JOC The Journal of Organic Chemistry

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Density Functional Theory Study of Hydrogen Atom Abstraction from a Series of *para*-Substituted Phenols: Why is the Hammett σ_p^+ Constant Able to Represent Radical Reaction Rates?

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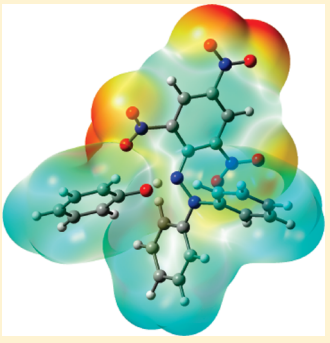
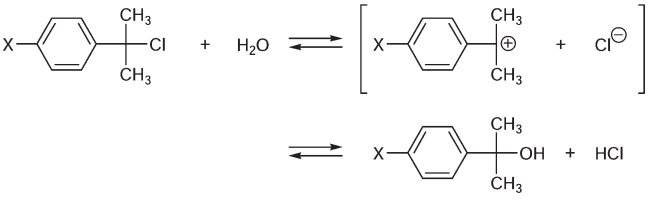
Supporting Information

ABSTRACT: The rate of hydrogen atom abstraction from phenolic compounds by a radical is known to be often linear with the Hammett substitution constant σ^+, defined using the S_N1 solvolysis rates of substituted cumyl chlorides. Nevertheless, a physicochemical reason for the above "empirical fact" has not been fully revealed. The transition states of complexes between the 2,2-diphenyl-1-picrylhydrazyl radical (**dpph**·) and a series of *para*-substituted phenols were determined by DFT (Density Functional Theory) calculations, and then the activation energy as well as the homolytic bond dissociation energy of the O−H bond and charge distribution in the transition state were calculated. The heterolytic bond dissociation energy of the C−Cl bond and charge distribution in the corresponding *para*-substituted cumyl chlorides were calculated in parallel. Excellent correlations among σ^+, charge distribution, and activation and bond dissociation energies revealed quantitatively that there is a strong similarity between the two reactions, showing that the electron-deficiency of the π-electron system conjugated with a substituent plays a crucial role in determining rates of the two reactions. The results provide a new insight into and physicochemical understanding of σ^+ in the hydrogen abstraction from substituted phenols by a radical.



INTRODUCTION

A number of quantitative structure−activity relationship (QSAR) studies on the antioxidant, enzymatic and cellular toxic activities of phenolic compounds have been reported by Hansch and Selassie and their co-workers.[1−7] The biological and chemical activities of phenolic compounds are attributed to the radical scavenging function of their phenolic hydroxyl groups (O−H). Mulder et al.[8] revealed that the H (hydrogen)-atom (H·) abstraction rates for a series of substituted phenolic compounds are correlated with the Hammett electronic substituent constant, sigma plus σ^+.

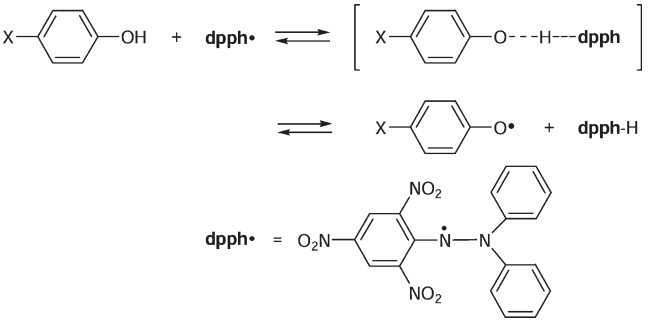


The Hammett σ^+ constant is defined using the S_N1 solvolysis rates (in 90% acetone/water at 298 K) of a series of *para* and *meta*-substituted cumyl chlorides, as expressed by eq I.[9] As Hansch et al. reported, σ^+ often becomes statistically significant in QSAR equations, when radical reactions are involved.

$$\log(k/k_0) = \rho\sigma^+ \qquad \text{(I)}$$

where the reaction constant ρ is taken to be −4.54. k and k_0 are rate constants of substituted and unsubstituted (X = H) cumyl chlorides, respectively.

