Elimination mechanisms in the anilinolysis of sulfamoyl chlorides in chloroform and acetonitrile

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The kinetics of the reaction of various sulfamoyl chlorides, $R^1R^2NSO_2Cl$ (R^1 = Ph, Me, c-C_6H_{11}, Bu^t, R^2 = H and R^1 = R^2 = Me and R^1 = R^2 = $PhCH_2$) with anilines in chloroform and acetonitrile have been studied. Reaction is first order in both chloride and aniline and pseudo first order and second order rate constants have been determined for various chlorides and *para*- and *meta*-substituted anilines. Hammett ρ values vary from −4.76 to −2.63 for varying $XC_6H_4NH_2$ depending on the halide, X. Substituents in $XC_6H_4NHSO_2Cl$ have only small effects on the rates. There is a *ca*. 10^6-fold rate difference between $PhNHSO_2Cl$ and $(PhCH_2)_2NSO_2Cl$ reacting with *p*-anisidine in chloroform at 25 °C. This finding, coupled with the observation of hydrogen/deuterium isotope effects, supports the operation of an elimination mechanism involving an *N*-sulfonylamine, [PhN=SO_2], as a transient species. In chloroform an E2-type mechanism is suggested, while in acetonitrile the activation parameters (ΔH, ΔS) may indicate a more E1cB-like E2 mechanism.

For quite a few years there has been widespread interest in the kinetics and mechanism of reactions of sulfonyl halides in hydrolysis, alcoholysis (including phenolysis) and aminolysis processes (Scheme 1) leading to sulfonic acid, sulfonate ester and sulfonamide products, respectively. This area has been authoritatively reviewed.[1] A number of mechanisms have been supported depending on substrate, reagents and solvents and these range from nucleophilic substitutions (S_N) through addition–eliminations (S_AN) to eliminations (E1, E2 and E1cB variants).

Studies on the mechanism(s) of reaction of the related sulfamoyl halides R = RNH or R^1R^2N in **1** [reaction (1)] have not

$$\underset{\mathbf{1}}{RSO_2X} + Y^- \longrightarrow RSO_2Y + X^- \qquad (1)$$

been extensive despite their importance as intermediates in the pharmaceutical and agrochemical industries[2] and their utility in the synthesis of sulfamides.[3]

The hydrolysis of *N*,*N*-disubstituted sulfamoyl halides $R^1R^2NSO_2Cl$ has been controversial, with both S_N1 and S_N2 processes being favoured by different groups.[4a–f] The kinetics of halide exchange using a ^{36}Cl label have been reported for *N*,*N*-dimethylsulfamoyl chloride.[4g] We could only find one piece of kinetic information on the reaction of a sulfamoyl halide with an amine, namely the rate of reaction of *N*,*N*-dimethylsulfamoyl chloride with piperidine in aqueous dioxane giving *N*,*N*-dimethyl-*N*′-piperidylsulfamide.[4a] This paucity of information on sulfamoyl group transfers to nitrogen centres prompted us to probe the kinetics and mechanism of such transfers using a series of anilines and a number of sulfamoyl chlorides.

Results and discussion

Preliminary studies using *N*-phenylsulfamoyl chloride and aniline at varying concentrations in chloroform showed that the UV kinetics were first order in chloride and in aniline. Second order rate constants were obtained from plots of k_{obs}, the pseudo first-order rate constant, determined using excess amine from plots of k_{obs} *vs*. [aniline]. The observed second order kinetics are compatible with the following mechanistic types: S_N2, S_AN, E2 and E1cB. However, the pronounced acidity of the N–H group in monosubstituted sulfamates compared to that of the C–H group in phenylmethylsulfonate esters, such as $PhCH_2SO_2OC_6H_4CH_3$-*p*,[5] which are well known to react *via* elimination mechanisms involving sulfenes,[6] suggests that sulfamoyl halides will be very likely to involve elimination pathways in their decomposition. King has shown that the analogous phenylmethylsulfonyl halides, $PhCH_2SO_2X$ react with aniline and other amines *via* an elimination path involving a sulfene.[7] Williams[8] has determined the acidities of the aryl methylsulfamates, $MeNHSO_2OAr$ in 50% EtOH–H_2O as being in the range 10.53 (Ar = C_6H_5) to 8.70 (Ar = *m*-$NO_2C_6H_4$). We feel that the pK_a of $PhNHSO_2Cl$ may be lower, *ca*. 7–8. This is based on comparison of this system with the sulfonamides shown. The pK_a values of the latter have been determined in water.[9] Comparison of the σ_p value for chlorine (0.227) with the σ values for a series of C_6H_4X groups indicated that the electronic demands of Cl would probably be best matched by *p*-nitrophenyl, which has σ_p = 0.23. The pK_a of $PhNHSO_2$-$C_6H_4NO_2$-*p* was found to be 7.50 in water and it is reasonable to consider that the pK_a of phenylsulfamoyl chloride should be *ca.* 7–8 in H_2O and *ca*. 9 in 50% EtOH.[10]

