According to Miller,[10] the quantity $Q_{X,Nu}$ can be written as eq 23 where $\chi\sigma_{R,X}N_{Nu}$ is the so-called interaction term.

$$Q_{X,Nu} = \beta\sigma_{R,X} + aN_{Nu} + \chi\sigma_{R,X}N_{Nu} + h \qquad (23)$$

Setting eq 22 equal to eq 23 and dividing through by $\sigma_{R,X}$ gives eq 24 which predicts that the slopes of the

$$\beta_{Nu} = \chi N_{Nu} + \beta \qquad (24)$$

line obtained from correlation with eq 17 will be a linear function of the nucleophilicity parameter, $N$. The same type of equation can be derived from the solvent variation. Thus,

$$\beta_{Sv} = \chi S_{Sv} + \beta \qquad (25)$$

Unfortunately, the data available here do not permit a test of eq 24 and 25.

The results obtained would undoubtedly be much improved if a wider range of $\sigma_R$ values could be studied. The largest range of $\sigma_R$ studied in this work encompassed only 0.14 $\sigma$ units. It is unlikely that a greater range of $\sigma$ will be studied as no substituent with $\sigma_R$ >0.21 is known, and it is unlikely that a substituent with $\sigma_R$ <0.07 would react at a measurable rate.

It is interesting to note that, although $\sigma_R^-$ values might have been expected to be the substituent constants most applicable to reactions involving carbanions, correlations with eq 12 are generally inferior to correlations with eq 3 in which $\sigma_R$ constants were used. This is partly due to the fact that values of $\sigma_R^-$ were not available for all substituents, and therefore in several cases all the members of the set could not be correlated by eq 12. Nevertheless, eq 12 is not successful in correlating this data. Thus no attempt was made to correlate data with the equation

$$Q_X = \beta\sigma^-_{R,X} + h \qquad (26)$$

# Why Increasing Concentrations of Ethylenediamine Cause the Rate of Exchange of Isobutyraldehyde-*2-d* to Rise, Then Fall, and Then Rise Again[1a,b]

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First-order rate constants for the deuterium exchange of about 0.06 *M* isobutyraldehyde-*2-d* in aqueous solution around pH 8.5 increase with increasing concentrations of added ethylenediamine and reach a maximum at diamine concentrations around 0.03 *M*. They then decrease, pass through a minimum around diamine concentrations of 0.1 *M*, and finally increase again. This behavior is explained in terms of the transformation of most of the limiting reagent to 2-isopropylimidazolidine (or its conjugate acid), which then catalyzes the exchange of remaining aldehyde. Exchange by this pathway is fastest when half the aldehyde has been transformed to imidazolidine. At higher concentrations of diamine most of the exchange arises from attack of the various bases present on the small amounts of iminium ions, such as $Me_2CDCH{=}NHCH_2CH_2NH_2^+$, which are present in equilibrium with the imidazolidine. Quantitative treatment of the data gives reasonable agreement with the experimental rate constants. A few measurements using *N*-methylethylenediamine also show a rate maximum and minimum, but *N,N'*-dimethylethylenediamine, which gives a considerably less basic and more hindered imidazolidine, shows no extrema.

In searching for bifunctional catalysts for the dedeuteration of isobutyraldehyde-*2-d*,[1b,2,3] it was observed that the rate of dedeuteration of ~0.06 *M* isobutyraldehyde-*2-d* in the presence of ethylenediamine around pH 8.38 at first increased, then decreased, and then increased again as the concentration of diamine was increased from zero to about 0.5 *M*. We developed a hypothesis, which included the formation of 2-isopropylimidazolidine and its action as a basic catalyst, to explain these results. To test this hypothesis (and for other reasons), the equilibrium constant for the formation of 2-isopropylimidazolidine from isobutyraldehyde and ethylenediamine was measured and the basicity constant of the imidazolidine was determined.[4] The way in which these results and additional kinetic measurements support our hypothesis will be described in the present paper.