In the case where σ^+ represents the relative rate of homolytic cleavage of an O−H bond, it has been known that the homolytic bond dissociation energy of the O−H bond (BDE(O−H)) follows the Hammett relationship as shown in eq II.[4,5,7,8,10−14]



However, the reason for the colinearity between σ^+ and BDE(O−H) is still not necessarily obvious.

$$BDE(\text{O}-\text{H}) = a\sigma^+ + \text{const} \qquad \text{(II)}$$

BDE(O−H) has been recognized to be a useful descriptor in QSAR analyses of antioxidants such as flavonoids and tocopherols,

Received: March 1, 2011
Published: April 18, 2011

Table 1. E_a, BDE_v(O−H), and *CT* Values for the H-Atom Abstraction from 13 *para*-Substituted Phenols by dpph· (Reaction A)

compound							
No.	X	σ_p^{+} [a]	σ_p [a]	E_a [b]	BDE_v(O−H) [b]	CT_v(X−Ph−O)^{MPA} [c]	CT_v(X−Ph−O)^{NPA} [c]
1a	$N(CH_3)_2$	−1.70	−0.83	0.63	75.5	0.032	−0.114
2a	NH_2	−1.30	−0.66	3.19	76.7	−0.022	−0.167
3a	CH_3O	−0.78	−0.27	6.49	79.6	−0.132	−0.274
4a	CH_3	−0.31	−0.17	9.55	83.0	−0.203	−0.341
5a	*t*-Bu	−0.26	−0.20	9.72	83.4	−0.200	−0.340
6a	Ph	−0.18	−0.01	8.93	82.8	−0.190	−0.326
7a	F	−0.07	0.06	9.70	83.3	−0.244	−0.386
8a	H	0.00	0.00	11.04	85.2	−0.244	−0.381
9a	Cl	0.11	0.23	9.98	84.1	−0.273	−0.411
10a	Br	0.15	0.23	10.00	84.3	−0.252	−0.407
11a	CF_3	0.61	0.54	11.83	87.9	−0.335	−0.467
12a	CN	0.66	0.66	11.02	87.3	−0.363	−0.493
13a	NO_2	0.79	0.78	11.44	89.3	−0.410	−0.536

[a] Taken from ref 51. [b] In kcal/mol. BDE_v denotes *BDE* in vacuum. [c] In esu. MPA and NPA denote Mulliken and natural population analyses, respectively. CT_v denotes *CT* in vacuum.

where it is generally difficult to apply σ^+ because of their skeletal structures and substitution patterns.

Because *BDE*(O−H) is an important descriptor for characterizing the radical scavenging activities of phenols, several experimental studies have been performed to measure *BDE*(O−H)s.[10,15−18] Also, a number of DFT (Density Functional Theory) calculations of *BDE*(O−H) of substituted phenols have been reported. The calculated *BDE*(O−H) values of phenols in the vacuum and solvent phases are known to nicely reproduce the corresponding experimental ones with considerable accuracy.[19−24] *BDE*(O−H) calculations explain that phenols with O−H groups in their *ortho*-positions, that is, cathecol and pyrogallol, can exhibit high free radical scavenging activity.[10,21,25−29]

Several H-atom abstraction mechanisms such as the hydrogen atom transfer (HAT) and proton-coupled electron transfer (PCET) ones[30−33] have been proposed based on theoretical calculations of the transition state (TS) according to each reaction mechanism. Using theoretical calculations, Foti et al.[34] showed that the reaction of phenols with 2,2-diphenyl-1-picrylhydrazyl radical (**dpph**·), where the structure of TS complex has no symmetry, occurs via a single pathway by a mechanism that has both HAT and PCET character. Ingold and his co-workers have energetically investigated the H-atom abstraction mechanism for a series of substituted phenols by **dpph**· by means of both experimental and theoretical approaches. Their publications have covered a broad range of research topics such as the solvent and inter/intramolecular hydrogen-bonding effects on the H-atom abstraction reaction for phenols.[14,27,29,34−43]

A linear relation between the activation energy (E_a) and *BDE*(O−H) (known as the Evans−Polanyi rule[44,45]), expressed by eq III, can be expected for a series of reactions of **dpph**· with substituted phenols.

$$E_a = \alpha BDE(\mathrm{O{-}H}) + \mathrm{const} \qquad \text{(III)}$$

As a result, the rate constant for H-atom abstraction is supposed to be linear with σ^+. Nevertheless, the reason for the linearity between σ^+ and the intrinsic reaction rate has not yet been fully elucidated in terms of the electronic structure of the reacting species involved in the reaction.