Table 1 Second order rate constants for the reaction of some mono- and disubstituted sulfamoyl chlorides $R^1R^2NSO_2Cl$ with *p*-anisidine in chloroform at 25 °C

R^1	R^2	k_2/dm^3 mol^{-1} s^{-1}
Ph	H	10.3
Bu	H	13.9
Ph	Me	1.3×10^{-5}
$PhCH_2$	$PhCH_2$	5.8×10^{-6}

$$PhNHSO_2Cl \rightleftharpoons Ph\bar{N}SO_2Cl + H^+$$

$$PhNHSO_2C_6H_4X \rightleftharpoons Ph\bar{N}SO_2C_6H_4X + H^+$$

Evidence for an elimination mechanism

The data in Table 1 support the operation of an elimination mechanism in the aminolysis of monosubstituted sulfamoyl chlorides, which are seen to react *ca.* 10^6 times more rapidly than disubstituted sulfamoyl chlorides. The latter probably react *via* bimolecular nucleophilic attack by the amine at the sulfur of the sulfamoyl centre. This test has also been used to show that monosulfamate esters, $RNHSO_2OR'$ react by a

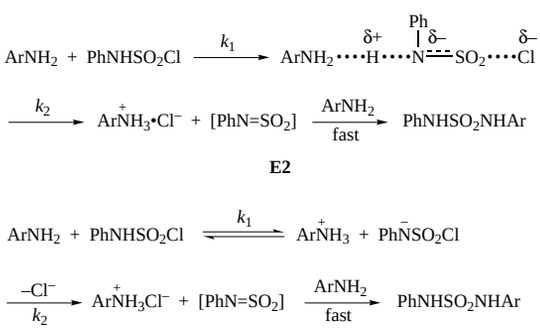
Table 2 Kinetic isotope effects for the reaction of *N*-phenylsulfamoyl chloride with anilines ($XC_6H_4NH_2$) in chloroform at 25 °C

X	k_H[a]/dm^3 mol^{-1} s^{-1}	k_D[b]/dm^3 mol^{-1} s^{-1}	k_H/k_D
p-OMe	10.3	3.9	2.6
		3.5	2.9
p-Me	3.1	0.78	4.0
		0.86	3.6
H	1.0	0.19	5.3

[a] From Table 3. [b] Using $PhNDSO_2Cl$ (97% D by ^1H NMR spectroscopy) and $CDCl_3$.

different mechanism to disulfamate esters R_2NSO_2OR'.[8,11] Further support for an elimination mechanism possibly involving an *N*-sulfonylamine [PhN=SO_2], came from the reaction of *N*-phenyl sulfamoyl chloride (**1**, R = PhNH, X = Cl) with *p*-anisidine-*N*D_2 (>90% D) (10 fold excess) in deuteriated chloroform. The product formed, *N*-phenyl-*N'*-*p*-anisylsulfamide, was fully deuteriated on both nitrogens. Had substitution taken place by amine attack at sulfur, a product containing only one deuterium would be expected, *i.e.* $PhNHSO_2NDC_6H_4OMe$-*p*. Fig. 1 shows the ^1H NMR spectra for the products of reaction when (*a*) non-deuteriated and (*b*) deuteriated materials were used. The possibility that the deuteriated anisidine might exchange with the starting sulfamoyl chloride or the product sulfamide seems unlikely since it is a weak base. This is supported by the fact that in our attempts to fully deuteriate *p*-anisidine, equilibration with DCl in D_2O for two days at room temperature resulted in only *ca.* 40% incorporation of deuterium. We synthesised the fully deuteriated material by a phase transfer method instead (see Experimental section).

