JOURNAL OF PHYSICAL ORGANIC CHEMISTRY
J. Phys. Org. Chem. **12**, 425–429 (1999)

Kinetics and mechanism of the pyridinolysis of benzenesulfonyl chlorides in methanol

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Received 8 August 1998; revised 26 October 1998; accepted 2 November 1998

ABSTRACT: The kinetics of reactions between Y-benzenesulfonyl chlorides and X-pyridines in methanol at 35.0 °C were investigated. Strong *para* π-acceptors, X = *p*-CN and *p*-COCH$_3$, give good linear fits to Brønsted-type plots with low β_X (=0.32–0.45) but show positive deviations from linear Hammett plots ($\rho_X = -1.98$ to -2.79). Excellent linear Hammett plots are obtained with substituent variations in the substrate with $\rho_Y = 0.6$–1.0 which are similar to those for the anilinolysis. These results support an S_N2 mechanism for the pyridinolysis of benzenesulfonyl chlorides. The cross-interaction constant ρ_{XY} is a small negative value (-0.48). Much smaller magnitudes of β_X, ρ_X and ρ_{XY} than the corresponding values for the anilinolysis suggest that the transition state is formed at a relatively earlier position along the reaction coordinate than for anilinolysis. Copyright © 1999 John Wiley & Sons, Ltd.

KEYWORDS: pyridinolysis; benzenesulfonyl chlorides; Brønsted plots; cross-interaction constant; S_N2 mechanism

INTRODUCTION

There has been considerable interest in the mechanism of solvolysis and aminolysis reactions of sulfonyl halides. Various mechanisms have been proposed depending on nucleophiles, substrate and solvents ranging from nucleophilic substitutions (S_N1 and S_N2) through addition–elimination (S_AN) to elimination ($E1$, $E2$ and $E1cB$ types). For example, various alkane and arene sulfonyl chlorides[1] (RSO$_2$Cl, where R = Me, Et, Pr^i, benzene, 1-naphthalene, 5-dimethylaminonaphthalene-1-, 1-anthracene, etc.) are known to undergo nucleophilic substitution reactions with solvents and amines through an S_N2 mechanism. On the other hand, Arcoria *et al.*[2] proposed an addition–elimination (S_AN) mechanism for the aminolysis of thiophene and furan sulfonyl chlorides. Recently, Spillane and co-workers[3] reported that various sulfonyl chlorides (R^{1}R^{2}NSO$_2$Cl, where R^1 and/or R^2 = Ph, Me, PhCH$_2$, c-C$_6$H$_{11}$, Bu^t, H) react with anilines in chloroform and acetonitrile via an $E2$-type mechanism.

In a previous study[4] we found that pyridine bases (XPy = XC$_5$H$_4$N) can provide an interesting and novel mechanistic probe for nucleophilic substitution reactions. Owing to the weak π-donor effect of strong π-acceptor groups,[5] e.g. CN, NO$_2$, under the influence of a positive charge at the neighboring (or *para* in the ring) position, the ratio $\delta pK_a/\delta\sigma = pK_a(para) - pK_a(meta)/(\sigma_p - \sigma_m)$ reverses in pyridine to positive (for CN and NO$_2$, the ratios are *ca* $+5$ and $+3$, respectively), in contrast to the negative values for other normal substituents (for CH$_3$,OCH$_3$,Br and Cl the ratios are -4, -5, -6 and -7, respectively). Thus in the reactions in which the N atom of pyridine becomes positively charged, the pK_a values of *p*-CN, *p*-NO$_2$, etc., reflect the substituent effect correctly since determination of pK_a involves a positive charge on N(XC$_5$H$_4$N $+$ H$^+$ $\rightarrow$ XC$_5$H$_4$N$^+$H). However, in other cases the pK_a values of such strong π-acceptors will not represent substituent effects correctly, i.e. the weak π-donor effect that was accounted for in the pK_a measurement will be absent. These different representations of the pK_a values will be reflected differently in the linear Brønsted plots depending on the charge types, positive or negative, of the N-moiety in the transition state (TS) or product. For example, in the Brønsted plots for the pyridinolysis of phenyl chloroformates,[4] *p*-CN and *p*-COCH$_3$ groups gave large negative deviations requiring enhanced pK_a values corresponding to the enhanced σ_p (σ_p^-) values in order to represent correctly through-conjugation of the electron-rich N-moiety in the TS.

