a calorimetric technique which makes possible the measurement of the heats of reaction of trimethylboron and diborane with the alkylpyridines. The results are in excellent agreement with the conclusions reached in the present paper Unpublished work with D. Gintis and L. Domash.

(10) H. C. Brown and R. M. Horowitz, Abstracts of Papers, Division of Organic Chemistry, American Chemical Society Meeting at Boston, Mass., April 2, 1951.

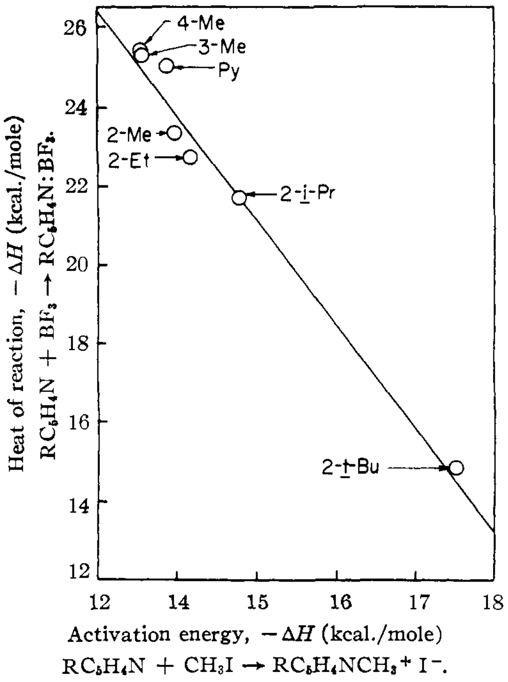

Fig. 4.—Relationship between the heats of reaction of the monoalkylpyridine bases with boron trifluoride and the activation energies for their reactions with methyl iodide.

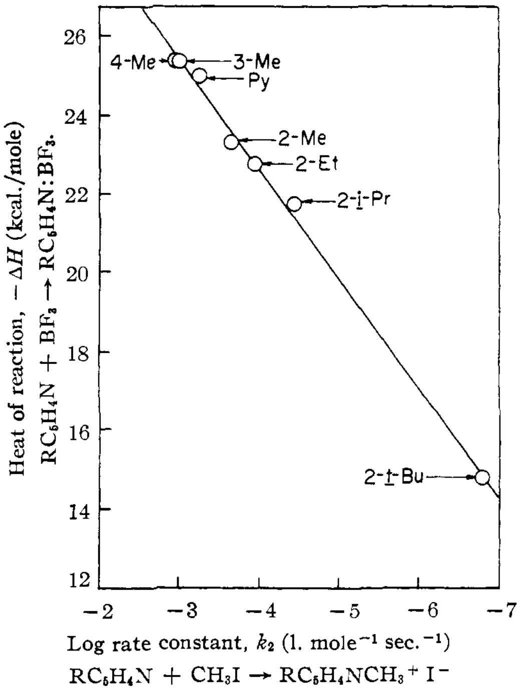

Fig. 5.—Relationship between the heats of reaction of the monoalkylpyridine bases with boron trifluoride and the logarithm of their rate constants for their reactions with methyl iodide.

Among these interactions may be mentioned the bulk steric effect (steric strain) discussed in the present paper, steric inhibition of resonance, hydrogen bonding, and field polar effects.[11] Consequently, no simple single modification of the Hammett relationship should be expected to permit the extension to all *ortho* substituted aromatics.

In cases where the sole important complicating factor is due to steric strain, the situation appears relatively simple. The present results support the conclusion that in such cases *ortho* substituted aromatic derivatives can be included in linear Hammett-type plots by utilizing reference reactions of similar steric requirements. This thesis will be developed in subsequent publications.

Experimental Part

Measurements of the heats of reaction of the pyridine bases were carried out using the mercury-well calorimeter described in the previous paper.[6] Typical data are reported in Table I. The pyridine bases used were samples which had been prepared previously and purified by Murphey[12] and Cahn.[3] Tetrahydropyran-boron trifluoride was prepared and purified as previously described.[6]

LAFAYETTE, INDIANA

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(11) A detailed discussion of these effects in the ionization of *ortho* substituted acids and bases is contained in a forthcoming publication by D. H. McDaniel and H. C. Brown.

(12) H. C. Brown and W. A. Murphey, THIS JOURNAL, **73**, 3308 (1951).