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CROSS-INTERACTION CONSTANTS AS A MEASURE OF THE TRANSITION STATE STRUCTURE. PART 9. THE DEGREE OF BOND FORMATION IN THE S_N2 TRANSITION STATE INVOLVING ANIONIC NUCLEOPHILES

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The second-order rate constants of the reactions between benzenesulphonyl chlorides and anionic nucleophiles, benzoates and cinnamates, in methanol at 30·0 °C are reported. A marked increase in rate found with a *p*-nitro substituent in the substrate indicated the development of an electron-rich centre on the S atom in the transition state. The two types of cross-interaction constants, ρ_{XY} and λ_{XY}, suggested that bond formation in the S_N2 transition state with anionic nucleophiles is greater than that for the corresponding reaction with aniline nucleophiles.

INTRODUCTION

In a previous paper,[1] we showed that the mixed Hammett–Brønsted type cross-interaction constant, λ_{XY} in equation (1), can be more useful than the Hammett type, ρ_{XY} in equation (2); the use of ΔpK_X ($=pK_X - pK_H$) enables us to avoid the complication arising from the fall-off of the substituent effect transmission to the reaction centre by a factor of ca 2 owing to a non-conjugating intervening CH_2 or CO group in the reactants.[2]

$$\log(k_{XY}/k_{HH}) = \beta_X \Delta pK_X + \rho_Y \sigma_Y + \lambda_{XY} \sigma_Y \Delta pK_X \quad (1)$$

$$\log(k_{XY}/k_{HH}) = \rho_X \sigma_X + \rho_Y \sigma_Y + \rho_{XY} \sigma_X \sigma_Y \quad (2)$$

On the other hand all of our previous work[3] on the application of cross-interaction constants to the elucidation of the transition state (TS) structure has been involved with the use of neutral nucleophiles, partly because the kinetics are clean and experimentally convenient. In this work we aim to show that the use of anionic nucleophiles is just as useful for the similar analysis of the TS structure. We can in fact provide a comparison of the degree of bond formation in the S_N2 TSs involving neutral and anionic nucleophiles.

We report here the results of kinetic studies on the reactions of substituted benzenesulphonyl chlorides (BSC) with two series of nucleophiles, benzoates and cinnamates, equation (3). The degree of bond formation in the TS and the mechanism are discussed in the light of the sign and magnitude of λ_{XY} and ρ_{XY} determined by multiple linear regression analysis[4] of the second-order rate constants using equations (1) and (2).

$$XRCOO^- + YC_6H_4SO_2Cl \rightarrow YC_6H_4SO_2OCOR + Cl^- \quad (3)$$

$R = C_6H_4$— or $C_6H_4CH{=}CH$—
$X = p\text{-}CH_3O$, $p\text{-}CH_3$, H or $p\text{-}Cl$
$Y = p\text{-}CH_3O$, $p\text{-}CH_3$, H, $p\text{-}Cl$ or $p\text{-}NO_2$

RESULTS AND DISCUSSION

In reaction (3), the anionic nucleophiles are added in the form of sodium salts. The reaction follows typical second-order kinetics, equation (4), and is first order with respect to each reactant.

$$\text{Rate} = k_2[\text{BSC}][\text{RCOO}^-] \quad (4)$$

The rate constant, however is, found to increase with increasing dilution of nucleophiles, i.e. at lower $[RCOO^-]$, as shown in Table 1. The downward drift in k_2 with increasing salt concentration can be accounted for by the ion-pairing of the salt at relatively higher salt concentration,[5] lowering the nucleophilicity of the anionic nucleophile and hence diminishing the second-order rate constant. This is supported by the relative insensitivity of k_2 to changes in neutral substrate concentration [BSC]. The k_2 values are reported in Tables 2 and 3 at a fixed salt concentration of $[RCOO^-] = 0{\cdot}02$ M.

The rate of reaction with both anionic nucleophiles is slower than the corresponding rate of reactions with

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Table 1. Effect of varying concentrations of sodium benzoate, sodium cinnamate and benzenesulphonyl chloride on the rate of the reaction in methanol at 30·0 °C

$[C_6H_5COONa]$ (M)	$[C_6H_5SO_2Cl]$ (M)	k_2 ($\times 10^3$ l mol^{-1} s^{-1})[a]
0·01	0·015	10·3 ± 0·08
0·02	0·010	9·13 ± 0·10
0·02	0·015	9·15 ± 0·11
0·02	0·017	9·14 ± 0·09
0·022	0·015	9·07 ± 0·13
0·035	0·015	8·92 ± 0·10
0·040	0·015	7·78 ± 0·11
$[C_6H_5CH{=}CHCOONa]$ (M)	$[C_6H_5SO_2Cl]$ (M)	k_2 ($\times 10^3$ l mol^{-1} s^{-1})[a]
0·01	0·012	16·1 ± 0·09
0·02	0·012	14·0 ± 0·10
0·02	0·016	14·3 ± 0·12
0·02	0·020	14·1 ± 0·11
0·02	0·025	14·5 ± 0·08
0·034	0·015	12·8 ± 0·12
0·04	0·015	12·1 ± 0·13

[a] The error limits shown are average deviations based on triplicate runs.

