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REACTIONS OF 2-THIOPHENESULPHONYL CHLORIDE WITH ANION AND NEUTRAL NUCLEOPHILES

SOLVENT EFFECTS ON NUCLEOPHILIC REACTIVITY CORRELATIONS

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Abstract—The reaction kinetics of 2-thiophenesulphonyl chloride with anion and neutral nucleophiles was studied in H_2O, D_2O and in protic solvents-H_2O (10% v/v) and aprotic solvents-H_2O (10% v/v) mixtures at 25°. Analysing the rate constants measured in water by Bronsted, Ritchie and Edwards equations the conclusion drawn that, for the nucleophilic order against the sulphonyl sulphur, basicity is of prime importance, although there may well be some dependence on polarizability and solvation. Solvent isotope effects show that the reactions occur by nucleophilic catalysis rather than by a general base mechanism. Water is the solvent in which there is the greater reactivity than in either protic solvents or aprotic–protic mixtures. By solubility measurements and applying Parker's equation the contributions of solvation energies of both reactants and transition states to the free energy of activation are calculated. Solvent effects on nucleophilic reactivities are discussed in terms of S parameters (similar to Ritchie N_+ parameters), and by the approach of multiparameter empirical correlations. The data point out that solvation plays a large role on nucleophilic order. A complete comprehension of the problem would require an equation that takes into some account solvent effects. The homogeneous comparison of 2-thiophenesulphonyl chloride data with those of α-disulphone, *p*-anisyl *p*-methoxybenzenesulphinyl sulphone and benzenesulphonyl chloride shows that the same factors are involved in driving the nucleophilic reactivity for these compounds.

Bimolecular reactions between anions and uncharged species, as well as some bimolecular reactions of other charge types, are often much faster in dipolar aprotic solvents than in protic ones.[1,2] This is mainly ascribed to the desolvation in dipolar aprotic solvents of the reactant anion, which outweighs any effect due to transition state anion or reactant molecule solvation.[3]

Protic–dipolar aprotic mixtures are very useful as reaction media for these types of reactions, especially where the anion is so poorly solvated by the pure dipolar aprotic solvent that it is difficult to find a soluble electrolyte to act as a source of the anion.

Some features already discussed for protic to dipolar aprotic solvent transfer are observed in slightly dampened form for transfer from protic to dipolar aprotic–protic mixture. Thus many reactions as reported in eqn (1)

$$X^- + S \leftrightarrows [XS^-]^{\neq} \rightarrow P \qquad (1)$$

are faster in the mixture than in protic solvents; then rates of anion–molecule reactions increase continuously with increasing the dipolar aprotic component of a protic–dipolar aprotic mixture.[2,4–6] A significant feature is that reactions are still accelerated markedly by small amounts of dipolar aprotic components.

One of the important questions regarding the behavior of reactions (1) is what factors principally determine the relative order of reactivity of a series of nucleophiles in a given substitution.

One can try to resolve this problem by a general approach, adapted from perturbation theory, which considers interaction between nucleophile and electrophile to involve three main factors: as (i) coulomb factors, (ii) electronic repulsion due to closed shells and (iii) orbital penetration.

A change in the nature of the nucleophile may produce a regular change in these factors which affects the activation energy in the same direction. This leads to a direct relationship between reactivity and affinity, usually represented as some kind of linear free-energy relationship.

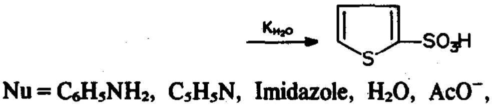
The Bronsted relationship is the most suitable of these for the treatment of the nucleophilic reactivities of a class of closely related nucleophiles which normally follow the pKa of their conjugate acids. Exceptions to the Bronsted equation must be examined on this basis and interpreted in terms of steric factors, anomalous solvation or some other specific effects.

Indeed, there is no reason to suppose that these factors will change in the same direction with changes in the nature of the nucleophile. In general, the first and the second factors will tend to change in the same direction whereas the third factor usually changes in the opposite direction. This situation leads to two extreme cases corresponding to a "soft" and "hard" nucleophilic order respectively, with the possibility of many nucleophilic orders between these limits.

Another factor, as important as those described previously in determining the nucleophilic order, is the solvent. In fact solvation energies usually change in the opposite direction with respect to (i) and (ii) and very often, they play an important or the most important role on reactions (1).

Recent papers[7–9] some of which compare reactions in gas phase with the same reactions in many solvents, support these ideas.

In order to give a contribution to this problem and particularly, to show solvent effects on the nucleophilic order, in this report we carried out the reactions (2) in protic solvents and in protic–dipolar aprotic mixtures



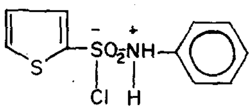
(2)

Nu = $C_6H_5NH_2$, C_5H_5N, Imidazole, H_2O, AcO^-, N_3^-, F^-, NO_2^-, $S_2O_3^{2-}$, SCN^-, Piperidine and morfoline.

The second route (K_{H_2O}) is referred to the nucleophiles (as C_5H_5N, AcO^-, NO_2^-, SCN^-) forming unstable intermediates which are decomposed by water.

DISCUSSION

For the reactions of 2-thiophenesulfonyl chlorides with anilines previously reported,[10] we postulated the S_AN mechanism in which the rate-determining step involved attack of the nucleophile on the sulphonyl group to give the intermediate:



An analogous mechanism may be hypothesized for the reactions (2).

Second order rate constants measured at 25° for the reactions (2) are reported in Table 1 and in Fig. 1 $\log k_2$ (in water) are plotted vs pKa's (Bronsted equation).

It is interesting that six anilines are well fitted by a correlation $\log k_2$–pK_a derived for nucleophiles as F^-, NO_2^-, N_3^-, C_5H_5N, which notoriously yield stable or metastable intermediates with sulphonylchloride compound. This seems further evidence for a S_AN mechanism, already proposed for such reactions with anilines as nucleophiles.

We obtained a good correlation ($r = 0.996$ and $\beta = 0.68$) except for $S_2O_3^{2-}$, AcO^-, SCN^- and imidazole; the correlation also included the values relative to the reactions between 2-thiophenesulphonyl chloride and substituted anilines.[10]

This shows that, if the solvent and the electrophile do not change, the basicity becomes an important factor in determining the nucleophilic reactivity for these reactions at the tetracoordinate sulphur. In fact, for a given series of nucleophiles N, reacting with a common center S, it follows that

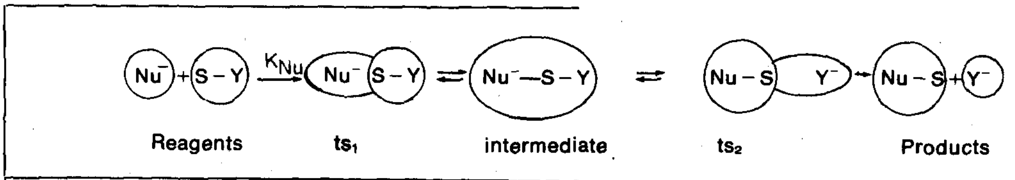
$$\Delta F = -RT \ln k = E_{NS} - (E_N + \Delta F_N^s) + \text{const} \qquad (3)$$

where E_{NS} is dissociation energy of the product NS formed; E_N is electron affinity of N; ΔF_N^s is solvation free energy of N; provided that differences in ΔS (change in entropy) are neglected.[11] It is immediately apparent that the equilibrium is determined by two factors:

(a) The interaction energy between N and S (E_{NS}).

