JOURNAL OF PHYSICAL ORGANIC CHEMISTRY, VOL. 5, 557–566 (1992)

SOLVENT EFFECTS IN AROMATIC NUCLEOPHILIC SUBSTITUTION REACTIONS IN NON-POLAR APROTIC SOLVENTS. INHIBITION BY ELECTRON-DONOR–ACCEPTOR (EDA) COMPLEXATION OF THE SUBSTRATE BY AROMATIC SOLVENTS

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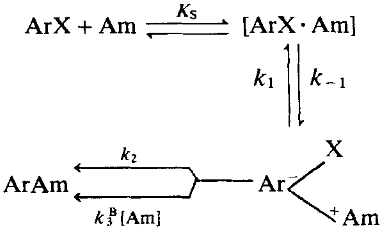
The reactions of *n*-butylamine and piperidine with 1-chloro-2,4-dinitrobenzene and 4-chloro-3-nitrotrifluoromethylbenzene were studied in *n*-hexane, benzene and mesitylene. The reactions seem to follow a bimolecular S_NAr mechanism for both substrates and amines. However, whereas in *n*-hexane they are base catalysed, in the aromatic solvents only mild acceleration is observed. The different behaviour of these reactions in the aromatic solvents in comparison with hexane is explained by the specific solvent effect exerted by the aromatic compounds, which solvates the aromatic reactant preferentially in view of its electron-donor properties. These conclusions were confirmed by kinetic studies in hexane-aromatic solvent binary mixtures. It can be concluded that the presence of electron-donor solvents may inhibit S_NAr reactions when association constant of the solvent with the substrate is greater than the EDA constants between the reactants. These specific solvent effects could also explain why only mild acceleration is observed in aromatic solvents

INTRODUCTION

We have long been interested in the role that electron-donor–acceptor (EDA) complexes between reactants play in aromatic nucleophilic substitution (S_NAr) mechanisms. The formation of such complexes has been considered either as a side-reaction[1] or as a pre-equilibrium to the formation of the σ-intermediate,[2–4] or even as providing an alternative mechanism of base catalysis.[5–7] Most of the studies have been performed with aliphatic and aromatic amines as nucleophiles. More recently, the formation of EDA complexes prior to the σ complex has been proposed for the reaction between hydroxide ion and nitroarenes in DMSO–H_2O solution.[8]

Previous studies on the formation of EDA complexes between aliphatic amines as n-donors and cyano- and nitro-substituted benzenes as π-acceptors[9] had raised the question of the role that these complexes might play in the S_NAr reaction of the nitro group in 1,2-dinitrobenzene (1,2-DNB) by amines. Primarily, based on the fact that 1,2-DNB forms stronger complexes than other aromatic dinitro compounds (1,3- and 1,4-DNB) with aliphatic amines, the formation of such complexes was proposed for the reaction of 1,2-DNB with primary[10] and secondary amines[11] in *n*-hexane as solvent.

Equation (1) shows the inclusion of an EDA complex formation prior to the zwitterionic σ intermediate in a typical bimolecular S_NAr mechanism, where ArX represents the aromatic substrate



(1)

Actually, in the reaction of 1,2-DNB with primary amines,[10] the formation of the EDA complexes between reactants was not kinetically distinguishable. However, the presence of such complexes was detected and quantified at zero time of reaction. In the case of

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0894-3230/92/090557-10$10.00

Received 27 December 1991
Revised 21 April 1992

secondary amines, such as piperidine (PIP), the behaviour of the rate coefficients with PIP concentration could be best explained in terms of the formation of the 1,2-DNB · PIP complex as in equation (1).

