

Theoretical studies on the base-catalysed rearrangement of 4,4'-disubstituted benzils in the gas phase and aqueous solution¹

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The base-catalysed rearrangements of disubstituted aryl benzils in the gas phase and in solution (water) have been investigated theoretically by the AM1 method. The solvent effects were accounted for using the Cramer–Truhlar SM2.1 solvation model. The calculated Gibbs free energy changes (ΔG^\ddagger) for the overall reactions (k_{obs}) are dissected into component parts, *i.e.* for the equilibrium step (K) of reactants \rightleftharpoons intermediate (ΔG_1^\ddagger) and rearrangement step (k_2) of intermediate \rightarrow transition state (ΔG_2^\ddagger); $\Delta G^\ddagger = \Delta G_1^\ddagger + \Delta G_2^\ddagger$. The Hammett ρ values for the migrating (ρ_X) and non-migrating rings (ρ_Y) are then calculated for each step. Thus, the overall $\rho(k_{\text{obs}})$ value can be dissected into two components, $\rho(K) + \rho(k_2)$. It has been shown that (i) the substituent effects of the 4,4'-disubstituted aryl benzils are not in general additive, $\rho(k_{\text{obs}}) \neq \rho_X + \rho_Y$, due to the cross-interaction term, ρ_{XY} , and (ii) in the gas phase, the equilibrium step is considerably more important than the rearrangement step, $\rho(K) \gg \rho(k_2)$, whereas in solution (water) the two steps contribute comparably, $\rho(K) \approx \rho(k_2)$. It is also notable that in the rearrangement step (k_2) the carbonyl carbon of the non-migrating ring actually becomes more electron-deficient [$\rho_Y(k_2) < 0$] on going from the intermediate to the transition state. This is in contrast to the migrating ring which becomes more electron-rich [$\rho_X(k_2) > 0$]. Fair agreement of the $\rho(k_{\text{obs}})$ values are obtained between those for the theoretical solution phase (6.7 in water) and for the experimentally observed [5.7 in 70% (v/v) aqueous Me_2SO] for the symmetrically disubstituted aryl benzils ($\sigma_X = \sigma_Y$).

The benzilic acid rearrangement involves the base-catalysed conversion of a 1,2-diketone **1** into an α -hydroxy carboxylic acid **4**. Scheme 1 shows the accepted pathway for pairs of substituted aryl groups (Ar_X and Ar_Y).² The reaction proceeds by reversible addition of a base, OH^- , to a carbonyl group (C^1) giving the intermediate **2**, followed by an intramolecular [1,2]-migration of a formally nucleophilic group (Ar_X^-) to the second carbonyl carbon (C^2) in the rate-determining step. The observable rate constant, k_{obs} , is composed of K , representing the equilibrium constant ($K = k_1/k_{-1}$), and the rate constant k_2 for the rate-limiting step, eqn. (1). The overall transition state

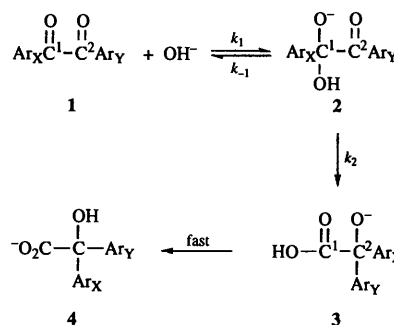
$$k_{\text{obs}} = Kk_2 \quad (1)$$

(TS) has been considered to resemble more closely the intermediate,^{2c,d} **2**. In disubstituted aryl (Ar_X and Ar_Y) benzils, electron-withdrawing substituents ($\delta\sigma > 0$) are known to accelerate and electron-donating substituents ($\delta\sigma < 0$) retard the rearrangement. The actual aryl group undergoing migration (Ar_X) has been determined by means of isotopic (¹⁴C) labelling in the monosubstituted benzils.^{2b} The aryl group (Ar_X) geminally attached to the OH group has been shown to migrate to the adjacent carbonyl carbon (C^2) with the non-migrating aryl group (Ar_Y). Bowden *et al.*^{2c,d} have shown that the Hammett ρ value for the symmetrically disubstituted ($\text{Ar}_X = \text{Ar}_Y$) benzils in 70% (v/v) aqueous Me_2SO is 5.70 using σ (and not 2σ) in the temperature range 30–60 °C. This ρ value for the overall rate process for the symmetrically disubstituted benzils (ρ_c) has been considered to reflect cumulative effects consisting of contributions from migrating ($\rho_X = 3.8_s$) and non-migrating ($\rho_Y = 1.8_s$) groups, eqn. (2). The breakdown of the cumulative

$$\rho_c = \rho_X + \rho_Y \quad (2)$$

ρ_c value into two contributing parts, eqn. (2), was estimated based on several model processes.

