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Proton Transfer from Cyanocarbon Acids. II.[1] General-Base-Catalyzed Detritiation and Bromination of Malononitriles. Rates of the Reverse Reactions[2,3]

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Abstract: The detritiation of malononitrile-*1-t* and *tert*-butylmalononitrile-*1-t* in aqueous acid and in buffer solutions is a general-base-catalyzed reaction whose slow step is a proton transfer from the cyanocarbon acid. Catalytic coefficients for carboxylate anions conform to the Brønsted relation with an exponent $\beta = 0.98 \pm 0.02$. The bases, hydroxide ion and solvent water, show sizable deviations from the Brønsted plot. Bromination of the two malononitriles and of their 1-D derivatives in aqueous solution is also general base catalyzed and gives rates which are independent of bromine concentration and closely comparable to the detritiation rates, indicating that these rates are also determined by a slow proton transfer from the carbon acids. The primary hydrogen isotope effects are very low for reactions of the malononitriles with the bases water and acetate ion. This fact and also the Brønsted coefficient of almost unity indicate a transition state in which the proton is almost fully transferred from the cyanocarbon acid to the attacking base. Dissociation constants for the acids ($pK^0 = 11.19$ for malononitrile and 13.10 for the *tert*-butyl derivative) permit a calculation of the rates of the reverse reactions of their carbanions with general acids, and also hydronium ion. Typical rate coefficients at 25° are 4.0×10^9 and $1.0 \times 10^8\ M^{-1}\ \text{sec}^{-1}$ for reaction of the anion of *tert*-butylmalononitrile with hydronium ion and chloroacetic acid, respectively. These rates as well as their calculated isotope effects and energies of activation indicate the reverse reactions to be virtually diffusion controlled. This is plausible for the indicated transition state but is a considerably different behavior from the "slow" proton transfers exhibited by other important categories of carbon acids.

In the previous study of this series[1] it was demonstrated that the detritiation of 1,4-dicyano-2-butene, a carbon acid of p$K \sim 21$, exhibited general-base catalysis and isotope effects consistent with a slow proton transfer (I). A Bronsted exponent of nearly unity was observed and is compatible with a transition state where the proton (or triton) is almost completely transferred to the base catalyst. In other words, the slow rate of proton transfer (k_1) is determined by an unfavorable acid–base equilibrium (Ia) whose reverse rate has attained a maximum value. This thesis was supported by calculation of approximate reverse rates which were on the order of the diffusion limit. These calculations, however, involved only a tentative pK for the cyanocarbon species because of difficulties in measurement for such a weak acid.

$$\text{RCL} + \text{B} \overset{k_1}{\rightleftharpoons} \text{RC}^- + \text{BL}^+ \quad \text{slow} \qquad \text{(Ia)}$$

$$\text{RC}^- + \text{HA} \rightleftharpoons \text{RCH} + \text{A}^- \quad \text{fast} \qquad \text{(Ib)}$$

It is of interest to extend these studies to additional cyanocarbon acids to determine whether the behavior observed for 1,4-dicyano-2-butene is typical of proton transfer from carbon activated with α-cyano groups. This would identify cyanocarbons as rather different from many other classes of carbon acids.[5]

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(1) Part I: E. A. Walters and F. A. Long, *J. Amer. Chem. Soc.*, **91**, 3733 (1969).

(2) Work supported by the Atomic Energy Commission.

(3) Presented in part at the 158th National Meeting of the American Chemical Society, New York, N. Y., Sept 1969.

(4) To whom requests for reprints should be sent.

(5) (a) M. Eigen, *Angew. Chem., Int. Ed. Engl.*, **3**, 1 (1964); (b) R. P. Bell, *Quart. Rev., Chem. Soc.*, **13**, 169 (1959).

We now present results on the proton transfer from malononitrile and *tert*-butylmalononitrile. These molecules were chosen because their pK values can easily be determined in the pH range; thus firm calculations of the rates of the reverse reactions may be made. In addition, the ionization of these stronger acids, unlike that of 1,4-dicyano-2-butene, is expected to show catalysis by the solvent water as well as by other general bases.

Detritiation of tritium-labeled molecules and bromination of 1-H and 1-D derivatives permit measurement of the rate coefficient k_1 in the forward direction in reactions I, since both bromination and detritiation are controlled by a slow proton (or trition) transfer from the carbon acid.

Experimental Section

Materials. Malononitrile was labeled with tritium by dissolving the solid (1.0 g) in tritiated water (50 mCi in 10 ml), stirring for 1 hr, and extracting with ether. The product was purified by recrystallization (ether–hexane) and by vacuum sublimation at 30–35°.

tert-Butylmalononitrile was kindly supplied by Dr. O. W. Webster of E. I. du Pont de Nemours and Co.; pure samples were obtained by vacuum sublimation at 70–80°. The material was tritiated by exchange in an ethyl acetate–tritiated water mixture containing 50 mCi and 0.5 g of NaOH/ml. *tert*-Butylmalononitrile-*1-d* was prepared by allowing the 1-H compound to exchange in a dioxane–D_2O mixture (50% v/v) for 20 hr. The nmr spectrum showed 97 ± 2% D in the 1 position after one exchange and 98 ± 2% D after a second.

Inorganic salts of Analar grade were dried before use, dioxane was refluxed with sodium and distilled, and allyl alcohol was distilled. Doubly distilled water was used for most experiments, and deuterium oxide was the ICN product containing 99.75% D. Hydrochloric acid solutions were Fisher volumetric standards. Aqueous buffer solutions were made up from standardized carboxylic acid solutions and standard sodium hydroxide. The pH ($= -\log [H_3O^+]$) of each buffer solution was calculated using pK values (25°, $I = 0.100$) which were derived by the Debye–Hückel approximation from equilibrium constants at zero ionic strength.[6] These pH values were confirmed with a Radiometer Model 4 pH meter.

