Base-Catalyzed Hydrogen Exchange of Phenylacetylene and Chloroform. Brønsted Relations and Normal Acid Behavior

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Abstract: Rates of detritiation of phenylacetylene-*t* and chloroform-*t* measured in amine buffer solutions show simple general base catalysis and give Brønsted relations with essentially unit exponents: $\beta = 0.99 \pm 0.05$ for phenylacetylene and $\beta = 1.12 \pm 0.05$ for chloroform. These results are taken to indicate that proton transfer is rapid and reversible and separation of the proton transfer products is the rate-determining step in these reactions, i.e., that phenylacetylene and chloroform are functioning as normal (in the Eigen sense) rather than as pseudo acids. Arguments based upon Marcus and Lewis-More O'Ferrall rate theory are made in support of this view. The data are also used to estimate aqueous solution pK_a's from these carbon acids: $pK_a = 20.0$ for phenylacetylene and 24.1 for chloroform.

Phenylacetylene and chloroform are weak carbon acids whose conjugate bases are carbanions in which the basic electron pairs presumably are localized on single carbon atoms. Electronic structures such as this are not typical of carbon bases: the basic electron pairs in most carbon bases are strongly delocalized over several atomic centers, and it is, in fact, this delocalization to which most carbon acids owe their acidity. It is commonly believed that the structural reorganization which accompanies delocalized carbon base formation is a major factor responsible for the intrinsic slowness of proton transfer from carbon, and that proton transfer between the oxygen and nitrogen basic centers of "normal"[1] acids and bases is fast because here the basic electron pairs are localized on single atoms.[1,2] This idea leads to the suggestion that phenylacetylene and chloroform might show behavior characteristic of normal acids rather than that typical of regular carbon "pseudo" acids. It is of interest to determine to what extent this is so.

An important respect in which normal acids differ from pseudo acids is the nature of their Brønsted correlations. Normal acids usually give biphasic Brønsted plots ("Eigen curves") with limbs of zero and unit slope connected by intermediate regions of relatively sharp curvature. Pseudo acids, on the other hand, give Brønsted plots in which this intermediate region is much broader and the curvature is often so gradual as to go undetected; pseudo-acid Brønsted plots are therefore generally linear and have slopes significantly greater than zero but less than one.

Construction of Brønsted plots for the acid-base reactions of phenylacetylene and chloroform is complicated by the fact that general base catalysis in these systems is difficult to detect and the requisite catalytic coefficients are consequently not easily determined. For example, in an early study of protium-tritium exchange of phenylacetylene in aqueous buffer solutions of tris(hydroxymethyl)methylamine, 2,6-lutidine, and ammonia, variations in rate with changes in buffer concentration were found to be small, and sometimes erratic, and accurate rate constants for buffer catalysis could not be determined.[3] Marginal general base catalysis was also once reported for protium-deuterium exchange of chloroform in methylamine buffers,[4] but a later study of this exchange using tritium as a tracer and piperidine and morpholine buffers produced only specific hydroxide ion catalysis.[5]

We have found that general base catalysis of protium-tritium exchange in these two acids is indeed weak. But by working carefully we have been able to measure reliable values of general base catalytic coefficients for both substances, and, with these, to construct accurate and informative Brønsted plots.[6]

Experimental Section

Materials. Phenylacetylene-*t* was prepared by exchange with tritiated water in the presence of a basic catalyst: 10 g of phenylacetylene (Chemical Samples Co.) was shaken overnight with 10 mL of tritiated water (10 mCi/mL) containing 5 g of dissolved sodium carbonate. The organic layer was then separated, dried over anhydrous sodium sulfate, and distilled, bp 141-142 °C. Chloroform-*t* was prepared in a similar manner using 0.1 M NaOH as the catalyst and shaking for 2 days. The distilled product had bp 61-62 °C.

Cyanoethylamine was prepared by the reaction of acrylonitrile with aqueous ammonia[7] and purified by distillation, bp 70-71 °C (10 mm). Titration with perchloric acid in acetic acid solution showed it to be 99.7% pure, and the Hinsberg test indicated the absence of secondary amines. Trifluoroethylamine was prepared by reducing trifluoroacetamide with lithium aluminum hydride.[8] It was purified as its hydrochloride salt by recrystallization from absolute ethanol; the amine was then recovered by neutralizing the salt with sodium hydroxide and the resulting product was distilled, bp 38-38.5 °C.

All other materials were best available commercial grades.

pK_a Determination. The pK_a of the conjugate acid of 2,2-dimethoxyethylamine was determined by measuring the pH of partly neutralized (HCl) solutions of the amine (Aldrich Chemical Co.) of known concentrations. Measurements were made with a Beckman Model 1019 Research pH meter on solutions thermostated at 25.0 ± 0.1 °C. Concentrations were calculated from the weights of solution components used.

Kinetics. Wholly aqueous buffer or hydroxide ion solutions were allowed to come to temperature equilibrium with the constant-temperature bath. Sufficient quantities of tritiated substrate were then added to give final substrate concentrations ca. 1×10^{-3} M in the case of phenylacetylene and 5×10^{-3} M in the case of chloroform, and the resultant mixtures were shaken vigorously for 30-40 s to effect dissolution. Portions of these reaction mixtures were then quickly transferred to screw-cap vials, taking care to leave as little air space as possible in order to minimize partitioning of the volatile substrates between solution and vapor phases, after which these vials were placed in the constant-temperature bath.

At appropriate times, vials were taken from the bath, and 10-mL aliquots were removed by volumetric pipet and quenched by running them into 60-mL separatory funnels containing 15 mL of toluene (accurately pipetted) and enough aqueous HCl to neutralize all of the base. The funnels and their contents were shaken, and the toluene layers were removed and dried over $CaCl_2$. Ten-milliliter aliquots of these dried toluene solutions were then combined with 10 mL of toluene-based counting solution (8 g of 2,5-diphenyloxazole and 0.1 g of 1,4-bis[2-(5-

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(4) Hine, J.; Peek, R. C.; Oaks, B. D. *J. Am. Chem. Soc.* **1954**, *76*, 827-829.
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(6) Part of this work was communicated in preliminary form: (a) Kresge, A. J.; Lin, A. C. *J. Chem. Soc., Chem. Commun.* **1973**, 761-762. b) Dahlberg, D. B.; Kresge, A. J.; Lin, A. C. *Ibid.* **1976**, 35-36.
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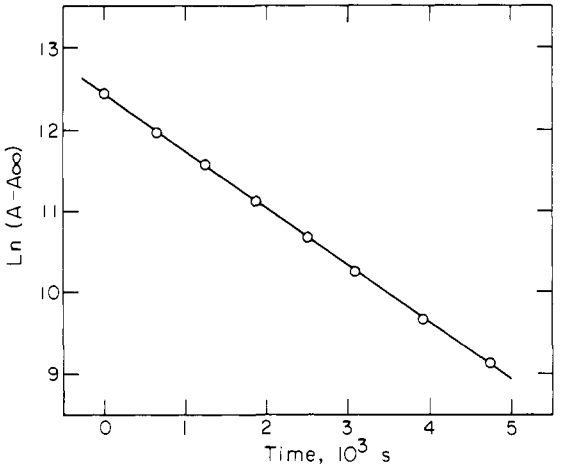


Figure 1. Sample first-order kinetic plot. Detritiation of phenylacetylene-*t* in aqueous tris(hydroxymethyl)methylamine buffer: $[BH^+] = [B] = 0.100$ M, ionic strength = 0.100 M, and temperature = 24.6 °C. Least-squares analysis gave $k_{obsd} = (6.994 \pm 0.040) \times 10^{-4}$ s^{-1} with standard deviation in ln $(A - A_\infty)$ = 0.0172 (1.7%) and correlation coefficient = 0.9999.

phenyloxazolyl)]benzene per liter), and the resulting mixtures were assayed for radioactivity using a Packard 314 Ex liquid scintillation counter. Measurements were continued for sufficiently long times to ensure good counting statistics (at least 10^5 counts).

