Computational Support for Tunneling in Thermal [1,7]-Hydrogen Shift Reactions

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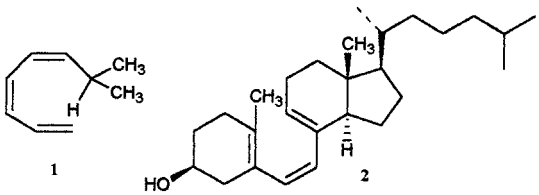
Density functional calculations have been performed for the [1,7]-hydrogen shift in two substituted 1,3,5-heptatrienes (**1** and **9**) for which kinetic data are available from the literature, including the observed kinetic isotope effects. For both cases the computed kinetic isotope effect was significantly smaller than that observed. These results provide further support for the presence of tunneling in thermal, antarafacial [1,7]-hydrogen shift reactions.

Introduction

Thermal [1,*n*]-hydrogen shifts in conjugated polyenes provide one of the best opportunities for observing tunneling in chemical reactions. For example the [1,7]-hydrogen shift in 1,3,5-heptatriene involves a degenerate reaction in which there is an antarafacial transfer of a hydrogen atom[1] of the methyl group to the methylene

group. The transition structure because of its antarafacial nature should have C_2 symmetry in which the migrating hydrogen is equidistant from the two terminal carbons (the one from which it is migrating and the one to which it is migrating). This unsubstituted system, however, is not easily studied kinetically because of its degenerate nature (product is the same as reactant). On the other hand, appropriate substitution of the 1,3,5-heptatriene system removes the degeneracy present in the parent system, allowing the kinetics to be studied more easily. Detailed kinetic studies have been reported for two such substituted heptatrienes, 7-methyl-1,3,5-octatriene (**1**)[2] and previtamin D_3 (**2**),[3] in which a [1,7]-hydrogen shift occurs. In both cases a large deuterium kinetic isotope



effect was observed and was taken as evidence for tunneling in the proton-shift reactions. Baldwin pointed out[2] that for **1**, two of the three criteria[4] for establishing the occurrence of tunneling were met: ($E_a^D - E_a^H$) considerably above 1.2 kcal/mol and A^D/A^H greater than unity. At the time it was not possible to meet the third criterion, an observed k_H/k_D greater than that calculated for the system in a semiclassical way,[4] because computational methods were not available that could even correctly predict the activation energies for this reaction. It is shown here that computational methods are now available to determine if this third criterion is met or not by Baldwin's results. Similar kinetic results have also been reported for previtamin D_3 (**2**).[3]

In 1985 we reported the results of SCF calculations in which a transition structure with C_2 symmetry was found for the [1,7]-antarafacial hydrogen shift in 1,3,5-heptatriene.[5] However, the computed activation energy (44 kcal/mol) was about twice the experimental value reported for a substituted 2,4,6-octatriene.[6] Before one can rely on a computed isotope effect, a method needs to be found that can at least accurately compute the activation energy for the deuterium system where tunneling is not expected. A recent report showed that density functional calculations with the B3LYP hybrid[7] and the 6-31G* basis set[8] reproduced[9,10] the experimental[11] activation energy for the [1,5]-hydrogen shift in 1,3-pentadiene. Encouraged by this, calculations[12] were undertaken of the kinetic isotope effects in the reactions of **1** and a substructure of **2**, and the results are presented here.

Results and Discussion

(3*Z*,5*Z*)-1,3,5-Heptatriene. As a further check on the reliability of the DFT method, the [1,7]-hydrogen shift in the parent triene, (3*Z*,5*Z*)-1,3,5-heptatriene, was studied. There are three conformers of this triene that must be considered in order to obtain the activation energy for the hydrogen shift reaction, *s-trans, s-trans* (**3**), *s-cis,*

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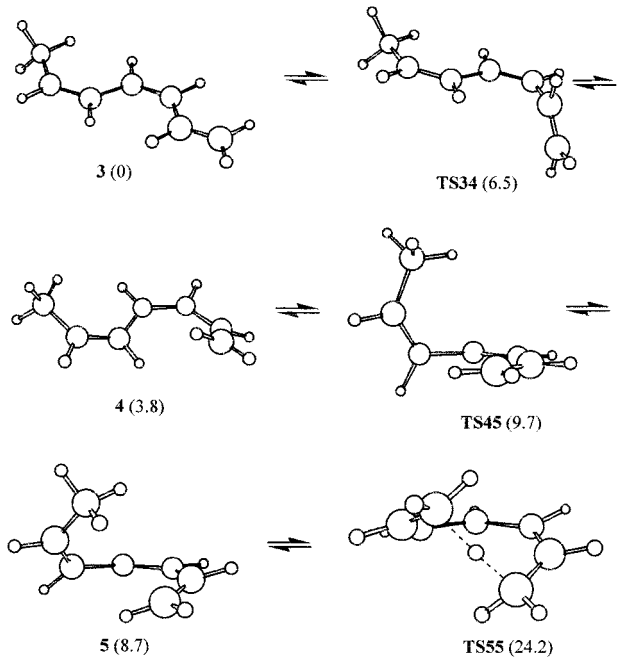