(b) The solution electron affinity ($E_N + \Delta F_N^s$) which is a function of the nucleophile and solvent only.

If the term (a) is more important than (b) it is expected the previously described behavior; *vice versa* factor (b) > factor (a) the correlation between reactivity and affinity is not good; probably the negative deviation from the Bronsted line of the points AcO^- and imidazole can be ascribed to these solvation phenomena. Taking into account solvation effects, the reaction mechanism can be depicted as



where the circles indicate the solvation shells.

When the rate-determining step is the attack, $K_{obs} = K_{Nu}$, and the nucleophile Nu^- is obliged to destroy its solvation shell partially to interact with the electrophile. If the term ΔF_N^s is larger than the others the reactivity is determined by solvation.

This is in accord with what was earlier reported,[10] that the reaction between benzenesulphonyl chloride and

Table 1. Second order rate constants k_2 for the reactions of 2-thiophenesulphonyl chloride with nucleophiles Nu in various solvents at 25°C

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

Solvents	Nu= NO_2^-	N_3^-	$S_2O_3^{--}$	F^-	AcO^-	C_5H_5N	$C_6H_5NH_2$	Im.	H_2O
1 Water$^{(b)}$	77.3	259	2849	57.7	7.47	713	709$^{(10)}$	125	0.0245
2 Heavy Water	80.1	-	-	-	8.76	552	589	128	-
3 Methanol$^{(c)}$	4.34	2.50	30.6	2.01	1.69	4.79	9.41	11.0	0.0100
4 Ethanol$^{(c)}$	5.27	4.58	-	1.74	0.483	5.31	5.45	9.42	0.000372
5 Propan-1-ol$^{(c)}$	3.85	3.32	-	-	0.428	2.46	3.12	-	0.000369
6 2-Methoxyethanol$^{(c)}$	37	0.632	-	-	2.46	8.49	3.77	-	0.00291
7 Acetonitrile$^{(c)}$	338	2.01	-	-	0.786	36.4	3.33	92.6$^{(d)}$	0.000389
8 Acetonitrile$^{(e)}$	395	-	-	-	4.37	35.5	5.86	225	-
9 Acetone$^{(c)}$	5.18	2.09	-	-	1.06	10.3	1.00	61.7	0.000271
10 Dioxane$^{(c)}$	60.4	-	-	-	7.82	4.63	0.753	32.3	0.00742
11 Dioxane$^{(f)}$	52.7	0.375	-	8.20	4.67	91.6	27.1	108	0.00556

(a) Values of k_2 are reproducible to $\pm$ 6%

(b) In this solvent the values of k_2 for p-anisidine and SCN^- are 2.317 and 0.00186 respectively.

(c) Mixtures with 10%(v/v) of water.

(d) In pure acetonitrile the value of k_2 is 0.195.

(e) Mixture containing D_2O in equal amount to (c).

(f) Mixture with 40%(v/v) of water. In this solvent the values of k_2 for morpholine and piperidine are 3.00 and 11.00 respectively.

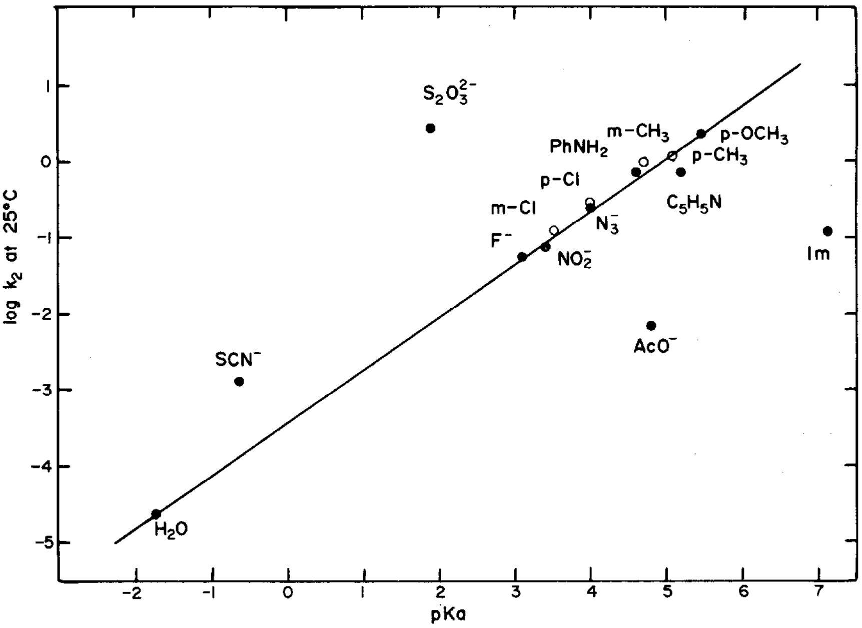


Fig. 1. Plot of log k_2 of 2-thiophenesulphonyl chloride with nucleophiles vs pKa in water.

imidazole was ruled by imidazole desolvation energy in the transfer protic–aprotic solvent. In the case of the acetate anion the negative charge is localized almost completely on the O atoms, which provide excellent sites for solvation by protic solvent. Furthermore, the Me group is small and will not impede much the approach of water molecules to the negative charge.

Clearly, the protonation (that is the model process for the Bronsted equation) for AcO^- and imidazole occurs by a different mechanism with respect to reactions (2). Probably in water the proton transfer can occur without requiring nucleophile desolvation.

Since the reactions of benzenesulphonylchloride with AcO^- and imidazole,[12] respectively, are analogous, we can conclude that the desolvation energy of the electrophile is very small.

The positive deviation of $S_2O_3^{2-}$ and SCN^- could be ascribed to high polarizability of these groups (orbital-controlled reactions).

