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The Acidic Behavior of Chloroform^{1,2}

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Abstract: The detritiation of chloroform in aqueous buffer solutions involves only hydroxide ion; general base catalysis is not observable. No reaction with water is observable at either 25 or 50°. The rate coefficient for the hydroxide ion reaction is $0.165 M^{-1} sec^{-1}$ at 25°, implying that the pK of chloroform is about 24. The primary hydrogen isotope effect for the proton removal process, determined by a new accurate method, is $k^H/k^D = 1.42$ at 25°. The entropy of activation for the aqueous detritiation by hydroxide is strongly positive; ΔS^\ddagger at 25° is +15 eu, about 25 eu above normal for k values in $M^{-1} sec^{-1}$ units. This value drops sharply as DMSO is added to the reaction system implying that desolvation of hydroxide ion is a major contributor to the positive entropy. The Brønsted β for the hydroxide ion reaction, as determined in DMSO-H₂O solvent mixtures using the Bell and Cox procedure, is 0.98. These several data strongly suggest that the proton removal reaction of chloroform is fully normal in the Eigen sense, even for reaction with hydroxide ion. This result is in considerable contrast to most other carbon acids, including the otherwise normal cyanocarbons, in that hydroxide reaction is usually anomalously slow and Brønsted coefficients often differ considerably from the limiting values of zero and unity.

Recent studies⁴ have demonstrated that simple cyano-substituted saturated hydrocarbons constitute a group of carbon acids whose proton transfer reactions in aqueous solution are almost fully normal in the Eigen sense.⁵ The distinguishing characteristics are: general base catalysis with a Brønsted exponent of virtually unity; reverse reaction rates (in the thermodynamically favored direction) which are within a factor of 10 of that expected for a diffusion-controlled process; very low primary hydrogen isotope effects for reaction of the carbon acid with bases. The essential normality of these cyanocarbon acids is graphically demonstrated by their "Eigen plots" of rate coefficients against ΔpK , plots which are strikingly similar to those for simple oxygen and nitrogen acids.⁴ The most likely explanation for this behavior is that only slight electronic and structural rearrangement is involved in going from the cyanocarbon acid to the carbanion.

Reaction of these cyanocarbon acids with the base hydroxide ion is, however, anomalously slow, a fact

(1) Work supported by a grant from the Atomic Energy Commission.

(2) Z. Margolin and F. A. Long, *J. Amer. Chem. Soc.*, **94**, 5108 (1972), give a preliminary communication on part of this study; also presented in part at the 161st National Meeting of the American Chemical Society, Los Angeles, Calif., April 1971.

(3) Author to whom requests for reprints should be sent.

(4) F. Hibbert and F. A. Long, *J. Amer. Chem. Soc.*, **94**, 2647 (1972), and earlier papers referred to therein.

(5) M. Eigen, *Angew. Chem., Int. Ed. Engl.* **3**, 1 (1964).

which was essential in permitting the high Brønsted exponents to be determined for the other bases. In addition to this anomalous slowness, the hydroxide ion reaction with these acids also exhibits a relatively large primary hydrogen isotope effect and an unexpectedly large *negative* entropy of activation.

In searching for a carbon acid which might be more fully normal than the cyanocarbons, a promising candidate is chloroform. The earlier studies of its acidity behavior by Hine and coworkers⁶ demonstrated for the reaction with hydroxide ion a relatively small hydrogen isotope effect and a positive entropy of activation. Since additionally the particularly simple structure of chloroform and its anion suggested minimal electronic rearrangement upon removal of a proton, it seemed desirable to repeat and extend these studies. The principal experimental procedure has been measurement of the rates of detritiation of tritium-labeled chloroform. However, a new and potentially quite useful experimental procedure for measuring primary isotope effects has also been applied to the reaction.

Experimental Section

Materials. Chloroform was labeled with tritium by adding 5 ml of chloroform to 5 ml of basic solution ($10^{-2} N$ NaOH) that

(6) (a) J. Hine, *J. Amer. Chem. Soc.*, **72**, 2438 (1950); (b) J. Hine, N. W. Burske, M. Hine, and P. B. Langford, *ibid.*, **79**, 1406 (1957).

contained tritiated water (100 mCi). The mixture was shaken for 5 days. After acidification the layers were separated; the chloroform was dried overnight with molecular sieve (4 Å) and then distilled.