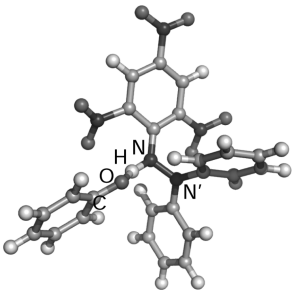
The Hammett σ^+ constant has been widely applied to express substitution effects on a variety of aromatic side-chain reactions during S_N1 benzylic solvolysis, where a positive charge on an aromatic ring conjugated with a substituent is generated.[46,47] Despite different categories of reaction mechanisms (radicalic and ionic reactions, that is, homolytic and heterolytic bond cleavage for H-atom abstraction and solvolysis, respectively), similarity in the electron-deficient intermediate structure between the two reactions, (**A**) H-atom abstraction from substituted phenols by **dpph**· and (**B**) benzylic S_N1 solvolysis, is expected to exist.

In this study, we examine the electronic structures of the TS complexes between **dpph**· and a series of 13 *para*-substituted phenols, using DFT calculations. In comparison with the electronic structures of the corresponding *para*-substituted cumyl chlorides in Reaction **B**, we quantitatively discuss why σ_p^{+} (σ^+ for substituents at the *para* position) can represent the reaction rate constant of Reaction **A**.

COMPUTATIONAL METHODS

All calculations were carried out using DFT with Gaussian09 package of programs.[48] The geometry of the TS complexes between **dpph**· and 13 *para*-substituted phenols, as well as those of the reactants and products in Reaction **A**, was fully optimized at the (U)B3LYP/6-31G(d) level. Following the geometry optimization, normal mode calculations were performed using the same basis set. Each TS complex was confirmed to have only one imaginary vibrational frequency mode. The activation energy (E_a) with *ZPE* (Zero-Point vibrational Energy) correction as well as the homolytic bond dissociation energy (BDE_v(O−H)) in vacuum with thermal energy correction (*ZPE*, translational, rotational, and vibrational contributions at 298 K) for Reaction **A** were calculated at the (U)B3LYP/6-311++G(2d,2p)//(U)B3LYP/6-31G(d) level (in vacuum), where a scaling factor of 0.9806[49] was used for the *ZPE* and thermal energy corrections. The heterolytic bond dissociation energy (BDE_w(C−Cl)) in water with thermal energy correction for Reaction **B** in the aqueous phase was calculated at the same level (optimized structure in vacuum) by means of CPCM (Conductor-like Polarizable Continuum Model (in water)) calculations.[50]

dx.doi.org/10.1021/jo200450p |*J. Org. Chem.* 2011, 76, 4564–4570



R_{TS}(O–H) = 1.232 Å (0.970)[1]
R_{TS}(N–H) = 1.242 Å (1.019)[2]
θ(O–H–N) = 158.9°
θ(C–O–H) = 121.4° (108.9)[1]
θ(N′–N–H) = 106.0° (118.8)[2]
φ(C–O–H–N) = −166.9°
φ(O–H–N–N′) = 52.4°

Figure 1. Structure of TS complex between and Compound **8a** (X = H) and **dpph**·. Values 1 and 2 in parentheses are corresponding ones in the reactant **8a** and the product **dpph**−H, respectively.

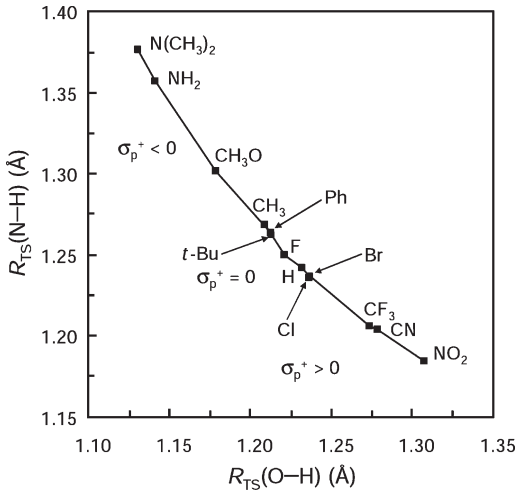


Figure 2. Plot between R_{TS}(O−H) and R_{TS}(N−H). R_{TS}(O−H) and R_{TS}(N−H) in TS complexes of **dpph**· with 13 *para*-substituted phenols are atomic distances from the phenolic hydrogen atom to the phenolic oxygen atom and to the nitrogen atom in **dpph**· (Ph−O---H---N−**dpph**), respectively.

