

Buffer Catalysis and Hydrogen-Deuterium Exchange of Heteroaromatic Carbon Acids

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Sir:

Buffer bases in aqueous solution catalyze the deprotonation of carbon acids such as ketones (2) and nitroalkanes (3). By contrast, there is some question about the magnitude of buffer-base catalysis in the deprotonation of heteroaromatic carbon acids at annular positions (4,5).

We present evidence that the hydrogen-deuterium exchange reactions of pyridinium ion (I) and pyridine 1-oxide (II) are not significantly catalyzed by buffer bases in aqueous solution. Deprotonation of I at positions *alpha* to the heteroatom was studied using neutral and anionic buffer bases in deuterium oxide. Deduteration of II at a position *gamma* to the annular heteroatom was examined using a neutral buffer base in water. Evidence has been presented that substrates such as I and II undergo H-D exchange reactions by simple deprotonation to give ylides (5,6) and carbanions (7) such as III and IV. Rates were determined by standard methods using NMR to follow the reactions (5,7).

Equation 1 describes the dependence of the pseudo-first order rate constant for exchange, $k\psi$, on the concen-

tration of deuteroxide ion (hydroxide ion) and buffer bases B. This equation may be applied to our results more conveniently when it has the form of equation 2 where k_2 is the second-order rate constant for reaction of the carbon acid with lyate ion and k_B a second-order rate constant

$$k\psi = k_2[\text{OD}^-] + k_B[\text{B}] \quad (1)$$

$$k\psi/[\text{OD}^-] = k_2 + k_B[\text{B}]/[\text{OD}^-] \quad (2)$$

for reaction with a general base B. Equation 2 has the form of an equation for a straight line, the intercept being k_2 and the slope k_B .

The results given in Table I show that $k\psi/[\text{OD}^-]$ (labelled as k_2) is essentially constant as the $[\text{B}]/[\text{OD}^-]$ or $[\text{B}]/[\text{OH}^-]$ ratio changes. For I the ratio of the concentrations of the bases varies by a factor of 9 and for II by a factor of 35. This means that k_B is insignificant. There is no evidence in these results for catalysis by buffer bases. In other words, the Brønsted β value for these reactions is essentially one.

These results may be interpreted in several ways; we have summarized possibilities elsewhere (5). We favor an

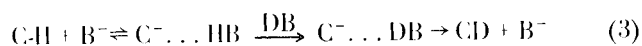
TABLE I

Kinetics of Hydrogen Exchange of 3,5-Dichloro-1-Methylpyridinium Chloride (I)
and 3,5-Dichloropyridine-4-*d* 1-Oxide (II) in Aqueous Buffers (a)

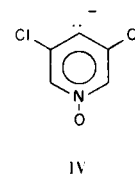
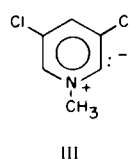
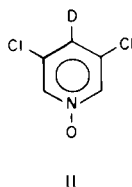
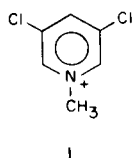
Cpd	pD or pH	[acid], M	[base], M	$k\psi$ (sec ⁻¹)	$10^{-5}[\text{B}]/[\text{OD}^-]$	k_2 (M ⁻¹ sec ⁻¹)
I (b)	7.41 (c)	0.010	0.010	4.1×10^{-6}	2.0	81
	7.63 (c)	0.09	0.15	6.8×10^{-6}	17.7	80
	8.01 (c)	0.04	0.15	2.0×10^{-5}	7.4	99
	8.07 (d)	0.46	0.27	1.9×10^{-5}	11.5	81
					$10^{-2}[\text{B}]/[\text{OH}^-]$	
II (e,f)	8.95	0.047	0.047	5.2×10^{-5}	2.8	0.30
	8.95	0.47	0.47	5.4×10^{-5}	27.6	0.32
	9.78	0.009	0.085	3.5×10^{-4}	0.8	0.30
	9.93	0.092	0.838	5.0×10^{-4}	5.2	0.31

(a) 1.0 Ionic strength; potassium chloride added; reactions followed by NMR; [Cpd] $\sim 0.5M$; $pK_W^D = 14.70$; $pK_W^H = 12.72$; $k_2 = (k\psi/K_w) \cdot [\text{H}]$ or $[\text{D}]$. (b) 30.0°. (c) $\text{D}_2\text{PO}_4^- - \text{DPO}_4^{-2}$. (d) Ethyl glycinate. (e) 75.0°. (f) Ethylenediamine buffer.

internal return mechanism (8), equation 3, where the isotope exchange process consists of two steps, ionization and substitution. If ionization is reversible and $\beta = 1$, substitution becomes the slow step. Substitution is not likely to be significantly dependent on acid-base properties. We favor this mechanism because negative charge is likely to be extensively localized; little solvent and structural reorganization should result during the ionization step. Consequently, reprotonation of the carbanion can be faster than substitution (9).



It will be of interest to determine whether other types of heteroaromatic carbon acids show significant buffer base catalysis for H-D exchange at annular positions. If substantial buffer catalysis is found and $\beta < 1$, then a mechanism similar to the one suggested here is not likely to operate.



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