

# Base-Catalyzed Isomerization of 3-Butenenitrile. Relative Nucleophilicities of Carbanions, Nitranions, Oxanions, and Thianions toward Hydrogen

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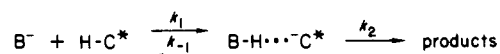
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**Abstract:** Rate constants for base-catalyzed isomerization of  $\text{CH}_2=\text{CHCH}_2\text{CN}$  to  $\text{CH}_3\text{CH}=\text{CHCN}$  in  $\text{Me}_2\text{SO}$  solution by families of carbanions ( $\text{C}^-$ ), nitranions ( $\text{N}^-$ ), oxanions ( $\text{O}^-$ ), and thianions ( $\text{S}^-$ ) have been measured. The relative catalytic effect of these anions at the same basicity is  $\text{S}^- > \text{O}^- > \text{N}^- > \text{C}^-$ . This order is the same as that observed previously for attack of families of anions of these types on a  $\beta$ -hydrogen atom in elimination reactions from cyclohexyl bromide, but it differs from that for attack on carbon in  $\text{S}_{\text{N}}2$  reactions:  $\text{S}^- \gg \text{C}^- > \text{O}^- > \text{N}^-$ . The Brønsted coefficients, which measure the sensitivity of the rates to changes in basicity, were in the range 0.8–1. These large values are consistent with previous values determined for deprotonation of  $\alpha$ -CN carbon acids, but not with the predictions of the Leffler–Grunwald rate–equilibrium equation. A review of the literature failed to provide support for the Leffler–Grunwald postulate that  $\beta$  will approach zero for exergonic proton transfers from carbon acids and unity for endergonic proton transfers. The results are rationalized by a two-step mechanism for proton transfers involving a hydrogen-bonded carbanion intermediate. The failure of substituent effects on protonations of carbanions to conform to those observed in the deprotonation of the corresponding carbon acids provides evidence against a one-step mechanism. Our observations argue against the application of the Hammond–Leffler postulate to most organic reactions over the usual reactivity ranges studied.

Proton transfer reactions have played a key role in the development of major concepts of organic chemistry, including the Brønsted equation,<sup>1</sup> the Hammett equation,<sup>2</sup> the Leffler–Grunwald rate–equilibrium expression,<sup>3</sup> and the reactivity–selectivity postulate.<sup>3</sup> Their usefulness as theoretical models stems from the fact that they are unique among organic reactions in that measurement of both rate and equilibrium constants is usually possible. The mechanisms of these reactions are complex, however. The studies of Eigen showed that fast proton transfer to a base,  $\text{B}^-$ , in water involving oxygen acids ( $\text{O}-\text{H}$ ) or nitrogen acids of the type  $^+\text{N}-\text{H}$  is not a simple one-step reaction but involves three steps, i.e., (1) formation of an H-bonded encounter complex,  $\text{B}^-\cdots\text{H}-\text{A}$ , (2) proton transfer to form a new complex,  $\text{B}-\text{H}^+\cdots\text{A}^-$ , and (3) separation into products,  $\text{BH} + \text{A}^-$ . These reactions all occur very rapidly, and it is difficult to determine which step is rate limiting.<sup>4</sup> In the 1960's the elegant studies of Cram and his students using chiral carbon acids,  $^+\text{C}-\text{H}$ , and isotopic labeling revealed a modified mechanistic scheme for slow proton transfers.<sup>5</sup> Hydrogen bonding of the base to these acids is weak and never rate limiting. Proton transfer is relatively slow and always important in determining the size of the rate constant. The general mechanistic pattern is that shown in Scheme I, where the two extremes encountered are  $k_{-1} \ll k_2$  ( $k_{\text{obsd}} = k_1$ ) and  $k_{-1} \gg k_2$  ( $k_{\text{obsd}} = K_e k_2$ ).

In most of the proton transfers studied the carbon acid,  $\text{H}-\text{C}^*$ , is much weaker than the conjugate acid of the base,  $\text{B}^-$ , making  $k_{-1}$  large and either greater than  $k_2$  or of the same order of magnitude. In either event both  $K_e$  and  $k_2$  are important in deciding the size of  $k_{\text{obsd}}$ . A rich variety of mechanistic possibilities has been observed for these reactions, centered around the chemistry of the H-bonded intermediate,  $\text{B}-\text{H}^+\cdots\text{C}^*$ , which can undergo intermolecular reactions with the solvent or other reagents and numerous intramolecular transformations.<sup>5,6</sup>

## Scheme I



Amines or oxanions have been most commonly used as bases for studies of proton transfers from carbon acids. By using families of amines (e.g., aliphatic amines, meta- and para-substituted anilines, or 3- and 4-substituted pyridines) or families of oxanions (e.g., carboxylate ions,  $\text{RCO}_2^-$ , phenoxide ions,  $\text{ArO}^-$ , or alkoxides,  $\text{RO}^-$ ), the sensitivities of the rates to changes in basicities can be determined from the slope ( $\beta$ ) of the Brønsted plot. Extended plots obtained by combining two or more of these families are known to be subject to considerable scatter, but this is unavoidable in aqueous media if studies over extended  $\text{p}K_{\text{HB}}$  regions are to be carried out, since the basicities of each amine or oxanion family can only be varied over a few  $\text{p}K_{\text{HB}}$  units. In contrast, we have found that in  $\text{Me}_2\text{SO}$  solution the range for a single family can be extended to as much as 10  $\text{p}K_2$  units and that when the basicity is changed by remote substitution the Brønsted equation is the most general and precise of all the linear free energy relationships.<sup>7</sup> These extended plots have allowed us to compare nucleophilicities of carbanions ( $\text{C}^-$ ), nitranions ( $\text{N}^-$ ), oxanions ( $\text{O}^-$ ), and thianions ( $\text{S}^-$ ) at the same basicity for several kinds of reactions. For example, for  $\text{S}_{\text{N}}2$  reactions with benzyl chloride the order is approximately the following:  $\text{S}^- (10^4) > \text{C}^- (10^2) > \text{O}^- (3) > \text{N}^- (1.0)$ .<sup>7c</sup> On the other hand, a different order,  $\text{S}^- (10^4) > \text{O}^- (10^2) > \text{N}^- (10) > \text{C}^- (1.0)$ , has been found for the nucleophilicities of these ions toward hydrogen in an E2 reaction with cyclohexyl bromide.<sup>8</sup> Relatively little quantitative information concerning donor atom effects in other types of deprotonation is available. Aliphatic amines have been found to be 5–10 times more reactive than phenoxide ions of the same basicity in the deprotonation of  $\text{CNCH}_2\text{CH}=\text{CHCH}_2\text{CN}$  in water.<sup>9</sup> Also, the rate of base-catalyzed isomerization of  $\Delta^5$ -cholesten-3-one to its conjugated isomer by  $\text{EtS}^-$  ion in  $\text{MeOH}$  has been shown to be only about

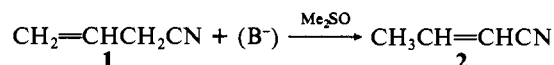
(1) Brønsted, J. N.; Pedersen, K. Z. *Phys. Chim.* **1924**, *108*, 185–235.  
 (2) Hammett, L. P. *J. Am. Chem. Soc.* **1937**, *59*, 96.  
 (3) Grunwald, E.; Leffler, J. E. "Rates and Equilibria in Organic Reactions"; Wiley: New York, 1964; pp 156–168.  
 (4) Eigen, M. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 1–19.  
 (5) Cram, D. J. "Fundamentals of Carbanion Chemistry"; Academic Press: New York, 1963; Chapters I, III, IV, and V.  
 (6) See Koch (Koch, H. F. *Acc. Chem. Res.* **1984**, *17*, 137–144) for a recent discussion of the role of hydrogen-bonded carbanions in deprotonation and elimination reactions.

(7) (a) Bordwell, F. G.; Hughes, D. L. *J. Org. Chem.* **1982**, *47*, 3224–3232.  
 (b) Bordwell, F. G.; Hughes, D. L. *Ibid.* **1980**, *45*, 3314–3320. (c) Bordwell, F. G.; Hughes, D. L. *Ibid.* **1982**, *47*, 169–170. (d) Bordwell, F. G.; Hughes, D. L. *J. Am. Chem. Soc.* **1984**, *106*, 3234–3239.  
 (8) Bordwell, F. G.; Mrozack, S. R. *J. Org. Chem.* **1982**, *47*, 4813–4815.  
 (9) (a) Walters, E. A.; Long, F. A. *J. Am. Chem. Soc.* **1969**, *91*, 3733–3739. (b) Hibbert, F.; Long, F. A.; Walters, E. A. *J. Am. Chem. Soc.* **1971**, *93*, 2829–2835.

