were based upon this analysis. A flask with a crease in the bottom which made two separate compartments was used, the quinone solution being placed in one compartment and the leuco dye mixture in the other. The solutions could then be mixed very rapidly by shaking the flask, after it had reached a constant temperature. The rapid mixing is quite necessary and a preliminary isotope effect of 1.5 was measured before the fast mixing technique was used. The two independent determinations of the isotope effect described in the Results Section were done to show that mixing rate problems had been overcome. The successful determination of relative rates in excess of a factor of 30, together with the unlikelihood that that factor could be higher, suggests that the isotope effect is reliable.

Dependence of the Primary Isotope Effect (k^{H}/k^{D}) on Base Strength for the Primary Amine Catalyzed Ionization of Nitroethane

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Abstract: Primary kinetic isotope effects (k^{H}/k^{D}) have been determined in both water and 50% dioxane–water (v/v) for the primary amine catalyzed ionization of nitroethane and nitroethane-1-d_2. In water the pK_a of nitroethane is 8.5 and the values of k^{H}/k^{D} appear to be maximal for amines whose conjugate acids possess pK_a values near 8.5 (*i.e.*, near ΔpK_a = 0). In the 50% dioxane–water solvent the pK_a of nitroethane is 10.7 and it would appear as though the maximum in k^{H}/k^{D}, if any, must pertain to amines of pK_a > 10. If one concludes that these results are not fortuitous then it follows that transition state symmetry is dependent upon ground-state basicity. Also, since the Brønsted plots for both k^{H} and k^{D} are linear one would be forced to conclude that the primary kinetic isotope effects are a more sensitive probe of transition state than are Brønsted plots.

Theoretical calculations[2] have indicated that the primary deuterium isotope effect (k^{H}/k^{D}) for the base (B:) catalyzed ionization of an acid (HA) should reach a maximum value when the difference in basicity of B: and A: (ΔpK) is small. Until recently experimental support of theory has been lacking.[3] This study deals with the determination of k^{H}/k^{D} in the region of ΔpK = 0 for the primary amine catalyzed ionization of nitroethane. Our objective has been to ascertain if a maximum in the primary isotope effect occurs and the sensitivity of the primary isotope effect to changes in the acidity of nitroethane due to change in solvent.[4] The relative usefulness of k^{H}/k^{D} and the Brønsted coefficient β in determining the position of the transition state along the reaction coordinate is considered.[5]

$$\Delta \mathrm{p}K = \mathrm{p}K(\mathrm{HA}) - \mathrm{p}K(\mathrm{BH}) \qquad (1)$$

Experimental Section

Apparatus. Kinetic measurements were made with a Gilford Model 2000 or a Zeiss PMQ II spectrophotometer. The Zeiss was equipped with a thermostated brass cuvette holder and the Gilford with dual thermospacers through which water was circulated at 30 ± 0.1°. Readings were recorded automatically with either a Honeywell or Servo Riter II recorder.

The pH's of the kinetic solutions were determined both prior to and at the completion of reactions, using a Radiometer Model 22 pH meter with a PHA 630 scale expander, and a combined glass calomel electrode (Radiometer G.K. 2021 C) thermostated at the temperature of each kinetic experiment.

Mass spectra were recorded on an AEI MS 902 mass spectrometer. All pmr spectra were taken neat (TMS as an internal standard) on a Varian HA 100 or a Jeolco C-60HL. A Loenco Model 15C-E vpc with a 16-ft 20M Carbowax column on 60–80 Chromosorb W was used for preparative collection of nitroethane-1-d_2. All calculations were performed on an Olivetti–Underwood Programma 101, and best least squares fit of points was used in plots of k_{obsd} *vs.* B_T. A microliter pipet (Ependorf) was used to deliver stock solutions of substrate and iodine.

Materials. Pyridine (Baker), piperidine (Matheson Coleman and Bell), and 1,2-diaminopropane were distilled from barium oxide, bp 116, 103, and 117°, respectively. Glycylglycine (Aldrich) and hydrochlorides of glycine ethyl ester (Eastman), 2,2,2-trifluoroethylamine (Pierce), ethylamine (Matheson Coleman and Bell), ethylenediamine (Eastman), and ammonia were recrystallized from ethanol-water mixtures and dried under vacuum over phosphorus pentoxide. Tris(hydroxymethyl)aminomethane (Matheson Coleman and Bell) and glycine (Fischer reagent) were used without further purification. Nitroethane (Aldrich) was distilled twice through a 9-in. Vigreux column, bp 113°. Deuterium oxide (Stohler Isotopes, 99.8% isotopically pure) was used without further purification. Spectral grade dioxane (Matheson Coleman and Bell) was refluxed over sodium metal and distilled under nitrogen through a 6-ft vacuum-jacketed column with glass helices (bp 102°) prior to each kinetic run. The resulting dioxane was tested for the presence of peroxides with potassium iodide paper, and with iodine with an excess of iodide by observing changes in absorption at 351 nm. Any solutions containing peroxides were discarded. All solutions containing dioxane were checked for the presence of peroxides prior to and at the completion of each kinetic run.