Application of the stationary-state hyprothesis to this mechanism gives equation (2), where k_A is the observed second-order rate constant.

$$k_A = \frac{k_1k_2 + k_1K_sk_3^B[\mathrm{Am}]}{(k_{-1} + k_2 + k_3^B[\mathrm{Am}])(1 + K_s[\mathrm{Am}])} \tag{2}$$

For $K_s[\mathrm{Am}] \gg 1$ and $k_2 + k_3[\mathrm{Am}] \ll k_{-1}$, a linear response to the nucleophile concentration such as depicted in equation (3) is obtained. This behaviour is characteristic of most base-catalysed reactions.

$$k_A = \frac{(k_1k_2K_s)}{k_{-1}} + \frac{k_1K_sk_3^B[\mathrm{Am}]}{k_{-1}} \tag{3}$$

On the other hand, whereas all the studied reactions were base catalysed in *n*-hexane, only mild acceleration was observed in benzene.[12] Also, the reactions seem to be inhibited in benzene and other electron-donor solvents.[13]

Kinetic studies of these reactions in hexane–donor solvent mixtures led us to propose that the preferential solvation exerted by these donor solvents through EDA complex formation with the aromatic substrate can explain the difference in reactivity of 1,2-DNB in these solvents with respect to *n*-hexane.

In this work we have extended these studies to the reaction of *n*-butylamine (*n*-BA) and piperidine (PIP) with other aromatic substrates, such as 1-chloro-2,4-dinitrobenzene (CDNB) and 4-chloro-3-nitrotrifluoromethylbenzene (CNTFB), in *n*-hexane, benzene, mesitylene and binary mixtures of hexane with the aromatic solvents.

The reactivity of CDNB toward aliphatic and aromatic amines has been extensively investigated in a variety of solvents.[14–18] However, no reports have been found for these reactions in *n*-hexane. Also, it was considered of interest to compare the previously found effects for the amino denitration reaction when chloride ion is the leaving group. The studies of the reaction with CNTFB allowed us to test these effects with the change in activation on the aromatic ring when a NO_2 group has been replaced with a CF_3 group.

RESULTS AND DISCUSSION

Reactions in *n*-hexane

The kinetics of the reactions of the amines, *n*-BA and PIP, with the aromatic substrates, CDNB and CNTFB, were studied in the presence of various excess of amounts of nucleophile under pseudo-first-order conditions. The reactions proved to be first order in the substrate and on division of the observed pseudo-first-order coefficient, k_ψ, by the appropriate concentration of amine, the second-order rate coefficient, k_A, was calculated.

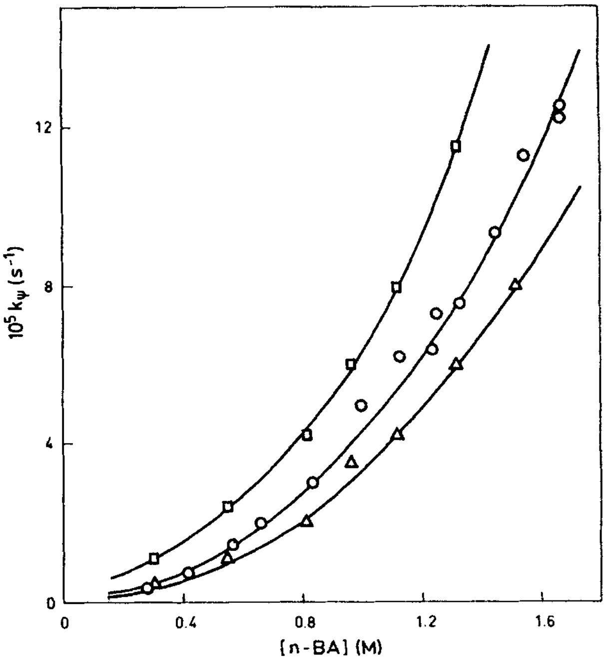


Figure 1. Dependence of k_ψ on amine concentration in the reaction of *n*-BA with CNTFB (*ca* 10^{-4} M) in *n*-hexane at different temperatures: (△) 20·0 ± 0·5; (○) 27·0 ± 0·5; (□) 35·0 ± 0·5 °C

