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NUCLEOPHILIC SUBSTITUTION REACTION OF BENZYL BENZENESULFONATES WITH ANILINES IN METHANOL-ACETONITRILE MIXTURES. PART 3.

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Abstract – Kinetic studies on the nucleophilic substitution reaction of *para*-nitrobenzyl benzenesulfonates with anilines in methanol-acetonitrile mixtures are reported. It was found that the reaction proceeds *via* a dissociative S_N2 mechanism with a more product-like transition state compared to that for substrate with a less electron attracting substituent. A stronger electron withdrawing substituent in the benzyl moiety and in the leaving group is shown to enhance both bond making and bond breaking but the enhancement of bond making was found to be greater than that of bond breaking.

In previous papers in this series,[1,2] we have reported the results of our studies on substituent and solvent effects on the transition state (TS) variation in the reaction of benzyl benzenesulfonates with anilines in methanol- acetonitrile (MeOH-MeCN) mixtures (1).

$$X-C_6H_4NH_2 + Y-C_6H_4CH_2OSO_2C_6H_4-Z \rightarrow X-C_6H_4\overset{+}{N}H_2CH_2C_6H_4-Y + {}^-O_3SC_6H_4-Z \qquad (1)$$

A more electron donating substituent (X) in the nucleophile and a more electron withdrawing substituent (Z) in the leaving group have been found to make the TS of the dissociative S_N2 process more product-like in addition to enhancing the rate of reaction (1). These experimental findings were in good accord with the theoretical predictions of the effects of substituents on the S_N2 TS variation.[3,4] On the other hand, it has been shown that predictions of effects of substituent (Y) in the benzyl moiety on the degree of substrate-leaving group(C_α-L) bond breaking in the S_N2 TS structure were shown to be complex[4]; a more electron withdrawing substituent is expected to increase the nucleophile-substrate ($N-C_\alpha$) bond formation, but the C_α-L bond cleavage is predicted to decrease in a "polarization-controlled" reaction whereas it is predicted to increase in a "charge-transfer-controlled" reaction.

Our preliminary results[2] have indicated that an electron withdrawing group (Y = *p*-Cl) retarded the rate with the TS of more product-like structure suggesting the possibility of a charge-transfer-controlled effect on the TS structure of the reaction (1); the C_α-L bond cleavage is enhanced as a result of a greater amount of charge transfer to the $\sigma^*(C_\alpha-L)$ orbital by the substituent, *i.e.*, Y = *p*-Cl, in the TS. This type of behavior was shown to predominate in an S_N2 TS involving a relatively short range interaction of the two reactants, especially when the C_α-L bond has a low lying LUMO (lowest unoccupied MO) of a strongly antibonding $\sigma^*(C_\alpha-L)$ orbital.[4]

In this work we report the results of further studies to elucidate the effect of an electron withdrawing substituent in the benzyl moiety on the S_N2 TS structure using *para*-nitrobenzyl benzenesulfonates (Y = *p*-NO_2) in reaction (1).

Result and Discussion

Substituent Effects : Second order rate constants k_2 for reactions of *para*-nitrobenzyl benzenesulfonates(Y= *p*-NO$_2$) with anilines in MeOH-MeCN mixtures are reported in Table 1. The rate is in general slower than that of the unsubstituted (Y=H) and the substrate with a less electron attracting (Y= *p*-Cl) substituent; k_2 values in 100 (v/v %) MeOH are 17.3,[2] 15.4[4] and 4.57 ($\times 10^{-3}$ l mol^{-1} sec^{-1}) for Y=H, *p*-Cl and *p*-NO$_2$ respectively with Z=X=H in reaction (1). Table 1 shows that the rate is faster for the nucleophile with a more electron donating substituent (X= *p*-CH$_3$O), the leaving group with a more electron withdrawing group (Z= *m*-NO$_2$) and the solvent of greater hydrogen bond donor acidity α (higher MeOH content)[5] as was found in the previous reports.[1,2]

Table 1. Second order rate constants ($k_2 \times 10^3$ l mol^{-1} sec^{-1}) for reactions of *p*-NO$_2$-benzyl benzenesulfonates with X-anilines in methanol-acetonitrile mixtures at 35°C

