Vibrationally Assisted Tunneling in a Hydrogen Atom Transfer Reaction

Brent A. Johnson, Yunfeng Hu, K. N. Houk,* and
Miguel A. Garcia-Garibay*

Department of Chemistry and Biochemistry
*University of California, Los Angeles, California 90095-1569*

Received March 9, 2001

Interest in tunneling reactions has increased recently thanks to refined theoretical models,[1,2] improved experimental techniques,[3] and the identification of tunneling reactions in several enzymatic processes.[4] In the past few years, we have analyzed the structural and electronic factors that affect the rate of hydrogen tunneling in *o*-methyl ketones (Scheme 1).[5,6] Reactions occur adiabatically in the triplet manifold (³**1**) by transfer of a hydrogen atom from the *o*-methyl group to the singly occupied n-orbital of the carbonyl oxygen to yield a triplet enol (³**E**).[7,8] Once the enol is in the ground state, the reaction is rapidly reversible. We have shown that rates of H-transfer become temperature independent below 30−50 K in *o*-methyltetralones and *o*-methylanthrones.[5] By using solvent effects to change the electronic configuration of the excited state, we have also shown that the reaction is most efficient for ketones with n,π* configurations.[5e] Finally, as expected for an adiabatic process, we obtained evidence that different triplet sublevels react with different tunneling rates.[5a]

In this communication, we describe a very unusual temperature dependence for the isotope effect in the reaction of 6,9-dimethylbenzosuberone (**1**) and d_8-6,9-dimethylbenzosuberone (d_8-**1**) (Scheme 1).[9] We discovered that the rates of H- and D-transfer are nearly identical ($k_H/k_D = 1.1$) between 60 and 4 K, under conditions where isotope effects of ca. 10^3 should be expected.[5,6a] To explain this, we propose a mechanism where the rate-limiting step is given by isotope-independent skeletal motions, i.e., an example of vibrationally assisted tunneling.[10]

Although the H-transfer reaction occurs in glasses and in crystals, we report here results in methylcyclohexane between

Scheme 1
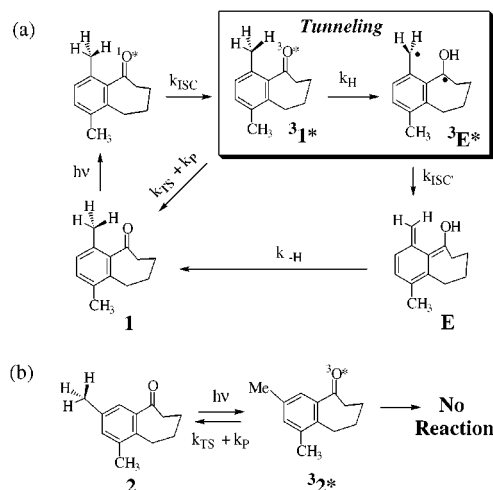
100 and 4 K. As in previous studies,[5] the rate of disappearance of the triplet ketone was determined by phosphorescence methods. We consider that the rates of triplet decay (k_{dec}) are given by the sum of thermal and radiative rates ($k_{TS} + k_P$, Scheme 1), plus the rate of the H-transfer reaction ($k_{H(D)}$, eq 1).

$$k_{dec} = k_{TS} + k_P + k_{H(D)} \qquad (1)$$

To obtain the value of k_H (k_D), we assume that ($k_{TS} + k_P$) is isotope independent and can be obtained from a model compound with a similar chromophore, for which no reaction is possible. In this case we selected 6,8-dimethylbenzosuberone (**2**) (Scheme 1b). The triplet decays from compounds **1**, d_8-**1**, and **2** were measured as a function of temperature, and the fitted data were used to calculate the rates of hydrogen or deuterium transfer according to eq 1.[11] An Arrhenius plot with H- and D-transfer rates obtained between 100 and 4K is shown in Figure 1. As expected, the rates of decay of **2** were constant over the entire temperature range and the value $k_{dec} = 32$ s^{-1} was assumed to represent $k_P + k_{TS}$ (marked with a line in Figure 1). The calculated reaction rates for **1** and d_8-**1** were constant between 4 and 50 K, with values of $k_H = 83$ s^{-1} and $k_D = 73$ s^{-1}, and a rapid increase was observed above 50−60 K. That reaction occurs at the lowest temperatures studied was shown by accumulation and detection of the product in ethanol glasses.[12,13]