Typical kinetic results are shown in Figure 1 and in Tables 1 and 2. As can be inferred, these reactions follow the kinetic law given in equation (4).

$$k_\psi = k'[\mathrm{Am}] + k''[\mathrm{Am}]^2 \tag{4}$$

where [Am] is the corresponding amine concentration and the ratio k''/k' is equal to k_3^B/k_2.[14] According to Bunnett and Garst,[19] when the values of these ratios are small (< 5) and the accelerating effect of the bases bear no relationship to their base strength, the reactions are not base catalysed. On the other hand, high values (> 50) indicate genuine base catalysis. However, and in agreement with a recent report,[18] we believe and show in this work that when the reactions are performed in solvents of low dielectric constant, relatively low values of the ratio may still indicate base catalysis.

Although the data for these type of reactions are usually analysed by the linearized form of equation (4):

$$k_\psi/[\mathrm{Am}] = k_A = k' + k''[\mathrm{Am}] \tag{5}$$

we have found that equation (5)[10] is much less sensitive than equation (4), particularly for the calculation of the k''/k' ratio and consequently to decide if the process is

Table 1. Rate constants for reactions of CDNB (*ca* 10^{-4} M) with *n*-BA and PIP in *n*-hexane at various temperatures

Amine	Temperature (°C)	Parameter	Values																		
n-BA	18·0 ± 0·5	$10^2[n\text{-BA}]$ (M)	5·0	10·1	15·2	20·2	25·3														
		$10^5 k_\psi$ ($\mathrm{s^{-1}}$)	0·86	3·17	7·21	13·60	24·20														
		$10^4 k_A$ ($\mathrm{s^{-1}\,l\,mol^{-1}}$)	1·72	3·14	4·74	6·74	9·56														
	26·0 ± 0·5	$10^2[n\text{-BA}]$ (M)	1·5	3·0	5·0	7·5	10·1	12·6	15·2	20·2	25·3	30·0	35·1	40·0	50·7						
		$10^5 k_\psi$ ($\mathrm{s^{-1}}$)	0·17	0·58	1·15	2·75	3·85	7·46	9·51	23·68	39·52	59·15	71·38	99·96	139·21						
		$10^4 k_A$ ($\mathrm{s^{-1}\,l\,mol^{-1}}$)	1·15	1·92	2·29	3·66	3·81	5·92	6·25	11·72	15·62	19·71	20·33	24·99	27·46						
	37·0 ± 0·5	$10^2[n\text{-BA}]$ (M)	5·0	10·1	15·2	20·2	25·3														
		$10^5 k_\psi$ ($\mathrm{s^{-1}}$)	2·08	5·88	12·09	23·35	45·05														
		$10^4 k_A$ ($\mathrm{s^{-1}\,l\,mol^{-1}}$)	4·16	5·82	7·95	12·55	17·81														
PIP	17·0 ± 0·5	$10^3[\mathrm{PIP}]$ (M)	10·0	30·0	50·0	71·0	91·0														
		$10^4 k_\psi$ ($\mathrm{s^{-1}}$)	1·41	5·13	9·94	15·50	22·0														
		$10^2 k_A$ ($\mathrm{s^{-1}\,l\,mol^{-1}}$)	1·41	1·71	1·98	2·18	2·4														
	26·0 ± 0·5	$10^3[\mathrm{PIP}]$ (M)	2·8	6·1	6·1	10·0	10·1	20·2	21·8	30·0	48·0	68·0	76·8	88·0	109·0	121·0	129·0	149·0	169·0	189·0	202·0
		$10^4 k_\psi$ ($\mathrm{s^{-1}}$)	0·61	1·39	1·34	2·35	2·50	5·06	5·10	7·35	12·98	20·08	24·02	25·79	37·15	42·91	43·76	56·69	68·32	79·88	99·09
		$10^2 k_A$ ($\mathrm{s^{-1}\,l\,mol^{-1}}$)	2·16	2·29	2·21	2·35	2·47	2·51	2·34	2·45	2·70	2·95	3·13	2·93	3·41	3·55	3·39	3·80	4·04	4·23	4·51