MeOH (v/v %)	Z	X= *p*-CH$_3$O	*p*-CH$_3$	H	*p*-Cl	*m*-NO$_2$
100	*p*-CH$_3$[a]	6.97	4.30	2.62	1.28	0.316
	H	12.6	7.94	4.57	2.36	0.499
	p-Cl	24.0	17.4	9.91	4.79	0.910
	m-NO$_2$	178	93.3	49.2	21.5	4.62
90	*p*-CH$_3$[a]	5.73	3.90	2.19	1.05	0.251
	H	10.7	6.61	3.98	1.08	0.398
	p-Cl	23.0	16.2	8.32	3.62	0.794
	m-NO$_2$	158	83.2	45.7	18.2	3.98
80	*p*-CH$_3$[a]	5.00	3.16	1.82	0.871	0.199
	H	9.12	5.45	3.16	1.51	0.316
	p-Cl	21.9	12.5	7.08	3.02	0.692
	m-NO$_2$	135	72.4	38.4	16.5	3.24
70	*p*-CH$_3$[a]	4.62	2.75	1.42	0.742	0.155
	H	7.41	5.01	2.47	1.26	0.240
	p-Cl	16.9	11.5	5.62	2.64	0.525
	m-NO$_2$	114	66.1	31.6	15.7	2.70
50	*p*-CH$_3$[a]	3.53	2.06	1.14	0.567	0.112
	H	6.09	3.56	1.81	0.810	0.155
	p-Cl	14.5	8.00	4.03	1.82	0.331
	m-NO$_2$	91.2	49.5	25.1	11.5	1.95

[a] : Data from reference 1.

Hammett ρ_X and Broensted β_N values for substituent changes in the nucleophile (with Y= *p*-NO$_2$) are summarized in Tables 2 and 3

Table 2. Hammett ρ_X values[a] for reactions of *p*-NO$_2$-benzyl benzenesulfonates with X-anilines in MeOH-MeCN mixtures at 35°C

Y	MeOH (v/v %)	Z= *p*-CH$_3$	H	*p*-Cl	*m*-NO$_2$
p-NO$_2$	100	-1.34	-1.42	-1.45	-1.57
	90	-1.36	-1.43	-1.50	-1.59
	80	-1.40	-1.46	-1.50	-1.61
	70	-1.46	-1.50	-1.53	-1.62
	50	-1.49	-1.60	-1.63	-1.66
p-Cl[b]	100	-1.05	-1.08	-1.11	-1.21
	80	-1.12	-1.18	-1.22	-1.33
	50	-1.20	-1.29	-1.31	-1.44
H[b]	100	-0.82	-0.84	-0.87	-0.97
	80	-0.94	-0.96	-1.01	-1.06
	50	-1.05	-1.05	-1.14	-1.20

[a] : Correlation coefficients ; r = 0.997±0.002. [b] : Data from reference 2.

Table 3. Broensted β_N values[a] for reactions of p-NO$_2$-benzyl benzenesulfonates with X-anilines in MeOH-MeCN mixtures at 35°C

Y	MeOH (v/v%)	Z= p-CH$_3$	H	p-Cl	m-NO$_2$
p-NO$_2$	100	0.45	0.48	0.49	0.53
	90	0.47	0.49	0.51	0.54
	80	0.48	0.49	0.51	0.54
	70	0.50	0.51	0.52	0.55
	50	0.50	0.54	0.55	0.56
p-Cl[b]	100	0.36	0.37	0.38	0.41
	80	0.38	0.40	0.41	0.45
	50	0.41	0.44	0.44	0.49
H[b]	100	0.28	0.29	0.30	0.31
	80	0.32	0.32	0.34	0.36
	50	0.36	0.36	0.39	0.41

a: Correlation coefficients ; $r=0.996\pm0.003$. b: Data from reference 2.

together with the corresponding values with Y=H and p-Cl. Magnitudes of these selectivity parameters, and hence the degree of the nucleophile-substrate (N-C$_\alpha$) bond making in the TS,[6,7] are seen to increase with a more electron withdrawing substituent in the leaving group (Z=m-NO$_2$) and in the substrate (Y=p-NO$_2$). These results are consistent with our previous experimental findings[1,2] as well as with theoretical predictions of substituent effects on the S$_N$2 TS structure[3,4] ; here again a good leaving group (Z=m-NO$_2$) leads to a greater degree of bond formation (larger $|\rho_X|$ and β_N) suggesting a concerted S$_N$2 mechanism for the reaction (1). The concerted nature of bond-making and -breaking is further supported by ρ_Z values obtained by changing substituents (Z) in the leaving group in Table 4.