5 times slower than by  $\text{MeO}^-$  ion, despite the much lower basicity of  $\text{EtS}^-$ .<sup>10</sup> Similarly,  $\text{EtS}^-$  in  $\text{MeOH}$  was found to be only about 15 times less effective than  $\text{MeO}^-$  ion in epimerizing menthone. In these examples it was estimated that at the same basicity  $\text{EtS}^-$  ion would be slightly more effective than  $\text{MeO}^-$  ion.<sup>10</sup> Information concerning the effectiveness of nitranions and carbanions in deprotonations has been lacking hitherto.<sup>11</sup> Our objective was to measure rate constants for deprotonations of a carbon acid with families of carbanions, nitranions, oxanions, and thianions and to compare the relative rates at the same basicity.

## Results

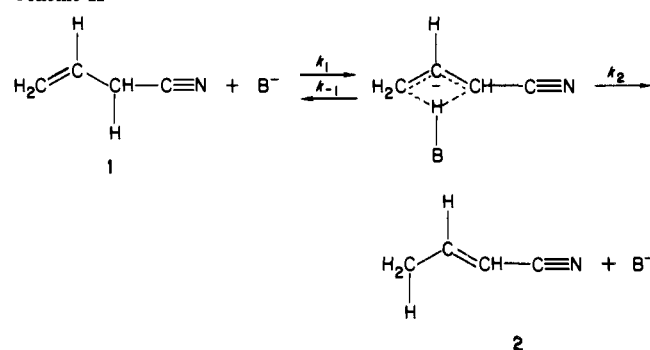
Ela and Cram found that *t*-BuOK/ $\text{Me}_2\text{SO}$  completely isomerizes allylbenzene to  $\beta$ -methylstyrene in 30 min,<sup>12</sup> but a preliminary NMR investigation showed that this isomerization requires a base with  $\text{p}K_{\text{HB}}$  higher than 20 to be fast enough to afford conveniently measurable rates. Since this would preclude our use of phenoxide or thiophenoxide ion families, we turned to a study of the rates of base-catalyzed isomerization of 3-butenenitrile to its conjugated isomers, *cis*- and *trans*-2-butenenitriles.



**Measurements of Rate Constants.** Rates of base-catalyzed isomerization of **1** to **2** in  $\text{Me}_2\text{SO}$  solution were followed by gas-liquid chromatographic (GC) analysis in the presence of the base and a 5–20% excess of its conjugate acid (HB). (The rates were found to be independent of the concentration of HB.) Since the base concentration remains unchanged throughout the run, the decrease in the concentration of **1** followed first-order kinetics. The rate constants were calculated from the slope of a plot of  $\ln \{([1]_0/[1])\}$  vs. time. The  $R^2$  values for these plots usually ranged from 0.99 to 0.999 with use of 4 or 5 aliquots for each run. Division of the first-order rate constants by the base concentration gave the second-order rate constants listed in Table I. The rate constants for oxanions, thianions, and nitranions were usually reproducible to better than  $\pm 10\%$ , but those for many of the carbanions tried were not, standard deviations of  $\pm 50\%$  being not uncommon. Often under seemingly identical conditions two runs would produce rate constants that differed by a factor of 2. Since the rates with carbanions were relatively slow and the  $\text{p}K_{\text{HB}}$  values relatively high, it is possible that reaction with adventitious oxygen caused problems. Details of the method used are given in the Experimental Section. The Brønsted plot for carbanions was constructed by using data for several families of carbanions and shows the expected scatter. A dashed line is used to indicate that the slope is not well-defined.

**The Acidity of 3-Butenenitrile in  $\text{Me}_2\text{SO}$  Solution.** It is not possible to measure the  $\text{p}K_{\text{a}}$  of 3-butenenitrile (**1**) in  $\text{Me}_2\text{SO}$  by the usual indicator method since our rate studies show that isomerization to 2-butenenitrile (**2**) catalyzed by an indicator anion with a  $\text{p}K_{\text{HB}}$  near the estimated  $\text{p}K_{\text{a}}$  will be about  $10^6 \text{ M}^{-1} \text{ s}^{-1}$ . A measurement carried out prior to the present rate studies in our laboratory gave an estimated apparent  $\text{p}K_{\text{a}}$  of about 25, which must be that of **2**. A mixture of *cis*- and *trans*-2-butenenitriles was not well behaved in a  $\text{p}K_{\text{a}}$  determination, however, values between 24.5 and 25.5 being obtained. The equilibrium constant between 3-butenenitrile and 2-butenenitrile has been found to be 200 in *t*-BuOH at 30 °C.<sup>13</sup> Adopting this value for  $\text{Me}_2\text{SO}$  solution places the  $\text{p}K_{\text{a}}$  of 3-butenenitrile at about 22.5, assuming an average value of 25 for 2-butenenitrile. An alternative value for this  $\text{p}K_{\text{a}}$  can be arrived at by the following reasoning. Since the  $\text{p}K_{\text{a}}$  values in  $\text{Me}_2\text{SO}$  for  $\text{CH}_2=\text{CHCH}_2\text{NO}_2$  and  $\text{PhCH}_2\text{NO}_2$  are 11.3 and 12.3, respectively,<sup>14</sup> one might expect the  $\text{p}K_{\text{a}}$  of

## Scheme II



$\text{CH}_2=\text{CHCH}_2\text{CN}$  to be about 1  $\text{p}K_{\text{a}}$  unit lower than that of  $\text{PhCH}_2\text{CN}$ , i.e., about 21.

## Discussion

**Mechanism of Isomerization of 3-Butenenitrile.** The behavior of families of bases toward 3-butenenitrile in  $\text{Me}_2\text{SO}$  is similar to that of families of bases toward 5-cyano-3-pentenitrile **3**<sup>9a</sup> and *tert*-butylmalononitrile **4**<sup>9b</sup> in aqueous media. Reactions of families of amine bases and phenoxide bases with 5-cyano-3-pentenitrile gave  $\beta$  values of 0.94 and 0.98, respectively.<sup>9</sup> (As mentioned earlier, rates for the latter were about a factor of 5 slower at the same basicity.) Reactions of a family of carboxylate ion bases with *tert*-butylmalononitrile also gave a  $\beta$  value near unity (0.98). The  $k^{\text{H}}/k^{\text{D}}$  isotope effects for these reactions were found to be small, which was interpreted to mean that the proton has been essentially completely transferred in the transition state.<sup>9b</sup> Pratt and Bruice extended the study with *tert*-butylmalononitrile to include the amine bases,  $\text{MeONH}_2$ ,  $\text{NH}_2\text{COCH}_2\text{NH}_2$ ,  $\text{H}_2\text{N-NH}_2$ , and  $\text{MeOCH}_2\text{CH}_2\text{NH}_2$ , and the oxanion bases  $\text{F}_3\text{CCH}_2\text{O}^-$  and  $\text{HO}_2^-$ .<sup>15</sup> The resulting line, which was constructed by using both  $\text{RCO}_2^-$  and amine bases, extended over about 9  $\text{p}K_{\text{a}}$  units with a slope of 0.80. In a related study with an optically active and isotopically labeled nitrile  $\text{C}_6\text{H}_5\text{C}^*\text{D}(\text{Et})\text{CN}$ , Cram and Gosser showed that reaction with  $\text{Pr}_3\text{N}$  in  $\text{CH}_3\text{OH}$  or  $\text{KHCO}_3$  in  $\text{HOCH}_2\text{CH}_2\text{OH}$  gave exchange with inversion, but that reaction with  $\text{Pr}_3\text{N}$  in *t*-BuOH gave isomerization.<sup>16</sup> In the first instance the  $\text{CH}_3\text{OH}$  and  $\text{HOCH}_2\text{CH}_2\text{OH}$  solvents bond at the back side of the H-bonded carbanion (Scheme I), but in the poorer H-bond donor solvent, *t*-BuOH, the  $\text{Pr}_3\text{N}$  base takes the deuterium ion on a conducted tour to the back side of the chiral carbon atom, stopping at an H-bond donor site along the way.<sup>16</sup> The conducted tour mechanism is analogous to numerous examples of base-promoted intramolecular 1,3-shifts of protons across allylic-type moieties including  $\text{PhCH}_2\text{CH}=\text{CH}_2$ ,  $\text{PhCH}(\text{CH}_3)\text{CH}=\text{CH}_2$ ,  $\text{Ph}_2\text{CDC}=\text{CPh}$ ,  $\text{PhCH}_2\text{C}\equiv\text{CH}$ , 5-methylcyclopentadiene, 3-methylindene,  $\Delta^5$ -cholestenone, and  $\text{PhCH}(\text{CH}_3)\text{N}=\text{CHR}$ .<sup>5</sup> There is every reason to believe, therefore, that the mechanism for isomerization of 3-butenenitrile is that shown in Scheme II.

