

# Theoretical studies on the gas-phase nucleophilic substitution reactions of benzyl chlorides with phenoxides and thiophenoxides

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**ABSTRACT:** Gas-phase nucleophilic substitution reactions of Y-benzyl chlorides with X-phenoxide and X-thiophenoxide nucleophiles were investigated theoretically using the PM3 semi-empirical MO method. The Leffler–Grunwald rate-equilibrium and Brønsted correlations predict that the degree of bond formation in the transition state (TS) is approximately 45 and 40% on the reaction coordinate for the phenoxides and thiophenoxides, respectively. For a weaker nucleophile, a later TS is obtained with an increased bond making and breaking. The variation of the TS structure with substituents in the nucleophile is thermodynamically controlled and is well correlated by rate–equilibrium relationships. In contrast, the TS variation (a tighter TS) with substituent (for a stronger acceptor Y) in the substrate is dependent only on variations of the intrinsic barrier and so cannot be correlated by such thermodynamically based rate–equilibrium relationships. The gas phase  $\rho_X$  and  $\rho_Y$  values are much greater in magnitude than those in solution. A similar gas-phase theoretical cross-interaction constant,  $\rho_{XY}$  (ca  $-0.60$ ), is obtained for both phenoxides and thiophenoxides, which is in good agreement with the experimental value ( $-0.62$ ) for the thiophenoxide reactions in MeOH at 20.0 °C. The oxy and sulfur anion bases lead to a similar TS structure, but a lower reactivity for the former is due to a greater endothermicity of the reaction. A relatively wide range variation of the reaction energies,  $\Delta G^\circ$ , can be ascribed to the loss of resonance stabilization of anion nucleophiles upon product formation. © 1998 John Wiley & Sons, Ltd.

**KEYWORDS:** cross-interaction constants; gas-phase nucleophilic substitution reactions; PM3 MO; benzyl chlorides; phenoxides; thiophenoxides

## INTRODUCTION

$S_N2$  reactions have played a fundamental role in the development of modern physical organic chemistry.<sup>1</sup> Based on kinetic studies on the effects of substituents, detailed mechanisms and transition-state (TS) structures of the reactions have been characterized. In this regard, linear free energy relationships (LFER) have played a pivotal role.<sup>12</sup> Although first-derivative parameters, the Hammett  $\rho_i$  and Brønsted  $\beta_i$  as shown in equations (1) and (2), respectively, are often used to examine the TS structure, they have a limitation in their scope of application as a measure of TS structure;  $\rho_i$  (or  $\beta_i$ ) can be a measure of  $r_{ij}$  (Scheme 1) only when the other reaction center,  $R_j$ , remains constant, because the efficiency of charge transmission between reaction centers  $R_i$  and  $R_j$  in bond making and breaking may differ for different reaction series.<sup>3</sup>

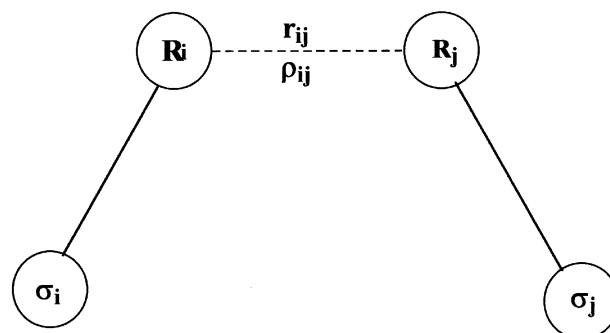
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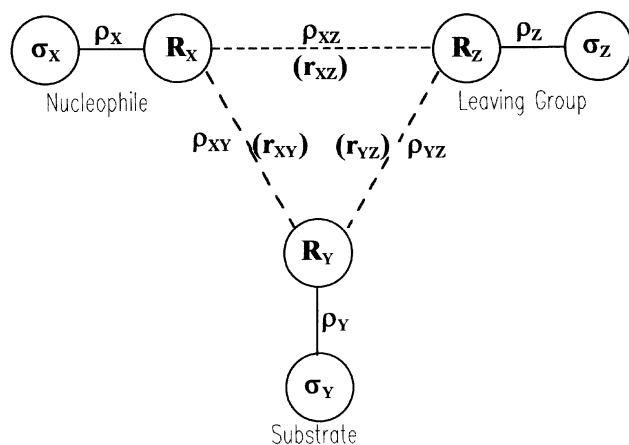
$$\rho_i = \partial \log k / \partial \sigma_i \quad (1)$$

$$\beta_i = \partial \log k / \partial pK_i \quad (2)$$

As a way of resolving this difficulty, we have introduced a second-derivative parameter, the cross-interaction constant,  $\rho_{ij}$ , in equation (3), which can be alternatively defined according to equation (4). A Taylor series expansion of  $\log k_{ij}$  around  $\sigma_i = \sigma_j = 0$  leads to a



Scheme 1.



Scheme 2.

simple second-order expression [equation (3)] with neglect of the pure second-order ( $\rho_{ii}$  and  $\rho_{jj}$ ) and higher order ( $\rho_{ijj}$ , etc.) terms. Here  $i$  and  $j$  represent any of three fragments, nucleophile (X), substrate (Y) and leaving group (Z) in Scheme 2, comprising a typical  $S_N2$  transition state.<sup>3</sup>

$$\log(k_{ij}/k_{HH}) = \rho_i\sigma_i + \rho_j\sigma_j + \rho_{ij}\sigma_i\sigma_j \quad (3)$$

$$\rho_{ij} = \partial^2 \log k_{ij} / \partial\sigma_i\partial\sigma_j = \partial\rho_j / \partial\sigma_i = \partial\rho_i / \partial\sigma_j \quad (4)$$

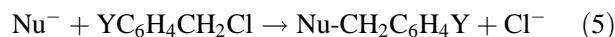
It has been shown that the magnitude of  $\rho_{XY}$  and  $\rho_{XZ}$  is inversely proportional to the distance,  $r_{XY}$  and  $r_{XZ}$ , respectively.<sup>34</sup> Moreover, we have shown that the  $\rho_{XZ}$  (and hence  $r_{XZ}$ , the tightness of the TS) is relatively constant and the TS tightness varies very little depending on the class of reaction,<sup>5</sup> at a primary carbon center the TS is tight with  $\rho_{XZ} \approx 0.33$ , but the TS for displacement at a secondary carbon is looser with  $\rho_{XZ} \approx 0.11$ . In a series of studies involving  $S_N2$  reactions of benzyl derivatives with various nucleophiles (mostly anilines and benzylamines) we obtained a relatively constant  $\rho_{XY}$  of  $-0.6$  to  $-0.8$ .<sup>36</sup>

These results were entirely based on the kinetic studies in solution. However, condensed-phase studies suffer from solvation and ion pairing effects, which are difficult, if not impossible, to separate from factors inherent to the mechanism. It is important to probe the electronic structures of TSs through substituent studies. On the other hand, gas-phase studies of substituent effects on the TS structure have been reported only for simple systems.<sup>78f</sup> The experimental difficulties involving complex reaction systems preclude at present such substituent studies on large substrates and nucleophiles as used in our solution kinetics.

