Secondary α-Hydrogen Kinetic Isotope Effects in Nucleophilic Additions to Ferrocenyl-stabilised Carbocations

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Summary The secondary α-hydrogen kinetic isotope effects upon the solvolyses of Fc_2C^+H (**1a**) and p-$MeOC_6H_4C^+HFc$ (**1b**) (Fc = ferrocenyl) in H_2O, H_2O–MeCN, and H_2O–MeOH (k_f^H/k_f^D = *ca.* 0·9), and upon the acid heterolyses of the corresponding alcohols (k_r^H/k_r^D = *ca.* 1·1), suggest that there is appreciable C····O bond formation in the transition state for carbocation solvolysis; for additions of HO^-, N_3^-, and BH_4^- to (**1a**), k_f^H/k_f^D = *ca.* 1·0, indicating 'early' carbocation-like transition states for these reactions, whereas intermediate values (k_f^H/k_f^D = *ca.* 0·96) are found for additions of primary amines.

Secondary α-hydrogen kinetic isotope effects (KIE) are a powerful tool in the elucidation of the mechanisms of nucleophilic substitutions and similar reactions,[1,2] but they have not been used to date to study nucleophilic additions to preformed carbocations in solution. We have measured these effects upon the rate constants k_f for additions to the cations (**1a**,**b**)[3] and k_r for acid heterolyses of the related alcohols (**2a**,**b**) (Fc = ferrocenyl; * denotes the position of isotopic replacement by deuterium).

FcC^+H^*R (**1**)

$FcCH^*(OH)R$ (**2**)

a; R=Fc

b; R=p-$MeOC_6H_4$

The KIE upon k_f for addition of anionic nucleophiles to (**1a**) are close to unity (Table 1),‡ suggesting that there is little or no change in the orbital hybridisation of the α-carbon in the transition states which, for these anion additions, are therefore akin to ion pairs. However, we found inverse KIE for addition of primary amines to (**1a**) (k_f^H/k_f^D = *ca.* 0·96; Table 1) and of water to (**1a**,**b**) (k_f^H/k_f^D = *ca.* 0·90; Table 2). In the transition states for these

Table 1. α-Hydrogen kinetic isotope effects on nucleophilic additions to (**1a**)[a,b]

Nucleophile	k_f^H/l mol^{-1} s^{-1}	k_f^H/k_f^D
HO^-	38·7	0·987 ± 0·020
N_3^-	2·61 × 10^4	1·012 ± 0·013
BH_4^-	1·89 × 10^3	0·999 ± 0·020
$MeNH_2$	6·53 × 10^2	0·955 ± 0·010
Bu^tNH_2	34·7	0·969 ± 0·014
$MeONH_2$	21·8	0·957 ± 0·004

[a] The rate constants and ratios given are each based upon 8—12 determinations, over a tenfold range of nucleophile concentrations; the k_f^H values given agree reasonably well with those quoted previously (ref. 3b), except for the hydroxide reaction where the earlier value was in error. [b] In H_2O–MeCN (1 : 1 w/w; mol fraction of H_2O = 0·695) at 25·0 °C.

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‡ Similarly, for the addition of HO^- to (**1b**) in water at 25·0 °C, k_f^H = 3·66 × 10^4 l mol^{-1} s^{-1} and k_f^H/k_f^D = 0·98 ± 0·05.

additions, it follows that there is appreciable bond formation between the reactants with corresponding change in the hybridisation at the reactive site. For the three amines studied, the KIE are of similar magnitude despite differences[3b] in their nucleophilicities towards (**1a**) and in their steric bulk.

TABLE 2. α-Hydrogen kinetic isotope effects on solvolysis of the cations (**1a**,**b**)[a]

Cation	k_f^H/s^{-1}	k_f^H/k_f^D	k_r^H/l mol^{-1} s^{-1}	k_r^H/k_r^D	$K_{R^+}^H/K_{R^+}^D$
(**1a**)	0·0266[b]	0·915 ± 0·024	37·2[b]	1·08 ± 0·02	0·847
	0·177[c]	0·896 ± 0·010			
(**1b**)	43·2[d]	0·874 ± 0·016	1·05 × 10^{3}[d]	1·15 ± 0·07	0·760

[a,b] As for Table 1. [c] In H_2O–MeOH (mol fraction of H_2O = 0·695) at 25·0 °C. [d] In H_2O at 25·0 °C.

The different behaviour of anionic and non-ionic nucleophiles does not depend upon their reactivities but on their charge. Ritchie has suggested[4] that anion desolvation may provide much of the free-energy barrier to additions of anions to preformed carbocations, and this would involve no significant hybridisation change at the α-carbon of the cation. Additions of both water and a primary amine to a carbocation involve both bond-making and proton loss; for amine addition in aqueous media, one must also consider the process of encounter between reactants, which does not involve rehybridisation at the reaction site. The observation[5] of general base catalysis of water addition to preformed carbocations suggests that, for this reaction [equation (1)], bond-making and proton loss are concerted. However, catalysis is relatively unimportant for amine addition [equation (2)]. This mechanistic difference

$$\mathrm{FcC^{+}HR + H_2O \rightleftharpoons \{[FcC(R)H\cdots O(H)\cdots H]^{+}\}^{\ddagger} \longrightarrow FcCH(OH)R + H^{+}} \qquad (1)$$

$$\mathrm{FcC^{+}HR + R'NH_2 \rightarrow FcCHRN^{+}H_2R' \xrightarrow{fast} FcCHRNHR' + H^{+}} \qquad (2)$$

between additions of water and of amines can be rationalised in terms of three-dimensional free-energy diagrams which have been discussed by several authors.[6]

The secondary isotope effects upon cation ⇌ alcohol equilibria in aqueous acidic media ($K_{R^+}^H/K_{R^+}^D$; Table 2) are as expected[1] for reactions involving $sp^2 \rightleftharpoons sp^3$ change in hybridisation at the reaction centre, and the KIE upon the forward (k_f) and reverse (k_r) reactions are relatively insensitive to solvent changes. The kinetic solvent isotope effect ($k_r^{H_2O}/k_r^{D_2O}$ = *ca.* 0·4) for acid heterolysis of tri-*p*-anisylmethanol[7] and several 1-ferrocenylalkanols[3a] can be interpreted in terms of a two-step mechanism [equation (3)].

$$\mathrm{ROH + H^{+} \overset{fast}{\rightleftharpoons} RO^{+}H_2 \rightleftharpoons R^{+} + H_2O} \qquad (3)$$

These observations are inconsistent with general base catalysis of water addition but it has been pointed out[8] that values of k_{H_2O}/k_{D_2O} do not necessarily distinguish between concerted and stepwise reactions when a proton is being transferred between electronegative atoms, and a model for conservation of its zero-point energy has been proposed.[9]

Our observed KIE for acid heterolyses (k_r^H/k_r^D) of the alcohols (**2a**,**b**) are close to that (1·08) estimated[10] indirectly from the rates of permanganate oxidation of Ph_2CH^*OH. The KIE for nucleophilic additions (k_f^H/k_f^D) to the carbocations (**1a**,**b**) give no support to the concept[11] of 'late' transition states for such reactions. The effects are consistent with the postulate[4] that water behaves somewhat differently from other nucleophiles, but indicate that HO^- behaves like other anionic nucleophiles in its reactions with preformed carbocations in aqueous solutions. The different KIE on addition of anionic and non-ionic nucleophiles suggest that different factors may govern their nucleophilicities towards carbocations and therefore may have a bearing on the interpretation of reactivities in terms of, for example, the N_+ scale.[4]

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