The extent of intramolecularity under the conditions of the experiment has not been determined, but the H-bonded intermediate is likely to be common to either an intramolecular or intermolecular mechanism.<sup>5</sup> The order of rate constants observed on changing the nature of the donor atom in the base, i.e.,  $\text{N} > \text{S}^- > \text{O}^- > \text{N}^- > \text{C}^-$ , can be accounted for in terms of Scheme II and the hypothetical reaction profile shown in Figure 1.

The  $k_1$  values can be equated approximately to the  $k_{\text{obsd}}$  values given in Table I since  $k_{-1}$  and  $k_2$  are both large and roughly equal. The  $k_{-1}$  values can be estimated from the  $\text{p}K_{\text{a}}$  value of **1** discussed in the previous section and the  $k_{\text{obsd}}$  and  $\text{p}K_{\text{HA}}$  values given in Table I to be of the order of  $10^6 \text{ M}^{-1} \text{ s}^{-1}$  for  $\text{C}^-$  bases,  $10^7$ – $10^8$  for  $\text{N}^-$  bases, and  $10^9$ – $10^{10}$  for  $\text{O}^-$  and  $\text{S}^-$  bases. The height of the first

(10) Bunnett, J. F.; Retallick, L. A. *J. Am. Chem. Soc.* **1967**, *89*, 423–428.

(11) A preliminary report of the present results has been published. See: Bordwell, F. G.; Hughes, D. L. *J. Org. Chem.* **1983**, *48*, 619–621.

(12) Ela, S. W.; Cram, D. J. *J. Am. Chem. Soc.* **1966**, *88*, 5791–5802.

(13) Prochazka, M.; Zelinka, J.; Vilim, A.; Cerny, J. V. *Collect. Czech. Chem. Comm.* **1970**, *35*, 1224–1234.

(14) Bordwell, F. G.; Bartmess, J. E.; Hautala, J. A. *J. Org. Chem.* **1978**, *43*, 3095–3101.

(15) Pratt, R. F.; Bruice, T. C. *J. Org. Chem.* **1972**, *37*, 3563–3564.

(16) Cram, D. J.; Gosser, L. *J. Am. Chem. Soc.* **1964**, *86*, 5457–5465.

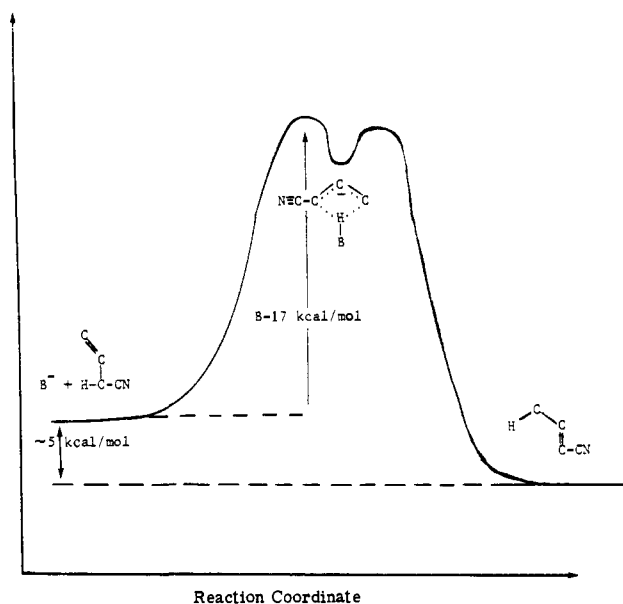


Figure 1. Hypothetical reaction profile for the base-catalyzed isomerization of 3-butenitrile to 2-butenitrile.

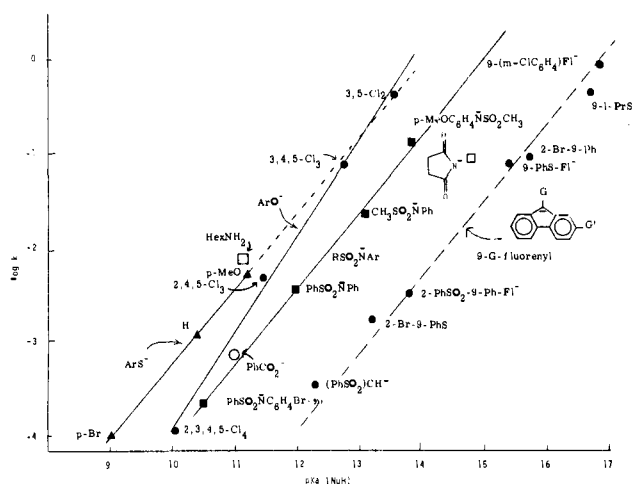


Figure 2. Brønsted plots for isomerization of 3-butenitrile to *cis*- and *trans*-2-butenitriles in Me<sub>2</sub>SO solution at 25 °C catalyzed by thianions (▲), oxanions (●), nitranions (■), carbanions (●), and a few orphan bases (*n*-hexylamine, benzoate ion, and succinimide ion).

barrier in Figure 1 can be related to the stability of the H-bonded intermediate by the restricted Hammond postulate.<sup>17a</sup> The intermediate is best stabilized when B-H is a good H-bond donor, such as <sup>+</sup>N-H, O-H, or S-H, leading to a lower transition-state energy and a higher value for *k*<sub>1</sub>. On the other hand, N-H and C-H bonds are poorer H-bond donors, even when the acidities of the H-B acids are the same, leading to higher energy transition states and lower rates. The H-bonding abilities <sup>+</sup>N-H > O-H > N-H > C-H correspond to the electronegativities of the atoms involved. The data are shown graphically in Figure 2. The  $\beta$  values for S<sup>-</sup>, N<sup>-</sup>, and C<sup>-</sup> ion bases are all about 0.8; that for the

O<sup>-</sup> ion bases appears to be slightly higher, but the data are not accurate enough or extensive enough to be sure. The oxanion bases are known to hydrogen bond to their conjugate acids in Me<sub>2</sub>SO, e.g., PhO<sup>-</sup>...HOPh, and their reactivity is no doubt reduced thereby.<sup>19</sup> This is not true for S<sup>-</sup>, N<sup>-</sup>, or C<sup>-</sup> bases. The reactivity order at the same basicity is O<sup>-</sup>, S<sup>-</sup> > N<sup>-</sup> > C<sup>-</sup>. This reactivity order is similar to that observed for dehydrobromination of cyclohexyl bromide by these same anion bases in Me<sub>2</sub>SO.<sup>8</sup> There are distinct differences in the deprotonation occurring in the CH<sub>2</sub>=CHCH<sub>2</sub>CN isomerization and *c*-C<sub>6</sub>H<sub>11</sub>Br elimination reactions, however. The S<sup>-</sup> and C<sup>-</sup> rate span is greater in the latter and S<sup>-</sup> ions are distinctly better than O<sup>-</sup> ions. Also, the  $\beta$  values are much smaller (~0.4).

The point in Figure 2 for the one neutral base, *n*-hexylamine, falls well above the nitranion line, and its reactivity is even greater at the same basicity than ArS<sup>-</sup> or ArO<sup>-</sup> ions. On the other hand, the point for the (ambident) nitranion derived from succinimide falls well below the sulfonamide line, and the point for the (more delocalized) benzoate ion falls below the phenoxide ion. The carbanion line must be looked on with reservations since the kinetics are relatively poor and several families were used to construct the line. There can be little doubt, however, that these carbanions are substantially less reactive than nitranions of the same basicity.

**Interpretation of  $\beta$  Values for Slow Proton Transfer by use of the Leffler-Grunwald Rate-Equilibrium Equation.** For the past 25 years chemists have been interpreting rates of reactions in terms of reactant-like and product-like transition states. The basis for this approach is a differential form of the Brønsted equation (eq 1), which was popularized by Leffler and Grunwald.<sup>3</sup>

$$\delta\Delta G^\ddagger = \beta\delta\Delta G^\circ \quad (1)$$

According to eq 1 a structural variation ( $\delta$ ) will cause related changes in the free energy of activation,  $\Delta G^\ddagger$ , and the overall free energy of the reaction,  $\Delta G^\circ$ . The proportionality constant,  $\beta$ , will vary, approaching zero for exergonic reactions and unity for endergonic reactions. This interpretation was based on postulates of Hammond<sup>17a</sup> and Leffler,<sup>17b</sup> which are often referred to as the Hammond-Leffler postulate (HLP). Since for proton transfers  $\beta$  measures the sensitivity of the rates to changes in basicity, a highly reactive intermediate, such as a strongly basic carbanion, would be expected to be less selective (lower  $\beta$ ) than a weakly basic carbanion in choosing a proton for reaction, the reactivity-selectivity postulate (RSP). If  $\beta$  changes as  $\Delta G^\circ$  changes, Brønsted (and Hammett) plots should curve. As experimental support for their postulates Leffler and Grunwald cited two kinds of experimental evidence: (1) the increase in Brønsted  $\beta$  values for deprotonation of a series of C-H acids by a family of RCO<sub>2</sub><sup>-</sup> ion bases as the reactions became more endergonic,<sup>20a</sup> and (2) the greater selectivity of the (*p*-Me<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>)<sub>2</sub>CH<sup>+</sup> cation than the (C<sub>6</sub>H<sub>5</sub>)<sub>3</sub>C<sup>+</sup> cation in choosing N<sub>3</sub><sup>-</sup> ion over H<sub>2</sub>O (*k*<sub>N</sub>/*k*<sub>W</sub> = 10<sup>3</sup> vs. 1.0) as a reactant partner in a competition reaction. Recently, in connection with the application of these two tests for RSP to S<sub>N</sub>2 reactions, we have had occasion to survey critically the experimentally evidence that has been presented in support of HLP and RSP.<sup>21</sup> Our conclusion with regard to proton transfer reactions was that the curvature observed in many, if not all, such Brønsted plots arises from causes other than changes in thermodynamics. We will first summarize the evidence upon which this conclusion is based and then show that an examination of the experimental values obtained for  $\beta$  fails to support the postulate that  $\beta$  approaches zero for exergonic reactions and unity for endergonic reactions.