Figure 1. The reaction pathway for the [1,7]-hydrogen shift in (3*Z*,5*Z*)-1,3,5-heptatriene. Energies relative to **3** (corrected for zero point energies) are given in parentheses in kcal/mol.

s-trans (**4**), and *s-cis, s-cis* (**5**). Minima were located on

3 **4** **5**

the potential energy surface which correspond to these conformers as well as the two transition structures that link these minima, **TS34** that links **3** and **4** and **TS45** that links **4** and **5** (see Figure 1). In addition, the transition structure in which the actual hydrogen shift occurs, **TS55**, was found. The structure of **TS55** is clearly antarafacial and very similar to that reported earlier at the SCF level.[5] Here the carbon−hydrogen bond distance of the migrating hydrogen was computed to be 1.370 Å and the C−H−C angle 150.6°. The structures of these minima and transition structures are depicted in Figure 1 and also shown in the figure are their energies relative to that of **3** (taken as 0). It is seen from the figure that the energies of the three minima increase, not unexpectedly, from **3** to **4** to **5**. The overall activation energy for the hydrogen shift is the energy difference (24.2 kcal/mol) between the lowest energy minimum, **3**, and the transition structure, **TS55**. The activation energy is close to that previously measured (21.6 kcal/mol) for a substituted triene system.[6] Of course the measured value would include tunneling if it is present and would give rise to a lower activation energy than that calculated, since the calculation does not take into account tunneling. It was therefore encouraging that not only was the calculated activation energy close to that of the experimental value, but it was higher than that observed. Since no detailed kinetic data are available for this parent system, the kinetic isotope effect was not calculated.

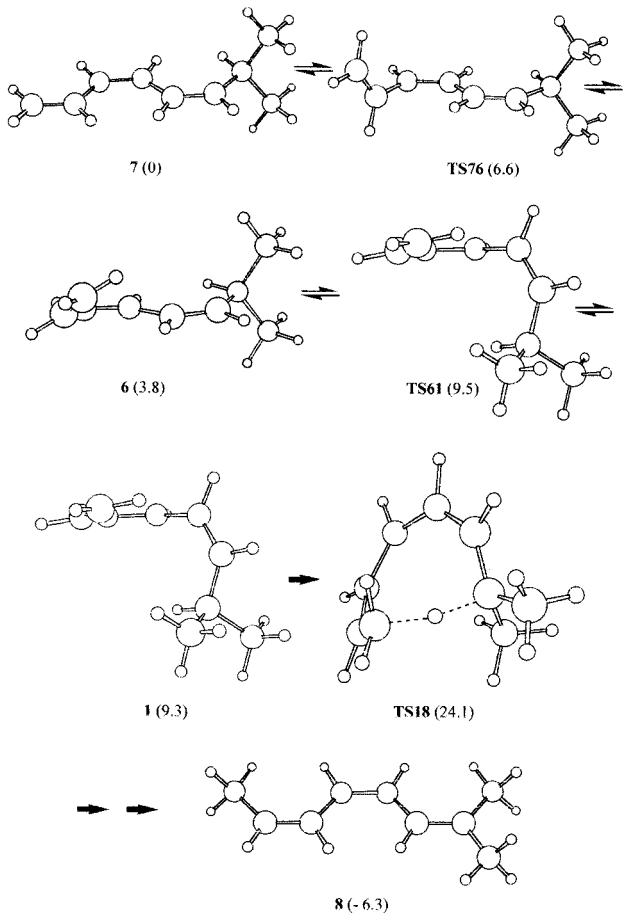
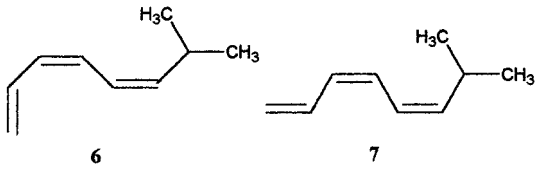


Figure 2. The reaction pathway for the conversion of **1** to **8**. Energies relative to **1** (corrected for zero point energies) are given in parentheses in kcal/mol.