Theory provides an alternative method for studying the  $S_N2$  mechanism involving relatively large reaction systems in the absence of solvation. Over the past two decades, the  $S_N2$  reaction has been extensively studied with *ab initio* methods, and many high-level studies have

been reported.<sup>8</sup> However, these studies also involved relatively simple reaction systems owing to the prohibitively long computational time required for a large system.

In this work, we used a relatively efficient semi-empirical MO method, PM3,<sup>9</sup> to investigate dually substituted  $S_N2$  reaction systems [equation (5)] for which *ab initio* calculations are not practical.



where  $\text{Nu}^- = \text{XC}_6\text{H}_4\text{O}^-$  and  $\text{XC}_6\text{H}_4\text{S}^-$  and  $\text{X} = \text{Y} = \text{H}$ ,  $p\text{-Cl}$ ,  $m\text{-CN}$ ,  $p\text{-CN}$  and  $p\text{-NO}_2$ .

The objectives of this work were threefold: (i) comparison of the theoretical gas-phase cross-interaction constants,  $\rho_{XY}$ , for the phenoxide and thiophenoxide nucleophiles with the corresponding experimental values in solution; (ii) study of substituent effects on the trends of transition state variations, namely whether a stronger electron acceptor substituent in the nucleophile X (and in the substrate Y) leads to an earlier (kinetically or intrinsically controlled reaction) or a later (thermodynamically controlled reaction) transition state; and (iii) study of the differences in the nucleophilic reactivity and mechanism between nucleophiles containing a first-row (O) and a second-row (S) nucleophilic center.

We were specifically interested in the comparison of the nucleophilicities of first- and second-row nucleophilic centers of comparable basicities, so we used oxy anions ( $\text{XC}_6\text{H}_4\text{O}^-$ ) and sulfur anions ( $\text{XC}_6\text{H}_4\text{S}^-$ ) with electron-withdrawing substituents,  $\sigma_X > 0$ ; these two anionic nucleophiles were shown to give comparable gas-phase proton affinities (see below).

Furthermore, we limited the substituents in the substrate ( $\text{YC}_6\text{H}_4\text{CH}_2\text{Cl}$ ) to those of electron acceptors ( $\sigma_Y > 0$ ) to ensure that the Hammett plots give linear correlations, not a U-shaped plot as normally observed for a wide variety of substituents including electron donors ( $\sigma_Y < 0$ ) and acceptors ( $\sigma_Y > 0$ ).<sup>10</sup> This choice of the Y substituents ( $\sigma_Y > 0$ ) also has an advantage of allowing a direct comparison of our theoretical gas-phase results with the experimental gas-phase data involving electron acceptor Y-substituents only.<sup>7k</sup>

Wherever applicable, we discuss our results in the light of available published gas-phase and/or condensed-phase experimental results.

## CALCULATION

The large number of heavy atoms (15–22) involved in the reaction system precluded the use of any *ab initio* MO method in this work. We therefore adopted a semi-empirical SCF MO method, PM3,<sup>9</sup> which is known to give reasonably reliable results for studies of reactivity and mechanisms.<sup>11</sup> Geometries and heats of formation ( $\Delta H_f^\circ$ ) of all stationary point species on the potential energy surface (PES), reactants (R), reactant ion–dipole

**Table 1.** Proton affinities<sup>a</sup> (*PA*) of nucleophiles in kcal mol<sup>-1</sup>

X	XC <sub>6</sub> H <sub>4</sub> O <sup>-</sup>	XC <sub>6</sub> H <sub>4</sub> S <sup>-</sup>
H	-345 (-391) <sup>b</sup> (-342) <sup>d</sup>	-338 (-351) <sup>c</sup>
<i>p</i> -Cl	-339	-334
<i>m</i> -CN	-334	-329
<i>p</i> -CN	-329 (-325) <sup>d</sup>	-327
<i>p</i> -NO <sub>2</sub>	-318 (-321) <sup>d</sup>	-320

<sup>a</sup> Experimental value of 367.2 kcal mol<sup>-1</sup> is used for  $\Delta H_f(\text{H}^+)$  following the procedure adopted by Dewar *et al.*<sup>37</sup> in their calculation of *PA*s using the AM1 method.

<sup>b</sup> Experimental *PA* for OH<sup>-</sup>.<sup>7g</sup>

<sup>c</sup> Experimental *PA* for SH<sup>-</sup>.<sup>7g</sup>

<sup>d</sup> Experimental *PA* reported by Lias *et al.*<sup>38</sup>

complexes (RC), transition states (TS), product ion-dipole complexes (PC) and products (P) were fully optimized without applying any symmetry constraints. All minima and TSs on the PES were characterized by confirming all positive and only one negative eigenvalues in the Hessian matrix, respectively.<sup>12</sup> Entropies of reaction,  $\Delta S^\circ$ , and of activation,  $\Delta S^\ddagger$ , were calculated at 298 K. All calculations were performed using the MOPAC 6.0 package.<sup>13</sup>

## RESULTS AND DISCUSSION

### Gas-phase basicities of nucleophiles

In order to compare the gas-phase basicities of the nucleophiles, phenoxides (XC<sub>6</sub>H<sub>4</sub>O<sup>-</sup>) and thiophenoxides (XC<sub>6</sub>H<sub>4</sub>S<sup>-</sup>), proton affinities (*PA*) were calculated. The results in Table 1 indicate that both anionic species are stabilized by delocalization of negative charge on O or S; the experimental *PA* of OH<sup>-</sup> is greater by 40 kcal mol<sup>-1</sup> than that of SH<sup>-</sup>, whereas the difference in the *PA*s of XC<sub>6</sub>H<sub>4</sub>O<sup>-</sup> and XC<sub>6</sub>H<sub>4</sub>S<sup>-</sup> is only 7 kcal mol<sup>-1</sup>. One might have expected a stronger basicity of anionic oxygen bases because of the higher electronegativity of O than S. This is only partly true. We note that as the electron-accepting power of the substituent X increases ( $\delta\sigma_X > 0$ ), the *PA* of the thiophenoxide eventually becomes greater than that of the phenoxide (for X = *p*-NO<sub>2</sub>). This can be ascribed to a more efficient negative charge delocalization of the anionic O base withdrawing a greater amount of anionic charge from the O than from the S atom in the thiophenoxides. This is apparent when *PA*s are compared with those of OH<sup>-</sup> and SH<sup>-</sup>;  $\Delta PA$  between the experimental *PA* of OH<sup>-</sup> and the calculated *PA* of C<sub>6</sub>H<sub>5</sub>O<sup>-</sup> is 46 kcal mol<sup>-1</sup>, whereas  $\Delta PA$  between the experimental *PA* of SH<sup>-</sup> and the calculated *PA* of C<sub>6</sub>H<sub>5</sub>S<sup>-</sup> is only 13 kcal mol<sup>-1</sup> (Table 1). In thiophenoxide bases, delocalization of negative charge involves a  $p\pi-d\pi$  type of overlap (with  $\Delta PA \approx 18$  kcal mol<sup>-1</sup> from