Rzepa and co-workers³ studied the mechanism of the benzilic acid and related rearrangements using the MNDO SCF–MO



Scheme 1

method. They considered also alternative classical anionic and single electron transfer (SET) pathways and the effects of substituents on these processes. The SET processes are found to have relatively high barriers and they concluded that a SET mechanism⁴ may apply to the migration of hydrogen rather than phenyl in the reaction of phenylglyoxal.

In this paper, we report a theoretical study on the base-catalysed rearrangement of 4,4'-disubstituted benzils using the AM1 SCF–MO procedure.⁵ This method has been shown to predict TS structures for a wide variety of molecular systems in reasonable accord with the results obtained from more time consuming *ab initio* calculations.⁶ Especially for the complex reaction systems, such as the one dealt with in this work, the use of the *ab initio* method is out of the question due to the excessive computer time required.

For disubstituted (X,Y) reaction systems, it has been shown that the cross-interaction constants, ρ_{XY} , are useful as a mechanistic tool for organic reactions in solution.⁷ A Taylor series expansion of $\log k_{XY}$ around $\sigma_X = \sigma_Y = 0$ leads to a simple second-order expression, eqn. (3a), assuming pure second order

$$\log(k_{XY}/k_{\text{HH}}) = \rho_X^0\sigma_X + \rho_Y^0\sigma_Y + \rho_{XY}\sigma_X\sigma_Y \quad (3a)$$

and higher order terms are negligible. In this equation, ρ_X^0 and

ρ_Y^0 represent ρ_X and ρ_Y values when $\sigma_Y = 0$ and $\sigma_X = 0$, respectively. The cross-interaction constant, ρ_{XY} , can be alternatively defined by eqn. (3b).

$$\rho_{XY} = \frac{\partial \rho_Y}{\partial \sigma_X} = \frac{\partial \rho_X}{\partial \sigma_Y} \quad (3b)$$

In this work, we aim to shed more light on the mechanism of the reaction (Scheme 1) by focusing specifically on the following two. (i) Our work in the past several years involving cross-interaction constants predict a non-additivity of the Hammett ρ value for a disubstituted reaction system,⁷ eqn. (4), in contrast

$$\rho_C \neq \rho_X + \rho_Y \quad (4)$$

to the additive cumulative effects assumed, eqn. (2), by previous workers.^{2c,d} Thus, theoretical determination of the cross-interaction constant, ρ_{XY} , should provide valuable mechanistic information.⁶ (ii) Experimentally obtained ρ_C (5.70) by Bowden *et al.*^{2c,d} represents the dependence of $\log(k_{XY})$ (for $X = Y$) upon σ_X , where k_{XY} is for the overall reaction pathway *i.e.* k_{obs} , and therefore is a complex quantity, eqn. (1). In other words, separation or decomposition of ρ_C (k_{obs}) into $\rho_C(K)$, $\rho_C(k_2)$, eqn. (5), was not possible experimentally. Since this

$$\rho_C(k_{obs}) = \rho_C(K) + \rho_C(k_2) \quad (5)$$

decomposition of $\rho_C(k_{obs})$ into its components is important in assessing the TS structure, we have carried it out theoretically.

We have varied the two substituents in the migrating phenyl (X) and non-migrating phenyl (Y) groups in **1** to give the symmetrically as well as non-symmetrically 4,4'-disubstituted benzils, with $X = Y = \text{CH}_3, \text{H}, \text{F}, \text{Cl}$ or NO_2 . In this work, we disregarded the SET mechanism.³

