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AN INTERPRETATION OF THE KINETICS OF BIMOLECULAR SUBSTITUTION BY ANIONIC BASES IN ALCOHOL-WATER MIXTURES

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IT has been difficult for many years to understand the large difference in behaviour of bimolecular nucleophilic substitution reactions between basic anions and organic halides in methanol-water mixtures and ethanol-water mixtures. If reactions of this type are studied initially in dry methanol and dry ethanol, and if water is then added to each of these solvents, the rate constant for alkaline hydrolysis falls in the case of ethanol-water mixtures, but, with methanol-water mixtures, rises initially, passes through a maximum, and then falls as still more water is added. This behaviour was observed by de Bruyn and Steger[1] for the alkaline hydrolysis of methyl and ethyl iodides and further examples are quoted by Bunnett and Zahler[2] for aromatic nucleophilic substitution reactions.

The fall observed with ethanol-water mixtures in the case of aliphatic halides (S_N2 reactions) is apparently in accordance with the behaviour

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[1] C.A.L. de Bruyn and A. Steger, Rec. Trav. Chim. **18**, 311 (1899); Z. Phys. Chem. **49**, 336 (1904).

[2] J. Bunnett and R.E. Zahler, Chem. Rev. **49**, 349 (1951).

expected on the basis of the Hughes-Ingold theory of solvent action,[3a] and the results of de Bruyn and Steger in ethanol-water mixtures have often[3a,4] been quoted as evidence supporting the theory. The initial rise in methanol-water mixtures is not expected and it would therefore appear that the methanol-water results are exceptional. The purpose of this communication is to introduce a different point of view, namely that it is the ethanol-water results which are atypical and to provide a reason for their lack of conformity.

In Table 1, results for various halides are collected and it is noteworthy that there is an initial rate increase in all cases in methanol-water mixtures. We have not observed any exception to this behaviour in these mixtures. The rate also rises initially in ethanol-water mixtures when sodium thiophenoxide is the added reagent and there is also some evidence[5] for an initial rise with sodium acetate and ethyl iodide in this medium.

In Fig. 1, results of various workers for the base composition in alkaline alcohol-water mixtures are given. These include results obtained in this department by kinetic methods similar in principle to those previously used in phenol-methanol mixtures.[6] Other workers have used thermodynamic methods. Although the curves should be regarded as approximate,

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[3] C.K. Ingold, *Structure and Mechanism in Organic Chemistry* a p. 348; b p. 349; c p. 460. Cornell University Press, Ithaca (1953).

[4a] A.E. Remick, *Electronic Interpretations of Organic Chemistry* p. 283. John Wiley, New York (1949); b K.J. Laidler, *Chemical Kinetics* p. 131. McGraw-Hill, New York (1950).

[5] S. Eagle and J.C. Warner, *J. Amer. Chem. Soc.* **61**, 488 (1939).

[6] B.D. England, *Chem. & Ind.* 1145 (1954).

TABLE 1

Influence of Added Water on the Overall Rate Constant for Bimolecular Nucleophilic Substitution by One or More Nucleophilic Reagents in Methanol and Ethanol. k_2 is in units of litre mole^{-1} sec^{-1}.

Organic halide	Nucleophilic reagent	Rate constant	"Volume %" water in solvent				
			0	10	20	30	40
			Ethanol-water mixtures				
CH_3I	$OEt^- + OH^-$	$k_2^{25} \times 10^3$	1.62	1.26	0.89	0.64	0.50
CH_3I	$C_6H_5S^-$[c]	$k_2^0 \times 10$	4.04	4.86	5.21	5.16	4.35
C_2H_5I[a]	$OEt^- + OH^-$	$k_2^{25} \times 10^4$	2.80	2.50	2.00	1.75	1.43
24DNCB[b]	$OEt^- + OH^-$	$k_2^{25} \times 10^2$	8.20	5.67	4.30	3.19	-
24DNCB	$C_6H_5S^-$	$k_2^0 \times 10^{-1}$	2.84	3.73	4.14	4.31	-
			Methanol-water mixtures				
CH_3I	$OMe^- + OH^-$	$k_2^{25} \times 10^4$	2.56	3.03	3.40	3.47	-
CH_3I	$C_6H_5S^-$	$k_2^0 \times 10$	1.10	1.29	1.62	1.96	2.20
C_2H_5I[a]	$OMe^- + OH^-$	$k_2^{25} \times 10^5$	8.75	11.3	13.1	16.0	16.0
24DNCB	$OMe^- + OH^-$	$k_2^{25} \times 10^2$	2.60	2.88	3.14	-	-
24DNCB	$C_6H_5S^-$	k_2^0	3.68	5.06	6.38	7.82	8.36

[a] Data from ref. 1. The constants here are probably in error by a nearly constant factor; we found this with the results of these authors for methyl iodide. All other measurements by present authors.

[b] 1-Chloro-2:4-dinitrobenzene.

[c] Thiophenoxide is probably converted in part to ethoxide, to methoxide and to hydroxide (in the more aqueous solvents).

