

Linear Free Energy Relationship and Kinetic Isotope Effects as Measures for the Transition State Variation. A Computational Study

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Linear free energy relationship (LFER) and kinetic isotope effects (KIEs) are frequently used experimental means to study reaction mechanisms, in particular the nature of transition states (TSs). Density functional theory (B3LYP/6-311+G**) calculations were carried out on a model reaction, acid-catalyzed ionization of phenylethyl alcohol, to analyze how experimentally observable properties, such as nonlinearity in the Hammett and Brønsted relations and variation in KIE, are related to a variation of the transition state structure and the mechanism. Several conclusions and insights were obtained: (1) Linear Hammett plots with a dual parameter treatment may not be evidence for an invariable TS structure for a series of reactions. (2) Variations of KIEs indeed reflect the variations of TS structures. (3) Nonlinear Brønsted plots cannot always be taken as evidence for a stepwise mechanism. (4) A TS structure in the gas phase may change much more easily than a TS structure in solution.

Introduction

Among traditional experimental means in physical organic chemistry, kinetic isotope effects (KIEs) and linear free energy relationship (LFER) have most frequently been used in studying organic reaction mechanism. Information on the transition state (TS) structure may be obtained from KIEs, especially used with a successive labeling technique, in which KIEs at multiple positions are measured for a given reaction.^{1–3} This technique allows one to induce the TS structure and to detect its variation for a series of related reactions. On the other hand, LFER provides information whether a series of reactions proceed via a same mechanism, presumably through similar TS structures.⁴

The Brønsted and Hammett relationships are the most frequently used LFER. The Brønsted equation relates the

substituent effects on a proton-transfer rate to those on an acid–base equilibrium, but it has also been used for an elementary reaction in general. A slope in a Brønsted plot normally shows a value between 0.0 and 1.0, although in some cases it is outside of the range; one such case is deprotonation of nitroalkane, well-known as a nitroalkane anomaly.^{5–9} Traditionally, the slope has been taken as a measure of the TS position along the reaction coordinate, under the implicit assumption that all reactions examined follow the same TS structure. Curved Brønsted plots can be obtained for a multistep reaction where the rate-determining step shifts with a substituent, and in fact, many experimentally observed curved plots have been taken as evidence for the change of the rate-determining step.^{10–15} However, when a TS structure varies along the reaction coordinate for a series of

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reactions, the Brønsted plot would also be curved, concave downward, giving a larger tangent for less reactive substrates and a smaller tangent for more reactive substrates.^{16,17}

Curved Hammett plots have been discussed in terms of a shift of the rate-determining step in a multistep reaction (concave downward curve) or of a variation of the reaction mechanism in a competitive reaction scheme (concave upward curve).^{18–21} However, except for the S_N1/S_N2 and the E2 borderline cases of benzylic systems, where substituents on the central carbon readily change the structure of the three-centered or four-centered TS,^{20,21} an unequivocal example of nonlinear Hammett plots due to a variation of the TS structure is rare. There are two possible reasons: first, substituents used in a Hammett treatment are often too small perturbation to induce TS variation detectable by a linear correlation, and second, a dual-parameter treatment, such as the Yukawa–Tsuno²² or Taft²³ treatment, can make an otherwise curved response linear.²⁴ Here fundamental questions arise in several ways: (1) whether and to what extent the TS structure varies with substituents for a series of reactions, (2) how such TS variations can be detected by KIE and LFER, and (3) can a curved Brønsted plot be taken as evidence for a shift of the rate-determining step for a multistep reaction as frequently argued in recent publications?^{10–13}

We report here ab initio MO and DFT computational results on KIEs and substituent effects for the k_A ionization reaction of a phenylethyl system for which the rate in solution and the equilibrium in the gas phase have been studied experimentally.^{25,26} The present study clearly

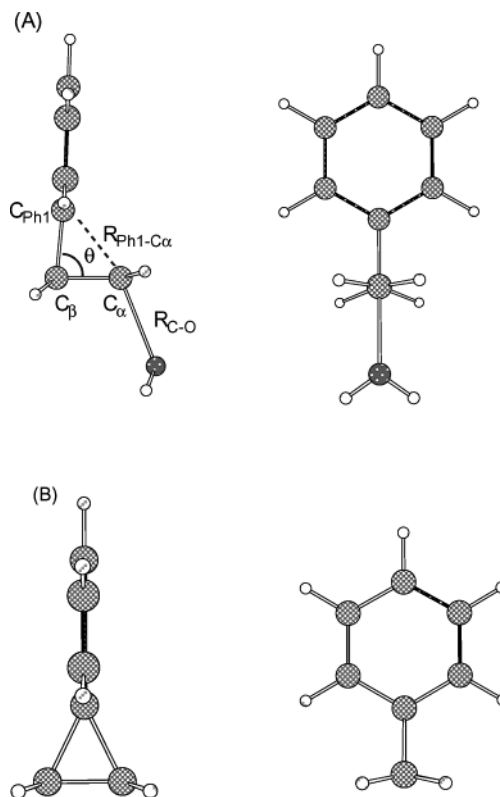


FIGURE 1. Structures of (A) the TS and (B) the phenonium ion of the parent compound.