Rate constants were calculated by least-squares analysis as slopes of plots of ln $(A_t - A_\infty)$ vs. time (A = counts per minute). Eight to ten values of A_t were generally used, and infinite-time radioactivities were determined after more than 15 half-lives. In the case of some very slow reactions, exchange was hastened for the determination of A_∞ through the addition of solid sodium hydroxide to the reaction mixture; this did not change the reaction volume significantly. Data obtained in this way conformed to the first-order rate law over the entire extent of reaction measured, which was always at least 4 half-lives. A sample kinetic plot is shown in Figure 1.

Results

pK_a Determination. pH measurements were made on two series of 2,2-dimethoxyethylamine buffer solutions of constant buffer ratio ($[BH^+]/[B] = 0.97$ and 0.38) and decreasing buffer concentration. Each series consisted of 12 solutions spaced roughly equally over the concentration range $[BH^+] = 0.09$–0.008 M. No other electrolyte was added, and the ionic strength (μ) was therefore equal to $[BH^+]$.

These data were extrapolated to zero ionic strength using the function given in eq 1 where b is the ionic interaction coefficient

$$\text{pH} + \log([BH^+]/[B]) - 0.5115\sqrt{\mu}/(1 + \sqrt{\mu}) = pK_a - b\mu \quad (1)$$

in the expression for the activity coefficient of BH^+, $\log y_{BH^+} = -0.5115\sqrt{\mu}/(1 + \sqrt{\mu}) + b\mu$. Least-squares analysis gave pK_a = 8.543 ± 0.002 and b = 0.178 ± 0.050; this result for 25 °C is consistent with the value, pK_a = 8.35, reported for 35 °C.[9]

Kinetics. First-order rate constants for the loss of tritium from phenylacetylene-*t* and chloroform-*t* were measured in buffer solutions of a number of primary amines, some secondary, tertiary, and aromatic amines, and two dibasic amines. Series of buffer solutions of constant buffer ratio but changing buffer concentration were used; buffer concentrations were generally varied by a factor of 10, and five concentrations were usually used to make up a series. Ionic strengths were kept constant at the relatively low value of 0.100 M in order to ensure that reliable estimates of solute activity coefficients could be made. For approximately half the amines, measurements were carried out in two such series of different buffer ratio, and for the rest, a single series were used. The results obtained are summarized in Tables S1–S3.[10]

(9) Hine, J.; Yeh, Y. Y.; Schmalsteig, F. C. *J. Org. Chem.* **1970**, *35*, 340–344.

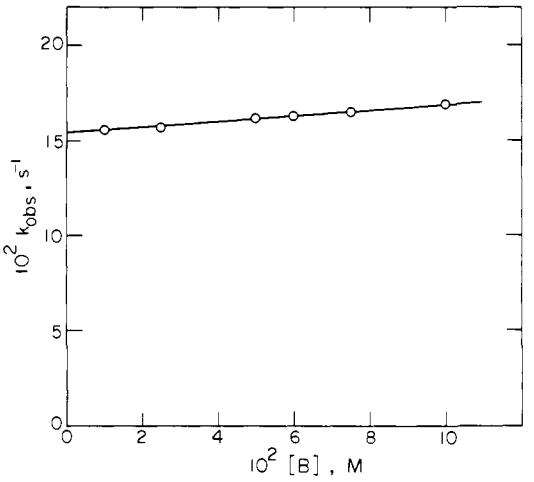


Figure 2. Sample plot showing dependence of observed first-order rate constants on buffer base concentration. Detritiation of phenylacetylene-*t* in aqueous 2,2-dimethoxyethylamine buffers: $[BH^+]/[B] = 1.00$, ionic strength = 0.100 M, and temperature = 24.6 °C. Least-squares analysis gave $k_B = (1.411 \pm 0.092) \times 10^{-3}$ M^{-1} s^{-1} with a standard deviation in k_{obsd} of 0.068×10^{-2} (0.4% of average value of k_{obsd}) and a correlation coefficient of 0.9916.

General base catalytic coefficients were evaluated by fitting observed first-order detritiation rate constants to the rate law given as eq 2. In a series of buffer solutions of constant buffer ratio

$$k_{obsd} = k_{HO^-}[HO^-] + k_B[B] \quad (2)$$

such as those used here, hydroxide ion concentrations generally remain constant. The first term of this rate law will therefore be constant, and observed rates of detritiation should thus increase linearly with increasing buffer base concentration. This behavior was observed for all of the buffer solutions examined here; a sample plot illustrating the relationship is shown in Figure 2. Though buffer catalysis in this example is unmistakable, it is also quite weak. This was commonly found to be the case throughout the present study; buffer catalysis, moreover, was generally weaker for hydrogen exchange in chloroform than in phenylacetylene.

This technique of keeping stoichiometric buffer ratios constant did not always succeed in preventing hydroxide ion concentrations from changing along a series of solutions. With two of the strongest bases used, methylamine and piperidine, significant hydrolysis of the amine to hydroxide ion and amine conjugate acid occurred, and the extent of this hydrolysis varied systematically with buffer concentration. The result was series of solutions whose hydroxide ion concentrations droped appreciably with decreasing buffer concentration, and this had the effect of exaggerating the dependence of k_{obsd} on buffer concentration. Such "buffer failure" was corrected for by adjusting observed rate constants to values they would have had under conditions of constant hydroxide ion concentration. This was accomplished by calculating the extent of hydrolysis and the concentration of hydroxide ion for each solution in a given series, noting the decrement, $\delta[HO^-]$, by which the hydroxide ion concentration of each successively more dilute solution fell below that of the most concentrated buffer in the series, and then adding the appropriate correction, $(k_{HO^-})(\delta[HO^-])$, to the observed rate constant for that solution. This method requires a prior knowledge of k_{HO^-}, and that was supplied for chloroform, the only substrate for which these adjustments were required, by separate rate measurements in sodium hydroxide solutions (see Table S4[10]). The method gives adjusted rate constants which, when analyzed according to eq 2, provide estimates of k_{HO^-} which are largely independent of the value put into the correction, provided that the correction is not large. It is significant, therefore, that for methylamine buffers, where the largest rate adjustement was 6%, analysis of the adjusted data gave $k_{HO^-} = 0.172$ M^{-1} s^{-1}, in good agreement with the directly

(10) Supplementary material.