Equilibrium Measurements. The dissociation constant of malononitrile has been measured many times;[7] an average value of pK^0 = 11.19 is used in this paper. The pK of *tert*-butylmalononitrile in aqueous solution at 25.0° and an ionic strength of 0.1 M was determined by a procedure using the absorption spectrum of *tert*-butylmalononitrile anion (Σ 2.06 × 10^4 cm^2 mol^{-1} at 2375 Å). At the wavelength used the extinction coefficient of the undissociated acid, determined in acidic solutions, is almost negligible.

All measurements were made on a Cary 14 instrument. Owing to the slow rate of dissolving of solid *tert*-butylmalononitrile and the instability of its anion in alkaline solutions, a dioxane solution of the cyanocarbon (0.01 ml) was injected directly into an aqueous solution (3.0 ml) contained in a thermostated cell. The measured absorbance readings were extrapolated to the time of mixing. A correction of approximately 2% to the first optical density reading was normally involved, and values were reproducible to ±1%. Measurements were taken in sodium hydroxide solutions (8.0×10^{-3}–0.100 M) containing varying concentrations of *tert*-butylmalononitrile.

A graphical method was used to compute both the extinction coefficient of the anion and a value of $K = 1.31 \pm .03 \times 10^{-13}$ for the dissociation constant of the cyanocarbon acid. An alternative method based on the extinction coefficient of the anion in 2 and 4 M sodium hydroxide solutions, in which the acid is almost completely dissociated, gave $K = 1.40 \pm .04 \times 10^{-13}$. The mean value was corrected using the Debye–Hückel approximation to give a dissociation constant, referring to infinite dilution, $K^0 = 7.9 \pm 4 \times 10^{-14}$ (pK^0 = 13.10 ± 0.02).

Kinetic Methods. The stability of malononitrile in aqueous solutions of acid pH is well known.[7] Before kinetic measurements were made with *tert*-butylmalononitrile it was examined under all reaction conditions and found to be comparably stable.

Detritiation. For reaction in aqueous buffer solutions the rate of dissolution of *tert*-butylmalononitrile-*1-t* is slow compared with its rate of tritium exchange. A dioxane solution of the labeled substrate was therefore injected into the reaction mixture to initiate each run. The volume of dioxane added in this way was only 0.05%. For the slower runs, rate coefficients determined for reactions initiated by addition of the solid to a fully aqueous solution were identical with those begun by adding a dioxane solution. Runs with malononitrile were usually begun by introduction of the solid.

The rates of detritiation were measured by the method of Halevi and Long.[8] Quenched samples of the reaction mixture were rapidly extracted with xylene (about 80% *tert*-butylmalononitrile was removed in a single extraction) and subjected to liquid scintillation counting (Packard TriCarb, Model 314DC). All reactions were carried out under pseudo-first-order conditions, and rate coefficients were calculated as gradients of log ($c_t - c_\infty$) against time plots, where c_t and c_∞ are the counts at time t and infinite time (at least ten half-lives), respectively. Reactions were followed for a minimum of three half-lives and the rate coefficients were reproducible to ±2% for *tert*-butylmalononitrile and to ±3% for malononitrile.

Bromination. The rate of bromination of malononitrile was measured by a spectrophotometric method and also by a product titration method. For *tert*-butylmalononitrile only the latter was used, since the spectral method was complicated by the precipitation of 1-bromo-*tert*-butylmalononitrile. All reactions were carried out with bromine in excess over malononitriles and at an ionic strength kept at 0.1 M with potassium bromide.

In the spectral method, a small volume (*ca.* 0.1 ml) of an aqueous solution of malononitrile was injected into the reaction mixture (3.0 ml) in a 1-cm quartz cuvette contained in the thermostated cell housing of a Cary 14 spectrophotometer. Typical initial concentrations were 4.1×10^{-3} M for malononitrile and 1.84×10^{-2} M for bromine. The decrease in bromine optical density (D) at 5090 Å was followed with time. The customary plot of log ($D_t - D_\infty$) *vs.* t was linear over two half-lives, and rate coefficients were obtained from the gradients.

The titration method was similar to that of Bell, *et al.*[9] A solution (5 ml) of one of the malononitriles in a reaction mixture containing all components except bromine was added to 20 ml of the reaction mixture. A typical reaction solution contained 2.85×10^{-3} M *tert*-butylmalononitrile and 4.69×10^{-2} M bromine together with 5.25×10^{-3} M hydrochloric acid. At a time t after the initiation of the reaction, bromination was stopped by adding a 30% solution of allyl alcohol (2–3 ml); then 4 ml of 3 M sodium acetate solution and a few crystals of potassium iodide were added. The liberated iodine was titrated with sodium thiosulfate solution (2×10^{-3} M) using starch as indicator. Further titrations were carried out at intervals of 30 min until no more iodine was produced; three titrations were usually sufficient. The total volume (V_t) of thiosulfate required for different reaction times (t) was determined. Plots of log ($V_\infty - V_t$) *vs.* t were linear over about two half-lives. First-order rate coefficients determined from these plots were normally reproducible to ±4%.

Brominations involving deuterated malononitriles in H_2O were carried out somewhat differently. For malononitrile-*1-d*$_2$ a concentrated solution of malononitrile in D_2O (about 0.5 M) was used to initiate the reaction; sufficient time was allowed for complete deuteration before the reaction was begun. For *tert*-butylmalononitrile, on the other hand, the solubility is such that this procedure introduces appreciable quantities of D_2O into the aqueous (H_2O) reaction mixture. Bromination of this malononitrile was therefore begun by introducing a dioxane solution of the deuterated solid. The volume of dioxane added was about 0.5% of the aqueous solution.

