JOC*Article*

Primary Semiclassical Kinetic Hydrogen Isotope Effects in Identity Carbon-to-Carbon Proton- and Hydride-Transfer Reactions, an ab Initio and DFT Computational Study

Scott Gronert* and James R. Keeffe*

Department of Chemistry and Biochemistry, San Francisco State University, 1600 Holloway Avenue, San Francisco, California 94132

sgronert@sfsu.edu; keeffe@sfsu.edu

Received March 22, 2006

$$\text{A—H} + \text{A}^- \xrightarrow[\text{transfer}]{\text{proton}} \text{A}^- + \text{A—H} \qquad \text{larger } k_H/k_D$$

$$\text{A—H} + \text{A}^+ \xrightarrow[\text{transfer}]{\text{hydride}} \text{A}^+ + \text{A—H} \qquad \text{smaller } k_H/k_D$$

Enthalpies of activation, transition state (ts) geometries, and primary semiclassical (without tunneling) kinetic isotope effects (KIEs) have been calculated for eleven bimolecular identity proton-transfer reactions, four intramolecular proton transfers, four nonidentity proton-transfer reactions, eleven identity hydride transfers, and two 1,2-intramolecular hydride shifts at the HF/6-311+G**, MP2/6-311+G**, and B3LYP/6-311++G** levels. We find the KIEs to be systematically smaller for hydride transfers than for proton transfers. This outcome is not the result of "bent" transition states, although extreme bending can lower the KIE. Rather, it is a consequence of generally greater total bonding in a hydride-transfer ts than in a proton-transfer ts, most prominently manifested as a reduced contribution from the zero-point vibrational energy difference between reactant and transition states (the ΔZPVE factor) for hydride transfers relative to proton transfers. This and other differences between proton and hydride transfers are rationalized by modeling the central ·C···H···C unit of a proton-transfer ts as a 4-electron, 3-center (4-e 3-c) system and the same unit of a hydride-transfer ts as a 2-e 3-c system. Inclusion of tunneling is most likely to magnify the observed differences between proton-transfer and hydride-transfer KIEs, leaving our qualitative conclusions unchanged.

Introduction

The use of the isotopes of hydrogen in mechanistic organic chemistry has long been of great utility.[1,2] The observation of primary kinetic isotope effects (KIEs), that is, isotopic rate ratios, k_H/k_D that are substantially greater than 1.0, for reactions in which isotopic substitution has been made at the transferred hydrogen, has enabled identification of the rate-determining step for multistep mechanisms in which one of the steps involves transfer of a hydrogen.

It was recognized in the early 1960s by Melander and by Westheimer that the magnitude of the "semiclassical" KIE, that part of the KIE not caused by differential tunneling of the isotopes, is influenced by the symmetry of the two partial bonds in the linear, three-center model for the hydrogen-transfer transition state (ts). When the force constants for the partial bonds between each of the two transfer termini and the hydrogen-in-flight are equal in the symmetrical stretching motion, the KIE will be at a maximum.[3,4] Otherwise a diminution in the isotopic rate ratio will be observed due to the presence of an isotopically sensitive symmetrical stretch in the ts, possibly accompanied by an increase in ts bending frequencies as well.[5] These ideas allowed a prediction that for proton transfer between bases of varying strength, a plot of k_H/k_D against ΔpK_a would go through a maximum at $\Delta pK_a \cong 0$, falling off on either side where the transfer termini are *not* equally basic. Qualitatively this prediction was confirmed by Bell and coworkers[6] and has been amply demonstrated by others as well,

---

[1] (a) Melander, L.; Saunders, W. H., Jr. *Reactions of Isotopic Molecules*; Wiley-Interscience: New York, 1980. (b) Saunders, W. H., Jr. In *Investigation of Rates and Mechanisms of Reactions*, 4th ed.; Bernasconi, C. F., Ed.; Wiley-Interscience: New York, 1986; Part 1, Chapter VIII.

[2] *Isotopes in Organic Chemistry*; Buncel, E., Lee, C. C., Eds.; Elsevier: New York, 1975−1987; 7 volumes.

[3] Melander, L. *Isotope Effects on Reaction Rates*; Ronald: New York, 1960; pp 24−32.

[4] Westheimer, F. H. *Chem. Rev.* **1961**, *61*, 265.

[5] Saunders, W. H., Jr. *Chem. Ind.* **1966**, 663.

[6] Bell, R. P. *The Proton in Chemistry*, 2nd ed.; Cornell University Press: Ithaca, NY, 1973; pp 262−265 and references therein.

10.1021/jo0606296 CCC: $33.50

although the observed maxima are quite broad for proton transfers to and from carbon. Similarly, Pryor and Kneipp[7] have shown isotope effect maxima for hydrogen-atom transfers occurring for reactions that are nearly thermoneutral. It must be acknowledged, however, that this appealingly simple view of isotope effect maxima has had its critics.[8a]

Other factors also affect the size of the primary KIE. Among them is the existence of tunneling, which will favor transfer of protium over deuterium, increasing k_H/k_D. Tunneling is expected to be greater for reactions in which curvature of the potential energy surface in the vicinity of the ts is large, that is, when the imaginary reaction coordinate frequency, $i\nu^{\ddagger}$, is large. In general it is thought that tunneling will amplify the isotope effect maximum for ergoneutral reactions with symmetrical transition states.[8b] Put another way, a smaller tunneling correction will lower KIE compared with processes in which tunneling makes a larger contribution. Because tunneling is a quantum mechanical fact, the issue is not whether it occurs, but to what extent. In at least one study of proton-transfer reactions, evidence for significant tunneling persists over a wide range of ΔpK_a.[9]

A third factor, heavy atom motion as part of the reaction coordinate, is argued to weaken the semiclassical isotope effect and perhaps the tunneling contribution as well.[10] Experimental evidence for this expectation has been given by Kaldor and Saunders.[11] It must be noted that, for some proton-transfer reactions in which heavy atom motion might be anticipated, KIE values remain large, even when $\Delta pK_a \neq 0$, possibly because of tunneling.[6,9]

A final factor that may affect the size of the primary KIE is transition state geometry, specifically, the angle formed by the two transfer termini and the transferred hydrogen. This angle, θ_{ts}, is at or very close to 180° for bimolecular proton-transfer reactions.[12] However, for bimolecular hydride transfers the angle can be 180° or somewhat smaller,[13] and for intramolecular hydrogen transfers of any sort it may be smaller yet. In 1970 More O'Ferrall,[14] following a suggestion by Lewis,[15] carried out a set of KIE calculations in which force constants were assigned according to specified geometries and bond orders, and the ts angle, θ_{ts}, was systematically varied. These calculations yielded isotope effects as determined by changes in zero-point vibrational energies (ZPVE) between reactant and transition states.[16] For transition states that are symmetrical in the Melander-Westheimer sense, the resulting KIE values were significantly diminished at ts angles of 150° and below, falling from 7.9 at $\theta_{ts} = 180°$ to 2.3 at 90° and 1.4 at 60°. These effects were shown to be only mildly sensitive to the symmetry of the bent transition state. The principal source of the smaller KIEs was traced to a "composite stretching and bending motion [in the transition state] of such high frequency as to offset the combined zero-point energy changes in the stretching vibration and one bending vibration in the reactants".[14] Another set of calculations was reported in 1973 by Saunders, who investigated linear and bent transition states in 1,2-elimination reactions.[17] He found that when the angle between carbon-2, its departing proton, and the base is bent, as in some syn eliminations, k_H/k_D is reduced. Experimental data consistent with these calculated results include small KIE values for 1,2-hydride shifts,[18] for presumed E2C elimination reactions,[19,20] and for some bimolecular hydride-transfer reactions.[21] Some, but not all, intramolecular (Ei) pyrolytic elimination reactions also exhibit relatively small KIE values as does the Cope elimination.[22] A complication regarding the interpretation of these results is that the extent of ts asymmetry is not clear.

In this study we report ab initio (HF/6-311+G** and MP2/6-311+G**) and DFT (B3LYP/6-311++G**) calculations of primary kinetic hydrogen isotope effects on identity inter- and intramolecular proton and hydride-transfer reactions between hydrogen donors and their conjugate hydrogen acceptors, that is, identity reactions with no thermodynamic bias. For comparison, four examples of nonidentity proton-transfer reactions are included. An overview of all systems examined in this work is found in Scheme 1. The principal variables investigated are (1) whether a proton or a hydride is being transferred, (2) the angle in the transition state formed by the donor and acceptor termini and the transferred hydrogen, and (3) the presence of isotopically sensitive motions, other than the symmetrical stretch, in the transition state.