## Results

The kinetics of the dedeuteration of isobutyraldehyde-*2-d* in the presence of ethylenediamine at 35° were studied at various concentrations and various pH's. The reaction was followed in the manner described previously[5,6] by acidifying the reaction mixture to stop the reaction (and to hydrolyze any imines, imidazolidines, etc., to aldehyde), extracting the aldehyde, and making proton magnetic resonance measurements to determine the extent of deuteration of the aldehyde. Satisfactory first-order rate constants were obtained in the various runs and their values are collected in Table I. Rate constants for the runs at pH 8.37 ± 0.14 using 0.060 ± 0.007 *M* isobutyraldehyde-*2-d* are plotted as open circles against the concentration of ethylene-

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[1] (a) This investigation was supported in part by Public Health Service Grants AM 06829 and 10378 from the National Institute of Arthritis and Metabolic Diseases and GM 18593 from the National Institute of General Medical Sciences. Abstracted in part from the Ph.D. Dissertation of K. W. Narducy, The Ohio State University, 1971. Direct correspondence to The Ohio State University. Part XIV in the series "Catalysis of α-Hydrogen Exchange." (b) For part XIII see J. Hine, E. F. Glod, R. E. Notari, F. E. Rogers, and F. C. Schmalstieg, *J. Amer. Chem. Soc.*, **95**, 2537 (1973). (c) NIH Predoctoral Fellow (No. F01 GM 41963), 1968–1971.

[2] J. Hine, F. E. Rogers, and R. E. Notari, *J. Amer. Chem. Soc.*, **90**, 3279 (1968).

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[4] J. Hine and K. W. Narducy, *J. Amer. Chem. Soc.*, in press.

[5] J. Hine, J. G. Houston, J. H. Jensen, and J. Mulders, *ibid.*, **87**, 5050 (1965).

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TABLE I

RATE OF DEDEUTERATION OF ISOBUTYRALDEHYDE-2-*d* IN THE PRESENCE OF ETHYLENEDIAMINE IN WATER AT 35°

| $[\mathrm{Me_2CDCHO}]_0$,[a] *M* | [Diamine],[a] *M* | pH[b] | $10^6k$, sec$^{-1}$ |
|---|---|---|---|
| 0.044 | 0.285 | 8.33 | 2.0 |
| 0.052 | 0.293 | 8.32 | 2.2 |
| 0.053 | 0.0127 | 8.72[c] | 3.4 |
| 0.053 | 0.0252 | 8.76[c] | 5.1 |
| 0.053 | 0.050 | 8.49[c] | 2.0 |
| 0.053 | 0.050 | 8.67[c] | 3.5 |
| 0.053 | 0.073 | 8.59[c] | 2.2 |
| 0.053 | 0.098 | 8.51[c] | 1.20 |
| 0.053 | 0.100 | 8.67[c] | 1.96 |
| 0.053 | 0.149 | 8.76[c] | 2.3 |
| 0.053 | 0.195 | 8.50[c] | 2.0 |
| 0.053 | 0.250 | 8.70[c] | 2.7 |
| 0.067 | 0.239 | 8.24 | 1.73 |
| 0.067 | 0.335 | 8.31 | 2.6 |
| 0.067 | 0.382 | 8.33 | 3.2 |
| 0.067 | 0.430 | 8.35 | 3.4 |
| 0.067 | 0.478 | 8.36 | 4.2 |
| 0.071 | 0.312 | 8.29 | 2.4 |
| 0.088 | 0.238 | 8.19 | 2.1 |
| 0.088 | 0.329 | 8.27 | 2.6 |
| 0.107 | 0.284 | 8.19 | 2.2 |
| 0.107 | 0.427 | 8.29 | 3.5 |
| 0.216 | 0.796 | 9.63 | 7.2 |
| 0.216 | 0.977 | 9.84 | 7.2 |
| 0.216 | 1.16 | 9.99 | 7.2 |

[a] Total concentration.[7] [b] Calculated unless otherwise noted. [c] Observed.

diamine in Figure 1.[7] Rate constants for the runs at PH 8.68 ± 0.09 using 0.053 *M* isobutyraldehyde-2-*d* are plotted as solid circles in the same figure. In each case the rate is seen to pass through a maximum at a diamine concentration around 0.03 *M*, then a minimum around 0.1 *M*, and then to increase with increasing concentrations of diamine.

Less detailed studies were made of the catalytic activities of *N*-methylethylenediamine and *N*,*N*′-dimethylethylenediamine in the exchange of 0.053 *M* isobutyraldehyde-2*d*. Rate constants obtained with the *N*-methyl compound are listed in Table II and those for the *N*,*N*′-dimethyl compound in Table III. The plots in Figure 2 show that the *N*-methyl compound at pH 8.51 ± 0.04 gives a maximum and then a minimum, but that with the *N*,*N*′-dimethyl compound at pH 8.66 ± 0.07 it is not clear that there are any extrema.