We obtained support for our interpretation by using Edwards equation

$$\log k/k_0 = \alpha E + \beta H.$$

In fact our data[a] are well accommodated by this equation (Fig. 2) and, what is important, the points

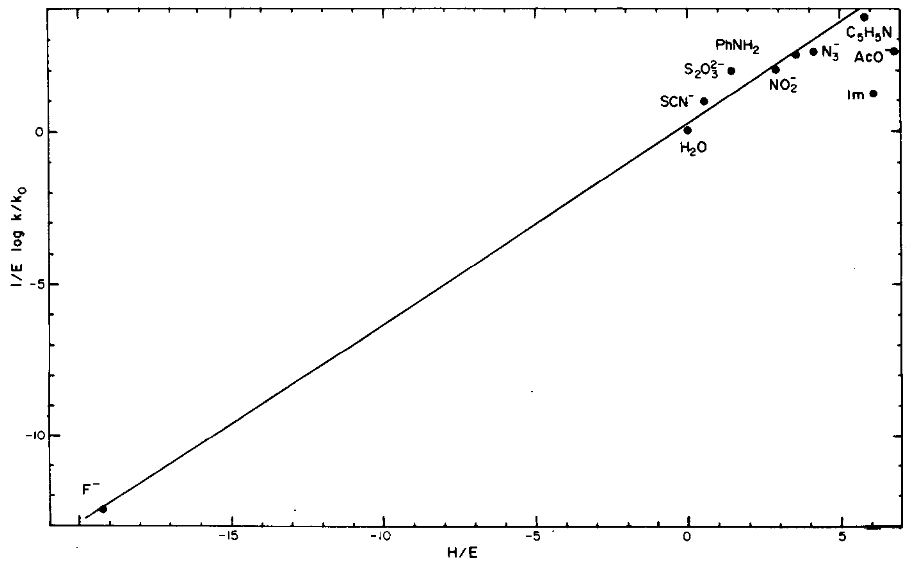


Fig. 2. Rate constants for reactions of 2-thiophenesulphonyl chloride with nucleophiles in water plotted according to the Edwards equation.

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[a] The correlation field is ranging over 10^4 orders of magnitude in rate, and the correlation is statistically reliable with a multiple correlation coefficient R = 0.93 and confidence level above 99% (Table 6).

relative to $S_2O_3^{2-}$ and SCN^- fall in the correlation line, meaning that for these nucleophiles the polarizability has a sensible effect ($\alpha = 0.73 \pm 0.30$, $\beta = 0.48 \pm 0.11$). However, the points AcO^- and imidazole are also scattered negatively from this line, showing that other factors than polarizability are important. This confirms our hypothesis that for AcO^- and imidazole solvation energies play a primary role.

In Fig. 3 the log K_2 are plotted against N_+[b] values. We obtained a fair correlation ($r = 0.97$, slope $= 0.96$) except for N_3^-. By comparing Fig. 2 with Fig. 1, two situations can be recognized.

First, desolvation energies have not the same weight for all nucleophiles; second, N_+ values do not reflect only the energies required to desolvate the nucleophiles but also other factors generally involved in determining the reactivity of a nucleophile.

By plotting N_+ values against pKa we note there is a rough proportionality for some nucleophiles meaning that in such a case N_+ values are not clean measures of desolvation energies.

A similar reasoning is valid also for pKa values; one could possible resolve the question by the inclusion of additional terms in Bronsted or in Ritchie correlations. We feel that for the success of such correlations it is necessary that various factors which drive the reactivity interact independently of each other; furthermore the existence of parameters which reflect these clean interactions are necessary.

Moreover, we tried to combine different parameters in order to obtain an equation which justified the nucleophilic order for the reactions here reported in water. So we found a two-parameters equation

$$\log k/k_0 = tH^c + fN_+^c \tag{4}$$

($t = 0.30 \pm 0.14$, $f = 0.33 \pm 0.16$, $R = 0.903$, c.l. $= 95\%$) statistically reliable for 8 points (except $S_2O_3^{2-}$ and SCN^-, for which we have not N_+ values).[d]

This confirms furtherly our interpretation that basicity, polarizability and solvation are three important elements in determining nucleophilic reactivity in this case. In fact without the points $S_2O_3^{2-}$ and SCN^- for which polarizability effect is more sensible, we find by equation (4) bridges the gap between observed and predicted values.

However other attempts to correlate all data by more complicated equations[e] give no improvements with respect to the single-parameter or Edwards equations and they are statistically unreliable. We can then conclude that, often, there are very specific interactions in a nucleophile–electrophile–solvent system which cannot be generalized for other systems different only in the nucleophile. In these cases deviations from single-parameter correlations or from Edwards equation are more meaningful than attempts to rationalize the whole picture by more complicated equations.

To obtain a better correlation with N_+ parameters we may try to correct such values. Ritchie has proposed that the observed second order rate constant for a substitu-

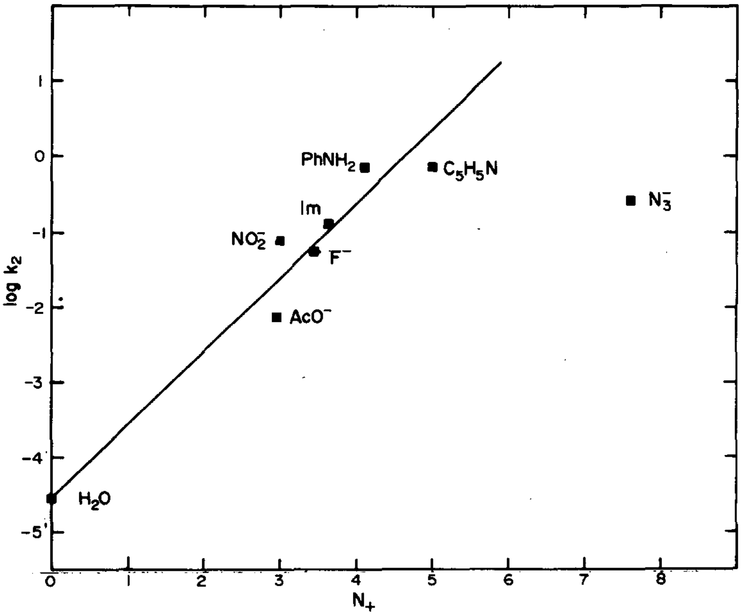

Fig. 3. Rate constants for reactions of 2-thiophenesulphonyl chloride with nucleophiles in water plotted vs N_+ values.

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[b] The N_+ values are parameters defined by Ritchie[13–16] equation

$$\log \frac{k_{Nu}}{k_{H_2O}} = N_+$$

where k_{Nu} is the rate constant for reaction of a given nucleophile Nu with a particular cation, k_{H_2O} is the rate constant for reaction of the same cation with water. N_+ is so a parameter characteristic of the nucleophile–solvent system and independent of the cation. For the author the N_+ values are measures of the nucleophile desolvation energies, the high N_+ the lower the energy required, although he no longer feels this correct.[17]

[c] H and N_+ values are Edwards and Ritchie parameters respectively.

[d] We have a better correlation by the equation $\log k/k_0 = aH + bn^{18}_{CH_3I}$ ($a = 0.29 \pm 0.10$, $b = 0.38 \pm 0.11$, $R = 0.89$, c.l. $= 99\%$) statistically reliable for 10 points (S_2O_3 and SCN^- enclosed) (Table 6).