Methods

All structures were built and optimized at the HF/3-21G or HF/6-31G* level using the MacSpartan Plus or Spartan 02 software package,[23] before carrying out geometry optimizations at HF/6-311+G**, MP2/6-311+G** (FC), and B3LYP/6-311++G** levels of theory using the Gaussian 03 suite of programs.[24] Conformational preferences were established using MacSpartan and usually at the higher HF and MP2 levels as well. Frequencies, partition functions, and zero-point vibrational energies (ZPVEs) were calculated at the same levels as used

---

(7) Pryor, W. A.; Kneipp, K. G. *J. Am. Chem. Soc.* **1971**, *93*, 5584.

(8) (a) A discussion with pertinent references is given by More O'Ferrall, R. In *Proton-Transfer Reactions*; Caldin, E. F., Gold, V., Eds.; Chapman and Hall: London, 1975; Chapter 8, pp 233−256. Motell, Boone, and Fink have shown that even when the partial bond force constants are far from equal, a large interaction force constant for the motion involving all three bodies in the three-center ts can preserve large KIEs; see: Motell, E. L.; Fink, W. H. *J. Am. Chem. Soc.* **1976**, *98*, 7152. Motell, E. L.; Boone, A. W.; Fink, W. H. *Tetrahedron* **1978**, *34*, 1619. (b) More O'Ferrall, R. In *Proton-Transfer Reactions*; Caldin, E. F., Gold, V., Eds.; Chapman and Hall: London, 1975; Chapter 8, pp 236−241.

(9) Keeffe, J. R.; Munderloh, N. H. *J. Chem. Soc. Chem. Comm.* **1974**, 17.

(10) (a) Bell, R. P. *Discuss. Faraday Soc.* **1965**, *39*, 16. (b) Katz, A. M.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1969**, *91*, 4469. (c) Reference 8, pp 241−242. (d) Reference 1b, pp 594−595.

(11) Kaldor, S. B.; Saunders, W. H., Jr. *J. Chem Phys.* **1978**, *68*, 1978.

(12) Keeffe, J. R.; Gronert, S.; Colvin, M. E.; Tran, N. L. *J. Am. Chem. Soc.* **2003**, *125*, 11730.

(13) Gronert, S.; Keeffe, J. R *J. Am. Chem. Soc.* **2005**, *127*, 2324.

(14) More O'Ferrall, R. *J. Chem. Soc. B* **1970**, 785.

(15) (a) Lewis, E. S.; Symons, M. C. R. *Q. Rev. Chem. Soc.* **1958**, *12*, 230. (b) Hawthorne, M. F.; Lewis, E. S. *J. Am. Chem. Soc.* **1958**, *80*, 4286.

(16) Bell's tunneling correction was also applied; see: Bell, R. P. *Trans. Farad. Soc.* **1959**, *55*, 1. See also ref 8 and ref 6, pp 270−289. For an early and thorough discussion of a KIE calculation using the force-field method see: Wiberg, K. B. *Physical Organic Chemistry*; John Wiley and Sons: New York, 1963; pp 351−359. Also: Wiberg, K. B.; Motell, E. L. *Tetrahedron* **1963**, *19*, 2009.

(17) Saunders, W. H., Jr. *J. Chem. Soc., Chem. Comm.* **1973**, 850.

(18) Collins, C. J.; Rainey, W. T.; Smith, W. B.; Kaye, I. A. *J. Am. Chem. Soc.* **1959**, *81*, 460.

(19) (a) Kevill, D. N.; Coppens, G. A.; Cromwell, N. H. *J. Am. Chem. Soc.* **1964**, *86*, 1553. (b) Kevill, D. N.; Weiler, E. D.; Cromwell, N. H. *J. Am. Chem. Soc.* **1966**, *88*, 4489.

(20) Biale, G.; Parker, A. J.; Stevens, I. D. R.; Takahashi, J.; Winstein, S. *J. Am. Chem. Soc.* **1972**, *94*, 2235.

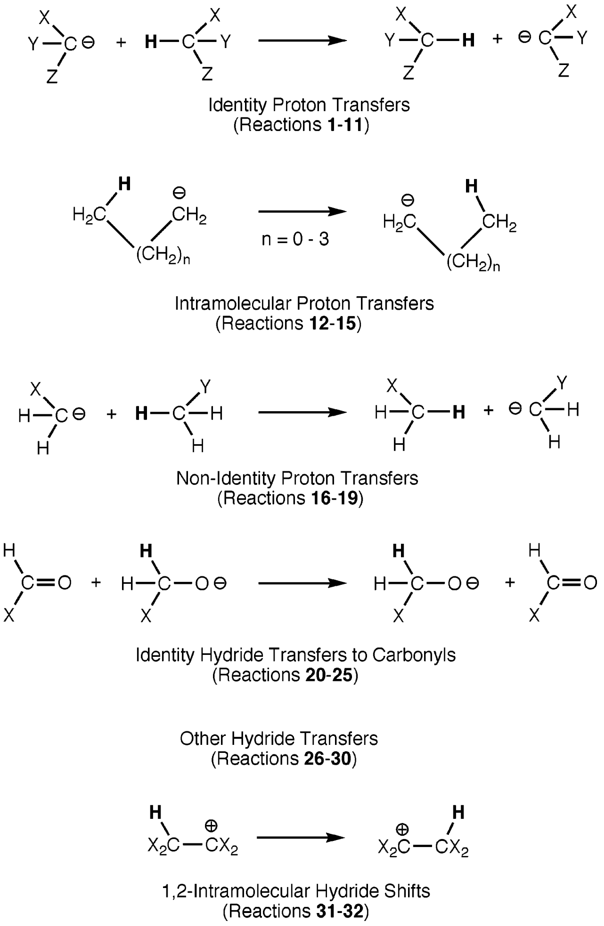
(21) Lewis, E. S.; Robinson, J. K. *J. Am. Chem. Soc.* **1968**, *90*, 4337.

(22) Chiao, W.-B.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1978**, *100*, 2802.

(23) Wavefunction, Inc., 18401 Von Karman Avenue, Suite 370, Irvine, CA 92612.

(24) Frisch, M. J., et al. *Gaussian 03*, Revision B04; Gaussian, Inc.: Pittsburgh, PA, 2003.

SCHEME 1. Overview of Systems



for the optimizations except for the bimolecular reactions involving tetrafluoroethylene (reactions 4 and 30) for which MP2 frequencies were not obtained, and the identity hydride transfer to pyridinium ion, reaction 27, which was calculated only at the B3LYP level. For purposes of calculating ΔH_{RXN} and $\Delta H^{\ddagger}$ values, the ZPVEs were scaled by 0.9135 (HF), 0.9748 (MP2), and 0.9806 (B3LYP) as recommended by Scott and Radom.[25] In previous work we have shown that there is no significant difference in MP2 ΔH_{RXN} and $\Delta H^{\ddagger}$ values whether using scaled HF or scaled MP2 ZPVE corrections.[12] We have also shown that calculated MP2/6-311+G** and B3LYP/6-311++G** ΔH_{ACID} values[12] and MP2/6-311+G** hydride ion affinities[13] provide excellent correlations with experimental results.