TABLE II

RATE OF DEDEUTERATION OF 0.053 *M* ISOBUTYRALDEHYDE-2-*d* IN THE PRESENCE OF *N*-METHYLETHYLENEDIAMINE IN WATER AT 35°

| [Diamine],[a] *M* | pH[b] | $10^6k$, sec$^{-1}$ |
|---|---|---|
| 0.095 | 8.50 | 2.9 |
| 0.097 | 8.48 | 3.0 |
| 0.199 | 8.55 | 1.5 |
| 0.199 | 8.52 | 2.1 |
| 0.400 | 8.49 | 2.6 |
| 0.484 | 8.54 | 2.7 |

[a] Total concentration.[7] [b] Observed.

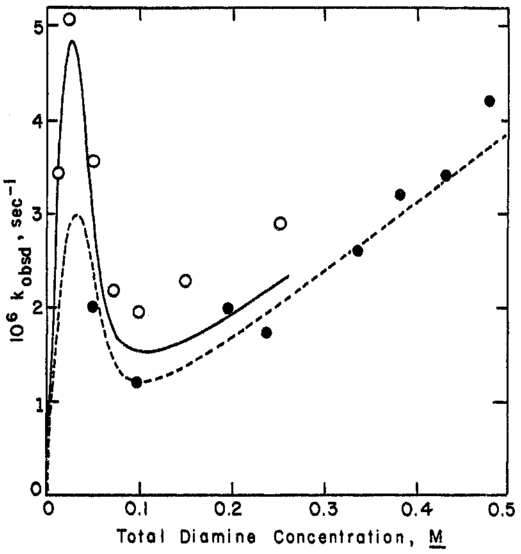

Figure 1.—Rate constants for the dedeuteration of isobutyraldehyde-2-*d* in water at 35° plotted against ethylenediamine concentration: ○, at pH 8.68 ± 0.09 and 0.053 *M* aldehyde; ●, at pH 8.37 ± 0.14 and 0.060 ± 0.007 *M* aldehyde. Lines constructed as described in text.

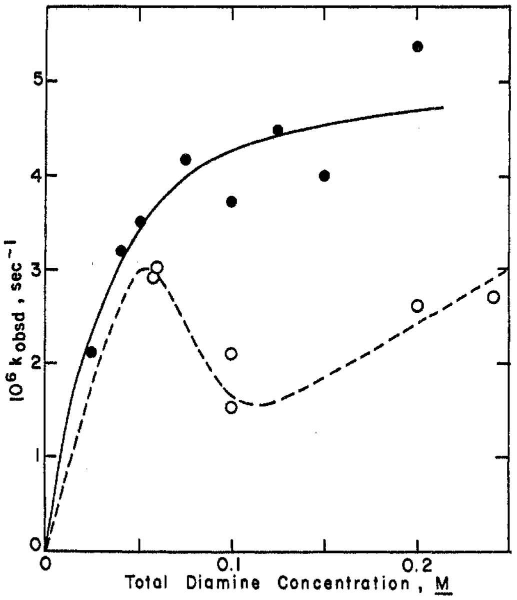

Figure 2.—Rate constants for the dedeuteration of isobutyraldehyde-2-*d* at initial concentrations of 0.053 *M* in water at 35°: ○, at pH 8.51 ± 0.04 in the presence of *N*-methylethylenediamine; ●, at pH 8.66 ± 0.07 in the presence of *N*,*N*′-dimethylethylenediamine. Lines constructed as described in text.

TABLE III

RATE OF DEDEUTERATION OF 0.053 *M* ISOBUTYRALDEHYDE-2-*d* IN THE PRESENCE OF *N*,*N*′-DIMETHYLETHYLENEDIAMINE IN WATER AT 35°[a]

| [Diamine], *M* | pH[b] | $10^6k$, sec$^{-1}$ |
|---|---|---|
| 0.025 | 8.60 | 2.1 |
| 0.040 | 8.63 | 3.2 |
| 0.050 | 8.63 | 3.5 |
| 0.075 | 8.64 | 4.2 |
| 0.100 | 8.66 | 3.7 |
| 0.125 | 8.67 | 4.5 |
| 0.150 | 8.67 | 4.0 |
| 0.200 | 8.73 | 5.4 |

[a] Total concentration.[7] [b] Calculated.