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[6] G. Kortun, W. Vogel, and K. Andrussow, "Dissociation Constants of Organic Acids in Aqueous Solution," Butterworths, London, 1961.

[7] (a) R. G. Pearson and R. L. Dillon, *J. Amer. Chem. Soc.*, **75**, 2439 (1953); (b) F. Hashimoto, J. Tanaka, and S. Nagakura, *J. Mol. Spectrosc.*, **10**, 401 (1963); (c) R. H. Boyd and C.-H. Wang, *J. Amer. Chem. Soc.*, **87**, 430 (1965); (d) K. Bowden and R. Stewart, *Tetrahedron*, **21**, 261 (1965).

[8] E. A. Halevi and F. A. Long, *J. Amer. Chem. Soc.*, **83**, 2809 (1961).

[9] (a) R. P. Bell, D. H. Everett, and H. C. Longuet-Higgins, *Proc. Roy. Soc., Ser. A*, **186**, 443 (1946); (b) R. P. Bell and J. E. Crookes, *ibid., Ser. A*, **286**, 285 (1965).

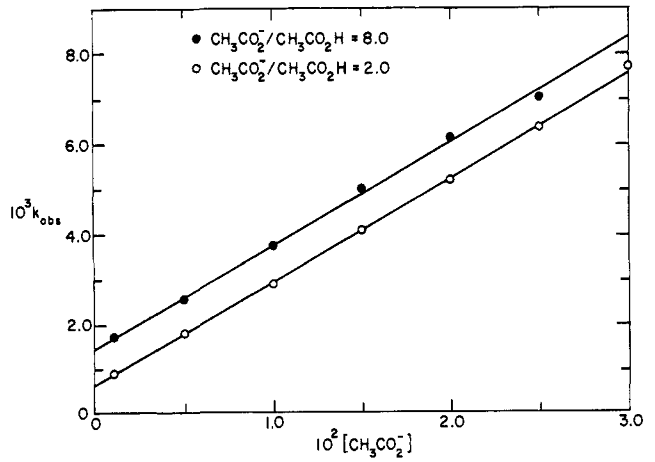

Figure 1. Acetate-catalyzed detritiation of *tert*-butylmalononitrile.

For *tert*-butylmalononitrile the V_∞ values after complete reaction corresponded exactly to those calculated assuming 1:1 stoichiometry of the bromination. For malononitrile in the spectral method, the decrease in bromine absorbance indicated 1.9 mol of bromine removed for each mole of malononitrile. The expected result is 2.0 mol. However, a stoichiometry of only 1:1.4 was calculated for the titration method. This may be connected with a less than complete liberation of iodine from potassium iodide by malononitrile dibromide.[9a]

Results

Detritiation of Malononitriles. The Water Reaction. The rates of detritiation of malononitrile-*1-t* and *tert*-butylmalononitrile-*1-t* were measured in hydrochloric acid solutions at an ionic strength $I = 0.100\ M$. Within the range of acidities studied ($[H_3O^+] = 1.0 \times 10^{-3}$–$0.100\ M$) the rates of detritiation were constant. The observed first-order rate coefficients at 25° can be converted to catalytic coefficients for detritiation for the base water by division by 55.5 M. The values are 1.51×10^{-4} and $5.89 \times 10^{-6}\ M^{-1}\ sec^{-1}$ for malononitrile and the *tert*-butyl derivative, respectively. Rates of detritiation were also measured at several temperatures for both malononitriles. The Arrhenius parameters shown in Table I were calculated from these data.[10]

Table I. Rate Coefficients and Activation Parameters for Water-Catalyzed Detritiation[a]

Temp, °C	Malononitrile $10^3 k_{obsd}$, sec^{-1}	*tert*-Butylmalononitrile $10^5 k_{obsd}$, sec^{-1}
5.1	1.08	
10.0		5.68
15.0		10.6
15.2	3.06	
25.0	8.37 ± 0.16	32.7 ± 0.2
35.0		91.4
45.0		236
Activation parameters; k, M^{-1} sec^{-1}		
$\Delta G^\ddagger$, kcal mol^{-1}	22.7	24.6
$\Delta H^\ddagger$, kcal mol^{-1}	16.2	18.5
$\Delta S^\ddagger$, cal deg^{-1} mol^{-1}	−21.8	−20.7
E_a, kcal mol^{-1}	16.8	19.1

[a] $I = 0.100$; $[H_3O^+] = 1.00 \times 10^{-3}\ M$.

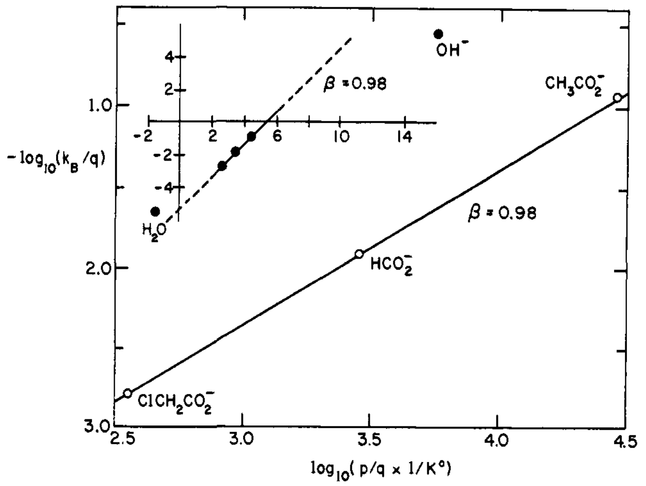

Figure 2. Brønsted plot for *tert*-butylmalononitrile.