Kinetic hydrogen isotope effects on proton and hydride-transfer reactions were obtained using calculated ZPVE and partition function values according to the method used by Glad and Jensen[26] and by Streitwieser and co-workers, eq 1.[27] In this equation the partition function ratios for translation, rotation, and excited vibrational states are expressed as Q^{R} and $Q^{\mathrm{R}*}$ for the isotopic reactants and as Q^{TS} and $Q^{\mathrm{TS}*}$ for the isotopic transition states. The exponential factor gives the contribution to the KIE from the zero-point energy changes between isotopic reactants and transition states.[28] For primary KIEs this factor will normally make the larger contribution.

$$\mathrm{KIE} = \left(\frac{Q^{\mathrm{TS}}}{Q^{\mathrm{TS}*}}\right)\left(\frac{Q^{\mathrm{R}*}}{Q^{\mathrm{R}}}\right) \mathrm{e}^{-(\Delta\Delta \mathrm{ZPVE}/RT)} \tag{1}$$

Several approximations are inherent in the method used. Vibrational frequencies are modeled as harmonic in nature, and no correction for tunneling is made. Thus, the KIEs reported here are "semiclassical" isotope effects. More elaborate and accurate variational transition state theory (VTST) methods would require consideration not only of tunneling and anharmonicity but of barrier recrossing and nonequilibrium effects and the possibility that protium and deuterium transition states have different geometries and force constants.[29,30] Calculated primary KIEs are likely to be increased somewhat were these considerations taken into account.[31]

Solution-phase KIE values for hydride transfer between NAD$^+$ analogues have been in the literature for some time.[32] These experimental values are larger than those reported here by about 2-fold. Kreevoy and co-workers have shown by the application of variational transition state theory that tunneling can account for the differences between the semiclassical and full KIEs.[32c]

Results and Discussion

Energetics.[33] Table 1 lists calculated enthalpies of activation for reactions of the light isotopomers in this study. These $\Delta H^{\ddagger}$ values represent the enthalpy differences between separated reactants and the transition states, intervening ion−molecule complexes being ignored for this purpose. Transition states having a single imaginary frequency were found for all of the reactions studied except for several of the hydride-transfer reactions for which the ts optimization produced stable addition complexes[13] or gave a ts at one or two computational levels but a complex at the other(s). These cases are identified in the footnotes to the tables. It is worth restating that the complexes formed by carbenium ions and hydride donors belong to a class of electron-deficient (hypovalent) species that, upon optimization of total bonding, often assume geometries that are decidedly nonclassical by Lewis structure standards.

Typically the $\Delta H^{\ddagger}$ values calculated at the HF level are significantly higher than those for the MP2 and B3LYP levels, with the latter two methods giving similar results. It is also noteworthy that the calculated ts imaginary frequencies are uniformly larger at the HF level, suggesting that the MP2 and

---

[25] Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 16502.

[26] Glad, S. S.; Jensen, F. *J. Phys. Chem.* **1996**, *100*, 227.

[27] Hasanayn, F.; Streitwieser, A.; Al-Rifai, R. *J. Am. Chem. Soc.* **2005**, *127*, 2249.

[28] Scaled frequencies and zero-point vibrational energies[25] were not used in the KIE calculations. We estimate that the effects of scaling would be small on the partition function contributions to the KIE values. The use of scaled ZPVE corrections lowers the calculated KIE values slightly as the recommended scaling factors are less than one. The effect is greatest for the HF/6-311+G** KIEs since that scaling factor is the smallest of the three.

[29] Truhlar, D. G.; Lu, D. H.; Tucker, S. C.; Zhao, X. G.; Gonzalez-Lafont, A.; Truong, T. N.; Maurice, D.; Liu, Y. P.; Lynch, G. C. *ACS Symp. Ser.* **1992**, *502*, 16.

[30] Alhambra, C.; Gao. J.; Corchado, J. C.; Villa, J.; Truhlar, D. G. *J. Am. Chem. Soc.* **1999**, *121*, 2253.

[31] But see Storer, J. W.; Houk, K. N. *J. Am. Chem. Soc.* **1993**, *115*, 10426.

[32] (a) Powell, M. F.; Bruice, T. C. *J. Am. Chem. Soc.* **1982**, *104*, 5834. (b) Ostovic, D.; Roberts, R. M. G.; Kreevoy, M. M. *J. Am. Chem. Soc.* **1983**, *105*, 7629. (c) Kim, Y.; Truhlar, d. G.; Kreevoy, M. M. *J. Am. Chem. Soc.* **1991**, *113*, 7837. (d) Kim, Y.; Kreevoy, M. M. *J. Am. Chem. Soc.* **1992**, *114*, 7116.

TABLE 1. Calculated Enthalpies of Activation (kcal/mol) for Proton- and Hydride-Transfer Reactions in This Study

reaction[a]	HF/6-311+G** $\Delta H^\ddagger$	MP2/6-311+G** $\Delta H^\ddagger$	B3LYP/6-311++G** $\Delta H^\ddagger$
Identity Proton Transfers			
1. $CH_3\mathbf{H} + CH_3^-$	18.2	6.8	5.9
2. $CH_3CH_2\mathbf{H} + CH_3CH_2^-$	16.8	4.0	4.7
3. $CH_3CH_2CH_2\mathbf{H} + CH_3CH_2CH_2^-$	17.0	4.3	5.3
4. $\mathbf{H}CF_2CF_2^+ + CF_2{=}CF_2$	34.5	7.9[b]	3.7
5. $CH_3O\mathbf{H} + CH_3O^-$	−21.5	−29.6	−27.4
5cx. $CH_3O\mathbf{H} + CH_3O^-$ complex formation[c]	−21.4	−28.3	−26.2
6. $\mathbf{H}CF_3 + CF_3^-$	−0.8	−8.9	−10.9
7. $\mathbf{H}CCl_3 + CCl_3^-$	−2.7	−20.8	−11.0
8. $\mathbf{H}CH_2CHO + {}^-CH_2CHO$	14.4	−1.1	−2.5
9. $\mathbf{H}CH_2CN + {}^-CH_2CN$	2.7	−9.6	−9.2
10. $\mathbf{H}CH_2NO_2 + {}^-CH_2NO_2$	7.0	−7.9	−8.7
11. $\mathbf{H}C{\equiv}CCH_3 + {}^-C{\equiv}CCH_3$	3.5	−4.9[d]	−5.0
Intramolecular Proton Transfers			
12. $\mathbf{H}CH_2CH_2^-$	56.5	46.2	45.7
13. $\mathbf{H}CH_2CH_2CH_2^-$	43.7	31.5	33.2
14. $\mathbf{H}CH_2CH_2CH_2CH_2^-$	26.3	14.1	15.2
15. $\mathbf{H}CH_2CH_2CH_2CH_2CH_2^-$ 24.2	12.6	13.9	
Nonidentity Proton Transfers[e]			
16. $\mathbf{H}CH_2CHO + {}^-CH_2CN$	6.5	−8.3	−8.8
17. $\mathbf{H}CH_2CN + {}^-CH_2CHO$	11.1	−0.3	−2.1
18. $\mathbf{H}CH_2NO_2 + {}^-CH_2CN$	−4.6	−16.2	−18.0
19. $\mathbf{H}CH_2CN + {}^-CH_2NO_2$	14.2	−0.7	−0.4
Identity Hydride Transfers to Carbonyls			
20. $\mathbf{H}CO_2^- + CO_2$	23.4	6.0	1.6
21. $\mathbf{H}COS^- + COS$ anti ts	29.1	6.6[f]	6.1
22. $\mathbf{H}COS^- + COS$ syn ts	28.5	6.6[f]	6.0
23. $\mathbf{H}CH_2O^- + H_2C{=}O$	10.6	−6.6	−11.7
24. $\mathbf{H}CHONH_2^- + HCONH_2$, (R,R) ts	19.4	0.2	1.3
25. $\mathbf{H}CHONH_2^- + HCONH_2$, (R,S) ts	21.3	3.4	3.3
Other Identity Hydride Transfers			
26. $\mathbf{H}CH_3 + CH_3^+$	−17.1[g]	−35.8[g]	−37.1[g]
27. 1,**4**-dihydropyridine[h]+ pyridinium$^+$	NA	NA	1.4
28. $\mathbf{H}CF_3 + CF_3^+$	34.1	17.1	11.6
29. $\mathbf{H}CCl_3 + CCl_3^+$	34.1	3.2[f]	11.2
30. $\mathbf{H}CF_2CF_2^- + CF_2{=}CF_2$	53.4	18.0[b]	15.9
1,2-Intramolecular Hydride Shifts			
31. $\mathbf{H}CF_2CF_2^+$ intramolecular	31.2	24.9	21.6
32. $\mathbf{H}C(CH_3)_2C(CH_3)_2^+$ intramolecular	7.9	3.7[i]	5.2