Calculations

Calculations were carried out using the standard AM1 procedure⁵ with full optimization of all geometric variables. All stationary points along the reaction coordinate were characterized by calculating the force-constant matrix and confirming all positive and only one negative eigenvalue for the intermediate and TS, respectively. Energetics are given in general terms of enthalpies (ΔH). However, in order to examine the free energy changes in aqueous solution, we calculated the entropy terms to give $\Delta G^\ddagger (= \Delta H^\ddagger - T\Delta S^\ddagger)$ for all the reactions of the substituted diaryl benzils. The solvent effects (in water) were accounted for by use of the SM2.1 model of the Cramer and Truhlar method.⁸ This quantum statistical continuum-dielectric model includes local-field terms representing solvent electric polarization, cavity creation, dispersion interaction, and change in solvent structure, and these terms are treated self-consistently with a solute electronic Hamiltonian. The free energy of solvation, ΔG_s° , calculated by this method is the difference between the gas-phase and the aqueous-phase free energies. Since in this model the SCF results are parametrized using experimental data, they implicitly include electron correlation and configuration mixing effects just as AM1 does for gas-phase solute energies. The empirical parametrization also allows for hydrophobic effects. In this work, we have done single point calculations with the gas-phase geometries due to the excessive computation times required.

Results and discussion

Gas-phase reaction

The benzoic acid rearrangement was found to be first order both in the benzil and hydroxide anion, proceeding stepwise as shown in Scheme 1;² thus the observed rate constant, k_{obs} , is a complex quantity, eqns. (6). The AM1 structures of reactant, **1**,

$$k_{obs} = \frac{k_1}{k_{-1} + k_2} k_2 \quad (6a)$$

$$\approx k_1, \text{ for } k_{-1} \ll k_2 \quad (6b)$$

$$\approx (k_1/k_{-1})k_2 = Kk_2, \text{ for } k_{-1} \gg k_2 \quad (6c)$$

intermediate, **2**, and the transition state (TS) involved in the rearrangement step, k_2 , and the rearranged product, **3**, are shown in Fig. 1 for some representative cases. Analysis of the total charges on the migrating ring and C-2 atom in the TS indicated that the greater the electronic charge on the migrating ring, the greater the positive charge on the C-2 atom, suggesting partial supply of the negative charge from the C_2 moiety. Moreover, the greater negative charge on the migrating ring is accompanied by a longer bond length of the two bonds between the migrating ring and C-1(d_1), and C-2(d_2) atoms, leading to a more stabilized TS with a lower activation barrier to the ring migration. Thus, when the substituent X is a stronger electron acceptor ($X = p\text{-NO}_2$) and Y is a stronger donor ($Y = p\text{-CH}_3$), the two bond lengths, d_1 and d_2 , are longest and the negative charge on the migrating ring and the positive charge on C-2 are greatest resulting in the most stabilized TS. These trends were the same both in the gas phase and in aqueous solution.

The energetics for the gas phase reactions are summarized in Table 1. Based on the calculated Gibbs free energy changes involved in the equilibrium step (ΔG_1°) and in the rate-limiting step (ΔG_1^\ddagger) of the rearrangement, the Hammett ρ values were evaluated at $T = 298$ K by using relations 7a and 7b. Such ρ

$$\rho(K) = \partial \log K / \partial \sigma = - \frac{1}{2.303RT} (\partial \Delta G_1^\circ / \partial \sigma) \quad (7a)$$

$$\rho(k_2) = \partial \log k_2 / \partial \sigma = \frac{1}{2.303RT} (\partial \Delta G_1^\ddagger / \partial \sigma) \quad (7b)$$

values, $\rho(K)$, $\rho(k_2)$ and $\rho(k_{obs})$, were each determined for the migrating ring substituent, σ_X , and non-migrating ring substituent σ_Y . In addition, from the changes in ρ_X with respect to σ_Y and/or in ρ_Y with respect to σ_X , eqn. (4b), the cross-interaction constants, ρ_{XY} , were derived.⁶ The sets of ρ values determined for the gas-phase reactions at 298 K are summarized in Table 2. Examination of Table 2 reveals that the ρ values for the migrating ring (ρ_X) are dependent on the substituent (Y) in the non-migrating ring and similarly the ρ_Y values are dependent on substituent X. On average, the $\rho_X(k_{obs})$ value is *ca.* 63% of the total value, $\rho(k_{obs}) = \rho_X(k_{obs}) + \rho_Y(k_{obs})$, and $\rho(K) = \rho_X(K) + \rho_Y(K)$ is *ca.* 90% of the total value, $\rho(k_{obs}) = \rho(K) + \rho(k_2)$. The former result shows that in the gas phase the effect of substituent on the non-migrating ring is also important (37%). In contrast the latter result indicates that the effects of substituents are largely reflected in the equilibrium step, *i.e.* addition of OH^- to benzils, and hence the overall TS should closely resemble the structure of the intermediate. This is due to the large exothermicity involved in the OH^- addition step, and hence in the gas phase $k_{obs} \approx k_1$ since $k_{-1} \ll k_2$, as given by eqn. (6b). This is also true for the symmetrically disubstituted case, *i.e.* $X = Y$, for which $\rho(K)$ (=13.0) is approximately 90% of the total, $\rho(k_{obs})$ *ca.* 14.7. When the $\rho(k_{obs})$ values are subjected to multiple regression analysis using eqn. (4a) with $\sigma_X = \sigma_Y$, we obtain eqn. (8). This result confirms that the effects