The temperature dependence of the isotope effect calculated from the rate data is shown in Figure 2. The figure reveals an isotope effect k_H/k_D of only 1.13 between 4 and 50 K and a surprising increase of up to 5.1 at about 100 K, when the glassy matrix began to soften. The results in Figures 1 and 2 were unexpected. Kinetic isotope effects, which originate from differences in zero-point energies between the two isotopomers, are expected to increase exponentially with decreasing temperatures, which is the opposite of Figure 2. Tunneling isotope effects are

(1) (a) Bell, R. P. *The Tunnel Effect in Chemistry*; Chapman and Hall: New York, 1980; pp 106−140.

(2) (a) Lee, S.; Hynes, J. T. *J. Chim. Phys. Phys.-Chim. Biol.* **1996**, *1996*, 1783−1807. (b) Truhlar, D. G.; Liu, Y.-P.; Schenter, G. K.; Garret, B. C. *J. Phys. Chem.* **1994**, *98*, 8396−8405. (c) Liu, Y.-P.; Lu, D.; Gonzalez-Lafont, A.; Truhlar, D. G.; Garret, B. C. *J. Am. Chem. Soc.* **1993**, *115*, 7806−7817.

(3) (a) Gol'danskii, V. I.; Benderskii, V. A.; Trakhtenberg, L. I. *Adv. Chem. Phys.* **1993**, *75*, 349. (b) Douhal, A.; Lahmani, F.; Zewail, A. H. *Chem. Phys.* **1996**, *207*, 477−498.

(4) (a) Kohen, A.; Klinman, J. P. *Chem. Biol.* **1999**, *6*, R191−R198. (b) Kohen, A.; Klinman, J. P. *Acc. Chem. Res.* **1998**, *31*, 397−404. (c) Rucker, J.; Klinman, J. P. *J. Am. Chem. Soc.* **1999**, *121*, 1997−2006.

(5) (a) Johnson, B. A.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **1999**, *121*, 8114. (b) Garcia-Garibay, M. A.; Gamarnik, A.; Bise, R.; Jenks, W. S. *J. Am. Chem. Soc.* **1995**, *117*, 10264−10275. (c) Johnson, B.; Gamarnik, A.; Garcia-Garibay, M. A. *J. Phys. Chem.* **1996**, *100*, 4697−4700. (d) Gamarnik, A.; Johnson, B. A.; Garcia-Garibay, M. A. *J. Phys. Chem.,* **1998**, *102*, 5491−5498.
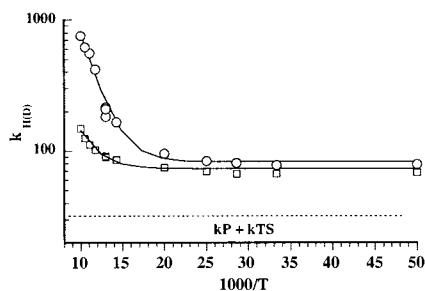
(6) For examples of H-atom tunneling of aromatic ketones in fluid solvents see: (a) Al-Soufi, W.; Eychmuller, A.; Grellmann, K. H. *J. Phys. Chem.* **1991**, *95*, 2022−2026. (b) Gritsan, N. P.; Khmelinski, I. V.; Usov, O. M. *J. Am. Chem. Soc.* **1991**, *113*, 9615−9620. (c) Smedarchina, Z.; Enchev, V.; Lavtchieva, L. *J. Phys. Chem.* **1994**, *98*, 4218−29.

(7) For an excellent review see: Wagner, P. J.; Park, B.-S. *Org. Photochem.* **1991**, *11*, 227−366.

(8) (a) Wagner, P. J.; Chen, C.-P. *J. Am. Chem. Soc.* **1976**, *98*, 239−241. (b)Haag, R.; Wirz, J.; Wagner, P. J. *Helv. Chim. Acta* **1977**, *60*, 2595−2607. (c) Scaiano, J. C. *Chem. Phys. Lett.* **1980**, *73*, 319−322. (d) Das, P. K.; Encinas, M. V.; Small, R. D., Jr.; Scaiano, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 6965−6970.