[a] The bolded hydrogen is the transferred hydrogen. [b] MP2 frequencies for the proton-transfer transition state in the tetrafluoroethyl cation + tetrafluoroethylene reaction were not obtained. The quoted activation enthalpy uses HF/6-311+G** ZPVE values. The same is true for the hydride transfer between tetrafluoroethyl anion and tetrafluoroethylene. The use of HF ZPVE values in place of MP2 values has been found to cause insignificant differences (-0.1 ± 0.5 kcal/mol) in 85 ΔH calculations [this work and see also Keeffe, J. R.; Gronert, S.; Colvin, M. E.; Tran, N. L. *J. Am. Chem. Soc.* **2003**, *125*, 11730−11745]. [c] Experimental values for ion−molecule complex formation between methanol and methoxide are $\Delta H_{CX} = -28.8 \pm 0.1$ kcal/mol [Barlow, S. E.; Dang, T. T.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1990**, *112*, 6832] and $\Delta H_{CX} = -29.3$ [Dodds, J. A.; Baer, S.; Moylan, C. R.; Brauman, J. I. *J. Am. Chem. Soc.* **1991**, *113*, 5942]. [d] Using HF frequencies the $\Delta H^\ddagger$ value is −4.1 kcal/mol. [e] ΔH_{RXN} for the gas-phase reaction of acetonitrile anion with acetaldehyde is −4.6 (HF), −8.0 (MP2), and −6.6 kcal/mol (B3LYP). The experimental value is approximately −7.5 kcal/mol. ΔH_{RXN} for the gas-phase reaction of acetonitrile anion with nitromethane is −18.7 (HF), −14.3 (MP2), and −17.7 kcal/mol (B3LYP). The experimental value is approximately −17 kcal.mol [Bartmess, J. E. In *NIST Standard Reference Database Number 69*; Mallard, W. G., Linstrom, P. J., Eds.; National Institute of Standards and Technology: Gaithersburg, MD, 2005; (http://webbook.nist.gov)]. [f] The reaction of thioformate with carbonyl sulfide produces an addition complex with no imaginary frequency when calculated at the MP2/6-311+G** level The same is true for the hydride transfer between chloroform and trichloromethyl cation. [g] The reaction of methane with methyl cation produces an addition complex, not a transition state [Gronert, S.; Keeffe, J. R. *J. Am. Chem. Soc.* **2005**, *127*, 2324−2333]. [h] The reaction is hydride transfer from C4 of the donor to C4 of the acceptor. [i] The 1,2-hydride shift in the tetramethylethyl cation produces, at the MP2 level, a symmetrically hydrogen-bridged cation with no imaginary frequency. This cation is an isomer of the optimized cation, with an enthalpy 3.7 kcal/mol higher.

B3LYP methods produce somewhat flatter potential energy surfaces along the reaction coordinate than does the HF method.[33]

A set of four intramolecular 1,*n* proton transfers, reactions 12−15, where $n = 2-5$, was examined in order to vary the transfer angle in the transition states. The enthalpies of activation (MP2) for these reactions are relatively large at 46.2, 31.5, 14.1, and 12.6 kcal/mol for the three-, four-, five-, and six-membered cyclic transfers, respectively. By comparison, bimolecular identity proton transfers between alkyl anions have calculated activation barriers of 4−7 kcal/mol. The larger values in the intramolecular cases can be ascribed to varying degrees of strain associated with the cyclic transition state arrays. Figure 1 shows the transition states, calculated at MP2/6-311+G**, for these reactions.

In the case of the 1,2-proton shift in the ethyl anion, an additional energetic difficulty arises because the concerted transfer is forbidden by conservation of orbital symmetry considerations. The transition state for this shift is unique in two other ways as well: (1) It has partial C···H bond lengths that are short for a proton transfer at 1.295 Å. Those in the

---

(33) See paragraph concerning Supporting Information at the end of this paper. Electronic energies, zero-point vibrational energies, ts imaginary frequency values, and Cartesian coordinates are reported therein.

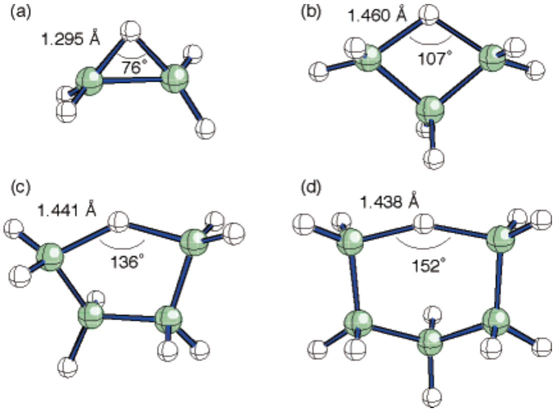


FIGURE 1. Structures of internal proton-transfer transition states (MP2/6-311+G**): (a) ethyl anion, (b) 1-propyl anion, (c) 1-butyl anion, and (d) 1-pentyl anion.

bimolecular methyl-to-methyl ts are 1.437 Å, and those for the other intramolecular proton transfers cluster around 1.45 Å, essentially the same as for bimolecular proton transfers. (2) NPA charge calculations[34] on the MP2 ts structures show that the transferred proton in the intramolecular ethyl anion ts is unusually positive at 0.33. This figure may be compared with 0.27 for the methyl-to-methyl ts, 0.24−0.28 for the other intramolecular proton transfers, and an average of 0.28 for previously studied intermolecular carbon-to-carbon proton transfers.[12] The picture that emerges for the intramolecular 1,2-shift ts is that it resembles somewhat a proton poised above and strongly attracted to a $(CH_2-CH_2)^{2-}$ dianion. Moreover, the dianion moiety is twisted by 45° about the C−C bond, presumably to ameliorate anion−anion repulsions.

Results for reaction 32, the degenerate 1,2-hydride shift in the 2,3-dimethyl-2-butyl cation, can be compared with solution-phase (superacid) data. All three computational methods produce a classical carbocation reactant with methyl (as opposed to hydrogen) hyperconjugation. Calculations at the HF and B3LYP levels lead to symmetrical transition states, whereas at the MP2 level a symmetrical structure, almost identical with those at the other levels but with no imaginary frequency, is obtained. This structure is 3.7 kcal/mol higher in enthalpy than the starting carbocation. Experimentally the rearrangement has $\Delta G^{\ddagger} = 3.0 \pm 0.1$ kcal/mol at −138 °C in SO_2ClF/SO_2F_2.[35] Presuming a small entropic disadvantage for the transition state leaves 3.0 kcal/mol as an upper limit for $\Delta H^{\ddagger}$, in reasonable agreement with our lowest computed value.

In our previous work on hydride transfers we found an excellent correlation between experimental hydride ion affinities (HIA) and computed enthalpies of hydride addition (ΔH_{ADD}) covering a wide range (275 kcal/mol) of reactivity, eq 2.[13] Using this correlation we give here estimates for the HIA values (kcal/mol) of five undocumented hydride acceptors: formamide (30.5), carbonyl sulfide (58.7), tetrafluoroethylene (74.6), trichloromethyl cation (258.2), and trifluoromethyl cation (294.5).

$$\mathrm{HIA} = (\Delta H_{\mathrm{ADD}} - 317.6)/1.02; \quad r^2 = 0.999; \quad n = 15 \qquad (2)$$

Transition State Geometries. Transition state partial C−H bond lengths, C···H···C angles (θ_{ts}), and point group indicators are given in Table 2. As noted earlier[13] calculated partial C−H lengths are smaller in hydride-transfer transition states than in proton-transfer transition states by an average of 0.10 Å (MP2/6-311+G**). Additionally, whereas the ts transfer angles for proton transfers are all very close to 180°, those for hydride transfers are more variable, some at or close to 180°, but others significantly bent. Both types of difference were discussed earlier as consequences of a model in which the proton-transfer ts resembles a four-electron, three-center (4-e 3-c) system while the hydride-transfer ts has a two-electron, three-center (2-e 3-c) system, both electrons occupying a bonding MO. Its geometry therefore adjusts to optimize orbital overlap and increase total bonding.[13]

In almost all identity reactions studied by us, the partial C···H distances in the ts are equal, as anticipated. For two hydride transfers, reactions 23 (HF only) and 25 (all three methods), unequal distances were calculated. This situation indicates that the reactant ion−molecule complex and the product ion−molecule complex are diastereomeric rather than identical or enantiomeric and, hence, that the transfer is not exactly an identity reaction.[12] Additionally, we call attention to the fact that in the transition states of some of the hydride-transfer reactions studied previously,[13] two stereocenters are generated. This opens the possibility of distinct (*R*,*R*) and (*R*,*S*) transition states for the transfer event. In this study only the hydride transfers between formamide and its hydride adduct (reactions 24 and 25) fit this description. Results for both paths are reported.