Further support for an elimination mechanism comes from a 'reverse' isotope experiment in which we probed the hydrogen deuterium kinetic isotope effect by synthesising $PhNDSO_2Cl$. Table 2 records the observed k_H and k_D values and the ratio k_H/k_D. The observation of these effects effectively rules out an $(E1cB)_{rev}$ mechanism and would point towards either an E2 or an $(E1cB)_{irrev}$ mechanism (Scheme 1). An $(E1cB)_{rev}$ mechanism



Scheme 1

involves a non-rate determining deprotonation equilibrium for which a kinetic isotope effect would not be expected.

Substituent effects

Hammett ρ values. The effects of varying substituents both in aniline and in sulfamoyl chloride have been probed. The results for various anilines are displayed in Tables 3–5, Table 6 (runs 1–4) and Table 7 and for sulfamoyl chloride in Table 8 and Table 6 (runs 2, 5 and 6). For the seven anilines in Table 3, a Hammett ρ of −3.57 (correlation coefficient, $r = 0.975$; stand. error = 0.364) at 25 °C in chloroform was obtained, in excellent agreement with the ρ obtained from the more limited plot for the four anilines (runs 1–4) in Table 6 which gave a ρ of −3.54 ($r = 0.997$; stand. error = 0.181). Changing the sulfamoyl chloride from *N*-phenyl- or *N*-methyl- to *p*-methylphenyl- and *p*-chlorophenyl- gave ρ values of −4.76 ($r = 0.99$; stand. error = 0.171) for the six anilines in the Table reacting with *N*-phenylsulfamoyl chloride.

Table 3 Second order rate constants for the reaction of *N*-phenylsulfamoyl chloride with anilines ($XC_6H_4NH_2$) in chloroform at 25 °C

X	λ/nm[a]	k_2/dm^3 mol^{-1} s^{-1}	log k_2	σ[b]	pK_a[c]
p-OMe	305	10.3	1.014	−0.2688	5.34
p-OEt	305	7.8	0.892	−0.24	5.20
p-Me	294	3.1	0.495	−0.17	5.08
H	287	1.0	0.002	0.0	4.60
m-OMe	287	0.39	−0.412	0.115	4.23
p-Cl	314	0.31	−0.507	0.227	3.98
p-Br	298	0.08	−1.1	0.232	3.86

[a] Analytical wavelength used. [b] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **23**, 458. 0.23 for *p*-nitrophenyl (see text) from C. Hansch and A. J. Lee, *Substituent Constants for Correlation Analysis in Chemistry and Biology*, Wiley-Interscience, New York, 1979, p. 128. [c] Refs B66, H16 (for *p*-OEt) and F14 (for *p*-CN in Table 7), D. D. Perrin, *Dissociation Constants of Organic Bases in Aqueous Solution*, Butterworths, London, 1965.

Table 4 Pseudo-first order rate constants for the reaction of *p*-methylphenylsulfamoyl chloride with anilines ($XC_6H_4NH_2$) in chloroform at 25 °C[a]

X	k_{obs}/s^{-1}	log k_{obs}	σ
p-OMe	0.88	−0.56	−0.268
p-OEt	0.65	−0.187	−0.24
p-Me	0.17	−0.769	−0.17
H	0.67	−1.187	0
m-OMe	0.012	−1.921	0.115
p-Cl	0.003	−2.511	0.227

[a] [Aniline] 6×10^{-4} mol dm^{-3}, [sulfamoyl chloride] 3.75×10^{-5} mol dm^{-3}.

Table 5 Pseudo first order rate constants for the reaction of *p*-chlorophenylsulfamoyl chloride with anilines ($XC_6H_4NH_2$) in chloroform at 25 °C[a]

X	k_{obs}	log k_{obs}	σ
p-OMe	0.71	−0.150	−0.268
p-OEt	0.52	−0.282	−0.24
p-Me	0.41	−0.384	−0.17
H	0.12	−0.907	0.0
m-OMe	0.07	−1.186	0.115
p-Cl	0.04	−1.45	0.227

[a] Concentrations of reactants as in Table 4 footnote.

