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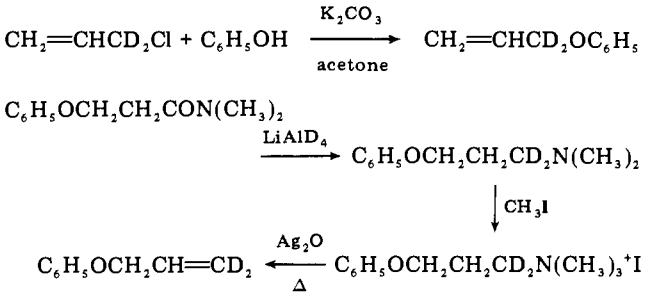
Received October 2, 1978

Secondary Deuterium Isotope Effects and Transition State Structure in the Aromatic Claisen Rearrangement

Sir:

The Claisen rearrangement of allyl aryl ethers is a classic example of the now familiar [3,3]-sigmatropic shift.[1] The intervention of the cyclohexadienone intermediate and its rapid enolization have been long established.[1] A concerted process leading to a transition state for the formation of the intermediate is supported by volume of activation measurements and on orbital symmetry grounds,[2] and a chair-like picture of this transition state provides a satisfactory rationalization of the observed stereoselectivity.[3,4] On the other hand, the relative insensitivity of reaction rates to polar substituent and solvent effects has been interpreted in terms of significant contributions of radical-pair-like structures to the transition state structure.[5] Unfortunately, the interpretation of such experiments is clouded by the fact that they depend upon alterations in transition state structure in order to produce observable effects. To clarify this picture it is important to understand the details of the bonding between the phenoxy and allyl moieties in the transition state, using an experimental approach which does not in itself alter the transition state structure. We report measurements of the secondary deuterium kinetic isotope effect attending deuterium substitution at the α and γ carbons of the allyl moiety and their interpretation in terms of transition state structure.

Scheme I



The deuterated allyl phenyl ethers required for this study were prepared as described in Scheme I, modeled on literature precedent.[6] All compounds exhibited NMR and IR spectra consistent with the structure shown. NMR analysis indicated >99% deuterium incorporation in the positions shown.

Kinetic experiments were carried out simultaneously on separate methyl salicylate solutions of allyl phenyl ether and its deuterated analogues at temperatures between 170 and 195 °C. Gas chromatographic analysis for allyl phenyl ether using an internal standard (anisole) and mechanical integration afforded concentration/time data which were fitted to the exponential form of the first-order rate equation by a standard nonlinear least-squares program.[7] At least 15 points, each the average of measurements on three ampules, were obtained for each run, covering 10–85% reaction. The derived isotope effects show no trend with temperature; hence averages for six runs with each compound are $k_H/k_{\alpha\text{-}D_2} = 1.18 \pm 0.02$ and $k_H/k_{\gamma\text{-}D_2} = 0.95 \pm 0.02$.[8]

Interpretation of these results in terms of transition state structure requires an estimate of the equilibrium isotope effects associated with the O–$CH_2(D_2)$ → =$CH_2(D_2)$ (α effect) and =$CH_2(D_2)$ → $C_6H_5CH_2(D_2)$–C (γ effect) conversions. Using the spectroscopically based calculations of Hartshorn and Shiner,[9] one may obtain an equilibrium α effect of 1.30 and a γ effect of 0.87, both calculated for two deuterium atoms at 185 °C. Gajewski and Conrad have recently provided experimental support for these calculations, observing an equilibrium α effect of 1.27 at 160 °C and a γ effect of 0.88 at 185 °C.[10] Thus the simplest interpretation of these results is that the C–H vibration frequencies at the α carbon for the transition state are approximately (1.18–1)/(1.27–1) or 57–77% of the way from those of allyl phenyl ether to those of the cyclohexadienone intermediate. In the same way, the C–H frequencies of the γ carbon in the transition state are about (0.95–1)/(0.88–1) = 22–62% of the way to those of the intermediate.