X = H to *p*-NO<sub>2</sub>) which is weaker than the  $p\pi-p\pi$  overlap in the phenoxides (with  $\Delta PA \approx 27$  kcal mol<sup>-1</sup> from X = H to *p*-NO<sub>2</sub>). This is also supported when relative stabilities (based on the relative heats of formation,  $\delta\Delta H_f$ ) of the two anionic nucleophiles are compared. A  $\delta\Delta H_f$  [=  $\Delta H_f(\text{S}) - \Delta H_f(\text{O})$ ] value relative to that for X = H ( $\delta\Delta H_f = 42.1$  kcal mol<sup>-1</sup>) represents an increase in the relative stability of the phenoxide due to an increase in the electron-withdrawing power of the substituent X; the increase in the relative (to X = H)  $\delta\Delta H_f$  values is 0, 2.4, 3.2, 6.4 and 10.9 kcal mol<sup>-1</sup> for X = H, *p*-Cl, *m*-CN, *p*-CN and *p*-NO<sub>2</sub> respectively. There is a large increase in the stability of the phenoxide anion compared with the thiophenoxide when the electron-withdrawing power of the substituent X increases from X = H to *p*-NO<sub>2</sub>, especially for X = *p*-CN and *p*-NO<sub>2</sub> for which direct (strong) delocalization of the anionic charge is so strong that a separate substituent scale,  $\sigma^-$ ,<sup>14</sup> is required. It is for such strongly delocalizing substituents that the phenoxide ions become weaker bases than the corresponding thiophenoxide ions. This is in line with a greater decrease in the  $pK_a$  value ( $\Delta pK_a = 2.72$ ) in water at 25 °C from X = H ( $pK_a = 9.86$ ) to X = *p*-NO<sub>2</sub> for phenols compared with a relatively small decrease ( $\Delta pK_a = 1.93$ ) under the same conditions for thiophenols ( $pK_a = 6.43$  for X = H).<sup>15</sup> However, there is no reversal in the order of  $pK_a$  in water, as we found with the gas-phase *PA*s, from C<sub>6</sub>H<sub>5</sub>OH > C<sub>6</sub>H<sub>5</sub>SH to *p*-NO<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>OH < *p*-NO<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>SH.

The *PA*s for XC<sub>6</sub>H<sub>4</sub>O<sup>-</sup> and XC<sub>6</sub>H<sub>4</sub>S<sup>-</sup> are comparable and differ by only -2-7 kcal mol<sup>-1</sup> and the choice of electron acceptor X is justified. For electron donor X the two *PA*s should have a greater difference.

### Energetics

Although there are two loosely bound ion-dipole complexes (RC and PC) on the PES, which is therefore a double-well type,<sup>1d</sup> the TSs are in all cases above the reactant levels,  $\Delta G^\ddagger > 0$ , so we disregarded the central barriers,  $\Delta G_0^\ddagger = G^\ddagger - G_{\text{RC}}$ , and considered only the activation energies,  $\Delta G^\ddagger$ , from the reactant levels. The energy data summarized in Tables 2 and 3 show that the reactions are mostly endothermic for both nucleophiles. This is again due to the enhanced stabilities of the anionic nucleophiles in the initial (reactant) states as a result of strong charge delocalization which is lost in the product, especially for the strong electron acceptor substituents. The endothermicities are greater for the phenoxides. Another aspect of interest is that the entropies of the TS are very low, *i.e.* the TSs are highly structured, for both reactions with the two nucleophiles, leading to  $\Delta S^\ddagger \approx -40$  cal K<sup>-1</sup> mol<sup>-1</sup> (e.u.). This is consistent with large negative  $\Delta S^\ddagger$  values observed experimentally for S<sub>N</sub>2 reactions in solution.

The two facts that the reactions are endothermic to

**Table 2.** Calculated heats of formation ( $\Delta H_f$ ) of reactants, activation energies and reaction energies for the reactions Y-benzyl chlorides with X-phenoxides (in kcal mol<sup>-1</sup>)

Y	X	$\Delta H_f$ (reactants)	Activation energies			Reaction energies		
			$\Delta H^\ddagger$	$-T\Delta S^\ddagger$	$\Delta G^\ddagger$	$\Delta H^\circ$	$-T\Delta S^\circ$	$\Delta G^\circ$
H	H	-32.69	16.53	11.95	28.48	-4.79	3.49	-1.30
	<i>p</i> -Cl	-45.71	19.20	12.03	31.23	1.46	3.58	5.04
	<i>m</i> -CN	-8.84	20.78	12.02	32.80	6.54	3.59	10.13
	<i>p</i> -CN	-14.36	23.48	12.10	35.58	11.43	3.73	15.16
	<i>p</i> -NO <sub>2</sub>	-70.12	28.22	12.05	40.27	22.33	3.25	25.58
<i>p</i> -Cl	H	-39.31	14.70	11.92	26.62	-4.87	3.41	-1.46
	<i>p</i> -Cl	-52.33	17.48	11.99	29.47	1.43	3.62	5.05
	<i>m</i> -CN	-15.46	19.15	12.02	31.17	6.48	3.68	10.16
	<i>p</i> -CN	-20.98	21.89	12.09	33.98	11.50	3.71	15.21
	<i>p</i> -NO <sub>2</sub>	-76.74	26.76	12.02	38.78	22.49	3.23	25.72
<i>m</i> -CN	H	2.83	11.79	12.09	23.88	-5.05	3.57	-1.48
	<i>p</i> -Cl	-10.19	14.66	12.18	26.84	1.37	3.70	5.07
	<i>m</i> -CN	26.68	16.50	12.16	28.66	6.59	3.59	10.18
	<i>p</i> -CN	21.16	19.25	12.25	31.50	11.58	3.69	15.27
	<i>p</i> -NO <sub>2</sub>	-34.60	24.28	12.19	36.47	22.78	3.31	26.09
<i>p</i> -CN	H	2.77	11.44	11.99	23.43	-4.99	3.48	-1.51
	<i>p</i> -Cl	-10.25	14.35	12.08	26.43	1.40	3.56	4.96
	<i>m</i> -CN	26.62	16.17	12.06	28.28	6.68	3.68	10.36
	<i>p</i> -CN	21.10	18.98	12.15	31.13	11.72	3.67	15.39
	<i>p</i> -NO <sub>2</sub>	-34.66	24.05	12.13	36.18	22.88	3.19	26.07
<i>p</i> -NO <sub>2</sub>	H	-40.86	8.34	12.51	20.85	-5.13	3.54	-1.59
	<i>p</i> -Cl	-53.88	11.39	12.60	23.99	1.36	3.72	5.08
	<i>m</i> -CN	-17.01	13.31	12.59	25.90	6.78	3.78	10.56
	<i>p</i> -CN	-22.53	16.21	12.67	28.88	11.85	3.74	15.59
	<i>p</i> -NO <sub>2</sub>	-78.29	21.45	12.59	34.04	23.20	3.29	26.49

**Table 3.** Calculated heats of formation ( $\Delta H_f$ ) of reactants, activation energies and reaction energies for the reactions Y-benzyl chlorides with X-thiophenoxides (in kcal mol<sup>-1</sup>)

