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REACTIONS OF AROMATIC SULPHONYL CHLORIDES WITH ANILINES

STUDIES OF SOLVENT EFFECTS BY THE APPROACH OF MULTIPARAMETER EMPIRICAL CORRELATIONS

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Abstract—The reaction kinetics of 5-substituted 2-thiophenesulphonyl chlorides with anilines were studied in fourteen pure solvents (protic and aprotic) and in mixed solvents at 25°. The approach of multiparameter equations to describe solvent effects according to the Palm-Koppel and Krygowski-Fawcett models was unsuccessful. Instead satisfactory single parameter linear correlations, one for protic solvents with positive slope and another for aprotic solvents with negative slope, were found by using the dielectric constant ϵ. An S_AN mechanism for these reactions was proposed, bond-making being the rate-determining step for protic solvents and bond-breaking for aprotic ones. The analysis of some data for the reactions of benzenesulphonyl chloride showed that the mechanism is analogous also for this substrate and the rate-determining step is depending on both solvent and nucleophile. Hammett ρ-values for the reactions of substituted 2-thiophenesulphonyl chlorides with aniline are in accord with the proposed mechanism. ρ-Values for the reactions of 2-thiophenesulphonyl chloride with substituted anilines are related to the solvent effects by equation $\rho = -15.7\,f(\epsilon) + 0.113E + 3.94$. The solvent effects on these values can be interpreted by the effect of the dielectric constant and the influence of H-bonding. Mixed solvents are characterized by the presence of a maximum rate.

Although the kinetics of solvolysis of some aromatic and aliphatic sulphonyl chlorides[1-4] and some reactions of nucleophilic substitutions[5-12] at tetracoordinate sulphur have been widely investigated, there is no attempt to study the solvent effects on the mechanism of these reactions by the approach of empirical parameters linear multiple regressions.

Some authors agree that solvent effects in this kind of substitutions are not correlated to the reaction rate by single parameter relationships, owing to the presence of specific solvation effects.[6]

A general theory describing solvent effects on physicochemical properties measured in solution has not been developed to date. However in many cases, reliable predictions can be obtained from empirical relationships. According to the Palm-Koppel model,[13] the solvent effect on the property A is described by a general correlation equation which gives the simultaneous separate calculation of the contributions of different types of non-specific solvent effect ("polarity" and "polarizability") and specific solvent-solute interaction (electrophilic and nucleophilic solvation) (1):

$$A = A_0 + yY + pP + eE + bB \qquad (1)$$

where y and p represent the susceptibilities of the process to the influences of solvent polarity and polarizability respectively, while e and b characterise the sensitivity of a given process towards electrophilic and nucleophilic solvation effects. In eqn (1):

$Y = \dfrac{\epsilon - 1}{2\epsilon + 1}$, where ϵ is the dielectric constant of the solvent;

$P = \dfrac{n^2 - 1}{2n^2 + 1}$, where n is the solvent refractive index;

$$E = E_T - 25.57 - 14.39\frac{\epsilon - 1}{\epsilon + 2} - 9.08\frac{n^2 - 1}{n^2 + 2},$$

where E_T is the Dimroth-Reichardt parameter;[14] $B = \nu^0_{OD} - \nu_{OD}$, ν^0_{OD} being the stretching frequency of OD band in deuterated methanol as a monomer in the gas phase (cm^{-1}), and ν_{OD} the corresponding value in the given solvent.