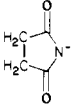
**The Question of Curvature in Brønsted Plots.** As mentioned earlier, proton transfer reactions provide unique opportunities for observing changes in  $\beta$  since both rate and equilibrium constants are usually accessible. We will confine our discussion here to

(17) (a) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334-338. By the "restricted Hammond postulate" we mean the original statement of the postulate as it applies to the structures of a transition state and reactive intermediate of similar energy occurring consecutively along a reaction coordinate. Hammond stated, however, that the value of the postulate derives from its application to highly endothermic reactions where the products will provide the best model for the transition state or to highly exothermic reactions where the reactants will provide the best models. This "generalized Hammond postulate" is sometimes referred to as the Hammond postulate,<sup>18</sup> and it is the basis for the rate-equilibrium equation and the reactivity-selectivity principle.<sup>3</sup> (b) Leffler (Leffler, J. E. *Science* **1953**, *117*, 340-341) had postulated earlier that the transition state would resemble the less stable side, reactants or products, of a chemical equilibrium.

(18) Lowry, T. A.; Richardson, K. S. "Mechanism and Theory in Organic Chemistry", 2nd ed.; Harper and Row: New York, 1981; p 197.

(19) Bordwell, F. G.; McCallum, R. J.; Olmstead, W. N. *J. Org. Chem.*, **1984**, *49*, 1424-1427.

**Table I.** Rates of Isomerization of 3-Butenenitrile to 2-Butenenitriles by Carbanion, Nitranion, Oxanion, and Thianion Bases in Me<sub>2</sub>SO Solution at 25 °C

|  | p <i>K</i> <sub>a</sub> <sup>a</sup> | [base] ( <i>M</i> ) | <i>k</i> ( <i>M</i> <sup>-1</sup> s <sup>-1</sup> ) <sup>c</sup> | ( <i>R</i> <sup>2</sup> ) <sup>d</sup> | average                 |
|--|--------------------------------------|---------------------|--|--|-------------------------|
| carbanion  |                                      |                     |  |  |                         |
| 9-( <i>m</i> -ClC <sub>6</sub> H <sub>4</sub> )Fl <sup>-</sup>                     | 16.85                                | 0.00287             | 0.927  | 0.979                                  |                         |
|  |                                      | 0.00127             | 0.914  | 0.992                                  | 0.92                    |
| 9- <i>i</i> -PrSFl <sup>-</sup>  | 16.9                                 | 0.00251             | 0.492  | 0.999                                  | 0.49                    |
| 2-Br-9Ph-Fl <sup>-</sup>   | 15.7                                 | 0.00209             | 8.34 × 10 <sup>-2</sup>  | 0.970                                  |                         |
|  |                                      | 0.00380             | 9.03 × 10 <sup>-2</sup>  | 0.998                                  | 8.7 × 10 <sup>-2</sup>  |
| 9-PhS-Fl <sup>-</sup>  | 15.4                                 | 0.0255              | 5.69 × 10 <sup>-2</sup>  | 0.998                                  |                         |
|  |                                      | 0.00492             | 4.82 × 10 <sup>-2</sup>  | 0.998                                  |                         |
|  |                                      | 0.00998             | 5.14 × 10 <sup>-2</sup>  | 0.988                                  | 5.2 × 10 <sup>-2</sup>  |
| 2-PhSO <sub>2</sub> -9Ph-Fl <sup>-</sup>   | 13.8                                 | 0.0126              | 2.58 × 10 <sup>-3</sup>  | 0.9998                                 |                         |
|  |                                      | 0.00728             | 3.65 × 10 <sup>-3</sup>  | 0.998                                  |                         |
|  |                                      | 0.0135              | 3.20 × 10 <sup>-3</sup>  | 0.997                                  | 3.1 × 10 <sup>-3</sup>  |
| 2-Br-9-PhS-Fl <sup>-</sup>   | 13.2                                 | 0.0123              | 1.43 × 10 <sup>-3</sup>  | 0.991                                  |                         |
|  |                                      | 0.0166              | 1.98 × 10 <sup>-3</sup>  | 0.962                                  |                         |
|  |                                      | 0.0179              | 1.03 × 10 <sup>-3</sup>  | 0.997                                  |                         |
|  |                                      | 0.0283              | 2.38 × 10 <sup>-3</sup>  | 0.9986                                 | 1.7 × 10 <sup>-3</sup>  |
| (PhSO <sub>2</sub> ) <sub>2</sub> CH <sup>-</sup>                                  | 12.25                                | 0.0313              | 3.31 × 10 <sup>-4</sup>  | 0.997                                  |                         |
|  |                                      | 0.0343              | 3.43 × 10 <sup>-4</sup>  | 0.9993                                 |                         |
|  |                                      | 0.0478              | 1.86 × 10 <sup>-4</sup>  | 0.9995                                 | 3.2 × 10 <sup>-4</sup>  |
| nitranion  |                                      |                     |  |  |                         |
| <i>p</i> -MeOC <sub>6</sub> H <sub>4</sub> NSO <sub>2</sub> Me <sup>-</sup>        | 13.84                                | 0.00761             | 0.121  | 0.995                                  |                         |
|  |                                      | 0.0144              | 0.114  | 0.999                                  | 0.118                   |
| C <sub>6</sub> H <sub>5</sub> NSO <sub>2</sub> CH <sub>3</sub> <sup>-</sup>        | 13.05                                | 0.00931             | 2.11 × 10 <sup>-2</sup>  | 0.998                                  |                         |
|  |                                      | 0.0160              | 2.29 × 10 <sup>-2</sup>  | 0.993                                  | 2.24 × 10 <sup>-2</sup> |
|  |                                      | 0.0193              | 2.31 × 10 <sup>-2</sup>  | 0.996                                  |                         |
| C <sub>6</sub> H <sub>5</sub> NSO <sub>2</sub> Ph <sup>-</sup>                     | 11.95                                | 0.0236              | 3.70 × 10 <sup>-3</sup>  | 0.995                                  |                         |
|  |                                      | 0.0265              | 3.94 × 10 <sup>-3</sup>  | 0.997                                  |                         |
|  |                                      | 0.0300              | 3.69 × 10 <sup>-3</sup>  | 0.996                                  | 3.78 × 10 <sup>-3</sup> |
| <i>m</i> -BrC <sub>6</sub> H <sub>4</sub> NSO <sub>2</sub> Ph <sup>-</sup>         | 10.50                                | 0.0286              | 2.25 × 10 <sup>-4</sup>  | 0.987                                  |                         |
|  |                                      | 0.04745             | 2.05 × 10 <sup>-4</sup>  | 0.994                                  | 2.15 × 10 <sup>-4</sup> |
|  | 14.8                                 | 0.00746             | 0.103  | 0.997                                  |                         |
|  |                                      | 0.00385             | 0.104  | 0.997                                  | 0.104                   |
|  |                                      |                     |  |  |                         |
| amine  |                                      |                     |  |  |                         |
| <i>n</i> -hexylamine   | 11.1 <sup>b</sup>                    | 0.01862             | 8.28 × 10 <sup>-3</sup>  | 0.996                                  |                         |
|  |                                      | 0.0290              | 8.52 × 10 <sup>-3</sup>  | 0.998                                  | 8.40 × 10 <sup>-3</sup> |
| thianion   |                                      |                     |  |  |                         |
| <i>p</i> -MeOC <sub>6</sub> H <sub>4</sub> S <sup>-</sup>                          | 11.19                                | 0.0273              | 5.02 × 10 <sup>-3</sup>  | 0.993                                  |                         |
|  |                                      | 0.0456              | 4.94 × 10 <sup>-3</sup>  | 0.994                                  | 4.98 × 10 <sup>-3</sup> |
| <i>p</i> -BrC <sub>6</sub> H <sub>4</sub> S <sup>-</sup>                           | 8.98                                 | 0.0320              | 9.90 × 10 <sup>-5</sup>  | 0.994                                  |                         |
|  |                                      | 0.0495              | 1.05 × 10 <sup>-4</sup>  | 0.990                                  | 9.98 × 10 <sup>-5</sup> |
| C <sub>6</sub> H <sub>5</sub> S <sup>-</sup>                                       | 10.28                                | 0.03445             | 1.13 × 10 <sup>-3</sup>  | 0.997                                  |                         |
|  |                                      | 0.0237              | 1.11 × 10 <sup>-3</sup>  | 0.997                                  | 1.2 × 10 <sup>-3</sup>  |
| oxanion  |                                      |                     |  |  |                         |
| 3,5-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub> O <sup>-</sup>                   | 13.55                                | 0.00251             | 0.371  | 0.994                                  |                         |
|  |                                      | 0.00281             | 0.462  | 0.997                                  |                         |
|  |                                      | 0.0066              | 0.426  | 0.999                                  | 0.420                   |
| 3,4,5-Cl <sub>3</sub> C <sub>6</sub> H <sub>2</sub> O <sup>-</sup>                 | 12.75                                | 0.0251              | 7.65 × 10 <sup>-2</sup>  | 2 pts                                  |                         |
|  |                                      | 0.00644             | 6.97 × 10 <sup>-2</sup>  | 0.996                                  |                         |
|  |                                      | 0.00677             | 6.61 × 10 <sup>-2</sup>  | 0.992                                  | 7.08 × 10 <sup>-2</sup> |
| 2,3,4,5-Cl <sub>4</sub> C <sub>6</sub> HO <sup>-</sup>                             | 10.0                                 | 0.01416             | 1.91 × 10 <sup>-4</sup>  | 0.996                                  |                         |
|  |                                      | 0.0258              | 1.29 × 10 <sup>-4</sup>  | 0.992                                  |                         |
|  |                                      | 0.0462              | 1.19 × 10 <sup>-4</sup>  | 0.996                                  |                         |
|  |                                      | 0.0603              | 9.30 × 10 <sup>-5</sup>  | 0.989                                  |                         |
|  |                                      | 0.0845              | 9.97 × 10 <sup>-5</sup>  | 0.992                                  | 1.09 × 10 <sup>-4</sup> |
| 2,4,5-Cl <sub>3</sub> C <sub>6</sub> H <sub>2</sub> O <sup>-</sup>                 | 11.4                                 | 0.032               | 4.64 × 10 <sup>-3</sup>  | 0.997                                  |                         |
|  |                                      | 0.0209              | 4.66 × 10 <sup>-3</sup>  | 0.997                                  | 4.65 × 10 <sup>-3</sup> |
| PhCO <sub>2</sub> <sup>-</sup>   | 11.0                                 | 0.272               | 6.15 × 10 <sup>-4</sup>  | 0.996                                  | 6.15 × 10 <sup>-4</sup> |