Y	X	$\Delta H_f$ (reactants)	Activation energies			Reaction energies		
			$\Delta H^\ddagger$	$-T\Delta S^\ddagger$	$\Delta G^\ddagger$	$\Delta H^\circ$	$-T\Delta S^\circ$	$\Delta G^\circ$
H	H	9.43	5.00	11.93	16.93	-8.61	3.47	-5.14
	<i>p</i> -Cl	-1.27	6.43	12.02	18.45	-4.35	3.30	-1.05
	<i>m</i> -CN	36.39	8.10	12.01	20.11	-0.24	3.69	3.45
	<i>p</i> -CN	34.14	8.60	12.10	20.70	2.14	3.36	5.50
	<i>p</i> -NO <sub>2</sub>	-17.14	11.28	12.06	23.34	9.02	3.37	12.39
<i>p</i> -Cl	H	2.80	3.17	11.64	14.81	-8.45	3.01	-5.44
	<i>p</i> -Cl	-7.90	4.69	11.72	16.41	-4.34	3.07	-1.27
	<i>m</i> -CN	29.76	5.91	11.78	17.69	0.33	3.01	3.34
	<i>p</i> -CN	27.51	6.99	11.78	18.77	2.23	3.11	5.34
	<i>p</i> -NO <sub>2</sub>	-23.77	9.79	11.75	21.54	9.31	3.30	12.61
<i>m</i> -CN	H	44.94	0.35	11.99	12.34	-8.70	3.50	-5.20
	<i>p</i> -Cl	34.24	1.96	12.05	14.01	-4.50	3.68	-0.82
	<i>m</i> -CN	71.90	3.35	12.15	15.50	0.36	3.65	4.01
	<i>p</i> -CN	69.65	4.70	12.19	16.89	2.18	3.67	5.85
	<i>p</i> -NO <sub>2</sub>	18.37	7.36	12.08	19.44	9.59	3.34	12.93
<i>p</i> -CN	H	44.88	-0.20	11.95	11.75	-8.58	3.34	-5.24
	<i>p</i> -Cl	34.18	1.44	12.07	13.51	-4.40	3.38	-1.02
	<i>m</i> -CN	71.84	2.81	12.14	14.95	0.42	3.39	3.81
	<i>p</i> -CN	69.59	3.95	12.17	16.12	2.16	3.68	5.84
	<i>p</i> -NO <sub>2</sub>	18.31	6.95	12.09	19.04	9.56	3.36	12.92
<i>p</i> -NO <sub>2</sub>	H	1.25	-3.56	12.53	8.97	-8.88	3.72	-5.16
	<i>p</i> -Cl	-9.45	-1.77	12.63	10.86	-4.63	3.75	-0.88
	<i>m</i> -CN	28.21	0.31	12.67	12.98	0.07	3.70	3.77
	<i>p</i> -CN	25.96	0.95	12.71	13.66	2.22	3.79	6.01
	<i>p</i> -NO <sub>2</sub>	-25.32	4.18	12.60	16.78	9.80	3.38	13.71

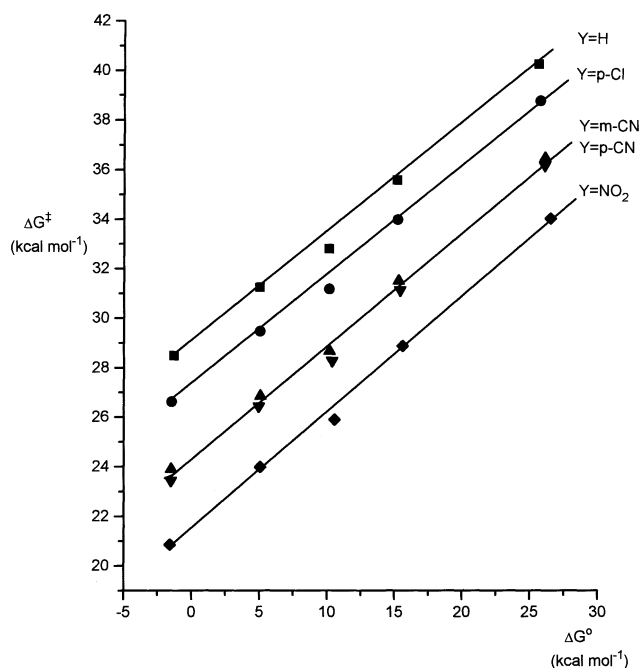


Figure 1. Plot of  $\Delta G^\ddagger$  versus  $\Delta G^\circ$

weakly exothermic and the TSs are highly structured, *i.e.* have very low entropy, will make the reaction unsuitable for gas-phase experimental studies.<sup>7g,16</sup>

The Leffler–Grunwald rate–equilibrium relationships for variations of substituents X [equation (6)] are shown in Fig. 1.

$$\delta\Delta G_X^\ddagger = \alpha\delta\Delta G_X^\circ \quad (6)$$

Excellent linearities (regression coefficients  $r \geq 0.99$ ) are found for all the plots with slopes  $\alpha$  ranging from 0.44 (Y = H) to 0.47 (Y = *p*-NO<sub>2</sub>) for phenoxides and from 0.36 (Y = H) to 0.42 (Y = *p*-NO<sub>2</sub>) for thiophenoxides. The excellent linearities obtained are an indication that the reactions occur by a single-step concerted process, since the relationship equation (6) applies only to an elementary reaction. The slope,  $\alpha$  (which can be defined alternatively by  $\rho_{\text{kin}}/\rho_{\text{eq}}$ ), is viewed as a measure of the TS structure;<sup>2c,17</sup> hence the values of 0.44–0.47 and 0.36–0.42 suggest that the reactions have progressed to *ca* 45 and 40% in the TS for the phenoxides and thiophenoxides, respectively. This is consistent with the Bell–Evans–Polanyi (BEP) principle,<sup>18</sup> since the more endothermic reactions of phenoxides lead to a later TS (*ca* 45%) than the less endothermic reactions of thiophenoxides (*ca* 40%).

A greater *endothermic* displacement leading to a later TS for phenoxides than for thiophenoxide is, however, in sharp contrast to the trends found for the gas-phase reactions of OH<sup>−</sup> and SH<sup>−</sup> by the *ab initio* calculations; the reaction of OH<sup>−</sup> exhibited much greater *exothermi-*

*city* than that of SH<sup>−</sup> with an earlier TS.<sup>19</sup> This is again due to a greater stability induced by the stronger resonance delocalization of the negative charge on O which is lost in the product.

Examination of Tables 2 and 3 reveals another interesting aspect of the rate–equilibrium relations: the  $\Delta G^\circ$  values are insensitive to variations of substituent Y in the substrates, *e.g.* for X = H, they vary from −1.3 to −1.6 kcal mol<sup>−1</sup> as Y is varied from H to *p*-NO<sub>2</sub>. This means that the Leffler–Grunwald relationship equation (6) does not apply. In this case  $\Delta G^\circ$  is approximately constant regardless of the substituent Y in the substrate ring, while the  $\Delta G^\ddagger$  values for the reaction are variable and dependent on the nature of Y [varying from 28.5 (Y = H) to 20.9 kcal mol<sup>−1</sup> (Y = *p*-NO<sub>2</sub>) for X = H]. Consequently, the plot of  $\Delta G^\ddagger$  vs  $\Delta G^\circ$  (which is equivalent to a Brønsted plot using carbon basicity instead of proton basicity; see below) for this reaction must be a straight line of infinite slope. This sort of anomalous Brønsted parameters is often observed,<sup>20</sup> *e.g.* for an identity exchange process of  $X^- + RX \rightleftharpoons XR + X^-$ ,<sup>7k</sup> and raises questions about using the Brønsted parameter,  $\alpha$ , as a measure of the TS structure. Such anomalous parameters are observed whenever the rate ( $\delta\Delta G^\ddagger$ ) is solely dependent on the intrinsic barriers,  $\delta\Delta G_0^\ddagger$ , as the simplified Marcus equation<sup>21</sup> [equation (7c)] indicates.