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(7) The concentrations given are "total" concentrations, without regard to how much of the compounds is actually transformed to imidazolidines, imines, etc., or to the state of protonation of the bases in the reaction mixtures.

## Discussion

We hypothesized that the formation of imidazolidines was very important in influencing the rate of exchange of isobutyraldehyde-*2-d* in the presence of ethylenediamine and some of its derivatives. Equilibrium constants for the formation of 2-isopropylimidazolidine are so large[4] that at reagent concentrations above 0.001 *M*, isobutyraldehyde and ethylenediamine react completely enough to transform most of the limiting reagent to the imidazolidine. Thus, when small amounts of diamine are added to aldehyde in the concentrations used in our kinetic runs, the diamine is transformed largely to the imidazolidine, which is the principal basic catalyst that acts on the remaining aldehyde. This component of the total reaction rate will reach a maximum (for a given pH and given aldehyde concentration) when half the aldehyde has been transformed to imidazolidine. In the presence of excess diamine the concentration of free aldehyde will be reduced to such a a low level that exchange *via* attack of imidazolidine on free aldehyde will be much less important. Exchange will also be taking place by attack of bases on iminium ions (such as $Me_2CDCH{=}NHCH_2CH_2NH_2^+$) that are present, and the rate of such exchange will increase monotonically with increasing diamine concentration.

Let us test this hypothesis by analyzing the rate data in terms of the suggested reaction mechanism. The rate constants obtained may be compared with values reported for somewhat similar processes in cases where a smaller number of possibilities made the interpretation of the kinetic data more straightforward. Exchange is assumed to take place entirely by the rate-controlling attack of various bases on the deuterated aldehyde (AD) or on one of the deuterated iminium ions, $Me_2CDCH{=}NHCH_2CH_2NH_2^+$ ($HDIm^+$) and $Me_2CDCH{=}NHCH_2CH_2NH_3^{2+}$ ($HDImH^{2+}$), present in the solution, as indicated in eq 1, in which *k* is a rate

$$v = \sum_i k_{B_i}[B_i][AD] + \sum_i k'_{B_i}[B_i][HDIm^+] + \sum_i k''_{B_i}[B_i][HDImH^{2+}] \tag{1}$$

constant for attack on aldehyde, *k'* is for attack on the iminium ion $HDIm^+$, and *k''* is for attack on the doubly charged iminium ion $HDImH^{2+}$. Secondary deuterium kinetic isotope effects and equilibrium isotope effects will be neglected, so that the equilibrium constant for formation of an imidazolidine or the rate constant for basic catalysis by an imidazolidine, for example, will be independent of whether there is a deuterium atom in the 2-isopropyl substituent of the imidazolidine or not. Since the observed rate constants were calculated in terms of $[AD]_t$, the total concentration of isobutyraldehyde-*2-d* in all forms, as shown in eq 2, we should transform eq 1 into such terms also.

$$v = k_{obsd}[AD]_t \tag{2}$$

In the paper[4] on equilibria the concentrations of imines and iminium ions are estimated to be no more than about 3% of those of the imidazolidine and imidazolidinium ions. Therefore we shall approximate $[AD]_t$ as shown in eq 3, in which Imid and $HImid^+$

$$[AD]_t = [AD] + [Imid] + [HImid^+] \tag{3}$$

are the imidazolidine and imidazolidinium ion, respectively.[8] The equilibrium constant $K_{app}$ was defined in the paper[4] on equilibria as shown in eq 4, in which

$$K_{app} = \frac{[Imid] + [HImid^+]}{[i\text{-}PrCHO][Da]_t} \tag{4}$$

*i*-PrCHO refers to both free and hydrated aldehyde and $[Da]_t$ is the concentration of diamine in all states of protonation. From the preceding, [AD] may be expressed in terms of $[AD]_t$ as shown in eq 5, in which

$$[AD] = \frac{[AD]_t}{1 + K_{app}[Da]_t} = f_A[AD]_t \tag{5}$$

$f_A$ is the fraction of the aldehyde originally added that is present in the free or hydrated form. If the equilibrium constants $K_I$ and $K_{IH}$ for the formation of the singly and doubly charged iminium ions, respectively, are defined as shown in eq 6 and 7, then $[HDIm^+]$