indicated that substituents on the migrating phenyl ring changed the TS structure and that such variation in the structure can be detected by KIEs and the Brønsted plot but not by the Hammett plot with a dual-parameter method.²⁷

Calculations and Results

The reaction considered in this study is shown in eq 1. Kinetic experiments in the literature have been done with arenesulfonate leaving groups in acidic media,²⁵ but to make the computation feasible, we used substituted phenylethyl alcohols as reactants, which, upon protonation, gave the final products, substituted phenonium ions plus water, in two consecutive steps. The choice of the system would be justified since the purpose of this study is not to calculate exact rate constants but to reproduce experimental trends and then to analyze the variation of the TS structures, KIEs, and reactivities with substituents. Substituted 2-phenylethyl alcohols, protonated 2-phenylethyl alcohols, TSs, and phenonium cations were fully optimized at the HF/6-31G*, B3LYP/6-31G*, B3LYP/6-311+G**, and MP2/6-31G* levels of theory with the Gaussian 98 suite of programs.²⁸ Full frequency analyses were carried out to confirm that the optimized structures were minima or saddle points. Thermochemical quantities such as entropy, enthalpy, and free energy were calculated from harmonic frequencies. The substituent

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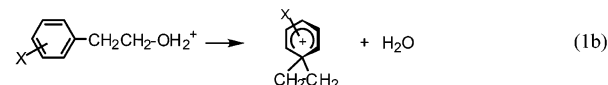
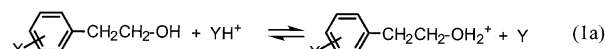
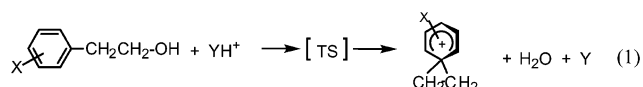
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TABLE 1. Structural Parameters of X-Substituted Phenonium Ions and TSs, Together with Selected Natural Population at Reactants, TSs, and Phenonium Ions^a

X	TS			phenonium ion		q_{Ar}^b			
	$R_{C-O} (n_{C-O})$	$R_{Ph1-C\alpha} (n_{Ph1-C\alpha})$	θ	$R_{Ph1-C\alpha}$	θ	reactant	TS	ion ^c	$\Delta q^e/\Delta q^d$
<i>p</i> -OMe	1.774 (0.32)	2.278 (0.08)	98.4	1.595	63.0	0.129	0.238	0.607	0.23
<i>p</i> -OH	1.824 (0.27)	2.245 (0.09)	96.6	1.600	63.2	0.121	0.253	0.591	0.28
<i>p</i> -Me	1.897 (0.21)	2.199 (0.10)	94.1	1.616	63.6	0.108	0.285	0.554	0.40
<i>m</i> -Me	1.942 (0.18)	2.172 (0.11)	92.7	1.628	63.9	0.103	0.299	0.530	0.46
H	1.973 (0.16)	2.152 (0.12)	91.6	1.631	64.0	0.099	0.306	0.521	0.49
<i>m</i> -OH	1.976 (0.16)	2.157 (0.12)	91.9	1.637	64.1	0.099	0.304	0.509	0.50
<i>p</i> -Cl	1.958 (0.17)	2.164 (0.11)	92.3	1.619	63.7	0.093	0.295	0.542	0.45
<i>m</i> -CHO	2.030 (0.13)	2.120 (0.13)	89.9	1.633	64.0	0.087	0.308	0.510	0.52
<i>m</i> -Cl	2.034 (0.13)	2.118 (0.13)	89.8	1.636	64.1	0.085	0.312	0.503	0.54
<i>p</i> -CHO	2.057 (0.12)	2.106 (0.14)	89.3	1.637	64.1	0.085	0.319	0.505	0.56
<i>m</i> -CN	2.099 (0.11)	2.080 (0.15)	87.9	1.641	64.2	0.076	0.330	0.487	0.62
<i>p</i> -CN	2.080 (0.11)	2.094 (0.14)	88.6	1.636	64.1	0.080	0.326	0.502	0.58
<i>m</i> -NO ₂	2.115 (0.10)	2.070 (0.16)	87.3	1.642	64.3	0.073	0.335	0.482	0.64
<i>p</i> -NO ₂	2.137 (0.09)	2.061 (0.16)	86.9	1.647	64.4	0.074	0.338	0.478	0.65

^a Structural parameters are at B3LYP/6-311+G**, and charges, at B3LYP/6-31G*. R refers to the bond length in Å, n is the Pauling bond order (see text), and θ is the bond angle at $C_\alpha-C_\beta-C_{Ph1}$ in degree. ^b Group positive charge on the $X-C_6H_4$ moiety based on natural population analysis. ^c Phenonium ion. ^d Change of the group positive charge between the reactant and the TS relative to that between the reactant and the phenonium ion.

effects on the stability of the phenonium ion were experimentally determined for bromide transfer reactions between substituted phenylethyl bromides and phenonium ions.²⁶ The results are compared with the substituent effects on the hydroxide transfer between phenylethyl alcohol and the phenonium ion.