RESULTS AND DISCUSSION

H-Atom Abstraction from *para*-Substituted Phenols by dpph· (Reaction A). By means of DFT calculations, we systematically determined the structure of the TS complex of **dpph**· with each of 13 *para*-substituted phenols in vacuum, as listed in Table 1, according to the structures reported by Foti et al.,[34] who computed TS complexes of **dpph**· with Compounds **3a** (X = OCH_3) and **8a** (X = H), as shown in Table 1.

The structure of the TS complex between **dpph**· and Compound **8a** is very close to the corresponding one reported by Foti et al., differences in bond lengths, bond angles, and dihedral angles between their and the present structures are within 0.0176 Å, 2.83, and 15.9 degrees, respectively. Figure 1 shows the structure of the TS complex between **dpph**· and Compound **8a** with major geometric parameters.

Figure 2 shows a plot of two crucially important distances in the structures of the TS complex between **dpph**· with Compounds **1a**−**13a**, R_{TS}(O−H) and R_{TS}(N−H), which are those from the phenolic hydrogen atom to the phenolic oxygen atom and to the nitrogen atom in **dpph**·, respectively. R_{TS}(O−H) and R_{TS}(N−H) synchronously vary in a correlative manner (r (correlation coefficient) = −0.985). As σ_p^+ decreases, R_{TS}(O−H) and R_{TS}(N−H) decrease and increase, respectively.

Table 2. Correlation Equations for the H-atom Abstraction from 13 *para*-Substituted Phenols by dpph· (Reaction A)

$Y = a\,X + const$ (n = 13)

eq no.	Y	X	a	$const$	r^a	s^b	F^c
T2−1a	E_a	σ_p^+	4.33	9.49	0.949	1.10	99.4
T2−1b	E_a	σ_p	6.14	8.56	0.869	1.73	34.0
T2−2a	BDE_v(O−H)	σ_p^+	5.47	84.2	0.988	0.661	442
T2−2b	BDE_v(O−H)	σ_p	8.21	83.0	0.958	1.21	124

[a] Correlation coefficient. [b] Standard deviation. [c] Ratio of regression and residual variances.

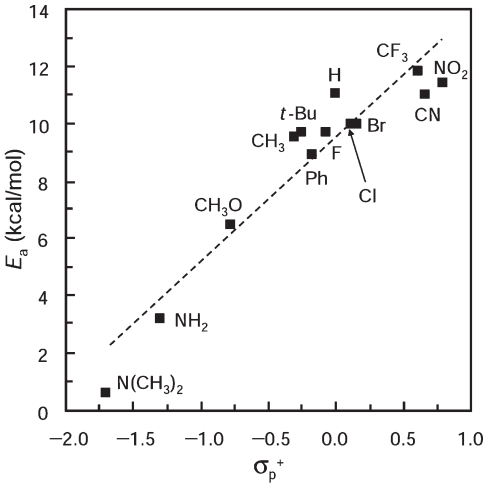


Figure 3. Plot between σ_p^+ and E_a. The dotted line is the regression line expressed by eq T2−1a in Table 2.

The activation energy, E_a, of the reaction between each compound with **dpph**· is listed in Table 1 along with the homolytic bond dissociation energy of the O−H bond, BDE_v(O−H). The calculated E_a value of Compound **8a**, 11.04 kcal/mol, is 1.5∼1.0 kcal/mol larger than the calculated and measured ones reported by Foti et al.,[34] 9.5 and 9.8 kcal/mol, respectively. However, the relative energy value (e.g., $\Delta E_a(X) = E_a(X) - E_a(X = H)$) is probably reliable enough to examine the linearity with other relative quantities for the congeneric series of compounds used in this study.

