

Kinetic Isotope Effects in Proton-transfer Reactions

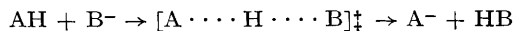
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RECENT results for the base-catalysed exchange of some aromatic hydrocarbons in firstly¹ a medium of lithium cyclohexylamide in cyclohexylamine, and secondly,² dimethyl sulphoxide containing potassium butoxide as base, have indicated considerable discrepancies in the relative rates of proton exchange. Hofmann *et al.*² suggested that the difference was due to greater charge delocalisation in the more polar solvent, whilst Streitwieser¹ suggested that ionisation may not be the true rate-determining step in the alkoxide–Me₂SO system. Further evidence³ in support of the latter viewpoint was apparently obtained when a k_D/k_T value of near unity resulted from the alkoxide-catalysed exchange of the methyl hydrogens of toluene, in sharp contrast to a k_H/k_D value in excess of 10 when the reaction was catalysed by lithium cyclohexylamide in cyclohexylamine.⁴ The absence of an isotope effect during racemisation studies using the *t*-butoxide–Me₂SO system has also been observed.⁵ The object of the present Communication is to show that the two widely different isotope effect values are not inconsistent and that both may relate to the

same rate-determining ionisation mechanism. Also implicit in this statement is the fact that the use of Me₂SO–base media may be a means of determining transition-state structure.

For the ionisation of weak carbon acids in the presence of a base catalyst (B) it is convenient to use a linear three-centre model:—



Kinetic isotope effect theory⁶ points to the fact that when the force constant (F_{22}) of the bond AH is equal to the force constant (F_{11}) of the bond HB the isotope effect will be a maximum. This condition is likely to be so when $\text{p}K_A(\text{HA}) - \text{p}K_A(\text{BH})$ is zero,⁷ and recently data has become available which seems to support this conclusion.^{7,8} Although no accurate value of the $\text{p}K_A$ of toluene is available it seems as if a value of 40 would be approximately correct. Similarly whilst no data is available for cyclohexylamine a similar solvent would be ammonia where a $\text{p}K_A$ at 25° of 35 has been suggested⁹ as compared to an experimentally obtained¹⁰

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value of 36. On this basis a large isotope effect of 10, which included a small secondary contribution, is not unexpected.

In the case of the *t*-butoxide–Me₂SO system the high basicity of the medium is due to the ability of Me₂SO to decrease the solvation of the butoxide ion. In other words for measurements in the *t*-butoxide–*t*-butyl alcohol–Me₂SO system the increase in the rate of ionisation as the concentration of Me₂SO is increased is due to the increasing ease with which the desolvation of the butoxide ion occurs. Consequently although the basicity of the medium as represented by *H*₋ is increasing, the position of the proton in the transition state remains substantially the same. This viewpoint is reflected in the results of a study¹¹ of the reaction of 2-arylethyl bromide with KOBu^t in Bu^tOH–Me₂SO, where *k*_H/*k*_D was found to remain constant within experimental error as the Me₂SO concentration increases, and also by unpublished results¹² of our own on the detritiation of acetophenone in OH⁻–Me₂SO where a log *k* against *H*₋ plot has a slope of +0.5 and is consistent with the known transition-state structure.¹³

Although no accurate p*K*_A values in Me₂SO are available, it can be assumed that any changes in going from aqueous media to Me₂SO would be similar for both PhCH₂⁻ and BuO⁻. If a value of

20 for p*K*_A of Bu^tOH is taken¹⁴ then p*K*_A(HA)–p*K*_A(HB) ~ 20, and as the anion of toluene will be a far more powerful base than the butoxide ion, the proton in the transition state will be very near the latter, the situation being [A⁻ · · · · H⁺B⁻]. Consequently a low value of *k*_H/*k*_D is to be expected,

and if the condition $f_{\ddagger}^{\dagger} > \frac{v_{\ddagger}^{\dagger HL}}{v_{\ddagger}^{\dagger DL}} f_{HA} \cdot f_B$ prevails,

where *v*_{HL}[‡] and *v*_{DL}[‡] are the decomposition modes of the vibrational frequencies (in wave-numbers), then an inverse isotope effect will be obtained.⁶

Approximate calculations¹⁵ of the magnitude of *k*_H/*k*_D can be made by taking *M*_B = 17, *M*_H = 1, and *M*_A = 100, and by assuming reasonable values of *F*₁₁/*F*₂₂, and a curvature parameter *d*, given by *F*₁₁*F*₂₂–*F*₁₂² of –0.1. Although no direct measurement of the *F*₁₁/*F*₂₂ ratio can be made, in view of the transition state suggested it would be expected that *F*₁₁ ≫ *F*₂₂, and the greater the difference p*K*_A(SH)–p*K*_A(HB) then the greater the ratio *F*₁₁/*F*₂₂ would become. For values of *F*₁₁/*F*₂₂ in excess of 10, the values of *k*_H/*k*_D seem to show little change and for the case of *F*₁₁/*F*₂₂ = 10 the resulting *k*_H/*k*_D value is 2.0, leading to *k*_D/*k*_T of near unity. Such a low value is therefore not incompatible with a rate-determining ionisation process.

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