$$\begin{aligned} \log(k_{XY}/k_{HH}) &= \rho_X^0 \sigma_X + \rho_Y^0 \sigma_Y + \rho_{XY} \sigma_X \sigma_Y \\ &= [\rho_X^0 + \rho_Y^0 + \rho_{XY} \sigma] \sigma, \text{ for } \sigma_X = \sigma_Y \\ &= [15.2 \pm 0.04 - (1.1 \pm 0.08) \sigma] \sigma \quad (8) \\ (r &= 0.994) \end{aligned}$$

of substituents on the two rings, X and Y, are not additive as we have been advocating, which is in contrast to the additivity assumed for the experimental ρ values by Bowden and co-

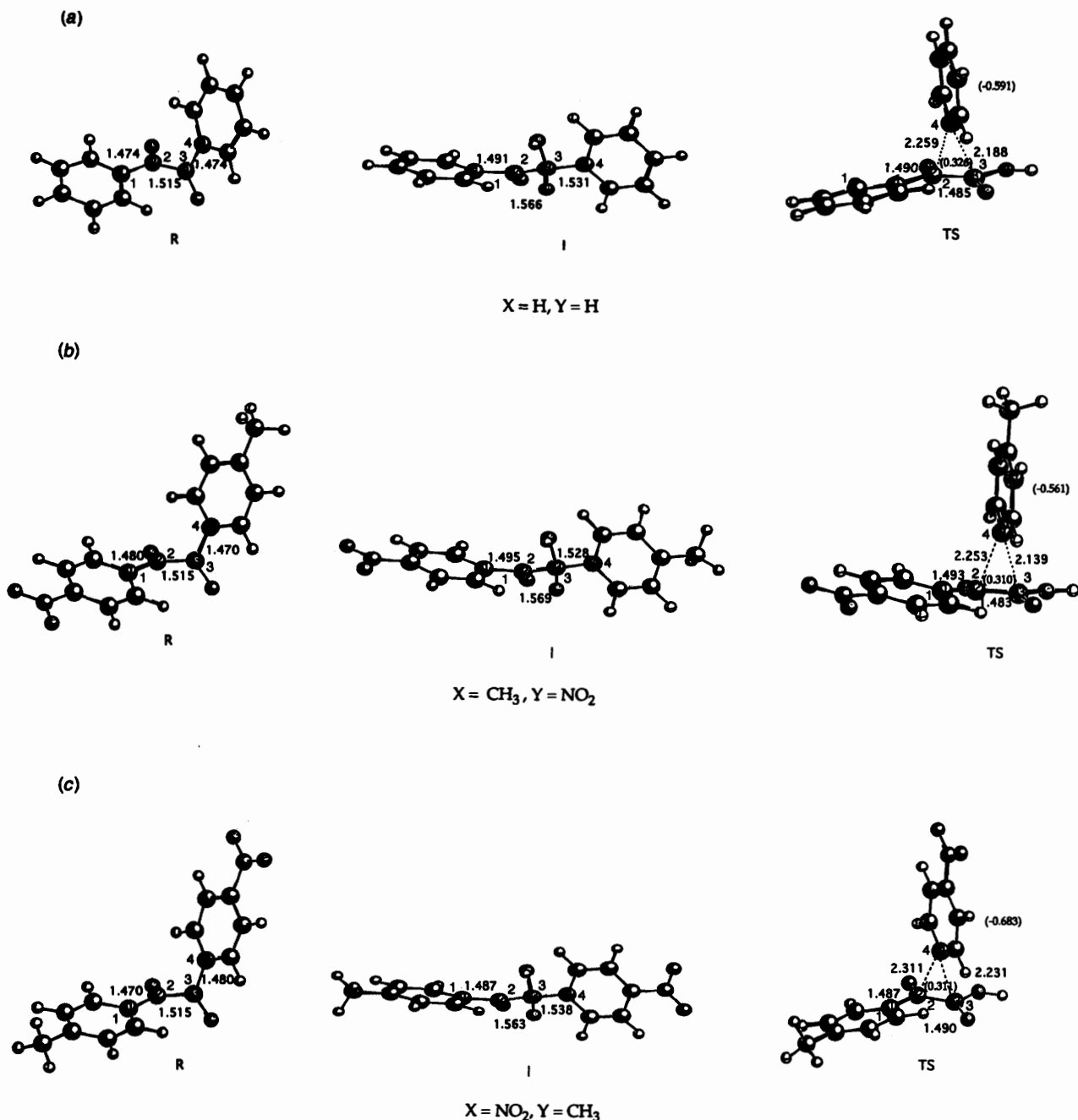


Fig. 1 Structures of reactants (R), intermediates (I) and transition states (TS). Bond length (Å) and charges (group charge on the migrating ring and charge on C-2 in electronic unit) are shown in parentheses.

workers.^{2c,d} The non-additivity is of course due to the cross-interaction between substituents X and Y, ρ_{XY} .⁷ Quite interesting features emerged in the results of Table 2 and eqn. (7) which are that (i) $\rho_Y(k_2)$ is negative. This means that in the migration of the X-ring, the carbonyl carbon on the non-migrating ring (Y) becomes more positively charged in the TS than that in the intermediate. This could be ascribed to a partial supply of the negative charge from the C-2 moiety in the TS or to the large negative charge carried by the migrating ring (X) inducing a partial positive charge on the carbonyl carbon on the Y-ring, and (ii) $\rho_{XY} = -1.1$ is not the simple ρ_{XY} obtained by using $\rho_{XY}(K)$ and $\rho_{XY}(k_2)$, i.e. $\rho_{XY}(k_{obs}) = \rho_{XY}(K) + \rho_{XY}(k_2) = -0.1 + (-0.5) = -0.6$. The ρ_{XY} value of -1.1 corresponds to twice of $\rho_{XY}(k_{obs})$ suggesting that the σ value used in eqn. (8) should be $2\sigma (= \sigma_X + \sigma_Y)$.

The $\rho(k_{obs})$ value of 14.7 for X = Y is ca. 2–3 times of the value experimentally observed (5.70) in 70% aqueous Me₂SO at 30.0 °C.^{2c,d} The dissection of the average $\rho(k_{obs})$ into average

ρ_X (63%) and ρ_Y (37%) is however in close agreement with that reported based on the experimentally derived values (67% vs. 33%).

Reactions in water

The energetics for the reactions in water calculated using the SM 2.1 model of Cramer and Truhlar⁸ are summarized in Table 3. The solvation energies (ΔG_{sol}) are given for the reactants, intermediates and TSs in Table 4. In contrast to the large exothermicity involved in the gas phase for the addition of OH⁻, the ΔG_1° values are small negative indicating a reversible nature of the addition of OH⁻ in solution with $k_{obs} = (k_1/k_{-1})k_2 = Kk_2$ [eqn. (1) = eqn. (6c)]. The Hammett ρ values for the reactions in solution (water) using eqns. (7a) and (7b) are collected in Table 5. We note that the $\rho_Y(k_2)$ values are all negative similarly to the negative values obtained in the gas phase (Table 2). Furthermore, the ρ values are in general greatly reduced; the

Table 1 Energetics (kcal mol⁻¹) for the gas-phase reactions (298 K)