Structures of Phenonium Ion and TS. Reactions of all substituted phenylethyl alcohols gave a symmetrical phenonium ion with the aromatic ring on the symmetry plane at all computational methods employed. In the TS as well as in the phenonium ion, the aromatic ring is bisected by the $C_\alpha-C_\beta-C_{Ph1}$ plane. The structures of the TS and the phenonium ion for the parent compound are schematically shown in Figure 1. Table 1 lists selected structural parameters of substituted phenonium ion and the TSs, together with a selected natural population. The table also lists the bond orders calculated according to the conventional Pauling's bond order–bond length expression (eq 2),²⁹

$$R = R^0 - 0.3 \ln n \quad (2)$$

where R and R^0 refer to bond lengths with bond order n and 1.0, respectively. It was found that the theory of calculations did not change much the phenonium ion structure. The structures of the TS depend slightly on the method; for example, for the parent compound, R_{C-O} and angle θ ($C_\alpha-C_\beta-C_{Ph1}$) at the TS are 2.15 Å and 84.6° (B3LYP/6-31G*), 2.00 Å and 85.8° (MP2/6-31G*), and 1.97 Å and 91.6° (B3LYP/6-311+G**), respectively. Substitution on the migrating phenyl ring did not change the phenonium ion structure much, although it did change the TS structure. Structural changes of phenylethyl alcohol and protonated phenylethyl alcohol with substituents or computational methods are small.

Activation and Reaction Energies. Table 2 listed the enthalpy and the free energy (in parentheses) for reaction 1 calculated at the different levels of theory for the parent as well as the *p*-OMe and *p*-NO₂ substituted substrates. It can be seen that at all levels of theory the difference between enthalpy and free energy does not depend on the substituent for the reaction energy, whereas the difference is substituent dependent for the activation energy. This is probably because the size of the entropy and hence the free energy depend much on low frequencies, which are less reliable than higher frequencies especially for compounds with weak interactions such as TS. In the present study, we used enthalpy in our discussion throughout. In Table 3 were summarized the activation and reaction enthalpies calculated for 14 different substituents at the HF/6-31G*, B3LYP/6-31G*, MP2/6-31G*, and B3LYP/6-311+G** levels of theory. As the proton source (YH^+) for the initial protonation equilibrium, we used protonated water trimer rather than the bare proton, but the choice of the proton source does not affect the substituent effects because the energy required for the proton transfer from the proton source is canceled out for different substituents. It is interesting to note that the activation barriers happened

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TABLE 2. Calculated Activation Enthalpies (Free Energies in Parentheses) and Reaction Enthalpies (Free Energies) for the Parent as well as *p*-Substituted 2-Phenylethyl Alcohols at Different Levels of Theory

method	activation energy			reaction energy		
	<i>p</i> -OMe	H	<i>p</i> -NO ₂	<i>p</i> -OMe	H	<i>p</i> -NO ₂
HF/6-31G*	18.8 (19.4)	22.0 (21.9)	34.7 (33.3)	9.3 (0.8)	23.7 (14.9)	43.7 (34.1)
B3LYP/6-31G*	18.5 (20.7)	23.8 (24.9)	36.1 (35.9)	15.6 (7.9)	28.9 (21.0)	44.7 (36.4)
B3LYP/6-311+G**	17.3 (18.7)	21.2 (21.8)	32.3 (31.9)	8.8 (0.6)	21.9 (13.3)	37.8 (28.8)
MP2/6-31G*	22.0 (24.1)	26.1 (27.9)	<i>a</i>	16.7 (9.1)	28.8 (20.9)	41.4 (33.5)

^a Transition state could not be determined.**TABLE 3.** Substituent Effects on the Activation and Reaction Enthalpies for Reaction 1^a