Table I. Summary of General Base Catalytic Coefficients for Detritiation of Phenylacetylene-*t* and Chloroform-*t* in Aqueous Solution at 24.6 °C, Ionic Strength = 0.100 M

base	pK(BH$^+$)	10^4k_B, M^{-1} s^{-1} phenylacetylene	10^4k_B, M^{-1} s^{-1} chloroform
ammonia	9.25[a]	95.0	0.0396
methylamine	10.62[b]		0.955
ethanolamine	9.50[c]		0.0402
2 methoxyethylamine	9.40[d]	127.0	0.0353
benzylamine	9.35[e]	193.0	
2,2-dimethoxyethylamine	8.54[f]	14.5	0.00463
tris(hydroxymethyl)-methylamine	8.07[g]	23.2	
2-cyanoethylamine	7.80[h]	4.29	
2,2,2-trifluoroethylamine	5.59[d]	0.0256	
piperidine	11.12[i]		1.60
N-methylbenzylamine	9.58[j]	355.0	
morpholine	8.49[k]	33.2	
N-methylmorpholine	7.41[l]	2.06	
imidazole	6.99[m]	0.616	
3-picoline	5.68[n]	0.00665	
2-aminoethylamine	9.93[o]	1030.0	0.425
2-ammonioethylamine	6.85[o]	9.58	
3-aminopropylamine	10.47[p]	9580.0	
3-ammoniopropylamine	8.49[p]	97.0	
hydroxide ion	15.74	2.44×10^6	1.63×10^3

[a] Bates, R. G.; Pinching, G. D. *J. Res. Natl. Bur. Stand.* 1949, *42*, 419–430. [b] Everett, D. H., Wynne-Jones, W. F. K. *Proc. R. Soc. London, Ser. A* 1941, *177*, 499–516. [c] Bates, R. G.; Pinching, G. D. *J. Res. Natl. Bur. Stand.* 1951, *46*, 349–352. [d] Love, P.; Cohen, R. B.; Taft, R. W. *J. Am. Chem. Soc.* 1968, *90*, 2455–2462. [e] Robinson, R. A.; Kiang, A. K.; *Trans. Faraday Soc.* 1956, *52*, 327–331. [f] This work. [g] Datta, S. P.; Grybowski, A. K.; Weston, B. A. *J. Chem. Soc.* 1963, 792–796. [h] pK(29°) = 7.7 (Soloway, S. S.; Lipschitz, A. *J. Org. Chem.* 1958, *23*, 613–615) adjusted to 25° using $-d(pK)/dT = (pK - 0.9)/T$ (Perrin, D. D. *Aust. J. Chem.* 1964, *17*, 484–488). [i] Bates, R. G.; Bower, N. E. *J. Res. Natl. Bur. Stand.* 1956, *57*, 153–157. [j] Carothers, W. H.; Bickford, C. F.; Hurwitz, G. J. *J. Am. Chem. Soc.* 1927, *49*, 2908–2914. [k] Hetzer, H. B.; Bates, R. G.; Robinson, R. A. *J. Phys. Chem.* 1966, *70*, 2869–2872. [l] Hall, H. K. *Ibid.* 1956, *60*, 63–70. [m] Christensen, J. J.; Izatt, R. M.; Wrathall, D. P.; Hansen, L. D. *J. Chem. Soc. A*, 1969, 1212–1223. [n] Brown, H. C.; Mihm, X. R. *J. Am. Chem. Soc.* 1955, *77*, 1723–1726. [o] Everett, D. H.; Pinsent, B. R. W. *Proc. R. Soc. London, Ser. A*, 1952, *215*, 416–429. [p] Bertsch, C. R.; Fernelius, W. C.; Block, B. P. *J. Phys. Chem.* 1958, *62*, 444–450.

measured value $k_{HO^-} = 0.163$ M^{-1} s^{-1}. The agreement in the case of piperidine buffers, $k_{HO^-} = 0.159$ M^{-1} s^{-1} vs. 0.163 M^{-1} s^{-1}, though even better, is probably less significant because the largest rate adjustement here was 31%.

Hydroxide ion concentrations of the buffer solutions required for these buffer failure corrections, and also for analysis of the kinetic data obtained in well-behaved buffers, were obtained by calculation. Thermodynamic dissociation constants of the amine conjugate acids (Table I) and activity coefficients, either recommended by Bates,[11] determined in the present work [for $(CH_3O)_2CHCH_2NH_3^+$], or estimated by the Debye–Hückel equation with an ion-size parameter of 6 Å,[12] were used for this purpose. Activity coefficients of neutral species were taken to be unity.

The data obtained for exchange of phenylacetylene in buffer solutions of the dibasic amines, $NH_2CH_2CH_2NH_2$ and $NH_2CH_2CH_2CH_2NH_2$, also required special treatment. These buffers were made up from diprotonated, BH_2^{2+}, and monoprotonated BH^+, species only; stoichiometric concentrations of free base, B, were zero. However, small amounts of free base were formed in the resulting solutions through the ionization of BH^+. Since B is a stronger base than BH^+, it could contribute significantly to the rate of hydrogen exchange even when present at low concentration, and this possibility was therefore taken into account by using the rate law of eq 3. Calculation of the concentrations

$$k_{obsd} = k_{HO^-}[HO^-] + k_B[B] + k_{BH^+}[BH^+] \quad (3)$$

of solution species in these buffers (vide infra) showed them to be well behaved in the sense that $[HO^-]$ was constant and that the ratio $[B]/[BH^+]$ $(=\gamma)$ did not change along a series of solutions of constant buffer ratio. Equation 3 could therefore be replaced by eq 4, which indicates that observed rate constants

$$k_{obsd} = k_{HO^-}[HO^-] + (k_B\gamma + k_{BH^+})[BH^+] \quad (4)$$

should be linear functions of $[BH^+]$. If, however, the free base B is kinetically significant, the slopes of these linear relationships, $(k_B\gamma + k_{BH^+})$, will not be constant but will increase with increasing γ. This was, in fact, found to be the case, and experiments were therefore performed at several buffer ratios and the quantity $(k_B\gamma + k_{BH^+})$ was separated into its constituent catalytic coefficients through its dependence on γ.

The solution-species concentrations needed for this analysis were calculated by solving the cubic equation which characterizes the two coupled dissociation equilibria, eq 5 and 6. The concentration

$$BH_2^{2+} \rightleftharpoons BH^+ + H^+ \quad (5)$$

$$BH^+ \rightleftharpoons B + H^+ \quad (6)$$

dissociation constants, Q, required for this purpose were obtained in the case of $NH_2CH_2CH_2NH_2$ (pQ_1 = 7.106 and pQ_2 = 9.958) by interpolating published values,[13] and in the case of $NH_2CH_2CH_2CH_2NH_2$ (pQ_1 = 8.75 and pQ_2 = 10.50) by applying estimated activity coefficient corrections to published[14] pK_a's. These estimates were based on the fact that the differences between pQ_1 and pK_1 is nearly the same for $NH_2(CH_2)_2NH_2$ as for $NH_2(CH_2)_6NH_2$, and that the same is true for the difference between pQ_2 and pK_2 for these amines as well;[13] average values of these differences were therefore used to estimate pQ's from pK_a's.