Y	X	ΔH_f^a				$\Delta G_1^{o,b}$	$\Delta G_1^{\ddagger,c}$	$\Delta G_1^{\ddagger,d}$
		R	I	TS	P			
CH ₃	CH ₃	-35.84	-102.81	-76.51	-105.04	-56.22	25.98	-30.24
	H	-27.96	-95.36	-69.05	-97.59	-56.61	25.88	-30.73
	F	-73.05	-143.35	-118.56	-146.05	-59.48	24.31	-35.17
	Cl	-34.68	-105.13	-80.96	-108.06	-59.62	23.80	-35.80
H	NO ₂	-22.36	-100.39	-81.20	-105.11	-67.21	18.91	-48.29
	CH ₃	-27.96	-95.38	-69.04	-97.59	-56.79	26.17	-30.62
	H	-20.07	-87.92	-61.57	-90.13	-56.81	25.92	-30.88
	F	-65.14	-135.92	-111.08	-138.60	-59.78	24.36	-35.42
	Cl	-26.77	-97.70	-73.47	-100.61	-59.96	23.83	-36.13
F	NO ₂	-14.39	-92.96	-73.69	-97.66	-67.64	18.92	-48.72
	CH ₃	-73.05	-143.97	-116.90	-146.05	-60.13	26.80	-33.35
	H	-65.14	-136.51	-109.44	-138.60	-60.39	26.67	-33.72
	F	-110.15	-184.42	-158.80	-186.90	-63.23	25.16	-38.08
Cl	Cl	-71.78	-146.18	-121.17	-148.89	-63.42	24.61	-38.74
	NO ₂	-59.21	-141.20	-121.04	-145.59	-71.08	19.83	-51.26
	CH ₃	-34.68	-106.00	-78.67	-108.06	-60.51	27.03	-33.49
	H	-26.77	-98.54	-71.22	-100.61	-60.80	26.86	-33.94
NO ₂	F	-71.78	-146.43	-120.56	-148.89	-63.68	25.37	-38.32
	Cl	-33.41	-108.20	-82.91	-110.88	-63.82	24.92	-38.90
	NO ₂	-20.85	-103.17	-82.73	-107.53	-71.46	20.14	-51.33
	CH ₃	-22.36	-103.49	-73.83	-105.11	-70.21	28.73	-41.50
	H	-14.39	-96.01	-66.41	-97.66	-70.59	29.19	-41.40
	F	-59.21	-143.68	-115.37	-145.59	-73.44	27.80	-45.63
NO ₂	Cl	-20.85	-105.40	-77.63	-107.53	-73.47	27.26	-46.31
	NO ₂	-7.76	-99.74	-76.41	-103.31	-81.00	23.08	-57.92

^a Heat of formation: R = reactants; I = intermediate, TS = transition state, P = product. ^b $\Delta G_1^o = G_1 - G_R$; ($\Delta G = \Delta H - T\Delta S$). ^c $\Delta G_1^{\ddagger} = G_{TS} - G_1$. ^d $\Delta G^{\ddagger} = G_{TS} - G_R$.

Table 2 Calculated Hammett ρ_X and ρ_Y values for the gas-phase reaction at 298 K

X or Y	CH ₃	H	F	Cl	NO ₂
$\rho_X(K)^a$	5.73	5.75	5.76	5.74	5.62
$\rho_X(k_2)^a$	3.77	3.83	3.71	3.65	3.15
$\rho_X(k_{obs})^a$	9.50	9.58	9.47	9.40	8.77
$\rho_Y(K)^a$	7.32	7.39	7.37	7.35	7.32
$\rho_Y(k_2)^a$	-1.41	-1.76	-1.86	-1.84	-2.24
$\rho_Y(k_{obs})^a$	5.91	5.63	5.50	5.52	4.99
$\rho_X(k_{obs}) + \rho_Y(k_{obs})$	15.41	15.21	14.97	14.92	13.76

For X = Y^b: $\rho(K) = 13.01$, $\rho(k_2) = 1.51$, $\rho(k_{obs}) = 14.66$

ρ_{XY}^c : $\rho_{XY}(K) = -0.10$, $\rho_{XY}(k_2) = -0.48$, $\rho_{XY}(k_{obs}) = -0.58$

^a Correlation coefficients were better than 0.96 in all cases ($r \geq 0.96$).

