Proton Transfer from Cyanocarbon Acids. I. General Base Catalyzed Detritiation of 1,4-Dicyano-2-butene-1-*t* in Aqueous Solution[1,2]

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Abstract: Detritiation of 1,4-dicyanobutene-1-*t* in water is a measurably slow base-catalyzed reaction at 25°. General base catalysis is observed with amine and phenolate bases; the Brønsted β is 0.94 for the phenolate bases and 0.98 for secondary amines. For hydroxide ion catalyzed detritiation the activation parameters are: E_a = 15.3 kcal mole^{-1} and $\Delta S^{\ddagger} = -21.5$ eu with k in M^{-1} sec^{-1} units. The primary hydrogen kinetic isotope effect is $k_H/k_D = 3.9$. No catalysis by the base water could be detected at 50°. A tentative value of 21 was obtained for the pK_a of this cyanocarbon. From these data approximate values have been calculated for the rates of the reverse reaction of carbanion with the conjugate acid species; these values approach the diffusion limit. Evidence that, for the systems studied, the fast process is not, however, actually diffusion controlled comes from the fact that the Brønsted α and β slopes have not attained their limiting values of zero and unity and from the further fact that a modest degree of steric hindrance is observed. Over-all, the data strongly suggest that the slow process is a straightforward bimolecular slow proton removal.

Among the common chemical reactions which occur in aqueous solution proton transfer, $RH + B = R^- + BH^+$ is special in that in many cases the rate of the reaction in at least one direction is diffusion controlled; *i.e.*, the rate-determining process is "physical" rather than "chemical". If one now considers slow proton transfers, *i.e.*, transfer reactions in which the rate is measurable by conventional means, it is clear that there are effectively two categories of reactions. In one category the rate of the proton transfer in one direction is diffusion controlled and so the reverse rate can be measurably slow only if the equilibrium is unfavorable. Thus if $R^- + BH^+$ is diffusion controlled, one expects the reverse reaction $RH + B$ to be slow only if the acid RH is very weak (more precisely, only if the ratio K_{RH}/K_{BH^+} is very small). For this category the slow step will show only the substituent and steric effects that characterize the over-all equilibrium and a primary kinetic isotope effect corresponding to the difference in acidities of RH and RD. Furthermore, if for a series of acids, the reaction $R^- + BH^+$ is diffusion controlled, the rate of the reverse reaction will vary directly with K_{eq} and hence inversely with K_a for the acids BH^+; the Brønsted slope for the base-catalyzed reaction will be identically unity and for the reverse reaction identically zero.

A second, and in a sense more "chemical", category of proton transfers is where neither the forward nor the reverse transfer has attained the diffusion-limited rate. An example is the protonation of azulene by a strong acid and its reverse deprotonation by water,[4] a reaction for which the activation energy is in the order of 15 kcal/mole in both directions. For this category substituent and steric effects can be different for rates and equilibria, and slopes of Brønsted plots for general catalysis can be intermediate between zero and unity.

Both the pK and the chemical type of the acid RH will influence the category into which its proton-transfer processes fall. Furthermore, for a given RH there can be a gradual change in category as the strength of the reacting base B is varied. To understand a given class of slow proton transfers, one needs a systematic variation of acid and base strengths with determination of Brønsted slopes, of temperature coefficients and of rates in both directions wherever possible. Among carbon base acids there have been extensive studies of ionization of ketones in aqueous media (usually by measuring the rate of halogenation)[5] and some studies of reactions of protonated aromatics, as, for example, the azulenes.[4]

Studies in aqueous solution of simple RC–H systems, where stabilization by tautomerization is minimal, have been less extensive. One example is the acetylenes, but details on pK's of the carbon acids have been uncertain and over-all the studies have been far from complete.[6]

The unsubstituted hydrocarbons themselves are too weakly acidic to span the range necessary to observe a change in category.[7] Introduction of strongly electron-withdrawing substituents increases hydrocarbon acidity. However, the carbanions produced on ionization frequently undergo tautomerization reactions, thereby complicating the study of simple ionization.

An extremely wide range of acidity ($-10 < pK_a < 30$) can be obtained with very simple structural modification of cyanocarbon acids;[8,9] ionization seems to be straightforward and reversible. The cyanocarbons are remarkably stable to hydrolysis; many of the nitriles are inert to hydrolysis in 80% sulfuric

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[2] Presented in part at the 155th National Meeting of American Chemical Society, San Francisco, Calif., April 1968.

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[4] J. Schulze and F. A. Long, *J. Am. Chem. Soc.*, **86**, 331 (1964); B. C. Challis and F. A. Long, *ibid.*, **87**, 1196 (1965).

[5] See, for example, R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959.

[6] (a) E. A. Halevi and F. A. Long, *J. Am. Chem. Soc.*, **83**, 2809 (1961); (b) R. E. Dessy, U. Okuzumi, and A. Chen, *ibid.*, **84**, 2899 (1962); (c) H. B. Charman, D. R. Vinard, and M. M. Kreevoy, *ibid.*, **84**, 347 (1962).

[7] A. Streitwieser, Jr., and J. H. Hammons, *Progr. Phys. Org. Chem.*, 3, 41 (1966).

[8] R. H. Boyd, *J. Phys. Chem.*, **67**, 737 (1963).

[9] O. W. Webster, *J. Am. Chem. Soc.*, **87**, 1820 (1965).

acid,[10] some showing no evidence of protonation under these conditions.