The detritiation of chloroform was also studied in dibasic amine buffers ($NH_2CH_2CH_2NH_2$). Here, however, the concentrations of B and BH^+ were comparable ($[B]/[BH^+] = 3$), since the buffers were made up from B and BH^+ with stoichiometric concentrations of BH_2^{2+} equal to zero. Under these conditions catalysis by the weaker base, BH^+, could be no greater than 1% of that of the stronger base, B, and it was therefore neglected.

Slope and intercept parameters in the relationship between observed rate constants and base concentration according to eq 2 or eq 4 were evaluated by linear least-squares analysis. The catalytic coefficients obtained in this way are assembled in Table I. Hydroxide ion catalytic coefficients were evaluated from the intercepts using hydroxide ion concentrations calculated as described above. In the case of phenylacetylene, the average of 24 separate values so obtained is $k_{HO^-} = 244 \pm 4$ M^{-1} s^{-1}. The standard deviation of the group from this mean is 20 or 8%, which attests to the general validity of this method of analysis. In the case of chloroform, eight separate values gave the average $k_{HO^-} = 0.164 \pm 0.005$ M^{-1} s^{-1} in excellent agreement with the directly measured value $k_{HO^-} = 0.163 \pm 0.004$ M^{-1} s^{-1} (Table S4). The standard deviation of this group, 0.014 or 9%, is also reasurringly small.

Some of the rate constants determined here have been measured before, and agreement between the present results and literature values is on the whole quite good. For example, the hydroxide ion catalytic coefficient reported for the detritiation of chloroform, $K_{HO^-} = 0.165$ M^{-1} s^{-1},[5] agrees very well with the present value, $k_{HO^-} = 0.163$ M^{-1} s^{-1}, and the agreement between the hydroxide ion catalytic coefficient reported for the detritiation of phenylacetylene, $k_{HO^-} = 267$ M^{-1} s^{-1},[3] and the value obtained here, k_{HO^-}

(11) Bates, R. G. "Determination of pH Theory and Practice"; Wiley: New York, 1973; p 49.
(12) Roy, R. N.; Robinson, R. A.; Bates, R. G. *J. Am. Chem. Soc.* **1973**, *95*, 8231–8235.
(13) Everett, D. H.; Pinsent, B. R. W. *Proc. R. Soc. London, Ser. A* **1952**, *215*, 416–429.
(14) Bertsch, C. R.; Fernelius, W. C.; Block, B. P. *J. Phys. Chem.* **1958**, *62*, 444–450.

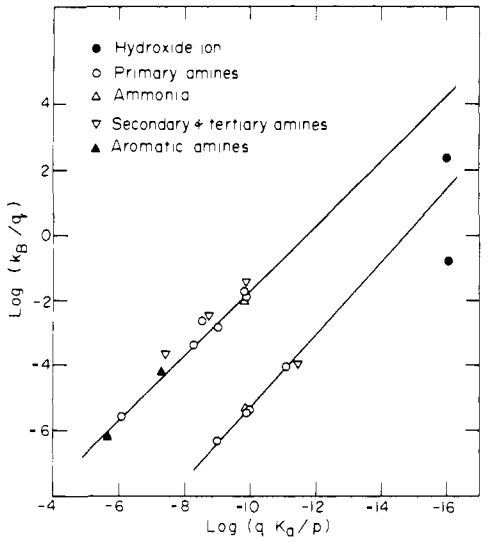


Figure 3. Brønsted relations for detritiation of carbon acids: upper line, phenylacetylene; lower line, chloroform.

= 244 M^{-1} s^{-1}, is also good. More approximate values were reported for the detritiation of phenylacetylene catalyzed by ammonia and tris(hydroxymethyl)methylamine, $k_B = 7.5 \times 10^{-3}$ and 4×10^{-3} M^{-1} s^{-1}, respectively,[3] but these are also consistent with the present values, $k_B = 9.5 \times 10^{-3}$ and 2.33×10^{-3} M^{-1} s^{-1}.

Activation Parameters. The detritiation of phenylacetylene in tris(hydroxymethyl)methylamine buffers was also measured at 35 and 45 °C. These data (Table S5[10]) were analyzed as described above for 25 °C, and the results, when combined with those for 25 °C, gave the following activation parameters: hydroxide ion catalysis, $\Delta H^{\ddagger} = 13.0 \pm 0.1$ kcal mol^{-1} and $\Delta S^{\ddagger} = -3.8 \pm 0.3$ cal deg^{-1} mol^{-1}; tris(hydroxymethyl)methylamine catalysis, $\Delta H^{\ddagger} = 12.5 \pm 0.3$ kcal mol^{-1} and $\Delta S^{\ddagger} = -28.6 \pm 1.1$ cal deg^{-1} mol^{-1}.

Brønsted Relations. The catalytic coefficients determined here for detritiation of phenylacetylene and chloroform by monobasic amines conform to the Brønsted relation, but, as Figure 3 shows, hydroxide ion rate constants fall below the general base correlation lines by considerable margins in a manner typical of proton transfer to and from carbon.[15] The lines in this figure were constructed using data for primary amines only, omitting tris(hydroxymethyl)methylamine; least-squares analysis gave the following values: for phenylacetylene, $\log (k_B/q) = (-11.146 \pm 0.369) - (0.991 \pm 0.045) \log (qK_a/p)$, and for chloroform, $\log (k_B/q) = (-16.468 \pm 0.524) - (1.117 \pm 0.052) \log (qK_a/p)$. Statistical factors $p = 3$, 2, and 1 were used for the conjugate acids of primary, secondary, and tertiary amines, respectively; $p = 2$ was also used for protonated imidazole, and $q = 1$ was used for all of the bases.

The catalytic coefficient for tris(hydroxymethyl)methylamine lies a factor of 2.3 above the correlation line for detritiation of phenylacetylene based upon other primary amines. The dibasic amines, 1,2-diaminoethane and 1,3-diaminopropane, also show positive deviations, the former 105% in the case of phenylacetylene and 220% for chloroform and the latter 460% in the case of phenylacetylene. Ammonia, on the other hand, fits in with the primary amines; it lies only 15% above the primary amine line for chloroform and 46% below that for phenylacetylene. The two secondary amines, benzylmethylamine and morpholine, lie above the phenylacetylene primary amine line, by 139 and 169%, respectively, and the tertiary amine *N*-methylmorpholine deviates still farther in the same direction, by 290%. Differences of this kind in the catalytic effectiveness of primary, secondary, and tertiary amines have been observed before, notably in the decomposition of nitramide[16] and the elimination of hydrogen chloride from 9-fluorenylmethyl chloride.[17] The present deviations, however, are somewhat smaller than the ones found previously, especially those for the elimination reaction. On the other hand, the single secondary amine used here for chloroform detritiation, piperidine, showed a negative deviation of 84%. Aromatic amines sometimes give negative deviations from Brønsted correlations,[16,17] but the two used here, imidazole and 3-methylpyridine, both for phenylacetylene detritiation, conformed respectably well to the primary amine line: the former was high by 53% while the latter was low by exactly the same factor.