We have also calculated the KIE values for four nonidentity proton-transfer reactions (reactions 16−19). These include the reaction between acetonitrile anion and acetaldehyde (and its reverse) and that between acetonitrile anion and nitromethane (and its reverse). The former has $\Delta H_{RXN} = -8.0$ kcal/mol, and the latter $\Delta H_{RXN} = -14.3$ kcal/mol, both calculated at the MP2 level. The transition states are unsymmetrical in the Hammond sense,[36] that is, they resemble the reactants more than the products, with respect to both partial C···H bond lengths and the amount of negative charge[34] in each moiety. Nevertheless, the KIE values associated with these thermodynamically unsymmetrical reactions are not reduced compared with the thermoneutral reactions; see Table 3. Perhaps this is not too surprising a result given that the experimental solution-phase proton-transfer reaction sets that give rise to variable isotope effects in fact show very broad or sometimes no maxima, with large KIEs persisting over a range of $\Delta pK_a \cong 12-13$ units (17 kcal/mol) or so.[6,9,37]

Energy Surfaces. As noted above the calculated ts imaginary frequencies are uniformly larger at the HF level suggesting that the MP2 and B3LYP methods produce somewhat flatter potential energy surfaces along the reaction coordinate than does the HF method.[33]

We also find that for a given computational method, proton-transfer transition states have larger imaginary frequencies than do hydride-transfer transition states.[33] The proton-transfer ts can be thought of as having a significant contribution from the ion triplet structure, $[A^-\cdots H^+\cdots A^-]$, that is, the partial covalent

---

[34] Natural population analysis (NPA) charges were obtained for the optimized MP2/6-311+G** and B3LYP/6-311++G** transition state structures.

[35] Saunders, M.; Kates, M. *J. Am. Chem. Soc.* **1978**, *100*, 7082.

[36] Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334.

[37] (a) Bordwell, F. G.; Boyle, W. J. *J. Am. Chem. Soc.* **1971**, *93*, 512. (b) Challis, B. C.; Miller, E. M. *J. Chem. Soc., Perkin Trans. 2* **1972**, 1618. (c) Kemp, D. S.; Casey, M. L. *J. Am. Chem. Soc.* **1973**, *95*, 6670.

TABLE 2. Selected Transition State Geometry Features for the Proton- and Hydride-Transfer Reactions in This Study

	HF/6-311+G**		MP2/6-311+G**		B3LYP/6-311++G**	
H donor (ts point group)[a]	d (C•••H), Å[b]	θ_{ts}, deg[c]	d (C•••H), Å[b]	θ_{ts}, deg[c]	d (C•••H), Å[b]	θ_{ts}, deg[c]
Identity Proton Transfers						
1. $CH_3\mathbf{H}$ (D3/D3h)	1.457	180	1.437	180	1.445	180
2. $CH_3CH_2\mathbf{H}$ (C1)	1.445	180	1.436	179.4	1.455	179.8
3. $CH_3CH_2CH_2\mathbf{H}$ (C2)	1.456	180	1.439	179.8	1.446	179.8
4. $\mathbf{H}CF_2CF_2^+$ (C1)	1.427	173.5	1.385	173.8	1.401	175.9
5. $CH_3O\mathbf{H}$ (C2)	1.191	178.4	1.201	176.4	1.208	177.5
5cx. $CH_3O\mathbf{H}$ (C1) complex formation[d]	1.575, 0.994	172.5	1.335, 1.101	175.5	1.370, 1.093	177.1
6. $\mathbf{H}CF_3$ (C1/D3h)	1.420	180	1.419	180	1.431	180
7. $\mathbf{H}CCl_3$ (D3/D3h)	1.396	180	1.382	180	1.398	180
8. $\mathbf{H}CH_2CHO$ (C1)	1.447	171.3	1.418	171.1	1.431	171.6
9. $\mathbf{H}CH_2CN$ (C1/C2h)	1.436	180	1.420	180	1.432	180
10. $\mathbf{H}CH_2NO_2$ (C1)	1.424	180	1.391	180	1.404	180
11. $\mathbf{H}C{\equiv}CCH_3$ (C1)	1.407	180	1.403	178.5	1.409	180
Intramolecular Proton Transfers						
12. $\mathbf{H}CH_2CH_2^-$ intramolecular (C1)	1.275	78.3	1.295	76.0	1.289	75.3
13. $\mathbf{H}CH_2CH_2CH_2^-$ intramolecular (C1)	1.456	107.9	1.460	107.0	1.469	107.2
14. $\mathbf{H}CH_2CH_2CH_2CH_2^-$ intramolecular (C2)	1.446	135.6	1.440	136.1	1.449	135.7
15. $\mathbf{H}CH_2CH_2CH_2CH_2CH_2^-$ intramolecular (Cs)	1.445	151.6	1.437	152.5	1.445	152.4
Nonidentity Proton Transfers[e]						
16, 17. $\mathbf{H}CH_2CHO + {}^-CH_2CN$ (C1)	1.485, 1.402	176.3	1.563, 1.310	175.8	1.536, 1.344	175.6
18, 19. $\mathbf{H}CH_2NO_2 + {}^-CH_2CN$ (C1)	1.494, 1.371	179.4	1.562, 1.286	179.2	1.544, 1.312	177.9
Identity Hydride Transfers to Carbonyls						
20. $\mathbf{H}CO_2^-$ (C2)	1.385	180	1.348	180	1.367	180
21. $\mathbf{H}COS^-$ (C1) anti ts	1.351	180	1.323	180[f]	1.347	180
22. $\mathbf{H}COS^-$ syn ts (C1)	1.354	151.9	1.324	161.0[f]	1.348	161.0
23. $\mathbf{H}CH_2O^-$ (C1)	1.416, 1.326	146.6	1.315	180	1.343	180
24. $\mathbf{H}CHONH_2^-$ (R,R) ts (C1)	1.376	151.4	1.326	153.3	1.350	162.3
25. $\mathbf{H}CHONH_2^-$ (R,S) ts (C1)	1.424, 1.335	153.2	1.309, 1.299	180	1.475, 1.263	164.3
Other Identity Hydride Transfers						
26. $\mathbf{H}CH_3$ (C1)[g]	1.241	115.2	1.232	103.2	1.242	109.6
27. 1,**4**-dihydropyridine (C2)[h]	NA		NA		1.357	175.1
28. $\mathbf{H}CF_3$ (C1/D3d)	1.315	180	1.307	179.9	1.331	179.6
29. $\mathbf{H}CCl_3$ (C1/C3)	1.310	180	1.292	180[f]	1.344	179.9
30. $\mathbf{H}CF_2CF_2^-$ (C1)	1.358	167.7	1.351	179.9	1.372	176.0
1,2-Intramolecular Hydride Shifts						
31. $\mathbf{H}CF_2CF_2^+$ intramolecular (C2v)	1.381	60.4	1.390	61.0	1.410	60.1
32. $\mathbf{H}C(CH_3)_2C(CH_3)_2^+$ intramolecular (C2)	1.321	64.1	1.317	65.1[i]	1.329	64.5

[a] The bolded hydrogen is the transferred hydrogen. The ts point groups are for MP2 structures. A slash indicates the structure virtually has the higher symmetry [b] Partial C•••H bond length(s) in the transition state. [c] The angle formed by the transferred hydrogen and the two carbon termini. [d] The hydrogen-bonded ion−molecule complex between methanol and methoxide$^-$. [e] ΔH_{RXN} for the gas-phase reaction of acetonitrile anion with acetaldehyde is −4.6 (HF), −8.0 (MP2), and −6.6 kcal/mol (B3LYP). The experimental value is approximately −7.5 kcal/mol. ΔH_{RXN} for the gas-phase reaction of acetonitrile anion with nitromethane is −18.7 (HF), −14.3 (MP2), and −17.7 kcal/mol (B3LYP). The experimental value is approximately −17 kcal/mol [Bartmess, J. E. In *NIST Standard Reference Database Number 69*; Mallard, W. G., Linstrom, P. J., Eds.; National Institute of Standards and Technology: Gaithersburg, MD, 2005; (http://webbook.nist.gov)]. [f] The reactions of thioformate with carbonyl sulfide and of chloroform with trichloromethyl cation produce addition complexes with no imaginary frequency when calculated at the MP2/6-311+G** level. [g] The reaction of methane with methyl cation produces an addition complex, not a transition state [Gronert, S.; Keeffe, J. R. *J. Am. Chem. Soc.* **2005**, *127*, 2324−2333]. [h] The reaction is hydride transfer from C4 of the donor to C4 of pyridinium ion. The point group is for the B3LYP structure. The two pyridinium moieties are gauche (semistacked) with respect to one another. The structure is similar in this respect to related transition states calculated by Wu et al. [Wu, Y.-D.; Lai, D. K.; Houk, K. N. *J. Am. Chem. Soc.* **1995**, *117*, 4100]. [i] The 1,2-hydride shift in the tetramethylethyl cation produces, at the MP2 level, a symmetrically hydrogen-bridged cation with no imaginary frequency. This cation is an isomer of the optimized cation, with an enthalpy 3.7 kcal/mol higher.

bond orders are relatively low.[12] This model suggests that along the reaction coordinate, on either side of the transition state, covalency increases sharply as a function of distance with a concomitant decrease in energy. The curvature along the reaction coordinate in the vicinity of the saddle point will then be substantial, resulting in large imaginary frequencies. By contrast hydride-transfer transition states, modeled as two-electron, three-center systems,[13] appear to have more bonding involving the two reaction termini and the transferred hydrogen. In such cases changes in total covalency will not be so sensitive a function of the position along the reaction coordinate, and the curvature near the ts will not be as sharp.