substituent	activation enthalpy	reaction enthalpy
<i>p</i> -OMe	18.8, <i>18.5</i> (22.0) [17.3]	9.3, <i>15.6</i> (16.7) [8.8]
<i>p</i> -OH	20.0, <i>19.9</i> (23.5) [18.8]	12.7, <i>18.7</i> (20.0) [12.6]
<i>p</i> -Me	20.2, <i>21.0</i> (23.9) [18.8]	17.8, <i>23.3</i> (24.1) [15.9]
<i>m</i> -Me	21.0, <i>22.1</i> (24.5) [19.6]	22.1, <i>26.3</i> (25.9) [19.1]
H	22.0, <i>23.8</i> (26.1) [21.2]	23.7, <i>28.9</i> (28.8) [21.9]
<i>m</i> -OH	23.7, <i>24.0</i> (26.7) [22.0]	27.4, <i>29.0</i> (28.2) [22.5]
<i>p</i> -Cl	26.0, <i>26.7</i> (29.3) [23.8]	27.7, <i>31.0</i> (31.2) [23.2]
<i>m</i> -CHO	27.6, <i>29.9</i> (31.8) [27.2]	30.5, <i>36.4</i> (36.4) [29.6]
<i>m</i> -Cl	26.6, <i>28.4</i> (30.4) [25.0]	31.4, <i>35.3</i> (35.1) [27.7]
<i>p</i> -CHO	28.1, <i>30.3</i> (31.4) [27.4]	33.3, <i>37.4</i> (35.6) [30.6]
<i>m</i> -CN	30.9, <i>33.5</i> (35.2) [30.0]	37.1, <i>41.8</i> (41.9) [34.6]
<i>p</i> -CN	32.0, <i>33.4</i> (34.8) [30.2]	38.8, <i>41.1</i> (40.2) [34.0]
<i>m</i> -NO ₂	32.0, <i>34.3</i> (35.8) [30.9]	38.5, <i>42.8</i> (43.0) [35.9]
<i>p</i> -NO ₂	34.7, <i>36.1</i> (–) [32.3]	43.7, <i>44.7</i> (41.4) [37.8]

^a Values are at the HF/6-31G*, B3LYP/6-31G*, (MP2/6-31G*) and [B3LYP/6-311+G**] levels of theory and are in kcal/mol.

to be similar at HF/6-31G* and B3LYP/6-311+G**, whereas the barriers tend to be higher at the MP2 method. The effects of substituents on the activation and reaction enthalpies are qualitatively the same for all the methods. We used the results at B3LYP/6-311+G** throughout in the paper, since the TS for the *p*-NO₂ substituted compound could not be optimized at the MP2 level.

Isotope Effects. Kinetic isotope effects for the acid-catalyzed ionization reaction of substituted phenylethyl alcohols were calculated from the isotopic shifts of frequencies at B3LYP/6-311+G** after scaling with the factor of 0.96³¹ by using Bigeleisen's equation³² and listed in Table 4. The overall reaction (eq 1) consists of two steps: the protonation equilibrium step (eq 1a) precedes the ionization step (eq 1b). Numbers shown in italic are the equilibrium IEs (EIEs) for protonation of the alcohols (eq 1a). All these IEs are at 25 °C.

A limited number of KIEs have been measured for the solvolyses of substituted phenylethyl arenesulfonates in acid media.^{33,34} For example, in the formolysis, phenylethyl nosylate gave the Ph1 carbon-14 KIE of 1.023 at 60 °C and phenylethyl tosylate gave α - and β -deuterium KIE of 1.17 and 1.00, respectively, at 75.3 °C. For the

TABLE 4. Kinetic Isotope Effects Calculated at B3LYP/6-311+G** for Reaction 1^a

	<i>p</i> -OMe	<i>p</i> -OH	<i>p</i> -Me	H	<i>p</i> -Cl	<i>p</i> -CHO	<i>p</i> -CN	<i>p</i> -NO ₂
α - ¹⁴ C	1.105	1.108	1.108	1.108	1.108	1.107	1.107	1.105
	<i>1.055</i>	<i>1.050</i>	<i>1.047</i>	<i>1.041</i>	<i>1.042</i>	<i>1.039</i>	<i>1.039</i>	<i>1.036</i>
α -D ₂	0.978	0.985	1.015	1.048	1.040	1.083	1.086	1.104
	<i>0.921</i>	<i>0.905</i>	<i>0.899</i>	<i>0.898</i>	<i>0.892</i>	<i>0.898</i>	<i>0.889</i>	<i>0.887</i>
β - ¹⁴ C	1.013	1.013	1.014	1.015	1.013	1.013	1.015	1.016
	<i>1.006</i>	<i>1.005</i>	<i>1.006</i>	<i>1.005</i>	<i>1.006</i>	<i>1.005</i>	<i>1.006</i>	<i>1.005</i>
β -D ₂	0.974	0.976	0.972	0.972	0.970	0.969	0.972	0.971
	<i>0.980</i>	<i>0.986</i>	<i>0.989</i>	<i>0.986</i>	<i>0.989</i>	<i>0.986</i>	<i>0.988</i>	<i>0.987</i>
Ph1- ¹⁴ C	1.014	1.015	1.019	1.025	1.021	1.024	1.025	1.028
	<i>1.010</i>	<i>1.009</i>	<i>1.008</i>	<i>1.010</i>	<i>1.008</i>	<i>1.007</i>	<i>1.007</i>	<i>1.007</i>