pK_a Determination. The pK_a of nitroethane in 50:50 (v/v) dioxane–water (μ = 0.2 with KCl at 30°) was determined by half-neutralization and serial dilution. The pK_a values for glycine, glycylglycine, 1,2-diaminopropane, tris, and 2,2,2-trifluoroethyl-

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(1) (a) A portion of the material to be submitted by J. E. D. in fulfillment of the requirement for the Ph.D. in Chemistry, University of California at Santa Barbara. (b) To whom inquiries should be addressed.

(2) (a) R. A. More O'Ferrall and J. Kouba, *J. Chem. Soc., B*, 985 (1967), and references therein. (b) W. J. Albery, *Trans. Faraday Soc.*, **63**, 200 (1967).

(3) (a) R. P. Bell and D. M. Goodall, *Proc. Roy. Soc.* (London), **A294**, 273 (1966); (b) J. L. Longridge and F. A. Long, *J. Amer. Chem. Soc.*, **89**, 1292 (1967), and references therein; (c) A. J. Kresge, D. S. Sagatys, and H. L. Chen., *ibid.*, **90**, 4174 (1968); (d) A. J. Kresge and Y. Chiang, *ibid.*, **91**, 1025 (1969).

(4) (a) J. F. Bunnett, *Angew. Chem. Intern. Ed. Engl.*, **1**, 225 (1962); (b) J. R. Jones, *Chem. Commun.*, 710 (1967); (c) A. F. Cockerell, *J. Chem. Soc., B*, 964 (1967); (d) A. F. Cockerell and W. H. Saunders, Jr., *J. Amer. Chem. Soc.*, 89, 4985 (1967).

(5) E. S. Lewis and L. H. Funderburk, *ibid.*, **86**, 2531 (1964),

amine in 50:50 (v/v) dioxane–water were determined titrimetrically (μ = 0.2 with KCl at 30°). Corrections for the mole fraction of dioxane and ionic strength were applied to the observed electrode reading.[6]

Kinetics. The rates of disappearance of nitroethane in the presence of piperidine, ethylamine, and ethylenediamine were followed by measuring the increase in absorbance of the anion of nitroethane at 240 nm. Stock solutions of nitroethane-1-d_2 in dioxane were prepared; and the reaction was initiated by the addition of 20 μl of the stock solution to *ca.* 2 ml of buffer, giving a solution of approximately 10^{-5} to 10^{-4} M. Doubly glass distilled water was used to prepare all solutions, and serial dilutions were made with 1.0 M potassium chloride. The reactions were carried out in Ŧ cuvettes. The concentration of nucleophile was always in large excess over that of nitroethane-1-d_2, reactions were followed to one half-life, and initial rates were calculated from plots of log ($\mathrm{OD}_\infty - \mathrm{OD}_t$) *vs.* time. To demonstrate that no exchange between anion and solvent was occurring, a solution of the sodium salt of nitroethane was placed in ethylenediamine at pH 9.80; no observable change in absorption at 240 nm was noted for periods in excess of 6 hr, indicating that no back-reaction occurs. Gregory and Bruice[7] found that no back-reaction between the anion of nitroethane and buffer could be detected for any of the amines used in the study under consideration. Also capture of the anion of nitroethane by hydronium ion has a rate constant of only 1.5×10^1 l./mole sec^{-1},[8] thus indicating that capture by water or buffer is slow. Values of $k_{\mathrm{OH}}{}^{\mathrm{H}}/k_{\mathrm{OH}}{}^{\mathrm{D}}$ calculated from the intercept of plots of k_{obsd} *vs.* total buffer for ethylamine, ethylenediamine, and piperidine gave a value of 9.3 (lit. value 9.3,[3a] 10.0 in D_2O[9]), thus indicating that once anion is formed, it does not pick up a proton from solvent or buffer. If the resulting carbanion had picked up a proton from solvent, this would result in an increasingly larger quantity of protium substrate, thus a much lower value for $k_{\mathrm{OH}}{}^{\mathrm{H}}/k_{\mathrm{OH}}{}^{\mathrm{D}}$ would be obtained.