Table 6 Pseudo-first order rate constants for the reaction of sulfamoyl chlorides ($RNHSO_2Cl$) with anilines ($XC_6H_4NH_2$) in chloroform at 20 °C[a]

Run	R	X	λ/nm	$k_{obs}/10^{-3}$ s^{-1}
1	Me	H	287	0.34
2		*p*-OMe	311	3.2
3		*p*-Cl	299	0.04
4		*p*-CN	270	0.0017[b]
5	c-C_6H_{11}	*p*-OMe	305	18.0
6	Ph	*p*-OMe	305	34.6

[a] [Aniline] 12×10^{-4} mol dm^{-3}, [sulfamoyl chloride] 0.75×10^{-4} mol dm^{-3}. [b] Estimated (see Experimental section).

Large negative ρ values, usually in the range of −2.0 to −2.9 for the aminolysis of sulfonyl halides are common[1] and more negative values have been reported. The reaction of phenylmethanesulfonyl halides with anilines (involving an elimination pathway with a sulfene intermediate[7] and a substrate that may be viewed as the carbon analogue of phenylsulfamoyl chloride) gives ρ values of *ca.* −3.50 for variation of the aniline base with a number of ring-substituted phenylmethanesulfonyl

Table 7 Second order rate constants for the reaction of *N*-phenylsulfamoyl chloride with anilines ($XC_6H_4NH_2$) in acetonitrile at 25 °C

X	k_2/dm^3 mol^{-1} s^{-1}	log k_2	σ [a]	pK_a [a]
p-Me	89.1	1.95	−0.17	5.08
H	20.3	1.31	0	4.60
m-OMe	11.2	1.05	0.115	4.23
p-Cl	2.68	0.428	0.227	3.98
p-CN	0.28	−0.55	0.66	1.74
p-NO_2	0.08	−1.12	0.778	1.00

[a] For σ and pK_a values see Table 3 footnotes *b* and *c*.

Table 8 Second order rate constants for the reaction of *para*-substituted phenylsulfamoyl chlorides ($XC_6H_4NHSO_2Cl$) with aniline at 25 °C in chloroform and with aniline in acetonitrile [a]

Chloroform		Acetonitrile	
X	k_2/dm^3 mol^{-1} s^{-1}	X	k_2/dm^3 mol^{-1} s^{-1}
p-OMe	0.98	*p*-Me	17.1
p-Me	0.88	H	20.3
H	1.01	*p*-Cl	34.8
p-Cl	0.84		

chlorides.[12] The ρ values of −3.57 (phenylsulfamoyl chloride) and −3.54 (methylsulfamoyl chloride) are strikingly close to this value for the related phenylmethanesulfonyl chloride system. Changing from chloroform to acetonitrile produces a lower ρ value of −3.09 and this would be expected on the basis of the change to a more polar solvent: the relative permittivities (ε) of chloroform and acetonitrile are 4.81 and 35.9, respectively.[13] For phenylmethanesulfonyl chloride the ρ values were measured in MeOH–CH_3CN mixtures varying from 100% MeOH (ε = 32.7 [13]) to 50% MeOH (v/v).

These ρ values determined here indicate that the anilines play a major role by proton abstraction in an E2 transition state or in the first step (k_1) of an $(E1cB)_{irrev}$ mechanism (Scheme 1). The much lower and higher ρ values measured for *p*-chlorophenyl- and *p*-methylphenylsulfamoyl chlorides of −2.63 (Table 5) and −4.76 (Table 4), respectively can be understood in terms of relative acid strength. The *p*-chloro compound should be more acidic than the parent sulfamoyl chloride and a diminished role can be envisaged for the anilines since the N–H is already weakened. However, in the *p*-methyl compound the hydrogen of the N–H bond should be more tightly held and consequently the bases will have a greater role.