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Contract/grant sponsor: Woosuk University.
Contract/grant sponsor: Chonju National University of Education.

CCC 0894–3230/99/060425–05 $17.50

This interesting mechanistic application of pyridine nucleophiles prompted us to probe the kinetics and mechanism of aminolysis of benzenesulfornyl chlorides:

$$\begin{aligned} &YC_6H_4SO_2Cl \\ &\quad + XC_5H_4N \xrightarrow[35.0\,^\circ C]{MeOH} YC_6H_4SO_2N^+C_5H_4X \\ &\quad + Cl^- \end{aligned} \tag{1}$$

In addition, we determined the cross-interaction constants,[6] ρ_{XY} in the equation

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

where X and Y are substituents in the nucleophile and substrate respectively, as a mechanistic criterion; it has been shown that ρ_{XY} is negative (-0.6 to -0.8) in S_N2 reactions whereas it is positive in the stepwise mechanism with rate-limiting departure of the leaving group.[7] The magnitude of ρ_{XY} for an S_N2 process is believed to be inversely related to the distance, r_{XY}, between nucleophile and substrate in the TS.[8] The reaction center, N, being within the ring, the magnitude of ρ_{XY}, i.e. the distance r_{XY}, will be of great interest as a probe of the TS structure.

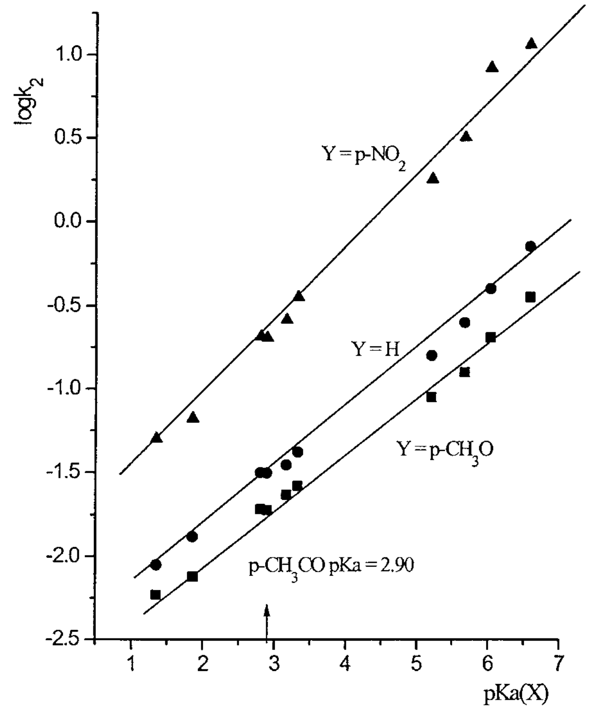

Figure 1. Brønsted plots (β_X) for the pyridinolysis of Y-benzenesulfonyl chlorides (for Y = p-CH_3O, H and p-NO_2) in MeOH at 35 °C

RESULTS AND DISCUSSION

The pseudo-first-order rate constants (k_{obs}) determined using excess pyridine (Py) obeyed second-order kinetics, and second-order rate constants k_2 were obtained from slopes of plots of k_{obs} versus [Py] as summarized in Table 1. The rates are faster with a stronger nucleophile ($\delta\sigma_X < 0$) and a stronger electron acceptor substituent in the substrate ($\delta\sigma_Y > 0$), which are compatible with the nucleophilic substitution at the sulfur atom which becomes more negatively charged in the TS. The rate constants, k_2, are comparable to or slightly lower than those corresponding values for the reactions with anilines;[1b] for example, the ratio of k_2 for p-methylaniline (pK_a = 5.10)/pyridine (pK_a = 5.21) in methanol at 35.0 °C ranges from *ca* 1.7 to 1.0 as the substituent Y in the substrate is varied from p-CH_3 to p-NO_2.