(9) Compounds **1** and d_8-**1** were prepared from *p*-xylene and *p*-xylene-d_{10}, respectively, by using reported procedures. Deuteration in d_8-**1** is localized on methyl and aromatic hydrogens.

(10) Vibrationally assisted tunneling has been analyzed in 1,4-sigmatropic shifts: (a) Chantranupong, L.; Wildman, T. A. *J. Am. Chem. Soc.* **1990**, *112*, 4151−4154. (b) Liu, Y.-P.; Lynch, G. C.; Truong, T. N.; Lu, D.; Truhlar, D. G.; Garret, B. C. *J. Am. Chem. Soc.* **1993**, *115*, 2408−2415.

(11) Decay rates were fitted to double exponential functions with pre-exponential parameters I_1 and I_2 and rate parameters k_1 and k_2. The fitted parameters were used to calculate average decay rates according to the following equation: $k_{ave} = (I_1/k_1 + I_2/k_2)/(I_1/k_1{}^2 + I_2/k_2{}^2)$. For a complete discussion of this procedure please see ref 5c, or, Johnson, B. A. Ph.D. Thesis, University of California, Los Angeles, 1999.

(12) The lifetimes of ground-state photoenols increase in polar solvents to the extent that they can be accumulated. See: Baron, U.; Bartlet, G.; Eychmuller, A.; Grellman, K.-H.; Schmitt, U.; Tauer, E.; Weller, H. *J. Photochem.* **1985**, *28*, 187−195.

(13) Although product formation confirms a tunneling reaction systematic errors may exist in Figure 1 to the extent that $k_P + k_{TS}$ may not be the same for test and model compounds. The larger decay rates of **1** and d_8-**1**, as compared to **2**, are consistent with a relatively efficient triplet state reaction.

Figure 1. Arrhenius plot of the calculated hydrogen (circles) and deuterium (squares) transfer rates of compounds **1** and d_8-**1** in a MCH glass between 100 and 20 K. The data were fitted using eq 2.
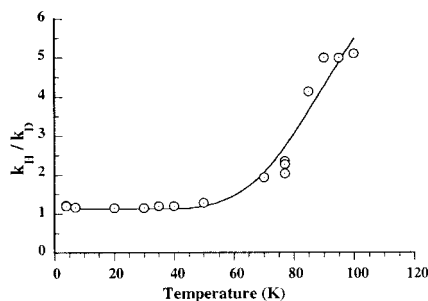

Figure 2. Isotope effects calculated from the hydrogen and deuterium transfer rates of **1** and d_8-**1** in MCH glass between 20 and 100 K.

expected to reach a constant value of ca. $k_H/k_D = 10^3$ when tunneling occurs from zero-point energy levels.[5,6]

The small difference in decay rates for **1** and d_8-**1** between 4 and 50 K indicates that H- and D-atom transfers are not rate-limiting in the decay of ^{3}**1***. The results in Figures 1 and 2 require H- and D-atom transfer to be preceded by an isotope and temperature-independent step. Given that reactions occur down to 4 K, we discard a preequilibrium process between structures with different reactivity. The results require a mechanism where tunneling is mediated by isotope-independent motions that occur from zero-point energy levels, which become non-rate-limiting after upper vibrational states are populated. The temperature dependence shown in Figures 1 and 2 can be fit by a model[10a] which assumes that reaction occurs by tunneling over the entire temperature range (eq 2). The observed rate is be given by a heavy-atom-limited zero-point-energy tunneling rate k_{ZPE}, which increases with contributions from a vibrationally assisted tunneling process, k_{VA}, and the temperature dependence of the rate constant is given by reaction promoting modes with energies $E_P = 250$ cal/mol, or 87 cm^{-1}.