Additionally we observe that the isotopic sensitivity of the imaginary frequency, expressed as the ratio $i\nu^{\ddagger}_{H}/i\nu^{\ddagger}_{D}$, is consistently larger for proton transfers than for hydride transfers. For proton transfers, including the intramolecular examples and the unsymmetrical reactions, the ratios are (HF) 1.38 ± 0.01, (MP2) 1.35 ± 0.04, and (B3LYP) 1.36 ± 0.03. For the hydride transfers the corresponding values are 1.17 ± 0.02, 1.07 ± 0.04, and l.13 ± 0.04. This result too is consistent with the presence of greater covalency in the hydride-transfer ts, a consequence of which is stronger coupling between the motion of the transferred hydrogen and the heavier termini and a reduction in the isotopic sensitivity of the imaginary frequency.[38]

KIE Values and Trends. General. Although the methods used here correlate very well with measured heats of reaction,[12,13] experimental results with which to compare calculated KIE values for gas-phase identity hydrogen-transfer reactions

---

[38] Reference 1a, page 39.

TABLE 3. Calculated Kinetic Hydrogen Isotope Effects[a] for the Proton- and Hydride-Transfer Reactions in this Study

H donor	HF			MP2			B3LYP		
	k_H/k_D	ZPVE[b]	Q[b]	k_H/k_D	ZPVE[b]	Q[b]	k_H/k_D	ZPVE[b]	Q[b]
Identity Proton Transfers									
1. $CH_3\mathbf{H}$	4.70	3.52	1.34	5.79	3.62	1.60	4.19	3.04	1.38
2. $CH_3CH_2\mathbf{H}$	4.64	3.96	1.17	4.49	3.84	1.17	4.57	3.90	1.17
3. $CH_3CH_2CH_2\mathbf{H}$	4.67	4.10	1.14	4.60	4.03	1.14	4.67	4.08	1.14
4. $\mathbf{H}CF_2CF_2^+$	5.48	5.34	1.03	NA	NA	NA	4.35	4.25	1.02
5. $CH_3O\mathbf{H}$	5.43	4.19	1.29	4.48	3.59	1.25	4.81	3.75	1.28
5cx. $CH_3O\mathbf{H} + CH_3O^-$ complex formation	1.07	0.85	1.26	2.21	1.77	1.25	2.07	1.65	1.26
6. $\mathbf{H}CF_3 + CF_3^-$	5.92	5.64	1.05	5.44	5.17	1.05	5.37	5.11	1.05
7. $\mathbf{H}CCl_3 + CCl_3^-$	5.82	5.63	1.03	5.28	5.11	1.03	5.42	5.23	1.04
8. $\mathbf{H}CH_2CHO$	5.04	4.27	1.18	4.83	4.09	1.18	4.71	4.00	1.18
9. $\mathbf{H}CH_2CN$	5.14	4.28	1.20	4.93	4.11	1.20	4.88	4.07	1.20
10. $\mathbf{H}CH_2NO_2$	5.01	4.16	1.21	4.77	4.03	1.18	4.95	3.94	1.26
11. $\mathbf{H}C{\equiv}CCH_3$	NA	NA	NA	4.60[d]	3.83	1.20	4.36	3.63	1.20
Intramolecular Proton Transfers									
12. $\mathbf{H}CH_2CH_2^-$	3.14	2.91	1.08	2.67	2.47	1.08	3.15	2.92	1.08
13. $\mathbf{H}CH_2CH_2CH_2^-$	4.44	4.03	1.10	4.40	3.98	1.10	4.45	4.04	1.10
14. $\mathbf{H}CH_2CH_2CH_2CH_2^-$	4.15	3.68	1.13	4.16	3.67	1.13	4.12	3.64	1.13
15. $\mathbf{H}CH_2CH_2CH_2CH_2CH_2^-$	4.25	3.79	1.12	4.25	3.76	1.13	4.11	3.64	1.13
Nonidentity Proton Transfers[e]									
16. $\mathbf{H}CH_2CHO + {}^-CH_2CN$	4.92	4.18	1.18	4.63	3.94	1.17	4.59	3.91	1.17
17. $\mathbf{H}CH_2CN + {}^-CH_2CHO$	5.34	4.35	1.20	4.97	4.17	1.19	4.94	4.14	1.19
18. $\mathbf{H}CH_2NO_2 + {}^-CH_2CN$	5.14	4.28	1.20	4.93	4.11	1.20	4.88	4.07	1.20
19. $\mathbf{H}CH_2CN + {}^-CH_2NO_2$	5.34	4.45	1.20	4.97	4.17	1.19	4.94	4.14	1.10
Identity Hydride Transfers to Carbonyls									
20. $\mathbf{H}CO_2^-$	NA	NA	NA	2.06	1.83	1.13	2.25	2.00	1.13
21. $\mathbf{H}COS^-$ anti ts	4.29	3.93	1.09	1.94[f]	1.75	1.11	2.72	2.42	1.12
22. $\mathbf{H}COS^-$ syn ts	4.01	3.64	1.10	1.85[f]	1.65	1.12	2.62	2.33	1.12
23. $\mathbf{H}CH_2O^-$	2.66	2.66	1.00	1.71	1.48	1.16	2.15	1.88	1.14
24. $\mathbf{H}CHONH_2^-$ (R,R) ts	NA	NA	NA	1.99	1.81	1.10	2.26	2.06	1.10
25. $\mathbf{H}CHONH_2^-$ (R,S) ts	NA	NA	NA	1.72	1.60	1.07	2.06	1.92	1.08
Other Identity Hydride Transfers									
26. $\mathbf{H}CH_3$	NA[g]	NA	NA	1.25[g]	1.03	1.21	1.37[g]	1.16	1.18
27. 1,**4**-dihydropyridine[h]	NA	NA	NA	NA	NA	NA	3.80	1.07	3.55
28. $\mathbf{H}CF_3$	3.67	3.60	1.02	2.37	2.30	1.03	2.85	2.78	1.03
29. $\mathbf{H}CCl_3$	7.22	7.18	1.01	3.08[f]	3.07	1.00	5.06	5.00	1.01
30. $\mathbf{H}CF_2CF_2^-$	4.63	4.53	1.02	NA[c]	NA	NA	4.08	3.95	1.03
1,2-Intramolecular Hydride Shifts									
31. $\mathbf{H}CF_2CF_2^+$	3.29	3.20	1.03	3.25	3.16	1.03	3.39	3.33	1.02
32. $\mathbf{H}C(CH_3)_2C(CH_3)_2^+$	3.44	3.42	1.01	2.53[i]	2.67	0.95	3.32	3.30	1.01