^b $r \geq 0.98$. ^c $r \geq 0.93$.

average $\rho(k_{obs})$ value is now only 7.0. The $\rho(k_{obs})$ value for the symmetrically disubstituted benzylics is 6.7, which is much closer to the experimental value (5.70) obtained in 70% aqueous Me₂SO at 30.0 °C^{2c,d} compared with that in the gas phase of 14.7. Both $\rho(K)$ [$= \rho_X(K) + \rho_Y(K)$] and $\rho(k_2)$ are ca. 50% of the total $\rho(k_{obs})$ indicating that now the overall TS resembles to a lesser extent to the structure of the intermediate which is in contrast to that in the gas phase for which nearly 90% of the overall substituent effects, $\rho(k_{obs})$, was ascribable to the effects on the equilibrium step. On the other hand, in water the importance of the migration step, k_2 , is greatly increased; in the gas phase, $\rho_X(k_{obs})$ is ca. 63% of the total ρ [$= \rho_X(k_{obs}) + \rho_Y(k_{obs})$], whereas it is ca. 80% in water. This is actually in worse agreement with the experimentally estimated value of 68% in 70% aqueous Me₂SO at 30.0 °C for symmetrically disubstituted benzylics.^{2c,d} The poor agreement could be due to: (i) the difference in the medium *i.e.* water vs. 70% aqueous Me₂SO, or (ii) the inaccuracies in either the AM1-SM2.1 model calculation or in the experimentally estimated value using the reaction constants expected for the extreme structures for the TS for the reaction based on several model processes. For the symmetrically disubstituted case, $\sigma_X = \sigma_Y$, multiple regression

Table 3 Energetics^a for the reaction in water (298 K)

Y	X	$\Delta G_{1, sol}^{o,b}$	$\Delta G_{1, sol}^{\ddagger,c}$	$\Delta G_{sol}^{\ddagger,d}$
CH ₃	CH ₃	-0.37	30.10	29.73
	H	-0.12	29.39	29.27
	F	-0.26	26.28	26.02
	Cl	-1.13	26.44	25.31
H	NO ₂	-2.56	20.91	18.35
	CH ₃	-0.50	30.44	29.95
	H	-0.50	29.58	29.09
	F	-0.64	26.50	25.84
	Cl	-0.62	26.63	25.48
F	NO ₂	-2.37	21.07	18.70
	CH ₃	-1.37	30.70	29.33
	H	-1.51	29.87	28.35
	F	-1.55	26.93	25.38
Cl	Cl	-2.12	27.04	24.92
	NO ₂	-3.33	21.56	18.23
	CH ₃	-2.35	30.89	28.52
	H	-2.14	30.18	28.05
NO ₂	F	-2.24	27.15	24.90
	Cl	-2.73	27.33	24.58
	NO ₂	-4.03	21.83	17.80
	CH ₃	-5.79	31.77	25.98
	H	-5.37	31.73	26.36
	F	-5.47	28.82	23.35
Cl	Cl	-6.04	28.88	22.84
	NO ₂	-7.00	23.60	16.59

^a kcal mol⁻¹. ^{b-d}: Same as footnotes of in Table 1, except that the ΔG values include solvation energy changes.

of $\log k_{XY} = (-1/2.303RT)[\Delta G_{obs}^{\ddagger}]$, where $\Delta G_{obs}^{\ddagger} = \Delta G_1^o + \Delta G^{\ddagger}$, using eqn. 4(a) gave the result in eqn. (9). Here again the ρ_{XY} value of -1.1 is greater by a factor of 2 ($\rho_{XY} = -0.6$) calculated separately for each component of $\rho_{XY}(k_{obs}) = \rho_{XY}(K) + \rho_{XY}(k_2)$, $\rho_{XY}(K) (= -0.3)$ and $\rho_{XY}(k_2) (= -0.3)$. Eqn. (9) again shows the non-additivity of the substituent effects on the rates in the distributed reaction system. In the gas phase, cross-interaction between X and Y is very small in the equilibrium step, $\rho_{XY}(K) = -0.1$. This is consistent with the relatively small structural changes within disubstituted benzylics during the addition

Table 4 The solvation energy changes, ΔG_{sol} in kcal mol⁻¹

Y	X	R	I	TS
CH ₃	CH ₃	-113.63	-57.78	-53.66
	H	-114.21	-57.80	-54.29
	F	-112.58	-53.40	-51.42
	Cl	-113.61	-55.13	-52.49
H	NO ₂	-115.97	-51.32	-49.33
	CH ₃	-114.21	-58.00	-53.73
	H	-114.35	-58.04	-54.38
	F	-112.77	-53.63	-51.50
F	Cl	-114.15	-55.35	-52.55
	NO ₂	-116.80	-51.53	-49.38
	CH ₃	-112.58	-53.86	-49.96
	H	-112.77	-53.89	-50.70
Cl	F	-111.31	-49.62	-47.85
	Cl	-112.65	-51.34	-48.90
	NO ₂	-115.56	-47.80	-46.08
	CH ₃	-113.61	-55.46	-51.60
NO ₂	H	-114.51	-55.48	-52.16
	F	-112.65	-51.21	-49.43
	Cl	-114.01	-52.93	-50.53
	NO ₂	-116.84	-49.39	-47.70
NO ₂	CH ₃	-115.97	-51.55	-48.50
	H	-116.80	-51.58	-49.03
	F	-115.56	-47.59	-46.57
	Cl	-116.84	-49.30	-47.68
	NO ₂	-120.35	-46.36	-45.84

