Effects of Metal Ions on Rates of Detritiation—New Probe in the Study of Metal–Substrate Interactions

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Summary The rate retarding effect of metal ions ($Cu^{2+} > Zn^{2+} \simeq Ni^{2+} >> MeHg^{+}$) on isotopic hydrogen exchange from the C(2) position of imidazole can be rationalised in terms of complex formation; the stability constants can be evaluated from the exchange rate constants.

The bell-shaped pH rate profile for detritiation from the C(2) position of imidazole closely resembles that found for benzimidazole,[1] where the mechanism, like that for many other heterocyclic compounds,[2] involves rate-determining hydroxide ion attack on the protonated species (BH_2^{+}). In such a case the pseudo-first order rate constant is given by equation (1).

$$k_{\mathrm{obs}} = \frac{kK_{\mathrm{w}}}{K_{\mathrm{a}} + \dfrac{K_{\mathrm{a}}K'_{\mathrm{a}}}{[\mathrm{H}^{+}]} + [\mathrm{H}^{+}]} \qquad (1)$$

where $K_{\mathrm{a}} = [\mathrm{BH}][\mathrm{H}^{+}]/[\mathrm{BH}_2^{+}]$, and $K_{\mathrm{a}}' = [\mathrm{B}^{-}][\mathrm{H}^{+}]/[\mathrm{BH}]$. The corresponding reaction in the presence of metal ions gives equation (2).

$$k'_{\mathrm{obs}} = \frac{kK'K_{\mathrm{w}}}{K'[\mathrm{H}^{+}] + K_{\mathrm{a}}K' + K_{\mathrm{a}}[\mathrm{M}n^{+}]} \qquad (2)$$

where $K' = [\mathrm{M}^{n+}][\mathrm{BH}]/[\mathrm{MBH}^{n+}]$, and $[\mathrm{M}^{n+}]$ is the free metal ion concentration. If $k_{\mathrm{obs}}/k'_{\mathrm{obs}} = R$, rearranging and taking logarithms leads to equation (3).

$$\log\left[\frac{1-R}{R}\right] = \log\,[\mathrm{M}^{n+}] + \log\left[\frac{K_{\mathrm{a}}}{K'([\mathrm{H}^{+}] + K_{\mathrm{a}})}\right] \qquad (3)$$

so that a plot of $\log\left[\frac{1-\mathrm{R}}{\mathrm{R}}\right]$ against $\log\,[\mathrm{M}^{n+}]$ should yield a straight line of unit slope; the stability constant of the complex, K' can be obtained from the intercept.

The results in the Table show that all the metal ions cause a rate-retardation, the effectiveness increasing in the order $Cu^{2+} > Zn^{2+} \simeq Ni^{2+} >> MeHg^{+}$. These findings are in contrast to the considerable rate enhancement brought about by Cu^{2+} and Zn^{2+} in the deuterium exchange of 1-methyl tetrazole[3] and the recent report[4] that $MeHg^{+}$ catalyses proton exchange between solvent water and purine nucleosides. This difference in behaviour is probably linked to the stability of the tritium atom in the metal-substrate complex.

Table Rates of detritiation of [2-^{3}H]-imidazole at 85 °C and pH 5·70 in the presence of metal ions.

Metal ion	Concentration/M	Relative rate[a]
Ni^{2+}	$5{\cdot}2 \times 10^{-4}$	0·72
	$5{\cdot}2 \times 10^{-3}$	0·36
	$2{\cdot}6 \times 10^{-2}$	0·12
	$5{\cdot}2 \times 10^{-2}$	0·069
Cu^{2+}	$5{\cdot}0 \times 10^{-4}$	0·385
	$5{\cdot}0 \times 10^{-3}$	0·022
Zn^{2+}	$5{\cdot}0 \times 10^{-3}$	0·32
$MeHg^{+}$	*ca.* 10^{-3}	0·76

[a] Relative to a value of $10{\cdot}0 \times 10^{-4}\ s^{-1}$ at 85 °C and pH 5·70 in the absence of metal ions.

The results for nickel are in good agreement with theory, leading to a pK' value of 2·45 ± 0·05 at 85 °C. The value at 25 °C is reported to be 3·00.[5] This present approach takes on an added significance in view of the occurrence of the imidazole ring system in many biologically important molecules. It can however be readily adapted to other compounds *e.g.* β-diketones, which have an exchangeable proton and which are known to complex with metal ions.

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