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DMSO-H₂O for Study of "Unobservable"
General Base Catalysis and Anomalous
Behavior of Hydroxide Ion¹

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Abstract

Studies of proton transfer rates to hydroxide ion in mixed DMSO-H₂O solvents show that with chloroform the Bronsted β is 1.0 whereas with 1,4-dicyanobutene-2, the β value is only 0.7. Comparison for the same two reactions in water of the primary hydrogen isotope effects, the β value for other bases, and the entropies of activation indicate that the hydroxide ion reaction is anomalously slow with the cyano-carbon, but normal for chloroform leading in the latter case to an example of "unobservable" general base catalysis.

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Sir: Recent studies by Eigen and others have greatly clarified the phenomenon of general acid-base catalysis.²⁻⁴ Eigen² has shown that for reactions of major categories of

² M. Eigen, *Angewandte Chemie, Int. Ed.*, 3, 1 (1964).

³ M. L. Bender, "Mechanisms of Homogenous Catalysis from Protons to Proteins," Part I, Wiley-Interscience, New York, New York, 1971.

⁴ R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y. 1959.

acids and bases in aqueous solution, there is a "normal" behavior in which the thermodynamically favored proton transfer occurs at a diffusion-controlled rate, i.e., with a rate independent of the strength of the catalyst and hence with a Brønsted coefficient of 0. The reverse process then occurs with a Brønsted coefficient of unity. Deviation from this limiting behavior normally occurs only in a transition region of a few pK units close to $\Delta \text{pK} = 0$, where ΔpK gives the pK difference for catalyst and substrate.

Many classes of carbon acids depart widely from this normal behavior in that they exhibit intermediate Brønsted coefficients of from 0.4 to 0.8 for wide ranges and large values of ΔpK .^{3,4} However it has recently been found that certain classes of carbon acids, presumably characterized by relatively small amounts of structural rearrangement on

reaction, show behavior very close to that of the Eigen normal acids. Thus, the proton removal reactions of a group of cyanocarbons exhibit general base catalysis with a Brønsted β of virtually unity, with a reverse reaction whose Brønsted α is almost zero and whose rate is within a factor of ten of that of a diffusion-controlled process.⁵⁻⁷

⁵ E. A. Walters and F. A. Long, J. Am. Chem. Soc., 91, 3733 (1969).

⁶ F. Hibbert, E. A. Walters and F. A. Long, J. Am. Chem. Soc., 93, 2829 (1971).

⁷ F. Hibbert and F. A. Long, J. Am. Chem. Soc., 93, 2836 (1971).

The strong implication, confirmed by the observed small primary hydrogen isotope effects, is that in the transition state the proton is virtually entirely transferred.

With cyanocarbon acids of pK values above about 12, it is only possible to observe the general base catalysis because the reaction rate for hydroxide ion is anomalously low and, indeed, anomalous rates with hydroxide ion are commonly observed with carbon acids. An important question is, are there carbon acids which will be normal in all respects, including normal behavior with hydroxide ion?

On the basis of its simple "electrostatic" nature, as well as Hine's studies of the haloforms⁸, a good candidate

⁸ J. Hine, N. W. Burske, M. Hine and P. B. Longford, J. Am. Chem. Soc., 79, 1406 (1957) and earlier papers.

for this normal behavior is chloroform. As Table I shows, the tritium removal reaction of hydroxide ion with tritiated chloroform exhibits a small primary hydrogen isotope effect⁹

⁹ The isotope effects were determined by a new, accurate method which involves measuring rates of tritium uptake by CHCl_3 and CDCl_3 from a tritiated aqueous solvent. Details of the method will be published shortly.

and a positive entropy of activation, both indicative of normal behavior with a fully transferred proton in the transition state. Studies with the weak base catalysts, piperidine and morpholine gave, however, no evidence of general base catalysis. A possible explanation is that there is no general base catalysis, i.e. the reaction mechanism does not involve a rate determining proton transfer.