This paper reports initial studies on proton transfer from cyanocarbon acids; evidence is presented for general base catalysis of detritiation of a weakly acidic substrate in an aqueous solution leading to the conclusion that the slow step is a proton-transfer reaction.

Experimental Section

Materials. Technical grade 1,4-dicyano-2-butene (Aldrich) was recrystallized from ethyl acetate–hexane before use, mp 73.7–74.3°; lit mp 72–73°.[11] Tritiation of the substrate to give 1,4-dicyano-2-butene-1-*t* was accomplished by dissolving 1.1 g of recrystallized compound in 30 ml of ethyl acetate. To this were added 10 ml of 0.5 *M* sodium carbonate solution and 1 ml of tritiated water (25–50 mCi); the mixture was shaken overnight in a bottle sealed with a silicon rubber stopper. After acidification the cyanocarbon was extracted from the aqueous phase with ethyl acetate and dried and the solvent removed *in vacuo*. The resulting pale yellow crystals were recrystallized from 1:1 ethyl acetate–hexane to give long white needles, mp 74°.

Liquid amines and phenols were all distilled immediately prior to preparation of the buffer solutions. Solid phenols were analytical reagent grade materials and were recrystallized before use.

Kinetic Methods. (A) Detritiation. With the exceptions noted below, the technique used to measure exchange rates was that of Halevi and Long.[6a] Reactions were studied at 25.0 ± 0.1° with an ionic strength of 0.100. The counting period on a Packard Tri-Carb scintillation spectrometer, Model 314-DC, was long enough to accumulate 10,000 counts for all samples except those very near the end of the reaction. A single extraction of cyanocarbon from the quenched aqueous solution by xylene was used to obtain samples for counting. Although only 68% of the dicyanobutene is removed from water in this extraction, preliminary experiments showed that when care is taken to reproduce accurately the volumes of liquids used for each sample the number of counts could be reproduced with an average deviation from the mean of 1.3%. By using a spring-loaded, self-filling syringe for sampling, exchange half-times as short as 10 sec could be measured. Except for very slow runs, the exchange was followed to greater than 90% completion. The observed first-order rate constants were obtained graphically from the usual log $(C_t - C_\infty)$ *vs.* *t* plots. Final values were taken after some 15 half-lives where practical; otherwise rate coefficients were calculated by the method of Swinbourne[12] using data for the first 90% reaction. These plots were accurately linear for all the experimental data.

For each catalyst the reaction was repeated at four or five different concentrations of the same buffer. Acidity of the reaction mixture was checked at the beginning of a run and again near the end with a Radiometer Model 4 pH meter. Runs were rejected if the pH of the reaction medium differed by more than 0.03 pH unit from the concentrated buffer or changed by more than the same amount during the course of the reaction.

Certain assumptions are made throughout this paper for calculation of hydroxide ion concentrations. Acid dissociation of ammonium compounds is an isoelectric process, $RNH^+ = RN + H^+$, so that the salt effect on the activity coefficient term of the dissociation constant

$$K_a = \frac{[RN][H^+]}{[RNH^+]}\,\frac{\gamma_{RN}\gamma_{H^+}}{\gamma_{RNH^+}}$$

is expected to be small. Bates has found[13] that the ionic strength effect on the thermodynamic pK_a of substituted ammonium ions at $I = 0.1$ is to decrease pK_a by about 0.06 unit. We have applied this correction to give concentration dissociation constants, K_a', and used these values to compute hydroxide ion concentration, from the equation

$$[OH^-] = \frac{K_W^c[RN]}{K_a'[RNH^+]}$$

where K_w^c is the concentration equilibrium constant for water.

The situation is slightly different for the phenol buffers since the equilibrium is of the type $ROH = RO^- + H^+$. The complete expression for calculation of hydroxide ion concentration is

$$[OH^-] = \frac{K_w^\circ}{K_a^\circ}\,\frac{[RO^-]}{[ROH]}\,\frac{\gamma_{RO^-}\gamma_{H_3O^+}/\gamma_{ROH}}{\gamma_{OH^-}\gamma_{H_3O^+}/a_{H_2O}}$$

where K_w° and K_a° are thermodynamic dissociation constants. At an ionic strength of 0.1 the activity coefficient terms cancel each other to a good approximation;[14] neglect of these terms introduces an uncertainty of less than 0.03 into pK_a. Hence, for phenol buffers hydroxide ion concentration was calculated from

$$[OH^-] = \frac{K_w^\circ}{K_a^\circ}\,\frac{[RO^-]}{[ROH]}$$

Some of the uncertainty in k_{OH^-} may be due to these two approximation procedures.

Sampling by simple xylene extraction was not satisfactory for solutions containing phenol buffers because the phenol which was extracted into the xylene along with substrate quenched the scintillations very efficiently. The technique was modified in the following way: a 10-ml aliquot of reaction medium was added to a separatory funnel containing 5 ml of 1.0 *N* HCl and 15 ml of Et_2O. These were shaken together, and 10 ml of the aqueous phase was removed and extracted a second time with 15 ml of xylene. The xylene solution was treated in the same manner as before. This technique was satisfactory because phenols are completely or almost completely miscible with ether while 1,4-dicyano-2-butene is virtually insoluble in it, permitting a separation of the two compounds. This added extraction step did not noticeably diminish the reproducibility of the sampling.