$$K_I = \frac{[i\text{-}PrCH{=}\overset{+}{N}HCH_2CH_2NH_2]}{[i\text{-}PrCHO][DaH^+]} \tag{6}$$

$$K_{IH} = \frac{[i\text{-}PrCH{=}\overset{+}{N}HCH_2CH_2NH_3^+]}{[i\text{-}PrCHO][DaH_2^{2+}]} \tag{7}$$

and $[HDImH^{2+}]$ may be expressed as shown in eq 8

$$[HDIm^+] = K_I[AD][DaH^+] \tag{8}$$

and 9. Substitution of these equations, which are

$$[HDImH^{2+}] = K_{IH}[AD][DaH_2^{2+}] \tag{9}$$

based on the well-founded assumption that the various equilibria concerned are established rapidly relative to the deuterium exchange reaction, into eq 1 gives eq 10.

$$v = \left(\sum_i k_{B_i}[B_i] + \sum_i k'_{B_i}[B_i]K_I[DaH^+] + \sum_i k''_{B_i}[B_i]K_{IH}[DaH_2^{2+}]\right)f_A[AD]_t \tag{10}$$

The bases from which basic catalysis might be expected are water, hydroxide ion, unprotonated diamine (Da), monoprotonated diamine, imidazolidine, imidazolidinium ion, the iminium ion $i\text{-}PrCH{=}NHCH_2CH_2NH_2^+$, and the imines $i\text{-}PrCH{=}NCH_2CH_2NH_2$ and $i\text{-}PrCH{=}NCH_2CH_2NH_3^+$. The known catalysis constant for water[5] shows that catalysis by attack of water on aldehyde would contribute only about 0.5% to reaction *via* attack on the aldehyde at the lowest diamine concentration used. Because of this inability of water to compete with the other bases in the solution, exchange *via* attack of water on the iminium ions was neglected. The imidazolidinium ion and the iminium ion should be too weakly basic (and the latter's concentration should be too low) for significant amounts of catalysis. Since no basic catalysis by imine was observed in runs using methylamine, where the imine was the most abundant nitrogen base present,[6] we have neglected catalysis by imine nitrogen atoms in the present case, where the relative concentration of imines is much lower. Significant amounts of catalysis by the primary amino group of the uncharged imine seem unlikely in view of its relatively low concentration and the fact that primary amines are not particularly effec-

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[8] Since nothing is gained in the present case by treating the aldehyde hydrate as a separate species, we shall define [AD] as the concentration of the deuterated aldehyde in both the free and hydrated form. This is analogous to the definitions of aldehyde concentrations used in calculating the various rate and equilibrium constants that we shall be using.

tive catalysts.[9,10] In a kinetic analysis of the values of $k_{\mathrm{obsd}}$ such catalysis by the imine would be indistinguishable from catalysis by its tautomer, the imidazolidine.

Increases in the diamine concentration at a given pH bring about decreases in the concentration of aldehyde and increases in the concentrations of iminium ions. For this reason the fraction of the reaction that proceeds through the aldehyde decreases as the concentration of diamine increases. The fraction of reaction involving the base hydroxide ion must also decrease with increasing concentration of diamine, since the hydroxide ion concentration remains constant, and the concentration of its competitors, the imidazolidine and the unprotonated and monoprotonated diamine, increases. These changes provide reasons for neglecting attack of hydroxide ions on the iminium ions, even though we do allow for attack of hydroxide ions on the aldehyde.

Neglect of the bases indicated and combination of eq 2 with eq 10 gives eq 11, in which the subscripts

$$k_{\mathrm{obsd}} = f_{\mathrm{A}}\{k_{\mathrm{h}}[\mathrm{OH^-}] + k_{\mathrm{i}}[\mathrm{Imid}] + k_{\mathrm{d}}[\mathrm{Da}] + k_{\mathrm{dh}}[\mathrm{DaH^+}] + (k'_{\mathrm{i}}[\mathrm{Imid}] + k'_{\mathrm{d}}[\mathrm{Da}] + k'_{\mathrm{dh}}[\mathrm{DaH^+}])K_{\mathrm{I}}[\mathrm{DaH^+}] + (k''_{\mathrm{i}}[\mathrm{Imid}] + k''_{\mathrm{d}}[\mathrm{Da}] + k''_{\mathrm{dh}}[\mathrm{DaH^+}])K_{\mathrm{IH}}[\mathrm{DaH_2^{2+}}]\} \quad (11)$$