^a Numbers in roman are the KIEs for the overall process (eq 1), and those in italic are the EIEs for the protonation of alcohol (eq 1a).

formolysis of *p*-methoxyphenylethyl tosylate, the carbon-14 KIEs at the phenyl-1, α - and β -positions, and the deuterium KIEs at the α and β positions were reported to be 1.022, 1.131, and 1.013, at 30 °C, and 1.20 and 0.97, at 50 °C, respectively. We did not expect exact agreement in the KIEs between theory and experiment because calculations were done for the reactions in the gas phase, whereas experiments were done in solution. Nevertheless, the agreement between the experimental and calculated KIEs is reasonably good in all positions, except for the deuterium KIE at the α -position. The protonation equilibrium showed normal (larger than unity) IEs (italicized numbers in Table 4) for all carbon isotopes. These EIEs are consistent with the structural variation upon protonation; that is, the protonation induced the change of the reactant structure on the way to the TS. Thus, for the parent compound, the protonation made the C α –O bond longer (1.429 to 1.611 Å), C β –C_{Ph1} bond longer (1.512 to 1.525 Å), and the C α –C β –C_{Ph1} angle smaller (112.3° to 105.2°). In contrast to these carbon EIEs, the deuterium EIEs on the protonation equilibrium were inverse, especially at the α -position. The α -D₂ EIEs became inverse because the protonation on the oxygen affects the strength and the mode of frequencies related to α -D. It is well-known that the magnitude of a secondary deuterium IE depends on the number of coordinates in which the deuterium atom is involved.³⁵ The α -D₂ KIE of the parent compound for the ionization step (eq 1b) was calculated to be 1.167, which is of reasonable magnitude for the KIE of this type of reaction, if one takes into account that the C–O bond is partly weakened upon protonation.

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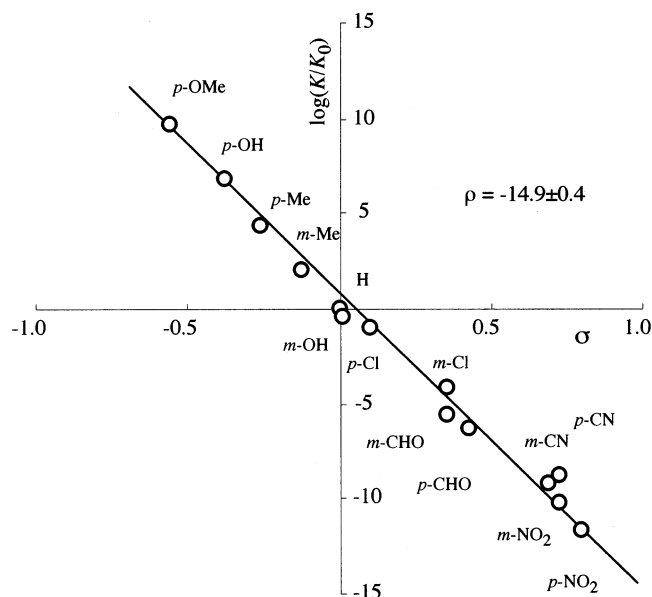


FIGURE 2. LArSR plot for the hydroxide transfer equilibrium of substituted phenylethyl alcohols and phenonium ions at 25 °C. $\rho = 14.9 \pm 0.4$, $r^+ = 0.65$.

Discussion

Substituent Effect on the Equilibrium Constant.

Linear aromatic substituent effect relationship (LArSR, eq 3), often called the Yukawa–Tsuno equation, has widely been used to analyze substituent effects on rates and equilibria.²² In eq 3, σ° is a normal substituent constant, the term $(\sigma^+ - \sigma^\circ)$ is the resonance substituent constant that measures the ability for π -delocalization of the π -electron donating substituent, and r^+ is a resonance demand parameter characteristic of a given reaction. This dual-parameter treatment allows one to examine the degree of exalted π -interaction between para π -donor substituents and a cationic reaction center.

$$\log(k/k_0) = \rho\{\sigma^\circ + r^+(\sigma^+ - \sigma^\circ)\} \quad (3)$$

Figure 2 shows the LArSR plots for the hydroxide transfer equilibrium of substituted phenylethyl alcohols. Substituent constants used in the present study are those derived from the gas-phase reactions.³⁶ The Hammett treatment gave a good straight line with the ρ value of -14.9 and the r^+ value of 0.65 . Thus, the degree of π -interaction relative to the polar/field effect of substituents (measure by the size of r^+) is larger than that for the ionization equilibrium of benzoic acid ($r^+ = 0.27$) and smaller than that for the ionization of cumyl chloride ($r^+ = 1.0$). Mishima and co-workers carried out gas-phase experiment on the bromide-transfer equilibrium between substituted phenylethyl bromides and phenonium ions with FT-ICR mass spectrometry and reported that the LArSR analysis of the stability of substituted phenonium ions gave a straight line correlation with $\rho = -12.6$ and $r^+ = 0.62$.²⁶ They argued that the magnitude of $r^+ = 0.62$ coincided with the r^+ value for the k_A solvolysis of