<sup>a</sup>The p*K*<sub>HA</sub> values of the anions measured in Me<sub>2</sub>SO solution by the method described by Matthews: Matthews, W. S. et al. *J. Am. Chem. Soc.* **97**, 7006–7014. <sup>b</sup>Kolthoff, I. M.; Chantooni, M.; Bhowmik, S. *J. Am. Chem. Soc.* **1968**, *90*, 23–28. <sup>c</sup>*k*<sub>obsd</sub> values for the disappearance of **1**. <sup>d</sup>*R*<sup>2</sup> for the slope of the plot of ln {[**1**]<sub>0</sub>/[**1**]} vs. time.

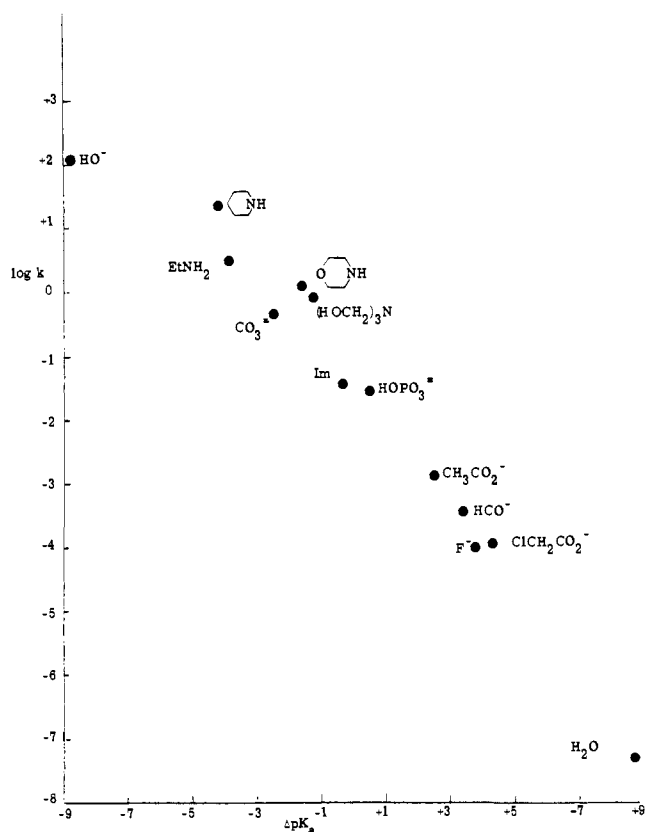
deprotonation of carbon acids by bases of the type studied by Bell<sup>20</sup> and those presented in Table I. In such studies the Brønsted plots are always linear when a single family of bases is used over a relatively small reactivity range, say 4–5 log units (Figure 2). Over larger reactivity ranges, curvature is sometimes observed. It is difficult to decide, however, whether this curvature is caused by

changes in Δ*G*<sup>o</sup> or for other reasons. The other reasons include (a) changes in the reaction mechanism,<sup>4,5,22</sup> (b) structural variations at or near the reaction site that cause changes in electronic, steric, and solvation effects, and (c) differences in the solvation of remote substituents. Most of the work has been carried out

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(22) A careful analysis by Murdoch (Murdoch, J. R. *J. Am. Chem. Soc.* **1980**, *102*, 71–78) has revealed that, in such proton transfers, intrinsic curvature and the curvature produced by a change in the rate-limiting step are not distinguishable unless unusually precise data are obtainable.



**Figure 3.** Brønsted plot for the deprotonation of phenylnitromethane by various bases in water at 15 °C. (Data taken from ref 23.)

in aqueous media where a single family of bases can be used over only a small reactivity range (1 or 2 log units). If a second family of bases with a different donor atom is used, appreciable scatter will be introduced into the plot, making it difficult to determine linearity or lack thereof. The problem is well illustrated by Figure 2 where four different donor atoms have been used. The range of reactivities at constant basicity, which extends over 2 log units, indicates the degree of scatter in a Brønsted plot where these families are mixed. An example typical of the problems encountered in aqueous media can be illustrated by reference to a Brønsted plot constructed from the data for deprotonation of  $\text{PhCH}_2\text{NO}_2$  by  $\text{RCO}_2^-$  ions, amines, and other bases (Figure 3).<sup>23</sup> A cursory examination of Figure 3 might lead one to conclude that the Brønsted plot is curved, an interpretation that has been applied to some Brønsted plots for proton transfers.<sup>24</sup> On the other hand, the points for  $\text{H}_2\text{O}$  and  $\text{HO}^-$  have for many years been considered to be "deviant,"<sup>20,25</sup> probably for solvation reasons.<sup>24d</sup> The authors apparently excluded those points, as well as the points for morpholine and piperidine, in arriving at a "good Brønsted line" with  $\beta = 0.57$ . (A least-squares analysis gives  $\beta = 0.578$  with  $R^2 = 0.966$ .) An equally good line is obtained with the morpholine and piperidine points included ( $\beta = 0.61$ ,  $R^2 = 0.965$ ). A careful examination of Figure 3 shows that all the points are "orphans" in the sense that they do not belong to a family where the donor atom has been kept constant and basicities have been changed by remote substitution, conditions that are essential if electronic, steric, and solvation effects are to be kept constant. Most of the scatter probably arises from changes in the nature of the donor atom since the three-point  $\text{RCO}_2^-$  ion family line

also has a slope of 0.57. ( $\text{RCO}_2^-$  ion families have been found by Bell and his students to give reasonably good Brønsted plots in numerous studies of proton transfer reactions.<sup>20</sup>) We conclude that there is no basis to consider that the Brønsted plot in Figure 3 is curved, although the evidence for linearity leaves much to be desired.

