Secondary Isotope Effects in the Reactions of Methyl-d_3-pyridines with Boron Trifluoride. Consideration of the Secondary Isotope Effect as a Steric Phenomenon[1,2]

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Abstract: The introduction of methyl-d_3 groups in the 3 or 4 position of pyridine results in no observable change in the heats of reaction of these bases with boron trifluoride over the normal derivatives. On the other hand, in the 2 position, there is observed a significant increase in the heat of reaction for the deuterium derivatives, corresponding to the smaller steric requirements of methyl-d_3 over methyl-d_0 groups. Use of a reference acid of smaller steric requirements, BH_3, causes the difference to disappear, consistent with the predictions of the steric interpretation, but contrary to the predictions of either of the two electronic interpretations, inductive or hyperconjugative, now under consideration. These results support the conclusion that the secondary isotope effects of deuterium arise predominantly from its smaller steric requirements.

Deuterium labeling of the methyl groups in 3- and 4-picoline has no observable effect on the rates of reaction of the bases with methyl iodide.[8] On the other hand, such labeling of the methyl groups in the 2 position in 2-picoline and 2,6-lutidine results in enhanced rates of reaction with methyl, ethyl, and isopropyl iodide.[8] The results appear to be in better agreement with the proposed steric interpretation of secondary isotope effects[9,10] than with the competing hyperconjugative[11] and inductive[12] interpretations. In order to test further the applicability of the steric interpretation, we undertook an investigation of the secondary deuterium isotope effects in the reactions of these labeled bases with Lewis acids. This technique had previously proven exceedingly valuable in providing a quantitative basis to the study of steric effects.[13]

Results

Values for the heats of reaction of 4-methyl-d_3-, 3-methyl-d_3-, 2-methyl-d_3-, and 2,6-dimethyl-d_6-pyridine and the corresponding normal bases with gaseous boron trifluoride were determined in nitrobenzene solution according to the procedure previously described,[14] but using an improved gas–liquid calorim-

eter.[15] It has previously been shown that the use of a Lewis acid of much smaller steric requirements, such as diborane, diminishes the steric effect while allowing the polar influences to come through unchanged.[16] Accordingly, the isotope effect in the reaction of 2,6-dimethyl-d_6-pyridine with diborane was also determined.

We were looking for small differences in the heats of reaction. Moreover, calorimetric techniques are notoriously imprecise. Consequently, we carried out six to fifteen individual determinations for each pyridine base under rigorously standardized conditions. These numerous individual determinations were averaged to obtain the isotope effect.

The individual results are reported in the Experimental Section. In Table I are summarized the final averaged values for the heats of reaction of the methylpyridines with boron trifluoride and diborane, together with the values for the isotope effects.[17] Previous values for the heats of reaction of the normal compounds are included for comparison. However, the values for the isotope effects are based entirely upon the present measurements using the same calorimeter, materials, and procedure for each of the determinations with a related pair of labeled and normal bases.

Discussion

It is apparent from the data that a 4-methyl-d_3 substituent exerts no significant effect ($\Delta H_H - \Delta H_D = -0.04$ kcal/mole) upon the heat of reaction of 4-picoline with boron trifluoride. In the case of the 3-methyl-d_3 substituent, the observed difference is larger ($\Delta H_H - \Delta H_D = -0.10$ kcal/mole), but still within the experimental uncertainty. Supporting the conclusion that this difference is not significant, only the inductive effect of the substituent should be operative

(1) Chemical Effects of Steric Strains. XX.

(2) Based in part on theses submitted by John G. Koelling and Gerald J. McDonald in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Purdue University, 1962 and 1964, respectively.

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(7) Dow Chemical Co. Fellow, 1961–1962.

(8) H. C. Brown and G. J. McDonald, J. Am. Chem. Soc., 88, 2514 (1966).

(9) L. S. Bartell, Tetrahedron Letters, No. 6, 13 (1960); J. Am. Chem. Soc., 83, 3567 (1961).

(10) (a) K. Mislow, R. Graeve, A. J. Gordon, and G. H. Wahl, Jr., ibid., 85, 1199 (1963); (b) ibid., 86, 1733 (1964); (c) A. Horeau, A. Nouaille, and K. Mislow, ibid., 87, 4957 (1965); (d) L. Melander and R. E. Carter, ibid., 86, 295 (1964).

(11) V. J. Shiner, Jr., Tetrahedron, 5, 243 (1959); V. J. Shiner, Jr., and J. S. Humphrey, Jr., J. Am. Chem. Soc., 85, 2416 (1963).