Table 2. Rate constants for reactions of CNTFB (*ca* 10^{-4} M) with PIP in *n*-hexane at various temperatures

Amine	Temperature (°C)	Parameter	Values										
PIP	18·0 ± 0·5	10[PIP] (M)	1·0	2·43	3·53	4·79							
		$10^4 k_\psi$ (s^{-1})	0·17	0·74	1·22	2·54							
		$10^4 k_A$ (s^{-1} l mol^{-1})	1·75	3·04	3·46	5·29							
	26·0 ± 0·5	10[PIP] (M)	1·44	1·97	1·99	2·40	3·53	4·23	4·81	5·51	5·76	5·92	6·36
		$10^4 k_\psi$ (s^{-1})	0·52	0·85	0·92	1·03	2·20	3·16	3·60	5·15	6·02	5·87	7·25
		$10^4 k_A$ (s^{-1} l mol^{-1})	3·60	4·30	4·62	4·29	6·24	7·47	7·48	9·34	10·46	9·90	11·39
	35·0 ± 0·5	10[PIP] (M)	1·0	2·43	3·53	4·79							
		$10^4 k_\psi$ (s^{-1})	0·42	1·51	3·21	5·50							
		$10^4 k_A$ (s^{-1} l mol^{-1})	4·19	6·24	9·10	11·47							

base catalysed or not according to the previously given criteria.

We therefore calculated the rate coefficients by fitting the experimental k_ψ values with [Am] through equation (4) by a least-squares procedure.[10] The results are given in Table 3.

The calculated activation parameters are given in Table 4. They show relatively low $\Delta H^{\neq}$ and large negative $\Delta S^{\neq}$ values. These values are consistent with the complexity of the proposed mechanism, suggesting the existence of a pre-equilibrium association between reactants, such as the EDA complexation between the substrate and the nucleophile.

As is observed, the uncatalysed step is hardly detected for the reactions studied. Hence, except for the case of the reaction between CDNB and PIP, where the value of k' can be significantly measured and the k''/k' ratio is small, these processes seem to be wholly base catalysed.

Since in the reaction of CDNB with PIP the results are uncertain, in order to test if the low value of k''/k' can be interpreted as base catalysis, the kinetics of the reaction were studied with the addition of DABCO as a non-nucleophilic but a stronger base in a non-polar solvent[20] than PIP. The data were fitted by an equation similar to equation (4) where k' is replaced with k_0, which is the value of k' when the base is the nucleophile itself. The results are given in Table 5. As can be seen, the value of k''/k' increases on addition of DABCO.

Moreover, by using pyrrolidine (PYR) as a nucleophile, which is also a stronger base than PIP, the ratio $k''/k' = 63 \cdot 2$ was obtained (Table 5). This evidence shows that although the k''/k' ratio for chlorine departure in CDNB with PIP is small in *n*-hexane, increasing the base strength of either the nucleophile or the catalyst increases the ratio. Therefore, we can consider that these reactions in *n*-hexane are also base catalysed.

It can be argued that the addition of a polar substance such as the nucleophile itself could affect the reaction rate by changing the properties of the medium. Hence, in order to test the sensitivity of these reactions

Table 3. Regression analysis of k_ψ for the reactions between *n*-BA and PIP with CDNB and CNTFB in *n*-hexane by equation (4)

