CH_3–CD_3 Isotope Effects in the Acid Catalysed Dienone–Phenol Rearrangement

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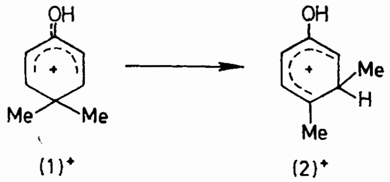
Summary $k(CH_3)/k(CD_3)$ has been determined for rate-determining methyl migration in the dienone–phenol rearrangement and is 1·144 ± 0·017.

IN a recent paper,[1] Schubert and LeFevre have suggested that reactions which involve 1,2-methyl migration in the rate-determining step will show a significant deuterium isotope effect. They observed that for the acid-catalysed rearrangement of 1,1-diphenyl-2-methylpropane-1,2-diol, the di(trideuteriomethyl) derivative reacted 1·18 ± 0·02 times slower than the unlabelled material, and that the entire isotope effect was due solely to the migrating methyl group.

In previous work,[2,3] we have shown that the acid-catalysed rearrangement of 4,4-dimethylcyclohexadienone (**1**) is a simple *A*-1 reaction involving a rate-determining methyl group migration and we now determine the CH_3–CD_3 isotope effect for this reaction. The CD_3 labelled cyclohexadienones [$^2H_3$]-(**1**) and [$^2H_6$]-(**1**) were prepared by published procedures[3] from the isotopic isobutyraldehydes.



These isotope effects were determined at 25° by monitoring the change in absorbance at 260 nm[3] with pairs of unlabelled (**1**) and [$^2H_3$]-(**1**) or [$^2H_6$]-(**1**). Fifteen determinations at several acid concentrations were made.

$$k\{\text{unlabelled-}(\mathbf{1})\}/k\{[^2H_6]\text{-}(\mathbf{1})\} = 1{\cdot}151 \pm 0{\cdot}016$$

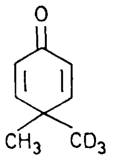
$$k\{\text{unlabelled-}(\mathbf{1})\}/k\{[^2H_3]\text{-}(\mathbf{1})\} = 1{\cdot}060 \pm 0{\cdot}012$$

Assuming that there is no isotope effect on the non-migrating methyl group, the isotope effect on the migrating methyl group $k(CH_3)/k(CD_3)$ can be computed independently from each of the isotope effects listed above.

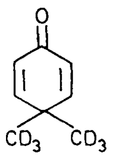
$$k\{[^2H_3]\text{-}(\mathbf{1})\}/k\{\text{unlabelled-}(\mathbf{1})\} = 1 + k(CD_3)/k(CH_3) \qquad (1)$$

$$k\{\text{unlabelled-}(\mathbf{1})]/k\{[^2H_6]\text{-}(\mathbf{1})\} = k(CH_3)/k(CD_3) \qquad (2)$$

Since $k\{\text{unlabelled-}(\mathbf{1})\}/k\{[^2H_6]\text{-}(\mathbf{1})\}$ is the product of both the migrational and non-migrational isotope effects and since the non-migrational isotope effect is expected to be $\geqslant 1$ (*cf.*, β-deuterium isotope effects in carbonium ion reactions[4]), the derived migrational isotope effect can be considered to be an upper limit.



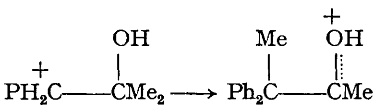
[$^2H_3$]-(1)



[$^2H_6$]-(1)

From the [$^2H_3$]-(**1**) isotope effect, $k(CH_3)/k(CD_3) = 1{\cdot}128 \pm 0{\cdot}026$ and from the [$^2H_6$]-(**1**) isotope effect, $k(CH_3)/k(CD_3) = 1{\cdot}151 \pm 0{\cdot}016$. A weighted average of these two results give $k(CH_3)/k(CD_3) = 1{\cdot}144 \pm 0{\cdot}017$ for the isotope effect on the migrating methyl group in the dienone–phenol rearrangement. These results indicate that the migrational isotope effect in the dienone–phenol rearrangement is similar to, although slightly smaller than, the only other published example.[1]

If, as has been suggested,[1] the origin of these methyl group isotope effect lies in a reduction of the C–H stretching and/or bending force constants due to the partial positive charge born by the methyl group in the transition state, then the "symmetrical" transition state should give rise to the largest methyl group isotope effect. This is so because the fractional positive charge on the migrating methyl group is a maximum for the symmetrical transition group. For Schubert's case, the rate-determining step is



$$\mathrm{P}\overset{+}{\mathrm{H_2C}}-\overset{\mathrm{OH}}{\overset{|}{\mathrm{C}}}\mathrm{Me_2} \longrightarrow \mathrm{Ph_2}\overset{\mathrm{Me}}{\overset{|}{\mathrm{C}}}-\overset{\overset{+}{\mathrm{OH}}}{\overset{\vdots}{\mathrm{C}}}\mathrm{Me}$$

$(\mathbf{3})^+$ $(\mathbf{4})^+$

The conversion $(\mathbf{3})^+ \rightarrow (\mathbf{4})^+$ is expected to be more nearly isoenergetic than $(\mathbf{1})^+ \rightarrow (\mathbf{2})^+$. [In fact, $(\mathbf{3})^+ \rightarrow (\mathbf{4})^+$ may actually be exothermic since $(\mathbf{4})^+$ is probably more stable than $(\mathbf{3})^+$]. Moreover, in $(\mathbf{2})^+$ the non-bonded electrons on oxygen are not able to conjugate effectively with the positive charge in the ring and $(\mathbf{2})^+$ is probably much less stable than $(\mathbf{1})^+$. According to Hammond[5] the transition state for the dienone–phenol rearrangement should be more 'product-like' than for the pinacol–pinacolone rearrangement studied by Schubert. This will result in a reduced methyl group isotope effect in the dienone-phenol rearrangement.

Thus, in addition to providing information concerning whether or not methyl group migration takes place in the rate-determining step,[6] it appears that CH_3–CD_3 isotope effects are capable of providing information about the structure of the transition state.

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