h, i, d, and dh refer to the bases hydroxide ion, imidazolidine, unprotonated diamine, and monoprotonated diamine, respectively. Since we have the equilibrium constants and acidity constants with which to calculate $f_{\mathrm{A}}$ and the concentrations of the five species shown, and since $k_{\mathrm{h}}$ is known, there are nine unknowns ($k_{\mathrm{i}}$, $k_{\mathrm{d}}$, $k_{\mathrm{dh}}$, $k'_{\mathrm{i}}K_{\mathrm{I}}$, $k'_{\mathrm{d}}K_{\mathrm{I}}$, $k'_{\mathrm{dh}}K_{\mathrm{I}}$, $k''_{\mathrm{i}}K_{\mathrm{IH}}$, $k''_{\mathrm{d}}K_{\mathrm{IH}}$, and $k''_{\mathrm{dh}} \cdot K_{\mathrm{IH}}$) in eq 11. We did not vary the concentrations of all the participating species sufficiently to permit the reliable determination of all these constants. In fact, because of various concentration interdependencies and for other reasons it is not clear that such variation would be possible. It is therefore not surprising that an unrestricted least squares treatment of the data in Table I did not give a plausible set of values for these unknowns.[11] For this reason certain restrictions were introduced. The rate constants for attack of the primary amines Da and DaH$^+$ on isobutyraldehyde-*2*-*d* were assumed to fall on a Brønsted line of slope 0.5 with the rate constant for attack by methylamine, the only other primary amine whose reactivity has been studied. (Values of 0.49 and 0.53 for the Brønsted $\beta$ have been found for 3- and 4-substituted pyridines and phenoxide ions, respectively.[5]) Using the estimate[10,12] that the $k_{\mathrm{m}}$ term observed using methylamine buffers[6] is about 90% owing to attack of amine on deuterioaldehyde gives a rate constant of $2.7 \times 10^{-3}$ $M^{-1}$ sec$^{-1}$ for methylamine, from which values of $1.1 \times 10^{-3}$ and $3.0 \times 10^{-5}$ $M^{-1}$ sec$^{-1}$ may be calculated for $k_{\mathrm{d}}$ and $k_{\mathrm{dh}}$, respectively. Since the *N*-methyliminium ion of isobutyraldehyde-*2*-*d* has been found to be only 84% as selective as the aldehyde toward attack by various bases,[10] we have assumed that this is also true for the iminium ions encountered in the present case. These assumptions give eq 12, in which there are only three unknowns. Least squares treatment of the data in Table I gave the values $1.45 \times 10^{-3}$ $M^{-1}$ sec$^{-1}$, 0.043 $M^{-2}$ sec$^{-1}$, and 0.50 $M^{-2}$ sec$^{-1}$ for $k_{\mathrm{i}}$, $k'_{\mathrm{i}}K_{\mathrm{I}}$, and $k''_{\mathrm{i}}K_{\mathrm{IH}}$, respectively. These values seem plausible.

$$k_{\mathrm{obsd}} - f_{\mathrm{A}}k_{\mathrm{h}}[\mathrm{OH^-}] = f_{\mathrm{A}}\{k_{\mathrm{i}}[\mathrm{Imid}] + 0.0011[\mathrm{Da}] + 0.00003[\mathrm{DaH^+}] + ([\mathrm{Imid}] + (0.0011/k_{\mathrm{i}})^{0.84}[\mathrm{Da}] + (0.00003/k_{\mathrm{i}})^{0.84}[\mathrm{DaH^+}])k'_{\mathrm{i}}K_{\mathrm{I}}[\mathrm{DaH^+}] + ([\mathrm{Imid}] + (0.0011/k_{\mathrm{i}})^{0.84}[\mathrm{Da}] + (0.00003/k_{\mathrm{i}})^{0.84}[\mathrm{DaH^+}])k''_{\mathrm{i}}K_{\mathrm{IH}}[\mathrm{DaH_2^{2+}}]\} \quad (12)$$

The value of $k_{\mathrm{i}}$ corresponds to 2-isopropylimidazolidine attacking isobutyraldehyde-*2*-*d* 30% more rapidly than does ethylenediamine (according to our estimated rate constant), although the latter amine is about three times as basic. However, secondary amines (if not too hindered) are known to be better catalysts than primary amines of similar basicity.[9] Our $k_{\mathrm{i}}$ is too small by a factor of about two to fall on a Brønsted plot of the points for piperidine, piperazine, and morpholine,[9] suggesting that 2-isopropylimidazolidine is somewhat more hindered than these other secondary amines.