As expected, σ_p^+ exhibits a nicer correlation with E_a (r = 0.949) than the Hammett constant σ_p defined from the ionization constant of a *para*-substituted benzoic acid in water at 298 K (r = 0.869), as summarized in Table 2. This result was very similar when other DFT calculations such as B971[52] and M06−2X[53] functionals with the same basis set (6-311++G(2d,2p)//6-31G(d)) were performed.

BDE_v(O−H) values listed in Table 1 are in close agreement with observed and calculated ones reported in a number of publications.[8,13,19,24] BDE_w(O−H) values calculated with B971 and M06−2X functionals are very similar with that with B3LYP (Table S1 in Supporting Information). σ_p^+ also exhibits nicer correlation with BDE_v(O−H) (r = 0.988) than σ_p (r = 0.958), as can be seen in eqs T2−2a and T2−2b (Table 2).

The relation among R_{TS}(O−H), R_{TS}(N−H), and σ_p^+, illustrated in Figure 2, is now well explainable with the Hammond postulate:[54] the smaller BDE_v(O−H) is (negative σ_p^+), the more TS resembles the reactant (shorter R_{TS}(O−H)), and the

dx.doi.org/10.1021/jo200450p |J. Org. Chem. 2011, 76, 4564–4570

Table 3. BDE_w(C−Cl) and *CT* Values for the S_N1 Solvolysis of 13 *para*-Substituted Cumyl Chlorides (Reaction B)

compound no.	X	σ_p^{+} [a]	σ_p [a]	BDE_w(C−Cl) [b]	CT_w(X−Ph−C(CH$_3$)$_2$)^{MPA} [c]	CT_w(X−Ph−C(CH$_3$)$_2$)^{NPA} [c]
1b	N(CH$_3$)$_2$	−1.70	−0.83	−7.1	0.196	0.177
2b	NH$_2$	−1.30	−0.66	−5.2	0.191	0.172
3b	CH$_3$O	−0.78	−0.27	2.6	0.181	0.163
4b	CH$_3$	−0.31	−0.17	7.1	0.175	0.156
5b	*t*-Bu	−0.26	−0.20	7.3	0.175	0.156
6b	Ph	−0.18	−0.01	8.0	0.170	0.152
7b	F	−0.07	0.06	10.2	0.169	0.151
8b	H	0.00	0.00	10.4	0.170	0.152
9b	Cl	0.11	0.23	11.4	0.162	0.145
10b	Br	0.15	0.23	11.6	0.162	0.145
11b	CF$_3$	0.61	0.54	15.9	0.157	0.140
12b	CN	0.66	0.66	16.8	0.150	0.134
13b	NO$_2$	0.79	0.78	18.6	0.146	0.131

[a] Taken from ref 51. [b] In kcal/mol. BDE_w denotes *BDE* in water. [c] In esu. MPA and NPA denote Mulliken and natural population analyses, respectively. CT_w denotes *CT* in water.

larger BDE_v(O−H) is (positive σ_p^{+}), the more TS resembles the product (shorter R_{TS}(N−H)). In fact, BDE_v(O−H) exhibits positive and negative correlations with R_{TS}(O−H) and R_{TS}-(N−H), respectively (r = 0.990 and −0.990).

As can be seen in Figure 3, the E_a values are significantly deviated from the regression line shown by the dotted line (r = 0.949), and appear to asymptotically approach a certain value when $\sigma_p^{+} > 0.5$. This may possibly correspond to a bilinear behavior of log k against BDE_v(O−H).[45] There are several conceivable reasons for why the linearity of σ_p^{+} with E_a is poorer than that with BDE_v(O−H). One of them is probably the present assumption that the pre-exponential factor (frequency factor) before the exp($-E_a/RT$) term in the expression of rate constant (k) takes a constant value common for all the H-atom abstraction from Compounds **1a**∼**13a** by **dpph**·. Strictly speaking, the relative value of pre-exponential factor is determined by the partition functions of each reactant (Compounds **1a**∼**13a**) and the corresponding TS, and the curvature of potential energy surface at TS.[32] Accordingly, the linearity of σ_p^{+} with E_a probably becomes worse. Also, it should be noted that solvation processes associated with the intrinsic H-abstraction are involved in the rate-determining step,[39−42,55,56] when correlation analysis of E_a and the observed apparent rate constant in a solvent is perfo-rmed.