Recently, Krygowski and Fawcett have reported a new model of solvation[15] which involves only two parameters instead of four.[13] It postulates that the solvent effect on a physicochemical quantity Q can be represented as a linear function of two independent but complementary parameters describing the Lewis acidity A and Lewis basicity B of the given solvent (2):

$$Q = Q_0 + \alpha A + \beta B \qquad (2)$$

where α and β are constants describing the sensitivity of the property Q to acidic and basic solvent properties. In this case E_T is chosen as a measure of Lewis acidity, while DN,[16] the Gutman donor number, is chosen as a measure of solvent basicity B. Thus, it is assumed that the solvent effect on the property Q can be described in terms of the regression plane (3):

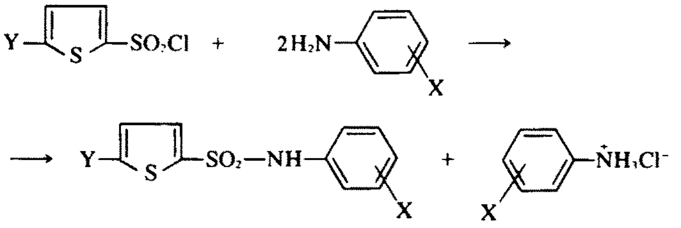
$$Q = Q_0 + \alpha E_T + \beta DN. \qquad (3)$$

Following these and other authors[13,15,17] we tested the applicability of multiparameter equations to nucleophilic substitutions at tetracoordinate sulphur, although if we are aware of the limitations inherent in this approach.

These limitations arise: (1) from the assumption that, to measure each solute-solvent interaction by a single parameter, it is necessary that these interactions work independently of each other,[18] (2) from the appropriate choice of the correlating parameter and (3) from the lack of the same parameters.

Besides it is necessary that the mechanism of the chemical process under examination does not change on changing the solvent.

The reactions examined in this paper (4) were carried out in fourteen pure solvents (Table 1) and in mixed solvents.

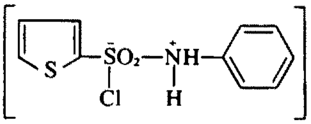


(4)

Y = H; X = *p*-OCH$_3$, *p*-CH$_3$, *m*-CH$_3$, H, *p*-Cl, *m*-Cl
Y = NO$_2$, Cl, CH$_3$; X = H

DISCUSSION

Recently two different reaction mechanisms for nucleophilic substitutions at tetracoordinate sulphur have been proposed: S_N2 and S_AN.[19–24] Previous work on the reactions of 2-thiophenesulphonyl halides with anilines[24] let us hypothesize the S_AN mechanism as the more probable, in which the rate-determining step involved attack of the aniline to the sulphonyl group to give the intermediate (5):



(5)

The rate constants values for the reactions carried out in pure solvents are reported in Table 1. Solvent effects for the reactions (4) could be explained in terms of the following solvent properties:

(a) The behaviour of the solvent as a dielectric in facilitating the separation of opposite charges from the initial state to the transition state (bond-making) and in the stretching of the S–Cl bond (bond-breaking);

(b) The ability of protic solvents to form H-bonds with the negative end of the intermediate and thus to stabilise the transition state relative to the initial state;

(c) The ability of aprotic solvents to provide electrophilic solvation by the positive end of their dipoles (dipole–dipole interactions), although such a solvation requires severe restriction of molecular motions with a large negative solvation entropy. (This type of solvation is poorer than that of protic ones and justifies the lower rate constants values);

(d) The ability of the medium to solvate the positive end of the intermediate by its nucleophilic solvation power.

When we applied the Palm–Koppel model we used the function $f(\epsilon) = (\epsilon - 1/2\epsilon + 1)$ as a measure of (a) while for (b) and (c) we used the electrophilicity parameter E and for (d) the parameter of basicity B.[13]

We could not test the effect of the parameter of basicity B for all solvents because the experimental values for the alcohols are not available.