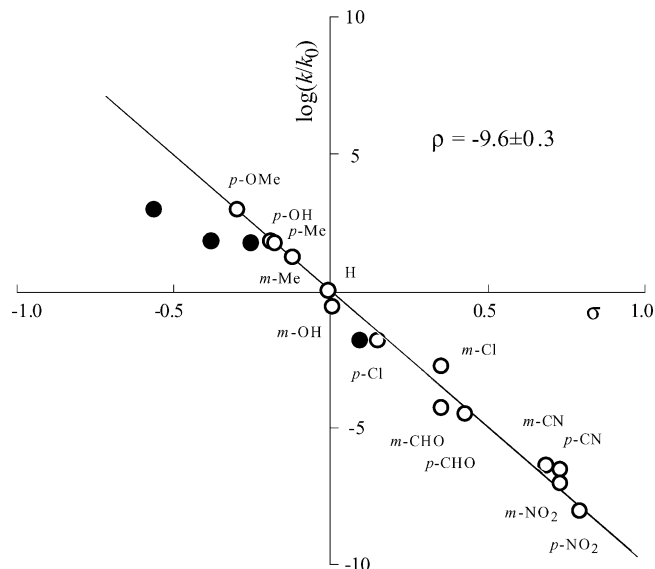


FIGURE 3. Substituent effects for the acid-catalyzed ionization of phenylethyl alcohol at 25 °C. Open circle with $r^+ = 0.27$ and filled circle with $r^+ = 0.65$.

2-ArCH₂CH₂OTs, indicating that the positive charge developed at the solvolysis TS leading to the phenonium ion is delocalized into the aromatic π -system in the same manner as that of the phenonium ion.^{25a} The calculated results on the hydroxide transfer and the previous experiment on the bromide transfer both in the gas phase gave similar r^+ values but slightly different ρ values. The small difference in ρ between the present calculation and the previous experiment may be due to the difference in the system (OH⁻ and Br⁻ transfer) and/or the limitation of the computational method. The important point here is that the straight-line correlation was observed with the extended Hammett treatment for the phenonium ion formation equilibrium in both the calculations and experiment with similar r^+ values.

Substituent Effect on the Reactivity. Calculated relative activation enthalpies for reaction 1 were converted to the $\log(k/k_0)$ scale at 25 °C as usually used in the Hammett correlation. The LArSR plot gave a reasonably good straight-line correlation with $r^+ = 0.27$ (Figure 3). The ρ value (-9.6) is smaller than that for the corresponding gas-phase equilibrium (-14.9 , Figure 2). Analogous LArSR plots for the rate constants of the k_A acetolysis of substituted 2-phenylethyl tosylates have been reported to give a straight line with $\rho = -3.87$ and $r^+ = 0.63$ at 115 °C.^{25a} Thus, the ρ value is much larger and the r^+ value is smaller in the gas-phase calculations than those in the solution experiment.

The LArSR analysis brought about three important mechanistic points for the gas-phase reaction. First, the linear correlation indicated that the reaction proceeded through the same mechanism for all substituted substrates. Second, the electronic effect of substituents on the stability of the TS is smaller ($\sim 64\%$) than that of the phenonium ion judging from the relative magnitude of the ρ values. This may be interpreted in terms of the TS position of roughly two-thirds along the reaction coordinate. The third and the most important point is that the r^+ value for the reaction is smaller than that for the equilibrium, in sharp contrast to the solvolysis reaction,

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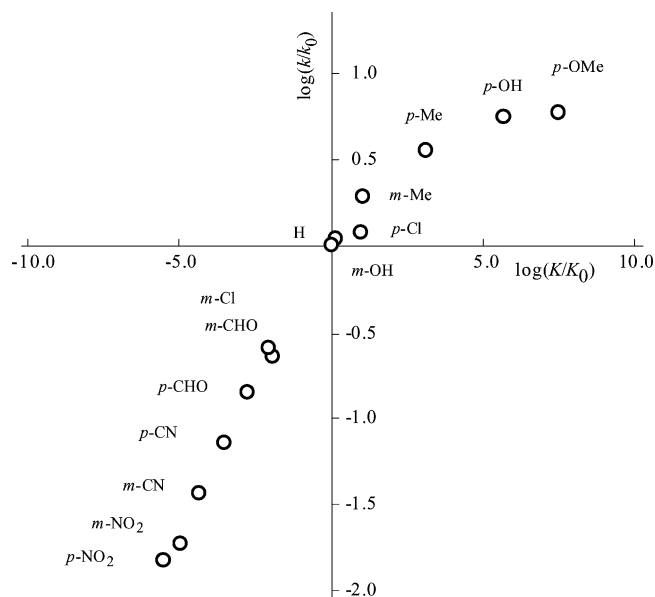