The correlation between the E_a and BDE_v(O−H) values in Table 1 nicely satisfies the Evans−Polanyi rule expressed by eq III.

$$E_a = 0.780\,BDE_v(\mathrm{O-H}) - 56.22$$
$$n = 13, r = 0.964, s = 1.14, F = 93.5 \qquad (1)$$

The coefficient value of BDE_v(O−H), 0.780, is within the empirically acceptable range for the Evans−Polanyi relation (0 < α < 1 in eq III).[57] Equation 1 suggests that BDE_v(O−H) is able to effectively represent the H-atom abstraction reaction rate for phenolic compounds such as flavonoids.

S_N1 solvolysis of *para*-substituted cumyl chlorides (Reaction B). We selected and calculated a series of substituted cumyl chlorides, each of which has a *para*-substituent identical to that of the corresponding phenol studied in the previous section. Table 3 lists the structures of 13 *para*-substituted cumyl chlorides along with the respective heterolytic (i.e., ionic) bond dissociation energies of the C−Cl bond (BDE_w(C−Cl)) in water. It is notable that BDE_w(C−Cl) takes a remarkably low energy value (−7.1∼18.6 kcal/mol). This is due to a large stabilization of energy (∼115 kcal/mol) arisen from hydration of the ionic products, X−Ph−C(CH$_3$)$_2^{+}$ and Cl^{-}.

As expected, BDE_w(C−Cl) shows a nearly perfect correlation with σ_p^{+} (r = 0.997). Meanwhile, the correlation coefficient with σ_p is slightly poorer (r = 0.976) than that with σ_p^{+}.

$$BDE_w(\mathrm{C-Cl}) = 10.5\,\sigma_p^{+} + 10.1$$
$$n = 13, r = 0.997, s = 0.670, F = 1587 \qquad (2)$$

Although it may be preferable to comparatively discuss the activation energy (E_a) difference between Reactions **A** and **B** quantitatively, it is difficult to computationally define an exact structure of a TS complex having a single imaginary vibrational frequency for Reaction **B** using the present continuous solvation model (CPCM), unless approaches such as those taken by Ruff et al.[58] (potential energy scan along the C−Cl distance) are performed. Alternatively, from the definition of σ_p^{+} in eq I, we assumed that the relative activation energy (ΔE_a(X) = E_a(X) − E_a(X = H)) is replaceable with $-2.303\,RT\,\rho\,\sigma_p^{+}$ (= 6.19 σ_p^{+} kcal/mol at 298 K), assuming k (rate constant) = const · exp($-E_a/RT$).

Hammett σ_p^{+} and Charge Distribution in Reactions A and B. The Hammond postulate suggests that the electronic structure of a TS complex for Reaction **B** resembles the reactant structure (X−Ph−C(CH$_3$)$_2$−Cl) more than that for Reaction **A**, because BDE_w(C−Cl) (−7.1∼18.6 kcal/mol) is much lower than BDE_v-(O−H) (75.5∼89.3 kcal/mol). Accordingly, we compared the electronic structure of a TS complex for Reaction **A** with that of the reactant structure for Reaction **B**.

Supposing a common characteristic charge distribution pattern, we focused on the (apparent) intramolecular charge transfer induced by a substituent in the TS complex and reactant structures for Reactions **A** and **B**, respectively. The level of charge transfer (*CT*) is defined as the sum of the net atomic charges of the leaving group having a substituted phenyl part in the reaction

dx.doi.org/10.1021/jo200450p |*J. Org. Chem.* 2011, 76, 4564–4570

Table 4. Correlation Equations between σ_p^+ and CT (Reactions A and B)

	$Y = a\,X + const$ (n = 13)						
eq no.	Y	X	a	$const$	r^a	s^b	F^c
T4−1a	$CT_v(X-Ph-O)^{MPA}$	σ_p^+	−0.169	−0.248	0.992	0.0162	703
T4−1b	$CT_v(X-Ph-O)^{NPA}$	σ_p^+	−0.163	−0.386	0.994	0.0143	841
T4−2a	$CT_w(X-Ph-C(CH_3)_2)^{MPA}$	σ_p^+	−0.0196	0.166	0.981	0.00300	276
T4−2b	$CT_w(X-Ph-C(CH_3)_2)^{NPA}$	σ_p^+	−0.0182	0.149	0.987	0.00229	407