In Table 8 the effects of a limited study of the variation of rates with varying substitutent in $XC_6H_4NHSO_2Cl$ are presented. In chloroform the reaction is virtually insensitive to changing substituent and interestingly a similar result was obtained in the hydrolysis in aqueous dioxane at 29 °C of the sulfamoyl azides ($RNHSO_2N_3$, R = Ph, *p*-ClC_6H_4 and *p*-$MeOC_6H_4$), which gave rates of 8.75, 6.68 and 8.68 ($\times 10^2$ min^{-1}) respectively.[14] In acetonitrile in our system there is a notable increase in rate with a change from an electron-donating to an electron-withdrawing substituent (Table 8). Also, it is noticeable that the rates are considerably faster in acetonitrile: k_{CH_3CN}/k_{CHCl_3} for *p*-Me, H and *p*-Cl being respectively 19.5, 20.1 and 41.4. The more polar solvent facilitates reaction and in the case of *p*-chlorophenylsulfamoyl chloride a 40-fold acceleration is found. The extra rate enhancement for the chloro compound may well be due to the fact that in either an E2 or $(E1cB)_{irrev}$ mechanism the chloro substituent will stabilise an intermediate *N*-sulfonylamine, whereas a *p*-methyl group or the unsubstituted parent compound would not provide such stabilisation; hence their 20-fold acceleratory action may be due simply to the change to the more polar solvent.

In Table 6 an approximately tenfold acceleration is noted from runs 2, 5 and 6 for a change in sulfamoyl chloride in the reaction with *p*-anisidine in chloroform at 20 °C. These data gave a very poor Taft plot when log k_{obs} was plotted *vs.* σ*. The rate constants do, however, increase with increasing σ*.

Table 9 Activation parameters for the reaction of *N*-phenylsulfamoyl chloride with anilines in chloroform and acetonitrile

Solvent	Substituent	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J K^{-1} mol^{-1}
$CHCl_3$ [a]	*p*-OMe	24.3 ± 4	−141.7 ± 12
	p-OEt	23.2 ± 2	−151.9 ± 5
	p-Me	23.4 ± 4	−154.5 ± 12
	H [b]	30.2 ± 2	−143.5 ± 6
	m-OMe [b]	53.6 ± 5	−73.2 ± 2
	p-Cl [c]	50.5 ± 7	−85.1 ± 23
CH_3CN [d]	H	17.7 ± 9	−160.4 ± 1
	m-OMe	26.5 ± 3	−136.2 ± 7
	p-Cl	37.3 ± 1	−112.0 ± 1

[a] Temperature range 298–313 K (four temperatures). [b] Temperature range 298–313 K (three temperatures). [c] Temperature range 298–317.5 K (three temperatures). [d] Temperature range 298–314 K (four temperatures).

Brønsted β values. Brønsted β values have been determined for the data in Tables 3 and 7 using pK_a values measured in water (see Table 3, footnote *c*). In $CHCl_3$ at 25 °C the β_{nuc} for aniline attack is 1.27 (n = 0.982, stand. error = 0.11) and in CH_3CN at 25 °C the value is 0.685 (n = 0.980, stand. error = 0.076). These Brønsted coefficients could be substantially in error since the rate data in the Tables should of course be plotted using pK_a values measured in the same solvents in which the rates were measured. At least, however, it may be taken that the β_{nuc} values for the reaction are reasonably positive. In agreement with this, β_{nuc} values of *ca.* 1.2 have been reported for the anilinolysis of phenylmethanesulfonyl chloride in 100% MeOH, 80% and 50% MeOH–CH_3CN (v/v) [12] and of *ca.* 0.6–1.1 for the elimination reaction of 2-arylethylquinuclidinium ions, $ArCH_2CH_2^+X$ in 60% DMSO–H_2O (v/v).[15] Using pK_a values for anilinium ions, determined in dimethyl sulfoxide (DMSO),[16] an approximate straight line is obtained when they are plotted against those determined in water. The values for *p*-Cl and *p*-NO_2 are available in DMSO,[16] and the other four pK_a values in DMSO required for the data in Table 7 were obtained by interpolation (for *m*-OMe and *p*-CN) and by a slight extrapolation (for *p*-Me and H). A plot of log k_2 values in Table 7 *vs.* these pK_a values gave a slope of 0.62 (r = 0.976, stand. error = 0.069). Since the relative permittivity of DMSO (ε = 46.5 [13]) is closer to that of acetonitrile (ε = 35.9) than H_2O (ε = 78.3 [13]) such a plot may be more meaningful and seems to point to a reasonable degree of proton transfer in the slow step of the elimination.