[e] $\text{Log } k/k_0 = aH + bn^{18}_{CH_3Br}$; $\log k/k_0 = aH + bn^{18} + cN_+$; $\log k/k_0 = aH + bE + cN_+$.

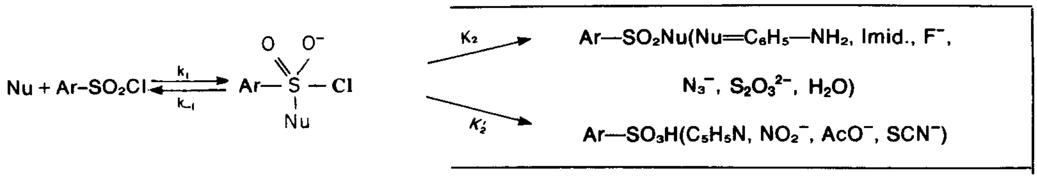
tion proceeding by the general mechanism

$$Nu + S\text{-}L \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Nu\text{-}S\text{-}L \xrightarrow{k_2} Nu\text{-}S + L$$

would be related to N_+ as follows:

$$\log k_{Nu} = \log k_0 + N_+ - \log(1 + k_{-1}/k_2)$$

where k_0 is the rate of reaction of S–L with water. In our case:



Since k_{-1}/k_2 with 2-thiophenesulphonylchloride is already much less than one for all nucleophiles studied except for NO_2^-, F^-, AcO^- and N_3^-, only the points relative to these nucleophiles would be altered by generally increasing the size of k_{-1}/k_2.

While the points C_5H_5N and N_3^- would be moved significantly closer to the correlation line, those for F^-, NO_2^-, AcO^-, $PhNH_2$ would be moved further away. A general increase in k_{-1}/k_2, therefore, does not lead to any significant improvement in the correlation.

Perhaps we must admit that there are different ratios k_{-1}/k_2 for various nucleophiles; this might be probable if the different intermediates formed in the reactions (2) eliminate the leaving groups at different rates (with different k_2 values).[f] In this case we think that the intermediate formed by N_3^- attack is very stable (a large ratio k_{-1}/k_2) and the N_+ value is decreased sensibly by the term $\log(1 + k_{-1}/k_2)$. Consequently the true value for N_3^- is not 7.6 but about 4.2.

Water effect

Contrary to what would be expected in general for reactions of anionic nucleophiles, water is the solvent in which there is a reactivity greater than in other solvents both protic and aprotic–protic mixtures. In order to understand this behavior the solubilities of the salts used as sources of anions were measured at 25° in the various solvents (Table 2).

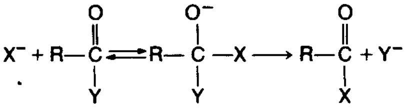
In this way we calculated the contribution of solvation energies of both reactants and transition states to the free energy of activation[g] by using the Parker[2,3,19,20] equation

$$\log \frac{k^s}{k^0} = \log {}^0\gamma^s_{X^-} + \log {}^0\gamma^s_S - \log {}^0\gamma^s_{SX^{\neq}}$$

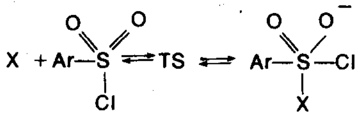
where the k's are the rate constants for the above reaction in the solvents 0 and s and the ${}^0\gamma^s$'s are the solvent activity coefficients for the nucleophile (X^-), the substrate (S) and the transition state ($SX^{\neq}$).

We neglected the term ${}^0\gamma^s_S$ because very likely its contribution is very small with respect to ${}^0\gamma^s_{X^-}$.

Parker *et al.*[21] reported that the reactions at CO carbon appeared to be less sensitive to dipolar aprotic solvent acceleration than the corresponding aromatic substitutions. They felt this was presumably due to greater solvation of the transition state (H-bonding from the protic solvent) because of the greater localization of the negative charge in the transition state of the former reaction.



We supported a similar explanation for the reactions (2). Also in this case we think the working mechanism is the S_AN,[10] in which the rate-determining step is the attack of the nucleophile on the sulphonyl group. Hence a pentacoordinate intermediate with localized negative charge is formed[h]



In this case a protic solvent has a double opposed effect, since it solvates both the nucleophile by H-bonding changing it in a less reactive species (decreasing the rate) and the transition state decreasing the activation free energy (increasing the rate).

Except for NO_2^- anion, the solvation of transition state is greater than that of reactants; hence the reactions are faster in water.

Sequences of nucleophilic reactivity

In the terminology of the theory of hard and soft acids and bases (HSAB), the sulphonyl sulphur, as the sulphonate,[23] can be characterized as an electrophilic center of a considerable degree of hardness. In fact, if we see the reactivity sequence in water:

$$\underset{\text{soft}}{S_2O_3^{2-}} > \underbrace{C_5H_5N \geq C_6H_5NH_2 > N_3^- > \text{Imid.} > NO_2^- >}_{\text{borderline}} \underbrace{F > AcO^- > SCN^- > H_2O}_{\text{hard}}$$

we can conclude that it is a borderline center.

However it is apparent that detailed solvent studies are essential for any discussion of nucleophilic reactivity. Pearson and Songstad stress that the HSAB principle is not a theory but a statement about experimental facts.[24] Although the approach appears to have some value, little

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[f] Indeed we have two k_2 values (k_2 and k_2') depending on the formation of an intermediate (function of the kind of nucleophile) which is or is not decomposed by water.

[g] Table 7 and Fig. 8.

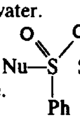
[h] Also Kice[22] postulates an intermediate  $Nu\text{—}S(O)(O^-)(Ph)$ SO_2Ph for the nucleophilic substitutions of α-disulphone.

Table 2. Solubilities of some salts measured at 25°C in various solvents (mol l^{-1})

Solvents/salts	NaN_3	NaF	$NaNO_2$	CH_3COONa	$Na_2S_2O_3.5H_2O$
H_2O	3.583	0.879(a)	10.17	4.992	2.922
D_2O	-	-	8.717	4.348	-
CH_3OH-H_2O(b)	0.719	0.009	0.853	2.905	0.158
C_2H_5OH-H_2O(b)	0.142	0.001	0.136	0.413	-
C_3H_7OH-H_2O(b)	0.136	-	0.127	0.087	-
CH_3CN-H_2O(b)	0.047	-	0.021	0.0013	-
CH_3COCH_3-H_2O(b)	0.128	-	0.053	0.0019	-
CH_3CN-D_2O(b)	-	-	0.027	0.0014	-

(a) J. H. Payne, J. A. C. S. 19, 947 (1937), found a value of 0.983

(b) Mixtures with 10% (v/v) of water

Table 3. Sequences of nucleophilic reactivity in various solvents for the reactions of 2-thiophenesulphonyl chloride with nucleophiles at 25°C