[a] Calculated according to eq 1 with $T = 298.15$ K and $P = 1$ atm using unscaled harmonic frequencies and ZPVE values; see text. The bolded hydrogen is the transferred hydrogen. [b] These are the contributions made to the isotopic rate ratio made by the zero point vibrational energy factor and the partition function factor, respectively; see eq 1 in text. [c] MP2 frequencies for the bimolecular reactions involving tetrafluoroethylene were not obtained. [d] Previously (ref 12) we reported this ts to have two imaginary frequencies in addition to the reaction coordinate. Recalculation gave a first-order saddle point. [e] ΔH_{RXN} for the gas-phase reaction of acetonitrile anion with acetaldehyde is −4.6 (HF), −8.0 (MP2), and −6.6 kcal/mol (B3LYP). The experimental value is approximately −7.5 kcal/mol. ΔH_{RXN} for the gas-phase reaction of acetonitrile anion with nitromethane is −18.7 (HF), −14.3 (MP2), and −17.7 kcal/mol (B3LYP). The experimental value is approximately −17 kcal/mol [Bartmess, J. E. In *NIST Standard Reference Database Number 69*; Mallard, W. G., Linstrom, P. J., Eds.; National Institute of Standards and Technology: Gaithersburg, MD, 2005; (http://webbook.nist.gov)]. [f] The reaction of thioformate with carbonyl sulfide produces an addition complex with no imaginary frequency when calculated at the MP2/6-311+G** level. The same is true of the reaction between chloroform and trichloromethyl cation. Thus the values quoted are equilibrium isotope effects upon complex formation. [g] The reaction of methane with methyl cation produces an addition complex, not a transition state [Gronert, S.; Keeffe, J. R. *J. Am. Chem. Soc.* **2005**, *127*, 2324−2333]. The quoted isotope effects are equilibrium effects upon complex formation. [h] The reaction is hydride transfer from C4 of the donor to C4 of pyridinium ion. [i] The 1,2-hydride shift in the tetramethylethyl cation produces, at the MP2 level, a symmetrically hydrogen-bridged cation with no imaginary frequency. This cation is an isomer of the optimized cation, with an enthalpy 3.7 kcal/mol higher.

are scarce or nonexistent. However, unpublished work in this laboratory on gas-phase E2 elimination reactions gives experimental KIEs in satisfactory agreement with computational results.[39] Additionally, we call attention to the experimental difference in isotopic hydrogen bond strengths for the complex formed between between methoxide ion and methanol in the gas phase, which has been reported to be 0.47 ± 0.11 kcal/mol, giving $K_H/K_D = 2.2 \pm 0.4$.[40] Anion−molecule complexes between alkoxide ions and their parent alcohols are similar in structure and energy to proton-transfer transition states. Therefore we have calculated the equilibrium isotope effect on the formation of the methanol/methoxide hydrogen-bonded complex and found $K_H/K_D = 1.1$ (HF), 2.2 (MP2), and 2.1 (B3LYP). We conclude that the MP2/6-311+G** and B3LYP/6-311++G**

---

(39) Gronert, S.; Fagin, A. E. Unpublished results. Experimental KIE values for activation-controlled, gas-phase E2 eliminations give primary KIEs (corrected for secondary effects), which are satisfactorily reproduced by computation at the HF/6-31+G* level.

(40) Barlow, S. E.; Dang, T. T.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1990**, *112*, 6832. In reality the gas-phase proton transfer between alcohols and their conjugate bases is probably barrier-free with an isotope effect similar to that for hydrogen bond formation. Computationally a transition state can be found, and a computational primary KIE is reported in Table 3.

computational levels in particular are adequate to our purpose. Glad and Jensen have previously reported that correlated methods give superior KIE results compared with HF methods.[26]

Table 3 contains the calculated KIE values, k_H/k_D, for the proton and hydride transfers, inter- and intramolecular, in this study. The total KIE values are sorted into contributions from ΔZPVE and the isotopic partition function ratios (Q ratios) according to eq 1. As expected for primary KIEs, the ΔZPVE factor dominates. The Q factor accounts for about 10−20% of the total KIE (averaging less than 10%) except in a few cases. As mentioned above, for several hydride transfers, transition state optimization produced stable addition complexes rather than transition states. In those cases the isotope effects reported in Table 3 are the equilibrium isotope effects for addition complex formation.

(1) KIE Magnitudes. We first note that although the calculated transition states for identity reactions are (except for reactions 24 and 25) symmetrical and therefore the real, symmetrical stretch in the ts involves no movement of the transferred isotope, the calculated KIEs are uniformly lower than the value of about 7−10 expected for complete loss of the reactant C−H stretch.[3,4] The most obvious source of the smaller values is the presence of isotope-sensitive motions in the transition state, incompletely matched in the reactant. In particular, a pair of degenerate (or almost degenerate) C···H···C bending modes is expected for a linear (or almost linear) ts, and these can be of higher frequency than those in the reactant. A case in point is the proton transfer between propyne and its conjugate base, reaction 11. Propyne is calculated[41] to have two $C_{sp}-C_{sp}-H$ bending modes at 617 cm^{-1}. In the transition state the degenerate bends are at 1362 cm^{-1}. Additionally, there are two stretching motions involving the C≡C moieties in which the isotope moves slightly. If loss of zero point vibrational energy from the original $C_{sp}-H$ stretch were the sole determining factor, a KIE of 10 or more (at 25 °C) would result. Clearly the reduced KIE has its origin in isotope-sensitive ts vibrations that are not fully compensated by reactant state motions involving the isotope.

(2) Hydride versus Proton Transfer. The principal result emerging from Table 3 is that identity *hydride*-transfer reactions have *smaller* primary kinetic isotope effects than do identity *proton*-transfer reactions. This is true even for hydride transfers proceeding through transition states that are linear about the C···H···C axis. Since the real, symmetrical stretching vibration in a linear, symmetrical, hydrogen-transfer transition state is not isotopically sensitive, it follows that more of the other real transition state vibrations are isotopically sensitive and have higher frequencies for hydride transfers than for proton transfers. This outcome too is in accord with the point made above that there is more total bonding in the two-electron, three-center (2-e 3-c) hydride-transfer ts than in the four-electron, three-center (4-e 3-c) proton-transfer ts. Direct confirmation of this statement is found in the ΔZPVE contributions to the KIEs: smaller for the hydride transfers and larger for the proton transfers.

(3) Transfer Angle. Another outcome of this work is that the KIE is not very sensitive to the extent of nonlinearity about the C···H···C trio of atoms. Figure 1 shows the transition states obtained at the MP2/6-311+G** level for a set of intramolecular 1,n proton-transfer reactions ($n = 2-5$). The KIE values in Table 3 show that only for the 1,2-proton shift in the ethyl anion is the isotope effect diminished. Thus, the transfer angle, θ_{ts}, has to fall below about 100° before k_H/k_D becomes significantly smaller than that for the bimolecular proton transfers between alkyl anions, all of which have linear transition states. Of course the unique features of the 1,2-proton shift discussed earlier could also contribute to the lowering of the KIE.

(4) Isotope-Sensitive Vibrations. What is the nature of the real, isotope-sensitive vibrations in hydride-transfer transition states, and why are such motions more important for hydride transfers than for proton transfers? The vibrations responsible for reduced KIEs are likely to be somewhat particular to each system examined, although as discussed above, for linear transition states a pair of degenerate bends is expected. Earlier force field models used simplified three- and five-center models that cannot be sensitive to structural variables further removed from the site of isotopic substitution.[14,22] Even though Wolfsberg and Stern's cutoff procedure[42] has been applied with some success,[1a] the reactions studied here are structurally diverse near the reaction centers and cannot be expected to be fit by a single, truncated model. Coupling of isotopically sensitive modes with other vibrations of like symmetry will therefore yield a set of vibrations particular to the individual substrate.

The greater the number of isotopically sensitive vibrations in the ts and especially the higher their frequencies, the greater will be the diminution of the ΔZPVE factor, hence the KIE. The proton transfer from propyne to propynyl anion was discussed above. It is instructive to look at a few other examples. Hydride transfer between fluoroform and trifluoromethyl cation (reaction 28) has a KIE less than 3.0 (MP2 and B3LYP), whereas that between chloroform and trichloromethyl cation (reaction 29) has KIE = 5.1 at B3LYP and even higher at HF (MP2 optimization gives a stable cation-molecule complex). The two systems seem similar, but examination of the real ts vibrations[41,43] shows several prominent features including a high frequency (1810 cm^{-1}, A2u) stretching mode in the fluoroform ts, in which the isotope is moving between the carbons along the transfer axis while pyramidalization/depyramidalization occurs at the carbons. Additionally there is a similar A2u motion at 830 cm^{-1} and a pair of degenerate C···H···C bending motions at 1330 cm^{-1} (Eu). In the chloroform ts the bending motions are almost unchanged at 1310 cm^{-1}, but the corresponding A2u frequencies are shifted to 1110 and 425 cm^{-1}. The consequences are a greater reduction in the ΔZPVE factor for the fluoroform hydride transfer than for the chloroform hydride transfer, determined *in this case* by the difference in real stretching frequencies, producing a significantly lower KIE for the former despite the apparent similarity of the two reactions.

Proton transfer between the two haloforms and their respective conjugate bases (reactions 6 and 7) have nearly identical KIEs. The contributions from the ΔZPVE factor are also identical. In the transition state of the fluoroform reaction the bending modes are present at 1580 cm^{-1}, and the A2u stretching modes are found at 1105 and 637 cm^{-1}. The net result is that the ΔZPVE contribution to the fluoroform *proton*-transfer KIE is about twice the size of that for the fluoroform *hydride* transfer.