(12) E. A. Halevi, Tetrahedron, 1, 174 (1957); E. A. Halevi, M. Nussim, and A. Ron, J. Chem. Soc., 866 (1963).

(13) For a review, with pertinent literature references, see H. C. Brown, ibid., 1248 (1956).

(14) H. C. Brown and D. Gintis, J. Am. Chem. Soc., 78, 5378 (1956).

(15) For details of the construction and operation of the calorimeter, consult the doctoral dissertations of J. Olcott and S. Bank, Purdue University, 1957 and 1960, respectively.

(16) H. C. Brown, D. Gintis, and L. Domash, J. Am. Chem. Soc., 78, 5387 (1956).

(17) As in the preceding paper[8] one of the referees recommended that a statistical analysis of the results be made. This analysis is reported in the Experimental Section. It confirms the conclusions reached on the basis of the simple arithmetical averages reported in Table I.

Table I. Isotope Effects in the Heats of Reaction of the Methyl-d_3-pyridines with Boron Trifluoride and Diborane[a]

| Pyridine	Ref acid	Previous value	Present value	Av dev[d]	$\Delta H_H - \Delta H_D$
		—Heat of reaction, $-\Delta H$— (kcal/mole)			
4-Methyl	BF$_3$	33.8[b]	33.61 ± 0.26 (11)		
4-Methyl-d_3	BF$_3$		33.57 ± 0.24 (12)		−0.04
3-Methyl	BF$_3$	33.6[b]	33.52 ± 0.11 (9)		
3-Methyl-d_3	BF$_3$		33.42 ± 0.23 (11)		−0.10
2-Methyl	BF$_3$	31.6[b]	31.12 ± 0.10 (15)		
2-Methyl-d_3	BF$_3$		31.28 ± 0.17 (14)		0.16
2,6-Dimethyl	BF$_3$	25.8[b]	25.61 ± 0.06 (7)		
2,6-Dimethyl-d_6	BF$_3$		25.84 ± 0.09 (7)		0.23
2,6-Dimethyl	$\frac{1}{2}$(BH$_3$)$_2$	16.3[c]	16.42 ± 0.08 (9)		
2,6-Dimethyl-d_6	$\frac{1}{2}$(BH$_3$)$_2$		16.40 ± 0.10 (6)		−0.02

[a] Nitrobenzene solution at 25° for the reactions: Py(soln) + BF$_3$(g) = Py:BF$_3$(soln) and Py(soln) + $\frac{1}{2}$ B$_2$H$_6$(g) = Py:BH$_3$-(soln). [b] See ref 16. The values are all corrected by 0.4 kcal/mole on the basis of more recent determinations of the heat of reaction of gaseous boron trifluoride with pyridine (ref 15). [c] See ref 16. [d] The figures in the parentheses give the number of individual measurements which were averaged.

from the 3 position and the observed change is in the wrong direction for such an effect.

In the 2 position the trideuteriomethyl substituent results in an enhanced heat of reaction of 0.16 kcal/mole. Again this is near the limit of our experimental uncertainty, and no conclusion can safely be drawn. (However, the statistical analysis[17] indicates a 96% confidence level that the observed difference is significant.)

On the other hand, the reaction of 2,6-dimethyl-d_6-pyridine with boron trifluoride is more exothermic than that of the normal base by 0.23 kcal/mole. This appears to be significantly larger than the combined average deviation in the two measurements. Moreover, the statistical analysis reported in the Experimental Section indicates a 99% confidence level that the observed difference is significant.

$-\Delta H = 25.61 \pm 0.06$

$-\Delta H = 25.84 \pm 0.09$
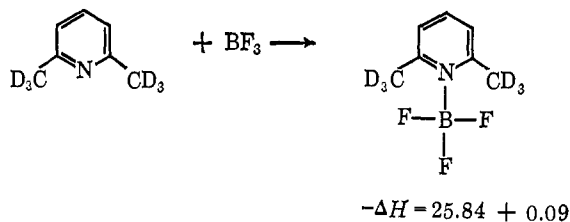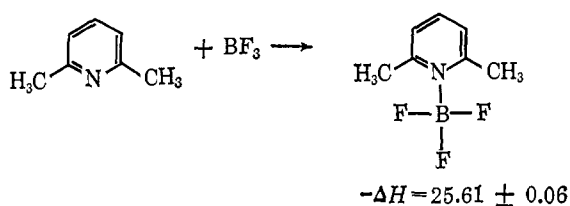
Finally, no isotope effect was observed in the heat of reaction of diborane with 2,6-dimethyl-d_6-pyridine.