(3*Z*,5*Z*)-7-Methyl-1,3,5-octatriene. There are several conformers that must be considered for (3*Z*,5*Z*)-7-methyl-1,3,5-octatriene, since the activation energy should be computed as the difference in energy between its lowest energy conformer and the transition structure for the [1,7]-hydrogen shift. Structure **1** corresponds to the *s-cis, s-cis* conformer and was found to be a minimum, although the conjugated π-system is far from planarity due to steric crowding that would exist in the planar structure (see Figure 2). In addition two other conformers were found to be minima, the *s-cis, s-trans* (**6**) and *s-trans, s-trans* (**7**). Conformer **7** was calculated to be the most stable of the three with **6** intermediate in stability between **1** and **7.** Of the three conformers (**1**, **6**, and **7**) only **7** has all of its sp^2 carbons atoms in a plane (see Figure 2). All three of these conformers were shown to be on the path connecting **7** with the rearranged product,

(12) The calculations were carried out with Gaussian 98W: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, Jr., J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; and Pople, J. A., Gaussian, Inc., Pittsburgh, PA, 1998 with the density functional method using Becke's three-parameter hybrid method (ref 7a) with the Lee−Yang−Parr correlation function (ref 7b) and the 6-31G* basis set (ref 8). Zero point energies and thermal corrections were all done with unscaled B3LYP/6-31G* frequencies obtained analytically with G98W.



6 7

(4*Z*,6*Z*)-2-methyl-2,4,6-octatriene (**8**). The reaction scheme shown in Figure 2 was established by finding not only the transition structure (**TS18**) in which the hydrogen transfer occurs, but also the transition structures **TS76** and **TS61** which link **7** to **6** and **6** to **1**, respectively. Energies in kcal/mol are shown in Figure 2 in parentheses relative to the lowest energy conformer (**7**) of the reactant. IRC calculations[13] beginning at the three transition structures further confirmed the scheme in Figure 2.

The computed structure of **TS18** clearly shows that the shift of the hydrogen is an antarafacial shift.[1] Since the symmetry in this transition structure is destroyed by the two extra methyl groups from that of the parent transition structure (C_2) in the reaction of (3*Z*,5*Z*)-1,3,5-heptatriene,[5] there is now a question of the position of the migrating hydrogen in the transition structure. It was computed to be very nearly equidistant from the two carbons between which it is migrating, with a distance of 1.375 Å from the original methylene carbon and 1.356 Å from the original methyl group carbon. This C−H−C angle is 158.3°. The energy of product **8** is calculated to lie 6.3 kcal/mol below that of **1** in agreement with Baldwin's finding that the conversion of **1** to **8** "followed clean first-order kinetics" and is not complicated by **1** being in equilibrium with **8** at the temperatures at which the rates were measured (60−115 °C).

The computed activation energy at 60 °C for the conversion of **1** to **8** is 23.2 kcal/mol for the nondeuterated case and 24.1 kcal/mol for the case in which the migrating hydrogen is replaced by deuterium. The corresponding experimental values obtained by Baldwin are 21.5 and 23.5 kcal/mol. While it appears at first sight that these observed activation energies are reproduced by calculation very nicely, it is the difference in these two values ($E_a^D - E_a^H$) that is of importance in considering whether tunneling plays a factor in this reaction. The computed difference is only 0.9 kcal/mol while the experimental difference is 2.1 kcal/mol, which is a disagreement by more than a factor of 2. More importantly the calculated value for the activation energy of the deuterated case (E_a^D) is in much better agreement with the experimental value (they differ by 0.6 kcal/mol) than is that for the calculated value of the nondeuterated case (E_a^H) and its experimental value (they differ by 1.7 kcal/mol). One expects that the tunneling effect will be much smaller in the deuterated case than in the nondeuterated case. The larger error in the nondeuterated case of the activation energy (computed vs observed) suggests that tunneling may very well be a factor in this reaction, since the rate of the nondeuterated case is predicted to be slower than that observed (our calculations of course do not take into account tunneling). These differences are reflected in the computed and observed kinetic isotope effects. At 60° we calculate k_H/k_D to be 3.89 which is roughly one-half of that observed by Baldwin (7.0). Hence

(13) Gonzalez C.; Schlegel H. B. *J. Chem. Phys.* **1989**, *90*, 2154. *J. Phys. Chem.* **1990**, *94*, 5523.