Activation data

Table 9 contains $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values for the reaction of phenylsulfamoyl chloride with anilines in chloroform and acetonitrile. The lower enthalpies in acetonitrile are immediately clear and the *ca.* 20-fold times faster reaction in this solvent has been referred to above. Acetonitrile, being more polar than chloroform, can provide greater stabilisation of the transition state. However, the lower enthalpies may indicate a shift to a more E1cB type mechanism, where proton removal is an important process occurring in the transition state. The enthalpies associated with proton dissociation of various anilinium ions in water lie in the range of *ca.* 16–30 kJ mol^{-1}.[17] Some data for different temperatures are plotted in Fig. 2.

The entropy data for acetonitrile compared to that for chloroform may also indicate a move to a mechanism with a greater charge build-up in the transition state and thus a somewhat greater change in entropy on going from ground state reactants to activation complex.

The evidence in support of E2 or $(E1cB)_{irrev}$ mechanisms has been given above. *A priori* the involvement of an *N*-

sulfonylamine is very likely. The general conditions for generation of an *N*-sulfonylamine[18] correspond to the reaction conditions used in this work. The likely mechanistic possibilities are shown in Scheme 1. The reaction may involve a central E2 type mechanism where departure of chloride and removal of the amino hydrogen in the sulfamoyl chlorides may both be concerted, or an $(E1cB)_{irrev}$ mechanism where a negative charge is first deposited on nitrogen prior to carbon–chlorine bond cleavage. In acetonitrile an E1cB-like E2 mechanism is proposed and in chloroform the mechanism may be shifted to a more E2 type.

Experimental

Solvents and starting materials

Chloroform was refluxed over PCl_5 for 12 h and fractionally distilled a number of times until a satisfactory low water content, which was determined by a Dean–Stark apparatus, was obtained. The solvent used in kinetic runs was distilled weekly and stored in an opaque container. Pyridine was left to stand for 24 h over KOH and then refluxed over fresh KOH, following which it was fractionally distilled. The first and last 10% of the distillate were discarded. Benzene stock solution was stored over $CaCl_2$ and was refluxed and fractionally distilled over CaH_2. It was stored over sodium wire. Acetonitrile was refluxed and distilled over CaH_2 and stored in a dark container. Light petroleum was fractionally distilled and stored over sodium wire at least 72 h before use.

Anilines. All liquid amines were refluxed over KOH and then fractionally distilled through an efficient Vigreux column, being sure to discard the first and last 15% of the distillate. All solid amines were sublimed or distilled under reduced pressure using a Kugel–Rohr distillation unit. All amines were stored under a nitrogen atmosphere at *ca.* 5 °C.

Sulfamoyl chlorides. These were prepared by the method of Kloek and Leschinsky,[19] except for *N*-methylsulfamoyl chloride, which was prepared by the method of Weiss and Schulze.[20]

Deuteriated materials. *p*-Anisidine-ND_2 was prepared as follows: *p*-anisidine (0.5 g, 4.1 mmol) was dissolved in $CDCl_3$ (10 ml) together with tetramethylammonium chloride (0.022 g, 0.2 mmol). To this was added 10 ml of D_2O and sodium deuteroxide (0.008 g, 0.2 mmol); the reaction mixture was stirred for 24 h following which time the organic and aqueous layers were separated and the aqueous layer was replaced with a fresh batch of 10 ml of D_2O, and the procedure was repeated. The layers were then separated and the chloroform was removed under vacuum. The deuteriated amine was purified by bulb to bulb distillation. The percentage of deuterium was determined by ^1H NMR spectroscopy to be 94%.

$PhNDSO_2Cl$ was prepared in >97% yield as follows: phenylsulfamoyl chloride (4.0 g, 0.021 mol) was added slowly to a solution of 15 ml of D_2O containing NaOD (0.021 mol). This solution was heated to 40 °C for 2 h to ensure the complete hydrolysis of the chloride to the sulfamic acid. The D_2O was removed under vacuum and the remaining sulfamate salt was recrystallised from 4:1 CH_3CN–D_2O. The percentage of deuterium incorporated into the sodium phenylsulfamate salt was estimated by ^1H NMR spectroscopy to be 98%. This was then reacted in the usual way in $[^2H_6]$benzene with phosphorus pentachloride to form the *N*-deuteriated phenylsulfamoyl chloride.