When extended Brønsted plots are constructed by using several families of bases, apparent curvature can arise even when the donor atom is kept constant because of differences in solvation. For example, in a study of the deprotonation of 4-(*p*-nitrophenoxy)-butan-3-one in water by 30 oxanion bases, definite curvature in the Brønsted plot was observed. The part of the plot constructed from phenoxide, acetate, oximate, and like ion bases was essentially linear with the usual scatter observed when mixed base families are used. The curvature was caused by the points for a series of alkoxide ions and hydroxide ion.<sup>26a</sup> The authors argue convincingly that at least the major part of this curvature is caused by slow rates resulting from enhanced solvation of alkoxide and hydroxide ions rather than from changes in  $\Delta G^\circ$ , and this view has since been supported by measurements of  $k_{\text{H}}/k_{\text{D}}$  isotope effects.<sup>26b</sup>

The changes in  $\beta$  values cited by Leffler and Grunwald as the most beautiful example supporting HLP and RSP were those of Bell for the deprotonation of  $\text{H}-\text{C}-\text{C}=\text{O}$  type carbon acids by a family of  $\text{RCO}_2^-$  ion bases.<sup>20a</sup> Here the structural variations were made in the electrophiles at the reaction site, i.e., the proton donor abilities of ketones,  $\beta$ -diketones,  $\beta$ -keto esters, and their halogenated derivatives were compared. Since the environment at the reaction site has been changed, it would not be surprising to find that  $\beta$  has been changed due to a change in mechanism, and/or because differences in the steric and electronic effects cause differences in solvation. Indeed, as pointed out by Kemp and Casey,<sup>27</sup> the data can actually be fitted better by two lines, one for monocarbonyl and one for dicarbonyl substrates, rather than a curve.

We conclude from these and other examples<sup>21</sup> that there are several factors that can cause Brønsted  $\beta$  values to change and that there is no compelling experimental evidence that a change in  $\Delta G^\circ$  is one of them.

Examination of Table II shows that most of the measurements have been carried out in water over small  $\Delta G^\circ$  ranges. In this medium nitroalkanes are the only monofunctional carbon acids for which deprotonations can be studied in the exergonic direction. For families of phenoxide ions and pyridines reacting with  $\text{O}_2\text{NCH}_2\text{CO}_2\text{Et}$ ,  $\beta = 0.65$ ; for pyridines reacting with  $\text{CH}_2=\text{C}-\text{HCH}_2\text{NO}_2$ ,  $\beta = 0.59$ ; for amines reacting with  $\text{C}_6\text{H}_5\text{CH}(\text{Me})\text{NO}_2$ ,  $\beta = 0.54$ ; for  $\text{RCO}_2^-$  ions and amines reacting with  $\text{PhCH}_2\text{NO}_2$ ,  $\beta = 0.57-0.6$ ; and for  $\text{RCO}_2^-$  and  $\text{ArO}^-$  ions reacting with  $\text{CH}_3\text{CH}(\text{NO}_2)_2$ ,  $\beta = 0.70$ . For a family of carboxylate ions reacting with fluoradene,  $\beta = 0.40$ , and for families of fluorenone ions and polyarylmethide ions reacting with  $\text{MeOH}$ ,  $\beta = 0.63$  and  $0.42$ , respectively. These values show no particular trend and no tendency to approach the zero value predicted by HLP. For the three examples with  $\text{PhCH}_2\text{NO}_2$ ,  $\text{O}_2\text{NCH}_2\text{CO}_2\text{Et}$ , and  $\text{CH}_3\text{CH}(\text{NO}_2)_2$ , which were studied over appreciable  $\Delta G^\circ$  ranges, and cover both the exergonic and endergonic regions, the average  $\beta$  values is  $0.68 \pm 0.3$ . For protonations of carbanions by  $\text{MeOH}$  in the exergonic region ( $-8.2$  to  $-33$  kcal/mol)  $\beta$  averaged 0.5.

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Table II. Brønsted  $\beta$  Values for Deprotonation of Carbon Acids