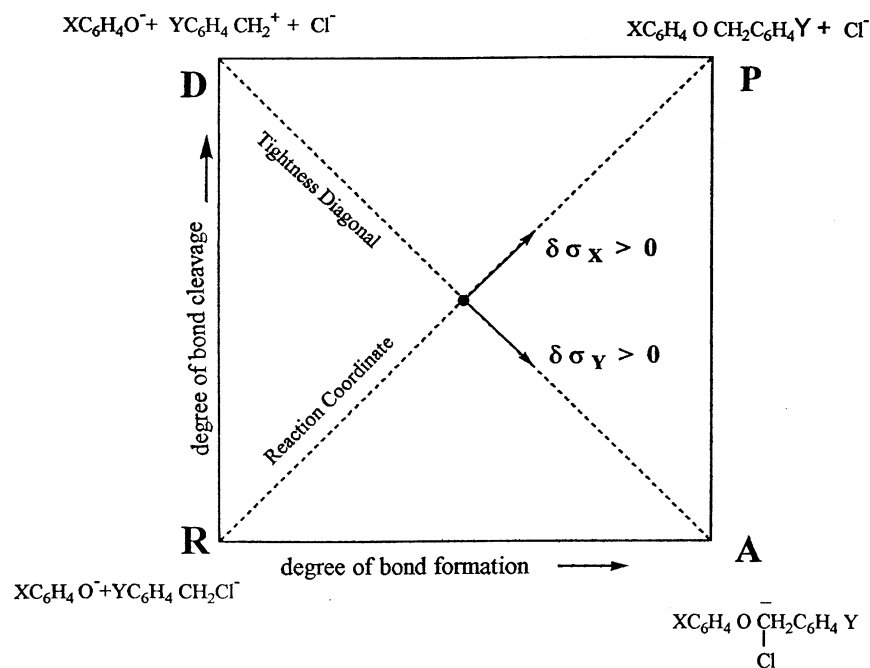
$$\Delta G^\ddagger = \Delta G_0^\ddagger + \Delta G^\circ/2 + (\Delta G^\circ)^2/16\Delta G_0^\ddagger \quad (7a)$$

$$\delta\Delta G^\ddagger \approx \delta\Delta G_0^\ddagger + \delta\Delta G^\circ \quad (7b)$$

$$\delta\Delta G^\ddagger \approx \delta\Delta G_0^\ddagger \text{ for } \delta\Delta G^\circ \approx 0 \quad (7c)$$

Equation (7b) requires that when  $\Delta G^\circ$  is constant within a certain series of reaction, the activation energy,  $\Delta G^\ddagger$ , (*i.e.* the rate) is function only of intrinsic barrier,  $\delta\Delta G_0^\ddagger$  [equation (7c)], and the reaction is therefore intrinsic barrier controlled.<sup>22</sup> For such an intrinsic barrier controlled reaction series, the Leffler–Grunwald relationship or the Brønsted equation does not hold, since any rate–equilibrium relationship [such as equation (6)] is thermodynamic in nature and only applies to thermodynamically controlled reaction series, *i.e.*  $\delta\Delta G_0^\ddagger < \delta\Delta G^\circ$  in equation (7b).<sup>3</sup> The variation of the intrinsic barrier represents movement along the tightness diagonal (line AD) in the More O’Ferrall–Jencks type plots (Fig. 2) and corresponds to a perturbation along the perpendicular coordinate on the PES.<sup>3</sup>

The effects of nucleophilicity and leaving ability on the rates in a concerted (S<sub>N</sub>2) process (*i.e.* in an elementary process) in general originate thermodynamically, and the Brønsted equation will apply satisfactorily to each effect separately.<sup>3</sup> However, the effects of substituents in the substrate on the rate in S<sub>N</sub>2 reactions are complex, since both bond formation and breaking are involved in the TS at the substrate reaction center. In a



**Figure 2.** More O'Ferrall–Jencks diagram. An acceptor Y shifts the TS towards corner **A**, making the TS tighter

sense, the effects of substituents in the substrate (Y) originate from a multiple electron process, not a simple electronic change, involving both bond formation and breaking simultaneously at the same reaction center. These effects are purely electronic and kinetic (intrinsic) in nature<sup>8a,23</sup> and not thermodynamic. This is why the effects of substituent in the substrate (Y) on the rates cannot be used in predictions of TS structures applying thermodynamically based methods, such as the magnitude of the Brønsted coefficients and movement along the reaction coordinate on the More O'Ferrall–Jencks diagram.<sup>3</sup>

In summary, the effects of substituents in the nucleophile (X) and leaving group (Z) on the rates of S<sub>N</sub>2 reactions at benzylic carbon are thermodynamically controlled and can be correlated by a rate–equilibrium relationship. In contrast, the effects of substituents in the substrate (Y) on the rates are kinetically or intrinsically

controlled and hence cannot be correlated by such thermodynamically based rate–equilibrium relationships.

#### Variations of TS structure and cross-interaction constants, $\rho_{xy}$

It was noted above that the rate–equilibrium relationship holds satisfactorily [equation (6)] for variations of substituent in the nucleophile, X. A similar plot based on the Brønsted equation [equation (8)] provides a Brønsted coefficient,  $\beta$ , which is a measure of bond making by a nucleophile in the TS.

$$\delta\Delta G_x^\ddagger = \beta\delta(PA_x) \quad (8)$$

Here the PAs of the anion nucleophiles are used to derive  $\beta$  instead of the reaction energies,  $\Delta G^\circ$  in equation

**Table 4.** The TS structures represented by various parameters for progress of the reaction

Nu <sup>-</sup>	Y	X	$\alpha$	$\beta$	$r_{(C-Nu)}^{\ddagger a}$	$\% \Delta n_{(C-Nu)}^{\ddagger}$	$r_{(C-Cl)}^{\ddagger a}$	$\% \Delta n_{(C-Cl)}^{\ddagger}$
XC <sub>6</sub> H <sub>4</sub> O <sup>-</sup>	H	H	0.44	0.43	1.929	43	2.188	49
		<i>p</i> -NO <sub>2</sub>			1.846	49	2.266	55
	<i>p</i> -NO <sub>2</sub>	H	0.47	0.48	1.929	43	2.151	46
		<i>p</i> -NO <sub>2</sub>			1.850	49	2.221	52
XC <sub>6</sub> H <sub>4</sub> S <sup>-</sup>	H	H	0.36	0.35	2.359	41	2.105	41
		<i>p</i> -NO <sub>2</sub>			2.274	48	2.153	46
	<i>p</i> -NO <sub>2</sub>	H	0.42	0.43	2.352	42	2.074	38
		<i>p</i> -NO <sub>2</sub>			2.276	47	2.121	43

<sup>a</sup> The PM3 bond lengths (Å) in the TS.