Solvents	Sequences
1 Water	$S_2O_3^{--} > C_5H_5N \geq C_6H_5NH_2 > N_3^- > Im > NO_2^- > F^- > AcO^- > SCN^- > H_2O$
2 Methanol(a)	$S_2O_3^{--} > Im > C_6H_5NH_2 > C_5H_5N > NO_2^- > N_3^- > F^- > AcO^- > H_2O$
3 Ethanol(a)	$Im > C_6H_5NH_2 > C_5H_5N \geq NO_2^- > N_3^- > F^- > AcO^- > H_2O$
4 2-Methoxyethanol(a)	$NO_2^- > C_5H_5N > C_6H_5NH_2 > AcO^- > N_3^- > H_2O$
5 Propan-1-ol(a)	$NO_2^- \geq N_3^- \geq C_6H_5NH_2 > C_5H_5N > AcO^- > H_2O$
6 Acetonitrile(a)	$NO_2^- > Im > C_5H_5N > C_6H_5NH_2 > N_3^- > AcO^- > H_2O$
7 Acetone(a)	$Im > C_5H_5N > NO_2^- > N_3^- > AcO^- \geq C_6H_5NH_2 > H_2O$
8 Dioxane(a)	$NO_2^- > Im > C_5H_5N > AcO^- > C_6H_5NH_2 > H_2O$
9 Dioxane(b)	$Im > C_5H_5N > NO_2^- > C_6H_5NH_2 > F^- \geq AcO^- > N_3^- > H_2O$

(a) Mixture with 10%(v/v) of water.
(b) Mixture with 40%(v/v) of water.

account is taken of solvent effects.[25] Analysis of solvent effects on the reactivity sequences, as reported in Table 3, supported that the borderline character is roughly kept on changing the solvent, notwithstanding the many inversions of nucleophilic reactivity. Such inversions are very important, because they point out that the solvent (solvation energy) plays a large role.

One of the most important effects of solvents on the reactants are their ability to form H bonding with the nucleophiles. Table 4 shows that the ratios $k_{anil.}/k_{nucl.}$ are larger or equal to unity in protic solvents, becoming less than unity in aprotic–protic mixtures.

This means that nucleophilic desolvation is becoming more important than aniline on diminishing the electrophilic power of solvents.

To analyse solvent effects on the reactions of 2-thiophenesulphonyl chloride with each nucleophile, we attempted single-parameters correlation by E,[i] B[i] and ϵ[i] values.

In every case no correlation fits experimental data.

Then according to Ritchie, we calculated some S parameters depending on nucleophile and solvent too by the equation $\log k_2/k_{H_2O} = S$. The S values obtained are reported in Table 5.

We tried to correlate each nucleophile reactivity on changing the solvent by S parameters. Indeed we obtained no satisfactory correlations. Therefore we applied two-parameters equations

$$Z = aX + bY + c$$

and the fit improved.

We observed that nucleophile solvent interactions are often specific and sometimes, differ from nucleophile to

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[i] Because we use 10% (v/v) H_2O-mixtures, we calculated E and B values by the expression

$$y_{mix.} = x_1y_1 + x_2y_2$$

where x_1, x_2 are molar fractions and y_1, y_2 pure solvents parameters.

Table 4. Ratios $k_{anil.}/k_{nucl.}$ for the reactions of 2-thiophenesulphonyl chloride with nucleophiles in various solvents at 25°C

Solvents	Nu= C_5H_5N	Imid.	NO_2^-	AcO^-	N_3^-	$E_m^{(a)}$
1 Water	0.99	5.67	9.17	94.9	2.74	21.8
2 Heavy Water	1.07	4.60	7.35	67.2	-	-
3 Methanol$^{(b)}$	1.96	0.86	2.17	5.57	3.76	16.3
4 Ethanol$^{(b)}$	1.03	0.58	1.03	11.28	1.19	14.3
5 2-Methoxyethanol$^{(b)}$	0.44	-	0.102	1.53	5.96	15.6
6 Propan-1-ol$^{(b)}$	1.27	-	0.810	7.29	0.94	14.2
7 Acetonitrile$^{(b)}$	0.09	0.04	0.099	4.24	1.66	9.2
8 Acetonitrile$^{(c)}$	0.17	0.03	0.015	1.34	-	-
9 Acetone$^{(b)}$	0.10	0.02	0.193	0.94	0.48	8.2
10 Dioxane$^{(b)}$	0.16	0.02	0.012	0.001	72.3	10.2
11 Dioxane$^{(d)}$	0.30	0.25	0.514	5.80	-	17.51

(a) Electrophilicity parameters of mixture; E values from I.A.Koppel and V.A.Palm, Advances in Linear Free Energy Relationships,(Ed. by N.V.Chapman and J.Shorter), chap.5.Plenum Press, New York(1972).

(b) Mixtures with 10%(v/v) of water.

(c) Mixture containing D_2O in equal amount to (b)

(d) Mixture with 40%(v/v) of water.

nucleophile. However the reactivity shows a fair dependence on E,[j] B[k] and S[l] parameters.

In conclusion for the various nucleophiles we have:

(a) NO_2^- (solvs 1–3, 5–8)

$$\log k_2 = 0.34S - 0.015B \qquad (r = 0.91)$$

(b) Imidazole (solvs 1–3, 6–8)

$$\log k_2 = 0.17S - 0.011B \qquad (r = 0.95)$$

(c) N_3^- (solvs 1–3, 5–7)

$$\log k_2 = 0.061E - 0.017B \qquad (r = 0.93)$$

(d) C_5H_5N (solvs 2–3, 5–8)

$$\log k_2 = 0.13S - 0.012B \qquad (r = 0.994)$$

(e) $C_6H_5NH_2$ (solvs 1–3, 5–8)

$$\log k_2 = 0.16E - 0.017B \qquad (r = 0.996)$$

It is worth noting that electrophile dependence on solvation is roughly constant (see B values) for all reactions, while the dependence on S values is more marked for anionic nucleophiles (NO_2^-).

Isotope effects

Though poorly understood theoretically, solvent isotope effects can be useful in determining reactions mechanisms. This tool must, however, be used cautiously. One should avoid the over interpretation of solvent isotope effects.

Isotope effects can seldom be used to distinguish between kinetically indistinguishable mechanisms such as general base and general acid or specific base mechanisms. Solvent isotope effects are, however, useful in differentiating between general base and nucleophilic reaction paths. The former mechanism is usually associated with a solvent deuterium isotope effect larger than 2 while the latter mechanism is usually associated with smaller isotope effects ranging from 0.8 to 1.9.[26]

Two quite different conclusions have been reached concerning the major determinant of this solvent isotope effect. According to one,[27,28] the major cause is the solvent isotope effect arising from ion–solvent interaction in the transition state; according to the other,[29] the major factor is related to the structural free energy difference in the initial state solvation shells. The first follows traditional ideas of solvation based on conclusions reached in mixed solvents; the second attaches greater importance to differences in the relative stability of the initial state solvation shell as between D_2O and H_2O.