Table 5 Calculated Hammett ρ_X and ρ_Y values for the reaction in water at 298 K

X or Y	CH ₃	H	F	Cl	NO ₂
$\rho_X(K)^a$	1.28	1.03	1.06	1.00	0.80
$\rho_X(k_2)^a$	4.56	4.64	4.54	4.52	4.23
$\rho_X(k_{\text{obs}})^a$	5.85	5.68	5.59	5.51	5.03
$\rho_Y(K)^a$	2.91	2.72	2.71	2.64	2.44
$\rho_Y(k_2)^a$	-0.81	-1.23	-1.23	-1.27	-1.41
$\rho_Y(k_{\text{obs}})^a$	2.10	1.49	1.39	1.38	1.03
$\rho_X(k_{\text{obs}}) + \rho_Y(k_{\text{obs}})$	7.95	7.17	6.98	6.89	6.06

For X = Y^b: $\rho(K) = 3.56$, $\rho(k_2) = 3.16$, $\rho(k_{\text{obs}}) = 6.73$

ρ_{XY} : $\rho_{XY}(K) = -0.28$, $\rho_{XY}(k_2) = -0.28$, $\rho_{XY}(k_{\text{obs}}) = -0.55$

^a Correlation coefficients were better than 0.96 in all cases ($r \geq 0.96$).

^b $r \geq 0.93$. ^c $r \geq 0.92$.

step of OH⁻, **1** \longrightarrow **2**; ρ_{XY} represents the change in the intensity of interaction between the two substituents, X and Y, accompanied with the equilibrium step, **1** \longrightarrow **2**. However in solution, $\rho_{XY}(K)$ ($= -0.28$) is just as large as $\rho_{XY}(k_2)$. This is an indication that in solution, cross-interaction becomes large through the water.

$$\begin{aligned} \log(k_{XY}/k_{HH}) &= [\rho_X^0 + \rho_Y^0 + \rho_{XY}\sigma]\sigma \\ &= [7.3 \pm 0.2 - (1.1 \pm 0.3)\sigma]\sigma \quad (9) \\ (r &= 0.90) \end{aligned}$$

We can summarize our findings in this theoretical work as follows. The substituent effects [$\rho(k_{\text{obs}}) \approx 15$] are much greater in the gas phase, than in aqueous solution [$\rho(k_{\text{obs}}) \approx 7$]. The

contribution of the migrating step $\rho(k_2)$ to the overall effects [$\rho(k_{\text{obs}})$] increases to ca. 50% in the aqueous solution, in contrast to a mere 10% contribution in the gas phase. On the other hand, the contribution of the substituent effects in the migrating ring [$\rho_X(k_{\text{obs}})$] to the overall effects $\rho(k_{\text{obs}})$ [$= \rho_X(k_{\text{obs}}) + \rho_Y(k_{\text{obs}})$] increases substantially in water (ca. 80%) relative to that in the gas phase (ca. 65%). In effect, the contribution of both the migration step and the migrating ring becomes much more important in water than in the gas phase. This trend is in good accord with the experimental results in aqueous Me₂SO solution. The effects of two substituents in the two rings are not strictly additive due to the cross interaction, ρ_{XY} , between the two and can be correlated with the simple second-order expression, eqn. (4a), the applicability of which has been advocated by us for mechanistic elucidations of various types of organic reactions in solution.

Acknowledgements

We thank the Ministry of Education (BSRI-95-3428) and Inha University for support of this work. One of us (C. K. K.) also thanks Inha University for a Postdoctoral Fellowship. Also we thank Professor Kiyull Yang (Gyeongsang University) for the computer facilities of the AMSOL program.

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Paper 6/01310D

Received 23rd February 1996

Accepted 11th June 1996