FIGURE 4. Brønsted relation for the ionization of protonated phenylethyl alcohol to phenonium ion at 25 °C.

which gave the r^+ value similar to that for the gas-phase equilibrium. If we plot the substituent effects on the ionization rates against the apparent σ values with $r^+ = 0.65$, the value that gave good correlation for the hydroxide transfer equilibrium, a curved plot is obtained with para electron-donating substituents (p -OMe, p -OH, p -Me, and p -Cl) deviate downward from the correlation line. The results, at first glance, appear to suggest that the relative contribution of the para electron-donating resonance effect over the polar/field effect is smaller at the TS than at the phenonium ion. However, the results may be related to variation of the TS structures with substituent as discussed below.

Brønsted-Type Plot. To apply the Brønsted-type relation to the present system, we took the elementary process of ionization of protonated phenylethyl alcohols to phenonium ions (eq 1b), and the substituent effects on the rate were plotted against those of the equilibrium in Figure 4. A curved correlation, concave downward, was obtained with a larger tangent slope for a less reactive reactant with a more electron-withdrawing substituent. The slopes calculated with the seven least reactive compounds (p -NO₂, m -NO₂, p -CN, m -CN, p -CHO, m -Cl, and m -CHO) and the three most reactive compounds (p -OMe, p -OH, and p -Me) are 0.36 and 0.05, respectively. Analogous treatment for the overall process (acid-catalyzed ionization, eq 1.) gave the slopes of 0.66 and 0.32 for the less reactive and more reactive sets of compounds, respectively, although the latter plot is not a real Brønsted-type treatment because this is a multi-step process. The biphasic correlation reflects the variation of the TS structure; the TS shifts from a product-like one to a reactant-like one when the substituent becomes more electron donating.

Substituent Effect on KIEs. Kinetic isotope effects are one of the most useful experimental methods for detecting variation of TS structure.¹ The variation of the TS structure suggested by LFER above should be reflected in the KIEs, and in turn, if one could measure the KIEs for the present reaction, one should observe

variations of the KIEs with substituents. The calculated KIEs in Table 4 indeed vary with substituents as expected. The Ph1-¹⁴C KIE is most straightforward in that it changes monotonically when the position of the TS changes along the reaction coordinate with a larger value for a later TS. A smaller Ph1-¹⁴C KIE (1.014) for $X = p$ -OMe and a larger one (1.028) for $X = p$ -NO₂ indicate that the TS lies earlier for a substrate with a more electron-donating substituent. The magnitude of α -D₂ KIE depends on the total bonding to C _{α} , and it is larger when the total bonding is smaller (looser TS). On the other hand, the magnitude of α -¹⁴C KIE depends on the balance (relative strength) of the two reacting bonds at the TS for an S_N2-type reaction, like the one considered in the present study, where one bond forms at the expense of another bond. The calculated KIEs at the α -position suggested that the total bond strength at the TS is larger with a more electron-donating substituent and the strength of the two reacting bonds (C_{Ph1}-C _{α} and C _{α} -O bonds) is less balanced for both electron-donating and -withdrawing sides (p -OMe and p -NO₂). Such trends in the TS structure were indeed observed in the calculations as shown below. The β -¹⁴C KIE increased slightly with a more electron-withdrawing substituent, consistent with a later TS with this substituent change. The deuterium KIEs at the β -position did not show appreciable variations.

Variations of the TS Structures. As Table 1 shows, the structure of the three-membered ring in the phenonium ion did not change much with substituents; the three-membered ring became slightly tighter with a more electron-donating substituent. In contrast, the C-O bond length (R_{C-O}) at the TS varied considerably with the substituent, from 1.77 Å for $X = p$ -OMe to 2.14 Å for $X = p$ -NO₂. The change of the C _{α} -C _{β} -C_{Ph1} angle (θ) is also large from 98° ($X = p$ -OMe) to 87° ($X = p$ -NO₂). Thus, the TS structure becomes more reactant-like with a more electron-donating substituent. These variations can more clearly be seen in Figure 5, where the C-O and C _{α} -C_{Ph1} bond orders were plotted against the reaction enthalpy. The group charge on the aromatic moiety becomes more positive in the reactant alcohol and in the phenonium ion with a more electron-donating substituent, which is consistent with the nature of the substituent. In contrast, the reverse trend was observed for the TS; the aromatic ring is more positively charged with a more electron-withdrawing substituent. The results can be rationalized in terms of the shift of the TS along the reaction coordinate. Thus, the TS lies later along the reaction coordinate, and the structure is closer to the phenonium ion with a more electron-withdrawing substituent. The ratio of the change of the group charge on the aromatic ring on going from the reactant to the TS over the corresponding change between the reactant and the phenonium ion ($\Delta q^\ddagger/\Delta q$) may be taken as a measure of the position of the TS along the reaction coordinate. The values in Table 1 clearly indicate the variation of the TS position with the substituent in the manner consistent with the Hammond postulate.³⁷