It may appear surprising at first sight that the secondary isotope effect should not merely decrease, but apparently vanish with the smaller reference acid diborane. However, the estimated steric strain for the reaction of diborane with 2,6-lutidine is approximately

$-\Delta H = 16.42 \pm 0.08$

$-\Delta H = 16.40 \pm 0.10$
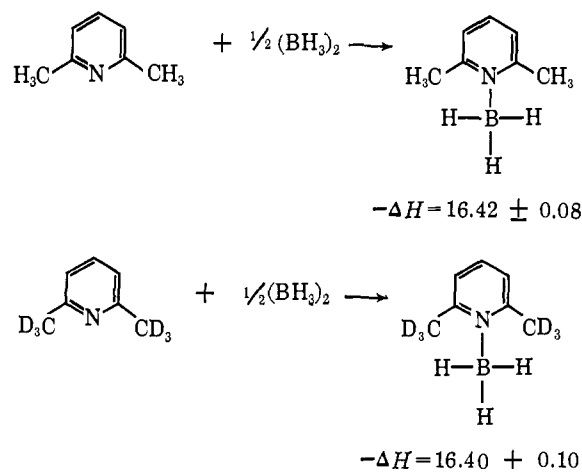
one-fourth of the corresponding strain for boron trifluoride.[16] A decrease of this magnitude would reduce the secondary isotope effect from 0.23 kcal/mole, observed with boron trifluoride, down to 0.06 kcal/mole, within the range of the experimental variation.

These results parallel closely those found in the rates of reaction of the methyl-d_3-pyridines with alkyl iodides.[8] The precision realized in the latter measurements was far higher than that achieved in the present calorimetric determinations. However, in both studies appreciable secondary isotope effects were observed only in the reactions of methylpyridines having methyl-d_3 substituents in the α positions. Although the observed effects are small, the similarity in the results of the two studies lends confidence that the observed changes are indeed due to true secondary isotope effects.

The liberation of more energy in the formation of boron trifluoride addition compounds of methylpyridines in which the α-methyl groups are labeled with deuterium suggests that such deuteration must stabilize the products. On the other hand, deuteration of the methyl groups more remote from the reaction center has no effect.

Since it was previously demonstrated that the stabilities of the addition compounds of alkylpyridines with Lewis acids vary markedly, and in a predictable manner, with the steric requirements of alkyl groups in the α position of the pyridine ring,[13,16] it is reasonable to examine whether the results are likewise consistent with the operation of a steric effect.[9,10] Indeed, in terms of this interpretation, the smaller steric requirements of a methyl-d_3 group as compared to a normal methyl group[18] would result in diminished steric interactions with the boron trifluoride group, giving rise to greater stability of the adduct. The absence of any observable effect from the presence of methyl-d_3 groups in the 3 and 4 positions is likewise consistent with the steric interpretation.

The results clearly rule out any significant hyperconjugative contributions[11] in the present case.[19] In the addition compounds there must be considerable positive charge on the nitrogen atom. Hyperconjuga-

(18) At the triple point deuterium and methane-d_4 have smaller molar volumes than hydrogen and normal methane: K. Clusius and K. Weigand, *Z. Physik. Chem.*, **B46**, 1 (1940).

(19) However, it should be clear that the present system can involve only relatively small hyperconjugative contributions. Consequently, it is not a good system for testing the importance of such hyperconjugation contributions to the secondary isotope effect.
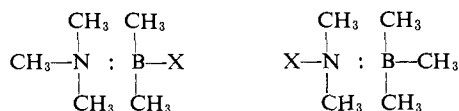
tion with the methyl substituents should provide electron density to stabilize the charge. Thus, in terms of this explanation, a methyl group in the 4 position should be just as effective as a methyl group in the 2 position, and both should stabilize the normal addition compound over the deuterium analogs. Clearly this is contrary to the experimental results.

The proposal of a differential inductive effect of hydrogen and deuterium[12] also predicts an enhanced stability of the boron trifluoride adducts of methyl-d_3-pyridines as a consequence of the proposal of a greater electron-donating ability of deuterium relative to hydrogen. However, an inductive effect would be expected to operate from the 3 and 4 positions nearly as effectively as from the 2 position. For example, a methyl substituent in the 2, 3, or 4 position of the pyridine ring results in a large, quite similar enhancement of the strength of the base.[20] Consequently, the failure to observe any effect of the methyl-d_3 group in the 3 or 4 position, either in the rate of reaction with methyl iodide[8] or in the heat of reaction with boron trifluoride, argues against a significant inductive contribution in the present system.