For all buffers with pK's below 10.10 iodine was employed as a scavenger to react rapidly with the anions of nitroethane and nitroethane-1-d_2. The kinetics were zero order, with $I_2 \approx 10^{-5}$ and buffer *ca.* 0.1–0.5 M. The decrease in absorption of iodine was followed at 351 nm ($\epsilon = 2.6 \times 10^4$).[10] Beer's law was found to hold for iodine in the concentration range 10^{-5} to 10^{-4} M in aqueous solution, but not in ammonia, glycine, and to a lesser extent in glycine ethyl ester. Other amines showed a similar but less marked deviation. Presumably this deviation is a consequence of complexation between amine and iodine, even though no charge-transfer band could be found for pyridine and iodine. It was shown that the complexing increases with increased concentration of amine and is strongest for ammonia and glycine, which have the highest pK_a's of the amines used with iodine as a scavenger.

A typical kinetic run was carried out as follows. Exactly 2 ml of buffer was pipetted into a Ŧ cuvette and thermostated in the spectrometer. Iodine from a stock solution (4.85×10^{-3} M) was delivered *via* a λ pipet (20 μl) into the cuvette. After mixing, 20 μl of a stock solution of nitroethane or nitroethane-1-d_2 (in acetonitrile) was delivered into the cuvette, mixed, and placed in the spectrophotometer and the loss of absorption followed at 351 nm. When the amines which complex strongly with iodine were used as buffers, iodine was added to the cuvette containing buffer until a specific absorbance was reached, *i.e.*, 0.5 and the reaction then initiated. Because solutions were run with the same buffer concentrations and at the same pH, all effects resulting from complexing cancelled out when one compares the rate of reaction of buffer with nitroethane and nitroethane-1-d_2. Calculations on a similar system[3a] have demonstrated that the first 75% of the iodination will be in error less than 2% with potassium iodide concentrations at 10^{-2} M. All kinetic runs using iodine as a scavenger contained 10^{-2} M potassium iodide. Optical density readings taken during the last 25% of the reactions were not used in determining k_{obsd}. A blank reaction (k_{blank}) for the loss of iodine from solutions containing all components save nitroethane was subtracted from values of k_{obsd} (obtained from plots of OD *vs.* time). Plots of $k_{\mathrm{obsd}} - k_{\mathrm{blank}}$ (*i.e.*, k_0, the zero-order rate constant) against free base concentration afforded slopes equal to either $k_{\mathrm{amine}}{}^{\mathrm{H}}$ or $k_{\mathrm{amine}}{}^{\mathrm{D}}$ Direct comparison of $k_{\mathrm{amine}}{}^{\mathrm{H}}/k_{\mathrm{amine}}{}^{\mathrm{D}}$ was possible when solutions were run at the same pH and buffer concentration (corrections for different substrate concentration were made by dividing either $k_{\mathrm{amine}}{}^{\mathrm{H}}$ or $k_{\mathrm{amine}}{}^{\mathrm{D}}$ by substrate concentration). Best results, with less deviation, were obtained when the reactions were carried out in this manner.

All rates carried out in dioxane–water 50:50 (v/v) were also performed with iodine as a scavenger. The procedure was similar to that described above, except that μ = 0.2 with KCl rather than μ = 1.0 (KCl) as was the case in aqueous solution. All rate data were obtained as described previously.

Preparation of Nitroethane-1-d_2. The procedure for the preparation of nitroethane-1-d_2 was essentially that of Bell and Goodall.[3a] However, complete removal of traces of $H_2O \cdot D_2O$ could be accomplished only by drying over molecular sieves and distillation at atmospheric pressure. The material so obtained was freed from reactive impurities by vapor phase chromatography (column temperature 80°, 18 psi, retention time *ca.* 18 min). A pmr spectra after chromatography indicated that no exchange had taken place.

Determination of Isotopic Content of Nitroethane-1-d_2. The mass spectrum of nitroethane does not contain a parent peak, and the determination of the isotopic content of nitroethane-1-d_2 by Bell and Goodall[3a] was based upon the molecular ions $[CH_3CD_2]\cdot^+$, $[CH_3CHD]\cdot^+$, etc. In our attempt to determine the isotopic content of nitroethane-1-d_2 we obtained different isotopic content for the same sample by varying the electron voltage from 6 to 70 eV. These results indicate that probable fragmentation of $[CH_3CHD]\cdot^+$ or $[CH_3CD_2]\cdot^+$ gives apparent enrichment of $[CH_3CH_2]\cdot^+$.