Surprisingly when we processed the kinetic results relative to the reaction between 2-thiophenesulphonyl chloride and aniline, the best correlation found for the fourteen solvents was only the following single-parameter equation (6):

$$\log k_2 = 0.138\,E - 3.973 \qquad (6)$$

Table 1. Second order rate constants for the reaction of 2-thiophenesulphonyl chloride with X-$C_6H_4NH_2$ in pure solvents at 25°C and Hammett ρ values

k_2 $10^{3(a)}$ $(l\ mol^{-1} sec^{-1})$

Solvents	X =	p-OCH$_3$	m-CH$_3$	p-CH$_3$	H	p-Cl	m-Cl	$\rho^{(b)}$
1 Water		-	1017	1224	709	284	135	-1.79
2 Methanol$^{(c)}$		32.8	6.90	13.5	5.62	1.79	0.974	-2.06
3 Ethanol		18.0	3.80	6.40	3.15(d)	1.02	0.530	-1.98
4 Propan-1-ol		11.7	3.05	3.99	1.87	0.728	0.369	-1.93
5 Propan-2-ol		10.3	2.12	3.78	1.83(d)	0.656	0.273	-2.04
6 Butan-1-ol		8.91	2.49	5.28	1.58	0.868	0.324	-2.02
7 2-Methoxyethanol		16.5	-	-	1.65	-	-	-
8 Benzyl alcohol		16.3	3.14	5.49	2.64	1.06	0.406	-1.97
9 Acetonitrile		16.4	1.84	4.28	1.20(d)	0.250	0.085	-3.06
10 Acetophenone		-	-	-	0.654	-	-	-
11 Acetone		3.21	0.373	0.913	0.260(d)	0.036	0.019	-3.28
12 Benzonitrile		-	-	0.709	0.240	0.0378	0.0106	-3.36
13 Nitroethane		-	0.155	0.408	0.0792	0.020	0.0061	-3.22
14 Nitrobenzene		-	0.087	0.402	0.0616	0.0129	0.0034	-3.53

(a) Values of k_2 were reproducible to ± 6%
(b) The ρ values were obtained without considering the measure relative to p-OCH$_3$. This point is scattered in all the solvents. To report it on the line of the other points we must use a value of σ= -0.40 ÷ -0.45.
(c) A.Arcoria, E.Maccarone, G.Musumarra and G.A.Tomaselli, *J.Org.Chem.*,38, 2457 (1973).
(d) A.Arcoria, E.Maccarone, G.A.Tomaselli, R.Calì and S.Gurrieri, *J.Heterocyclic Chem.*, 12, 333 (1975).

with R = 0.901 and s = 0.439 (confidence level above 99.9%). All the dual parameters correlations were statistically unreliable. As reported in Fig. 1, the correlation is rather poor, because aprotic solvents (except MeCN) do not lie on the line of hydroxylic solvents. The failure of the multiparameter equations could be ascribed to the different interactions with solutes of the two classes of solvents (protic and aprotic ones) which do not justify a unitary statistical treatment. Nevertheless multiparameter treatment for the two separated classes of solvents was also unsuccessful.

Then we focused our attention on single parameter equations, because their use is not only justified but necessary when a single type of solvation interaction occurs (and the correlating parameter reflects this kind of interaction) or such an interaction is prevailing over others.[13]

Using E values the single parameter correlations were fair only for the protic solvents, including water (R = 0.94) (Fig. 1). In this case, the positive sign of the E parameter coefficient indicates a more electrophilic stabilisation of the transition state with respect to the initial state, in which there are not localized negative charges.

Moreover, satisfactory single parameter correlations were found plotting log k_2 vs ϵ or $f(\epsilon)$ (Fig. 2). In fact we obtained a correlation with R = 0.999 for the alcohols (except for benzyl alcohol) and another for aprotic solvents with R = 0.96 (except for acetonitrile). We found interesting the existence of two separate lines, one with a positive slope and the other with a negative slope and considered this trend diagnostic for the elucidation of the reaction mechanism.