Table 2. Second-order rate constants, k_2 ($\times 10^3$ l mol^{-1} s^{-1}),[a] and Hammett coefficients for the reactions of (Y) benzenesulphonyl chlorides with (X) sodium benzoates in methanol at 30·0 °C[b]

	Y					
X	p-CH$_3$O	p-CH$_3$	H	p-Cl	p-NO$_2$	ρ_Y[c]
p-CH$_3$O	5·62 ± 0·05	7·41 ± 0·07	11·5 ± 0·08	15·1 ± 0·10	75·9 ± 0·18	0·75
p-CH$_3$	5·31 ± 0·07	6·92 ± 0·03	10·6 ± 0·11	13·5 ± 0·09	66·7 ± 0·11	0·70
H	4·79 ± 0·04	6·12 ± 0·04	9·12 ± 0·09	12·9 ± 0·08	53·5 ± 0·09	0·67
p-Cl	4·17 ± 0·06	5·25 ± 0·08	7·59 ± 0·06	9·33 ± 0·06	40·7 ± 0·10	0·62
ρ_X[d]	−0·26	−0·30	−0·37	−0·42	−0·55	

[a] The error limits shown are average deviations based on triplicate runs.

[b] $[XC_6H_4COONa]$ = 0·02 M; $[YC_6H_4SO_2Cl]$ = 0·015 M.

[c] Correlation coefficients > 0·997 at the 99% confidence level. Ordinary σ values are used except for Y = p-NO$_2$[11] (see text).

[d] Correlation coefficients > 0·998 at the 95% confidence level. Ordinary σ values are used.[12]

Table 3. Second-order rate constants, k_2 ($\times 10^3$ l mol^{-1} s^{-1}),[a] and Hammett coefficients for the reactions of (Y) benzenesulphonyl chlorides with (X) sodium cinnamates in methanol at 30·0 °C[b]

	Y					
X	p-CH$_3$O	p-CH$_3$	H	p-Cl	p-NO$_2$	ρ_Y[c]
p-CH$_3$O	8·93 ± 0·12	11·1 ± 0·13	16·6 ± 0·13	21·9 ± 0·18	97·3 ± 2·0	0·67
p-CH$_3$	8·69 ± 0·09	10·7 ± 0·11	15·7 ± 0·12	20·3 ± 0·13	91·1 ± 2·8	0·65
H	8·09 ± 0·10	9·93 ± 0·08	14·3 ± 0·14	18·5 ± 0·14	79·8 ± 2·2	0·64
p-Cl	7·52 ± 0·12	9·12 ± 0·11	12·9 ± 0·11	16·6 ± 0·11	67·5 ± 1·4	0·61
ρ_X[d]	−0·15	−0·17	−0·22	−0·24	−0·32	

[a,c,d] See Table 2.

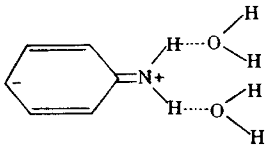
[b] $[XC_6H_4CH{=}CHCOONa]$ = 0·02 M; $[YC_6H_4SO_2Cl]$ = 0·015 M.

Table 4. AM1 HOMO levels (eV) based on full optimization, pK_a and k_2 values for various nucleophiles reacting with benzenesulphonyl chloride

Nucleophile	CMO[a]	LMO[b]	pK_a[c]	k_2 ($l\,mol^{-1}\,s^{-1}$)
$C_6H_5NH_2$	−8·522	−14·729	4·60	$11\cdot5\times10^{-2}$[d]
$C_6H_5CH_2NH_2$	−10·052	−15·665	9·35	2·30[e]
$C_6H_5COO^-$	−4·673	−6·204	4·204	$9\cdot12\times10^{-3}$[f]
$C_6H_5CH{=}CHCOO^-$	−4·691	−6·207	4·438	$14\cdot3\times10^{-3}$[f]

[a] Canonical MO.
[b] Localized MO.
[c] At 25 °C in water.[7]
[d] At 35·0 °C in MeOH.[13]
[e] At 35·0 °C in MeOH.[14]
[f] At 30·0 °C, this work.

