Secondary Deuterium Isotope Effects in the Cope Rearrangement

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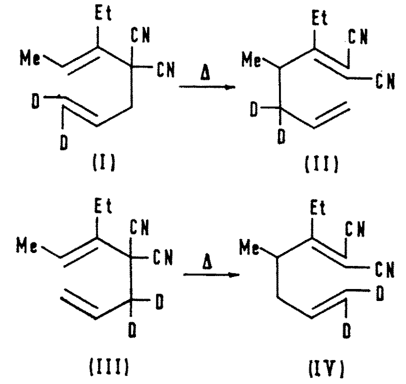
WE report on kinetic secondary deuterium isotope effects observed during the thermal rearrangement of [6,6-$^{2}H_{2}$]-3,3-dicyano-2-ethyl-1-methylhexa-1,5-diene (I) and the [4,4-$^{2}H_{2}$]-labelled compound (III). Compound (I) was prepared from [3,3-$^{2}H_{2}$]allyl chloride, sodium ethoxide, and 1,1-dicyano-2-ethylbut-1-ene by the method described by Cope.[1] [3,3-$^{2}H_{2}$]Allyl chloride was prepared from [1,1-$^{2}H_{2}$]-allyl alcohol and thionyl chloride by a modification of the method of Young *et al.*[2] Compound (III) was prepared correspondingly from [1,1-$^{2}H_{2}$]allyl chloride.[1] The rearrangements were performed in n-decane solution at 85° and rates were followed by measuring the increase in the absorption at 238 nm. due to the product formed.† The rates were followed simultaneously for deuteriated and undeuteriated compounds. The results of kinetic measurements are given in the Table. The energy and entropy of activations (25·8 kcal./mole and −11 e.u.) for this reaction were determined by Cope.[3]



Secondary deuterium isotope effects in the Cope rearrangements at 85°

Compound[a]	k_H/k_D	Atoms D/molecule	$\Delta\Delta F\ddagger/n$ (cal./mole)
(I)[b]	0·94±0·02[c]	1·87[d]	−26
(III)[b]	1·19±0·03[c]	1·94[e]	+66

[a] 0·1 mg. in 10 ml. of n-decane. [b] $k_H = 1{\cdot}17 \times 10^{-5}$ sec.$^{-1}$. [c] Average of four measurements. Uncertainties are standard errors. [d] There are 0·07 atoms D in position 4. Deuterium content and the position of label were determined by n.m.r. [e] In position 4 as determined by n.m.r.

These results can be rationalized as follows:

Shiner *et al.*[4] discussed recently some factors influencing the magnitude of secondary α-deuterium isotope effects in solvolytic reactions. They observed that the change of the alkyl group in reactions of alkyl halides has little influence on the magnitude of the isotope effect, while the reverse is true if the leaving group is changed. This is apparently due to the fact that the HCX force constants in the reactants change much more strongly with a change of the leaving group than do the force constants in the transition state. Therefore the difference in the force constants involving the HCX bending motion in the reactant are responsible for the observed differences in magnitude of α-isotope effects. It seems that the α-isotope effect varies with the degree of stretching of the C–X bond (if X is the same) in the transition state in a manner shown in the upper curve of Figure.

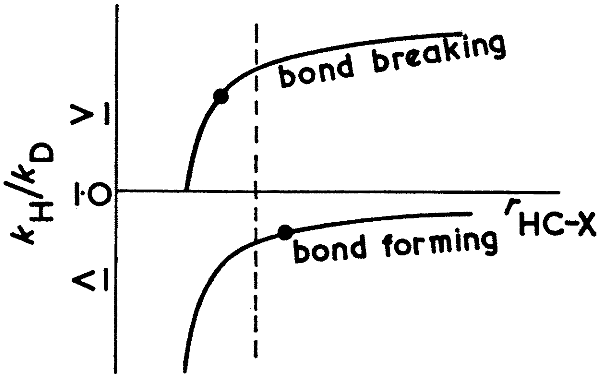


FIGURE. *Possible correlation between the magnitude of isotope effects and degree of bonding in the transition state (see text).*

If this correlation is correct, then small changes of the C–X distance in the reaction transition state will have a large influence on the magnitude of the α-effect only if the bond-breaking process is not far advanced. In solvolyses of alkyl halides the transition state resembles the carbonium-ion intermediate in which the covalent bond to the leaving group is completely broken, which explains the results discussed by Shiner.[4]

Such a correlation also explains the observation that the same α-effect is observed for $k_{\text{ionisation}}$ as for $k_{\text{solvolysis}}$ in a case where "internal return" is important.[5] By the principle of microscopic reversibility, the same situation pertains also in the (inverse) case of bond formation. Thus, the magnitude of the α-effect will be significantly changed only if the formation of the new bond is far advanced in the reaction transition state. For such a process the correlation given in the lower part of the Figure should be valid. An indication that solvolytic reactions conform to this correlation is found in π-participating systems.[6]

The isotope effects measured in the Cope rearrangement and reported here can be discussed in an analogous manner. The rate changes observed correspond to α-effects in solvolytic reactions with the *only* difference that here the HCC force constant changes are responsible for the effect.

In the rearrangement investigated, the products (II) and (IV) are more stable than the reactants. Therefore, the cyclic transition state must resemble more the reactant

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† The temperature was measured in a constant-temperature bath. The temperature in the cell was not accurately known because of experimental difficulties but was about 5° lower and constant to ±0·1°.

than the product. In other words neither the C-3–C-4 bond-breaking process nor the C-1–C-6 bond-forming process are very far advanced in the transition state. The situation is depicted in the Figure by black dots on the appropriate curves. It can be seen that a larger normal ($k_H/k_D > 1$) than the corresponding inverse effect can be expected in the reactions of (I) and (III), which explains the observed differences in the $\Delta\Delta F^{\ddagger}/n$ values (see Table). If the degree of bond fission were the same as the degree of bond formation (symmetrical transition state) the corresponding isotope effects would fall on the vertical dotted line. McMichael observed α-effects of similar magnitudes in the case of the Claisen rearrangement.[7]

We have also studied the thermodynamic isotope effect in the degenerate Cope rearrangement of [1,1,6,6-$^2H_4$]biallyl and an effect of 1·40 was observed.[8] Taking into account the experimental errors involved, this result is in complete agreement with the above discussion. By extending Shiner's reasoning to this case it seems that in reactions where C–C bonds are being broken in the rate-determining step, a maximum α-effect of about 10% can be expected.

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[5] S. Borčić and D. E. Sunko, *Croat. Chem. Acta*, 1961, **33**, 77.

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[7] We thank Dr. K. D. McMichael (Washington State University) for exchanging this information prior to publication.

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