**Table 5.** Calculated bond lengths in Å and bond order ( $n^\ddagger$ ) in the TS for the reactions Y-benzyl chlorides with X-phenoxides

Y	X	Reactants		TS			Products		Bond order	
		$r_{(C-C)}^a$	$r_{(C-Cl)}$	$r_{(C-C)}^a$	$r_{(C-Cl)}$	$r_{(C-O)}$	$r_{(C-C)}^a$	$r_{(C-O)}$	$n_{(C-Cl)}^\ddagger$	$n_{(C-O)}^\ddagger$
H	H	1.484	1.788	1.473	2.188	1.929	1.503	1.419	0.51	0.43
	<i>p</i> -Cl	1.484	1.788	1.473	2.205	1.909	1.503	1.419	0.50	0.44
	<i>m</i> -CN	1.484	1.788	1.473	2.216	1.897	1.503	1.420	0.49	0.45
	<i>p</i> -CN	1.484	1.788	1.473	2.233	1.880	1.502	1.420	0.48	0.46
<i>p</i> -Cl	<i>p</i> -NO <sub>2</sub>	1.484	1.788	1.473	2.266	1.846	1.502	1.422	0.45	0.50
	H	1.484	1.788	1.474	2.179	1.928	1.503	1.419	0.52	0.43
	<i>p</i> -Cl	1.484	1.788	1.474	2.197	1.908	1.503	1.419	0.51	0.44
	<i>m</i> -CN	1.484	1.788	1.474	2.207	1.896	1.502	1.420	0.50	0.45
<i>m</i> -CN	<i>p</i> -CN	1.484	1.788	1.474	2.224	1.880	1.502	1.420	0.48	0.46
	<i>p</i> -NO <sub>2</sub>	1.484	1.788	1.474	2.256	1.846	1.502	1.422	0.46	0.50
	H	1.485	1.786	1.475	2.171	1.929	1.504	1.418	0.53	0.43
	<i>p</i> -Cl	1.485	1.786	1.475	2.187	1.910	1.504	1.418	0.51	0.44
<i>p</i> -CN	<i>m</i> -CN	1.485	1.786	1.475	2.198	1.897	1.503	1.418	0.50	0.45
	<i>p</i> -CN	1.485	1.786	1.475	2.213	1.881	1.503	1.419	0.49	0.46
	<i>p</i> -NO <sub>2</sub>	1.485	1.786	1.475	2.244	1.848	1.503	1.421	0.47	0.49
	H	1.485	1.786	1.475	2.167	1.929	1.504	1.418	0.53	0.43
<i>p</i> -NO <sub>2</sub>	<i>p</i> -Cl	1.485	1.786	1.475	2.183	1.909	1.504	1.418	0.52	0.44
	<i>m</i> -CN	1.485	1.786	1.475	2.194	1.897	1.504	1.419	0.51	0.45
	<i>p</i> -CN	1.485	1.786	1.475	2.209	1.881	1.504	1.420	0.49	0.46
	<i>p</i> -NO <sub>2</sub>	1.485	1.786	1.476	2.240	1.847	1.503	1.422	0.47	0.49
<i>p</i> -NO <sub>2</sub>	H	1.485	1.784	1.477	2.151	1.929	1.505	1.417	0.54	0.43
	<i>p</i> -Cl	1.485	1.784	1.477	2.167	1.910	1.505	1.417	0.53	0.44
	<i>m</i> -CN	1.485	1.784	1.477	2.177	1.898	1.505	1.418	0.52	0.45
	<i>p</i> -CN	1.485	1.784	1.477	2.192	1.882	1.505	1.419	0.51	0.46
	<i>p</i> -NO <sub>2</sub>	1.485	1.784	1.477	2.221	1.850	1.504	1.421	0.48	0.49

<sup>a</sup>  $r_{(C-C)}$  denotes the bond length between benzyl carbon and *ipso*-carbon of the benzene ring.

(6) for the calculation of  $\alpha$ . Comparison of the two parameters in Table 4 shows good general agreement between the two. The agreement between  $\alpha$  and  $\beta$  indicates that sensitivity of the reaction center (on R) with variation of substituents X in the nucleophile in the addition with a methyl cation (methyl cation affinity or carbon basicity) is similar to that with a proton (proton affinity or proton basicity). The relationship of proton basicity to carbon basicity has been explored in the past.<sup>24</sup> A good correlation between the two is expected since the heats of formation of the two types of adducts (H—R and CH<sub>3</sub>—R) are normally correlated well<sup>7f,25</sup>

We have also shown in Table 4 bond lengths (Å) of the forming (C—Nu) and cleaving bonds (C—Cl) and calculated percentage bond order changes,  $\% \Delta n^\ddagger$  [equation (9)]<sup>26</sup> {which is derived by substituting the Pauling bond order<sup>27</sup>,  $n = \exp [(r_o - r)/a]$ , for percentage bond order changes} involved for the two bonds on going from the reactant to the TS. In equation (9),  $r^\ddagger$ ,  $r_R$  and  $r_P$  denote bond length in the TS, reactant and product (Tables 5 and 6), respectively.

$$\% \Delta n^\ddagger = \frac{[\exp(-r^\ddagger/a) - \exp(-r_R/a)]}{[\exp(-r_P/a) - \exp(-r_R/a)]} \times 100 \quad (9)$$

A constant  $a = 0.6$  was adopted in the calculation. This constant must be selected depending on the type of

bonds. For covalent bonds,  $a = 0.26$  is more appropriate and  $a = 0.9$  is also applicable to certain types of bonds.<sup>8i,28</sup> The most suitable value of  $a$  should be selected by confirming the bond order conservation,  $\sum n_i^\ddagger = n_{(C-Cl)}^\ddagger + n_{(C-Nu)}^\ddagger = 1.0$ . When the bond order conservation was considered,  $a = 0.26, 0.6$  and  $0.9$  gave  $\sum n_i^\ddagger = 0.35-0.38, 0.94-0.97$  and  $1.21-1.24$ , respectively. Hence it is apparent that for our reaction systems  $a = 0.6$  is the best choice. It should be noted that the bond order,  $n^\ddagger$ , and percentage bond order change,  $\% \Delta n^\ddagger$ , in the TS are related by the equations

$$n_{(C-Cl)}^\ddagger = 1 - \% \Delta n_{(C-Cl)}^\ddagger \quad (10a)$$

$$n_{(C-Nu)}^\ddagger = \% \Delta n_{(C-Nu)}^\ddagger \quad (10b)$$

Reference to Table 4 reveals that the progress of bond cleavage in the TS is greater than that of bond formation in the reactions of phenoxides, whereas the reverse is true, *i.e.* the degree of bond cleavage is smaller than that of bond formation, in the reactions of thiophenoxides. The degrees of bond formation, represented by  $\% \Delta n^\ddagger$ , in the phenoxide reactions agree satisfactorily with those represented by the rate-equilibrium coefficients,  $\alpha$  and  $\beta$ . There are, however, significant, but not large, differences between the two methods. In general, the degree of bond cleavage in the TS increases with a stronger electron acceptor in the nucleophile ( $X = p\text{-NO}_2$ ) and in the