Liquid amines were distilled before the preparation of the buffer solutions. Dimethyl sulfoxide was stirred with calcium hydride for several days and distilled under vacuum. CDCl_3 was obtained from the International Chemical and Nuclear Corp. (99.8% D per atom) and was used without further purification. Hydrochloric acid solutions were Fisher volumetric standards. Sodium hydroxide solutions were prepared by adding distilled water to the BDH Chemicals Ltd. standardized sodium hydroxide. The HTO used was the ICN product containing 100 mCi/ml, and the scintillation solution was prepared by adding toluene to 2,5-diphenyloxazole and 1,4-bis[2-(4-methyl-5-phenyloxazolyl)]benzene which are produced by Packard.

Detritiation. The rates of detritiation were measured by the method of Halevi and Long.⁷ Quenched equal samples of the reaction mixture were extracted with standard aliquots of toluene (about 70% extraction) and subjected to liquid scintillation counting (Packard Tricarb, Model 314DC). All reactions were carried out under pseudo-first-order conditions, and rate constants were determined from the slope of the straight line that was observed by plotting $\log(C_t - C_\infty)$ as a function of time, where C_t is the count at time t and C_∞ is the count at time infinity.

Isotope Effects. The technique for measuring isotope effects was to follow the uptake of tritium from the aqueous solvent during the early stages of the reaction (never more than 10%) of the two acidic species Cl_3CH and Cl_3CD . Two volumetric flasks containing the basic solution (10^{-3} *N* NaOH) and tritiated water (10 mCi/100-ml flask) were thermostated for 0.5 hr in a bath at 25°. The tritiated water was prepared as a stock solution containing 100 mCi/l., and for all the isotope effect experiments the same stock solution was used. Sixteen separating funnels were prepared with 5 ml of HCl to quench the reaction and 15 ml of toluene to extract the chloroform.

After the solution in the volumetric flask was thermally equilibrated, 10 μl of chloroform was added to one flask and 10-ml aliquots were transferred to the separating funnels. There is no need in this procedure for an aliquot at time infinity. The next step was to add 10 μl of chloroform-*d* to the second flask and take 10-ml aliquots. After taking all the aliquots from both flasks, all 16 separating funnels were treated as one run. The water layer was dumped, 2 ml of HCl (0.1 *N*) was added, and every funnel was shaken for 30 sec. This procedure of washing with 2 ml of HCl was repeated four times. Preliminary experiments with blanks showed that four washings were sufficient to rid toluene samples of tritiated water so that the count from a blank was close to background. Hence, in the experiments, after the fourth washing, a 10-ml aliquot was taken from the toluene layer and was subjected to liquid scintillation counting. A counting period of 100 min (10,000 counts or more) was used for all samples. Counts for the two compounds, chloroform and chloroform-*d*, were plotted as a function of time, and two straight lines with different slopes were observed (Figure 2). According to the equations for calculating the isotope effect, the ratio of the slopes is equal to $k^{\text{H}}/k^{\text{D}}$ which is the desired isotope effect. The isotope effect was measured at two temperatures, 25 and 0°.

Dimethyl Sulfoxide-Water-Sodium Hydroxide. Dimethylsulfoxide-water solutions were made up by volume and the sodium hydroxide was added (10^{-2} *N*). The ionic strength was kept constant (0.1) by adding KCl. The detritiation of chloroform was followed by the same procedure described before and was measured at 25 and 0°.

Results

Hydroxide Ion Catalyzed Detritiation of Chloroform.

The rates of detritiation of chloroform were measured in both unbuffered and buffered solutions. For the unbuffered experiments the base was sodium hydroxide and the rates were measured at 25° and ionic strength of 0.1. Five different concentrations of NaOH in the range of 0.001 to 0.05 *M* were used. The reaction was found to be first order in hydroxide and the rate

coefficient for the hydroxide ion reaction is $0.165 \pm 0.002 \text{ M}^{-1} \text{ sec}^{-1}$.

The rates for the hydroxide reaction were studied at five different temperatures from 0 to 35°, ionic strength 0.1, and sodium hydroxide concentration 0.01 *N*. Activation parameters calculated at 25° from rate coefficients in $\text{M}^{-1} \text{ sec}^{-1}$ units are $E_a = 23.7 \text{ kcal mol}^{-1}$; $\Delta H^\ddagger = 23.1 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = 15.5 \text{ cal deg}^{-1} \text{ mol}^{-1}$; $\Delta G^\ddagger = 18.5 \text{ kcal mol}^{-1}$.