Let us look at the following reaction scheme (7):

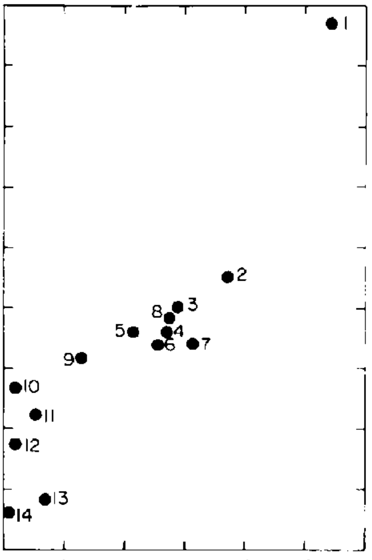


Fig. 1. Plot of log k_2 vs electrophilicity parameter (E) of the solvents (1–14) as in Table 1.

Figures 1 and 2 show that in protic solvents the reaction rate constants become larger by both ϵ and E increasing. In aprotic solvents, k_2 values do not depend on E to any extent but they show a strong dependence on ϵ. In fact a comparison between two aprotic solvents with equal E values shows that the reaction is faster in the solvent with the smaller ϵ value.

$$\text{Reagent} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [\overset{\delta}{\text{N}}{}^{+}\text{------}\overset{\delta}{\text{S}}{}^{-}\text{–X}] \rightleftharpoons [\overset{+}{\text{N}}\text{–}\overset{-}{\text{S}}\text{–X}] \rightleftharpoons [\overset{+}{\text{N}}\text{–S------}\overset{-}{\text{X}}] \xrightarrow{k_2} \text{P} \qquad (7)$$

$$\text{TS}_1 \qquad\qquad \text{i} \qquad\qquad \text{TS}_2$$

Analysing solvent effects on the first step (bond-making) and on the second step (bond-breaking) we have:

(a) Protic solvents:

1st step favored by ϵ increases[a]

2nd step favored by E increases[b]

(b) Aprotic solvents:

1st step favored by ϵ increases[a]

2nd step unfavored by ϵ increases[c]

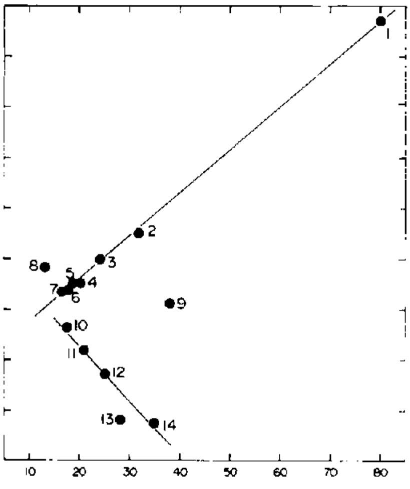


Fig. 2. Plot of log k_2 vs dielectric constants of the solvents (1–14) as in Table 1.

In order to interpret this behaviour we can assume that the rate determining step in protic solvents is bond-making while in aprotic solvents is bond-breaking. In these media, in fact, as the Cl electrophilic solvation

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[a] Since the reaction goes from a neutral initial state to a transition state with separate charges, the larger is the ϵ value the lower is the electrostatic energy connected with this transition.

[b] Owing to the presence of a negative localized charge, electrophilic solvation of the transition state by hydrogen bonding will accelerate the reaction rate.

[c] The application of electrostatic and transition state theories to an ion-dipole reaction gives the following equation:

$$\ln k = \ln k' + \frac{N_A Z^2 e^2}{RT} \frac{\epsilon - 1}{2\epsilon} \left(\frac{1}{r^*} - \frac{1}{r}\right),$$

where Ze is the charge and r is the radius of the ion. Since $r^* > r$, a linear relationship between ln k and $(\epsilon - 1/2\epsilon)$ of negative slope is predicted.[25]

In our case a plot of log k_2 vs $(\epsilon - 1/2\epsilon)$ for the aprotic solvents gave a straight line with r = 0.96 and negative slope.

occurs by ion-dipole interactions, the reaction rate must be slower when the dielectric constant is larger. An increase in ϵ weakens the dipolar interaction forces, making the chloride ion a bad leaving group.