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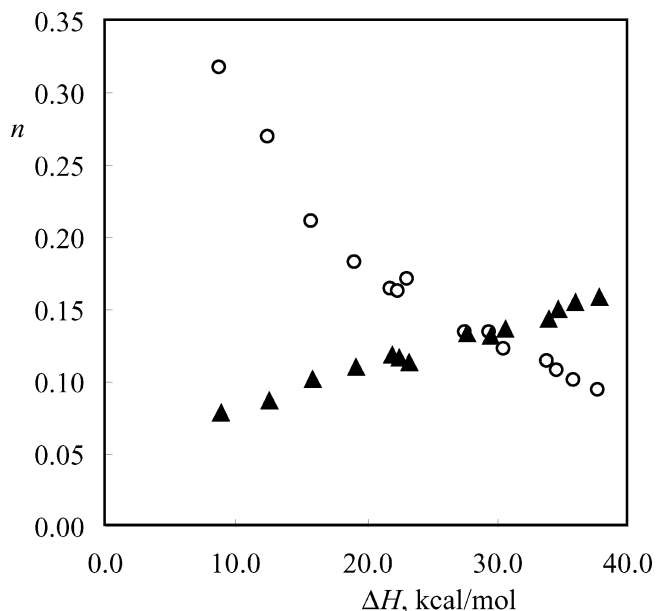


FIGURE 5. Variation of the TS bond orders vs the reaction enthalpy. Open circles refer to $n_{\text{C-O}}$ and closed triangles denote $n_{\text{C}\alpha\text{-Ph1}}$.

Concluding Remarks

The computational results shown above can be summarized as follows. First, analyses of the substituent effects by means of the dual-parameter treatment (LArSR) gave straight lines for both the rate and the equilibrium of the gas-phase acid-catalyzed ionization process. The fact can be taken as evidence that the reaction follows a single mechanism regardless of the substituent. Second, the Brønsted plot for the ionization of the protonated alcohols gave a curved correlation, consistent with the variation of the TS according to the reactivity of the substrate within the same mechanistic framework. Third, the KIEs varied with substituent in a manner consistent with the TS variations with a more reactant-like structure for a more reactive substrate. Fourth, the calculated TS structures confirmed the TS variation expected from the Brønsted plot and the KIEs.

One of the important messages from the results is that a linear Hammett correlation on rates can arise even though the TS varies with substituent. The linearity in the present reaction was attained probably because the dual-parameter treatment masked a possible curvature of the plot. On the other hand, it should be noted that if a single-parameter treatment with an appropriate set of σ values was used, a curved Hammett plot was obtained, just like in the Brønsted plot. Thus, caution should be paid in the use of a dual-parameter treatment for estimating the TS structure and its variation from LFER

analyses. The fact that the Brønsted plot gave a curved correlation raises another point of interest. In the literature, a curved or biphasic plot has often been taken as evidence for a shift of the rate-determining step in a multistep process.¹³ In other words, a single concerted mechanism has often been expected to give a straight-line correlation. However, the present study clearly indicated that such an argument may not be true in some cases and that a curved Brønsted plot can arise from a variable TS.

Finally, comments should be given as to why the r^+ values in the gas phase and in solution were different for the k_{A} ionization reactions. A similar magnitude of the r^+ value for the solvolysis to that in the gas-phase equilibrium may arise from a substituent-independent TS structure in solvolysis. Here, the positive charge is delocalized into the aromatic π -system at the TS in a manner similar to that of the phenonium ion.²⁶ On the other hand, the small r^+ value in the gas-phase reaction is considered to arise from the change of the TS structure with substituent. A more reactive substrate has a more reactant-like TS, and thus the effect of the substituent becomes smaller. Such a TS variation should result in a curved correlation if a single-parameter correlation is used as in the Brønsted plot, but the curvature can be masked in the dual-parameter treatment by a gradual change of the relative importance of the two parameters with substituent. This constant/variable TS structure argument is supported by the substituent effect on the Ph1-¹⁴C KIE; that is, the experimental Ph1-¹⁴C KIE in solution is nearly substituent independent (1.022 for X = OMe and 1.023 for X = H), whereas the calculated Ph1-¹⁴C KIE in the gas phase is 1.014 for X = OMe and 1.025 for X = H. Clearly the TS varies with substituent in the gas phase, whereas it does not change much in solution, probably due to a large variation of the activation energy in the gas phase as well as a multiple interaction mechanism available in the solution phase.

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Supporting Information Available: Optimized Cartesian coordinates, enthalpy, and reaction coordinate frequencies (for TS) for substituted phenylethyl alcohols, protonated alcohols, TSs, and phenonium ions at B3LYP/6-311+G**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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