General-Base Catalysis. The detritiation of *tert*-butylmalononitrile-*1-t* was studied in acetate, formate, and monochloroacetate buffer solutions. By systematic variation of buffer ratios and concentrations, the individual contributions to the observed rate from the bases water, hydroxide, and carboxylate ions were determined. A typical plot of buffer concentration against rate coefficient for two ratios of an acetic acid–acetate buffer is shown in Figure 1. The catalytic coefficient for the buffer anion is calculated from the gradient. The intercept contains contributions from hydroxide ion and solvent water; using the catalytic coefficient for water, that for hydroxide can therefore be calculated. Hydroxide ion makes only a very small contribution in all but the acetate buffer solutions. In these other cases the intercept of plots like Figure 1 corresponds exactly with the water-catalyzed detritiation. All the data were treated by least-squares analysis, and the resulting catalytic coefficients for detritiation are shown in Table II.

Table II. Base-Catalyzed Detritiation, 25°

$$RCT + B \xrightarrow{k_B} RC^- + BT^+$$

Base (B)	pK^0 [a]	k_B, M^{-1} sec^{-1} *tert*-BuCH(CN)$_2$	$CH_2(CN)_2$
H_2O	−1.74	5.89×10^{-6}	1.51×10^{-4}
$ClCH_2CO_2^-$	2.85	3.25×10^{-3}	
HCO_2^-	3.75	2.52×10^{-2}	1.23
$CH_3CO_2^-$	4.76	0.231	
OH^-	15.75	2.48×10^{5}	

[a] See ref 6.

The data for *tert*-butylmalononitrile are shown in Figure 2 as a plot of the Brønsted relationship (1),[11]

$$\log k_B/q = \beta \log [(p/q)(1/K^0)] + \text{constant} \qquad (1)$$

where k_B is the base catalytic coefficient and K^0 the dissociation constant of the conjugate acid of the base B. The statistical factors for carboxylate anions were taken as $p = 1$, $q = 2$. For the acid–base pairs H_2O–OH^- and H_3O^+–H_2O the values $p = 2$, $q = 1$ and $p = 3$, $q = 2$ were used, respectively.[12] Rate coefficients

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(10) In part I of this series[1] the activation parameters for the hydroxide-ion-catalyzed detritiation of 1,4-dicyano-2-butene were calculated incorrectly. We are indebted to Professor J. Hine for pointing out this mistake. The corrected values (k, M^{-1} sec^{-1}) are: $E_a = 15.3$ kcal mol^{-1}, $A = 3.5 \times 10^{10}\ M^{-1}$ sec^{-2}, $\Delta G^\ddagger = 18.4$ kcal mol^{-1}, $\Delta H^\ddagger = 14.7$ kcal mol^{-1}, and $\Delta S^\ddagger = -12.4$ eu.

(11) J. N. Brønsted, *Chem. Rev.*, 5, 322 (1928).

(12) (a) R. P. Bell, "Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p 159; (b) V. Gold and D. C. A. Waterman, *J. Chem. Soc. B*, 839 (1968).

Table III. Bromination of Malononitriles[a]

Temp, °C	10^2k, sec^{-1}		10^4k, sec^{-1}	
	$CH_2(CN)_2$	$CD_2(CN)_2$	*tert*-$BuCH(CN)_2$	*tert*-$BuCD(CN)_2$
0.0	0.202[b]			
10.0	0.584[b]			
25.0	2.86 ± 0.06 (3)[c]	1.90 ± 0.06 (2)		
25.0	2.86 ± 0.18 (4)[d]		5.36 ± 0.14 (4)	3.68

[a] $[Br_2] = 0.01–0.10\,M$; $[HCl] = 1 \times 10^{-3}–8 \times 10^{-3}\,M$; $I = 0.10$; k = observed rate coefficient. [b] Data from ref 7a. [c] Spectral method. [d] Product titration method.

for carboxylate anions conform to eq 1 with $\beta = 0.98 \pm 0.02$; *i.e.*, the Brønsted exponent is practically unity. The bases water and hydroxide ion have been deliberately neglected in Figure 2 since these species often show deviations from Brønsted plots.[1,13] The measured β is similar to that observed in the amine- and phenoxide-ion-catalyzed detritiation of 1,4-dicyano-2-butene.[1]

In eq 1 it should be noted that K^0 refers to the dissociation of the proton acid, whereas k_B is for a detritiation reaction. The catalytic coefficient referring to proton transfer should preferably be used. However, provided the primary isotope effect does not change between formate and acetate ions, the Brønsted exponent will be unchanged. Evidence that this is true for much more drastic changes in the base catalyst is discussed below.

Table II contains catalytic coefficients for the water- and formate-ion-catalyzed detritiation of malononitrile and *tert*-butylmalononitrile. As noted by Bell,[14] Brønsted relationships can be generated by varying either of the conjugate pairs involved in an acid–base equilibrium. We can therefore consider the two malononitriles as general acids in the transfer of a proton to the bases formate ion and water. Using statistically corrected pK values for these cyanocarbon acids, Brønsted exponents α of 0.90 ± 0.05 and 1.06 ± 0.05 for transfer to water and formate ion, respectively, were obtained.