amines, as shown in Table 4, where we have given the highest occupied MOs (HOMOs) of the nucleophiles both calculated by AM1.[6] Examination of LMO–HOMOs indicates that the lone-pair levels in the anionic nucleophiles are substantially higher than those in the amines; benzoates and cinnamates are therefore soft bases having relatively low pK_a values.[7] One anomaly in Table 4 is that aniline has a much lower pK_a value despite the lower HOMO. This is mainly due to resonance and inductive effects of the benzene ring[8a] but is also partially due to the nucleophilic solvation of water enhancing the lone-pair electron delocalization (I). Since this type of delocalization cannot occur in benzylamine, its pK_a is high, as expected from the low HOMO level. The reactivity order, however, parallels the basicity of the nucleophiles, since in the charge-controlled reaction[9] the more basic nucleophile is more nucleophilic; this is in line with the HSAB principle:[10] since the sulphonyl reaction centre is a hard acid, a hard base, i.e. a more basic nucleophile, will react faster, as in Table 4.


(I)

The rate is faster with a more electron-donating substituent (EDS) in the nucleophile (X = *p*-OCH_3) and with a more electron-withdrawing substituent (EWS) in the substrate (Y = *p*-NO_2). We note a marked increase in rate with a strong EWS, Y = *p*-NO_2, suggesting the development of an electron-rich reaction centre at the sulphonyl S which is in strong resonance with the EWS.[11] It therefore appears that bond formation in the TS is fairly extensive between the reaction centre, S, and the anionic nucleophile. This is supported by a better linear correlation in the Hammett plots with σ^- instead of σ for Y = *p*-NO_2.[11] The ρ_X and ρ_Y values determined are shown in Tables 2 and 3.

For both anionic nucleophiles, the magnitude of ρ_X (<0) increases with a more EWS in the substrate and the (positive) ρ_Y value increases with a more EDS in the nucleophile. These trends in the selectivity parallel those of the reactivity so that the reactivity–selectivity principle does not hold.

Since ρ_Y increases ($d\rho_Y > 0$) with a more EDS($d\sigma_X < 0$) in the nucleophile, and $|\rho_X|$ increases

Table 5. Cross-interaction constants, ρ_{XY} and λ_{XY}, obtained by multiple linear regression of rate constants using equations (1) and (2)

Reaction			ρ_X	ρ_Y	ρ_{XY}	r[a]	β_X	λ_{XY}	r[a]
$XC_6H_4COO^-$	$+\ YC_6H_4SO_2Cl$	$\xrightarrow[30\cdot0\,^{\circ}C]{MeOH}$	−0·37	0·69	−0·33	0·997	0·38	0·33	0·996
$XC_6H_4CH{=}CHCOO^-$	$+\ YC_6H_4SO_2Cl$	$\xrightarrow[30\cdot0\,^{\circ}C]{MeOH}$	−0·22	0·63	−0·22	0·998	0·62	0·44	0·998
$XC_6H_4CH_2NH_2$	$+\ YC_6H_4SO_2Cl$	$\xrightarrow[35\cdot0\,^{\circ}C]{MeOH}$	−1·38	1·52	−0·39	0·999	1·40	0·39	0·999
$XC_6H_4NH_2$	$+\ YC_6H_4SO_2Cl$	$\xrightarrow[35\cdot0\,^{\circ}C]{MeOH}$	−2·14	0·96	−0·70	0·998	0·72	0·20	0·998

[a] Correlation coefficients at the 99% confidence level.

($d|\rho_X| > 0$ or $d\rho_X < 0$) with a more EWS ($d\sigma_Y > 0$) in the substrate, the sign of ρ_{XY} should be negative. This is borne out in Table 5, which summarizes the cross-interaction constants, λ_{XY} and ρ_{XY}, determined by

$$\rho_{XY} = \frac{\partial \rho_Y}{\partial \sigma_X} = \frac{\partial \rho_X}{\partial \sigma_Y} = \frac{\partial^2 (k_{XY}/k_{HH})}{\partial \sigma_X \sigma_Y} < 0 \qquad (5)$$

multiple linear regression of the second-order rate constants in Tables 2 and 3 using equations (1) and (2). The fact that the cross-interaction constants are non-zero indicates substantial bond formation in the TS, which considered together with the fairly good leaving group, Cl^-, involved suggests a concerted, i.e. S_N2, mechanism. The possibility of an addition–elimination mechanism with a rate-limiting addition step cannot be precluded entirely. However, we are here concerned only with the degree of bond formation irrespective of whether concerted bond breaking occurs (S_N2) or not (addition–elimination). The size of $|\rho_{XY}|$ for benzoates is approximate half of that for the reaction with aniline nucleophile; this is reasonable if the degree of bond formation is approximately the same for a group (CH_2 or CO) between the reaction centre and substituent reduces ρ values by a factor of 2·4–2·8.[2] An extra conjugative intervening group, CH=CH, in cinnamates should also reduce ρ values by slightly more than the same factor (less than 0·16)[2b] so that the value of $|\rho_{XY}| = 0\cdot22$ indicates a relatively greater degree of bond formation compared with benzoates.