$$k_{H(D)} = k_{ZPE} + k_{VA}\exp(-250/RT) \qquad (2)$$

While there are great uncertainties in the fitted values of k_{VA} for H and D, the value of E_P, which is associated with the energy of the promoting mode, is relatively well determined. To identify vibrations that may promote the tunneling process, we carried out a single-crystal X-ray diffraction analysis of compound **1**, and a vibrational analysis of stationary points on the triplet surfaces of **1** and d_8-**1** obtained with the UB3LYP/6-31G* method (Figure 2).[14] Ketone **1** crystallizes in the space group $P2_1/c$ with two molecules per asymmetric unit (molecules A and B). Molecules **1**A and **1**B crystallize in boat conformations with the planes of the carbonyl and phenyl groups making dihedral angles of −48.8 (**1**A) and 53.4° (**1**B). The two structures are very similar and only molecule A is shown in Figure 3. The closest distances between the tunneling hydrogen and the carbonyl oxygen are 2.63 and 2.69 Å, for **1**A and **1**B, respectively. These are smaller than
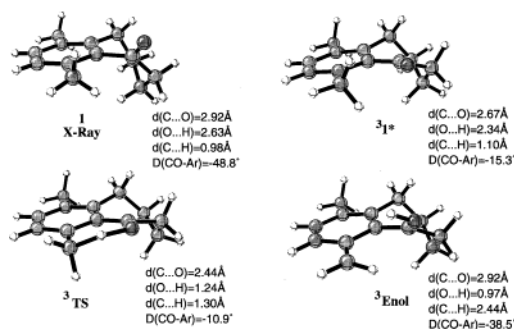
Figure 3. X-ray and calculated structures of 6,9-dimethylbenzosuberone (**1**) with a few structural parameters listed.

the sum of the van der Waals radii for hydrogen and oxygen (2.7 Å), which is commonly observed for reactions occurring in the solid state.[15] Both **1**A and **1**B minimized to the same B3LYP/6-31G* ground-state structure (not shown). The vertical triplet state calculated with the UB3LYP/6-31G* method is 8.0 kcal/mol above a relaxed structure which was assumed to be the starting point for the reaction. The structures of the triplet ketone (^{3}**1***), transition state (^{3}**TS**), and enol (^{3}**E**) shown in Figure 3 indicate that adiabatic H-transfer in the triplet surface is a least motion process with very small structural changes. The zero-point-energy-corrected barriers for the reactions ^{3}**1** and d_8-^{3}**1** predict a normal primary kinetic isotope effect with activation energies of 6.2 and 7.3 kcal/mol, respectively. The calculated heats of reactions are −4.3 and −4.0 kcal/mol for the protio and deutero compounds. In agreement with orbital symmetry considerations, the reaction coordinate is characterized by planarization of the carbonyl and phenyl groups to maximize orbital overlap between the transferring-ring hydrogen and the singly occupied carbonyl n-orbital.[5,7] The dihedral angle D(CO−Ar) changes from −58.8° in the ground state to −15.3°, −10.9°, and −38.5° as the structure evolves along the triplet surface from the excited-state ketone to transition state to triplet enol product. At the same time, the distance between carbon donor and oxygen acceptor changes from 2.67 to 2.44 to 2.92 Å, and the position of the hydrogen in the transition state is almost halfway between reactant and product. A close analysis of the low-frequency modes in the triplet ketone shows that hydrogen transfer from carbon to oxygen may be facilitated by modes involving oscillation of the methyl group, at 154 cm^{-1}, and coplanarization of the carbonyl and phenyl groups, at 65.8 cm^{-1}. These occur at 106.7 and 62.7 cm^{-1}, respectively, for the deuterated compound. The later frequency is in good agreement with the experimental value of ca. 87 cm^{-1}, suggesting that the skeletal mode may be the most important tunneling-promoting motion.

In conclusion, our results suggest that tunneling is the main reaction mechanism for **1** over the temperature range investigated. The small isotope effect below 60 K requires a mechanism where H-transfer is not the rate-limiting step. Based on a simple picture derived from the X-ray structure of **1** and triplet state surface stationary points obtained with the UB3LYP/6-31G* method, we propose that tunneling in **1** occurs with assistance of a reaction-promoting skeletal bending mode. Work in progress includes detailed kinetics measurements in crystals and direct dynamics calculations.

Supporting Information Available: Stationary points and energies for the reaction of **1** and d_8-**1**, normal modes postulated to assist the tunneling reaction, X-ray structures and tables for **1** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

(14) Electronic structure and vibrational calculations were carried out using the Gaussian 98 suite of programs.

(15) Scheffer, J. R. *Solid State Organic Chemistry*; Desiraju, G. R., Ed.; VCH: Amsterdam, 1987; pp 1−45.