We don't wish to discuss a question as important as this, even if the data relative to AcO^- and NO_2^- ($k_{D_2O}/k_{H_2O} = 1.2$, $\text{solub}_{D_2O}/\text{solub}_{H_2O} < 1$) seems to support the second conclusion. However a contribution from both the transition state and initial state interactions cannot be excluded.

In fact if we consider the kinetic solvent isotope effect between CH_3CN–H_2O and CH_3CN–D_2O mixtures for nucleophiles as NO_2^-, AcO^-, $C_6H_5NH_2$ and imidazole we

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[j] The positive coefficient of E means a larger solvation of negative charges at the transition state.

[k] The negative coefficient of B means a larger solvation of positive charges at initial state. We think that, in this case, B parameter reflects the solvation energy of electrophile (2-thiophenesulponyl chloride). Increasing B, the solvation energy increases and the rate is slower.

[l] If Ritchie's assumption is valid, such values reflect nucleophile desolvation energy. But, as we observed previously, the ratio k_{Nu}/k_{H_2O} is not depending only on solvation; in fact for the reactions here reported in water it is depending also on nucleophile basicity and polarizability. However, keeping nucleophile constant if we change solvent, solvent effects can be interpreted by S parameters. In this case if data are well fitted, two cases may occur:

(i) Nucleophile solvation plays a primary role on reactivity;

(ii) Solvation has not a fundamental weight, but experimental data are fitted by S parameters because other effects compensate each other.

Table 5. S parameters calculated at 25°C from the reactions of 2-thiophenesulphonyl chloride with nucleophiles Nu in various solvents

Solvents		S							
	Nu=	NO_2^-	N_3^-	$S_2O_3^{--}$	AcO^-	C_5H_5N	$C_6H_5NH_2$	Im	F^-
1 Water(a)		3.50	4.02	5.06	2.48	4.46	4.46	3.71	3.37
2 Methanol(b)		2.64	2.40	3.49	2.23	2.68	2.97	3.04	2.30
3 Ethanol(b)		4.15	4.09	-	3.11	4.15	4.17	4.40	3.67
4 Propan-1-ol(b)		4.02	3.95	-	3.06	3.82	3.93	-	-
5 2-Methoxyethanol(b)		4.10	2.34	-	2.93	3.46	3.11	-	-
6 Acetonitrile(b)		5.94	3.71	-	3.30	4.97	3.93	5.38	-
7 Acetone(b)		4.28	3.89	-	3.59	4.58	3.57	5.36	-
8 Dioxane(b)		3.91	-	-	3.02	2.79	2.01	3.64	-
9 Dioxane(c)		3.98	1.83	-	2.92	4.22	3.69	4.27	3.17

(a) In this solvent the value of S for SCN^- is 1.88
(b) Mixtures with 10%(v/v) of water.
(c) Mixture with 40%(v/v) of water. In this solvent the values of S for morpholine and piperidine are 5.73 and 6.30 respectively.

Table 6. Data used in correlation equations for the reactions of 2-thiophenesulphonyl chloride with nucleophiles Nu in water at 25°C

Nu	$\log k/k_o$	$E_N^*(E^o+2.60)$	$H^*(pka+1.74)$	$n^*_{CH_3I}$	$N_+^{(a)}$
1 F^-	3.372	-0.27	5.189	2.70	3.45
2 $C_6H_5NH_2$	4.462	1.78	6.321	5.70	4.10
3 C_5H_5N	4.464	1.20	6.970	5.23	5.00
4 NO_2^-	3.499	1.73	5.110	5.35	3.04
5 N_3^-	4.024	1.58	6.480	4.00	7.60
6 SCN^-	1.881	1.83	1.039	6.70	-
7 H_2O	0.000	0.00	0.000	0.00	0.00
8 $S_2O_3^{--}$	5.066	2.52	3.640	8.95	-
9 AcO^-	2.484	0.95	6.490	4.30	2.95
10 Im	3.708	-1.44(b)	8.840	4.97	3.66

* Values from R.G.Pearson, Advances in Linear Free Energy Relationships,(Ed. by N.V.Chapman and J.Shorter), chap.6, p 293 Plenum Press, New York(1972).
(a) From reference 17.
(b) Interpolated by us.

have ratios $k_D/k_H = 1.1$, 5.5, 1.7 and 2.4 respectively. Solubility measurements (for NO_2^- and AcO^-) show that in this case initial state solvation cannot be invoked to justify such a solvent isotope effect.

Therefore, we must ascribe it to a differential transition state solvation. Perhaps the system CH_3CN-D_2O is less structured than CH_3CN-H_2O and solvates negative charges with minor loss of energy.

An alternative explanation for AcO^- and imidazole deviations from the correlation $\log k_2$-pka is that these two nucleophiles react by a general catalytic mechanism rather than by a nucleophilic catalysis. This explanation, however, is not supported by solvent isotope effects measurements because we find a ratio $k_H/k_D = 0.85$–1.29 for NO_2^-, AcO^-, C_5H_5N, $C_6H_5NH_2$ and imidazole according to a nucleophilic catalysis.

From the comparison with Kice's results[23] (Fig. 4), it is evident that, although there is some scatter, the change in α-disulphone reactivity in general parallels that in 2-thiophenesulphonyl chloride.

The point for N_3^- shows some deviation from the correlation line in the direction of being more reactive toward the disulphone compound. We therefore interpret these results to mean that when nucleophilic substitution at disulphone and sulphonyl compound involves the same mechanism the reactivity pattern for a series of nucleophiles toward $-SO_2$–SO_2– will roughly parallel the one they exhibit toward $-SO_2Cl$, even though the rates for all the substitution involving the disulphone compound are faster than those for the sulphonyl compound. Also the data relative to *p*-anisyl *p*-methoxybenzenesulphinyl sulphone (Fig. 5) are fitted by S parameters.

From these comparisons we can conclude that the same factors are involved in driving the reactivity for the reactions examined.

