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A Semiempirical Investigation of Identity Reaction Proton Transfers*

William H. Saunders, Jr.

Department of Chemistry, The University of Rochester,
Rochester, New York 14627, USA

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A semiempirical investigation of identity-reaction proton transfers using the AM1 and PM3 methods has been carried out. Enthalpy differences between separated reactants and the ion-dipole complex (well depth) and between the complex and the transition structure (barrier height) were calculated. A comparison of carbon-to-carbon and oxygen-to-oxygen proton transfers led to the unexpected result that barriers were higher for the latter than for the former, in contrast to experimental observations in solution. The calculated values are compared with experiment and with *ab initio* calculations where possible, and the reliability of semiempirical calculations of well depths and barrier heights is assessed.

INTRODUCTION

Proton transfers, especially those to and from carbon, play a central role in many organic reaction mechanisms. It has long been known that carbon acids almost always deprotonate much more slowly than oxygen or nitrogen acids of comparable acidity. The latter are usually classed as »normal« or »Eigen« acids, the name arising from the discovery by Eigen that protons bound to electronegative atoms are abstracted by bases at a diffusion controlled (or close to diffusion controlled) rate when the deprotonation is exoergic.[1] That carbon acids deprotonate more slowly has been attributed to the necessity for electronic and heavy-atom reorganization in a developing resonance-stabilized carbanion.[2–4] The role of solvation or solvent reorganization remains uncertain because of the difficulty of separating solvent effects from intrinsic effects for reactions carried out in solution.

An obvious answer is to isolate the intrinsic effects by operating in the gas phase. Ion cyclotron resonance studies of proton transfers from carbon give rates that are well below encounter rates, suggesting significant barriers.[5–7] Obtaining barrier heights from the data, however, requires assumptions concerning energy-level

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[*] Dedicated to the memory of Professor Tibor Škerlak

spacings in the transition structure. In contrast, the energies of the reactants, ion-dipole complex and the transition structure are readily calculable by SCF-MO methods. Not many results were available in the literature at the time the present study was begun, and most of those did not deal with carbon acids yielding delocalized anions. Carbon acids yielding localized anions were reported to show sizable barriers to deprotonation,[8–10] but the few reports on carbon acids yielding delocalized anions were conflicting.[11,12]

COMPUTATIONAL PROCEDURES

For an initial exploration, semiempirical methods were chosen. They have the advantage over *ab initio* methods of requiring much less computer time and were thus suitable for rapid examination of a range of carbon and oxygen acids. For the same reason, they are potentially applicable to much larger systems than *ab initio* calculations. In order to eliminate any thermodynamic contribution to the calculated barriers, identity reactions were chosen:

$$A^- + HA \rightarrow AH + A^-$$

Because the products are identical with the reactants, calculations were further facilitated by the need to calculate only the energies of the reactants, the reactant ion-dipole complexes and the transition structures.

The calculations utilized the Mopac version 6.0[13] – specifically, the AM1[14] and PM3[15] methods. The semiempirical heats of formation were used without correction for zero point energy differences, for the calculations are parametrized to match experimental heats of formation and so implicitly include the corrections. Frequency and force calculations showed that all species were stationary points, with no negative eigenvalues for stable species and only one for transition structures.

RESULTS AND DISCUSSION

The results are summarized in Tables I and II. The well depth is the enthalpy difference between reactants and the ion-dipole complex. As expected, there is an enthalpy decrease on forming the complex because of attraction between the anionic base and the dipolar proton donor. The barrier height is measured from the ion-dipole complex to the transition structure. Finally, TS *vs.* reactants is the enthalpy difference between the transition structure and the separated reactants.

Qualitatively, most of the well depths are in a reasonable range, varying from –1 to –21 kcal mol^{-1} by AM1, and –6 to –29 kcal mol^{-1} by PM3 (excluding in both cases the special case of acetaldehyde enolate + acetaldehyde enol). Good agreement with high-level *ab initio* calculations is obtained in a number of cases. For hydroxide ion + water, the well depths of –21 (AM1) and –26 (PM3) compare well with the SCF-CI value of –25 kcal mol^{-1}.[16] Similarly, the –11 (AM1) and –14 (PM3) values bracket nicely the –12 kcal mol^{-1} found at MP2/6 – 31 + G^*//6 – 31 + G^* for acetaldehyde enolate + acetaldehyde.[17] The AM1 and PM3 values for acetonitrile conjugate base + acetonitrile are fairly far apart, but their average (–15) is close to the –16 kcal mol^{-1} at MP2/6 – 31 + G^*//6 – 31 + G^*.[18]

The well depths for the hydrocarbons, however, do not compare favorably with those from high-level *ab initio* calculations by Scheiner's group. Methane and methyl