An alternative explanation is that the proton transfer behavior is fully normal in the Eigen sense, i.e. general catalysis with a Brønsted slope of $\beta = 1$ and with hydroxide ion behaving normally according to its pK . As is well known, for reaction in water the latter situation results in the phenomenon of "unobservable general base catalysis", in that the rate with hydroxide ion overwhelms that of other bases.¹⁰

¹⁰ See for example the discussion in L. P. Hammett, "Physical Organic Chemistry," 2nd Edition, McGraw-Hill, New York, New York, 1970, pages 322-323.

It is possible to examine the second alternative by studying the proton transfer to hydroxide ion in the mixed solvent $\text{DMSO-H}_2\text{O}$. Using plausible assumptions it can be shown for reaction of a substrate SH with hydroxide ion that the ΔpK difference for substrate and catalyst for the mixed solvent case is given by¹¹

¹¹ R. P. Bell and B. G. Cox, J. Chem. Soc. (B), 194 (1970).

$$\begin{aligned}\Delta pK &= pK_{SH} - pK_{H_2O} \\ &= pK_{SH}^{\circ} - H_- - \log \{ [H_2O] / [OH^-] \}\end{aligned}$$

Thus, for a mixed solvent, one may replace the usual Brønsted or Eigen plot by a plot of $\log k_{OH^-}$ versus the function, $H_- + \log \{ [H_2O] / [OH^-] \}$.

Bell and Cox¹¹ applies this procedure to reaction of menthone with OH^- in DMSO- H_2O solvents and found an intermediate β value of 0.48, close to that predicted. We have now applied it to the detritiation of chloroform; For comparison, we have also studied 1,4-dicyanobutene as an example of a cyanocarbon acid which exhibits an anomalously slow rate of reaction with hydroxide ion but is otherwise almost normal.⁵ The rate studies involved hydroxide ion concentrations of from 0.001 to 0.05 M and solvents with weight percent DMSO ranging from 0 to 60%. H_- values were taken from Bowden.¹² The resulting Brønsted β for chloroform is

¹² K. Bowden, Chem. Rev., **66**, 119 (1966).

virtually unity, whereas that for the cyanocarbon is only 0.7 (Figure 1.). Data for entropies of activation and for hydrogen isotope effects (Table I) support the conclusion that hydroxide ion is behaving anomalously with the cyanocarbon, but normally with chloroform. We conclude that the mixed DMSO- H_2O solvent permits study of anomalous behavior of hydroxide ion as well as detection of "unobservable" general base catalysis, and that proton removal from chloroform is characterized by general base catalysis with a Brønsted β of unity.

A preliminary interpretation of these results is that the anions of most carbon acids are characterized by a dispersed charge which makes hydrogen bonding with the water molecule difficult and which in turn causes a low rate of proton transfer to the anion, and, via the equilibrium, to an anomalously low reverse rate with OH^- also. With the anion of chloroform, there is minimal dispersion of the anionic charge and the reaction of the anion with water can attain the diffusion limited rate, i.e. can behave normally. Further experiments to test this hypothesis are in progress but in the meantime, it is fair to conclude that in favorable circumstances carbon acids can behave as normally as those of oxygen or nitrogen.

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Table I.

Comparison of proton transfer behavior; values for aqueous reaction unless otherwise indicated.

	<u>HCCl₃</u>	<u>1,4-dicyano- butene-2</u>
Aqueous OH ⁻ rate, k^{OH^-} in M ⁻¹ sec ⁻¹	0.165	0.198
Brønsted Coefficients:		
Phenolate ions	n.o. ^a	0.94
Amines	n.o.	0.98
OH ⁻ in DMSO-H ₂ O	0.98	0.71
Entropy of Activation, e.u. ^b :		
Hydroxide ion	+15	-10
Morpholine	n.o.	-11
Phenolate ion	n.o.	+5
Primary isotope effect, k^H/k^D :		
Hydroxide ion	1.4	3.5
Morpholine	n.o.	1.7
Phenolate ion	n.o.	1.4

^a n.o. is for "not observable"

^b for k values in M⁻¹ sec⁻¹ units

FIGURE CAPTION

Figure 1. Dependence of rate of proton transfer upon $\text{H}^+ + \log \{[\text{H}_2\text{O}] / [\text{OH}^-]\}$ in aqueous dimethyl sulphoxide.