Bromination of Malononitriles. The rates of bromination of malononitrile, malononitrile-*1-d*$_2$, *tert*-butylmalononitrile, and *tert*-butylmalononitrile-*1-d* were measured in aqueous hydrochloric acid solutions at 25.0°. The rates were independent of bromine concentration ($1 \times 10^{-2}–10 \times 10^{-2}\ M$) and acid concentration ($1 \times 10^{-3}–8 \times 10^{-3}\ M\ H_3O^+$). At lower bromine or higher acid concentration the first-order plots were not linear nor were the rate coefficients constant. Similar behavior has been observed in other zero-order bromination reactions.[7a,15] Pseudo-first-order rate coefficients for solvent-water-catalyzed bromination of the malononitriles are shown in Table III. For malononitrile, since two protons are replaced in the bromination, the rate of ionization of a single proton was taken as half the observed rate of bromination by assuming that monobromomalononitrile is much more reactive than malononitrile itself.[7a]

The rate of bromination of malononitrile has been measured previously at 0 and 10° by a conductometric method,[7a] and from these data a rate coefficient at 25° was calculated. The agreement at 25° between our measured rate coefficient ($k = 2.86 \times 10^{-2}$ sec^{-1}) and that calculated from Pearson and Dillon's data ($k = 2.62 \times 10^{-2}$ sec^{-1}) is reasonable in view of the extrapolation involved for the latter and the differences in ionic strength.

The rate of bromination of *tert*-butylmalononitrile was measured in aqueous acetate–acetic buffer solutions at 25° and an ionic strength $I = 0.200$. The rates were independent of bromine concentration. A linear dependence of the rate on the concentration of acetate ion was observed, as shown in Table IV. The data were not of sufficient precision, however, to allow calculation of the rate of the hydroxide-ion-catalyzed reaction. Because of the formation of acid in the bromination, solutions with lower buffer concentrations or buffer ratios in which the contribution from hydroxide ion would be larger could not be used.

Table IV. Base-Catalyzed Bromination of Malononitriles[a]

$10^2[CH_3CO_2^-]$, M	$[CH_3CO_2^-]/[CH_3CO_2H] = 1.00$ 10^3k_{obsd}, sec^{-1}	$[CH_3CO_2^-]/[CH_3CO_2H] = 0.500$ 10^3k_{obsd}, sec^{-1}
2.00	11.2	8.64
3.00	14.2	12.8
4.00	16.8	18.4
5.00	22.3	20.0
6.00	26.0	24.8
7.00	31.3	28.2
8.00	34.0	33.3
k_B, M^{-1} sec^{-1}	0.409	0.397

[a] $[Br_2] = 2.65 \times 10^{-2}–7.18 \times 10^{-2}\ M$, $I = 0.200$, $[BuCH(CN)_2]_{init} = 1.0 \times 10^{-3}\ M$.

To summarize the results, the second-order rate coefficients for bromination are: for $CH_2(CN)_2$, $k_{H_2O} = 5.16 \times 10^{-4}\ M^{-1}$ sec^{-1}; for *tert*-$BuCH(CN)_2$, $k_{H_2O} = 9.66 \times 10^{-6}\ M^{-1}$ sec^{-1} and $k_{OAc^-} = 0.403\ M^{-1}$ sec^{-1}, this last being for $I = 0.2$ instead of $I = 0.1$.

Discussion

The finding of general-base catalysis in the detritiation and bromination of malononitriles and the kinetic details of the bromination (rate coefficients which are independent of bromine and acid concentrations) identify both as involving rate-determining proton (or triton) transfer as in

$$\begin{array}{lll} RCT + B \xrightarrow{k^T} RC^- + BT^- & \text{slow} & \\ RC^- + HA \longrightarrow RCH + A^- & \text{fast} & \text{(II)} \end{array}$$

$$\begin{array}{lll} RCH\ (\text{or } RCD) + B \xrightarrow{k^H \text{ or } k^D} RC^- + BH^+ & \text{slow} & \\ RC^- + Br_2 \longrightarrow RCBr + Br^- & \text{fast} & \text{(III)} \end{array}$$

Brønsted Catalysis. The Brønsted exponent is often regarded as a good indication of the position of the

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(13) For example, R. P. Bell and O. M. Lidwell, *Proc. Roy. Soc., Ser. A*, 176, 88 (1940); R. P. Bell, R. D. Smith, and L. A. Woodward, *ibid., Ser. A*, 192, 479 (1948).

(14) Reference 12a, p 160.

(15) R. P. Bell and M. Spiro, *J. Chem. Soc.*, 429 (1953).

transition state along the reaction coordinate.[16] If we adopt this idea, the measured exponent for carboxylate ions in the detritiation of *tert*-butylmalononitrile indicates a transition state in which the proton is almost completely transferred from the carbon acid. This interpretation is strengthened by the very similar Brønsted coefficients which are generated when the base catalyst is left unchanged but the cyanocarbon acid is varied. This is not always the case; for proton transfer from a series of nitroparaffins,[17] variation of the nitroparaffin entity gives $\alpha = -0.7$, but variation of base catalyst gives $\beta = 0.5$. Clearly, both cannot refer to the degree of proton transfer.