[a] Correlation coefficient. [b] Standard deviation. [c] Ratio of regression and residual variances.

species: Reaction **A**, X−Ph−O in the TS complex [in vacuum, denoted as $CT_v(X-Ph-O)$] and Reaction **B**, X−Ph−$C(CH_3)_2$ in the reactant [in water, $CT_w(X-Ph-C(CH_3)_2)$]. Tables 1 and 3 list $CT_v(X-Ph-O)$ and $CT_w(X-Ph-C(CH_3)_2)$, respectively. The atomic charge is not a physically observable quantity, and the value depends on definitions and procedures including a choice of atomic orbital basis set functions. However, the results shown later are probably less influenced by the above problem, again because the colinearity between two relative quantities within a congeneric series of compounds was of major interest in this study. We performed two types of population analyses, Mulliken[59] and natural[60] population analyses (abbreviated as MPA and NPA, respectively), with B3LYP/6-31G(d) instead of B3LYP/6-311++G(2d,2p)//B3LYP/6-31G(d), because the addition of diffuse functions (denoted by a plus sign (+) in 6-311++G(2d,2p)) often makes it difficult to interpret the obtained charge distribution chemically.[60]

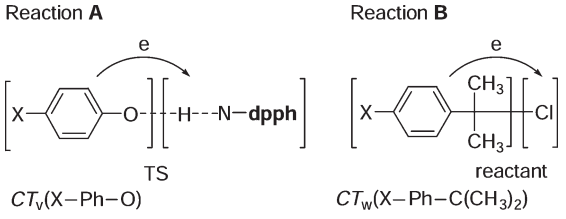


Table 4 lists the correlation equations of CT with σ_p^+, showing excellent correlations ($r > 0.98$). Equations T4−1a and T4−1b for Reaction **A**, as well as eqs T4−2a and T4−2b for Reaction **B**, give nearly the same coefficient and constant values with nearly equivalent statistical qualities. The excellent linearity of σ_p^+ with CT shown by eqs T4−1a and T4−1b and eqs T4−2a and T4−2b indicates that CT from the substituted phenyl into the remaining parts represents the relative reaction rate constant in both Reactions **A** and **B** quantitatively. Conversely, a *para*-substituent has a decisive effect on the charge distribution in the reaction intermediate, where the generation of an electron-deficient system conjugated with the substituent accelerates the reaction rate linearly depending on CT.

Comparison of the Relative *BDE*, E_a, and *CT* Values between Reactions A and B. For simplicity, the relative BDE_v(O−H) and BDE_w(C−Cl) values of Compounds **8a** and **8b** (X = H) are denoted as $\Delta BDE(\mathbf{A})$ and $\Delta BDE(\mathbf{B})$, respectively. Likewise, $\Delta E_a(\mathbf{A})$ and $\Delta E_a(\mathbf{B})$ are for Reactions **A** and **B**, respectively. $[CT_v(X-Ph-O)^{MPA} - CT_v(H-Ph-O)^{MPA}]$ of the TS complex and $[CT_w(X-Ph-C(CH_3)_2)^{MPA} - CT_w(H-Ph-C(CH_3)_2)^{MPA}]$ of the reactant are simplified as $\Delta CT_{TS}(\mathbf{A})$ and $\Delta CT_{RE}(\mathbf{B})$, respectively. Equations 3−5 are correlation equations between the above quantities in Reactions **A** and **B**.

$$\Delta BDE(\mathbf{A}) = 0.518\,\Delta BDE(\mathbf{B}) - 0.840 \quad n = 13, r = 0.987, s = 0.689, F = 407 \tag{3}$$

$$\Delta E_a(\mathbf{A}) = 0.700\,\Delta E_a(\mathbf{B}) - 1.55 \quad n = 13, r = 0.949, s = 1.10, F = 99.4 \tag{4}$$

$\Delta E_a(\mathbf{B})$ in eq 4 was estimated from the σ_p^+ value, as described previously.

$$\Delta CT_{TS}(\mathbf{A}) = 8.80\,\Delta CT_{RE}(\mathbf{B}) + 0.0251 \quad n = 13, r = 0.988, s = 0.0194, F = 451 \tag{5}$$