An even more striking result is the absence of any observable isotope effect in the heat of reaction of 2,6-dimethyl-d_6-pyridine with diborane. It was previously shown that diborane and boron trifluoride are equally sensitive to the polar influence of alkyl substituents in the 3 and 4 positions of the pyridine nucleus.[13,16] However, the much smaller steric requirements of BH_3, as compared to BF_3, result in far smaller steric strains in the reactions with α-substituted pyridine bases.[16] Thus the observation that the isotope effect of 0.23 kcal/mole in the reaction of 2,6-dimethyl-d_6-pyridine with boron trifluoride vanishes in the corresponding reaction with diborane is consistent with the proposed steric isotope effect, but is inexplicable in terms of the inductive isotope effect. This result also parallels the increase in the isotope effects in the reactions of 2-methyl-d_3-pyridine with alkyl iodides of increasing steric requirements.[8]

Thus, in all major respects the isotope effects in the rates of reaction of the methyl-d_3-pyridines with alkyl iodides parallel the effects in their heats of reaction with Lewis acids. The observation that significant isotope effects occur only with those labeled bases having methyl-d_3 groups located in a position where a steric effect can operate, together with the sensitivity of the isotope effect to the steric requirements of the reagent, strongly supports the conclusion that the fundamental origin of the secondary isotope effect in these reactions must reside in the decreased steric requirements of the methyl-d_3 substituents.

Application of a Test for Steric vs. Polar Basis. An important test of steric vs. polar contributions is provided by the relative effect of a substituent on the acidic and basic portion of a molecular addition compound.[13] For example, the introduction of electro-

negative substituents, such as halogen (–I), into the boron component results in a stronger acid and an enhanced stability (in the absence of large steric effects). In the amine component, such electronegative substituents reduce the base strength and decrease the stability of the addition compound. Thus, a polar effect manifests itself through opposing influences accompanying its presence in the acid or basic component. On the other hand, if X is a group with a low polar effect but large steric requirements (such as t-butyl), there would be observed a decrease in stability accompanying the introduction of X both in the amine or the boron component.
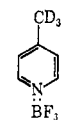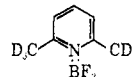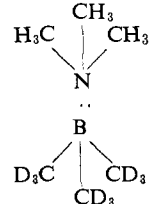
Fortunately, it is now possible to apply this test to resolving the present problem of secondary isotope effects. In the present study we have examined the effect of deuterium substitution in the amine component of the molecular addition compound. The effect of deuterium substitution on the boron component was previously examined.[21] It was observed that trimethylboron-d_0 forms a more stable addition compound with trimethylamine than does normal trimethylboron. In other words, the following equilibrium tends to the right, with an equilibrium constant of 1.25.

$$(CD_3)_3B + (CH_3)_3B:N(CH_3)_3 \rightleftharpoons (CH_3)_3B + (CD_3)_3:N(CH_3)_3$$
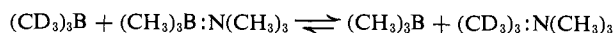
Thus, in the present study deuterium substitution in the basic component brings about an increase in the stability of the addition compound. Likewise, substitution of deuterium in the acidic component results in an increase in the stability of the molecular addition compound. Clearly this is contrary to the predicted operation of a polar influence and in accordance with the predicted effect of a steric influence.

The summary in Table II clearly establishes the superiority of the steric interpretation.

Table II. Predicted and Observed Secondary Isotope Effects in Molecular Addition Compounds

Compd	Inductive theory	Hyperconjugative theory	Steric theory	Obsd effect
	Predicted isotope effects[a]		
CD₃-pyridine·BF₃	Inverse	Normal	None	None
D₃C-pyridine-CD₃·BF₃	Inverse	Normal	Inverse	Inverse
(CH₃)₂ amine / D₃C-B(CD₃)CD₃	Normal	Inverse	Inverse	Inverse

[a] Predicted for formation of addition compound from its components.

CH₃ CH₃
| |
CH₃—N : B—X
| |
CH₃ CH₃

CH₃ CH₃
| |
X—N : B—CH₃
| |
CH₃ CH₃

(20) H. C. Brown and X. R. Mihm, *J. Am. Chem. Soc.*, **77**, 1723 (1955). The pK_a values are: pyridine, 5.17; 4-methyl-, 6.02; 3-methyl-, 5.68; 2-methylpyridine, 5.97.

(21) P. Love, R. W. Taft, Jr., and T. Wartik, *Tetrahedron*, **5**, 116 (1959).

Consideration of the Secondary Isotope Effect[22] as a Steric Phenomenon. The original observations that deuterium substitution in the β position of a compound undergoing solvolysis to a carbonium ion resulted in a rate retardation led to the proposal of an important hyperconjugative contribution.[23] On the other hand, the rate retardation resulting from α-deuterium substitution cannot be accounted for in this manner,[24] but can be rationalized in terms of steric[9] influences.