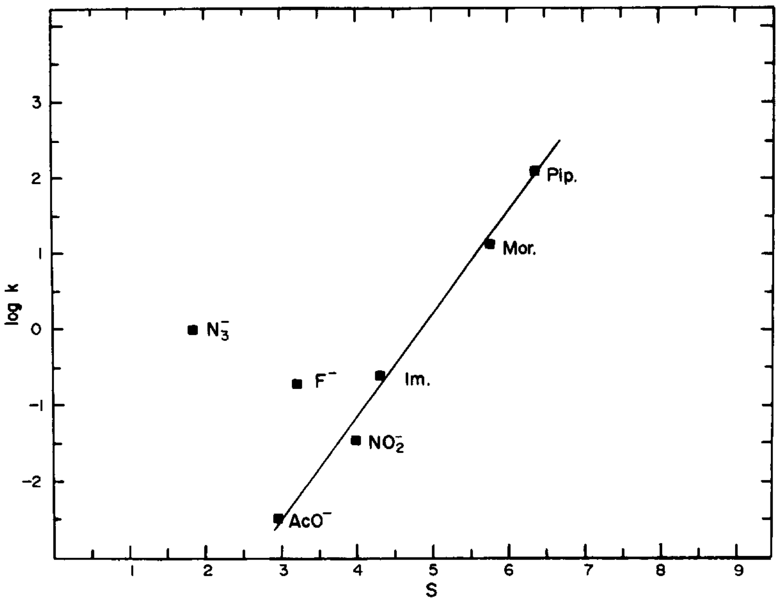

Fig. 4. Rate constants for phenyl α-disulphone with nucleophiles plotted vs S parameters in 60% dioxane.

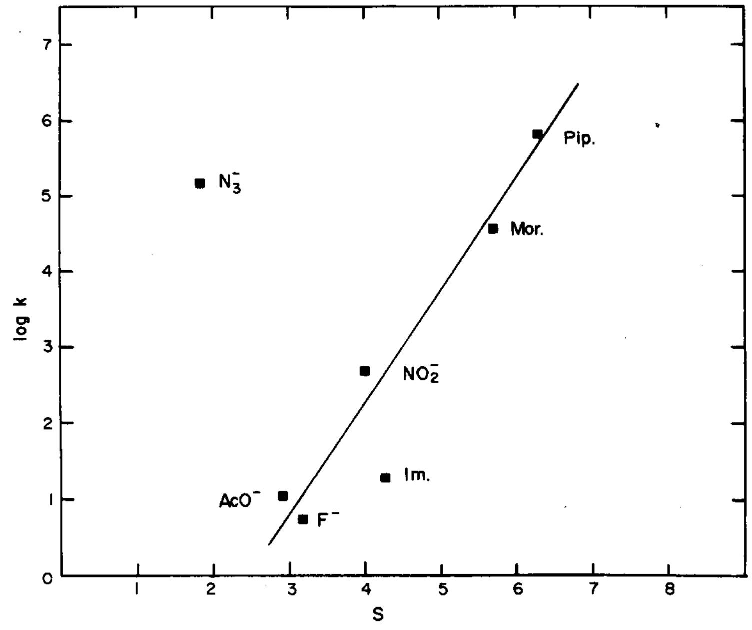

Fig. 5. Plot of log k_{Nu} for p-anisyl p-methoxybenzenesulphinyl sulphone vs S parameters for nucleophiles in 60% dioxane.

Finally our results (in water) may be compared with those obtained for nucleophilic reactions on benzenesulphonyl chloride[12] (Fig. 6). The rates show good correlation indicating that the two reactions are similar with respect to structure of transition state and factors determining nucleophilic order.

CONCLUSIONS

From the previous analysis the conclusion indicates that, for the nucleophilic order against the sulphonyl (and sulphinyl) sulphur, basicity and solvation are of prime importance, although there may be some dependence on polarizability.

It is apparent that the use of LFER's such as Bronsted or Edwards equations is possible only in water because in other solvents it is necessary to know the values of pka or E for each nucleophile. Therefore for the nucleophilic order treatment, it would be convenient to test the possible use of relationships, whose parameters are a measure of some nucleophile properties in the gas phase (as IP or AP and so on) and whose solvent dependence is well known. It is well to point out again that a knowledge of solvent role is necessary to understand nucleophilic order and basicity-nucleophilicity correlations.[30] In fact a complete comprehension of the problem would require an equation that also takes into account solvent effects.

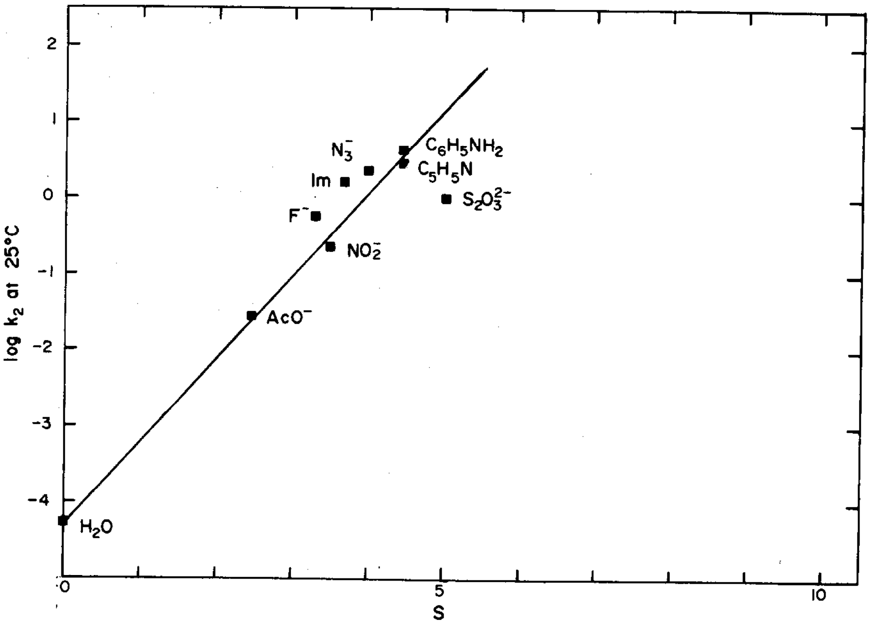

Fig. 6. Plot of log k_2 for benzenesulphonyl chloride vs S parameters for nucleophiles in water.

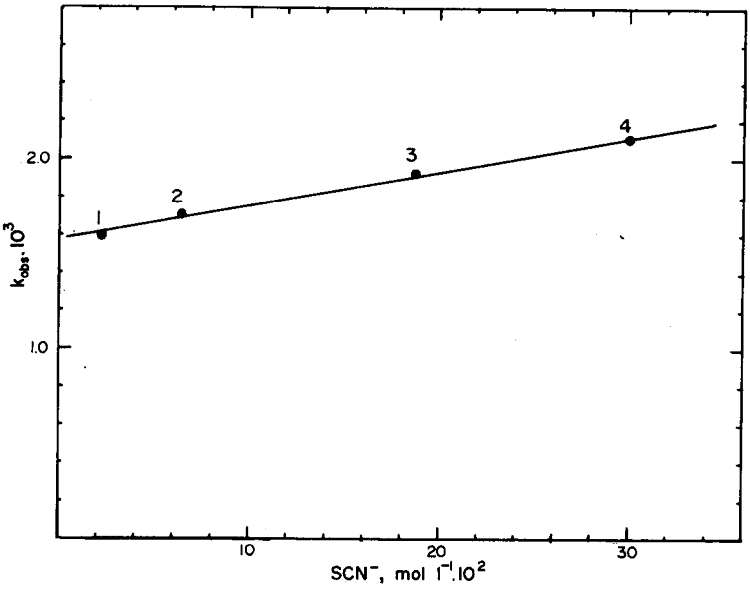

Fig. 7. Rates of hydrolysis of 2-thiophenesulphonyl chloride in water at 25°C as a function of SCN^- concentration.