Water Reaction. An attempted detritiation of chloroform with H_2O acting as a base was made at 25 and 50° in aqueous solutions which contained 0.01 *M* hydrochloric acid and 0.09 *M* sodium chloride to suppress the hydroxide ion contribution. At 25° the experimental procedure was the same as for the detritiation by hydroxide ion. For studies at 50° sealed ampoules were used to contain the aqueous solutions. For each temperature the resultant samples were held for a period of 3 weeks. No change of counts was observed during this period. The conclusion is that the water catalyzed reaction is very slow even at 50°. This is the expected result for such a weak acid as chloroform, particularly if a large Brønsted β coefficient is assumed.

General Base Catalysis. The detritiation of chloroform was studied in piperidine buffer solutions ($\text{p}K_a = 11.07$) at 25° and morpholine ($\text{p}K_a = 8.492$) buffer solutions at 49.4°. The buffer solutions were prepared by adding HCl to the base. The buffer ratio was 1:1 for piperidine and 4:1 for morpholine. Ionic strength was 0.1 for all solutions. The piperidine buffer solution was diluted to four different piperidine concentrations, keeping constant the buffer ratio and therefore the hydroxide concentration. The rate constants for the detritiation of chloroform as a function of base concentration are shown in Table I. The rate

Table I. Dependence of Detritiation Rate of Chloroform in Concentration of General Base (Ionic Strength 0.1 *M*)

No. of runs	Temp, °C	Base and concn	10% <i>k</i> , sec ⁻¹
2	25	0.1 <i>M</i> piperidine	3.46
3	25	0.04 <i>M</i> piperidine	3.54
2	25	0.02 <i>M</i> piperidine	3.39
2	49.4	0.2 <i>M</i> morpholine	1.46
2	49.4	0.1 <i>M</i> morpholine	1.45

of the reaction does not vary when the buffer concentration is changed. In each case, the slope of a plot of k vs. concentration of general base, which should give the rate coefficient for the morpholine or piperidine reaction, is zero. The only contribution that can be seen is the contribution from the hydroxide ion present in the buffer solution. This conclusion, that no general base catalysis is observable, agrees with the earlier studies of Hine⁶ which were also for aqueous solutions.

Given that the only contribution to the rates of Table I comes from hydroxide ion, one may use the $\text{p}K$ values and buffer ratios to calculate the magnitude of the rate coefficient for the hydroxide reaction. From the piperidine data at 25° the result is $k_{\text{OH}^-} = 0.13 \text{ M}^{-1} \text{ sec}^{-1}$. This value is about 20% lower than that measured by direct experiments with sodium hydroxide

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

solutions, a not unusual discrepancy for studies of this sort.

DMSO-H₂O. Studies in DMSO-H₂O mixtures containing small known amounts of hydroxide ion constitute a different procedure for observing general base catalysis. The original analysis by Bell and Cox⁸ gives the rationale and develops the necessary equations. Experimentally, one simply measures detritiation rates in the mixed solvents containing known amounts of hydroxide ion. In our case, the latter was normally constant at 0.01 normal. If one can assume that the substrate species SH behaves like an H⁻ acidity function indicator, then the following equations apply.

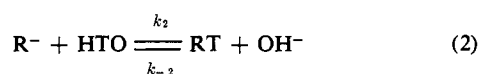
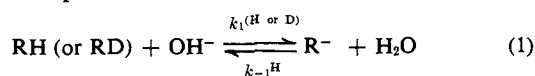
$$H_- = pK_{SH}^0 - \log \{[SH]/[S^-]\}$$

$$\Delta pK = pK_{SH} - pK_{H_2O} =$$

$$pK_{SH}^0 - H_- - \log \{[H_2O]/[OH^-]\}$$

It follows that a plot of $\log k$, where k is the second-order rate coefficient of the hydroxide ion reaction *vs.* the function $H_- + \log \{[H_2O]/[OH^-]\}$, is the equivalent of a Brønsted or Eigen plot of $\log k$ *vs.* pK . Figure 1 gives the results of these experiments.

Isotope Effect. In order to measure the primary isotope effect k^H/k^D for reaction of chloroform with hydroxide ion, a new procedure was developed. The method involves following the uptake of tritium by Cl_3CH and Cl_3CD from an aqueous (H₂O) solution during the initial zero-order phase of the reaction. The relevant equations are



Note that for reaction of RD *via* step 1 the reverse process will be $R^- + H_2O$ since HDO will be present only in vanishingly small amounts for this initial reaction, *i.e.*, for reactions which are effective for $t = 0$.