TABLE I

Identity reaction proton transfers by AM1

Base	Substrate	Well Depth[a]	Barrier Height[b]	TS *vs.* Reactants[c]
$^{-}CH_2NO_2$	CH_3NO_2	–11.9	1.2	–10.7
$^{-}CH_2CHO$	CH_3CHO	–10.8	5.7	–5.1
$^{-}CH_2CN$	CH_3CN	–10.8	0.03[d]	–10.77
$^{-}CH_2COOMe$	CH_3COOMe	–7.4	2.5	–4.9
$^{-}CH_2COCH_3$	CH_3COCH_3	–13.0	7.3	–5.7
$CH_2CHCH_2^-$	$CH_3CH{=}CH_2$	–5.1	5.7	0.6
$C_6H_5CH_2^-$	$C_6H_5CH_3$	–4.0	9.7	+5.7
CH_3^-	CH_4	–12.7	0.0	–12.7
CH_2CH^-	CH_2CH_2	–15.3	0.0	–15.3
HCC^-	$HCCH$	–19.6	0.0	–19.6
$^{-}CH_2CHO$	$CH_2{=}CHOH$[e]	–32.7	5.6	–32.0
MeO^-	MeOH	–13.1	4.5	–8.6
EtO^-	EtOH	–12.7	4.6	–8.1
OH^-	H_2O	–21.0	0.9[f]	–20.1
NH_2^-	NH_3	–12.7	2.9	–9.5
$FC_2H_4O^-$	FC_2H_4OH	–15.6	4.7	–10.9
$C_6H_5O^-$	C_6H_5OH	–13.8	7.4	–6.4

[a] ΔH_f(ion-dipole complex) – ΔH_f(separated reactants) in kcal mol^{-1}. [b] ΔH_f(TS) – ΔH_f (ion-dipole complex) in kcal mol^{-1}. [c] Barrier Height + Well Depth in kcal mol^{-1}. [d] Even though the maximum between the reactant complex and product complex is barely above the complexes in energy, the force-constant matrix of the symmetrically hydrogen bonded species has one negative eigenvalue, clearly characterizing the species as a transition state. [e] Oxygen-to-oxygen proton transfer. [f] The proton is not symmetrically located in the transition state; the symmetrical species is at a shallow minimum (–0.5) between the two maxima.

anion give a complex that is only about 2 kcal mol^{-1} more stable than the separated species.[8] Similarly, the well depth for ethylene + vinyl anion is only –4.9 kcal mol^{-1},[10] and for acetylene + acetylenyl anion –11 kcal mol^{-1}.[9] In these cases, the semiempirical calculations overestimate the strength of bonding between the components to the extent of giving symmetrically hydrogen bonded complexes in all three cases by AM1 and in two of three cases by PM3. The complex between toluene and benzyl anion is too large for *ab initio* calculations at a meaningful level, but Han and Brauman estimate a well depth of *ca.* –12 kcal mol^{-1} by analogy to other experimental results.[19] In this case, the semiempirical calculation appears to underestimate the well depth. That this is not just a matter of size and dispersion of the charge by resonance can be seen by comparing phenoxide + phenol with methanol and ethanol + their respective alkoxides, where the well depth changes little.

Although the well depths are often in qualitative or even quantitative agreement with the results of high-level calculations, the barriers must be viewed with some skepticism. The most obvious generalization is that the barriers for the carbon acids run lower than the barriers for comparable oxygen acids, especially in the PM3 calculations. This is precisely the reverse of what is found in solution. If it represented physical reality, it would mean that barriers in solution are primarily the consequence of solvent effects.

For the carbon acids yielding localized anions, methane ethylene and acetylene, the barriers are nonexistent in five calculations and trivially small in one (PM3 on

TABLE II

Identity reaction proton transfers by PM3

Base	Substrate	Well Depth[a]	Barrier Height[b]	TS *vs.* Reactants[c]
$^{-}CH_2NO_2$	CH_3NO_2	–17.8	0.4	–17.4
$^{-}CH_2CHO$	CH_3CHO	–14.4	1.4	–13.0
$^{-}CH_2CN$	CH_3CN	–18.8	0.10[d]	–18.7
$^{-}CH_2COOMe$	CH_3COOMe	–12.8	0.58	–12.3
$^{-}CH_2COCH_3$	CH_3COCH_3	–16.5	0.80	–15.7
$CH_2CHCH_2^-$	$CH_3CH{=}CH_2$	–8.6	0.4	–8.2
$C_6H_5CH_2^-$	$C_6H_5CH_3$	–5.7	2.7	3.0
CH_3^-	CH_4	–20.7	0.04[d]	–20.7
CH_2CH^-	CH_2CH_2	–23.9	0.0	–23.9
C_2H^-	C_2H_2	–29.0	0.0	–29.0
$^{-}CH_2CHO$	$CH_2{=}CHOH$[e]	–37.3	11.2	–26.1
MeO^-	MeOH	–19.4	10.2	–9.2
EtO^-	EtOH	–19.1	10.3	–8.8
OH^-	H_2O	–26.3	5.3[f]	–21.0
NH_2^-	NH_3	–15.4	7.4	–8.0
$FC_2H_4^-$	FC_2H_4OH	–21.5	10.1	–11.4
$C_6H_5O^-$	C_6H_5OH	–17.1	12.8	–4.3