This treatment shows that the solvent basicity makes no contribution while its dipolar properties are important in determining its interactions with the solutes. In protic solvents there is also some contribution from acidity, owing to the transition state which bears a net negative charge. The free energies of transfer, reported in Table 2 support this interpretation.

In fact the data show that in spite of the enthalpic advantage in the dipolar aprotic solvent, rate constants are higher in methanol owing to a dominating contribution from an unfavorable entropy of transfer of the transition state from methanol to acetonitrile. This means that the transition state for the reaction of 2-thiophenesulphonyl chloride with aniline is considerably better solvated by a protic solvent as expected for an addition-elimination mechanism rather than a concerted one-step mechanism. In the former case the transition state would resemble the intermediate, have more developed and localized charges, and be better solvated in a protic solvent.[7]

The kinetic data obtained for the reaction between benzenesulphonyl chloride and aniline in protic solvents fit in well with a single parameter equation. In fact plotting the values reported in Table 3 vs ϵ we obtain a good linear correlation with $R = 0.98$. If for methanol we use the Rogne value[21] the correlation improves ($R = 0.992$).

Since this reaction is faster in methanol and the change in solution heats of reagents is small (from methanol to acetonitrile) it seems reasonable to conclude that the entropy change for this reaction will play a dominant role and the mechanism is analogous to that of 2-thiophenesulphonyl chloride.

On the contrary, the multiparameter treatment (Palm–Koppel model) applied to the reactions of benzenesulphonyl chloride with imidazole[7] (Table 3) was successful. We obtained the following expression (8):

$$\log k_2 = 94.37\frac{\epsilon - 1}{2\epsilon + 1} - 0.09028\,E - 44.33 \qquad (8)$$

with $R = 0.956$ and $s = 0.299$ (confidence level above 99.9%) which explains 91% of the solvent effects.

In this case there is no change[a] of mechanism on changing the solvent and the addition of nucleophile is the rate-determining step. The negative sign of the parameter E coefficient suggests that the more important electrophilic solvation is that of the initial state with respect to

Table 2. Energies of transfer of reactants and transition state for the reaction of 2-thiophenesulphonyl chloride with aniline from methanol to acetonitrile at 25°

	$\delta\Delta H^{(a)}$ Kcal mol^{-1}	$\delta\Delta S$ cal mol^{-1} K^{-1}	$\delta\Delta G$ Kcal mol^{-1}
Reagents	1.33	3.10$^{(b)}$	0.406$^{(b)}$
Activation	-5.06	-20.21	0.963
Transition State	-3.73	-17.11	1.369

(a) Ref. 5
(b) see EXPERIMENTAL

Table 3. Second order rate constants k_2 for the reaction of benzenesulphonyl chloride with aniline and imidazole at 25° in various solvents

Solvent	$\varepsilon^{(e)}$ (at 25°C)	$E^{(e)}$	k_2, l mol^{-1} sec^{-1} Aniline	 Imidazole
Methanol	32.65	14.94	0.0588$^{(a)}$, 0.0686$^{(b)}$	0.0883$^{(c)}$
Ethanol	24.30	11.57	0.0417$^{(a)}$	0.0696$^{(c)}$
Propan-1-ol	20.1	10.58	0.0303$^{(a)}$	0.0473$^{(c)}$
Butan-1-ol	17.1	10.30	0.0240$^{(a)}$	-
Pentan-1-ol	13.9	-	0.0185$^{(a)}$	-
Hexan-1-ol	13.3	-	0.0151$^{(a)}$	-
Heptan-1-ol	11.1	-	0.0148$^{(a)}$	-
Acetonitrile	37.5	5.21	0.0145$^{(d)}$	3.20$^{(c)}$
Nitromethane	38.57	5.15	-	2.97$^{(c)}$
Benzonitrile	25.20	0.82	-	1.60$^{(c)}$
Water	80.10	21.8	-	1.91$^{(c)}$