Isotope Effects. The primary isotope effects for these reactions were calculated from the data for detritiation (Tables I and II) and for bromination (Tables III and IV), but further details of these and the solvent isotope effects are given in a subsequent paper.[18] For the present discussion only the conclusions from the primary isotope effect studies are needed. These are that for both malononitriles and for the two catalysts H_2O and acetate ion all of the data concur in demonstrating the unusually low value of $k^H/k^D = 1.48 \pm 0.02$. These isotope effects are about the lowest ever observed for proton transfer from carbon. An isotope effect $k^H/k^D = 1.66$–1.76 was observed by Cram[19] and coworkers in the racemization of 1-phenylmethoxyethane and its 1-D derivative in dimethyl sulfoxide–*tert*-butyl alcohol–potassium *tert*-butoxide at 80°. The rate of racemization is thought to measure the rate of exchange in this reaction. In the hydroxide-ion-catalyzed exchange of dichlorofluoromethane, Hine[20] observed an isotope effect $k^H/k^D = 1.52$. Finally, Bell and Crookes[9b] observed $k^H/k^D = 1.97$ for the water-catalyzed bromination of ethyl malonate. In other slow proton transfers from carbon the primary isotope effect has been shown to have maximum values (around 7) when the proton is held equally by the two atoms between which it is being transferred, that is, when the transition state is symmetrical.[21] Low isotope effects have been associated with reactions where the proton is either only slightly or almost completely transferred from the carbon moiety in the transition state. The low values observed here are compatible with our conclusion from Brønsted exponents that the proton is fully transferred to the base catalyst when the transition state is reached. The similarity of isotope effects for catalysis by water and acetate ion implies that the degree of proton transfer is the same for each. This similarity combined with the extremely low isotope effects is good evidence that the proton is completely transferred. Otherwise, one would expect a change in the isotope effect when the strength of the catalyzing base is changed, as here, by as much as 6 pK units.[21]

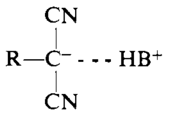
As the subsequent paper shows, one can use these primary isotope effects along with equilibrium data to calculate primary isotope effects for the reverse reactions. The results for reactions of the *tert*-butylmalononitrile anion in the solvent water to give the two products RCH and RCD are

$$(k_{\mathrm{RC^-+H_3O^+}})/(k_{\mathrm{RC^-+DH_2O^+}}) = 1.02$$

$$(k_{\mathrm{RC^-+HOAc}})/(k_{\mathrm{RC^-+DOAc}}) = 1.40$$

The absence of a primary isotope effect in the hydronium ion case and the small effect for reaction of acetic *vs.* deuterioacetic acid are compatible with reactions in which little change occurs in the force constants of the isotopic bond on going to the transition state. This is the expected result for a diffusion-controlled process. Another way to express this is to note that the kinetic isotope effect in the forward direction is identically the equilibrium isotope effect, indicating a transition state with properties very similar to the products RC^- and H_3O^+ or RC^- and HOAc.

Structure of the Transition State. All of the results so far discussed are in agreement with the proposal that the transition state for these cyanocarbon proton-transfer reactions (except perhaps the reaction with hydroxide ion) is one in which the proton is fully transferred to the attacking base.



$$\mathrm{R{-}\overset{\displaystyle CN}{\underset{\displaystyle CN}{C^-}}\cdots HB^+}$$

In a broad sense this result is in turn compatible with the recent theoretical analyses of Marcus[22] who has concluded that the Brønsted exponent is by itself a useful measure of the degree of proton transfer. Our results support this conclusion.

One can, however, ask about a finer grained aspect of the transition state structure, namely the arrangement of waters of solvation around it. This was demonstrated to be important in Eigen's early analyses of fast reactions between ions[23] and in recent years Kreevoy[24] notably has concerned himself with the question of whether water molecules form a chain through which the proton transfer is actually accomplished, *i.e.*, whether a better representation of the transition state is

$$\mathrm{RC^- \cdots (H_2O)_n \cdots HB^+}$$

For the present case some contribution to an answer can be obtained from the rates of the reverse reaction, to which we now turn.

Rates of the Reverse Reaction. It is possible, given rate coefficients in the forward direction and equilibrium data for the ionization of malononitriles, to derive detailed information about the reverse reactions between malononitrile anions and general acids. Two areas will be discussed: the magnitude of the rates of the reverse reactions (free energies of activation) and their heats of activation.

The rates of triton removal from *tert*-butylmalononitrile by formate, chloroacetate, and hydroxide ions were converted to rates of proton transfer using

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(16) Reference 12a, Chapter 10; J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," Wiley, New York, N. Y., 1963, p 157; R. A. Marcus, *J. Phys. Chem.*, 72, 891 (1968).

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(19) D. J. Cram, C. A. Kingsbury, and B. Rickborn, *ibid.*, **83**, 3688 (1961).

(20) J. Hine and N. W. Burske, *ibid.*, **78**, 3337 (1956).

(21) R. P. Bell and D. M. Goodall, *Proc. Roy. Soc., Ser. A*, **294**, 273 (1966); J. L. Longridge and F. A. Long, *J. Amer. Chem. Soc.*, **89**, 1292 (1967); A. J. Kresge, D. S. Sagatys, and H. L. Chen, *ibid.*, **90**, 4174 (1968); J. E. Dixon and T. C. Bruice, *ibid.*, **92**, 905 (1970).

(22) R. A. Marcus, *J. Phys. Chem.*, **72**, 891 (1968); A. O. Cohen and R. A. Marcus, *ibid.*, **72**, 4249 (1968); R. A. Marcus, *J. Amer. Chem. Soc.*, **91**, 7224 (1969).

(23) M. Eigen, *Z. Elektrochem.*, **64**, 115 (1960).

(24) M. M. Kreevoy and J. M. Williams, Jr., *J. Amer. Chem. Soc.*, **91**, 6809 (1969).