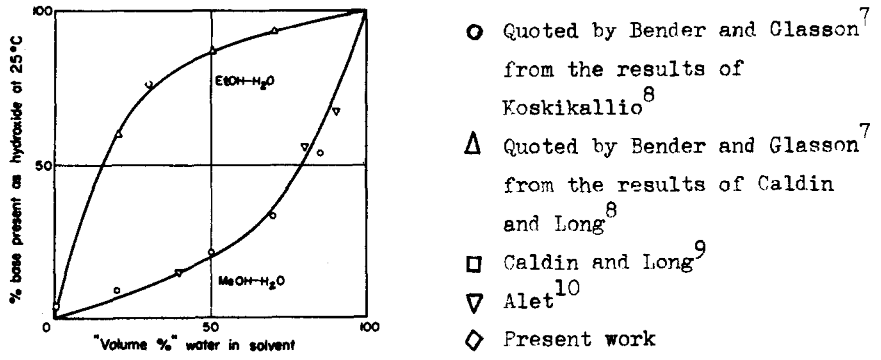

FIG. 1.

it is apparent that there is a surprisingly large proportion of hydroxide in alkaline ethanol-water mixtures containing only a small percentage of water; the corresponding proportion in methanol-water mixtures is very much less.

The mixture of anionic bases arises from the equilibrium $ROH + OH^- \rightleftharpoons H_2O + OR^-$. Although the existence of these equilibria has been recognised by many authors, others[3b,3c,11] appear sometimes to have ignored the existence of a second nucleophilic anion in alkaline ethanol-water mixtures. It now seems that the dominating factor causing the

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[7] M.L. Bender and W.A. Glasson, *J. Amer. Chem. Soc.* **81**, 1590 (1959).

[8] J. Koskikallio, *Suomen Kemistilehti* **30B**, 111 (1957).

[9] E.F. Caldin and G. Long, *J. Chem. Soc.* 3737 (1954).

[10] (Miss) I.R. Alet, *M. Sc. Thesis*, Wellington, N.Z. (1958).

[11] G.H. Grant and C.N. Hinshelwood, *J. Chem. Soc.* 258 (1933).

decrease in the overall rate of substitution in these mixtures, as water is added initially, is the progressive change of nucleophilic reagent from ethoxide to hydroxide. Previously[3a,4] the decrease in rate in S_N2 reactions has been attributed to the effect of the changing solvent on the solvation of initial and transition states, thereby increasing the activation energy of the reaction of the halide with a single nucleophile, and it would seem that this factor plays only a minor role in alkaline methanol- and ethanol-water mixtures near the 100% alcohol region.

Sodium thiophenoxide should be less susceptible to conversion into hydroxide as water is added for, although it is a strong nucleophilic reagent, it is relatively weak as a base.[12]

With alkaline methanol-water mixtures and with thiophenoxide in both methanol- and ethanol-water mixtures, what is apparently being observed in the initial stages of adding water is an influence of the changing solvent on the rate of reaction of the halide with a single nucleophilic reagent - this term being intended to include both a fully formed anion and loose complexes of the same ion with cations or with the solvent. There is evidence[13] for the existence of such complexes and for the importance of ion pairing in determining reaction rates in various media. At the moment it is plausible to attribute the increase in rate to the progressive dissociation of alkoxide, thiophenoxide and possible hydroxide ion pair complexes with cations as the solvent is made more aqueous.

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[12] P.B.D. de la Mare and C.A. Vernon, J. Chem. Soc. 41 (1956).

[13] J.D. Reinheimer, W.F. Kieffer, S.W. Frey, J.C. Cochran and E.W. Barr, J. Amer. Chem. Soc. **80**, 164 (1958); S. Winstein, L.G. Savedoff, S. Smith, I.D.R. Stevens and J.S. Gall, Tetrahedron Letters No. 9, 24 (1960).

Fig. 1 also lends credence to the view that the fall in rate which is eventually observed after the initial rise is again due to change of nucleophile to hydroxide. Such a change should result in a decrease in the overall rate for, although unambiguous data on the relative nucleophilicity of hydroxide and alkoxides is scanty, the relatively low reactivity of hydroxide has been stressed by Bunnett and Davis[14] and Bender and Glasson[7] and Alet[10] have found that it is less than that of methoxide and ethoxide when measurements are made in the same solvent.

That rate constants representing the simultaneous attack of two nucleophiles on a single halide do not drift during a run is not surprising in view of a treatment given previously.[6] The nucleophiles are in equilibrium throughout and the ratio of hydroxide and alkoxide concentrations remains virtually constant during a run despite the fact that they are being used up at different rates by the substitution processes. Moreover[6] the isolation of a large yield of alkyl ether does not necessarily mean that the constant obtained is largely characteristic of alkoxide.

Alkaline ethanol-water mixtures have been a popular medium for the investigation of substitution reactions, elimination reactions and mixtures of these types, as well as for mechanistic studies of more complex reactions. It is evident that a considerable re-interpretation of the results that have been obtained is now necessary.

We acknowledge the benefit of correspondence with Professor E.D. Hughes.

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[14] J.F. Bunnett and G.T. Davis, J. Amer. Chem. Soc. **76**, 3011 (1954); Ibid. **80**, 4337 (1958).