The cross-interaction constants, λ_{XY}, do not suffer from such complications, and the magnitudes can be compared in a straightforward manner without any such considerations of the fall-off of the susceptibility for substituent effect transmission to the reaction centre. As expected from the $|\rho_{XY}|$ values, cinnamate series have a higher value of λ_{XY}, suggesting a greater degree of bond formation involved in the TS. Both benzoates and cinnamates have larger λ_{XY} values than the aniline series ($\lambda_{XY} = 0\cdot20$), but they have similar values to that for the benzylamine series ($\lambda_{XY} = 0\cdot39$). It is interesting that for benzoates the magnitudes of the two cross-interaction constants are the same, $|\rho_{XY}| = |\lambda_{XY}|$, which reflects the original definition of the σ values, i.e. $\sigma_X = -\Delta pK_X$, using benzoic acids.[7] This is also true for benzylamines, $\sigma_X = -\Delta pK_X$.

The two types of nucleophiles, amines and anions, form separate families of nucleophiles in that the amines have much lower HOMOs than the anions, so that the amines are hard but anions are soft bases; anilines, however, are made softer by the solvation effect. Within a family of nucleophiles the reactivity is intrinsically controlled,[3g,15] and a more product-like TS, i.e. a greater degree of bond formation with larger ρ_{XY} and λ_{XY}, is formed by a more basic nucleophile.[3g,15]

We conclude that the degree of bond formation in the TS with anionic nucleophiles is in general greater than that with neutral nucleophiles under similar reaction conditions. Anionic nucleophiles transfer a larger amount of charge to the reaction centre in bond formation so that the use of σ^- constants is warranted for the strong electron-withdrawing *para* substituents in the substrate owing to the strong resonance between the relatively electron-rich reaction centre and EWS.

EXPERIMENTAL

Materials. Substituted benzenesulphonyl chlorides were purified as described previously.[14] Sodium benzoates and cinnamates were recrystallized from suitable solvents[16] and their purities were checked by m.p. and ^1H NMR determinations.

Kinetic procedures. The rate measurements were carried out under second-order conditions, fixing the concentrations of sodium benzoates and cinnamates at 0·02 M and those of benzenesulphonyl chlorides at 0·015 M in methanol at 30·0 ± 0·05 °C. The chloride ion was titrated by Volhard's method[17] following a procedure similar to that of Mishra *et al.*[16] The standard deviation of the individual second-order plot was well within 1% and the agreement between triplicate runs were usually within 1–3%.

Product analysis. The reaction mixtures were kept overnight and the solvent, methanol, was removed. The residual liquid was extracted with carbon tetrachloride and dried with anhydrous sodium sulphate. After removing the solvent, the residue was examined by thin-layer chromatography (TLC), IR and NMR spectrometry and elementary analysis. TLC with 20% ethylacetate–hexane showed spots at

$$R_F = 0\cdot53\ (C_6H_5COOSO_2C_6H_5)$$

and

$$0\cdot44\ (C_6H_5CH{=}CHCOOSO_2C_6H_5).$$

$C_6H_5COOSO_2C_6H_5$: ν_{max}(neat), 3030 (CH arom.), 1715 (C=O, sym. str.), 1580 (C=C, arom.), 1295 (CO) and 1180 cm^{-1} (SO_2); δ (60 MHz; CCl_4), 6·65–7·78 (10H, phenyl). Found: C, 59·46; H, 3·81; O, 24·48; S, 12·25. Calculated for $C_{13}H_{10}O_4S$: C, 59·53; H, 3·85; O, 24·40; S, 12·22%. $C_6H_5CH{=}CHCOOSO_2C_6H_5$): ν_{max}(neat), 3015 (CH, arom.), 2905 (CH, alkene), 1720 (C=O, sym. str.), 1620 (C=C, alkene), 1570 (C=C, arom.), 1290 (CO), 1175 cm^{-1} (SO_2); δ (60 MHz; $CDCl_3$), 6·40–8·01 (10H arom. and 2H olef.). Found: C, 62·53; H, 4·14; O, 22·28; S, 11·05. Calculated for $C_{15}H_{12}O_4S$: C, 62·48; H, 4·20; O, 22·20; S, 11·12%.

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