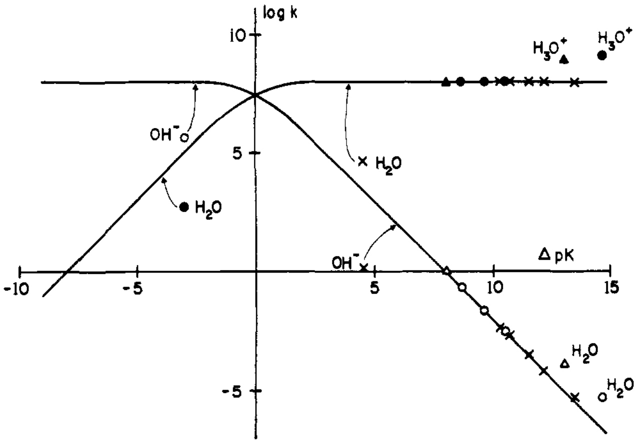

Figure 3. Forward and reverse rates of proton transfer from cyanocarbon acids. Open and closed points represent forward and reverse rate coefficients, respectively: for *tert*-butylmalononitrile, ○ and ●; for malononitrile, △ and ▲; for 1,4-dicyano-2-butene, × and ×. Statistical corrections on rate coefficients and equilibrium constants are included.

the measured isotope effect (k^H/k^T) for transfer to acetate ion. Since the isotope effect remains essentially constant on changing the base catalyst from acetate to water, it is likely to be the same also for formate and chloroacetate ions. This may not be true for hydroxide ion, however, and therefore our assumption introduces a slight uncertainty into the proton-transfer rate in this case. Rate coefficients for proton transfer were then combined with dissociation constants (K_{RCH} and K_{BH^+}) to calculate rate coefficients for the reaction between carbanions (RC$^-$) and general acids (BH$^+$).

$$\mathrm{RCH} + \mathrm{B} \overset{K}{\rightleftharpoons} \mathrm{RC}^- + \mathrm{BH}^+$$

$$K = k_1/k_{-1} = K_{RCH}/K_{BH^+} \qquad k_{-1} = k_1(K_{BH^+}/K_{RCH})$$

The results of these calculations are shown in Table V. The uncertainty in the rate coefficients is about ±8%.

Table V. Reverse Rates for Malononitriles[a]

$$\mathrm{RCH} + \mathrm{B} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{RC}^- + \mathrm{BH}^+$$

B	BH$^+$	k_1, M^{-1} sec^{-1}	$10^{-8}k_{-1}$, M^{-1} sec^{-1}
	Malononitrile		
H_2O	H_3O^+	5.16×10^{-4}	26
HCO_2^-	HCOOH	4.20	1.2
	tert-Butylmalononitrile		
H_2O	H_3O^+	9.66×10^{-6}	40
OH^-	H_2O	4.32×10^{5}	9.2×10^{-6}
$ClCH_2CO_2^-$	$ClCH_2CO_2H$	5.66×10^{-3}	1.01
HCO_2^-	HCO_2H	4.38×10^{-2}	0.98
$CH_3CO_2^-$	CH_3CO_2H	0.403	0.88

[a] I = 0.100, temperature = 25.0°.

The most significant feature of the k_{-1} values of Table V is that for all of the carboxylic acid reactions they are almost constant at 1×10^8 M^{-1} sec^{-1}. The magnitude of this value implies virtually a diffusion-controlled process. The constancy indicates a Brønsted α of zero, consistent with the observed β of 0.98. The reverse rate coefficients for hydronium ion are in the order of 3×10^9 M^{-1} sec^{-1}, *i.e.*, about 30-fold larger than for the carboxylic acids. This is about the difference normally observed in diffusion rates[5a] and is further evidence that the essential controlling step is diffusion. The higher rate for hydronium ion is usually attributed to the abnormal mobility of the proton in water. Interestingly, the H_3O^+ deviation from the Brønsted α plot (see Figure 3) offers a rationalization of the comparable deviation of the point for water from the associated Brønsted β plot, in that the enhanced reverse rate for H_3O^+ can be thought of as dictating, through the equilibrium, an enhanced activity of water as a base catalyst. In this sense the position of the water point is normal.

A revealing way to compare these various data is the Eigen-type plot of Figure 3, which includes also the data for another cyanocarbon acid, 1,4-dicyano-2-butene.[1] A first notable point is that in the region of $\Delta pK > 6$ the data for these different cyanocarbon acids fall nicely on the same two Brønsted lines.[25] This offers further confirmation of the conclusion that these proton transfers belong to the simple "physical" class whose rates depend essentially on diffusion limits and on the free energy requirements for the ionization.

The departure of points for the H_2O–H_3O^+ pair from the lines of Figure 3 has already been commented upon and is as expected. The large negative deviation for the OH^-–H_2O pair is, however, much more difficult to interpret, especially since there is evidence that with other carbon acids, *e.g.*, $CHCl_3$,[26] this deviation does not occur. For the *tert*-butylmalononitrile case, in the absence of data for $\Delta pK = 0$ the deviation could perhaps be rationalized by assuming a very unsymmetrical Eigen plot which extrapolated to much lower limiting rates on the negative ΔpK side. However, this would not resolve the similar deviations for the dicyano-2-butene case. Tentatively we assume that the OH^-–H_2O results are truly anomalous and suspect that they relate in some way to the effects of cyanocarbon species on the structure of water. This point, as well as rate behavior in the region of $\Delta pK = 0$, is being investigated further. It is worth noting that, at least for the dicyano-2-butene species, had not OH^- shown a negative deviation, general-base catalysis would not have been observable.

It is important to note that both for carboxylic acids and for hydronium ion the reverse rates of Table V are about a factor of 10 smaller than the "normal" values of 10^9 and 4×10^{10} M^{-1} sec^{-1}, respectively, as listed in Eigen's tabulation.[5a] The accuracy of the rate and equilibrium data here is sufficiently high that the tenfold smaller size of our reverse rates is significant. This factor of 10 implies that an additional $\Delta G^{\pm}$ of 1.4 kcal mol^{-1} is needed, beyond that for diffusion, to reach the transition state for the process. A possible explanation is that some

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(25) Actually, the excellent fit for 1,4-dicyano-2-butene results from assuming a value of 20 for the pK of this acid rather than using the tentative value of 21 given in the earlier publication.[1] Use of pK = 21 would raise all of the points for this species by one unit in log k and one unit in ΔpK. A further point is that, except for the H_2O–H_3O^+ pair, all of the acid–base catalyst pairs of Figure 3 belong to the same charge type, X^-–HX. The dicyanobutene molecule was also studied with neutral amine bases, R_2NH–$R_2NH_2^+$, and, as expected from Eigen's earlier studies and discussions, these latter data fall about half a unit of log k above those for the X^- category.