At the present time secondary isotope effects are commonly discussed and analyzed in terms of these three classical effects: hyperconjugative, inductive, and steric.[22] It is unfortunate that no really satisfactory quantitative treatment for any of these effects is yet available. Qualitative predictions based on any one of these effects frequently lead to conflicting answers. Consequently, it is always possible to account for an observed result, but it is not possible to make predictions with any confidence. Nevertheless, wide use has been made of secondary isotope effects in exploring reaction mechanisms. One must admire the courage of those who have relied upon such evidence.

In the course of our review of the literature on secondary isotope effects, we were impressed by the fact that with very few exceptions secondary isotope effects are exceedingly small unless the deuterium is in the neighborhood of the reaction center. This is suggestive of a steric effect, but does not require it. Inductive effects may be very small and fall off rapidly with distance. Much more persuasive was the frequency with which we could predict the observed direction of the secondary isotope effect in terms of steric considerations alone. Considered merely as a mnemonic device, it can be very helpful to be able to predict, with such a high degree of reliability, the direction of the secondary isotope effect. In view of our well-known predilection for simple hypotheses,[25] it appeared desirable to give serious consideration to the possibility that steric effects play a dominant role in the secondary isotope phenomenon.

For example, simple steric considerations provide a consistent rationalization for the normal isotope effects in the solvolysis of α-deuterio tosylates,[26] the normal isotope effects in the solvolysis of β-deuterio chlorides[27] and tosylates,[26] the inverse isotope effects in the hydrolysis of methyl-d_3 iodide[28] and propyl-γ-d_3 iodide,[29] the normal isotope effects in the hydrolysis of α-deuterio ketals,[30] the normal isotope effect in the hydrolysis of acetyl chloride-d_3[31] and the inverse isotope effect in the hydrolysis of ethyl acetate-d_3,[31] the normal isotope effects in the dissociation of α-deuterio hemi-

ketals,[32] the inverse isotope effects in the addition of bromine[33] and methyl radicals[34] to α-deuterio olefins, the inverse isotope effect in the Diels–Alder reaction of cyclopentadiene with maleic anhydride-d_2[35] and the normal isotope effects in the decomposition of the Diels–Alder adducts of 2-methylfuran with maleic anhydride-d_2 and of 2-methylfuran-5-d with maleic anhydride,[36a] the inverse isotope effect in the isomerization of maleic acid-2,3-d_2,[36b] the inverse isotope effect in the reaction of trimethyl-d_9-boron with trimethylamine,[21] the inverse isotope effect in the quaternization of triethyl-α-d_2-amine,[37] the normal isotope effect in the thermal decomposition of azobis-α-phenylethane-α,α'-d_2,[36c] the identical normal isotope effects in the mutarotation of D-glucose-1-d and fully deuterated D-glucose,[38] the inverse isotope effect in the reaction of pyridine bases with methyl-d_3 iodide,[39] the inverse isotope effect in the complexing of deuterated olefins with silver ion,[40] and many others.

It has been suggested that the isotope effect observed in the rates of racemization of 9,10-dihydro-4,5-dimethylphenanthrene, undoubtedly of steric origin, may not be compatible with a steric explanation for the much larger rate effects accompanying α- and β-deuterium substitution in solvolyzing systems.[10b] However, it should be apparent that our quantitative approaches to the magnitudes of these interactions[9] leave much to be desired. We do not have any good estimate of the strains in the initial states or the extent to which such strains may be relieved in the transition states for SN1 reactions. In the absence of a truly quantitative theory, we find the remarkable consistency exhibited by the qualitative trends to be more persuasive.

Opposed to this large number of observations which can be simply correlated in terms of the relative steric requirements of hydrogen and deuterium, we know of only two cases where the results appear to be inexplicable in terms of the steric explanation. It has been reported that p-methyl-d_3-benzhydryl chloride undergoes solvolysis at a rate that is 2 to 6% slower than the corresponding hydrogen compound.[41a] More recently it has been reported that the solvolysis of dimethylpropynyl-d_3-carbinyl chloride proceeds at a rate only 0.92 that of the hydrogen analog.[41b] The steric interpretation would predict no significant difference in these two isotopic systems. As was pointed out, the wide variation in the reported isotope effect (k_H/k_D = 1.02 to 1.06) with solvent for p-methyl-d_3-benzhydryl chloride is inexplicable in view of the similarity in ordinary substituent effects observed in these solvents. In the second case, there is a possibility that the