Hydroxide ion catalyzed detritiation was studied as a function of temperature. Dilute (0.011 *N*), unbuffered solutions of $Ba(OH)_2$ were used for these studies and precautions were taken to exclude contamination by carbon dioxide.

(B) Dedeuteration. A sample of 1,4-dicyano-2-butene was partially deuterated by shaking an ethyl acetate solution of substrate over a basic mixture of H_2O and D_2O. The resulting compound contained an atom fraction of deuterium of about 0.3. Hydroxide-catalyzed dedeuteration studies were performed in the usual manner. The cyanocarbon from each aliquot was isolated and analyzed for deuterium by means of a Picker-Nuclear MS 9 mass spectrometer operating at an ionizing voltage of 12 eV. At this low voltage no follow-on decompositions of the parent ion occur so that the relative intensities of the parent peaks of the mono- and undeuterated species could be used to determine the fraction of deuterium remaining in any sample. First-order rate coefficients were computed from these data by a least-squares technique.

(C) Solvent Isotope Effect. Buffer solutions in D_2O were prepared by partial neutralization of triethylamine with DCl in D_2O. Detritiation experiments were replicated three times. A completely analogous set of runs was performed with buffer solution in H_2O. Under the chosen conditions of buffer ratio and triethylamine concentration about 4% of the observed rate was due to hydroxide ion catalysis and this was corrected for. Ionic strength was brought to 0.400 with NaCl for these experiments.

Equilibrium Measurements. The method of Dolman and Stewart[15] was employed to prepare $DMSO–H_2O–OH^-$ solutions of known basicity; care was exercised to avoid contamination by adventitious water. Dicyanobutene in DMSO was added to the medium by means of a calibrated syringe inserted through a rubber septum. The resulting solution of carbanion in DMSO was transferred to a quartz cell which was tightly stoppered, and the uv spectrum was recorded on a Cary Model 14 instrument. Since the anion is sensitive to oxygen, these experiments were conducted in an atmosphere of dry N_2. A shoulder on the anion peak at 300 mμ was used to calculate carbanion concentration in the samples. The anion maximum could not be observed because it was obscured by solvent. Media with H_- base strengths varying between 17.5 and 21.5 were used for the experiments. A preliminary p*K* of 21 was computed for 1,4-dicyano-2-butene. Although this scale was established for ionization of aromatic amines a calibration test with the carbon acid fluorene (pK = 18.5) strongly suggested that the scale is also appropriate to ionization of carbon acids.

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[10] H. Fischer and D. Rewicki, *Progr. Org. Chem.*, 7, 116 (1968); E. M. Arnett, *Progr. Phys. Org. Chem.*, **1**, 278 (1963).

[11] P. Kurtz, *Ann.*, 572, 23 (1951).

[12] E. S. Swinbourne, *J. Chem. Soc.*, 2371 (1960).

[13] H. B. Hetzer, R. G. Bates, and R. A. Robinson, *J. Phys. Chem.*, 67, 1124 (1963); R. G. Bates, *Ann. N. Y. Acad. Sci.*, **92**, 341 (1961).

[14] H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolyte Solutions," Reinhold Publishing Corp., New York, N. Y., 1950, p 525.

[15] D. Dolman and R. Stewart, *Can. J. Chem.*, 45, 911 (1967).

Results and Discussion

A matter of first concern is establishment of the nature of the exchange process. Melting points and mass and nmr spectra of substrate were unchanged after treatment with a medium more basic than those used for rate studies. On partial deuteration the methylene peaks in the nmr spectrum decreased while the vinyl resonance collapsed to a singlet; no new peaks appeared. We conclude that detritiation and dedeuteration are simple hydrogen-exchange processes which involve no molecular rearrangement or double bond migration.

Preliminary experiments indicated that detritiation was catalyzed by hydroxide ion and other bases. In order to evaluate the catalytic activity of these bases, it is first necessary to identify the role of solvent as a base.

Water Reaction. Solutions of tritiated cyanocarbon in 0.01 M hydrochloric acid and 0.09 M sodium chloride were thermostated at 25 and 50° for periods of 6.7×10^5 sec (8 days) and 1.0×10^6 sec (12 days), respectively. Aliquots were removed periodically and sampled for tritium remaining in the cyanocarbon by the usual technique. The reaction at 25° had an average of 3563 ± 45 cpm over the 8-day period and the experiment at 50° had 7363 ± 130 cpm over the longer period. No trend with time was observed in either case. The listed counting uncertainties fall within the precision limits of the sampling method, so no water-catalyzed detritiation is apparent. It is possible to place an upper limit on this reaction rate, however. A form of the first-order rate equation for low degree of turnover to product gives the maximum observed rate at 50° as

$$k_{\text{obsd}} = \frac{1}{\Delta t}\frac{\Delta C}{C} = 1.7 \times 10^{-8}\ \text{sec}^{-1}$$

where ΔC is the average deviation from the mean at the end of the observation period $t = 10^6$ sec, and C is the average counts per minute at $t = 0$ sec. The corresponding rate coefficient for bimolecular reaction with water is $3 \times 10^{-10}\ M^{-1}\ \text{sec}^{-1}$. Applying the Arrhenius equation, with use of a value for the frequency factor of $A = 2 \times 10^{10}\ M^{-1}\ \text{sec}^{-1}$ as determined in this laboratory for the very similar detritiation reaction of malononitrile with water, leads to an energy of activation of ≥ 29.2 kcal/mole. From this the bimolecular catalytic constant for water at 25° has a maximum value of $8 \times 10^{-12}\ M^{-1}\ \text{sec}^{-1}$. Combining this with the measured pK_a, and applying an appropriate isotope effect correction, a value of $10^{11}\ M^{-1}\ \text{sec}^{-1}$ can be computed for the maximum rate of recombination of 1,4-dicyano-2-butene anion with hydronium ion. This is on the order of magnitude of a diffusion-controlled process. Since the water-catalyzed rate of detritiation may well be slower than the estimated maximum, a smaller value for the rate of the reverse step is entirely possible. Thus, our data are consistent with, but do not require, a diffusion-limited reaction for the recombination process, $R^- + H_3O^+$.