Preparation of *N*-phenyl-*N′*-*p*-anisylsulfamide

Non-deuteriated material. *N*-Phenylsulfamoyl chloride (0.25 g, 0.0013 mol) was dissolved in dry chloroform (50 ml) and *p*-anisidine (0.32 g, 0.0026 mol) was added. The solution was stirred for 2 h at room temperature, by which time complete reaction had occurred. The *p*-anisidine hydrochloride which forms precipitated from solution and was filtered off; removal of the solvent under vacuum gave crude product sulfamide (0.341 g, 94%). This was flash chromatographed to yield the pure product (87%). δ_C 55.190, 114.186, 117.919, 121.904, 122.490, 128.929, 130.667, 138.433, 155.831 ppm. ^1H NMR spectrum in $[^2H_6]$DMSO, see Fig. 1(*a*).

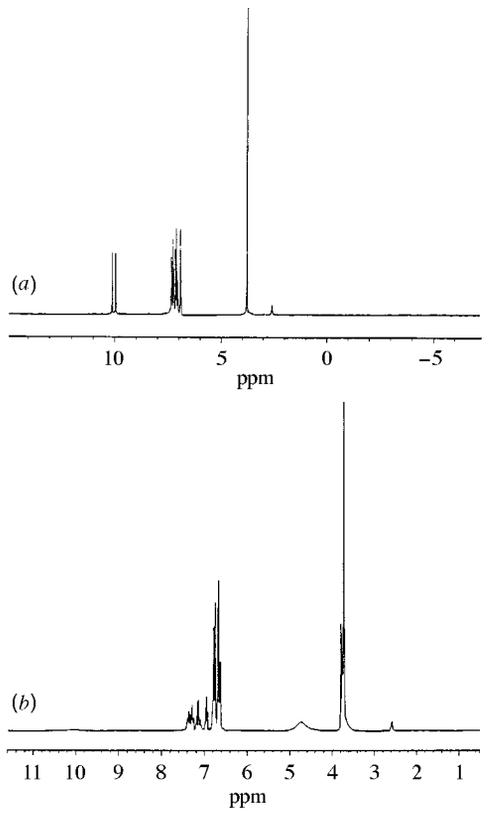


Fig. 1 ^1H NMR spectra for (*a*) $PhNHSO_2NHC_6H_4OCH_3$-*p* and (*b*) $PhNDSO_2NDC_6H_4OCH_3$-*p*

Deuteriated material. This reaction was conducted as in the previous experiment, except that a 10:1 molar ratio of *p*-anisidine-ND_2 to phenylsulfamoyl chloride was used. The product sulfamide was redissolved in $[^2H_6]$DMSO (in $CDCl_3$ the ^1H NMR signals for the amino hydrogens fall under the aromatic peaks) and its ^1H NMR spectrum was recorded, see Fig. 1(*b*). Two deuterium atoms, one on each of the nitrogens, are indicated and thus the reaction product is $PhNDSO_2ND$-C_6H_4OMe-*p*.

Kinetic measurements

The reactions between various aromatic amines and the sulfamoyl chlorides were carried out at 25 ± 0.2 and 20 ± 0.2 °C unless otherwise stated in the text and were monitored by UV spectroscopy using a Shimadzu 260 instrument. Reactions were generally followed by monitoring the decrease in absorbance of the amine peak at a suitable wavelength (see Tables 3 and 6). The reactions were started by the addition of 1 ml of a sulfamoyl chloride stock solution to an equal volume of the appropriate amine solution equilibrating in a quartz cuvette in the sample holder of the instrument. The initial sulfamoyl chloride concentration was 3.75×10^{-5} mol dm^{-3} (runs at 25 °C) and 0.75×10^{-4} mol dm^{-3} (runs at 20 °C). Amine concentrations varied from 4.5×10^{-4} mol dm^{-3} to 24×10^{-4} mol dm^{-3}. Plots of $|A_t - A_\infty|$ as a function of time were found to be linear for over 90% reaction (>3 half lives). From 15 to 20 points were used in each plot. Second order rate constants were determined from plots of k_{obs} as a function of amine concentration, the best line being determined by least-squares analysis. Some typical plots are shown in Fig. 2. Rate constants (Tables 1–8) were accurate to within ±5% based on replicate runs. The reaction of *p*-cyanoaniline in $CHCl_3$ with $MeNHSO_2Cl$ was extremely slow and the spectral changes were very small (thus the method of initial rates was not used). The pseudo first-order