EXPERIMENTAL

Materials. 2-Thiophenesulphonyl chloride was obtained following the procedure described.[31]

Anilines were commercial products (Carlo Erba) purified by several distillations or crystallizations, while imidazole is a commercial product (Aldrich) of high purity. Reagent grade inorganic sodium salts were used. D_2O is a Carlo Erba product (RPE) at 99.7%.

Kinetic procedure. Rate measurements for reactions of 2-thiophenesulphonyl chloride with water, nitrite, acetate, thiocyanate, pyridine, imidazole and anilines 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.[32,33] The reagent concentrations ranged from *ca.* 0.0002 to *ca.* 0.003 mol for 2-thiophenesulphonyl chloride and from *ca.* 0.01 to *ca.* 0.2 mol for the nucleophiles, depending on the reaction rates and salts solubility.

The first order rate constants (k_{obs}) were obtained from the slope of conventional plots of la(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.

With the nucleophiles azide, fluoride and thiosulphate the second-order rate constants were obtained from the infinity titres,[12] applying the equation

$$\frac{k_0}{k_n N} = \frac{V}{V_0 - V}$$

where k_0 and V_0 are observed first-order rate constants and

Table 7. Free energies of transfer $\delta\Delta G_t$ of transition state for the reactions of 2-thiophenesulphonyl chloride with some nucleophiles from water to various solvents at 25°C

$\delta\Delta G_t^*$(Kcal mol^{-1})

Solvents	Nu= N_3^-	F^-	NO_2^-	AcO^-	$S_2O_3^{--}$
1 D_2O	-	-	0.0702	-0.0125	-
2 $CH_3OH^{(a)}$	3.699	4.701	3.174	0.912	4.413
3 $C_2H_5OH^{(a)}$	4.302	6.089	4.145	2.339	-
4 n-$C_3H_7OH^{(a)}$	4.517	-	4.372	4.092	-
5 $CH_3CN^{(a)}$	5.444	-	2.788	6.221	-
6 $CH_3CN^{(b)}$	-	-	2.546	5.161	-
7 $CH_3COCH_3^{(a)}$	4.827	-	4.713	5.819	-

* Calculated by the equation $\delta\Delta G_t = \delta\Delta G^{\neq} + \delta\Delta G_r$, where $\delta\Delta G^{\neq}$ are activation energies differences and $\delta\Delta G_r$ are reactants free energies differences in the two solvents compared.

(a) Mixtures with 10%(v/v) of water.

(b) Mixture containing D_2O in equal amount to (a).

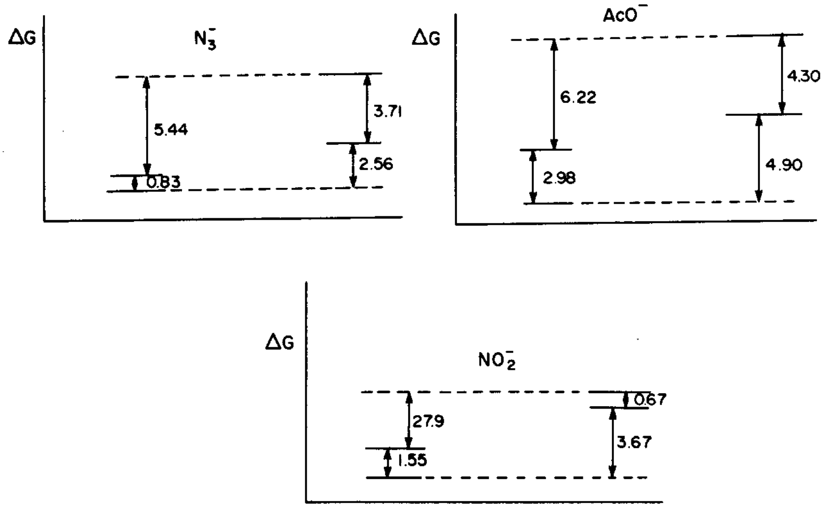

Fig. 8. Transfer energies of transition state and reactants from water to acetonitrile for the reactions of 2-thiophenesulphonyl chloride with N_3^-, AcO^- and NO_2^-.

infinity titre respectively in a reaction without added nucleophile; V is the infinity titre in a reaction with added nucleophile.

Although not identified, some of the assumed products are well known.[34]

Thus aromatic sulphonyl chlorides react readily in aqueous solution with aniline, NaF and NaN_3 to yield sulphoanilide, sulphonyl fluoride and sulphonyl azide respectively. 2-Thiophenesulphonyl chloride reacts with acetate to give a mixed anhydride.[35]

Rate measurements for the reactions of 2-thiophenesulphonyl chloride with piperidine and morpholine in dioxane-water were measured in a stopped-flow spectrophotometer[m] by monitoring the increase in optical density with time at 290 nm, a wavelength where the formed sulphoanilide has a strong absorption.

Solubility measurements. The solubilities of the salts used as source of anions were performed by atomic absorption technique.

After drying, the salts were dissolved at 45°, in the various solvents used, to obtain saturated solutions, which were thermostated at 25° for 24 hr. Such solutions were carried at atomic absorption spectrophotometer (Perkin–Elmer mod 300, equipped by a digital voltmeter) and Na concentration was measured by an oxidizing air–acetylene flame ($\lambda = 589.6$ nm), after dilution in case of need.

To prepare standard solutions having known concentrations of the metal to be determined, we dissolved 2.542 g of NaCl in 1 litre of the same solvent as that of sample.

Hydrolysis of 2-thiophenesulphonyl chloride SCN^- catalysed. Rogne[12] reports that benzenesulphonyl chloride in water does not react with SCN^-. We find, instead, for 2-thiophenesulphonyl chloride some reactivity. Figure 7 shows a plot of k_{obs} vs C_{SCN^-}. One can see that, while there is some increase in rate with increasing C_{SCN^-}, the intercept on the k_{obs} axis at $C_{SCN^-} = 0.00$, which represents the contribution to k_{obs} from the reaction of the sulphonyl chloride with hydroxide ion present in the solution is larger than the increase in rate brough on by the addition of 0.30 M NaSCN. Because the SCN^--catalyzed reaction constituted only a portion of the total reaction rate of 2-thiophenesulphonyl chloride, even at high SCN^- concentration, we don't consider the k value relative to this nucleophile so much. However, our interpretation is not affected by the presence or absence of this value.

Method of calculation. The calculations of multiple linear regression coefficients were done by use of a programme established by us on the CDC 7600 computer of "Centro di Calcolo Interuniversitario dell'Italia NO".[10]

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[m] Mod. Durrum 131.

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