Hydroxide Ion Reaction. Hydroxide ion catalyzed detritiation was measured in both unbuffered and buffered media. In order to have conveniently measurable rates, a maximum hydroxide ion concentration of 0.01 M could be used in the unbuffered system; $Ba(OH)_2$ was chosen as the source of hydroxide. At 25° and an ionic strength of 0.1 the hydroxide ion catalytic constant k_{OH^-} was found to be 0.205 ± 0.006 $M^{-1}\ \text{sec}^{-1}$. Hydroxide ion concentration was varied over a factor of 4, and the reaction was found to be accurately first order in hydroxide.

Ammonia (pK_a = 9.18)[16] and morpholine (pK_a = 8.43)[17] buffers were also used to measure k_{OH^-}. Catalytic coefficients for the base form of the buffers was determined by varying free amine concentration at a constant buffer ratio. Least-squares slopes of plots of k_{obsd} *vs.* [amine] gave catalytic constants for ammonia, $k_B = 4.90 \times 10^{-5}\ M^{-1}\ \text{sec}^{-1}$, and morpholine, $k_B = 1.46 \times 10^{-4}\ M^{-1}\ \text{sec}^{-1}$.

Dependence of the rate on hydroxide ion concentration was then determined by varying both ammonia and morpholine buffer ratios through a factor of 4. The rate coefficient for hydroxide, k_{OH^-}, was obtained from plots of $[OH^-]$ *vs.* $(k_{\text{obsd}} - k[B])$; the values were $k_{OH^-} = 0.188$ and $0.225\ M^{-1}\ \text{sec}^{-1}$ from ammonia and morpholine buffers, respectively. Estimates of k_{OH^-} could also be made from k_{obsd} *vs.* [B] plots for the other buffers used in this study; these values all lie between those given above so we have taken $k_{OH^-} = 0.207 \pm 0.020\ M^{-1}\ \text{sec}^{-1}$ at 25°. Although this uncertainty is somewhat larger than desired, it appears to be random and lacks a systematic change with catalyst strength. It should be noted that direct determination of k_{OH^-} gave the very similar value of $0.205 \pm 0.006\ M^{-1}\ \text{sec}^{-1}$.

The rate of the hydroxide ion catalyzed detritiation was measured as a function of temperature over the range of 5–35° in water with an ionic strength of 0.1. The results were treated in the usual fashion to obtain a set of activation parameters (Table I). A substantial activation energy and a large negative entropy of activation (or equivalently a low frequency factor) are consistent with a reaction proceeding by a slow proton abstraction. Pearson and Dillon[18] have compiled a list of activation energies and entropies for slow proton transfers from β-diketones and nitroalkanes; the activation energies lie in the range of 14–23 kcal mole^{-1} and the entropies of activation lie between −15 and −26 eu. The results for detritiation of dicyanobutene lie well within this range, and the conclusion is that the hydroxide ion catalyzed detritiation shows typical behavior for a slow proton removal from a weak acid species.

Table I. Activation Parameters for Detritiation of 1,4-Dicyano-2-butene by Hydroxide Ion in Water

$E_a = 15.3$ kcal mole^{-1}
$A = 3.7 \times 10^8\ M^{-1}\ \text{sec}^{-1}$
$\Delta H^{\ddagger} = 14.7$ kcal mole^{-1}
$\Delta S^{\ddagger} = -21.5$ eu (for k in $M^{-1}\ \text{sec}^{-1}$)
$\Delta G^{\ddagger} = 21.1$ kcal mole^{-1}

The transfer process with hydroxide ion is $RH + OH^- = R^- + H_2O$; the rate in the forward direction and an approximate pK are available. These can be combined with $K_w{}^c$ to give a bimolecular rate coefficient for reaction between the cyanocarbon anion and water. The calculated result is $k_r = 1 \times 10^6\ M^{-1}$

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(16) R. G. Bates and G. D. Pinching, *J. Res. Natl. Bur. Std.*, **42**, 419 (1949).

(17) H. B. Hetzer, R. G. Bates, and R. A. Robinson, *J. Phys. Chem.*, **70**, 2869 (1966). This paper gives the thermodynamic pK_a of morpholinium ion as 8.492.

(18) R. G. Pearson and R. L. Dillon, *J. Am. Chem. Soc.*, **75**, 2439 (1953).