Isotopic purity was ultimately established by proton magnetic resonance. A neat sample of nitroethane-1-d_2 showed no α protons. In a control experiment using $H_2O \cdot D_2O$, it was established that 1% H_2O could be detected by the spectrometer. Thus the isotopic content of nitroethane-1-d_2 was set as 99% and corrections made on $k^{\mathrm{H}}/k^{\mathrm{D}}$ assuming 1% protonium in the deuterated substrate.

Results

The rate expression for proton abstraction from nitroethane is provided by eq 2[7,8]

$$k_0 = (k_{\mathrm{spon}} + k_{\mathrm{OH}}[\mathrm{HO}^-] + k_{\mathrm{B}}[\mathrm{B}])[\mathrm{S}] \qquad (2)$$

where k_0 is the zero-order rate constant for disappearance of iodine, k_{spon} is the spontaneous rate and k_{B} the rate constant for buffer-catalyzed ionization by the basic component of the buffer [B]. Plots of k_0 *vs.* $[B_T]$, where $[B_T] = [B] + [BH]$, provide $k_B[S]$ as slope and $k_{\mathrm{spon}} + k_{\mathrm{OH}}[\mathrm{HO}^-]$ as intercept (see Figure 1). By dividing the slope by [S] and correcting for the fraction of free base the term k_B is obtained. In practice, the same conditions of pH and $[B_T]$ were employed for each amine with both protio and deuterio substrates so that $\mathrm{slope}^{\mathrm{H}}[S_1]/\mathrm{slope}^{\mathrm{D}}[S_2] = k^{\mathrm{H}}/k^{\mathrm{D}}$, where $[S_1]$ and $[S_2]$ represent the concentrations of deuterio and protio substrates employed. No results were found to be incompatible with the rate expression described above.

That iodine is removed by complexing with amine has been shown to be true for most all amines used in this study. Complex formation was found to be instantaneous and to be followed by a slow loss of molecular iodine which is proportional to the amine concentration. The rate of iodine consumption was corrected by subtracting the rate of iodine consumption in a solution containing only buffer (see Experimental Section). The rate constant k_0 varies linearly with the concentration of amine (Figure 1) indicating that complex formation does not alter the rate of reaction between iodine and the carbanion.

Because a small quantity of protio compound is present in the deuterated substrate, and since only a small fraction of the total substrate is used up during the reaction, one must correct the observed rate constant for the fraction of protonated species present. Therefore, the true value of k^{D} is obtained only after the fol-

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(6) L. G. Van Uitert and W. C. Fernelius, *J. Amer. Chem. Soc.*, **76**, 5887 (1954).

(7) M. J. Gregory and T. C. Bruice, *ibid.*, **89**, 2327 (1967).

(8) R. G. Pearson and D. L. Dillion, *ibid.*, **75**, 2429 (1953).

(9) Wynne-Jones W. F. K., *J. Chem. Phys.*, **2**, 381 (1934).

(10) M. L. Bender and A. Williams, *J. Amer. Chem. Soc.*, **88**, 2502 (1966).

lowing correction is applied

$$k^D = (k_B - fk_B^H)/(1 - f) \qquad (3)$$

where k_B^H represents the observed rate constant for nitroethane and $f (= 0.99)$ is the fraction of nitroethane impurity in the deuterated material used in obtaining k_B. Because the value of f cannot be obtained more accurately (by mass spectrometry) a possible uncertainty of 10% exists in its determination. However, this uncertainty does not affect the general outcome of the study and in most every case is much smaller than the experimental uncertainty associated with the rates themselves. Results are provided in Table I.

Table I. Primary Deuterium Isotope Effects Determined *via* Zero-Order Kinetics (Solvent Water, μ = 1.0, 30°)

Amine	pH range	Protio: deuterio no. of k_{obsd}	pK_a	k^H/k^D
$CF_3CH_2NH_2$	5.60–5.90	20:20	5.63	7.2 ± 0.2
1,2-Diaminopropane	7.10–7.60	10:10	7.13	8.3 ± 0.2
Glycine ethyl ester	7.55–7.82	15:15	7.75	7.5 ± 0.5
Tris	8.08–8.65	20:15	8.15	8.5 ± 0.2
Glycylglycine	8.10–8.34	10:10	8.40	9.6 ± 0.4
Ammonia	9.18–9.38	20:15	9.33	10.0 ± 0.5
Glycine	9.18–9.66	15:15	9.63	7.8 ± 0.5