(22) For an excellent review and discussion of secondary isotope effects, see E. A. Halevi, *Progr. Phys. Org. Chem.*, **1**, 109 (1963).
(23) (a) E. S. Lewis and C. E. Boozer, *J. Am. Chem. Soc.*, **74**, 6306 (1952); (b) V. J. Shiner, Jr., *ibid.*, **75**, 2925 (1953).
(24) A. Streitwieser, Jr., and R. C. Fahey, *Chem. Ind.* (London), 1417 (1957).
(25) P. E. Peterson, C. Casey, E. V. P. Tao, A. Agtarap, and G. Thompson, *J. Am. Chem. Soc.*, **87**, 5163 (1965).
(26) A. Streitwieser, Jr., R. H. Jagow, R. C. Fahey, and S. Suzuki, *ibid.*, **80**, 2326 (1958).
(27) V. J. Shiner, Jr., J. W. Wilson, G. Heinemann, and N. Solliday, *ibid.*, **84**, 2408 (1962).
(28) J. A. Llewellyn, R. E. Robertson, and J. M. W. Scott, *Can. J. Chem.*, **38**, 222 (1960).
(29) K. T. Leffek, J. A. Llewellyn, and R. E. Robertson, *J. Am. Chem. Soc.*, **82**, 6315 (1960).
(30) V. J. Shiner, Jr., and S. Cross, *ibid.*, **79**, 3599 (1957).
(31) M. L. Bender and M. S. Feng, *ibid.*, **82**, 6318 (1960).

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(34) M. Matsuoka and M. Szwarc, *J. Am. Chem. Soc.*, **83**, 1260 (1961).
(35) D. E. Van Sickle, *Tetrahedron Letters*, No. 19, 687 (1961).
(36) (a) S. Seltzer, *ibid.*, No. 11, 457 (1962); (b) *J. Am. Chem. Soc.*, **83**, 1861 (1961); (c) *ibid.*, **83**, 2625 (1961).
(37) E. S. Lewis, *Tetrahedron*, **5**, 143 (1959).
(38) N. C. Li, A. Kaganove, H. L. Crespi, and J. J. Katz, *J. Am. Chem. Soc.*, **83**, 3040 (1961).
(39) K. T. Leffek and J. W. MacLean, *Can. J. Chem.*, **43**, 40 (1965).
(40) R. J. Cvetanović, F. J. Duncan, W. E. Falconer, and R. S. Irwin, *J. Am. Chem. Soc.*, **87**, 1827 (1965).
(41) (a) V. J. Shiner, Jr., and C. J. Verbanic, *ibid.*, **79**, 373 (1957). The significance of this observation has been questioned because of its smallness and apparent large solvent dependency: M. J. S. Dewar, "Hyperconjugation," The Ronald Press, New York, N. Y., 1962, p 141. (b) V. J. Shiner, Jr., and G. S. Kriz, Jr., *J. Am. Chem. Soc.*, **86**, 2643 (1964).

solvolysis of this derivative involves a concerted attack of solvent on the δ-methyl during ionization. Consequently, it is exceedingly important that these two isotope effects be confirmed and these doubts put to rest. We plan to undertake such a study.

Secondary deuterium isotope effects have been applied in numerous studies of reaction mechanism. Invariably the electronic interpretations of the effects of deuterium labeling were applied in analyzing the results of these studies. They have included investigations of the enolization of ketones,[42] the hydrolysis of carboxylic acid derivatives,[31] the Diels–Alder reaction,[36a] the benzoylation of aniline,[43] the thermal decomposition of azobis-α-phenylethane,[36c] neighboring hydrogen,[44] carbon[45] and phenyl[46] participation in solvolysis reactions, the addition of methyl radicals to olefins,[34] the isomerization of maleic acid,[36b] the pyrolysis of cyclopropane[47] and cyclobutane,[48] the deoxymercuration reaction,[49] and the air oxidation of cumene.[50]

The successful correlation of so many secondary isotope effects in terms of the relative steric requirements of hydrogen and deuterium suggests that a reevaluation of the data and the conclusions of these investigations may lead to new and fruitful interpretations.

In conclusion, it is important to recognize that this suggestion that the dominant factor in the secondary isotope effect may be steric in origin can only be considered to be a speculation at present. However, the steric hypothesis does provide a simple, highly reasonable interpretation of the great majority of the available data. As we have pointed out, in the great majority of cases, with remarkably few exceptions, a simple consideration of the effect of the smaller steric requirements of deuterium and deuterium-substituted groups provides a direct, unambiguous prediction of the direction of the observed effect. Not only does it organize and systematize the enormous mass of available information, but, as has been demonstrated in the present and other recent studies, it is capable of making reliable predictions in totally new systems, not previously explored. Consequently, it deserves serious objective consideration in a reexamination of the physical basis for the secondary isotope effect.