From a plot of log $k_{\mathrm{B}}$ *vs.* log $k'_{\mathrm{B}}K_{\mathrm{I}}$ in the case where $k'_{\mathrm{B}}$ is the rate constant for attack of base on and $K_{\mathrm{I}}$ is the equilibrium constant for formation of the *N*-methyliminium ion of isobutyraldehyde-*2*-*d*,[10] a value of 0.013 $M^{-2}$ sec$^{-1}$ would be calculated for $k'_{\mathrm{i}}K_{\mathrm{I}}$ if it referred to the *N*-methyliminium ion. Since $k'_{\mathrm{B}}K_{\mathrm{I}}$ for a given base has been found to increase with increasing acidity of the primary ammonium ion from which the iminium ion is formed,[13] a larger value than this would be expected for our $k'_{\mathrm{i}}K_{\mathrm{I}}$, which refers to the iminium ion formed from monoprotonated ethylenediamine, and a still larger value would be expected for $k''_{\mathrm{i}}K_{\mathrm{IH}}$, which refers to the iminium ion formed from diprotonated ethylenediamine. The values we have obtained are in agreement with these expectations.

From the constants obtained using eq 12, the observed rate constants may be calculated with a standard deviation of 13% and an average deviation of 10%. These constants, a pH of 8.68, and an aldehyde concentration of 0.053 $M$ were used to calculate the solid curve in Figure 1, and with a pH of 8.37 and an aldehyde concentration of 0.060 $M$ they were used to calculate the dashed curve. Part of the deviations of the points from the respective lines arises from the fact that most points refer to a slightly different set of conditions from those from which the lines were calculated.

In eq 12 all the rate constants were taken as being independent of the ionic strength. Two of these constants, $k'_{\mathrm{dh}}$ and $k''_{\mathrm{dh}}$, govern reactions between ions. The data were also treated by using the Davies equation[14] (which takes the form of eq 13 at 35°) to calculate

$$\log \gamma = -0.52Z^2\left(\frac{\sqrt{\mu}}{1 + \sqrt{\mu}} - 0.2\,\mu\right) \quad (13)$$

activity coefficients and using the Brønsted method[15] to calculate the ionic strength effect on the rate con-

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[9] J. Hine and J. Mulders, *J. Org. Chem.*, **32**, 2200 (1967).

[10] J. Hine, J. Mulders, J. G. Houston, and J. P. Idoux, *ibid.*, **32**, 2205 (1967).

[11] Some of the values were negative. If the computer program was modified to prohibit negative values, some values were zero and some of the nonzero values had implausible relative magnitudes. Furthermore, some of the values could be changed greatly (provided others were also) with very little effect on the sum of the squares of the deviations from the $k_{\mathrm{obsd}}$ values.

[12] The value of $k_{\mathrm{m}}$ listed near the end of ref 10 resulted from an arithmetic error.

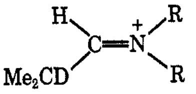
[13] J. Hine, B. C. Menon, J. Mulders, and J. P. Idoux, *J. Org. Chem.*, **32**, 3850 (1967).

[14] C. W. Davies, *J. Chem. Soc.*, 2093 (1938).

[15] J. N. Brønsted, *Z. Physik. Chem.*, **102**, 169 (1922); **115**, 337 (1925).

stants. The values of $k_i$ and $k'_iK_I$ obtained were within 3% of the values obtained neglecting such ionic strength effects, but $k''_iK_{IH}$ was much smaller (0.040 $M^{-1}$ sec$^{-1}$) and the standard deviation of the fit increased to 14%. We feel that this procedure, which requires the evaluation of the activity coefficients of a triply charged ion, is not very reliable and, largely because the $k''_iK_{IH}$ value obtained is implausible, prefer the treatment in which ionic strength effects on rate constants were neglected. Nevertheless we feel that the value of $k''_iK_{IH}$ obtained is much less reliable than the values of $k'_iK_I$ and $k_i$. Other sets of restrictions on the nine constants in eq 11 led to implausible sets of rate constants with values of $k'_iK_I$, $k''_iK_{IH}$, and other constants that often differed considerably from the values obtained by the method described above, but the values of $k_i$ were all constant within 15%.