In the reaction of ethylamine, ethylenediamine, and piperidine there is no back-reaction of BH with carbanion (see Experimental Section).[7] For this reason the formation of nitroethane anion, with these amines, could be followed spectrophotometrically without the necessity of iodine as a trapping agent. Under the conditions where $[B_T] \gg$ [substrate] + [anion], the system is simplified to the pseudo-first-order conditions of eq 4

$$-\overset{|}{\underset{|}{C}}-H, D \xrightarrow{k_B[B]} -\overset{|}{\underset{|}{C}}^- \qquad (4)$$

for which the kinetic equation pertains

$$k_1 = k_{spon}' + k_{OH}'[HO^-] + k_B'[B] \qquad (5)$$

For eq 5, k_1 is the observed pseudo-first-order rate constant and the remaining terms are the first-order counterparts of the expressions of eq 2. By plotting k_1 *vs.* [B] one obtains as slope k_B' and as intercept (k_{spon}' + $k_{OH}'[HO^-]$). Because k_{spon}' has been determined to be quite small (*i.e.*, 1×10^{-9} or 5.3×10^{-7} sec^{-1})[3a,11] it could be neglected in the pH range and [B] values employed so that k_{OH}^H/k_{OH}^D could be determined directly from the plots of k_1 *vs.* [B]. The data for the three amines reacting with nitroethane and nitroethane-1-d_2 under the pseudo-first-order conditions are recorded in Table II.

For reactions carried out in 50:50 (v/v) dioxane–water solvent, iodine was employed as an anion scavenger. Because peroxides oxidize iodide to iodine[12] it was necessary to remove all peroxides from the dioxane. For this reason, dioxane was freshly distilled before each kinetic run and no solution containing dioxane was kept over a period of 6 hr. The kinetics in this solvent system were obtained in the same manner as those run in aqueous media using iodine as an anion scavenger (Table III).

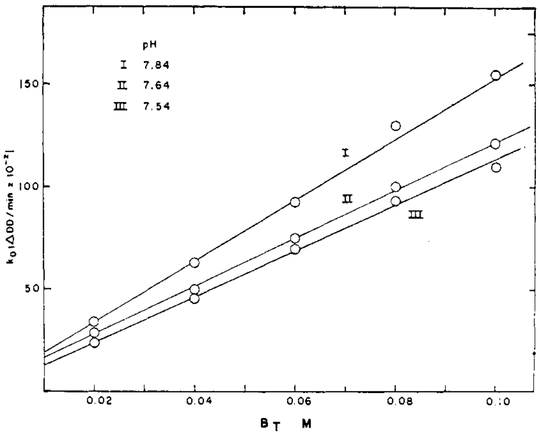

Figure 1. Plots of the zero-order rate constants (k_0) for amine (ethylenediamine)-catalyzed ionization of nitroethane in 50:50 (v/v) dioxane–water *vs.* concentration of amine buffer.

Table II. Primary Deuterium Isotope Effects Determined by Pseudo-First-Order Kinetics (Solvent Water)

Amine	pH range	No. of k_{obsd}	k^D, M^{-1} min^{-1}	pK_a	k^H/k^D
Ethylenediamine	9.76–10.34	15	1.10	10.10	6.7 ± 0.3
Ethylamine	10.67–10.74	15	1.20	10.69	6.4 ± 0.3
Piperidine	10.07–11.09	15	4.86	11.10	8.1 ± 0.3
Hydroxide		10	107		9.3

Table III. Primary Deuterium Isotope Effects Determined *via* Zero-Order Kinetics in 50:50 (v/v) Dioxane–Water[a] (μ = 0.2, 30°)

Amine	pH range	Protio: deuterio no. of k_{obsd}	pK_a' of amine[b]	k^H/k^D
$CF_3CH_2NH_2$	5.56–5.78	15:15	5.51	4.7 ± 0.2
1,2-Diaminopropane	7.83–8.31	10:10	7.51	8.3 ± 0.2
Ethylenediamine	7.54–7.84	15:15	7.29	7.8 ± 0.2
Glycylglycine	8.46–8.64	10:10	8.61	7.3 ± 0.1
Tris	8.47–8.77	15:15	8.63	7.7 ± 0.2
Glycine	9.68–10.05	10:10	10.01	8.2 ± 0.1

[a] pK_a of nitroethane in 50:50 (v/v) dioxane-water is 10.71. [b] pK_a of amine determined at 30°, μ = 0.2 (KCl).