Table 4. Hammett ρ_Z values[a] for reactions of p-NO$_2$-benzyl benzenesulfonates with X-anilines in MeOH-MeCN mixtures at 35°C

Y	MeOH (v/v%)	X= p-CH$_3$O	p-CH$_3$	H	p-Cl	m-NO$_2$
p-NO$_2$	100	1.60	1.52	1.45	1.38	1.34
	90	1.64	1.54	1.50	1.41	1.37
	80	1.63	1.56	1.51	1.45	1.39
	70	1.61	1.57	1.54	1.51	1.43
	50	1.62	1.59	1.55	1.52	1.45
p-Cl[b]	100	1.41	1.42	1.41	1.35	1.24
	80	1.51	1.50	1.49	1.43	1.30
	50	1.57	1.59	1.58	1.48	1.35
H[b]	100	1.29	1.33	1.33	1.24	1.22
	80	1.38	1.43	1.43	1.33	1.28
	50	1.51	1.52	1.52	1.45	1.35

a: Correlation coefficients ; $r=0.994\pm0.005$. b: Data from reference 2.

We find in this Table that a stronger nucleophile (X=p-CH$_3$O) has a greater ρ_Z value indicating more extensive bond cleavage in the TS.

In contrast, kinetic isotope effects studies of Ando et al.[8] on the reaction of benzyl benzenesulfonates with N,N-dimethyl anilines, however, have shown that the TS becomes more reactant-like when a nucleophile becomes more nucleophilic or when a leaving group becomes a better one. On the other hand substituent effect studies of Yoh[9] on the same reaction have shown that a more electron donating substituent on the nucleophile led to a greater degree of bond formation (larger $|\rho_X|$) in agreement with our results.

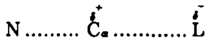
A more electron withdrawing substituent in the substrate ($Y=p-NO_2$) seems to enhance both the $N-C_\alpha$ bond making (greater $|\rho_X|$ and β_N values in Table 2 and 3) and the $C_\alpha-L$ bond breaking (greater ρ_Z values in Table 4). This is in agreement with the results of Ando et al[8] that the substituent $Y=m-Br$ gave more product-like TS.

The MO models for predictions of substituent effects on the S_N2 TS structure[3,4] can nicely accommodate these phenomena. It has been shown[4] that an electron withdrawing substituent in the substrate as well as in the leaving group is predicted to facilitate both bond formation and bond breaking in a charge-transfer-controlled process, in which the effect of the charge transfer (E_{ct}) component on bond breaking predominates over that of the polarization (E_{pl}) term[10-13]

Inspection of Tables 2 and 4 reveals that the $|\rho_Z|$ values are greater than the $|\rho_X|$ values for the substrate with $Y=H$, whereas the two selectivity parameters exhibit no significant difference for the substrate with $Y=p-NO_2$. This can be rationalized as follows: when the electron withdrawing power of the substituent (Y) in the substrate increases, the increase in the degree of bond breaking becomes less than that of bond making at the TS; although both the $N-C_\alpha$ bond making and $C_\alpha-L$ bond breaking increases ($\Delta \ell_{N-C_\alpha}>0$ and $\Delta \ell_{C_\alpha-L}>0$), the ratio $R=(\Delta \ell_{C_\alpha-L})/(\Delta \ell_{N-C_\alpha})$ decreases for the substrate with a strong electron withdrawing substituent,

$$R=\frac{\Delta \ell_{C_\alpha-L}}{\Delta \ell_{N-C_\alpha}}<1.0 \qquad (2)$$

This means that the dissociative S_N2 TS (I) becomes less polar for



$$N\cdots\cdots\cdots\overset{\delta^+}{C_\alpha}\cdots\cdots\cdots\cdots\overset{\delta^-}{L}$$