For reaction of RH, the rate law is

$$\frac{d[RT]}{dt} = k_1^H \frac{k_2}{k_{-1}} \frac{[RH][HTO]}{[H_2O]} [OH^-] \quad (3)$$

For reaction of the RD species the analogous rate law is

$$\frac{d[RT]}{dt} = k_1^D \frac{k_2}{k_{-1}} \frac{[RD][HTO]}{[H_2O]} [OH^-] \quad (4)$$

Using $\gamma^{H(\text{or } D)}$ for the atom fraction of tritium in the aqueous solvent for the two cases, we have

$$\frac{(d[RT]/dt)^H}{(d[RT]/dt)^D} = \frac{k_1^H [RH][OH^-]^H \gamma^H}{k_1^D [RD][OH^-]^D \gamma^D} \quad (5)$$

It is convenient to design the experiments so that $[RD]_0 = [RH]_0$, $[OH^-]^D = [OH^-]^H$, and $\gamma_0^H = \gamma_0^D$. If further we use δ as the atom fraction of tritium in the RH or RD species⁹

$$\frac{(d[RT]/dt)^H_{t \rightarrow 0}}{(d[RT]/dt)^D_{t \rightarrow 0}} = \frac{(d\delta/dt)^H_{t \rightarrow 0}}{(d\delta/dt)^D_{t \rightarrow 0}} = \frac{(k_1^{OH^-})^H}{(k_1^{OH^-})^D} \quad (6)$$

(8) R. P. Bell and B. G. Cox, *J. Chem. Soc. B*, 194 (1970); 783 (1971).

(9) The normal symbols for atom fraction of tritium in aqueous solvent and in substrate are β and α , respectively. We have shifted to γ and δ to avoid confusion with the long established use of α and β for Brønsted coefficients.

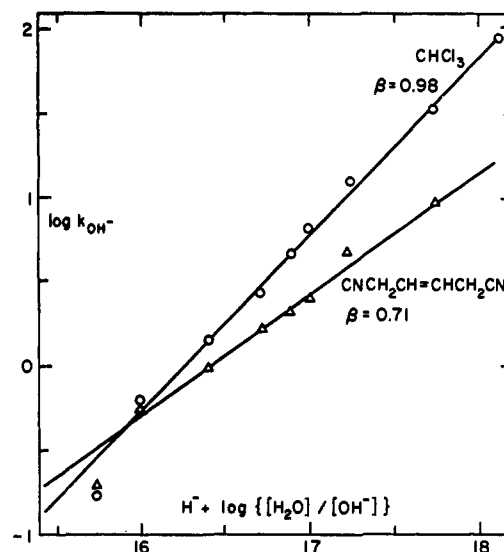


Figure 1. Determination of Brønsted coefficient β for two carbon acids from rates in H₂O-DMSO-hydroxide mixtures.

In other words, for this simple case the ratio of initial rates of tritium uptake by the two reactants gives directly the primary isotope effect. Slightly more involved, but reasonably obvious, equations hold (see eq 5) when the resulting conditions, *e.g.*, γ_0 values, differ for the two cases.¹⁰

For chloroform, experiments were made separately for the H and D compounds with otherwise identical conditions. Successive samples were removed during the early stage of the reaction, and counts due to tritium of the recovered chloroform were plotted against time, two straight lines were observed (Figure 2); the ratio of their two slopes gives k^H/k^D . Four sets of experiments with CCl_3H and CCl_3D at 25° gave $k^H/k^D = 1.42 \pm 0.01$ and at 0° $k^H/k^D = 1.6$.

Discussion

This discussion will use the data of the previous section to demonstrate that chloroform is an example of a fully normal acid in the Eigen sense. From the studies of Eigen and others, the essential character-

(10) This general procedure can also be used for a reaction subject to general catalysis to obtain the primary hydrogen isotope effect for reaction with a buffer ion. The equation for reaction of RH in a buffer solution of A⁻ and HA and subject to general base catalysis is

$$\left(\frac{d\delta}{dt}\right)_{t \rightarrow 0} = k_1^{OH^-} \left(\frac{k_2}{k_{-1}}\right)_{OH^-} \gamma_0 [OH^-] + k_1^{A^-} \left(\frac{k_2}{k_{-1}}\right)_{A^-} \gamma_0 [A^-] + k_1^{H_2O} \left(\frac{k_2}{k_{-1}}\right)_{H_2O} \gamma_0 [H_2O]$$

Hence, for solutions of increasing buffer concentration but constant buffer ratio (so $[OH^-]$ stays constant)

$$\frac{\partial (d\delta/dt)_{t \rightarrow 0}}{\partial [A^-]} = k_1^{A^-} \left(\frac{k_2}{k_{-1}}\right)_{A^-} \gamma_0$$