As noted above, hydroxide ion catalytic coefficients do not fit into these amine-based Brønsted correlations: in the case of phenylacetylene, hydroxide ion falls below the primary amine line by a factor of 75 and for chloroform the deviation amounts to a factor of 175. It is these deviations, in fact, which allow general base catalysis to be observed in these systems, for in both cases the Brønsted exponents are very large; it is a mathematical consequence of the Brønsted relation that lyate ion catalysis will overwhelm general base catalysis in systems with large Brønsted exponents provided that the lyate species obey the correlation as well.[18]

It is likely that these hydroxide ion deviations are due in part to electrostatic repulsion between the negative charge of this ion and the negative charge generated on the substrate in these carbanion-forming reactions. It is significant, therefore, that positively charged amines give deviations in the opposite direction: the catalytic coefficient for phenylacetylene detritiation by 2-ammonioethylamine lies above the primary amine line by a factor of 10 and that for 3-ammoniopropylamine, by a factor of 1.6.

Discussion

Brønsted Relations. Both of the hydrogen-exchange reactions investigated here give Brønsted plots which are linear and have essentially unit slope: for phenylacetylene, $\beta = 0.99 \pm 0.05$, and for chloroform, $\beta = 1.12 \pm 0.02$. These are similar to the Brønsted correlations produced by the proton transfer reactions of normal acids in the region where these processes are thermodynamically uphill and where separation of the proton-transfer products, eq 9, rather than the proton transfer step itself, eq 8, of the overall three-step reaction scheme, eq 7–9, is rate-determining.[1] These

$$AH + B \rightleftharpoons AH{\cdot}B \quad (7)$$

$$AH{\cdot}B \rightleftharpoons A{\cdot}HB \quad (8)$$

$$A{\cdot}HB \rightleftharpoons A + HB \quad (9)$$

correlations contrast with the behavior of ordinary carbon pseudo acids whose uphill proton transfers give Brønsted exponents considerably less than 1, even under conditions of appreciable reaction endoergonicity; for example, the ionizations of acetone and isobutyraldehyde, whose acid strengths in aqueous solution are comparable to those of the presently investigated carbon acids, give $\beta = 0.69$[19] and 0.49–0.53,[20] respectively, when measured with a series of amine proton acceptors not unlike those used here.

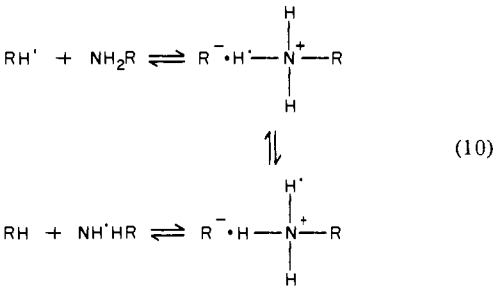
Anomalously large Brønsted exponents are sometimes found for proton transfer from carbon to normal bases in systems where other evidence leaves little doubt that the carbon acid is functioning as a pseudo and not as a normal species; a notable example of this behavior is the ionization of certain nitro compounds.[21] It is now known, however, that such inflated exponents are the result of a buildup of negative charge in the proton-transfer transition state on the carbon atom from which the proton is being trans-

(15) Kresge, A. J. *Chem. Soc. Rev.* **1973**, *2*, 475–503.
(16) Bell, R. P. "The Proton in Chemistry"; Cornell University Press: Ithaca, N.Y., 1973; pp 217–219.
(17) Spencer, T. A.; Kendall, M. C. R.; Reingold, I. D. *J. Am. Chem. Soc.* **1972**, *94*, 1250–1254.
(18) Bell, R. P., "Acid-Base Catalysis"; Oxford University Press: London, 1941; pp 93–95.
(19) Hine, J.; Cholod, M. S.; King, R. A. *J. Am. Chem. Soc.* **1974**, *96*, 835–845.
(20) Hine, J.; Houston, J. G.; Jensen, J. H.; Mulders, J. *J. Am. Chem. Soc.* **1965**, *87*, 5050–5059.
(21) Bordwell, F. G.; Boyle, W. J., Jr.; Hautala, J. A.; Yee, K. C. *J. Am. Chem. Soc.* **1969**, *91*, 4002–4003. Fukuyama, M.; Flanagan, P. W. K.; Williams, F. T., Jr.; Frainier, L.; Miller, S. A.; Shechter, H. *Ibid.* **1970**, *92*, 4689–4699. Bordwell, F. G.; Boyle, W. J., Jr.; Yee, K. C. *Ibid.* **1970**, *92*, 5926–5932. Bordwell, F. G.; Boyle, W. J., Jr. *Ibid.* **1971**, *93*, 511–512; **1972**, *94*, 3907–3911. Bordwell, F. G.; Bartmess, J. E.; Hautala, J. A. *J. Org. Chem.* **1978**, *43*, 3107–3113.

ferred; this negative charge is then later dispersed to other parts of the molecule by delocalization.[22] Since the carbanionic products of the present proton-transfer reactions, $PhC{\equiv}C^-$ and Cl_3C^-, are species in which negative charge delocalization does not take place, this phenomenon cannot be operating here. It is also known, moreover, that anomalous Brønsted exponents occur in proton transfers between pseudo acids and normal bases only when the variation needed to produce a correlation is effected by changing the structure of the acid; when the acid is held constant and the base is changed, as was done in each of the present correlations, these otherwise anomalous systems give ordinary noninflated exponents. It is most unlikely, therefore, that the unit Brønsted exponents observed here are inflated values, and it would seem safe to conclude that they are a genuine indication of the similarity of the present reactions to uphill proton transfers between normal acids and bases.[23]

Marcus and Other Rate Theories. Further insight into the nature of the present systems may be obtained by applying certain theories, such as Marcus rate theory,[25] through which various properties of proton-transfer reactions may be calculated. This approach has recently been used with considerable success in analyzing proton-transfer reactions with a view to determining the conditions under which the various steps on the three-step reaction scheme of eq 7–9 are rate-determining.[26] Before these theories may be applied here, however, an alternative to separation, eq 9, as the step following proton transfer, eq 8, required to complete the present hydrogen-exchange processes must be considered.