(a) L.V.Kuritsyn, *Izv. Vyssh.Ucheb.Zaved., Khim.Khim.Tekhnol.*, 1037 (1969); *Chem.Abstr.*, 72, 30895 (1970).
(b) O.Rogne, *J.Chem.Soc.(B)*, 1855 (1971).
(c) O.Rogne, *J.Chem.Soc.Perkin II*, 1760 (1973).
(d) E.Maccarone, G.Musumarra, G.A.Tomaselli, Ref (28)
(e) *Advances in Linear Free Energy Relationships*, eds N.V.Chapman and J.Shorter Plenum Press, London and New York, 1972, p. 254.

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[a] The plot of $\log k_2$ vs $f(\epsilon)$ (single parameter correlation) provides two lines, with *positive* slopes, both for protic and aprotic solvents.

the transition state. In fact, as the heats of solution measured by Rogne[7] show that, in the transfer from methanol to acetonitrile, imidazole is more desolvated (more reactive) by 3.03 kcal in the aprotic solvent, while for benzenesulphonyl chloride there are no appreciable changes.

In methanol H-bonds between the solvent and the nucleophile make the imidazole less reactive than in acetonitrile, and the reaction rate is slower. However Rogne's conclusion that the imidazole–sulphonyl chloride transition state is considerably better solvated by a dipolar aprotic relative to a protic solvent is affected by the lack of the entropies of solution.

The application of the Krygowski–Fawcett model[15] to the reaction of 2-thiophenesulphonyl chloride with aniline was not possible for all the solvents because D_N values are available only for few protic solvents (methanol, ethanol and water). However the analysis of the fraction of the disposable data indicated once again the failure of the multiparameter treatment for this reaction and showed that the solvent basicity (expressed both by B and D_N parameters) does not play an important role. Also for the reaction between benzenesulphonyl chloride with imidazole, for which the Palm–Koppel model was successful, the Krigowski–Fawcett treatment failed, pointing out that for this reaction there is no contribution from solvent basicity.

ρ Values

The ρ[a] values for substituents in thiophenesulphonyl chloride seem in accord with the proposed mechanism (Table 5).

From the Scheme (7) if $k_{-1} \gg k_2$ (9):

$$k_{obs} = \frac{k_1 k_2}{k_{-1}} = K k_2 \tag{9}$$

from which, assuming the two steps are governed by Hammett laws, we have[27] (10):

$$\log \frac{k_{obs}}{(k_0)_{obs}} = \sigma(\rho_1 + \rho_2) \tag{10}$$

where ρ_1 is referred to the first step (bond-making) and ρ_2 to the second (bond-breaking).

For a nucleophilic substitution, a decrease in electronic density on the S atom favours the bond-making, increasing $\rho(\rho_1 = \text{positive})$, but is unfavourable to the bond-breaking decreasing $\rho(\rho_2 = \text{negative})$.

As the observed ρ value is the algebraic sum of $\rho_1 + \rho_2$, it becomes more negative passing from methanol to nitroethane (as shown in Table 5), if the bond-breaking becomes more important.

The values for the substituents in the nucleophile are well correlated by a dual parameters equation (11):

$$\rho = -15.7f(\epsilon) + 0.113E + 3.94 \tag{11}$$

with the coefficient of multiple regression R = 0.972 (which explains the 94.5% of solvent effects) and standard deviation s = 0.19 (cl = 95%). The reaction medium effect on these values can be ascribed mainly to the solvent effects on the transition state stability.

In aprotic solvents, in which electrophilic solvation is poorer than in alcohols, and in which delocalization

Table 4. Second order rate constants for the reaction of 2-thiophenesulphonyl chloride with p-anisidine in mixtures of methanol with some aprotic cosolvents at 25°

Aprotic	Volume (%) of methanol					
Cosolvents	95	85	75	55	15	5
CH_3CN	38.3	46.0 (b)	42.7	39.6	28.2	-
CH_3COCH_3	38.4 (b)	30.2	26.3	19.6	11.1	7.2
C_6H_6	36.6 (b)	29.0	16.1	9.6	3.7	1.2
$C_6H_5NO_2$	35.3 (b)	32.5	24.1	16.3	8.8	3.8

(a) Values of k_2 were reproducible to ±6%.
(b) Maximum rate.