Then for parallel initial stage experiments with RH and RD, and with the other concentrations identical as before

$$\frac{\partial [(d\delta/dt)_{t \rightarrow 0}] / \partial [A^-]^H}{\partial [(d\delta/dt)_{t \rightarrow 0}] / \partial [A^-]^D} = \frac{(k_1^{A^-})^H}{(k_1^{A^-})^D} \quad (i)$$

The experimental procedure is implicit in eq i. For RH and for RD a set of experiments is done, each with constant buffer ratio but varying buffer concentrations, other concentrations being identical. For each experiment the δ *vs.* t slope is obtained; for each set of experiments these slopes are plotted as a function of buffer concentration. These final slopes are used in eq i to give $(k_1^{A^-})^H / (k_1^{A^-})^D$. This extended procedure was used in obtaining the isotope effects listed in Table II for morpholine and phenolate ions reacting with 1,4-dicyanobutene-2.

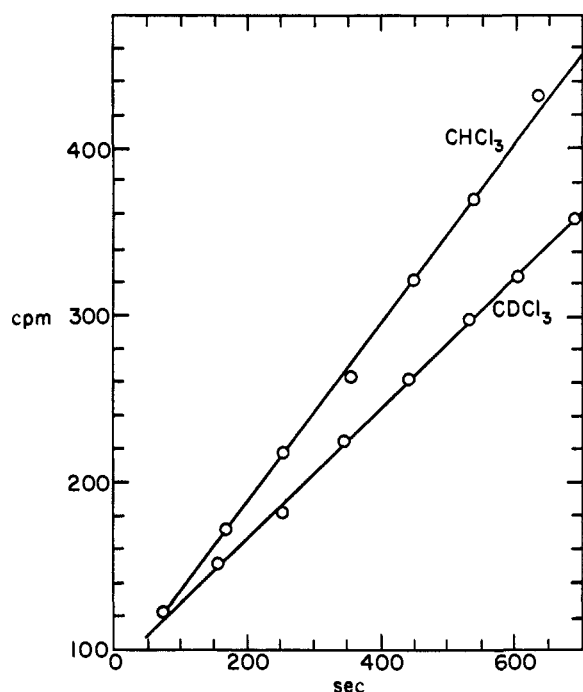


Figure 2. Plots of tritium uptakes, in counts per minute, for CHCl_3 and CDCl_3 during the initial stage of the reaction in tritiated aqueous solutions containing $0.001 M$ hydroxide ion, 25° .

istics of a normal proton transfer system, $\text{HA} + \text{B}^- = \text{A}^- + \text{HB}$, occurring in aqueous solution are as follows.

(a) When the transfer process is in the thermodynamically favored direction, the rate of proton transfer will be diffusion controlled and will hence operate at a rate independent of the ΔpK difference, where ΔpK gives the difference between the acidities of HA and HB.

(b) In the reverse, "slow" direction, the reaction will therefore exhibit general catalysis with a Brønsted coefficient, α or β , of unity.

(c) These limiting Brønsted slopes will hold generally except for a small changeover zone in the region of $\Delta pK = 0$.

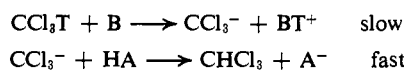
(d) In the transition state, the proton will be virtually entirely transferred to one base or the other, the exception being the region close to $\Delta pK = 0$ where intermediate proton transfer will occur.

(e) As a consequence of this transition state behavior, primary hydrogen isotope effects for the proton transfer process will normally be quite small.

(f) The solvent generated acid-base pair, $\text{H}_2\text{O}-\text{OH}^-$, will behave normally, *i.e.*, in accord with the pK of H_2O , but the other solvent pair, $\text{H}_3\text{O}^+-\text{H}_2\text{O}$, will show slightly faster rates than expected from the pK value because of the high diffusion rate available uniquely to hydronium ion.

These various characteristics have been demonstrated by Eigen and others for a variety of oxygen and nitrogen acids. Most carbon acids depart from this normal behavior widely. The question then is, where stands chloroform?