All of the proton acceptors used here were amines, and the immediate products of the proton-transfer steps were therefore hydrogen-bonded ammonium ion-carbanion ion pairs. Simple rotation of the ammonium ion within such an ion pair would bring a new hydrogen into hydrogen-bonding position, and collapse of this species back to carbon acid and amine would then effect exchange, eq 10. Such a mechanism however, is possible only



(10)

with primary and secondary amines; tertiary amines do not have the required additional hydrogen. Terrtiary amines, however, were found to catalyze exchange in the present systems at rates which correlate well with those for primary and secondary amines (Figure 3), and this indicates that this mechanism is not operative here. Rotation mechanisms have also been excluded as likely reaction paths for hydrogen exchange in amine hydrates.[27]

This leaves separation of the proton-transfer products and replacement of the ammonium ion by a new entity as the exchange-completing step in the presently studied systems. The question of whether the presently studied acids are normal or

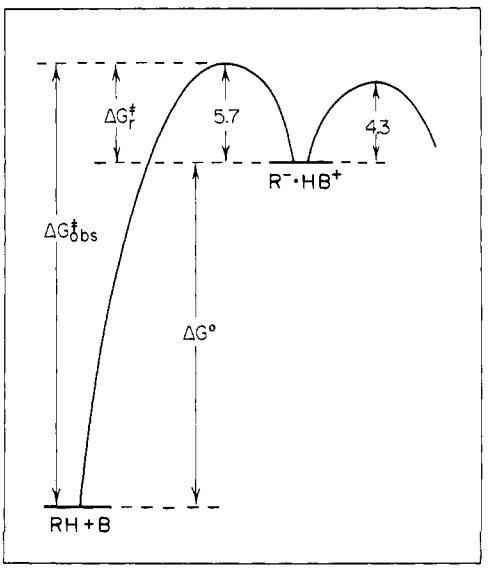


Figure 4. Hypothetical free-energy profile for phenylacetylene or chloroform ionizing as a pseudo acid; numbers are in units of kcal mol^{-1}. The barrier on the right, 4.3 kcal mol^{-1}, is the lower limit for separation of the proton transfer products, and the barrier on the left, 5.7 kcal mol^{-1}, is the lower limit consequently required for reversal of the proton-transfer step if proton transfer is to be rate determining.

pseudo species then reduces to whether the reaction barrier for this step is lower or higher than the barrier for reversal of the proton-transfer step. Information on this matter may be obtained by applying Marcus rate theory. One way of preceeding is to assume that proton transfer is, in fact, rate determining and then to compare the Brønsted exponent predicted by Marcus theory on this basis with the exponent actually observed. If agreement is obtained, the assumption is supported; if, on the other hand, the predicted exponent is significantly different from the one observed, the assumption may be taken as incorrect and the conclusion that the acid is not a pseudo but is rather a normal species may be reached.

A Marcus theory expression which is useful for this purpose is that of eq 11, in which $\Delta G^{\ddagger}$ is the free energy of activation and

$$\beta = \frac{\Delta G^{\ddagger}}{\Delta G^{\circ}} - \sqrt{\left(\frac{\Delta G^{\ddagger}}{\Delta G^{\circ}}\right)^2 - \left(\frac{\Delta G^{\ddagger}}{\Delta G^{\circ}}\right)} \qquad (11)$$

ΔG° is the free energy of reaction for the proton-transfer step. If proton transfer is to be rate determining, $\Delta G^{\ddagger}$ must be equal to the observed free energy of activation for the isotope exchange reaction, $\Delta G^{\ddagger}_{obsd}$, as illustrated in Figure 4.[28] The value of $\Delta G^{\ddagger}_{obsd}$ varies with the strength of the catalyzing base, but a representative calculation may be performed for a hypothetical base, with $-\log (qK_a/p) = 8.00$ which corresponds to the midpoint of the present Brønsted correlation for phenylacetylene (Figure 3). This gives $\Delta G^{\ddagger}_{obsd} = \Delta G^{\ddagger} = 21.8$ kcal mol^{-1}.

An estimate of ΔG° may be based upon the requirement that this quantity must differ from $\Delta G^{\ddagger}_{obsd}$ by the free energy of activation for reversal of the proton-transfer step, $\Delta G^{\ddagger}_r$, $\Delta G^{\circ} = \Delta G^{\ddagger}_{obsd} - \Delta G^{\ddagger}_r$, and that, if proton transfer is to be rate determining, $\Delta G^{\ddagger}_r$ must exceed the barrier for separation of the proton-transfer products by a significant amount, e.g., 1.4 kcal mol^{-1}, which corresponds to an order of magnitude in rate constant.

(22) Kresge, A. J. *J. Am. Chem. Soc.* **1970**, *92*, 3210–3211. Kresge, A. J. *Can. J. Chem.* **1974**, *52*, 1897–1903. Kresge, A. J. In "Proton Transfer Reactions"; Caldin, E. F., Gold, V., Eds.; Chapman and Hall: London, 1975; pp 179–199.

(23) It has been suggested before, on the basis of different arguments,[5] that chloroform is a normal rather than a pseudo acid, and normal acid behavior has also been claimed for certain cyano carbons and disulfones.[24]

(24) For summaries of the evidence see Bell, R. P., ref 16, pp 211–213. Hibbert, F. In "Comprehensive Chemical Kinetics"; Bamford, C. H., Tipper, C. F. H., Eds.; Elsevier: New York, 1977; Chapter 2.

(25) Marcus, R. A. *J. Phys. Chem.* **196**,, *72*, 891–899. Kresge, A. J. *Chem. Soc. Rev.* **1973**, *4*, 475–503.

(26) Murdoch, J. R. *J. Am. Chem. Soc.* **1972**, *94*, 4410–4418; **1980**, *102*, 71–78.

(27) Grunwald, E.; Ralph, E. K. *J. Am. Chem. Soc.* **1967**, *89*, 4405–4411. Grunwald, E.; Ralph, E. K. *Acc. Chem. Res.* **1971**, *4*, 107–113.

(28) Although $\Delta G^{\ddagger}_{obsd}$ refers to a detritiation reaction, isotope effects in the present systems are small,[5,6a,29] and the results obtained pertain, to close approximation, to all isotopes of hydrogen. Strictly speaking, moreover, $\Delta G^{\ddagger} = \Delta G^{\ddagger}_{obsd} - w^r$, where w^r is a work term representing the free energy required to assemble the reactants into a complex within which proton transfer can take place. Inclusion of w^r in the calculation, however, does not alter the qualitative conclusion to be reached; it does change the value of β calculated by eq 11 somewhat, but the change is in a direction (to lower values) which actually reinforces the argument made.

(29) Kresge, A. J.; Lin, A. C. *J. Am. Chem. Soc.* **1975**, *97*, 6257–6258.

Evaluation of ΔG° therefore requires knowledge of the reaction barrier for the separation step. Barriers for such a process, i.e., dissociation of ammonium ion–carbanion ion pairs in aqueous solution, appear not to have been measured, but an estimate might be based upon known rates of dissociation of hydrogen-bonded amine hydrates.[27] These are of the order of 10^{10} s^{-1} and range up to 2×10^{11} s^{-1} for the ammonia–water complex. The barriers for this process are believed to consist principally of London dispersion interactions, which will surely be greater for the present systems than for ammonia and water. Rate constants lower than 2×10^{11} s^{-1} would therefore seem to be appropriate in the present case; a conservative upper limit might be 5×10^{10} s^{-1}, which corresponds to a barrier of 2.9 kcal mol^{-1}. Since the separating entities in the present systems are oppositely charged ions, a Coulombic attraction term must be added to this London dispersion barrier. For singly charged ions 3 Å apart, this amounts to 1.4 kcal mol^{-1} when the dielectric constant of the intervening medium is taken as 80, a value appropriate to bulk water. The effective dielectric constant in the present system is likely to be considerably less than this, and that will raise the energy of attraction; 1.4 kcal mol^{-1} is therefore once again a safe limit, and it is consequently quite unlikely that the barrier for the separation step in the present system is less than 2.9 + 1.4 = 4.3 kcal mol^{-1}.