The Brønsted-type plots are presented in Fig. 1. We note that the linearities are good and two strong π-acceptors, p-CH_3CO and p-CN, do not deviate from the linear plots. The pK_a value of p-cyanopyridine was available in the literature[10] (1.86), but that of p-acetylpyridine was not, so we correlated five available pK_a values of π-acceptor *para* substituents (p-$CONH_2$, 3.61; p-COC_6H_5, 3.35; p-CN, 1.86; p-C_6H_5, 5.35; and p-NO_2, 1.39)[10,11] with their σ_p and obtained the equation p$K_a = -(5.12 \pm 0.23)\sigma_p + 5.39 \pm 0.12$, $r = 0.997$, $n = 5$. We then calculated the pK_a value of p-acetylpyridine (pK_a = 2.83) from this equation using $\sigma_p = 0.50$. Brønsted β values (β_X) determined from the slopes are shown in Table 1. The β_X values (0.33–0.46) are relatively small so that the stepwise mechanism with rate-limiting leaving group departure (for which $\beta_X \approx 0.8$–1.0) can be safely precluded. These Brønstead coefficients could be somewhat in error since the rate data (in methanol) should be plotted using pK_a values measured in methanol, not in water. However, the magnitude of β_X is significantly lower (by about half) than the corresponding values (β_X = 0.63–0.85) determined under the same reaction conditions for the reactions with anilines.[1b] These two results, linear plots for the strong π-acceptors and lower β_X values, suggest that positive charge develops on the reaction center N of the pyridine in the TS but charge development is much weaker so that the TS is much earlier along the reaction coordinate with pyridines than with anilines.

The Hammett plots are shown in Fig. 2 for variation of the substituents (Y) in the substrate. Excellent linearities are obtained with fairly small slopes (ρ_Y) of 0.6–1.0, which are comparable to the corresponding values for the reactions with anilines under the same reaction conditions ($\rho_Y \approx 0.6$–1.0).[1b] Better fits with σ_p^- for Y = p-NO_2 suggest relatively strong negative charge development on S in the TS. The positive ρ_Y suggests that the sulfur atom becomes more negative in the TS with a greater degree of bond making by the nucleophile than leaving group departure.

We finally attempted Hammett plots for substituent variations in pyridine (Fig. 3). We note that the two

Table 1. Rate constants, k_2 ($\times 10^2$ l mol^{-1}s^{-1}), for the reactions of Y-benzenesulfonyl chlorides with X-pyridines in methanol at 35 °C