(26) J. Hine, N. W. Burske, M. Hine, and P. B. Langford, *J. Amer. Chem. Soc.*, 79, 1406 (1957); unpublished work in this laboratory.

restructuring of the solvation shells is needed. The transition state for a pure diffusion process must be a simple encounter complex between the two fully solvated species. It is plausible that a proton transfer to a carbon acid anion requires the attacking acid to be adjacent to the carbon anion, *i.e.*, that transfer through an intervening solvent shell has only a low probability. In a sense the fact that reactions of many carbon anion bases are "slow," *i.e.*, are far from attaining a diffusion-limiting rate even when the situation is thermodynamically favorable, lends support to the idea that requirements for proton transfer may be relatively more demanding for carbon bases than for others, *e.g.*, oxygen or nitrogen bases.

Some further confirmation that the reverse reactions behave very nearly like a diffusion-controlled process comes from a calculation of $\Delta H^{\ddagger}$ for the reactions. The available data on the thermodynamics of ionization of malononitrile[7c] together with the activation parameters for water-catalyzed detritiation of malononitrile permit a calculation of the activation parameters for the reaction between hydronium ion and malononitrile anion. First, the activation data for detritiation were converted to proton transfer. The isotope effect ($k^{\mathrm{H}}/k^{\mathrm{T}}$) was assumed to result from a difference in activation energies for the two isotopic reactions.[27] A statistical factor was also applied; this affects only the entropy of activation. These activation parameters were then combined with Boyd's data and the resulting parameters for the reverse reaction are shown in Table VI and Figure 4.

Table VI. Thermodynamic Parameters[a]

$CH_2(CN)_2 + H_2O \rightleftharpoons CH(CN)_2^- + H_3O^+$

	ΔG, kcal mol^{-1}	ΔH, kcal mol^{-1}	$T\Delta S$, kcal mol^{-1}	ΔS, eu
Forward	22.0	15.9	−6.1	−20.4
Equilibrium	15.28	13.4	−1.9	−6.4
Reverse	6.7	2.5	−4.2	−14.0

[a] Rate coefficients in M^{-1} sec^{-1}; temperature, 25°.

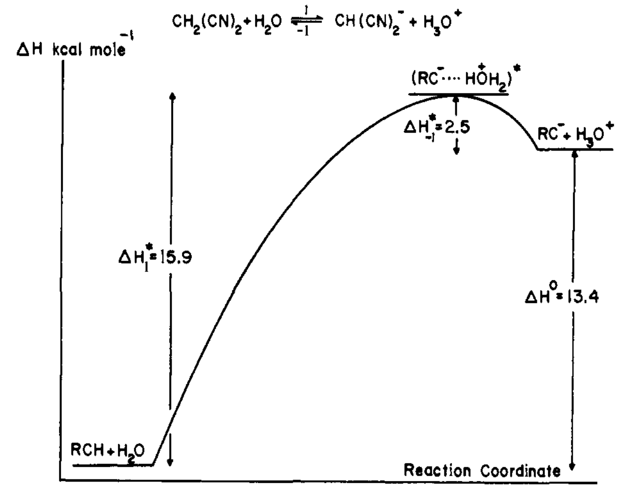

Figure 4. Activation parameters for proton transfer from malononitrile.

The energy of activation is that expected for a diffusion rate.[28] In terms of the Hammond postulate[29] the activation energies of Figure 4 place the transition state at a position close to products on the reaction coordinate. The magnitude of the entropy change is greater than that expected of a diffusion rate. This reflects the fact that the rate coefficients are slightly lower than the diffusion limit and may be a consequence of some restructuring of the solvation shells.

Comparison with Other Carbon Acids. Perhaps the most significant result of these studies is the demonstration that one group of carbon acids, the cyanocarbons, shows proton-transfer behavior which is virtually "normal," *i.e.*, almost the same as found for oxygen- or nitrogen-base acids of comparable strength. For example, Figure 3 is very reminiscent of the original Eigen plot for proton transfer from phenol.[30] Studies near to $\Delta pK = 0$, however, are needed to provide confirmation of this.

It is well known[5] that there are other categories of carbon acids, *e.g.*, nitroparaffins, β-diketones, and azulinium ions, where proton transfer is notably slow. The indication that this slow behavior is not an invariable property of carbon acids makes it important to understand the causes for the different behavior. It may be, for example, that the slow reactions occur when the negative charge of the carbanion is dispersed far from the reaction site. If so, even a cyanocarbon system such as p-nitrobenzyl cyanide[31] may behave quite differently from the molecules studied here. This general point is being investigated.

Acknowledgment. We wish to thank Mrs. Sue Garcia and Mrs. Diane Parchomchuk for technical assistance.

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[27] Reference 12a, Chapter 11.

[28] E. F. Caldin, "Fast Reactions in Solution," Wiley, New York, N. Y., 1964, Chapter 12.

[29] G. S. Hammond, *J. Amer. Chem. Soc.*, 77, 334 (1955).

[30] Figure 9b of ref 5a.

[31] E. F. Caldin and E. Harbron, *J. Chem. Soc.*, 2314 (1962).