The structure of the transition state, at least insofar as it is reflected in C–H bonding frequencies at the α and γ carbons of the allyl moiety, is entirely consistent with the long-held concerted description of the mechanism of the Claisen rearrangement.[1] Alternatives such as a fragmentation–recombination (diradical) mechanism would be expected to show little or no γ effect if fragmentation were rate determining and an essentially equilibrium α effect if recombination were rate determining. A mechanism involving rate-determining formation or decomposition of a diyl species would be consistent with the stereochemical results[3,4] but should show a nearly equilibrium γ effect and little or no α effect. Clearly, the ob-

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served isotope effects are consistent with neither the diradical nor the diyl picture.

It is desirable to relate the α and γ effects to the degree of bonding between C_α and O and between C_γ and C_{ortho} in the transition state. If a linear[11] relationship between isotope effect and bond order is assumed, then these results imply a bond order of ~0.23–0.43 for the C_α–O bond and bond order of 0.22–0.62 for the C_γ–C_{ortho} bond. Using this approach a transition state structure in which bond making and bond breaking have proceeded to the same extent cannot be excluded, but a "looser" transition state structure,[12,13] one in which bond breaking has proceeded to a greater extent than bond making, seems more consistent with this work, as well as with the earlier kinetic and stereochemical results.[3,4] In this picture, the lag of bond making relative to bond breaking is responsible for a major portion of the activation energy. An alternative, significantly nonlinear relationship between isotope effect and bond order suggested by Humski, Malojčić, Borčić, and Sunko,[14] would suggest a tighter transition state, in which both the C_α–O and C_γ–C_{ortho} bond orders are greater. Quantitative information with which to refine and evaluate these approaches is not yet available, but we prefer the linear assumption for its simplicity and its qualitative consistency with the stereochemical evidence.

Further, the direct evidence that we have obtained for a concerted transition state structure is entirely consistent with the interpretation of solvent and substituent effects advanced by Rhoads.[15] Such a concerted transition state structure would be expected to change as substituent electronic demands are varied, leading to insensitivity to polar substituent effects and curvature in attempted linear free-energy correlations.[16]

Finally, it is instructive to compare these results with those of Gajewski and Conrad for the rearrangement of allyl vinyl ether.[10] Their results support an early transition state for that exothermic reaction. Our results support a later transition state for a rate-determining step which is endothermic by some 3–5 kcal/mol.[17] This pattern is consistent with Hammond postulate[19] (parallel effect)[20] predictions. Comparison with other hetero-Cope processes is deferred to the full paper.

Acknowledgments. Grateful acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. It is a pleasure to acknowledge fruitful correspondence with Professor J. J. Gajewski and his gracious agreement on simultaneous publication.

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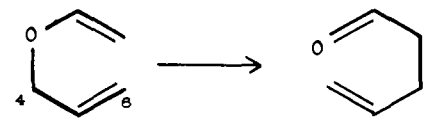
Aliphatic Claisen Rearrangement Transition State Structure from Secondary α-Deuterium Isotope Effects

Sir:

In a previous paper[1] it has been demonstrated that the secondary α-deuterium kinetic isotope effects on bond breaking and bond making in the all-carbon 3,3-sigmatropic (Cope) rearrangement vary relative to one another as a logical function of substitution.[2] Thus, the transition state structure for nearly degenerate 3,3 shifts resembles either two allyl radicals or cyclohexane-1,4-diyl depending on whether radical stabilizing substituents are on C_3 and C_4 or on C_2 and C_5, respectively.

The 3,3 rearrangement of allyl vinyl ether (AVE) presents a more difficult problem since the reaction is highly exothermic (17 kcal/mol),[3] a worthwhile characteristic of a useful reaction whose stereospecificity,[4] though not so high as the Cope rearrangement,[5] makes it a powerful synthetic tool.[6] The lower preference for chair over boat transition states in the aliphatic Claisen rearrangement relative to the Cope rearrangement has been attributed[4] to the exothermicity which requires that the transition state more resemble reactant than product (the parallel[2] or Hammond postulate effect[7]). Remaining questions about the rearrangement concern the effect of substituents at various positions which, in turn, require information about the transition state, specifically the extent of bond breaking and bond making. We here report that the KIE's at C_4 and C_6 in the 3,3 shift of 3-oxa-1,5-hexadiene (AVE) reveal that indeed the transition state "comes early" and that it involves much more bond breaking than making in contrast to the all-carbon 3,3 shift of relatively unperturbed 1,5-dienes.[1]



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