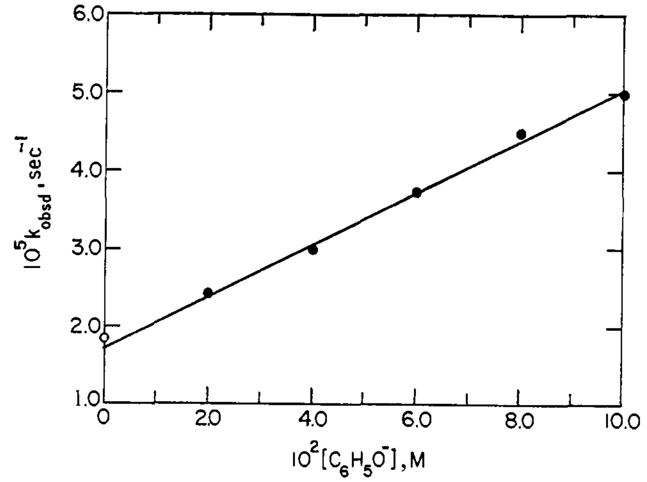

Figure 1. First-order rate coefficients for detritiation with phenol buffers, $I = 0.1$ and $[B^-]/[BH] = 0.998$. The line was drawn by least-squares analysis of the data and the circled point is a calculated intercept based on $k_{OH^-} = 0.205\ M^{-1}\ sec^{-1}$.

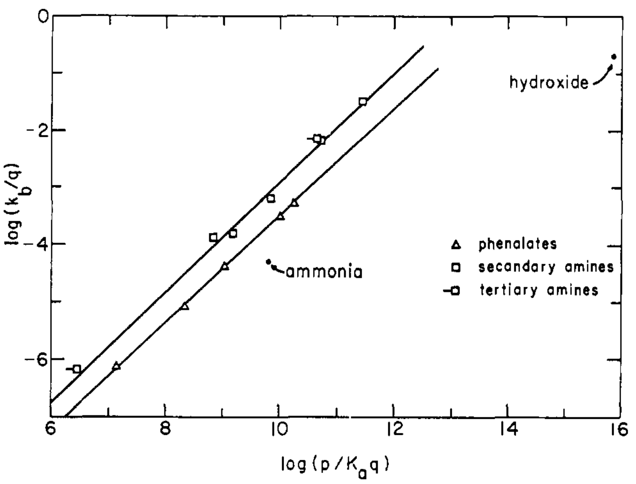

Figure 2. Brønsted plot for detritiation of 1,4-dicyano-2-butene by phenolate and secondary amine bases; points for hydroxide ion and ammonia and two points for tertiary amines are also included.

sec^{-1}. Even with recognition of a possible large uncertainty in the cyanocarbon acidity, this value is considerably below the diffusion limit.

General Base Catalysis. Studies with ammonia and morpholine buffers mentioned above gave strong indication of a general base catalyzed detritiation. A more systematic set of experiments was performed with two different base types; a group of anionic bases, phenolates, and another group of uncharged bases, secondary amines, were employed to determine the Bronsted β. Figure 1 is a representative example of the technique employed to determine the catalytic coefficients and demonstrates the large contribution to the rates which is made by the general base catalysis. In Figure 2 the catalytic constants for phenolates and secondary amines are shown on a Bronsted plot; the straight lines of this diagram were determined by a least-squares procedure. Both rate and equilibrium constants were corrected with statistical factors p and q, where p is the number of equivalent protons in the acidic form of the buffer and q is the number of equivalent sites which can add a proton.[19] The two classes of bases generate distinctly different lines while maintaining the same, or very similar, slopes; for phenolates $\beta = 0.94 \pm 0.02$ and for secondary amines $\beta = 0.98 \pm 0.08$. The catalytic constants are listed in Table II.

The Bronsted correlation for phenolate anions is quite good; this probably reflects the fact that, with limitation of changes to only a single substituent, there are relatively minor structural perturbations on the overall system. On the other hand, agreement among the amines is considerably less satisfactory, the average deviation of log k_b from the calculated value is 0.14. Probable explanations for the observed scatter are a greater uncertainty of the dissociation constants for amines in 0.1 M aqueous salt solutions and relatively larger structural variations among the bases caused by introduction of substituents at or near the basic site. The possibility of steric hindrance will be considered in a latter section.

The two tertiary amines for which catalytic constants were determined, 3,4-lutidine and triethylamine, fall almost on the same Brønsted plot as do the secondary amines (Figure 2). Apparently the structural alterations between the amine types are not large enough to cause demonstrably different behavior. The fact that lutidine is an aromatic molecule while the others are all aliphatic seems also to be unimportant. These results are in marked contrast to the amine-catalyzed decomposition of nitramide, where separate parallel Brønsted lines are observed for each of the four amine classes: primary, secondary, tertiary, and tertiary

Table II. Catalytic Coefficients for Detritiation of 1,4-Dicyano-2-butene-1-*t* in Water at 25°, $I = 0.1$

Base	$[B^-]/[BH]$	pK_a	$10^7 k_b$, M^{-1} sec^{-1}
Phenolates			
p-Cresol	0.995	10.262[a]	5610
Phenol	0.998	9.998[a]	3310
m-Chlorophenol	0.887	9.02[a]	428
m-Nitrophenol	4.32	8.399[a]	87.9
p-Nitrophenol	2.56	7.149[a]	7.30

Base	$[B]/[BH^+]$	pK_a	$10^4 k_b$, M^{-1} sec^{-1}
Secondary amines			
Piperidine	1.00	11.12[b]	363
3-Methylpiperidine	1.12	11.07[b]	127
Diethylamine	0.804	10.67[b]	77.5
l-Ephedrine	3.72	9.546[b]	6.96
Diethanolamine	3.94	8.883[b]	1.67
Morpholine	4.19	8.492[c]	1.46