Discussion

Values for primary deuterium isotope effects in the primary amine catalyzed ionization of nitroethane and nitroethane-1-d_2 are recorded in Tables I, II, and III. To avoid differences in zero point energy, a single set of substrates (nitroethane and nitroethane-1-d_2) was employed and primary amines were used as catalyst to minimize the tunneling which results from sterically hindered substrates and bases.[13] In Figure 2 there is plotted the pK_a of the conjugate acids of the amine catalysts *vs.* the primary isotope effect (k^H/k^D). In Figure 2 the main plot pertains to reactions carried out

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(11) R. Junell, *Z. Phys. Chem.*, **A141**, 71 (1929).

(12) A large number of workers have noted an initial increase in absorption when using iodine as a scavenger. This same result occurs when peroxides are present in the reaction mixture.

(13) (a) E. S. Lewis and J. D. Allen, *J. Amer. Chem. Soc.*, **86**, 2022 (1964); (b) E. S. Lewis and J. K. Robinson, *ibid.*, **90**, 4337 (1968).

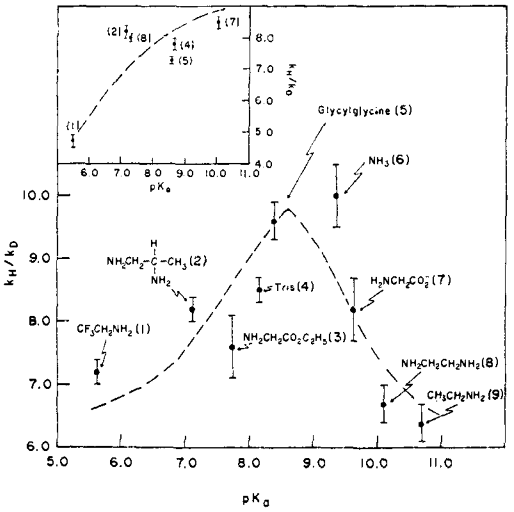

Figure 2. Plot of pK_a of primary amine catalyst *vs.* the ratio of the rate constants for the ionization of nitroethane and nitroethane-1-d_2. Main plot is for solvent water, 30°, $\mu = 1.0$ with KCl. Inset plot is for solvent 50% dioxane-water (v/v), 30°, $\mu = 0.2$ with KCl. Point 8 in Figure 2 uses the second ionization constant for ethylenediamine, whereas point 8 in inset of Figure 2 uses the first ionization constant. The dotted lines have no theoretical significance, and only serve as visual aids to illustrate where $\Delta pK = 0$.

in solvent water while the inset plot pertains to reactions carried out in 50% dioxane:water (v/v). In the plots of Figure 2 the points for the diamines refer to the species AH^+ as catalyst (eq 6) except for ethylenediamine in

$$AH_2^{2+} \underset{+H^+}{\overset{K_{a_1} \atop -H^+}{\rightleftarrows}} AH^+ \underset{+H^+}{\overset{K_{a_2} \atop -H^+}{\rightleftarrows}} A \qquad (6)$$

water where the species A is the catalyst. Therefore, for all diamines save ethylenediamine in water the primary isotope effect has been plotted *vs.* pK_{a_1} whereas for the latter pK_{a_2} has been employed. Since the rates of amine-catalyzed ionization of substrates has been determined within 1 pH unit of the amine pK_a, catalysis by the weakly basic carboxyl groups of glycine and glyclyglycine may be ignored.

Inspection of Figure 2 reveals that the isotope effects determined in water are rather large and appear to approach a maximum in the vicinity of the pK_a of nitroethane (*i.e.*, $\Delta pK_a = 0$). That the apparent maxima in k^H/k^D in the vicinity of $\Delta pK_a = 0$ is likely not fortuitous is supported by the results obtained in 50% dioxane-water (v/v). In this solvent the pK_a of nitroethane is 10.71 as compared to 8.5 in water; however, the pK_a values for the conjugate acids of the primary amines are increased on the average but *ca.* 0.1 pH unit on transfer from water to the dioxane-water solvent. Therefore, $\Delta pK_a = 0$ at an amine pK_a of 10.71 in the dioxane-water solvent. Inspection of the inset of Figure 2 reveals that the values of k^H/k^D no longer rise and fall in the vicinity of $pK_a = 8.5$ but appear to increase toward $pK_a = 10.71$. It was not possible to ascertain if the primary isotope effects decrease for amines of pK_a greater than 10.0 since for these amines a rapid reaction of the amine (and HO^-) with iodine occurs.