Experimental Section

Materials. The pyridine bases and nitrobenzene are described in the accompanying paper.[8] The ordinary pyridine bases and the nitrobenzene were stored over calcium hydride, whereas the deuterated bases were stored over barium oxide. Boron trifluoride was introduced into the vacuum line and purified through the anisole addition compound.[14] Two samples exhibited vapor pressures of 302 and 303 mm at $-111.8°$. Diborane was prepared in the high-vacuum line by dropwise addition of a solution of sodium borohydride in diglyme to a solution of boron trifluoride in diglyme. The diborane which was generated was fractionated twice through a $-111.8°$ carbon disulfide slush bath and a $-129.6°$ n-pentane slush

(42) W. D. Emmons and M. F. Hawthorne, *J. Am. Chem. Soc.*, **78**, 5593 (1956).

(43) J. J. Elliott and S. F. Mason, *Chem. Ind.* (London), 488 (1959).

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Table III. Statistical Analysis of the Significance of the Values of $\Delta H_B - \Delta H_D$ for the Reactions of Related Pairs of Pyridine Bases with Boron Trifluoride and Diborane

Pyridine bases compared	Evaluated t	Confidence level, %	Conclusion: Means
4-Methyl- and 4-methyl-d_3[a]	0.233	53	Not significantly different
3-Methyl- and 3-methyl-d_3[a]	0.711	75	Not significantly different
2-Methyl- and 2-methyl-d_3	1.95	96	Significantly different
2,6-Dimethyl- and 2,6-dimethyl-d_6[a]	4.33	99	Significantly different
2,6-Dimethyl- and 2,6-dimethyl-d_6[b]	0.29	60	Not significantly different

[a] Reference acid, boron trifluoride.   [b] Reference acid, diborane.

bath. The purified diborane exhibited tensimetric homogeneity with a vapor pressure of 225 mm at $-111.8°$.

Calorimetric Procedure. A complete description of the manipulation of the calorimetric apparatus has been published.[14] However, because of the small effects that were under investigation, it was necessary to introduce a number of refinements. A 0.2 M solution of the pyridine base in nitrobenzene was dried over calcium hydride with magnetic stirring. The calcium hydride was allowed to settle, and a 17.52-ml aliquot of the clear solution was placed in the gas–liquid calorimeter[15] by means of a calibrated pipet. The calorimeter was attached to the vacuum line and immersed in a constant temperature bath maintained at 24.65°. Boron trifluoride, measured as a gas in a calibrated volume in the vacuum line, was introduced into the solution in the calorimeter through a one-way valve. Time–temperature data were automatically recorded on a Brown Millivolt recorder. This was achieved by attaching the leads from a thermistor immersed in the solution to a Sargent thermistor bridge, which in turn was connected to the recorder. The thermistor was calibrated for each series of runs with a thermometer certified by the National Bureau of Standards. The Regnault–Pfaundler method was applied for the evaluation of the final temperature from the time–temperature curve.[51] The value for the heat of reaction was given by the expression $\Delta H = C_p \Delta T / \Delta n$, where ΔT is the difference between the initial and final temperatures of the solution, Δn is the amount of boron trifluoride used, and C_p is the total heat capacity of the calorimeter and solution.

With diborane the procedure was similar to that described for the measurements with boron trifluoride. However, the reaction of diborane with the pyridine base in solution is not as fast as the reaction with boron trifluoride. Consequently, the reaction chamber of the calorimeter was evacuated in the runs with diborane to facilitate rapid reabsorption of any diborane which might be passed through the solution without undergoing reaction.

The following values were obtained for the reactions with boron trifluoride (values in parentheses were excluded in the calculation of the mean since they differed from the mean by more than twice the standard deviation): (4-methylpyridine) (32.43), 33.80, 34.11, 33.92, 33.61, 33.12, 33.91, 33.73, 33.10, 33.57, 33.57, 33.24; (4-methyl-d_3-pyridine) 34.14, 33.34, 32.99, 33.63, 33.55, 33.76, 33.43, 33.93, 33.46, 33.67, 33.75, 33.15; (3-methylpyridine) (32.95), 33.51, 33.25, 33.65, 33.71, 33.66, 33.53, 33.52, 33.54, 33.31; (3-methyl-d_3-pyridine) 32.69, 33.77, 33.62, 33.47, 33.32, 33.98, 33.42, 33.53, (32.75), 33.45, 33.32, 33.70; (2-methylpyridine) 30.91, 31.18, 31.07, 31.19, (30.61), 31.13, 31.08, 30.90, 31.24, 31.32, 31.01, 31.07, 31.27, 31.23, 31.09, 31.13; (2-methyl-d_3-pyridine) 31.15, (31.88), 31.44, 31.52, (30.80), 31.36, 31.15, 31.07, 31.39, 31.48, 31.45, 31.57, 31.05, 31.12, 31.09, 31.15; (2,6-dimethylpyridine) 25.62, 24.59, 25.68, 25.72, 25.59, 25.62, 25.56; (2,6-dimethyl-d_6-pyridine) 25.80, 25.75, 25.92, 25.94, 25.67, 25.86, 25.95.