Base	$[B]/[BH^+]$	pK_a	k_b, M^{-1} sec^{-1}
Miscellaneous			
Hydroxide	. . .	15.53[d]	2.07×10^{-1}
Triethylamine[e]	0.235	10.65[b]	7.56×10^{-3}
Ammonia	1.31	9.245[f]	4.90×10^{-5}
3,4-Lutidine	4.00	6.46[b]	6.84×10^{-7}

[a] G. Kortüm, W. Vogel, and K. Andrussow, "Dissociation Constants of Organic Acids in Aqueous Solution," Butterworth & Co., Ltd., London, 1961. [b] D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution," Butterworth & Co., Ltd., London, 1965. [c] Reference 17. [d] $-$Log $K_w{}^c/55.5$. [e] $I = 0.4$. [f] Reference 16.

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(19) S. W. Benson, "The Foundations of Chemical Kinetics," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, p 565; D. M. Bishop and K. J. Laidler, *J. Chem. Phys.*, **42**, 1688 (1965).

heterocyclic amines.[20] Our observation does not negate the usual explanation for distinctive behavior for each class of amine base.[21] In the present case the conjugate acid of the catalyst is virtually formed in the transition state which makes it reasonable that structural variations will have a relatively minor role. But for nitramide decomposition, with $\beta = 0.64$, sensitivity to base and solvent properties should be approaching a maximum. Even in the present case ammonia is enough different from the other amines to have a catalytic coefficient smaller than expected by a factor of 10.

Hydroxide ion is some three powers of ten less effective kinetically than predicted from an extrapolation of the phenolate correlation. Similar anomalous behavior of the acid or base resulting from self-dissociation of water is rather common. For example, in the general acid catalyzed hydrolysis of cyanoketene–dimethylacetal the rate coefficient for hydronium ion is several powers of ten below the Brønsted line for carboxylic acids.[22] Both the solvated proton and hydroxide ion are such unique species in an aqueous solution that deviation from a Brønsted correlation is not surprising. The precise reasons for the direction and magnitude of the observed differences are not clear but they probably involve a combination of factors related to hydrogen bonding and solvation of the ions. It is important to note that without the anomalously low rate for hydroxide ion, demonstration of general base catalysis would have been virtually impossible. With $\beta = 0.94$ and a "normal" hydroxide reaction, the added effects from weak base catalysts would have been essentially within the experimental error of the hydroxide effect alone.

Mechanistically, general catalysis is a necessary concomitant of a rate-determining proton transfer; the above data, therefore, provide firm evidence for base-catalyzed slow proton removal from 1,4-dicyano-2-butene.

Evidence for general base catalysis of the proton removal from carbon bases has not usually been as obvious as in this instance. For example, detritiation of phenylacetylene by several bases was observed,[6a] but quantitative interpretation was complicated by salt and solvent effects, leading to the conclusion that only a somewhat inconclusive case for general catalysis could be made. In contrast, catalytic coefficients of 15 separate bases were determined in the present study.

Catalytic constants for hydroxide ion catalyzed detritiation of phenylacetylene and 1,4-dicyano-2-butene at 25° are 276 and 0.207 M^{-1} sec^{-1}, respectively; for catalysis by ammonia the respective constants are 7.5×10^{-3} and 4.9×10^{-5} M^{-1} sec^{-1}. The fact that the catalytic coefficients are larger for phenylacetylene than for 1,4-dicyano-2-butene while phenylacetylene is thought to be a weaker acid implies that the reverse process for phenylacetylene, $R^- + BH^+$, approaches more nearly to full diffusion control.

Isotope Effects. The rate of triethylamine-catalyzed detritiation of substrate was measured in H_2O and D_2O at 25°. The ratio of rates in these two solvents was found to be $k_{Et_3N}{}^{H_2O}/k_{Et_3N}{}^{D_2O} = 1.24$. This number is the pure "medium" effect, more specifically to be identified as a secondary solvent isotope effect. Similar ratios have been measured in comparable reactions with other base catalysts and have been found to lie in the range $1.14 < k_B{}^{H_2O}/k_B{}^{D_2O} < 1.26$.[23]

The ratio of rates of hydroxide ion catalyzed dedeuteration and detritiation at 25° with an ionic strength of 0.1, k_D/k_T, was found to be 1.8. Converting this to a primary deuterium isotope effect by the use of the relationship of Swain *et al.*,[24] $(k_H/k_D)^{1.442} = k_H/k_T$, leads to $k_H/k_D = 3.9$. This is approximately one-half of a "full" kinetic isotope effect. Variation of primary isotope effects has received considerable theoretical attention recently,[25] and there are definite indications that the effect passes through a maximum[26] in the vicinity of $\Delta pK = 0$, where ΔpK is the difference in acidity between substrate and catalyst. On the basis of these correlations a ΔpK of 5, as existing here, should be associated with an isotope effect of about 6.5 rather than the value of 3.9 found in the present case. This apparent anomaly is a direct result of the fact that the reverse reaction rate is close to diffusion controlled; *i.e.*, the rate of reaction is determined by the thermodynamics of ionization. Hence, the primary kinetic isotope effect is almost precisely the isotope effect on the cyanocarbon acidity. An estimate of the magnitude of the deuterium isotope effect on acidity of carbon acids can be made from the data on keto–enol equilibria of Long, *et al.*,[23a,b] who report isotope effects on both the keto–enol equilibrium and enol ionization for the two substrates 2-acetylcyclohexanone and methylacetylacetone. These values can be combined to give the isotope effect on the ionization of the keto form

$$K_a{}^{KH}/K_a{}^{KD} = \frac{K_{eq}{}^{H}}{K_{eq}{}^{D}}\,\frac{K_a{}^{EH}}{K_a{}^{ED}}$$