Some of our results can be compared to that of other authors. The relative magnitudes of k^H/k^D near $\Delta pK = \pm 5$ (see Figure 2) are in good agreement with those of Longridge and Long[3b] and are in accord with the magnitudes that might be expected if Bell and Goodall[3a] had extended their study within this range. It should be noted that no k^H/k^D values as high as 19.5 reported for the reaction of 2,6-lutidine and 2-nitropropane (where $\Delta pK = 1$) were obtained (in a separate experiment using nitroethane-1-d_2 and pyridine a value of 9.2 was obtained, thus indicating that pyridine gives a higher k^H/k^D ratio than do corresponding primary amines). The smaller values of k^H/k^D obtained with primary amines are most likely a result of little steric hindrance and consequently a smaller tunnelling correction. Values of k^H/k^D greater than 10 have not been observed where tunnelling corrections have been shown to be small (near $\Delta pK = 0$). Thus in this study and that of Long[3b] the maximum value for k^H/k^D near $\Delta pK = 0$ approaches a value of approximately 10.

The lines drawn in Figure 2 have no theoretical significance but are merely present as visual aids. Although no firm conclusion can be drawn concerning the shape of plots of the primary isotope effect *vs.* pK_a of the base, one might anticipate from previous work that the plot will rise and fall near $\Delta pK_a = 0$.[1a,14] The large effect that the symmetry of the transition state has upon k^H/k^D values is somewhat surprising. Over a range of only 3 pH units k^H/k^D changes *ca.* 3 units (Figure 2). If this trend continued, one would anticipate no kinetic isotope effect approximately 9 pH units from $\Delta pK_a = 0$. This is generally not observed.[15]

If it were possible to draw a smooth continuous curve rising and then falling about $\Delta pK_a = 0$, one would anticipate that the symmetry of such a curve would be affected by secondary isotope effects. These secondary isotope effects arise from changes in the force constants of the C–H bonds which are not broken in passing from reactant to transition state, and also to changes in hybridization at carbon. When strong bases are used, *i.e.*, ethylamine, the transition state should resemble reactants and little change in hybridization will result in a small secondary isotope effect. However, with weak bases, as trifluoroethylamine, the transition state will be close to carbanion, necessitating considerable rehybridization and a concomitantly larger secondary isotope effect. A value of 1.18 has been reported for the secondary isotope effect of hydroxide ion reacting with nitroethane.[3a] Since the secondary isotope effect should be dependent upon the strength of the base it does not seem reasonable to employ a value of 1.18 as a constant correction for the range of base strengths used in the present investigation. Therefore no corrections for secondary isotope effects have been applied in this study.

Previous work concerning the effect of solvent change on primary kinetic isotope effects has been sparse. Cockerill[4c,d,16] and coworkers have noted that the k^H/k^D ratio for HO^--catalyzed β elimination from $PhCH_2CH_2S^+(CH_3)_2$ and $PhCD_2CH_2S^+(CH_3)_2$ depends upon the concentration of dimethyl sulfoxide in aqueous dimethyl sulfoxide solutions. They proposed that increasing k^H/k^D with increasing dimethyl sulfoxide con-

(14) R. P. Bell, *Discussions Faraday Soc.*, 39, 16 (1965).

(15) F. H. Westheimer, *Chem. Rev.*, 61, 265 (1961).

(16) A. F. Cockerill, S. Rottschaefer, and W. H. Saunders, Jr., *J. Amer. Chem. Soc.*, 89, 901 (1967).

centration was due to desolvation of HO^- with a concomitant increase in its basicity. The pK_a values determined for both the amines and nitroethane in the present study must give a direct measure of their relative basicities in the transition state; if this were not the case k^H/k^D would remain relatively constant with changes in solvent. Therefore, a change in solvent affects transition state symmetry, which in turn results in a shift in the k^H/k^D maximum, as well as alteration of the magnitude of k^H/k^D [$CF_3CH_2NH_2$ $k^H/k^D = 7.2$ (water) and 4.8 in dioxane–water 50:50 (v/v)].