(I)

the substrate with $Y=p-NO_2$, since an increase in the $N-C_\alpha$ bond formation will increase dispersal of the charge localized on the C_α atom as a result of extensive $C_\alpha-L$ bond breaking. This is consistent with the slower rate for the substrate with $Y=p-NO_2$, compared to that with $Y=H$, since the TS with increasing dispersal of charge is less polar and hence will be less stabilized by the polar solvent.[14-16]

Hammett ρ_Y^+ values determined by the plot of log k_2 *vs* σ^+ substituent constant for the three compounds, *i.e.*, for $Y=H$, p-Cl and $p-NO_2$, are summarized in Table 5. The negative sign of the ρ_Y^+ values indicates positive

Table 5. Hammett ρ_Y^+ values[a,b] for reactions of benzyl benzenesulfonates with X-anilines in MeOH-MeCN mixtures at 35°C

Z	MeOH (v/v %)	$X=p-CH_3O$	$p-CH_3$	H	p-Cl	$m-NO_2$
$p-CH_3$[c]	100	−0.69	−0.78	−0.84	−1.06	−1.25
	90	−0.72	−0.74	−0.84	−1.04	−1.23
	80	−0.71	−0.77	−0.83	−1.03	−1.21
	70	−0.69	−0.75	−0.81	−1.02	−1.20
	50	−0.66	−0.72	−0.79	−0.90	−1.16
H	100	−0.56	−0.68	−0.84	−0.89	−1.21
	90	−0.59	−0.65	−0.75	−0.95	−1.23
	80	−0.55	−0.60	−0.73	−0.87	−1.10
	70	−0.56	−0.60	−0.75	−0.85	−1.10
	50	−0.55	−0.60	−0.73	−0.91	−1.13
p-Cl	100	−0.66	−0.69	−0.80	−0.97	−1.27
	90	−0.61	−0.65	−0.81	−1.01	−1.23
	80	−0.59	−0.72	−0.83	−1.00	−1.15
	70	−0.65	−0.67	−0.86	−1.10	−1.19
	50	−0.57	−0.68	−0.83	−0.95	−1.15
$m-NO_2$	100	−0.35	−0.57	−0.71	−0.89	−1.11
	90	−0.38	−0.58	−0.70	−0.92	−1.07
	80	−0.42	−0.62	−0.73	−0.88	−1.05
	70	−0.47	−0.62	−0.78	−0.84	−1.07
	50	−0.53	−0.64	−0.76	−0.84	−1.04

a: Correlation coefficients; $r=0.945\pm0.050$. *b*: Kinetic data from references 1, 2 and this work. *c*: Data from reference 1.

charge development at the benzyl carbon (C_α) in the TS, which in turn implies that the C_α–L bond breaking is advanced than the N–C_α bond making since the positive charge developed as a result of the C_α–L bond breaking ($\rho_{break} < 0$) is greater than the negative charge transferred from the nucleophile ($\rho_{form} > 0$) in the N–C_α bond formation.

$$\rho_Y{}^+ = \rho_{break} + \rho_{form} < 0 \qquad (3)$$

$$|\rho_{break}| > |\rho_{form}|$$

It is reasonable to assume that $\rho_{break} = a\,\rho_Z$ and $\rho_{form} = b\,\rho_X$ where a and b are positive proportionality constants, and in general $a \neq b$. The magnitude of $\rho_Y{}^+$ value can then be given as

$$|\rho_Y{}^+| = |a\,\rho_Z| - |b\,\rho_X| \qquad (4)$$

Thus a greater degree of bond making (greater $|\rho_X|$) by a more electron donating substituent in the nucleophile (X= p–CH_3O) gives a smaller $|\rho_Y{}^+|$ value (for $|a\,\rho_Z|$ =const.) in Table 5. Similarly we should expect a greater $|\rho_Y{}^+|$ value for the leaving group with a more electron withdrawing substituent (Z= m–NO_2) (for $|b\,\rho_X|$ = const.) since the C_α–L bond cleavage will be more advanced (greater $|\rho_Z|$). However we find in Table 5 that the $|\rho_Y{}^+|$ value is actually smaller for a better leaving group (Z= m–NO_2). This is in fact consistent with our conclusion above that although the N–C_α bond making and the C_α–L bond breaking are concerted, the increase in the bond formation ($\Delta|b\,\rho_X| > 0$) is greater than that in the bond breaking ($\Delta|a\,\rho_Z| > 0$) for the substrate and leaving group with a more electron withdrawing substituent, *i.e.*, $\Delta|b\,\rho_X| > \Delta|a\,\rho_Z|$. Thus the net result will be a decrease in the $|\rho_Y{}^+|$ value; $\Delta|\rho_Y{}^+| < 0$ since $\Delta|\rho_Y{}^+| = \Delta|a\,\rho_Z| - \Delta|b\,\rho_X|$ and $\Delta|b\,\rho_X| > \Delta|a\,\rho_Z|$.