For 2-acetylcyclohexanone $K_a{}^{KH}/K_a{}^{KD} = 3.8$ and for methylacetylacetone $K_a{}^{KH}/K_a{}^{KD} = 3.4$, numbers which although referring to the two solvents H_2O and D_2O are nevertheless in the vicinity of the kinetic isotope effect for proton removal from 1,4-dicyano-2-butene.

Steric Hindrance. Steric inhibition of rates of general base catalyzed reactions can sometimes be effected by surrounding the base with bulky substituents. This is usually tested by employing pyridine or 3,4-lutidine and 2-methyl- and 2,6-dimethylpyridine as catalysts. In such reactions as general base catalyzed mutarotation of glucose, hydrolysis of methylethylene phosphate,[27] and iodination of ketones and nitromethane,[28] 2,6-lutidine is a much poorer catalyst than would be expected on the basis of its ionization constant. The unhindered member of this series, 3,4-lutidine, proved to be such a weak base for the detritiation of 1,4-

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[28] J. A. Feather and V. Gold, *Proc. Chem. Soc.*, 306 (1963); *J. Chem. Soc.*, 1752 (1965).

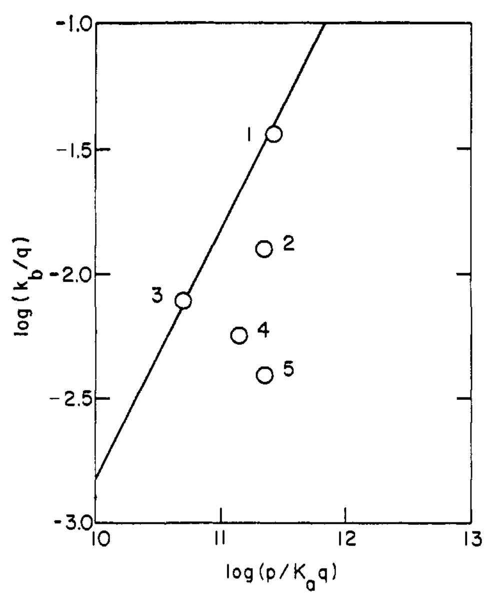

Figure 3. Brønsted correlation of sterically hindered piperidine catalysts: (1) piperidine, (2) 3-methylpiperidine, (3) diethylamine, (4) 2,6-dimethylpiperidine, (5) 2,2,6,6-tetramethylpiperidine. The solid line is that generated by unhindered secondary amines. The point for diethylamine is included for clarification of the scale.

dicyano-2-butene that the prospect of significantly lower rates resulting from steric hindrance with 2,6-lutidine made reaction times unacceptably long. An assortment of methyl-substituted piperidine catalysts was employed because of their more basic properties; the results are given in Figure 3 and Table III.

Table III. Catalytic Coefficients of Some Methyl-Substituted Piperidines at 25°

Catalyst	Log p/K_aq^a	Log k_b	Δ Log $k_b{}^b$
Piperidine	11.42	−1.44	−0.03
3-Methylpiperidine	11.37	−1.90	−0.44
2,6-Dimethylpiperidine	11.13	−2.25	−0.57
2,2,6,6-Tetramethylpiperidine	11.37	−2.41	−0.94

[a] D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution," Butterworth & Co., Ltd., London, 1965. [b] Deviation from the Brønsted catalysis law is given by $\Delta \log k_b = \log k_b - \beta \log p/K_aq - \log G$, where $\beta = 0.98$ and $\log G = 12.658$, parameters derived from catalytic behavior of secondary amines.

Departure of the catalytic efficiency of the base from that estimated from the Brønsted behavior of similar bases is expressed as

$$\Delta \log k_b = \log k_b - \beta \log p/K_aq - \log G$$

where log k_b is the experimental rate coefficient, and the parameters β and G arise from the correlation of unhindered secondary amines. Values of Δ log k_b increase with the number of methyl groups on carbon atoms adjacent to the basic site. Although the rate of detritiation as catalyzed by 2,2,6,6-tetramethylpiperidine, the most hindered base, is ninefold slower than predicted by the Brønsted law, this retardation is surprisingly modest when compared with the magnitudes of similar effects in solvolysis reactions.[29] In bromination of ketones and nitromethane, which are general base catalyzed slow proton transfers, 2,6-lutidine was found to be slower than expected by factors ranging from 7 to 13.[28] Clear evidence of a steric effect was not observed, however, in the hydration of acetaldehyde by carboxylic and alkylpyridinium acids.[30] Because of a general lack of data on steric hindrance to proton-transfer processes, it is difficult to comment on the relative magnitude of this effect; it is not even apparent whether the small effect contains mechanistic information or whether it is due to differences between alkylpiperidines and pyridines. It may be pointed out, however, that molecular models suggest no obvious reason why the nitrogen atom is inherently less encumbered in 2,2,6,6-tetramethylpiperidine than in 2,6-lutidine.