**Table 6.** Calculated bond lengths in Å and bond order ( $n^\ddagger$ ) in the TS for the reactions Y-benzyl chlorides with X-thiophenoxides

Y	X	Reactants		TS			Products		Bond order	
		$r_{(C-C)}^a$	$r_{(C-Cl)}$	$r_{(C-C)}^a$	$r_{(C-Cl)}$	$r_{(C-S)}$	$r_{(C-C)}^a$	$r_{(C-S)}$	$n_{(C-Cl)}^\ddagger$	$n_{(C-O)}^\ddagger$
H	H	1.484	1.788	1.474	2.105	2.359	1.488	1.828	0.59	0.41
	<i>p</i> -Cl	1.484	1.788	1.474	2.116	2.339	1.488	1.830	0.58	0.43
	<i>m</i> -CN	1.484	1.788	1.474	2.130	2.310	1.488	1.828	0.57	0.45
	<i>p</i> -CN	1.484	1.788	1.474	2.132	2.309	1.487	1.831	0.56	0.45
	<i>p</i> -NO <sub>2</sub>	1.484	1.788	1.473	2.153	2.274	1.488	1.828	0.54	0.48
<i>p</i> -Cl	H	1.484	1.788	1.474	2.094	2.367	1.488	1.830	0.60	0.41
	<i>p</i> -Cl	1.484	1.788	1.474	2.106	2.342	1.488	1.830	0.59	0.43
	<i>m</i> -CN	1.484	1.788	1.474	2.118	2.321	1.488	1.830	0.58	0.44
	<i>p</i> -CN	1.484	1.788	1.474	2.122	2.312	1.488	1.831	0.57	0.45
	<i>p</i> -NO <sub>2</sub>	1.484	1.788	1.474	2.143	2.277	1.488	1.831	0.55	0.48
<i>m</i> -CN	H	1.485	1.786	1.475	2.091	2.357	1.489	1.827	0.60	0.41
	<i>p</i> -Cl	1.485	1.786	1.475	2.102	2.337	1.489	1.826	0.59	0.43
	<i>m</i> -CN	1.485	1.786	1.475	2.111	2.320	1.489	1.829	0.58	0.44
	<i>p</i> -CN	1.485	1.786	1.475	2.115	2.312	1.489	1.826	0.58	0.45
	<i>p</i> -NO <sub>2</sub>	1.485	1.786	1.475	2.139	2.275	1.489	1.827	0.56	0.47
<i>p</i> -CN	H	1.485	1.786	1.475	2.087	2.357	1.488	1.829	0.61	0.42
	<i>p</i> -Cl	1.485	1.786	1.475	2.098	2.338	1.488	1.829	0.60	0.43
	<i>m</i> -CN	1.485	1.786	1.475	2.111	2.319	1.488	1.829	0.58	0.44
	<i>p</i> -CN	1.485	1.786	1.475	2.114	2.309	1.488	1.830	0.58	0.45
	<i>p</i> -NO <sub>2</sub>	1.485	1.786	1.475	2.135	2.275	1.489	1.827	0.56	0.47
<i>p</i> -NO <sub>2</sub>	H	1.485	1.784	1.476	2.074	2.352	1.489	1.825	0.62	0.42
	<i>p</i> -Cl	1.485	1.784	1.476	2.085	2.335	1.489	1.825	0.51	0.43
	<i>m</i> -CN	1.485	1.784	1.476	2.099	2.309	1.489	1.825	0.60	0.45
	<i>p</i> -CN	1.485	1.784	1.476	2.101	2.308	1.489	1.825	0.59	0.45
	<i>p</i> -NO <sub>2</sub>	1.485	1.784	1.476	2.121	2.276	1.489	1.825	0.57	0.47

<sup>a</sup>  $r_{(C-C)}$  denotes the bond length between benzyl carbon and *ipso*-carbon of the benzene ring.

substrate (Y = *p*-NO<sub>2</sub>) for both phenoxides and thiophenoxides. In contrast, however, the degree of bond formation in the TS is insensitive to the substituent (Y) in the substrate for both types of nucleophiles. This is reminiscent of the failure of the rate–equilibrium relationship [equation (6)] for variation of substituent Y in the substrate, discussed earlier. This is, however, in direct contradiction to more advanced bond formation reflected in larger  $\alpha$  and  $\beta$ . We therefore conclude that the rate–equilibrium relationships [equations (6) and (8)] provide a better measure of the progress of bond making in the TS than the measure of progress based on bond order changes [equation (9)].

Overall, the TS is earlier on the reaction coordinate for the thiophenoxides than for the phenoxides (see above) and the TS becomes tighter with a stronger electron acceptor substituent Y in the substrate. A tighter TS for a stronger acceptor Y is in accord with the experimental results of S<sub>N</sub>2 reactions at benzylic carbon in the gas phase,<sup>7k</sup> in MeOH<sup>29</sup> and in 20% aqueous DMSO.<sup>30</sup> These conclusions are also consistent with our earlier analyses based on the energetics that the variation of TS structure with the nucleophile is thermodynamically controlled (a weaker nucleophile leads to a later TS), whereas the TS variation with the substituent Y in the substrate is intrinsically controlled. The effects of substituents in the substrate (Y) reflect changes in the intrinsic barrier, a

shift on the tightness diagonal in the More O'Ferrall–Jencks type plots (Fig. 2).

On the other hand, a greater degree of bond cleavage and of bond formation in the TS with a stronger acceptor substituent in the nucleophile (X) is consistent with that expected from the thermodynamic barrier controlled reaction series, a shift towards the product corner, P, on the reaction coordinate in Fig. 2.

We have calculated the Hammett coefficients,  $\rho_X$  and  $\gamma$  in equation (11) and the cross-interaction constants,  $\chi_{XY}$  in equations (3) and (4) with  $i, j = X$  and Y.

$$\delta\Delta G^\ddagger / -2.3RT = \rho\sigma \quad (11)$$

Owing to the strong electron delocalization of a strong acceptor X, the use of the  $\sigma^-$  scale was required.<sup>14</sup> The results at  $T = 298$  K are given in Table 7 and show that the magnitude of  $\rho_X^-$  for the phenoxides is greater (by *ca* 1.8-fold) than that for the thiophenoxides, in agreement with the predictions based on the larger  $\alpha$  and  $\beta$  values for the former. However, there is only a 3–5% increase in the progress of bond formation based on the increase in  $\alpha$  and  $\beta$  ( $\Delta\alpha = \Delta\beta = +3$ –5%) for phenoxides than for thiophenoxides, but the  $\rho_X^-$  values for the phenoxides are greater by *ca* 1.8-fold than for the thiophenoxides. Hence the magnitude of  $\rho_X^-$  exaggerates the increase in the degree of bond making and is therefore of questionable



**Table 7.** Simple Hammett  $\rho$ -values<sup>a</sup> and cross-interaction constants,  $\rho_{XY}$ .<sup>a</sup>

X or Y	H	<i>p</i> -Cl	<i>m</i> -CN	<i>p</i> -CN <sup>b</sup>	<i>p</i> -NO <sub>2</sub> <sup>b</sup>		
XC <sub>6</sub> H <sub>4</sub> O <sup>-</sup>	$\rho_X^-$	-6.53	-6.74	-6.98	-7.05	-7.30	$\rho_{XY} = -0.60$
	$\rho_Y^-$	4.30	4.09	3.91	3.80	3.52	
		(4.57) <sup>c</sup>					
XC <sub>6</sub> H <sub>4</sub> S <sup>-</sup>	$\rho_X^-$	-3.50	-3.68	-3.90	-4.00	-4.26	$\rho_{XY} = -0.59$ ( $\rho_{XY} = -0.62$ ) <sup>e</sup>
	$\rho_Y^-$	4.43	4.22	3.97	3.93	3.65	
		(4.77) <sup>c</sup>					
		(6.40) <sup>d</sup>					

<sup>a</sup> Regression coefficients are better than 0.98 in all cases.