	pK_a[a]	p-CH$_3$O	p-CH$_3$	H	p-Cl	m-Cl	m-NO$_2$	p-NO$_2$	ρ_Y[b]
p-CH$_3$O	6.58	35.5	52.5	70.8	83.2	158	324	1148	0.98 ± 0.07 (0.993)[c]
p-CH$_3$	6.03	20.4	27.6	39.9	61.2	89.1	239	832	1.08 ± 0.03 (0.998)
m-CH$_3$	5.67	12.6	19.5	25.1	38.9	57.5	110	318	0.91 ± 0.04 (0.998)
H	5.21	8.91	11.8	15.9	24.0	33.9	63.1	178	0.86 ± 0.02 (0.999)
m-CONH$_2$	3.33[d]	2.63	3.82	4.17	5.62	9.77	17.4	35.5	0.76 ± 0.06 (0.998)
m-CH$_3$CO	(3.17)[e]	2.34	2.95	3.50	5.18	6.11	10.1	26.0	0.68 ± 0.03 (0.998)
m-Cl	2.81	1.91	2.45	3.16	4.07	5.37	9.33	20.6	0.68 ± 0.02 (0.999)
p-CH$_3$CO	(2.90)[f]	1.89	2.42	3.14	4.06	5.34	9.30	20.2	0.68 ± 0.02 (0.999)
p-CN	1.86	0.759	0.977	1.32	1.74	2.04	3.31	6.61	0.61 ± 0.03 (0.997)
m-CN	1.35	0.589	0.708	0.891	1.10	1.62	2.40	5.01	0.62 ± 0.03 (0.997)
β_x		0.33 ± 0.01 ($r = 0.997$)	0.34 ± 0.01 ($r = 0.997$)	0.35 ± 0.01 ($r = 0.997$)	0.36 ± 0.01 ($r = 0.999$)	0.38 ± 0.01 ($r = 0.997$)	0.41 ± 0.02 ($r = 0.995$)	0.46 ± 0.02 ($r = 0.995$)	
ρ_x[g]		-1.99 ± 0.09 ($r = 0.993$)	-2.08 ± 0.10 ($r = 0.993$)	-2.16 ± 0.08 ($r = 0.995$)	-2.19 ± 0.11 ($r = 0.992$)	-2.30 ± 0.07 ($r = 0.997$)	-2.50 ± 0.09 ($r = 0.996$)	-2.79 ± 0.11 ($r = 0.995$)	

[a] pK_a values in water at 25 °C taken from Ref. 9.
[b] The σ and σ_p^- values were taken from Ref. 9.
[c] Correlation coefficient.
[d] Taken from Ref. 11.
[e] Calculated values using p$K_a = -5.65\ (\pm 0.16)\sigma + 5.20\ (\pm 0.06)$, $r = 0.994$, $n = 23$.
[f] Calculated values using p$K_a = -5.55\ (\pm 0.36)\sigma_p + 5.65\ (\pm 0.21)$, $r = 0.994$, $n = 4$.
[g] The two π-acceptors, p-CN and p-COCH$_3$, are excluded. Correlation coefficients are better than 0.993 in all cases.

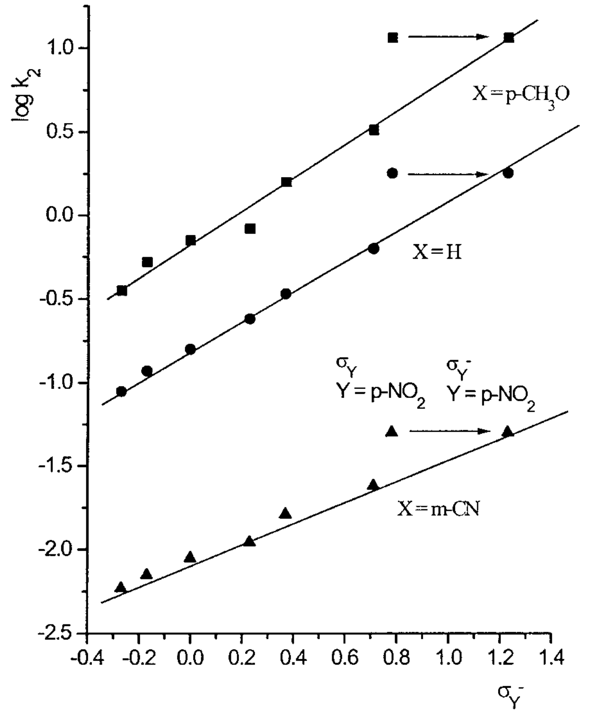

Figure 2. Hammett plots (ρ_Y) for the pyridinolysis of Y-benzenesulfonyl chlorides (for X = p-CH$_3$O, H and m-CN) in MeOH at 35 °C