[a] ΔH_f(ion-dipole complex) – ΔH_f(separated reactants) in kcal mol^{-1}. [b] ΔH_f(TS) – ΔH_f(ion-dipole complex) in kcal mol^{-1}. [c] Barrier Height + Well Depth in kcal mol^{-1}. [d] Even though the maximum between the reactant complex and product complex is barely above the complexes in energy, the force-constant matrix of the symmetrically hydrogen bonded species has one negative eigenvalue, clearly characterizing the species as a transition state. [e] Oxygen-to-oxygen proton transfer. [f] The proton is not symmetrically located in the transition state; the symmetrical species is at a shallow minimum (–0.1) between the two maxima.

methane + methyl anion). High-level *ab initio* calculations give significant barriers for all three reactions: methane 12–13, ethylene 9.6 and acetylene 2.5 kcal mol^{-1}.[8–10]

The oxygen acids yielding localized anions give barriers that appear to be too high, by comparison with both *ab initio* calculations and experience in solution. Although AM1 does give a low barrier for the water + hydroxide reaction, in agreement with *ab initio* calculations,[16,19] PM3 gives a barrier of 5 kcal mol^{-1}. Both predict a shallow minimum at the symmetrically hydrogen bonded species, a probable artifact which has no counterpart in the *ab initio* calculations. The alcohol + alkoxide reactions, with barriers of 4.5–10.3 kcal mol^{-1}, are in disagreement with high-level calculations on methanol + methoxide, which predict a barrier smaller than one kcal mol^{-1}.[20] There is one report in the literature of a study of alcohol-alkoxide proton transfers by ICR in which the efficiencies found could be interpreted by RRKM theory as requiring substantial barriers.[21] The authors, however, resist this interpretation and suggest other reasons for the low efficiencies.

For carbon acids that yield delocalized anions, experimental ICR data point to significant barriers for gas phase proton transfers, although the exact magnitudes depend on the assumptions made in RRKM calculations.[5–7] The results of *ab initio* calculations are more mixed. The barrier to proton transfer from propene to hydroxide ion was found to be about 4 kcal mol^{-1}, but no barriers were found for proton transfer from acetaldehyde to hydroxide, amide, or fluoride.[11,12] More recent, *ab initio* calculations, however, have found sizable barriers to identity-reaction proton transfers involving acetaldehyde, acetonitrile and propene.[17,18,22,23] At the highest levels studied, the barriers ranged from 6 (for acetonitrile) to more than 20 (for propene) kcal mol^{-1}. While these results are at various levels (some with correlation corrections, some without), they agree that the barriers are in all cases considerable.

The semiempirical calculations yield barriers to this class of carbon-to-carbon proton transfers that are much lower than the *ab initio* barriers where direct comparisons are possible, and also lower than the experimental results suggest. The PM3 method gives barriers that are substantially lower than those from AM1 calculations.

The oxygen-to-oxygen proton transfers from acetaldehyde enol to acetaldehyde enolate and from phenol to phenoxide are cases where an Eigen acid yields a delocalized conjugate base. The results show more resemblance to the other Eigen acids than to carbon acids yielding delocalized anions. The unusually deep well for the acetaldehyde enol reaction is doubtlessly a consequence of the high energy of the enol relative to the aldehyde. Experimental studies of this reaction can be expected to be difficult. An *ab initio* investigation is planned.

CONCLUSIONS

The semiempirical methods AM1 and PM3 can in the case of oxygen acids and carbon acids of moderate acidity such as acetone, acetaldehyde, and acetonitrile yield values for the gas-phase stabilities of ion-dipole complexes that are qualitatively or even quantitatively reasonable by comparison with experiment or *ab initio* calculations. They overestimate the stabilities of complexes between simple carbon acids and their conjugate bases. Both methods usually overestimate barriers to proton transfers from oxygen to oxygen, and underestimate the barriers for carbon-to-carbon proton transfers. Of the two, PM3 seems to do somewhat better on well depths and AM1 on barriers heights.

One is forced to conclude that the semiempirical methods cannot be relied upon to give quantitative accounts of the energy profiles of gas-phase proton transfers. On the other hand, they can often serve as qualitative or semiquantitative models under circumstances where high-level *ab initio* calculations are impractical. These circumstances include large systems such as benzyl anion + toluene or phenoxide + phenol, and smaller systems where detailed investigation of the energy surface is required.

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SAŽETAK

Poluiskustveno istraživanje reakcija prijenosa protona

William H. Saunders, Jr.

Provedena su semiempirijska (AM1 i PM3) istraživanja reakcija prijenosa protona. Izračunane su entalpijske razlike među odvojenim reaktantima i ion-dipolnim kompleksom, kao i među kompleksom i prijelaznim stanjem. Suprotno eksperimentalnim opažanjima u otopini, iz usporedbe prijenosa protona među ugljkovim s onim među kisikovim atomima slijedi neobičan zaključak, da je barijera viša u drugom slučaju. Pouzdanost semiempirijskih proračuna visinâ barijere procijenjena je usporedbom ovih vrijednosti s eksperimentalnima i onima izračunanim metodama *ab initio*.