<sup>b</sup>  $\sigma^-$  value is used.

<sup>c</sup>  $\rho_Y$  value calculated using  $\Delta H^\ddagger$  instead of  $\Delta G^\ddagger$ .

<sup>d</sup> Experimental gas-phase  $\rho_Y$  value using  $\Delta E^\ddagger$  at 350 K for the identity chloride exchange.<sup>7k</sup>

<sup>e</sup> Experimental value in MeOH at 20.0 °C.<sup>29</sup>

reliability as a quantitative measure of bond making in the TS.

Experimentally in methanol at 20.0 °C, the  $\rho_X$  values with XC<sub>6</sub>H<sub>4</sub>S<sup>-</sup> are much smaller, ranging from -0.28 (Y = *p*-CH<sub>3</sub>O) to -0.96 (Y = *p*-NO<sub>2</sub>),<sup>29</sup> than the corresponding gas-phase values in Table 7 ( $\rho_X = -3.50$  to -4.26). The  $\rho_X$  values for the reactions of XC<sub>6</sub>H<sub>4</sub>S<sup>-</sup> with phenylbenzyltrimethylammonium ions in DMF at 0 °C were -1.54 to -1.83.<sup>23a</sup> Clearly, the PM3 gas-phase  $\rho_X$  values are much greater than those in solution.

The experimental gas-phase  $\rho_Y$  value for the thermoneutral S<sub>N</sub>2 reactions of Cl<sup>-</sup> + YC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl ⇌ YC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl + Cl<sup>-</sup> at 350 K (with Y = H, *m*-OCH<sub>3</sub>, *m*-F, *m*-Cl and *m*-CF<sub>3</sub>) determined by plotting the effective activation energy,  $\Delta E^\ddagger$  (the energy difference between separated reactants and the S<sub>N</sub>2 TS) versus  $\sigma$  was +6.4 ( $r = 0.98$ ).<sup>31</sup> The  $\Delta E^\ddagger$  values determined by the semi-empirical AM1 method<sup>32</sup> gave a similar trend, although the S<sub>N</sub>2 barrier heights were *ca* 7–8 kcal mol<sup>-1</sup> higher than the gas-phase experimental values.<sup>31</sup> On the other hand, the PM3  $\rho_Y$  values obtained similarly using  $\Delta H^\ddagger$  instead of  $\Delta G^\ddagger$  were +4.57 ( $r = 0.97$ ) and +4.77 ( $r = 0.97$ ) for C<sub>6</sub>H<sub>5</sub>O<sup>-</sup> and C<sub>6</sub>H<sub>5</sub>S<sup>-</sup>, respectively, at 298 K. The agreement between the experimental and theoretical (PM3) values is satisfactory considering the different nucleophiles and temperatures involved. However, the use of  $\Delta G^\ddagger$  [equation (11)] gave smaller values of  $\rho_X^- = +4.3$  and +4.4 for C<sub>6</sub>H<sub>5</sub>O<sup>-</sup> and C<sub>6</sub>H<sub>5</sub>S<sup>-</sup>, respectively. The  $\rho_Y$  value calculated for the reactions of XC<sub>6</sub>H<sub>4</sub>S<sup>-</sup> with YC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl in MeOH at 20.0 °C was 0.58.<sup>3</sup> Again, the  $\rho_Y$  value in solution is much smaller than the gas-phase values. The smaller  $\rho_X$  and  $\rho_Y$  values in solution than in the gas phase are mostly due to the short-range solute–solvent dispersion and polarization effects.<sup>33</sup>

We note that the  $\rho_Y$  values are all positive, since electron-withdrawing Y substituents are used in both cases.<sup>7k</sup> The positive  $\rho_Y$  indicates that the reaction center, C<sub>o</sub>, becomes more negatively charged in the TS and the overall TS structure is relatively tight. It is well known

that for electron-donating Y substituents  $\rho_Y$  often changes sign to negative and the TS becomes looser.<sup>10</sup> Also, when better leaving groups, such as (CH<sub>3</sub>)<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>Z<sup>23a</sup> and <sup>-</sup>OSO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>Z<sup>3</sup>, are used, negative  $\rho_Y$  values are obtained with looser TSs.

The magnitude of  $\rho_{XY}$  is similar for the two reaction series with  $\rho_{XY} \approx -0.60$ , which corresponds to *ca* 40–45% progress of the reactions (Table 4). The gas-phase theoretical values of -0.60 is in excellent agreement with the experimental value of -0.62 for the thiophenoxide series in MeOH at 20.0 °C reported by Waszczylo and Westaway,<sup>29</sup> and is well within the range of  $\rho_{XY}$  (-0.6 to -0.8) found for S<sub>N</sub>2 reactions at benzylic carbon in various solvents.<sup>3,6</sup> One might suspect that the agreement is fortuitous, since the PM3 result is the value in the gas phase. However, this agreement in  $\rho_{XY}$ , despite the large difference found in the magnitudes of  $\rho_X$  and  $\rho_Y$  determined experimentally in solution<sup>23a</sup>, and determined in the gas phase, suggests that  $\rho_{XY}$  may be independent of environmental effects and may constitute an intrinsic property for a reaction. There is both experimental and theoretical evidence in support of this contention.<sup>5,34</sup>

In contrast to an intuitive expectation that bond formation will be more extensive with a sulfur base than an oxy base since (i) the former has a greater polarizability, (ii) the carbon basicity of sulfur is larger than that of oxygen in solution<sup>35</sup> and (iii) the sulfur-centered anions have lower anodic peak potentials with greater reactivity towards benzyl chloride in MeCN compared with oxygen-centered anions,<sup>36</sup> the degree of bond making with the sulfur base in the TS is smaller than, or similar to, that with the oxygen base in the gas phase even though the PAs are similar ( $\Delta PA \approx +7$  to -2 kcal mol<sup>-1</sup>).

The difference in the reactivity between the two nucleophiles ( $\delta\Delta G^\ddagger$ ) is strongly dependent on the endothermicities of the reactions for the two bases, which in turn are dependent on the loss of resonance stabilization in the reactant nucleophiles upon product formation. A greater endothermicity for the phenoxide is

reflected also in a greater degree of bond cleavage, which is another source of a higher activation barrier for the phenoxides.

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