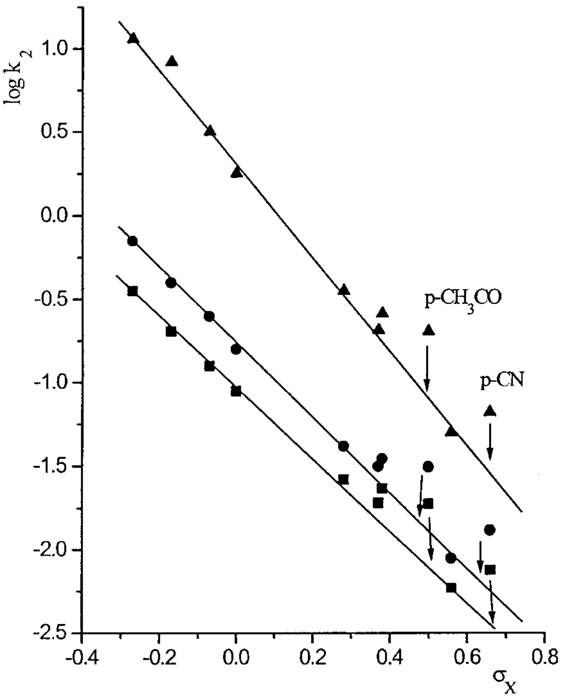

Figure 3. Hammett plots (ρ_X) for the pyridinolysis of Y-benzenesulfonyl chlorides (for Y = p-CH$_3$O, H and p-NO$_2$) in MeOH at 35 °C

strong π-acceptor *para* substituents, p-CH$_3$CO and p-CN, exhibit strong positive deviations from the otherwise linear Hammett plots. This anomalous behavior of the strong *para* π-acceptor can be attributed to the weak π-donor effect of such *para* substituents under the influence of positive charge[5] developed on N at the TS. The Hammett substituent constants, σ, for the strong para π-acceptor represent normal electron acceptor effects only, which are determined from the standard reactions, ionization equilibria of benzoic acids. Here the reaction center, the carbonyl carbon, is exocyclic and does not involve a cationic charge in the product so that the weak π-donor effect of the π-acceptor under the influence of positive charge is absent. However, for a strong *para* π-acceptor, the weak π-donor effect is represented in the pK_a value (since the pK_a determination involves cationic charge at N) and owing to this weak π-donor effect the pK_a value is somewhat enhanced beyond that expected from the purely π-acceptor ability. This is why the π-acceptors deviated positively from the plots of pK_a versus σ[10] and the ratio δp$K/\delta\sigma$ is positive for such substituents. Thus for pyridines the pK_a and σ scales represent different electronic effects for strong *para* π-acceptors.

It becomes clear that whenever the reaction center N on pyridine becomes positively charged in the TS or in the product, log$k$(or log$K$) versus pK_a will be linear but log$k$ (or log$K$) versus σ will be non-linear with respect to such *para* π-acceptors. In other cases, e.g. no positive charge development on N, such a *para* π-acceptor will behave normally with log$k$ (or log$K$) versus σ plots but will deviate negatively in log$k$ (or log$K$) versus pK_a plots. Such an example is encountered in the pyridinolysis of methyl[4,12] and phenyl chloroformates;[4] in the former, linear Brønsted plots were obtained in a stepwise mechanism with rate-limiting departure of the leaving group from a tetrahedral intermediate in which the N on pyridine is positively charged, whereas in the latter, the *para* π-acceptors exhibited negative deviations in the Brønsted plots but behaved normally with σ_p^- in the Hammett plots.[4]

Since in the present work the *para* π-acceptors, p-CN and p-CH$_3$CO, behaved normally in the Brønsted plots but showed positive deviations in the Hammett plots, the reaction center N on pyridine must be more positive in the TS. The ρ_X values determined excluding the two *para* π-acceptors ranged from -1.99 (Y = p-CH$_3$O, $r = 0.993$) to -2.79 (Y = p-NO$_2$, $r = 0.995$), which are numerically similar to those for the reaction with anilines (-1.96 to -2.65)[1b] but are actually much smaller (by *ca* 1/2.8) when the fall-off factor of *ca* 2.8 is taken into consideration. The lower ρ_X and β_X values compared with those for the reaction with anilines are indicative of a lower degree of bond making in the TS for the reaction with pyridines. Since the ρ_Y values are smaller, the TS for reactions with pyridines must be at an earlier position along the reaction coordinate. This is reasonable since for pyridines the reaction center, N, is within the ring so that close approach towards the π-electron-rich SO$_2$ moiety of the substrate will cause fairly strong π–π repulsion between those on the pyridine ring and the SO_2 moiety and the TS will be formed at a relatively longer distance, r_{XY}.