This estimate leads to $\Delta G^\circ = 21.8 - 4.3 - 1.4 = 16.1$ kcal mol^{-1}, and that, when inserted into eq 11 along with $\Delta G^\ddagger = 21.8$ kcal mol^{-1}, gives $\beta = 0.66$. This result is in complete disagreement with the experimentally determined value for phenylacetylene, $\beta = 0.99 \pm 0.05$, and that indicates that the assumption upon which this calculation was based, namely that proton transfer is the rate-determining step, is incorrect. Separation must therefore be rate determining, and phenylacetylene must be functioning as a normal rather than as a pseudo acid. The unit Brønsted exponent actually observed is therefore not a kinetic property of the proton-transfer step, i.e., is not an indication of the structure of the proton-transfer transition state; it is a consequence rather of the proton-transfer step serving as a preequilibrium preceding the rate-determining separation process.

This conclusion concerning the normal acid nature of phenylacetylene stems from a feature of Marcus theory which requires a proton-transfer process with a near-unit Brønsted exponent to have a very late transition state and consequently a very low barrier for the reversal process; reversal is therefore faster than the separation process which follows it, and proton transfer is not the rate-determining step. This Hammond-postulate[30] type of behavior may be illustrated by using a rearranged form of eq 11, eq 12,

$$\Delta G^\ddagger = [\beta^2/(2\beta - 1)]\Delta G^\circ \quad (12)$$

to calculate the barrier expected for reversal of the proton-transfer step if β really had the experimentally observed value 0.99. This calculation gives $\Delta G^\ddagger = 16.102$ kcal mol^{-1}, and, since $\Delta G^\circ = 16.1$ kcal mol^{-1}, the barrier for the reverse reaction must have the very low value 0.002 kcal mol^{-1}. Use even of $\beta = 0.90$, a number which is two standard deviations below the most probable value $\beta = 0.99$, gives only 0.20 kcal mol^{-1} for the barrier to reversal of the proton-transfer step: this still falls far short of the 4.3 kcal mol^{-1} estimated as the conservative lower limit to the barrier for the separation step.

Simple Marcus theory upon which these considerations have been based has the somewhat unrealistic feature of being applicable only over a limited range of ΔG°. When it is applied to systems in which ΔG° runs close to those limits, such as, for example, reactions with very large Brønsted exponents, it may therefore give unrealistic answers. Various alternative relationships between $\Delta G^\ddagger$ and ΔG° have been proposed to remedy this situation; a particularly straightforward and mathematically simple one is the hyperbolic expression recently proposed by Lewis and More O'Ferrall.[31] This new rate theory accomodates all values of ΔG° from plus to minus infinity, and it might therefore be more properly applicable to the present problem than is Marcus theory. The counterpart of eq 11 provided by Lewis–More O'Ferrall theory is given as eq 13. Use of this expression with the values

$$\beta = 1/(2 - \Delta G^\circ/\Delta G^\ddagger) \quad (13)$$

of $\Delta G^\ddagger$ and ΔG° detailed above gives $\beta = 0.79$, which is greater than the $\beta = 0.66$ provided by Marcus theory but still significantly short of the experimental value of $\beta = 0.99 \pm 0.05$. A rearranged form of eq 13, eq 14, may also be used to calculate the Lewis–

$$\Delta G^\ddagger = [\beta/(2\beta - 1)]\Delta G^\circ \quad (14)$$

More O'Ferrall theory barrier for reversal of the proton-transfer step using an experimentally derived value of β. This gives 0.16 kcal mol^{-1} with $\beta = 0.99$, and 2.0 kcal mol^{-1} with $\beta = 0.90$, both of which are again far short of the 4.3 kcal mol^{-1} estimated as the lower limit to the barrier for separation of the proton-transfer products. Lewis–More O'Ferrall theory therefore leads to the same general conclusion as Marcus theory, namely, that separation and not proton transfer is the rate-determining step in hydrogen exchange of phenylacetylene and that this substance is therefore acting as a normal and not as a pseudo acid.

These calculations were performed with limits of $\Delta G^\ddagger$ or β and ΔG° which give the closest correspondence between calculated and required quantities; use of other allowed values would simply increase the already significant discrepancies and thereby reinforce the arguments. Use of a work term, w^r, has the same effect. Similar calculations for chloroform also lead to the same conclusion.

The Separation Step. When the proton-transfer products separate in the rate-determining step of these isotope exchange reactions, the ammonium ion partner of the original ion-pair product could be replaced by either another ammonium ion, eq 15, or by a solvent water molecule, eq 16. In the latter case this

$$RH' + RNH_2 \rightleftharpoons R^-\cdot H'NH_2R^+ \rightarrow R^-\cdot HNH_2R^+ \quad (15)$$

$$RH' + RNH_2 \rightleftharpoons R^-\cdot H'NH_2R^+ \rightarrow R^-\cdot HOH \quad (16)$$

unsymmetrical reaction scheme would have to be accompanied by another, mirror-image, path to give an overall symmetrical mechanism.[32]

These two mechanisms differ in the stoichiometry of their rate-determining transition states. They will therefore have different rate laws, the third-order expression of eq 17 for the

$$-d[RH']/dt = k[RH'][RNH_2][RNH_3^+] \quad (17)$$

mechanism of eq 15 and the effectively second-order expression of eq 18 for the mechanism of eq 16, and they might be distin-

$$-d[RH']/dt = k[RH'][RNH_2][H_2O] \quad (18)$$

guished on this basis. The essential difference between these two expressions is a quadratic dependence of observed rate constant ($-d[RH']/[RH']dt$) upon buffer concentration for eq 17 and a linear dependence for eq 18. This, in principle, is an easily distinguishable difference, but in practice in the present case distinction becomes difficult because buffer catalysis is so weak. For example, in a series of kinetic runs conducted at constant buffer ratio but varying buffer concentration, most of the reaction occurs through catalysis by hydroxide ion (see Figure 2), and the data fit eq 17 just about as well as eq 18. Comparison of kinetic results for the same buffer system at different buffer ratios offers a somewhat more critical test, inasmuch as such data cover a wider variation in the product $[RNH_2][RNH_3^+]$, and here a definite preference for eq 18 over eq 17 is apparent (see Table S-7). The distinction is especially clear in the case of phenylacetylene exchange determined in tris(hydroxymethyl)methylamine buffers where a series of measurements were made over a tenfold variation in buffer ratio; analysis of these data according to eq 17 gives a negative rate constant whereas eq 18 produces a realistic positive

(30) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334–338.
(31) Lewis, E. S.; Shen, C. C.; More O'Ferrall, R. A. *J. Chem. Soc., Perkin Trans. 2* **1981**, 1084–1088.
(32) Burwell, R. L; Pearson, R. G. *J. Phys. Chem.* **1966**, *70*, 300–302. Abraham, M. H.; Dodd, D.; Johnson, M. D.; Lewis, E. S.; More O'Ferrall, R. A. *J. Chem. Soc. B* **1971**, 762–766.