This shows that an increase in the accepting ability by introducing an electron sink (Y=Z= electron withdrawing group) in the substrate enhances bond making more than bond breaking.

The extent of bond breaking is substantially greater than that of bond formation at the TS of the reaction (1), but the variation in the degree of bond breaking ($\Delta\ell_{C_\alpha-L}$ and $\Delta|a\,\rho_Z|$) with the substituent changes in the substrate (Y=H→Y= p–NO_2) or in the leaving group (Z= p–CH_3→Z= m–NO_2) is less than that of bond making ($\Delta\ell_{N-C_\alpha}$ and $\Delta|b\,\rho_X|$). This is reasonable since bond breaking is already far advanced in the TS so that further change in the degree of bond breaking will be less compared to the changes occuring in the less extensive bond making.

Solvent Effects: The rate in Table 1 is seen to decrease as the polarity (π^*) of solvent[5] increases with the MeCN content. Table 2 and 4 show that the changes in the $|\rho_X|$ are greater than those in the $|\rho_Z|$ as solvent composition is changed, which is in agreement with our conclusion above that change in the degree of bond making is greater than that of bond breaking (provided that the a and b are not much different). Since the polarity of the dissociative S_N2 TS, (I), is determined by the degree of bond breaking $|a\,\rho_Z| > |b\,\rho_X|$ in eq (4), the TS will be less stabilized in the more polar solvent since the increase in the bond breaking, $\Delta|a\,\rho_Z|$, is less than that in the bond making, $\Delta|b\,\rho_X|$, as the polarity of solvent increases with the MeCN content; in the TS (I), greater degree of bond making will give more delocalization of the positive charge developed on the benzyl carbon C_α over the N–C_α bond so that the stabilization will be less in the more polar solvent.[14–16]

This is consistent with slower rate found in the more polar solvent of higher MeCN content in Table 1.

Conclusion

Nucleophilic substitution reaction of *para*–nitrobenzyl benzenesulfonates with anilines in MeOH–MeCN mixtures proceeds by a dissociative S_N2 reaction in which bond breaking is ahead of bond formation in the TS. The reaction was found to be a rare example of the charge–transfer–controlled process where the effect of an electron withdrawing substituent in the substrate is determined by the charge transfer E_{ct} term so that the substituent enhances both bond–making and –breaking. It was however notable that the enhancement of bond making is greater than that of the bond breaking in this type of reaction.

EXPERIMENTAL

Materials : All materials are as reported [1,2] except *para*-nitrobenzyl benzenesulfonates (p-$NO_2C_6H_4CH_2OSO_2C_6H_4$-Z) which were prepared by the method in the literatures[8,9,10] and were recrystallized more than twice from anhydrous ether. Melting points (uncorrected) were as follows [Z, mp (°C)] : H, 89-90(lit.[9] 90-91°C) ; p-Cl 128-131(lit.[9] 130-131 °C) ; m-NO_2, 107-108(lit.[9] 109-110°C).

Kinetic Procedures : All the kinetic procedures and determination of second order rate constants k_2 are as described previously.[1] Methanolysis rates of the compounds studied were found to be less than 10^{-2} times[17] of the k_2 values in Table 1 so that they were neglected. Excellent linearities between conductivity and product concentration were evidenced in the excellent linearities obtained in all Guggenheim plots ($r > 0.999$). Initial concentrationo of the esters were $1.0-3.5 \times 10^{-4}$ M and those of anilines were over 10^2 times of the ester concentration. The second-order rate constants, k_2, were obtained from the slope of the plots of (more than four) k_2, were obtained from the slope of the plots of (more than four) k_{obs} *vs.* [aniline].

$$k_{obs} = k_2 \text{ [aniline]}$$

Good second order kinetics ($r > 0.999$) were obtained in all cases.

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