Table 5. Second order rate constants k_2 at 25° for the reaction of 5-substituted 2-thiophenesulphonyl chlorides with aniline in various solvents and Hammett ρ values

Solvents	$5-NO_2$	5-Cl	H	$5-CH_3$	ρ
CH_3OH (b)	167.1	10.98 (c)	5.62	5.05	1.10 ± 0.07 (d)
CH_3CN	14.8	1.81	1.20	0.899	0.85 ± 0.01
$C_2H_5NO_2$	0.576	0.133	0.0792	0.0776	0.63 ± 0.05

(a) Values of k_2 were reproducible to ±6%.
(b) E.Maccarone, G.Musumarra and G.A.Tomaselli, *Ann.Chim.*, 63, 861 (1973).
(c) The value of k_2 (12.25) reported in refer. (b) is erroneous.
(d) Standard deviation relative to a confidence level > 99%.

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[a] The appropriate form of the Hammett equation, considering the heteroatom as a substituent[26,27] and assuming the additivity of substituent effects, is: $\log k = \rho(\sigma_x + \sigma_{\alpha s}) + \log k_0$. In this case we calculated ρ values from the plot of log k against σ_x assuming the constancy of $\sigma_{\alpha s}$ and using σ^- values (R = 0.9998 in MeCN) rather than σ(R = 0.98 in MeCN) for X substituents. This is reasonable because the existence of a negative charge on the sulphonyl group in the intermediate causes different conjugation between the sulphonyl group and the substituent in the initial state and in the transition state.

charges are less, the N atom bears a greater positive charge: hence ρ increases.[a]

In protic solvents ρ is reduced due to a strong solvation by H-bonds to the negative end of the transition state.

Reaction order

Also in aprotic solvents reported in Table 1 the reaction order is unitary with respect to the nucleophile because the interactions between the medium and the leaving group are still effective. In benzene,[28] which is an inert solvent from the dipolar interactions point of view, in order that the bond S–Cl stretching should facilitate the Cl^- departure in the transition state, the nucleophile must act as a catalyst. However the reaction in this solvent is more complicated because of the presence of both catalytic effects and aniline association phenomena.

Mixed solvents

When two solvents of different character are mixed, their selectivity with respect to the solute varies with the composition. Therefore, a study of the reaction rate in mixed solvents is useful to analyse the reaction rate dependence on the solvent nature. For this aim we correlated k_2 with the molar fraction. If there is no selectivity the plot of k_2 vs the solvent composition is linear. However, in our case there is a maximum rate for the mixture 0.88 MeOH/0.12 MeCN and for the mixtures 0.97 MeOH/0.03 MeCOMe, 0.98 MeOH/0.02 C_6H_6, 0.98 MeOH/0.02 C_6H_5–NO_2 (Table 4).

A maximum rate in mixed solvents was observed by Foon and Hambly[1] and by Ciuffarin *et al.*[6] for the neutral hydrolisis of aliphatic sulphonyl chlorides in water–dioxane and water–acetone mixtures and for the reactions of benzene–sulphonyl chloride with pyridine and primary amines in water–dioxane, water–acetonitrile and water–ethanol mixtures. Both groups of research workers have ascribed the maximum rate to the break-up of the protic solvent structure for the cosolvent addition, because the maximum was present only at the lowest temperatures (0–15°) where the protic solvent has the most organised structure. Hambly and Foon considered the maximum rate "as resulting from a change in the initial reactants rather than from a change in the nature of the activated complex".