Presumably β is an index of the per cent transfer of H^+ from an acid "HX" to a base "B" in the transition state.[17] Thus, changes in β are generally interpreted as a change in the position of the transition state along the reaction coordinate. Theoretical calculations[18] indicate that both β and k^H/k^D should change as the symmetry of the transition state is altered. Yet numerous examples[19] exist where β is linear throughout an extended pH range. It is important to point out that the Brønsted plot for the ionization of acetylacetone with a variety of catalysts undergoes a transition from $\alpha = 0$ to $\alpha = 1$ as do "normal" acids, but that the transition occurs over a substantially wide pK range.[20] Experimentally, curvature is not detectable over a range of approximately 10 pK units. It has been established that log k^H is a linear function of pK_a for primary amine catalyzed ionization of nitroethane (pK_a of amine 5–10.7, many of the same amines were used in this study). Plots of log k^H and log k^D *vs.* pK_a for identical amines, used in both studies, indicate that the β's are within experimental error ($r = 0.98$ without ammonia) of one another; 0.55 and 0.59, respectively (see Figure 3 and Table IV). If all experimental points fit exactly on the Brønsted plot for k^H and k^D, the value of k^H/k^D for all amines investigated would be identical. The rise and fall of k^H/k^D in the vicinity of $\Delta pK_a = 0$ is reflected in small deviations of the value of log k^H and log k^D from the Brønsted plots. Thus, experimentally, changes in β are undetectable over the range studied, but significant changes in k^H/k^D are apparent. A possible explanation for this discrepancy is that k^H/k^D is a very sensitive probe for transition state symmetry, particularly near $\Delta pK = 0$, whereas, changes in β are noted with more extreme changes in the position of the transition state along the reaction coordinate or with an actual change in the energy curves for the reaction under consideration. It is conceivable that the values of k^H/k^D plotted in Figure 2 result from random variation of points from the Brønsted lines for log k^H and log k^D. It might be argued that this is rather unlikely when the results of the solvent change are considered. Systems are now under investigation which should provide evidence as to whether the value of k^H/k^D is maximized near $\Delta pK_a = 0$ for nitroalkanes in general.[21]

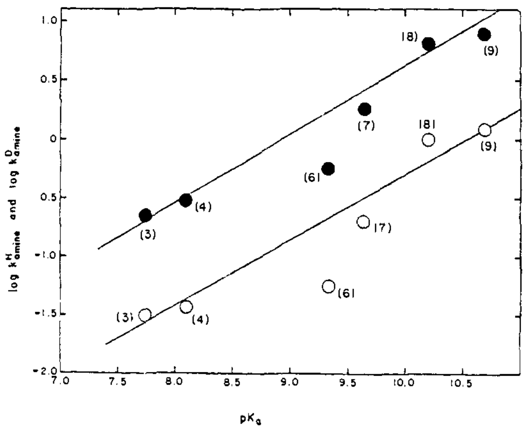

Figure 3. Brønsted plot for amine-catalyzed ionization of nitroethane (●) and nitroethane-1-d_2 (○) [$r = 0.98$ for both protium and deuterium, excluding ammonia].

Table IV. Rate Constants for k^H and k^D for the Brønsted Plot of Log k^H and Log k^D *vs.* pK_a (See Figure 3)[a]

Amine	k_{amine}^H, M^{-1} min^{-1}	k_{amine}^D, M^{-1} min^{-1}	pK_a
Glycine ethyl ester	0.23	0.030	7.75
Tris	0.31	0.0360	8.15
Ammonia	0.56	0.056	9.33
Glycine	1.71	0.208	9.63
Ethylenediamine	6.7	1.01	10.10
Ethylamine	7.7	1.24	10.69

[a] The protio substrate has a correlation coefficient of 0.984, while that of deuterium has a correlation coefficient of 0.979. Both values are reported without ammonia (ammonia is known to fall below Brønsted plots for primary amines).

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[17] (a) J. E. Leffler and E. Grundwald, "Rates and Equilibria of Organic Reactions," John Wiley & Sons, Inc., New York, N. Y., 1963, p 241; (b) G. S. Hammond, *J. Amer. Chem. Soc.*, 77, 334 (1955).

[18] R. A. Marcus, *J. Phys. Chem.*, 72, 891 (1968).

[19] R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p 158; (b) R. P. Bell, "Acid-Base Catalysis," Oxford University Press, London, 1941, Chapter V, pp 82–85.

[20] M. Eigen, *Angew. Chem. Intern. Ed. Engl.*, 3, 1 (1964).

[21] Lewis and Funderburk (ref 4) have reported a correlation between k^H/k^D and β for the ionization of nitropropane catalyzed by substituted pyridines. Their findings also indicate that k^H/k^D may rise and fall around a maxima.