The expected mechanism for the detritiation of chloroform is



The rate-limiting step here is a slow proton transfer from the carbon acid to the base and general base catalysis would be expected. Because chloroform is a very weak acid ($pK > 21$), the only experimentally accessible slow proton transfer process is the base-catalyzed reaction; *i.e.*, in an Eigen plot of $\log k$ vs. ΔpK , the only accessible region is that with ΔpK positive, implying that one would expect a Brønsted β of unity and a Brønsted α of zero, the latter being for the diffusion limited reverse process. The experimental data for the chloroform detritiation process are collected in Table II and compared with similar

Table II. Comparison of Proton Transfer Behavior (Values for Aqueous Reaction Unless Otherwise Indicated)

	HCCl_3	1,4-Dicyano-butene-2
Aqueous OH^- rate, k^{OH^-} in $M^{-1} \text{sec}^{-1}$	0.165	0.198
Brønsted coefficients		
Phenolate ions	NO ^a	0.94
Amines	NO	0.98
OH^- in DMSO- H_2O	0.98	0.71
Entropy of activation, eu ^b		
Hydroxide ion	+15	-10
Morpholine	NO	-11
Phenolate ion	NO	+5
Primary isotope effect, $k^{\text{H}}/k^{\text{D}}$		
Hydroxide ion	1.4	3.5
Morpholine	NO	1.7
Phenolate ion	NO	1.4

^a NO is for "not observable." ^b For k values in $M^{-1} \text{sec}^{-1}$ units.

data for one of the simple cyanocarbon acids, 1,4-dicyanobutene-2. For the latter, the Brønsted coefficients for phenolate ions and amines are from studies of Walters and Long.¹¹ The other data are from recent accurate studies done for this comparison.¹²

General Base Catalysis. An important preliminary point is that for an acid as weak as chloroform, with all bases *including hydroxide* behaving normally and a Brønsted β of unity, general base catalysis should *not* be observable. This is because of the well-known phenomenon of hydroxide ion domination of base catalysis for buffer mixtures in aqueous solution. Hammett,¹³ for example, has shown that experimentally it is virtually impossible to determine a Brønsted α or β in aqueous solution larger than about 0.85. As another way to demonstrate the difficulty for the specific case of general base catalysis, consider the following equations. Let the total rate of reaction for conditions of base catalysis be given by $V = \Sigma k_B \cdot C_B C_S$. For a buffer mixture, under the plausible assumption that for a very weak acid there will be no measurable reaction of water as a base, one has $V = V_{\text{A}^-} + V_{\text{OH}^-} = (k_{\text{A}^-} C_{\text{A}^-} + k_{\text{OH}^-} C_{\text{OH}^-}) C_S$. Here A^- is the base species of the buffer mixture of HA and A^- which is being used to hold hydroxide ion constant. The ratio of rates for the two bases of in-

(11) E. A. Walters and F. A. Long, *J. Amer. Chem. Soc.*, **91**, 3733 (1969).

(12) Z. Margolin and F. A. Long, to be submitted for publication.

(13) L. P. Hammett, "Physical Organic Chemistry," 2nd ed, McGraw-Hill, New York, N. Y., 1970, p 322.

terest, the buffer species whose rate coefficient is desired and the inescapable hydroxide ion, is

$$\frac{V_{A^-}}{V_{OH^-}} = \frac{k_A \cdot C_{A^-}}{k_{OH^-} \cdot C_{OH^-}} = C_{HA} \left(\frac{K_{HA}}{K_W} \right)^{1-\beta}$$

where C_{HA} is the concentration of the acidic component of the buffer and K_{HA} and K_W are ionization constants for HA and water, respectively.

Recall next that buffer concentrations cannot rise above about 0.1 M, otherwise the dilute solution approximations which are an essential simplification will fail. The implication then is that when β is equal to unity, the maximum available ratio of rates for buffer ion relative to hydroxide ion is only 0.1, and this is virtually impossible to detect experimentally.¹⁴

In view of this analysis, the fact that general base catalysis is not observable for the detritiation of chloroform suggests that it belongs to the category of fully normal acids with a Brønsted β of unity. To test this, experiments were performed with the mixed solvent system DMSO-H₂O and with hydroxide ion as a base. Simply put, the strong increase in basicity which occurs when DMSO is added to aqueous hydroxide ion solutions constitutes a method to obtain a change in ΔpK by changing the solvent instead of by changing the base. This method was first used by Bell and Cox⁵ and later applied by Melander¹⁵ and commented on by Jones.¹⁶ The results of applying this procedure to the two acids, chloroform and 1,4-dicyanobutene-2,¹² are shown in Figure 1. The significant facts are that the cyanocarbon acid, for which the aqueous hydroxide ion reaction is anomalously slow, shows an intermediate Brønsted β of 0.7 whereas chloroform exhibits a Brønsted β of virtually unity. Interestingly, therefore, the lack of observable general catalysis for aqueous solutions and the data for the mixed solvent give in combination strong evidence that chloroform is behaving as a normal acid.