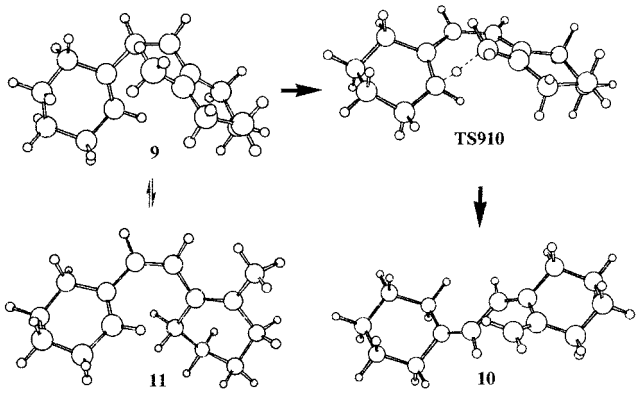
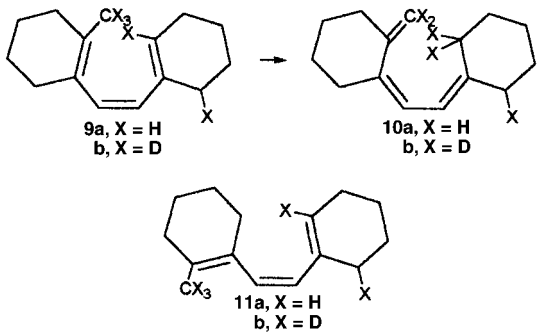


Figure 3. The reaction path for the [1,7]-hydrogen migration in the conversion of **11** to **10**.

the third "hallmark" mentioned by Baldwin is also satisfied by these calculations for the conversion of **1** to **8**.

Previtamin D_3 (2). Okamura measured the kinetic isotope effect and activation energies for the [1,7]-hydrogen shift in **2**, as well as the equilibrium constants between **2** and its rearranged product, of the nondeuterated system and deuterated system containing five deuteriums.[3] To make the calculations tractable at the DFT level compound **9** was chosen as a model for **2**, which would give **10** on rearrangement. Structure **9** corresponds



to the *s-cis, s-cis* conformer; a second conformer **11** (*s-cis, s-trans*) was found which is of lower energy than **9** (see Figure 3). The potential energy surface is quite flat here with the energy difference between **9** and **11** calculated to be only 0.5 kcal/mol. The transition structure **TS910** for the [1,7]-hydrogen shift was found and is shown in Figure 3. In the transition structure the migrating hydrogen is even more unsymmetrically displaced between the two carbons than in **TS18**, it being 1.406 Å from the original methyl carbon and 1.341 Å from the carbon to which it is migrating. The C−H−C angle (150.8°) is also smaller than in **TS18**.

The computed activation energy at 80 °C for the deuterated case **11b** to **10b**) is 21.4 kcal/mol and is in good agreement with the measured value of 21.9 kcal/mol for **2**, while agreement for the activation energy of the conversion of nondeuterated **11a** to **10a** (computed: 20.8, experimental: 19.6) is not as good. The computed difference in activation energies ($E_a^D - E_a^H$) is only 0.6 kcal/mol vs the experimental value of 2.3 kcal/mol. This is reflected in the large disagreement between the computed (2.4) and experimental (6.2) isotope effects (k_H/k_D). This disagreement supports the proposal that tunneling plays a role in the migration of the hydrogen from

11a to **10a.** Okamura also measured the equilibrium constants for **2** and its rearranged product and for **2** containing five deuteriums. Equilibrium constants computed at 60 °C (6.2 and 6.5, respectively) compare well with his experimental values for **2** (5.37 and 5.42). This suggests that the choice of **9** as a model for **2** is an appropriate one.

Conclusions

For the two cases studied here it was found that the computed activation energy for the [1,7]-shift of a deuterium is in much better agreement with the experimental value than is the case for the [1,7]-shift of a hydrogen. In both cases the activation energy for the hydrogen shift was computed to be larger than that observed which in turn leads to the computed kinetic isotope effects (k_H/k_D) to be significantly smaller than those observed for **1** and **2**. This is exactly the effect that Bell suggested should be found for systems in which tunneling plays a role.[4] Hence the DFT calculations on **1** and **9** reported here lend further support to the insight that tunneling in such hydrogen transfers plays a crucial role.

Supporting Information Available: Cartesian coordinates, total energies, frequencies, and thermochemical data for structures **1**, **3**−**11**, **TS34**, **TS45**, **TS55**, **TS76**, **TS61**, **TS18**, and **TS910**. This material is available free of charge via the Internet at http://pubs.acs.org.

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