| substrate(s)   | base (families)                                  | solvent                             | $\beta$    | $\Delta G^\circ$ range <sup>a</sup> | ref |
|--|--|-------------------------------------|------------|-------------------------------------|-----|
| A. $\alpha$ -Carbonyl Substrates   |  |                                     |            |                                     |     |
| CH <sub>3</sub> COCH <sub>3</sub>  | RCO <sub>2</sub> <sup>-</sup>                    | H <sub>2</sub> O                    | 0.88       | +18 to +21                          | 20a |
| CH <sub>3</sub> COCH <sub>3</sub>  | pyridines  | H <sub>2</sub> O                    | 0.65, 0.73 | +15 to +18                          | 29  |
| cyclohexanone  | pyridines  | H <sub>2</sub> O                    | 0.52, 0.73 | +15 to +18                          | 29  |
| menthone   | H <sub>-</sub> acidity function                  | H <sub>2</sub> O/Me <sub>2</sub> SO | 0.48       |                                     | 30  |
| H <sub>3</sub> COCH <sub>2</sub> CH <sub>2</sub> OC <sub>6</sub> H <sub>4</sub> NO <sub>2</sub> - <i>p</i> | oxanions   | H <sub>2</sub> O                    | 0.75       | +14 to +20.5                        | 26a |
| CH <sub>2</sub> (COCH <sub>3</sub> ) <sub>2</sub>  | RCO <sub>2</sub> <sup>-</sup>                    | H <sub>2</sub> O                    | 0.48       | +3 to +8                            | 24a |
| CH <sub>2</sub> (COOEt) <sub>2</sub>   | RCO <sub>2</sub> <sup>-</sup>                    | H <sub>2</sub> O                    | 0.79       | +11 to +14                          | 31  |
| CH <sub>3</sub> COCH <sub>2</sub> SO <sub>3</sub> <sup>-</sup>   | pyridines  | H <sub>2</sub> O                    | 0.75       | +9.6 to +19                         | 32  |
| 9-CO <sub>2</sub> MeFlH  | RCO <sub>2</sub> <sup>-</sup>                    | Me <sub>2</sub> SO                  | 0.40       | -3.3 to +0.5                        | 33  |
| CH(COOMe) <sub>3</sub>   | RCO <sub>2</sub> <sup>-</sup>                    | H <sub>2</sub> O                    | 0.72       | +4.1 to +6.8                        | 32  |
| GC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> CT(CN) <sub>2</sub>   | H <sub>2</sub> O                                 | H <sub>2</sub> O                    | 0.61       | +17 to +18.5                        | 34  |
| PhCH <sub>2</sub> CN(CN) <sub>2</sub>  | RCO <sub>2</sub> <sup>-</sup>                    | H <sub>2</sub> O                    | 1.00       | +8.4 to +9.6                        | 34  |
| PhCT(CN) <sub>2</sub>  | H <sub>2</sub> O                                 | H <sub>2</sub> O                    | 0.61       | +17 to 18.5                         | 34  |
| GC <sub>6</sub> H <sub>4</sub> CT(CN) <sub>2</sub>   | ClCH <sub>2</sub> CO <sub>2</sub> <sup>-</sup>   | H <sub>2</sub> O                    | 0.98       | +11 to +12                          | 34  |
| PhCH <sub>2</sub> CH(COMe)CO <sub>2</sub> Et   | RCO <sub>2</sub> <sup>-</sup>                    | H <sub>2</sub> O                    | 0.44       | +9.5 to +12                         | 34  |
| ArCH <sub>2</sub> CH(COMe)CO <sub>2</sub> Et   | MeCO <sub>2</sub> <sup>-</sup>                   | H <sub>2</sub> O                    | 0.76       | +6.8 to +8.6                        | 34  |
| PhCH <sub>2</sub> CH(COMe) <sub>2</sub>  | RCO <sub>2</sub> <sup>-</sup>                    | H <sub>2</sub> O                    | 0.44       | +7.7 to +10.5                       | 34  |
| ArCH <sub>2</sub> CH(COMe) <sub>2</sub>  | MeCO <sub>2</sub> <sup>-</sup>                   | H <sub>2</sub> O                    | 0.58       | +5.8 to +6.8                        | 34  |
| ArCH <sub>2</sub> CH(COMe) <sub>2</sub>  | H <sub>2</sub> O                                 | H <sub>2</sub> O                    | 0.48       | +15.5 to +17                        | 34  |
| B. $\alpha$ -Cyano Substrates  |  |                                     |            |                                     |     |
| <i>t</i> -BuCH(CN) <sub>2</sub>  | RCO <sub>2</sub> <sup>-</sup>                    | H <sub>2</sub> O                    | 0.98       | +11 to +14                          | 9b  |
| <i>t</i> -BuCH(CN) <sub>2</sub>  | RCO <sub>2</sub> <sup>-</sup> , amines           | H <sub>2</sub> O                    | 0.8        | +2.0 to +14                         | 15  |
| <i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> CN                                 | amines   | H <sub>2</sub> O                    | 0.61       | +14 to +18                          | 35  |
| CNCH <sub>2</sub> CH=CHCH <sub>2</sub> CN  | ArO <sup>-</sup>                                 | H <sub>2</sub> O                    | 0.94       | +12 to +18                          | 9a  |
| CNCH <sub>2</sub> CH=CHCH <sub>2</sub> CN  | 2° amines  | H <sub>2</sub> O                    | 0.98       | +14 to +17                          | 9a  |
| CNCH <sub>2</sub> CH=CHCH <sub>2</sub> CN  | H <sub>-</sub> acidity function                  | H <sub>2</sub> O/Me <sub>2</sub> SO | 0.7        |                                     | 36  |
| CH <sub>2</sub> =CHCH <sub>2</sub> CN  | 9-R-Fl <sup>-</sup>                              | Me <sub>2</sub> SO                  | 0.8        | +6.8 to +12                         | b   |
| CH <sub>2</sub> =CHCH <sub>2</sub> CN  | ArNSO <sub>2</sub> R <sup>-</sup>                | Me <sub>2</sub> SO                  | 0.8        | +11 to +16                          | b   |
| CH <sub>2</sub> =CHCH <sub>2</sub> CN  | ArS <sup>-</sup>                                 | Me <sub>2</sub> SO                  | 0.8        | +15 to +18                          | b   |
| CH <sub>2</sub> =CHCH <sub>2</sub> CN  | ArO <sup>-</sup>                                 | Me <sub>2</sub> SO                  | 1.0        | +12 to +16                          | b   |
| C. $\alpha$ -Sulfonyl Substrate  |  |                                     |            |                                     |     |
| (EtSO <sub>2</sub> ) <sub>2</sub> CHCH <sub>3</sub>  | RCO <sub>2</sub> <sup>-</sup> , ArO <sup>-</sup> | H <sub>2</sub> O                    | 0.8        | +9.6 to +14                         | 37  |
| D. $\alpha$ -Nitro Substrates  |  |                                     |            |                                     |     |
| ArCH <sub>2</sub> NO <sub>2</sub>  | HO <sup>-</sup>                                  | H <sub>2</sub> O                    | 1.5        | -14 to -11.5                        | 38  |
| ArCH <sub>2</sub> NO <sub>2</sub>  | morpholine                                       | H <sub>2</sub> O                    | 1.3        | -2.8 to 0                           | 38  |
| ArCH <sub>2</sub> NO <sub>2</sub>  | 2,4-lutidine                                     | H <sub>2</sub> O                    | 1.3        | 0 to +2.8                           | 38  |
| ArCH <sub>2</sub> NO <sub>2</sub>  | PhCO <sub>2</sub> <sup>-</sup>                   | Me <sub>2</sub> SO                  | 0.92       | -2.4 to +1.3                        | 39  |
| GCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> NO <sub>2</sub>   | lyate ion  | 50% MeOH                            | 1.7        |                                     | 46  |
| GCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> NO <sub>2</sub>   | pyridine   | 50% MeOH                            | 1.8        |                                     | 46  |
| ArCH <sub>2</sub> NO <sub>2</sub>  | lyate ion, RCO <sub>2</sub> <sup>-</sup>         | 50% H <sub>2</sub> O/-<br>MeOH      | 1.4        | +9.6 to +11                         | 41  |
| C <sub>6</sub> H <sub>5</sub> CH(Me)NO <sub>2</sub>  | amines   | H <sub>2</sub> O                    | 0.54       | -6.4 to -3                          | 40  |
| PhCH <sub>2</sub> NO <sub>2</sub>  | amines, RCO <sub>2</sub> <sup>-</sup>            | H <sub>2</sub> O                    | 0.57       | -5.5 to +5.8                        | 21  |
| O <sub>2</sub> NCH <sub>2</sub> COOEt  | ArO <sup>-</sup> , pyridines                     | H <sub>2</sub> O                    | 0.65       | -5.5 to +5.5                        | 32  |
| CH <sub>2</sub> =CHCH <sub>2</sub> NO <sub>2</sub>   | pyridines  | H <sub>2</sub> O                    | 0.59       | -2.8 to 0                           | 42  |
| CH <sub>3</sub> CH(NO <sub>2</sub> ) <sub>2</sub>  | RCO <sub>2</sub> <sup>-</sup> , ArO <sup>-</sup> | H <sub>2</sub> O                    | 0.70       | -7.4 to +5.5                        | 25  |
| E. Hydrocarbon Substrates  |  |                                     |            |                                     |     |
| PhC≡CH   | amines   | H <sub>2</sub> O                    | 0.99       | +14 to +21                          | 43  |
| CHCl <sub>3</sub>  | amines   | H <sub>2</sub> O                    | 1.12       | +21 to +28                          | 43  |
| CHCl <sub>3</sub>  | H <sub>-</sub> acidity function                  | H <sub>2</sub> O/Me <sub>2</sub> SO | 0.98       |                                     | 36  |
| fluoradene   | ArCO <sub>2</sub> <sup>-</sup>                   | Me <sub>2</sub> SO                  | 0.40       | -3.1 to +0.5                        | 33  |
| fluorenes  | MeO <sup>-</sup>                                 | MeOH                                | 0.37       | -0.7 to +10                         | 44  |
| polyarylmethanes   | MeO <sup>-</sup>                                 | MeOH                                | 0.58       | +16 to +24                          | 45  |
| F. Heterocyclic Substrate  |  |                                     |            |                                     |     |
| benzoxazoles   | amines   | H <sub>2</sub> O                    | 0.65-0.42  | +14 to +21                          | 27  |

<sup>a</sup> Estimated from  $1.37 \Delta pK_a$ ;  $\Delta pK_a = pK_a(\text{substrate}) - pK_{HB}$  (the conjugate acid of the base, B<sup>-</sup>). These values are approximate since  $pK_a$ (substrate) and  $pK_{HB}$  often must be estimated. <sup>b</sup> Present Work.

localized carbanions and are observed also with  $\alpha$ -sulfonyl carbon acids, chloroform, and phenylacetylene. The  $\alpha$ -cyano carbon acids differ from nitroalkanes and  $\alpha$ -keto carbon acids in that  $\beta$  values are near unity when the substituent changes are made in *either the acids or the bases*. The pattern of substituent effects on the forward and reverse rates remains the same as for nitroalkanes, however. For the deprotonation of GC<sub>6</sub>H<sub>4</sub>CT(CN)<sub>2</sub> substrates the deprotonation rates are sensitive to substituent effects, but the reverse rates appear to be essentially unaffected by substituents although they are considerably below the diffusion-controlled limit. Bell attributes this to the presence of a constant additional activation barrier arising from the necessity to reorganize the solvation shell.<sup>34</sup> This description is essentially that given above for

protonation of nitronate ions, suggesting that solvent reorganization from nitrogen to carbon may be important for even these relatively localized carbanions. It is noteworthy in this regard that *p*-CN, as well as *p*-COPh and *p*-NO<sub>2</sub> functions exhibit enhanced solvation in phenoxide ions in either aqueous or Me<sub>2</sub>SO solution, as judged by comparisons of substituent effects on phenol acidities in the gas phase with those in solution phases.<sup>47</sup> These enhanced solvation effects will, of course, be much larger in anions containing  $\alpha$ -CN,  $\alpha$ -COPh, and  $\alpha$ -NO<sub>2</sub> functions. They can account for the larger effects of  $\alpha$ -alkyl substitution on kinetic than on equilibrium

(47) Mishima, M.; McIver, R. T., Jr.; Taft, R. W.; Bordwell, F. G.; Olmstead, W. N. *J. Am. Chem. Soc.* **1984**, *106*, 2717-2718.

acidities, which are frequently in inverse directions.<sup>38,48</sup> They can also account for the observation that substitution of a nitro group for an  $\alpha$ -hydrogen atom in  $\text{CH}_3\text{CH}_2\text{NO}_2$  to give  $\text{CH}_3\text{CH}(\text{NO}_2)_2$  causes increases in the deprotonation rates,  $k_{\text{H}_2\text{O}}$  and  $k_{\text{HO}^-}$ , of  $10^{4.45}$  and  $10^{4.84}$ , respectively, whereas the equilibrium acidity is increased by only 3.44  $\text{pK}_a$  units.<sup>25</sup>