Isotope Effects. The listed values of the primary hydrogen isotope effects of Table II are consistent with the studies of general base catalysis. The low values for hydroxide ion with chloroform and for morpholine and phenolate ion with the cyanocarbon acid are indicative of a fully transferred proton. The higher value of 3.5 for hydroxide ion reacting with the cyanocarbon acid is consistent with the intermediate Brønsted β found in the DMSO-H₂O mixtures and also consistent with the anomalously slow reaction rates which hydroxide shows in reacting with this cyanocarbon acid in purely aqueous solutions.

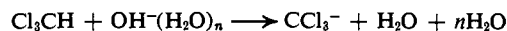
Entropy of Activation. From a transition state point of view, the implication of this analysis is that the proton from chloroform is virtually fully transferred to hydroxide ion in the transition state for the transfer

(14) Given this restriction, one may reasonably ask whether Brønsted coefficients of unity can ever be determined? The answer, of course, is yes and for two rather different reasons. Sometimes hydroxide ion shows an anomalously slow rate and hence falls off the Brønsted curve so that the above equations do not apply. This is the case with simple cyanocarbon acids. A far more important situation occurs when the studies are being made at ΔpK values close to zero. Then, because of its greater base strength, rates for hydroxide ion can reach the diffusion limiting rate, and hence fall below the line for $\beta = 1$ established by weaker bases for this reason. This is typically the situation for the intermediate strength acids and bases which Eigen and coworkers have studied by fast reaction techniques. A similar argument applies to determination of a Brønsted α of unity where the potentially interfering ion is hydronium ion.

(15) L. Melander and N. Bergman, in press.

(16) J. R. Jones, *Progr. Phys. Org. Chem.*, **9**, 241 (1972).

reaction. As the equation below illustrates, this implies that there should be an entropy of activation which is much more positive than expected for a normal bimolecular process.



Since hydroxide ion is known to be heavily solvated, this proton transfer process will generate one water molecule as a product and will release three or four others from the solvation shell of hydroxide ion. Since the chloroform anion is much larger than hydroxide, it will be much less solvated, and the net effect will be a significant release of water molecules. This in turn translates into a sizable positive entropy of activation.

A rough estimate of the expected effect can be made using the approach of Schalager and Long¹⁷ who calculated that each release of a water molecule in an aqueous solution should lead to a positive contribution to the entropy of reaction of about 5 eu. If we assume four water molecules are effectively released in forming the transition state of the hydroxide ion reaction, this would contribute +20 to the entropy of activation. Recall also that for a normal bimolecular reaction with rate coefficients in $M^{-1} \text{sec}^{-1}$ units, the "collision theory" expectation is a ΔS^* of about -11 eu. Hence, the expected entropy of activation for the above reaction is roughly +10 eu. The observed ΔS^* value of +15 eu is in the expected direction and in a rough sense about of the expected magnitude. The considerably smaller entropy of activation which is exhibited for the reaction of dicyanobutene with hydroxide is also evidence of the substantial difference between the two systems.

Some further evidence on the importance of the desolvation of hydroxide ion in the development of a positive ΔS^* value is given in Table III which lists ΔS^*

Table III. Detritiation of $CTCl_3$ by OH^- in DMSO-H₂O Solutions

n_{H_2O}	k_{OH^-} , $M^{-1} \text{sec}^{-1}$, 25°	E_a , kcal/mol	$\Delta S^*_{25^\circ}$, eu
1	0.165	23.8	15.5
0.973	0.306	23.1	14.7
0.941	0.635	22.2	13.1
0.910	1.42	21.7	12.9
0.870	4.43	20.8	12.1
0.829	12.6	19.6	10.4
0.797	33.4	18.6	8.7
0.764	91	17.1	5.7

values for the chloroform-hydroxide reaction in H₂O-DMSO solvent mixtures. It is well established that the solvation of hydroxide decreases as DMSO is added to an aqueous solution. As Table III shows, in parallel with this, the entropy of activation of the chloroform detritiation also decreases.