The Reverse Reaction, R⁻ + BH, and the Character of the Transition State. Using the tentative value of pK_a = 21 for the cyanocarbon acid, one can calculate for the various catalysts the rates of the reverse reactions, but to do this some preliminary corrections must be made on the data of Table II. Since pK_a is for the ordinary hydrogen species, the rates of interest are

$$H_2C(CN)CH{=}CHCH_2(CN) + B \underset{k_r}{\overset{k_f}{\rightleftharpoons}} H_2C(CN)CH{=}CH\bar{C}H(CN) + BH^+$$

To obtain k_f from the observed detritiation rates, one must correct for the primary isotope effect, a factor of 7.1, and also for the statistical effect of the four equivalent hydrogens, a factor of 4. Application of these leads to the k_r values of Table IV.

Table IV. Calculated Rate Coefficients for the Recombination of 1,4-Dicyano-2-butene Anion with Acids at 25°, $R^- + BH = RH + B^-$

BH	$10^5k_f{}^H$, M^{-1} sec^{-1}	$K_a{}^{BH}$	$10^{-8}k_r{}^H$, M^{-1} sec^{-1}
Water	5.89×10^5	1.80×10^{-16}	0.01
Ammonium	1.39×10^2	5.69×10^{-10}	8
Piperidinium	1.03×10^5	7.59×10^{-12}	80
Diethylammonium	2.20×10^4	5.36×10^{-11}	120
l-Ephedrinium	1980	2.85×10^{-10}	60
Diethanolammonium	475	1.31×10^{-9}	60
Morpholinium	415	3.22×10^{-9}	300
p-Cresol	1600	5.46×10^{-11}	9
Phenol	940	1.00×10^{-10}	9
m-Nitrophenol	25	3.98×10^{-9}	10
p-Nitrophenol	2.08	7.09×10^{-8}	15

Since pK_a is of low accuracy it is the comparative data of Table IV which have the greater significance. The absolute values of k_r may be in error by a substantial factor.

In the interesting analysis by Eigen[31] of simple proton-transfer reactions, it is noted that an important consequence of the existence of a diffusion-controlled limiting rate is that when ΔpK for the reacting acid and base species becomes sufficiently large, one reaction, the "fast" process, becomes diffusion controlled with

(29) E. L. Eliel, "Stereochemistry of Carbon Componds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 379; A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 93; E. R. Thornton, "Solvolysis Mechanisms," Ronald Press Co., New York, N. Y., 1964, p 91.

(30) R. P. Bell, M. H. Rand, and K. M. A. Wynne-Jones, *Trans. Faraday Soc.*, **52**, 1093 (1956).

(31) M. Eigen, *Angew. Chem.*, **75**, 489 (1963).

therefore a Brønsted coefficient, say α, of zero. Consequently for the reverse, "slow" process, since $\alpha + \beta = 1$, the Brønsted coefficient β must be identically unity. As the ΔpK becomes smaller, the "fast" process will become less rapid than the diffusion limit and α can rise above zero. Correspondingly, β will become less than unity. Implicit in this analysis is the proposal that once the Brønsted slopes have departed from zero and unity, they become functions of ΔpK so that Brønsted plots are really curved.

The striking feature of the data of Table IV is that, except for reactions with the acids H_2O and ammonium ion, the values of k_r are close to those expected for a diffusion-controlled rate. This is, of course, consistent with the facts that the Brønsted slopes, *e.g.*, of $\alpha = 0.05$ and $\beta = 0.94$, for the phenols are close to the limiting values of zero and unity and that the kinetic isotope effect is low. Actually the fact that the Brønsted slopes are not quite the limiting values, combined with evidence for steric effects, suggests that the reaction is not yet fully diffusion controlled. This conclusion, incidentally, is probably more significant than any reached from the somewhat approximate values of the k_r values themselves.

The implication of these remarks to the transition state for the reaction is that structurally this must have very nearly the dimensions of an "encounter" species from diffusion of R^- toward BH. From the standpoint of the detritiation process, this says that the hydrogen being removed is almost entirely transferred from RH to B at the transition state.

This same conclusion could have been arrived at in another way. Brønsted slopes are commonly interpreted as indicating the degree to which the transition states resemble reaction products;[32] this concept was recently given theoretical support by Marcus,[33] who equated the Brønsted exponent α (or β) to the order of the bond being formed in the reaction. The β of approximately unity for the present reaction, then, indicates that the bond between the base catalyst and the proton is almost completely formed in the transition state.

Recalling that the reverse reaction of carbanion with phenols occurs at close to the diffusion-controlled rate, it is of interest to speculate on the reason for the generally faster reaction of amine bases as compared to the phenols, *e.g.*, the two separate lines of Figure 1. A plausible explanation is that, since the reverse reaction for the amines, $R^- + R_3NH^+$, occurs between oppositely charged ions, electrostatic interaction causes the rate to be larger than for the phenol case. This, then, is reflected, *via* the equilibrium, into a faster rate for the forward reaction. Calculation by conventional means does in fact indicate that the ion–ion diffusion rate should be faster than that for ion–molecule by a factor of about 2.5; this is roughly the observed effect.[34]

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(32) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, p 157; reference 4, Chapter 10.

(33) R. A. Marcus, *J. Phys. Chem.*, 72, 891 (1968).

(34) K. Wiberg, "Physical Organic Chemistry," John Wiley & Sons, Inc., New York, N. Y., 1964, p 324.