A kinetic equation like eq 11 may be written for the dedeuteration of isobutyraldehyde-*2-d* in the presence of *N*,*N'*-dimethylethylenediamine, but the relative rate of exchange *via* iminium ions may be affected by the fact that the only iminium ions possible are of the type of ion **1**, formed from a secondary amine. In a study of catalysis of the dedeuteration of isobutyraldehyde-*2-d* by simple secondary amines, no evidence for reaction *via* iminium ions was obtained.[9] Least squares treatments with plausible restrictions gave sets of rate constants that corresponded to some exchange *via* iminium ions and permitted the calculation of the $k_{obsd}$ values in Table III with standard deviations around 10%. However, when catalysis *via* iminium ion formation was completely neglected and only the restriction (based on a Brønsted $\beta$ of 0.5) that $k_{dh} = 0.0259k_d$ was made, values for the two unknowns of $4.8 \times 10^{-5}$ and $3.5 \times 10^{-3}$ $M^{-1}$ sec$^{-1}$ were obtained for $k_i$ and $k_d$, respectively. The $k_{obsd}$ values may be calculated with a standard deviation of 11% from these rate constants, which were also used (with a pH of 8.66 and an aldehyde concentration of 0.053 *M*) in constructing the solid line in Figure 2. The value for log $k_d$ falls about 0.2 log units below the line in the Brønsted plot for morpholine, piperazine, and piperidine, suggesting that the open-chain diamine is slightly more hindered than the cyclic amines. Brønsted plots of log $k_i$ indicate that 1,3-dimethyl-2-isopropylimidazolidine is more hindered than *N*-methylmorpholine but no more hindered than a number of tertiary amines. Hindrance would be expected in view of the fact that the isopropyl group would have to be cis to at least one adjacent methyl group or cis to the unshared electron pair that is involved in removal of deuterium. In view of the plausible magnitude of the rate constants and the smallness in the improvement of the fit to the observed data obtained when catalysis *via* the formation of intermediate iminium ions is taken into account, we conclude that there may be some such catalysis, but it has not been established by our observations.



**1**

With *N*-methylethylenediamine we do not have equilibrium constants for reactions with isobutyraldehyde to form imidazolidines or imidazolidinium ions. Even if we did, the unsymmetrical nature of this base would make the detailed interpretation of kinetic data considerably more complicated than in the case of ethylenediamine or its *N*,*N'*-dimethyl derivative. Hence the dashed line in Figure 2 is simply a smooth curve that approximates the kinetic data.

Although a rate maximum and subsequent minimum is found with ethylenediamine and its *N*-methyl derivative, none appears with *N*,*N'*-dimethylethylenediamine. There are probably two major reasons for this. First, the equilibrium constant for the formation of an imidazolidine from isobutyraldehyde and *N*,*N'*-dimethylethylenediamine is only about one third as large as in the case of ethylenediamine itself. Second, 2-isopropylimidazolidine, which is 16 times as basic as its *N*,*N'*-dimethyl derivative and considerably less hindered, is a much better catalyst for the dedeuteration of isobutyraldehyde-*2-d*.

## Experimental Section

The reagents used in this study have been described previously.[4,5] In some of the kinetic runs the pH of the reaction solution (which we take as $-\log a_{H^+}$, with activity coefficients being calculated from the Davies equation[14]) was not measured but was calculated from the concentrations of the various reagents that had been added and the relevant acidity constants and equilibrium constants for imidazolidine formation.[4] In some other kinetic runs the amount of hydrochloric acid or sodium hydroxide added was not carefully measured, but the pH was determined by use of a Radiometer pH meter (26c) and glass electrode (202b or 202c). In the remaining cases, in which the amount of added acid and the pH were both carefully measured, there were differences between the observed and calculated pH as large as 0.1. In the runs carried out using ethylenediamine and its *N*-methyl derivative, the reaction solutions were prepared from the free amine and the appropriate amount of standard hydrochloric acid. With *N*,*N'*-dimethylethylenediamine the dihydrochloride was used and the appropriate amount of standard sodium hydroxide was added.

In least squares treatments of the data it was the sum of the squares of the *fractional* deviations that was minimized.

**Registry No.**—Isobutyraldehyde-*2-d*, 4303-51-9; ethylenediamine, 107-15-3; *N*-methylethylenediamine, 109-81-9; *N*,*N'*-dimethylethylenediamine, 110-70-3.