The evidence, as summarized in Table II, is persuasive that chloroform is behaving normally in its proton transfer reaction with hydroxide ion, but it should be noted that there are one or two places where the evidence is either weak or missing. First, although the simple proton transfer mechanism listed earlier for chloroform

(17) L. J. Schalager and F. A. Long, *Advan. Phys. Org. Chem.*, **1**, 1 (1963).

is entirely plausible and persuasive, it would have been helpful to have more explicitly eliminated all reasonable alternatives. Regrettably, the difficulties in eliminating alternative mechanisms are well known. Second, as more specific positive evidence, it would have been helpful to determine the rate coefficient for the reverse reaction between the chloroform anion and water to demonstrate that it had attained the limiting diffusion-controlled rate. This rate could be calculated if an independent and precise value of the pK^0 of chloroform were available, but the difficulties of obtaining precise pK 's for very weak acids are also well known.¹⁸

Comparison with Other Carbon Acids. These results with chloroform raise two important general questions about carbon acids. The first is, why is chloroform so far the sole example of full normality for a carbon acid? The related question is, why are other carbon acids commonly nonnormal in the Eigen sense? To respond to these questions, it is necessary to say something about carbon acids in general and also something about reactions with the particular base hydroxide ion.

Eigen has pointed out that to obtain the diffusion limited reaction which is characteristic of the thermodynamically favored normal proton transfers, it is necessary that there be formation of a hydrogen bond between the acid and base species. Only then can the "chemical energy of activation" be negligible relative to the activation energy for the diffusion process. It is commonly postulated that hydrogen bonds to carbanions are weak. Apparently to form a sufficiently firm hydrogen bond to satisfy the Eigen criterion requires that the charge of the carbanion be pretty well concentrated on the carbon atom. Chloroform is particularly favorable for this in that the CCl_3^- carbanion will almost surely preserve its tetrahedral structure¹⁹ and negligible structural rearrangement should occur. Hence, the carbon will retain a large fraction of its negative charge.

In contrast, almost all of the other carbon acids which have been studied have anions which are considerably stabilized by rearrangement. To appreciate this point, one need only think of ketones and nitroparaffins as typical examples. Even for the simple cyanocarbon acids whose behavior approaches normality, there is presumably some structural and electronic rearrangement in forming the anion, since the

(18) If one accepts the conclusion that the reaction of chloroform and hydroxide ion is normal and applies an Eigen plot, one can calculate a pK of 24 for chloroform. This value cannot be used in the above argument, however, since the reasoning would then be entirely circular.

(19) R. Hoffmann, private communication.

anion $(CN)_3C^-$ is known to be planar.²⁰ It is entirely possible that this planarity carries over to the carbanions of the malononitriles and other simple cyanocarbon species. It is not surprising, therefore, that chloroform is the first carbon acid which appears to demonstrate fully normal acidic behavior.

There remains the special problem of why hydroxide ion as a base so commonly shows anomalous behavior (relative to the pK of its conjugate acid) in its reactions with carbon acids and why, however, this anomalous behavior seems not to be encountered with chloroform. A preliminary point on this is to note that it has frequently been postulated that there is a difference between the relative ability of species to form hydrogen bonds and their acid-base properties.²¹ If, indeed, the capability of carbanions to form hydrogen bonds is relatively weak, then the effectiveness of the donor species in forming such bonds will be of great importance. If, for some reason, a solvent water molecule is less effective, relative to its pK , in forming hydrogen bonds, then one might find that rates between solvent water and carbanion did not reach the diffusion limiting value, although rates for other acids, substituted ammonium ions and the like, could reach this limit with carbanions. Slowness of solvent water in reacting as an acid with carbanions would, *via* the equilibrium for the process, be directly reflected in anomalously slow rates for hydroxide ion and the respective carbon acid. To summarize this argument, it is that the H_2O-OH^- pair has a general tendency toward slowness which reflects the comparatively weak hydrogen bonding capability of solvent water. The chloroform carbanion, however, is sufficiently strong in hydrogen bonding ability to overcome this tendency, leading to the observed normality.

As a subsidiary point to the above argument, one might reasonably ask why the H_2O-OH^- pair usually turns out to be normal in the proton transfer rate studies which Eigen and coworkers have made using fast reaction techniques. The answer is that almost all of these studies have been made with acid-base pairs which form hydrogen bonds much more easily than do the carbon acids. Also, the existence of diffusion-limited rates means that a given partner, *e.g.*, OH^- or H_2O , need only be "good enough" to permit attainment of this limit, a limit which once attained obscures any remaining differences in hydrogen bonding ability.

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(20) R. Desiderato and R. L. Sass, *Acta Crystallogr.*, **18**, 1 (1965).

(21) E. M. Arnett and E. J. Mitchell, *J. Amer. Chem. Soc.*, **93**, 4052 (1971).