Equations 3 and 4 suggest that a strong similarity exists between Reactions **A** and **B** in terms of the substitution effects on both kinetic and equilibrium free-energy changes. From the experimental rate constants (k) of Compounds **3a**, **4a**, **5a**, and **8a** (in *n*-heptane) reported by Litwinienko et al.,[39] the ρ value for Reaction **A** is estimated to be −3.97 ($\log k = \rho\,\sigma_p^+ + \text{const}$, r = 0.999). The ratio of the ρ values between Reactions **A** and **B** gives 0.874 (= −3.97/−4.54), which is not so far from the coefficient value (0.700) in eq 4. The coefficient value (8.80) in eq 5 is remarkably greater than those in eqs 3 and 4. This seems to reflect differences in the susceptibility of the charge distribution to the reaction rate between Reactions **A** and **B**. At present, it is difficult to explain the large coefficient value of $\Delta CT_{RE}(\mathbf{B})$. Although Ruff et al.[58] reported $\Delta CT_{TS}(\mathbf{B})$ values ($\Delta CT(\mathbf{B})$ in TS) of *para*- and *meta*-monosubstituted cumyl chlorides, their procedure to determine TS (potential energy search along the C−Cl distance) is inadequate for quantitative discussion. More rigorous procedure to quantitatively discuss the electronic structure of TS for the S_N1 solvolysis of benzylic compounds is expected to appear in the near future.[61]

As noted above, eqs 3−5 quantitatively indicate a strong similarity in the substituent effects on the kinetic and equilibrium energetic profiles and charge distribution patterns between Reactions **A** and **B**. Thus, the linear free-energy principle (LFEP) represented by σ_p^+ is well applicable to Reaction **A**, which is usually considered to belong to a different category of reactions from that of the reference one, that is, Reaction **B**.

CONCLUSION

The present study shows a direct quantitative relation of σ_p^+ with the relative activation energy (ΔE_a) of the reactions between **dpph**· and a series of *para*-substituted phenols. The colinearity of the activation energy (E_a) with the homolytic bond dissociation energy of a phenolic O−H bond (BDE_v(O−H)) guaranteed the fact that BDE_v(O−H) is generally usable as a

dx.doi.org/10.1021/jo200450p |J. Org. Chem. 2011, 76, 4564–4570

significant descriptor that represents a radical reaction rate effectively in QSAR of phenolic compounds such as flavonoids and tocopherols.[28,62−72] Population analysis quantitatively indicated a strong similarity in the charge distribution between the transition state complexes of **dpph·** with *para*-substituted phenols and the reactants of the corresponding *para*-substituted cumyl chlorides, where a substituent effect on the π-electron system governs the reaction rate: the relative reaction rate constant in both reactions varies linearly depending on the level of substituent-induced intramolecular charge transfer between the leaving and remaining parts in the transition state and reactant structures for the H-atom abstraction from phenols and solvolysis of cumyl chlorides, respectively: generation of an electron-deficiency in the π-electron system accelerates the reaction rate. Differences between σ and σ^+ emerge remarkably in the strongly electron-deficient π-conjugated TS of the H-atom abstraction from phenols by **dpph·**. Consequently, σ^+ can represent the electronic structure of TS more adequately than σ, due to differences in the original definition between these two LFEP descriptors.

The results obtained in this study allow a new physicochemical understanding of "why σ^+ can represent the reaction rate of H-atom abstraction from phenolic compounds by a radical".

■ ASSOCIATED CONTENT

Supporting Information. Optimized Cartesian coordinates of TS complexes of **dpph·** with Compounds **1a**∼**13a** (Reaction **A**) and those of Compounds **1b**∼**13b** (Reaction **B**), along with additional information. Table S1 lists BDE_w(O−H) values calculated with B971/6-311++G(2d,2p)//B3LYP/6-31G(d) and M06−2X/6-311++G(2d,2p)//B3LYP/6-31G(d). This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENT

This work was supported by Grants-in-Aid for Scientific Research (No. 20590036) from the Ministry of Education, Culture, Sports, Science and Technology. We wish to thank Professor Toshio Fujita (Kyoto University, Japan) for his instructive suggestions.

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