The following values were obtained for the reactions with diborane: (2,6-dimethylpyridine) 16.42, 16.34, 16.24, 16.32, 16.53,

(51) W. P. White, "The Modern Calorimeter," The Chemical Catalog Co., Inc., New York, N. Y., 1928, p 40.

16.62, 16.43, 16.40, 16.45; (2,6-dimethyl-d_6-pyridine) 16.26, 16.33, 16.48, 16.32, 16.56. 16.45.

The mean values and the average deviations are summarized in Table I.

Statistical Analysis.[52] A statistical analysis of the data was carried out to establish whether the observed differences between ΔH_H and ΔH_D were significant. The procedures were similar to those used in the preceding paper.[8] The results are summarized in

Table III and support the conclusions previously reached based on a visual examination of the average values and average deviations reported in Table I.

Stability Constants of Magnesium Porphyrin–Pyridine Complexes. Solvent and Substituent Effects[1]

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Abstract: The stability constants for the reaction, magnesium porphyrin monopyridinate + pyridine $\rightleftharpoons$ magnesium porphyrin dipyridinate, have been determined for a series of variously substituted magnesium porphyrins. Comparison of the substituent effects observed in the case of the magnesium porphyrins to those obtained earlier for nickel porphyrins provided insight into the nature of the metal-to-porphyrin bonding. The effect of substitution in the 4 position in the pyridine ring was also examined. These results suggest that d–π bonding between transition metals in porphyrins and pyridine ligands is not very important.

There has been considerable controversy in the literature concerning the state of solvation of chlorophyll in the leaf and in solution. The differences of opinion have been based primarily on spectral observations. One group of investigators has held that the divergence of the spectrum in the leaf from that in solution can be best accounted for by its state of aggregation while the other group has preferred to consider the chlorophyll as occurring in the leaf in combination with a protein, as does heme in hemoglobin.

The question of chlorophyll aggregation in solution was investigated by Katz, Closs, Pennington, Thomas, and Strain.[3] They concluded that the chlorophyll molecules were aggregated in noncomplexing solvents by way of intermolecular complexing between the carbonyl groups on the periphery of the chlorophyll ring and the magnesium at the center of another molecule.

Wei, Corwin, and Arellano[4] observed that magnesium porphyrins readily form dipyridine complexes. Corwin and Wei[5] found that magnesium porphyrins and chlorins form monoaquo and monomethanol complexes, substantiating earlier observations of Fischer[6] who prepared methanolate complexes of magnesium

porphyrins, and of Byrne, Linstead, and Lowe[7] who studied the hydration of magnesium phthalocyanin.

Miller and Dorough[8] made a quantitative study of the magnesium tetraphenylporphin and chlorin stability constants in pyridine–benzene mixtures. They obtained their stability constants by analyzing changes in the visible spectrum of the magnesium tetraphenylporphin and chlorin as the pyridine concentration was changed. These observations have led us to examine the complexing of magnesium porphyrins with nitrogen bases.

Results and Discussion

Although the magnesium porphyrins readily form dipyridinate complexes, solution of the magnesium porphyrin in a variety of solvents, including pure pyridine, does not yield the spectrum of the pure dipyridinate. Instead a spectrum having two Soret peaks and a more subtly altered visible spectrum is obtained. Dilution of the ligand increases the intensity of the shorter wavelength Soret peak and decreases the intensity of the longer wavelength Soret peak. This behavior is characteristic of an equilibrium between two different states of ligancy in solution, analogous to that described by Baker, Brookhart, and Corwin[9] for Ni(II) and Cu(II) porphyrin–piperidine complexes. The spectra of magnesium deuteroporphyrin IX dimethyl ester in a complexing solvent (pyridine) and a noncomplexing solvent (2,6-lutidine) are shown in Figures 1 and 2.

The stereoelectronic effect of the ligand on the porphyrin π system proposed earlier by Corwin,

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