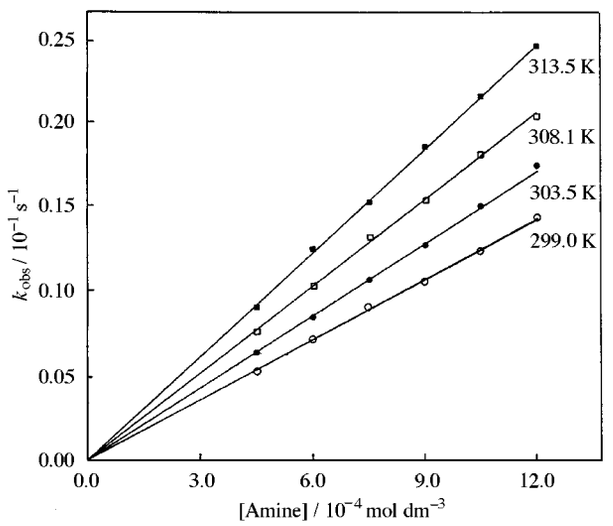


Fig. 2 Plots of pseudo first order rate constants as a function of amine concentration at four different temperatures for the reaction of phenylsulfamoyl chloride (3.75×10^{-5} mol dm^{-3}) with *p*-ethoxyaniline ($4.5–12 \times 10^{-4}$ mol dm^{-3}) in chloroform

rate constant for this reaction, k_{obs} (Table 6), was estimated as follows: (i) $MeNHSO_2Cl$ (1.0×10^{-4} mol dm^{-3}) was reacted with *p*-anisidine (4.0×10^{-4} mol dm^{-3}) in chloroform at 20 °C, a half-life of 4.6 min being observed; (ii) the sulfamoyl chloride (0.025 mol dm^{-3}) was reacted with *p*-cyanoaniline (0.1 mol dm^{-3}) in chloroform at 20 °C, a half-life of 35 min being observed; the reaction was performed in 100 ml of solution, with appropriate dilution of sample in chloroform prior to absorbance readings. The above results (i) and (ii) indicate that *p*-cyanoaniline is 1902 (35/4.6 × 250) times less reactive than *p*-anisidine towards *N*-methylsulfamoyl chloride. Thus an estimated rate constant for the reaction of *N*-methylsulfamoyl chloride (0.75×10^{-4} mol dm^{-3}) and *p*-cyanoaniline (12.0×10^{-4} mol dm^{-3}) in chloroform at 20 °C is 1.003×10^{-4} min^{-1} (0.190 76/1902 min^{-1}) or $0.001\,67 \times 10^{-3}$ s^{-1}.

Product runs

Since the reaction of sulfamoyl chlorides with amines is a well documented synthetic route to unsymmetrical sulfamides, extensive product studies were not carried out. TLC analysis, to ensure that clean reactions were occurring, was performed, however. Bearing in mind the careful drying of the solvents and amines which was carried out the formation of sulfamic acids by reaction of H_2O with the sulfamoyl chlorides would be negligible. Product runs with *N*-methylsulfamoyl chloride (5 mmol) and with aromatic amine (10 mmol) in chloroform (2 ml) were carrried out by refluxing for 40 min. The usual work-up for sulfamides gave from the appropriate amine the following: *N*-methyl-*N′*-phenylsulfamide, 71%, mp 80–81 °C, *N*-methyl-*N′*-*p*-anisylsulfamide, 96%, mp 86–87 °C and *N*-methyl-*N′*-*p*-chlorophenylsulfamide, 97%, mp 112–113 °C. The yields are yields of crude product. A product run with phenylsulfamoyl chloride (0.25 g, 1.3×10^{-3} mol) and *p*-anisidine (0.32 g, 2.6×10^{-3} mol) in $CHCl_3$ (50 ml) was carried out at room temperature over 2 h and 94% crude sulfamide was formed. After purification an 87% yield of pure sulfamide giving C, H and N microanalyses within ±5% and good ^{13}C and ^{1}H NMR spectra (see above) was obtained. Sulfamides were purified by recrystallisation using EtOH–H_2O (50/50 v/v) or flash chromatography. Characterisation was by IR spectroscopy, mp or $^{13}C/^{1}H$ NMR spectroscopy.

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