---

[41] (41) Calculated and visualized at the B3LYP/6-31+G* level within the Spartan 02 modeling package.[23] Almost identical frequencies are found at the MP2/6-311+G** and B3LYP/6-311++G** levels in the Gaussian output.

[42] (42) (a) Wolfsberg, M.; Stern, M. J. *Pure Appl. Chem.* **1964**, *8*, 225. (b) Wolfsberg, M.; Stern, M. J. *J. Chem. Phys.* **1966**, *45*, 4105.

[43] (43) We note that hydride transfer from the haloforms to the corresponding trihalomethyl cations has an eclipsed ts for fluoroform at both MP2 and B3LYP levels. Likewise the chloroform ts is eclipsed at B3LYP.

A Unifying Conceptual Framework. We model the reaction site of a proton-transfer transition state as four-electron, three-center (4-e 3-c) bonding array in which the HOMO is antibonding (taking into account a repulsive interaction between the transfer termini). By contrast the hydride-transfer ts is pictured as a two-electron, three-center (2-e 3-c) array in which the HOMO is bonding.[13] A useful analogy likens the proton-transfer ts to the allyl anion and the hydride-transfer ts to the allyl cation.[44] Further evidence that there is greater bonding in the 2-e 3-c structure than in the 4-e 3-c structure comes from comparison of the activation enthalpies for rotation about a C−C linkage in the allyl cation and anion. Our unpublished MP2/6-311+G**//HF/6-311+G** computations place the rotational barrier for the cation at 35.1 kcal/mol while that for the anion is only 20.3 kcal/mol.

Previous computational work shows that an ion-triplet structure, $[A^-\cdots H^+\cdots A^-]$, makes a significant contribution to the proton-transfer ts[12,45] but that the analogous $[C^+\cdots H^-\cdots C^+]$ contributor is not important for the hydride-transfer ts.[13] The limiting case for the 4-e, 3-c ts leads to an energy surface in which bond breaking is virtually unaccompanied by bond formation. Proton transfers between electronegative atoms such as nitrogen and especially oxygen come closest to inhabiting this category having little or no barrier to the passage of the proton between properly positioned basic sites.[12,46] The proton transfers between carbons reported here also have substantial $[C^-\cdots H^+\cdots C^-]$ character at the ts, albeit not to the extent described for O and N.[12] On the other hand, the limiting case for the 2-e, 3-c ts leads to bond breaking compensated by an equal amount of bond formation.[13] Hydride transfers fall more or less into this category having more bonding at the ts, and flatter energy surfaces along the reaction coordinate than do proton transfers.

It must not be imagined that all proton-transfer transition states are exactly alike or that all hydride-transfer transition states are exactly alike. For example, the amount of bonding in the 2-e, 3-c hydride-transfer ts can vary. At one extreme lie the carbocation-alkane complexes; these are not transition states but stable species possessing a 2-e 3-c bond, and with very small equilibrium isotope effects. Closer to the other limit could be the hydride-transfer ts in the chloroform system. Weaker 2-e, 3-c bonding in that case leads to a ts more greatly resembling a proton-transfer ts, consequently a larger KIE. Between these two extremes are the bulk of the hydride transfers reported here and previously.[13] For these we often find formation of stable complexes rather than transition states when using correlated methods. When transition states are found they are characterized by relatively small imaginary frequencies and by small KIEs.

Conclusions

Proton-transfer transition states and hydride-transfer transition states are fundamentally different. The former can be modeled as a four-electron, three-center molecular orbital array (analogous to an allyl anion), and the latter as a two-electron, three-center structure (analogous to an allyl cation).[13,44] Consequences of this difference include the following:

(1) The primary, semiclassical KIE is smaller for hydride transfer than for proton transfer. This result is principally expressed by smaller ΔZPVE contributions to the hydride-transfer KIE than for proton transfers. Specifically, more bonding in hydride-transfer transition states generates a larger number of isotopically sensitive, real ts vibrations. Some of these are bending motions; others are stretching modes of relatively high frequency which reduce the ΔZPVE factor in eq 1. The frequencies of these motions are sensitive to the details of molecular structure near the transfer termini.

(2) The correlated methods, MP2/6-311+G** and B3LYP/6-311++G**, appear to reproduce heats of reaction and heats of activation better than the HF/6-311+G** level of theory. KIE values are similar for the three methods although the HF calculation does relatively poorly for the formation of the hydrogen-bonded complex between methoxide and methanol.

(3) Partial C···H bond distances in the hydride ts are shorter, allowing better overlap between the ends of the C···H···C triad, enhancing total bonding.[13]

(4) The greater bonding in a hydride-transfer ts can, in some cases, be further aided by bending the C···H···C transfer angle, θ_{ts}, or by otherwise bringing the two halves of the ts closer together. Sufficiently increased bonding can lead to a stable addition complex with a 2-e 3-c bond rather than a transition state.[13]

(5) Curvature of the energy surface along the reaction coordinate in the vicinity of the transition state is sharper for proton transfers, leading to larger imaginary frequencies than for hydride transfers. Moreover, the isotopic ratio of imaginary frequencies, $i\nu_H/i\nu_D$, is larger for proton-transfer transition states than for hydride-transfer transition states. This result supports the premise of greater covalency in the hydride-transfer ts, a consequence of which is stronger coupling between the motion of the transferred hydrogen and the heavier termini, and a reduction in the isotopic sensitivity of the imaginary frequency.[38]

(6) Proton-transfer transition states have significant ion-triplet character, $[C^-\cdots H^+\cdots C^-]$,[12,45] while the bonding changes in a hydride-transfer ts occur more synchronously.[13]

Other conclusions from this work are,

(7) Bent transition states can reduce the KIE,[14] but only when the transfer angle, θ_{ts}, falls considerably below 180°, in our calculations at or below about 100°.

(8) Proton-transfer reactions in which ΔH_{RXN} differs from zero by as much as 14 kcal/mol are unsymmetrical in the Hammond sense,[36] but still have calculated semiclassical KIEs as large as those for thermoneutral reactions.[8a]

Although tunneling has been neglected in these calculations, its inclusion is likely to magnify the differences between proton-transfer and hydride-transfer KIEs. The simplistic Wigner tunneling contribution[47] to the isotope effect, for example, is greater the larger the imaginary frequency. Our results show

---

(44) (a) Swain, C. G.; Wiles, R. A.; Bader, R. F. W. *J. Am. Chem. Soc.* **1961**, *83*, 1945. (b) Sorensen, T. In *Stable Carbocation Chemistry*; Prakash, G. K. S., Schleyer, P. v. R., Eds.; Wiley-Interscience: New York, 1997; Chapter 3.

(45) (a) Gronert, S. *J. Am. Chem. Soc.* **1993**, *115*, 10258. (b) Bernasconi, C. F.; Wenzel, P. J.; Keeffe, J. R.; Gronert, S. *J. Am. Chem. Soc.* **1997**, *110*, 44008. (c) Pross. A.; Shaik, S. *J. Am. Chem. Soc.* **1982**, *104*, 1129. (d) Harris, N.; Wei, W.; Saunders, W. H., Jr.; Shaik, S. *J. Am. Chem. Soc.* **2000**, *122*, 6754. (e) Wei, W.; Shaik, S.; Saunders, W. H., Jr. *J. Phys. Chem. A* **2002**, *106*, 11616.

(46) (a) Swain, C. G.; Kuhn, D. A.; Schowen, R. L. *J. Am. Chem. Soc.* **1965**, *87*, 1553. (b) Eliason, R.; Kreevoy, M. M. *J. Am. Chem. Soc.* **1978**, *100*, 7037.

(47) Wigner, E. *Z. Phys. Chem. B* **1932**, *19*, 203. See also ref 1a, pages 36−39.

this frequency to be uniformly larger for proton transfers. Therefore we regard our conclusions to be qualitatively valid.

Acknowledgment. Support from the National Science Foundation (CHE-0348809) is gratefully acknowledged by S. G. We also appreciate helpful comments from Professors A. J. Kresge, E. L. Motell, R. A. More O'Ferrall, and W. H. Saunders, Jr.

Supporting Information Available: Electronic energies, zero-point vibrational energies, imaginary frequencies for transition states, and Cartesian coordinates for all structures, as well as the complete ref 24. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0606296