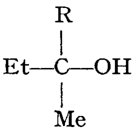
Secondary Deuterium Isotope Effect on Lewis Basicity: Tris(dipivaloylmethanato)-europium as a Simple and Effective Probe

By JEREMY K. M. SANDERS and DUDLEY H. WILLIAMS*
(*University Chemical Laboratory, Lensfield Road, Cambridge* CB2 1EW)

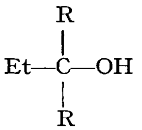
Summary Investigation of equilibrium isotope effects *via* competition experiments with the paramagnetic shift reagent Eu(dpm)$_3$ is described and it is shown that in the aliphatic alcohols studied deuterium is effectively more electropositive than protium; the method may be extended to other substituents.

THERE has been considerable interest recently in the effect of remote deuterium substitution on the Lewis basicity of a molecule; aliphatic acids deuteriated in the alkyl chain are weaker than their protium analogues and similarly deuteriated amines are stronger bases than the protium compounds.[1,2] Ultimately all secondary isotope effects have to be related to changes in zero-point energies and force constants but to what extent these changes manifest themselves as 'inductive,' 'steric,' or 'hyperconjugative' effects is a matter for discussion,[1] and this discussion has been hampered by lack of reliable data, the conventional potentiometric techniques for measuring pK changes being limited to acids and amines.[2] We report here a novel method using the paramagnetic shift reagent Eu(dpm)$_3$.[3]†



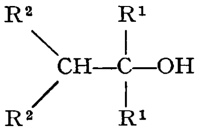
$Et{-}C(R)(Me){-}OH$

(**1**; R = H)
(**2**; R = D)



$Et{-}C(R)_2{-}OH$

(**3**; R = CH_3)
(**4**; R = CD_3)



(**5**; R^1 = R^2 = CH_3)
(**6**; R^1 = CD_3, R^2 = CH_3)
(**7**; R^1 = CH_3, R^2 = CD_3)

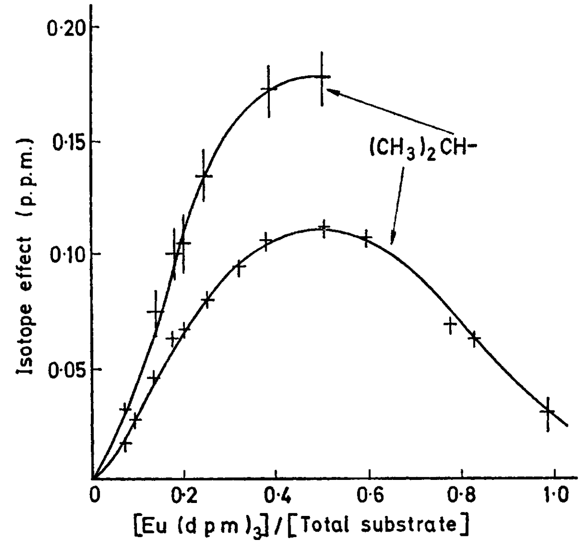


FIGURE. *Variation of isotope effect with molar ratio, using* (**5**) *and* (**6**) (*each* 0·11M *in* CCl$_4$).

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† The first examples of isotope effects in Eu(dpm)$_3$-shifted spectra have recently been reported by deBoer *et al.*[4] and by Hinckley *et al.*[5] We thank Dr. deBoer for communicating his results to us prior to publication.

Substrates (**1**)—(**7**) were used for this study, their syntheses being unexceptional.

Addition of Eu(dpm)$_3$ to mixtures of deuteriated and undeuteriated analogues causes a splitting of the resonances, and experiments on non-equimolar mixtures reveal that the resonance due to the deuteriated species which are shifted furthest. *E.g.* in a solution in CCl$_4$ of (**3**) and (**4**) (each 0·13M) containing Eu(dpm)$_3$ (0·04M) the methylene protons of the ethyl group appear as a quintet because the quartet of (**4**) is shifted 7 Hz (at 100 MHz) further than that of (**3**). Similarly the methyl triplet is split by a 3 Hz non-equivalence.

At sufficiently high concentrations of shift reagent the isotope effect decreases to zero as shown in the Figure for the pair (**5**), (**6**). Line-width and signal-to-noise considerations prevented accurate monitoring of the methine proton at high Eu(dpm)$_3$ concentrations, but in the spectra at highest concentrations of shift reagent it was clear that the isotope effect had decreased to almost zero. The maximum effect is seen at an analogous molar ratio to the bifunctional competition cases described elsewhere,[6–9] and clearly the deuteriated compound is competing more effectively for the shift reagent, Δ_{lim} (the limiting shift) being effectively the same in each case.

We have shown elsewhere[6] that the shift gradient $G(\text{H}_k)_i$ of the k'th proton in the i'th substrate in a mixture of x substrates is given by equation (1), where S_j are the substrate concentrations and K_j are the equilibrium constants for the association in equation (2). The stoicheiometry of the adduct is 1:1.[6] Thus, for an equimolar mixture of deuteriated and undeuteriated species we may write down equation (3); the ratio of the observed gradients is thus the ratio of equilibrium constants, and in the Table are gathered the isotope effect data for the substrates (**1**)—(**7**), both in terms of K_D/K_H and in terms of $\Delta(\Delta G)$, the difference in free energy change. G_D/G_H remains constant up to a molar ratio of *ca.* 0·25 and decreases thereafter.

$$G(\text{H}_k)_i = \Delta_{\text{lim}} \times K_i S_i/(1 + \sum_{j=1}^{x} K_j S_j) \qquad (1)$$

$$(\text{substrate})_j + \text{Eu(dpm)}_3 \overset{K_j}{\rightleftarrows} (\text{adduct})_j \qquad (2)$$

$$G_D/G_H = K_D/K_H \qquad (3)$$

Attenuation of isotope effects along an alkyl chain

Substrate pair	K_D/K_H	$\Delta(\Delta G)^a$ (cal/mol)	$\Delta(\Delta G)$ per deuterium (cal/mol/D)
(**1**), (**2**)	1·023 ± 0·002	−13·7 ± 1·4	−13·7 ± 1·4
(**3**), (**4**) (**5**), (**6**)	1·035 ± 0·03	−20·7 ± 1·3	−3·45 ± 0·21
(**5**), (**7**)	1·008 ± 0·001	−4·5 ± 0·5	−0·75 ± 0·08

[a] $\Delta(\Delta G) = \Delta G_D - \Delta G_H = -RT \ln (K_D/K_H)$.

The most striking aspect of these results is their very great precision; we have shown[6] that ΔG for the association is *ca.* −3 kcal/mol and yet we can measure $\Delta(\Delta G)$ with an accuracy of ±1 cal/mol. Presumably the observed isotope effect is due to the change in lone-pair Lewis basicity which is in itself caused by the deuterium substitution. As can be seen from the Table, the effect, measured in terms of $\Delta(\Delta G)$, attenuates by a factor of approximately four per intervening bond.

Further studies with Eu(dpm)$_3$ could further clarify such isotope effects, and indeed the method is applicable to other substituent effects and to physical methods other than n.m.r. spectroscopy.

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