The positive sign of the E coefficient of previous correlation showed that in the reactions reported in this paper the transition state solvation is more important than the initial state one. The addition of the cosolvent to methanol "depolymerises" it increasing the amount of protic solvent available to make H-bonds with the negative end of the intermediate. Hence the reaction rate increases. A further addition of the aprotic solvent, decreasing the electrophilic solvation power of the medium, makes the reaction rate lower.

This is in agreement with the report by Shatskaya *et al.*[11] who found a maximum rate for the reaction of *p*-nitrobenzenesulphonyl bromide with *p*-anisidine in nitrobenzene-cyclohexane mixtures at 25° and ascribed it "to high polarity of the transition state and greatly differing polarities of the solvent components".

Our conclusion is that in aprotic solvents specific solvent effects on $\Delta G^{\neq}$ must be small or nonexistent, because the variation in rate constants is due very largely to the electrostatic continuum effect. In protic solvents other effects such as H bonding may play an important role in reducing (increasing) the free energy of the transition state (reagents), decreasing (increasing) the value of $\Delta G^{\neq}$ and therefore increasing (decreasing) the reaction rate constants.

EXPERIMENTAL

Materials. 2-Thiophenesulphonyl chloride and 5-substituted 2-thiophenesulphonyl chlorides were obtained following the procedures described.[29]

Anilines were commercial products (Carlo Erba) purified by several distillations or crystallizations.

The solvents used throughout were commercial products (Carlo Erba); no special purification was undertaken, since several experiments showed that elaborate purification was unnecessary.

Kinetic procedure. For the solvents miscible with water, rate measurements were done by a digital pH meter, Amel Model 333, equipped by a motorized burette, Amel Model 233, by continuous titration of the acid produced with 0.1 N NaOH, following the procedure described.[24,30] The reagent concentrations ranged from *ca.* 0.0002 to *ca.* 0.0003 for 2-thiophenesulphonyl chlorides and from *ca.* 0.004 to *ca.* 0.2 mol for the anilines, depending on the reaction rates.

In the other solvents rate measurements were done by mixing standard solns of 2-thiophenesulphonyl chloride derivatives and aniline in stoppered vessels at constant temp. At intervals, the ppt of anilinium chloride was filtered off. The ppt was washed several times with benzene, dissolved in water and titrated with 0.1 N NaOH using phenolphthalein as indicator. The concentration range was 0.006–0.015 M for the sulphonyl chloride derivatives and 0.4–0.8 M for the anilines.

The first order rate constants (k_{obs}) were obtained from the slope of conventional plots of ln (a–x) vs time, using the least-squares method.

The mixed solvents were obtained by mixing suitable volumes of each component of the mixture at 25°, and measured by calibrated burettes.

Entropies of solution. The entropies of solution of 2-thiophenesulphonyl chloride and aniline in the transfer from methanol to acetonitrile were obtained by combining the heats of soln[5] and the free-energy changes, which were measured by measuring distribution coefficients between each solvent and a third immiscible solvent (Cyclohexane) at 25°.

Method of calculation. If Y is the observations vector (log K_2), X the matrix of solvent dependent parameters, β the coefficient of the vectors which must be estimated and ϵ the vector of errors, we can define the model

$$Y = X\beta + \epsilon \qquad (1)$$

$$b = (X'X)^{-1}X'Y. \qquad (2)$$

The least squares estimate **b** of β is the vector of the coefficients. The solutions to the eqn (1) were found (eqn 2) by use of a programme established by us on the CDC 7600 computer of "Centro di Calcolo Universitario dell'Italia NO".

This programme gives the least squares estimate of b and some statistical data which are a measure of the "goodness" of the model of solvation used (Overall F-test, Partial F-test, etc.). To find the best regression equation we used the stepwise regression procedure.[31]

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[a] The larger ρ in aprotic than in protic solvents can be ascribed also to bond-making which is advanced over bond-breaking, in accord to the proposed mechanism.

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