The 70 rate data in Table 1 were subjected to multiple regression analysis using Eqn. (2) to determine the cross-interaction constant ρ_{XY} for the pyridinolysis of benzenesulfonyl chlorides. The ρ_{XY} obtained was -0.48 ± 0.09 with $r = 0.977$. The negative ρ_{XY} is consistent with the S_N2 mechanism. However the magnitude is much smaller than those for anilinolysis (-0.70 and -0.75),[6] especially when the fall-off *ca* 2.8 is considered from pyridine to aniline ($\rho_{XY} = -0.48 \rightarrow -0.17$). The much lower magnitude of ρ_{XY} is again an indication of an earlier TS, i.e. bond making at a longer distance, r_{XY}, between the pyridine nucleophile and substrate in the TS, which is in line with the conclusion reached from the lower values of β_X and ρ_X (see above).

In summary, the strong *para* π-acceptors, $X = p$-CN and p-CH_3CO, give good linear fits to Brønsted-type plots but deviate positively from Hammett plots, log$k$ versus σ_X. The slopes, β_X and ρ_X (obtained excluding the two *para* π-acceptors), are considerably lower than the corresponding values for the reactions with anilines. These results together with the similar magnitude of ρ_Y suggest that the pyridinolysis of benzenesulfonyl chlorides proceeds by an S_N2 process in which the TS is at a relatively earlier position along the reaction coordinate than that in anilinolysis. The proposed mechanism is also supported by a small negative cross-interaction constant, $\rho_{XY} = -0.48$.

EXPERIMENTAL

Materials. Merck HPLC-grade methanol was used throughout. Pyridine nucleophiles from Aldrich (GR grade) were used without further purification. Benzenesulfonyl chlorides (Aldrich) were used as supplied.

Rate constants. Rates were measured conductimetrically at $35.0 \pm 0.05\,°C$. The conductivity bridge used in this work was a laboratory-made computer automatic A/D converter conductivity bridge. Pseudo-first-order rate constants, k_{obs}, were determined by the Guggenheim method[13] with a large excess of pyridine (Py); $[\text{substrate}] = 1 \times 10^{-3}$ M and $[Py] = 0.03$–0.25 M. Second-order rate constants, k_2, were obtained from the slope of a plot of k_{obs} vs [Py] with more than five concentrations of pyridine. The k_2 values in Table 1 are the averages of more than three runs and were reproducible to within ±3%.

Product analysis. Benzenesulfonyl chloride was reacted with excess *m*-acetylpyridine with stirring for more than 15 half-lives at 35.0 °C in methanol, and the products were isolated by evaporating the solvent under reduced pressure. The product mixture was treated by column chromatography (silica gel, 20% ethyl acetate–*n*-hexane). Analysis of the product gave the following results: $C_6H_5SO_2N^+C_5H_4{-}p{-}CH_3CO$, m.p. 42–43 °C; NMR (250 MHz, $CDCl_3$), δ_H, 2.8 (3H, s, CH_3CO), 7.4–9.2 (9H, m, C_5H_4N, C_6H_5); IR, ν_{max} (KBr) 2900 (CH, aromatic), 1710 (C=O); mass spectrometry, $m/z = 262$ (M^+); analysis: calculated for $C_{13}H_{12}NO_3S$, C 59.5, H 4.58; found, C 59.6, H 4.57%.

Acknowledgements

We thank Woosuk University and Chonju National University of Education for support of this work.

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