**Summary and Conclusions.** Rate constants for base-catalyzed proton transfers occurring in the isomerization of  $\text{CH}_2=\text{CHC}-\text{H}_2\text{CN}$  to  $\text{CH}_3\text{CH}=\text{CHCN}$  in  $\text{Me}_2\text{SO}$  solution at  $\text{pK}_{\text{HB}} = 11$  are in the order  $\text{N} > \text{S}^-$ ,  $\text{O}^- > \text{N}^- > \text{C}^-$  when compared at the same basicity. The rate span of about 2 log units observed (Figure 2) corresponds to the extent of scatter that would be observed in a Brønsted plot constructed with the assumption that these bases belonged to a single family. An example of the scatter occurring in such a Brønsted plot may be observed in Figure 3. Scatter of this nature makes it difficult, if not impossible, to verify the curvature in the Brønsted plots predicted by the rate-equilibrium relationship (eq 1). Verification of such curvature is complicated further by differences in solvation of different types of anions and particularly by the fact that proton transfers do not occur by simple one-step mechanisms. Support for a two-step mechanism for proton transfers from carbon acids is provided by the failure of substituent effects on the reverse, protonation reaction, to conform to those observed in the deprotonation reaction, as is required by a one-step mechanism. The prediction that  $\beta$  in eq 1 should approach zero for exergonic reactions and unity for endergonic reactions is shown not to be borne out by experiment. Instead,  $\beta$  varies from 0.40 to 1.7 (Table II). The failure of eq 1 is attributed to the general adherence of base-protonated proton transfers from carbon acids to Cram's mechanism wherein an intermediate hydrogen-bonded carbanion is the initial "product". The proton transfers in Table II can be represented by hypothetical reaction profiles of the type shown in Figures 1 and 4. We conclude that the complexity of mechanisms for proton transfers renders a simple interpretation of  $\beta$  in terms of the extent of proton transfer in the transition state as unreliable. The lack of evidence for changes in  $\beta$  that can be clearly related to changes in  $\Delta G^\circ$  removes the experimental underpinning for the application of the Hammond-Leffler postulate to most organic reactions over the usual reactivity ranges studied.<sup>27</sup>

### Experimental Section

**Materials.** 3-Butenenitrile was distilled at atmospheric pressure, bp 117–120 °C, to give a colorless liquid. GC analysis showed <1% impurity. However, titration of anions of  $\text{pK}_a > 15$  in  $\text{Me}_2\text{SO}$  showed that about 4% acidic impurity was present. Titration of an acid anion of  $\text{pK}_a$  10.3 showed no impurity, so the acidity of the impurity was about 12 to 13 in  $\text{Me}_2\text{SO}$ .

The phenols were commercially available solids that were recrystallized from hexane and vacuum sublimed. The sulfonamides were prepared from the appropriate sulfonyl chloride and substituted aniline. The thiophenols were either recrystallized (*p*-Br) or vacuum distilled. The carbon acids were primarily indicators whose syntheses have been described before.<sup>7</sup>

**Kinetic Measurements.** All reactions were carried out under a blanket of argon in cuvettes sealed on top with three-way stopcocks, as previously described.<sup>7</sup>

In order to calculate the second-order rate constants for the isomerization reactions, the concentration of the base had to be known accurately. This was accomplished by two methods, depending on whether the anion was colored or not.

**Method I. For Colored Anions.** The procedure for generating colored anions is the same as that used for a  $\text{pK}_a$  run.<sup>7</sup> Briefly, weighed amounts of  $\text{Me}_2\text{SO}$  and stock dimsyl were added to the cuvette. Aliquots of the indicator solution were added and weighed, and the resulting absorbances at a fixed wavelength were recorded after each addition. From this a Beer's law plot was constructed and an  $\epsilon$  for the anion determined. Then, about a 10% excess of the indicator was added to make sure no dimsyl was left in the cuvette. After equilibration at 25 °C, a solution of 3-butenitrile (~0.1 mL of 300 mM solution) was added to start the reaction. The resulting drop in absorbance due to dilution and an acidic impurity was recorded, and the final anion concentration was calculated

from this absorbance and the  $\epsilon$ . The concentrations of the anions ranged from 1 mM for the fast reactions ((9-*m*-ClC<sub>6</sub>H<sub>4</sub>Fl<sup>-</sup>) to 15 mM for the slower reactions (2-PhSO<sub>2</sub>-9-PhFl<sup>-</sup>).

**Method 2. For Colorless Anions.** This method involved titrating the colorless acid (AH) with stock dimsyl in the presence of a colored indicator (HIn) of lesser acidity than AH. (1) First the empty reaction cuvette was tared and an indicator was chosen that was several  $\text{pK}_a$  units less acidic than the acid being titrated. Often, 9-PhFlH ( $\text{pK}_a = 17.9$ ) or 9-PhCH<sub>2</sub>FlH ( $\text{pK}_a = 21.3$ ) were used. (2) Two or three drops of the indicator solution (~50 mM) along with  $\text{Me}_2\text{SO}$  were added to the tared cuvette and weighed. The amount of  $\text{Me}_2\text{SO}$  added depended on what final anion concentration was desired. (3) A solution of the acid (AH) was added and weighed. (4) The stock dimsyl solution (~100 mM) was added slowly with shaking until the faint color of the indicator anion (In<sup>-</sup>) appeared, and weighed. (5) This was back-titrated with a drop or two of AH solution to barely quench the anion color, and weighed. (6) Another small amount of AH was added (~10% excess) to ensure that no residual dimsyl was left. (7) After equilibration at 25 °C, 3-butenitrile was added to begin the reaction.

The [A<sup>-</sup>] concentration was calculated from eq 2, where [AH]<sub>0</sub> is the concentration of the stock acid (AH) solution, and the numbers refer to the weight of the cuvette in the steps outlined above.

$$[\text{A}^-] = [\text{AH}]_0 \left( \frac{(3 - 2 + 5 - 4)}{7 - 1} \right) \quad (2)$$

Concentrations of 2 to 80 mM of [A<sup>-</sup>] were prepared in this way.

**GC Analysis.** The reactions were followed by comparing the ratios of *cis*- and *trans*-2-butenitrile to 3-butenitrile by gas chromatography (Varian 3700). Under the conditions of the GC (10% carbowax column at 50 °C), *cis*-2-butenitrile eluted at 11 min, *trans*-2-butenitrile at 16 min, and 3-butenitrile at 19 min.

For each run, 4 to 5 aliquots of the reaction mixture were analyzed at roughly evenly spaced intervals. To quench the reaction, an aliquot containing 0.1 to 0.2 mL of the reaction mixture was removed by syringe and poured into 1 mL of water containing 1 drop of acetic acid. This was extracted by shaking for 5 s with 0.2 to 0.3 mL of hexane. (Hexane was used because the butenenitriles are soluble in it but  $\text{Me}_2\text{SO}$  and most of the acids used were not.) About 1  $\mu\text{L}$  of this hexane solution was injected into the GC.

Several standard solutions of the butenenitriles in hexane were analyzed, and it was found that the ratios of 2-butenitrile to 3-butenitrile as determined by GC peak areas closely matched (within 1%) the ratios determined by weight. However, it was found that in the workup procedure, the extracted ratios were not the same as those in the reaction mixture. Consequently, a working curve was made. The working curve was made by simulating reaction conditions and workup, except that no anion was added. The curve was derived from 9 points ranging from 20% 3-butenitrile to 90% 3-butenitrile. For the standard solutions, a mixture of 2-butenitrile that contained 52% *cis*/48% *trans* was used (obtained from fractional distillation). After the workup procedure, GC analysis showed 62% *cis*/38% *trans*, very close to the ratios obtained from most of the reaction mixtures. After the working curve was established, three standards were run under exact reaction conditions, one containing 2-PhSO<sub>2</sub>-9-PhFlH, one containing 3,4,5-Cl<sub>3</sub>C<sub>6</sub>H<sub>2</sub>OH, and one containing PhSO<sub>2</sub>NHPh. These points all fall close to the working curve, showing that the type of nucleophile present did not affect the extraction ratios. Examination of the curve showed that 2-butenitrile is extracted more favorably than 3-butenitrile. Thus, when GC analysis shows 33% 3-butenitrile, there is actually 50% present in the reaction mixture. Because of this, many of the reactions were only followed to 60 or 70% completion.

As intimated above, the ratio of *cis*- to *trans*-2-butenitrile was about 1:1 in these reactions and varied only  $\pm 3\%$  for reactions with different nucleophiles. Czech workers reported a *cis*/*trans* ratio of 59/41 for this compound in *t*-BuOH.<sup>13</sup>

For three of the colored nucleophile ions, 9-PhSFl<sup>-</sup>, 9-(*m*-ClC<sub>6</sub>H<sub>4</sub>)Fl<sup>-</sup>, and 2-PhSO<sub>2</sub>-9-PhFl<sup>-</sup>, the absorbance of the indicator anion did not change during the entire time required for complete isomerization. This showed that the anion concentration was not decreasing during the reaction, ruling out any side reactions such as the Michael addition of the anion to the product 2-butenitrile.

Dimethyl sulfoxide slowly isomerized 3-butenitrile to 2-butenitrile (~10% reaction per week). Consequently, solutions of the nitrile in  $\text{Me}_2\text{SO}$  were kept frozen.

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