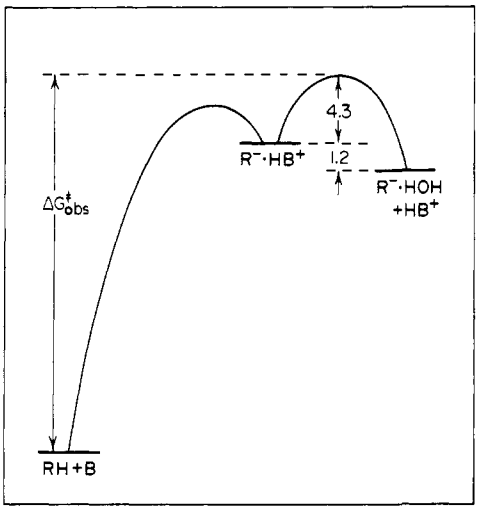


Figure 5. Free-energy profile for phenylacetylene or chloroform ionizing as a normal acid; numbers are in units of kcal mol^{-1}.

value. This, therefore, indicates that, in the rate-determining separation step of these isotope exchange reactions, the ammonium ion–carbanion ion pair is converted to a carbanion hydrate, as shown in eq 16, and rapid collapse of this hydrate then produces exchanged substrate.

Aqueous Solution pK_a's of Phenylacetylene and Chloroform. This assignment of a detailed mechanism to the separation step of the isotope exchange reactions of phenylacetylene and chloroform identifies the products of these reactions as water solvated carbanions, similar to the species formed when these substances ionize as acids in aqueous solution, eq 19; this makes these systems

$$\text{R-H} \rightleftharpoons \text{R}^-_{(aq)} + \text{H}^+_{(aq)} \qquad (19)$$

especially suitable for use in estimating the aqueous solution pK_a's of phenylacetylene and chloroform.

These estimates may be made in the manner outlined in Figure 5. The observed free energy of activation for hydrogen exchange by a representative base, $\Delta G^{\ddagger}_{obsd}$ is equal to the barrier for the separation step, plus the free energy of reaction for conversion of the ammonium ion–carbanion ion pair to an aquated carbanion and a free ammonium ion, eq 20, plus the free energy change for

$$\text{R}^-\cdot\text{HB}^+ + \text{H}_2\text{O} \rightleftharpoons \text{R}^-\cdot\text{HOH} + \text{HB}^+ \qquad (20)$$

a reaction, eq 21, whose equilibrium constant is the ratio of acid

$$\text{RH} + \text{B} \rightleftharpoons \text{R}^- + \text{HB}^+ \qquad (21)$$

dissociation constants of RH and HB$^+$. The barrier for the separation steps has been estimated to be 4.3 kcal mol^{-1} or greater, and $\Delta G^{\ddagger}_{obsd}$ and the pK_a of HB$^+$ are fixed by the Brønsted correlation for exchange. The only quantities not known are therefore the pK_a of RH and ΔG for the reaction of eq 20; if the latter can be estimated, the pK_a of RH may be calculated.

In the process of eq 20, a pole–pole Coulombic interaction is replaced by a pole–dipole interaction. The former was estimated above as 1.4 kcal mol^{-1}, and the latter can be calculated as 0.2 kcal mol^{-1}; this puts the potential energy of R$^-$·HOH 1.2 kcal mol^{-1} above that of R$^-$·HB$^+$.[33] This energy difference will be offset by a concentration effect stemming from the fact that one of the reactants in eq 20 is also the solvent and is therefore present in greater abundance than the other species. If this concentration effect is treated as an entropy change and the potential energy difference is equated with an enthalpy change, a free energy change of −1.2 kcal mol^{-1} may be estimated for the process of eq 20.

When this result is combined with $\Delta G^{\ddagger}_{obsd}$ for exchange in phenylacetylene catalyzed by a hypothetical base with pK_a(BH$^+$) = 8.00, an acidity constant for the carbon acid which corresponds to pK_a = 20.0 is obtained. A similar calculation for chloroform using a base with pK_a(BH$^+$) = 10.00, which is the midpoint of the Brønsted correlation for this substrate, gives pK_a = 24.1 for this carbon acid.

This estimate of the pK_a of phenylacetylene in aqueous solution is appreciably lower than the values measured recently in dimethyl sulfoxide solution, pK_a = 28.7,[34] and cyclohexylamine solution, pK_a = 23.2.[35] The differences, however, are consistent with the expected greater solubility and consequent greater stability of unionized phenylacetylene in organic solvents such as dimethyl sulfoxide and cyclohexylamine than in water, coupled with the known ability of hydroxylic solvents such as water to stabilize localized anions. The pK_a of chloroform appears not to have been measured directly, but an estimate, pK_a = 24, which is in good agreement with the present value, has been made on the basis of hydroxide ion catalyzed rates of tritium exchange in aqueous solution.[5]

Acknowledgment. We are grateful to the National Sciences and Engineering Research Council of Canada, the donors of the Petroleum Research Fund administered by the American Chemical Society, and the National Science Foundation of the United States for their financial support of this research.

Registry No. Phenylacetylene, 536-74-3; chloroform, 67-66-3; chloroform-*t*, 86013-86-7; phenylacetylene-*t*, 696-51-5; ammonia, 7664-41-7; methylamine, 74-89-5; ethanolamine, 141-43-5; 2-methoxyethylamine, 109-85-3; benzylamine, 100-46-9; 2,2-dimethoxyethylamine, 22483-09-6; tris(hydroxymethyl)methylamine, 77-86-1; 2-cyanoethylamine, 151-18-8; 2,2,2-trifluoroethylamine, 753-90-2; piperidine, 110-89-4; *N*-methylbenzylamine, 103-67-3; morpholine, 110-91-8; *N*-methylmorpholine, 109-02-4; imidazole, 288-32-4; 3-picoline, 108-99-6; 2-aminoethylamine, 107-15-3; 2-ammonioethylamine, 26265-69-0; 3-aminopropylamine, 109-76-2; 3-ammoniopropylamine, 26265-70-3; hydroxide ion, 14280-30-9; tritium, 10028-17-8.

Supplementary Material Available: Tables S1–S7 of rate constants (16 pages). Ordering information is given on any current masthead page.

(33) Both the pole–pole and the pole–dipole interaction energies were calculated with the dielectric constant for the surrounding medium set equal to that of bulk water, 80; use of a lower value would raise each energy and increase their differences. But that would have a minimal effect on the pK_a estimate, for the pole–pole interaction, which dominates this difference, also enters, in an opposite sense, into the calculation of the barrier for the separation step.

(34) Bordwell, F. G.; Algrim, D.; Fried, H. E. *J. Chem. Soc., Perkin Trans. 2* **1979**, 726–728.

(35) Streitwieser, A., Jr.; Reuben, D. M. F. *J. Am. Chem. Soc.* **1971**, *93*, 1794–1795.