Aromatic *substrate*	*Amine*	Temperature (°C)	k' (s^{-1})	k'' (s^{-1} l mol^{-1})	k''/k' (l mol^{-1})	t_c[a]	t_t[b]	n[c]
CDNB	*n*-BA	18·0 ± 0·5	0	$3 \cdot 60 \times 10^{-3}$	∞	2·16	5·84	5
		26·0 ± 0·5	0	$5 \cdot 74 \times 10^{-3}$	∞	1·16	3·01	13
		37·0 ± 0·5	0	$6 \cdot 65 \times 10^{-3}$	∞	1·89	5·84	5
	PIP	17·0 ± 0·5	$1 \cdot 39 \times 10^{-2}$	$1 \cdot 12 \times 10^{-1}$	8·1	23·00	5·84	5
		26·0 ± 0·5	$2 \cdot 05 \times 10^{-2}$	$1 \cdot 18 \times 10^{-1}$	5·7	25·99	2·90	19
CNTFB	*n*-BA	20·0 ± 0·5	0	$3 \cdot 93 \times 10^{-5}$	∞	0·72	4·03	7
		27·0 ± 0·5	0	$4 \cdot 38 \times 10^{-5}$	∞	1·02	3·06	14
		35·0 ± 0·5	0	$5 \cdot 94 \times 10^{-5}$	∞	0·41	4·60	6
	PIP	18·0 ± 0·5	0	$1 \cdot 04 \times 10^{-3}$	∞	0·24	9·92	4
		26·0 ± 0·5	0	$1 \cdot 67 \times 10^{-3}$	∞	0·54	3·25	11
		35·0 ± 0·5	0	$2 \cdot 07 \times 10^{-3}$	∞	2·64	9·92	4

[a] t_c ($n - 2$, $k' = 0$), Student's *t*-test value of the correlation calculated with $k' = 0$.

[b] t_t (n − 2, 0·005), tabulated *t* values for a 99·5% confidence level. Note that if this value is smaller than the calculated *t* value, the hypothesis $k' = 0$ can be disregarded.

[c] Number of points.

Table 4. Activation parameters for the reactions studied in hexane

Aromatic substrate	Amine	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta S^{\neq}$ (JK^{-1} mol^{-1})[a]	Correlation coefficient
CDNB	*n*-BA	21 ± 2	−218 ± 2	0·984
CNTFB	*n*-BA	18 ± 3	−267 ± 3	0·970
CNTFB	PIP	27 ± 1	−206 ± 1	0·998

[a] At 26 °C.

Table 5. Kinetic results for the reactions of CDNB[a] with PIP in the presence of DABCO and TEA, and for the reaction of CDNB[a] with pyrrolidine (PYR) in *n*-hexane

Amine	Temperature (°C)	Parameter	Values					
DABCO[b]	30·0 ± 0·5	10^3[DABCO] (M)	4·0	7·3	14·7	22·0	28·5	35·3
		$10^4 k_\psi$ (s^{-1})	1·66	1·72	1·93	2·06	2·15	2·28
		k''/k^0 (l mol^{-1})[c]	19·22					
TEA[c]	27·0 ± 0·5	10^2[TEA] (M)	0·0	5·0	10·0	15·0	20·0	
		$10^3 k_\psi$ (s^{-1})	3·23	3·11	3·18	3·12	3·19	
PYR	27·0 ± 0·5	10^3[PYR] (M)	7·2	12·0	19·2	26·3	31·1	
		$10^4 k_\psi$ (s^{-1})	3·81	7·16	14·73	24·18	31·95	
		k''/k' (l mol^{-1})	63·18					

[a] $[\mathrm{CDNB}]_0 = 1 \times 10^{-4}$ M.
[b] $[\mathrm{PIP}]_0 = 5 \times 10^{-3}$ M.
[c] $[\mathrm{PIP}]_0 = 1 \times 10^{-1}$ M.

to a change in the polar properties of the medium and by considering that, in general, non-cyclic tertiary amines cannot be good catalysts owing to their high steric requirement[11] and that the polarity of triethylamine (TEA) is similar to those of the studied amines, TEA was used as an additive. Kinetic studies at a constant nucleophile concentration with increasing amounts of TEA showed that this compound induces not even a small acceleration of these reactions (Table 5). We conclude that the acceleration effects are not medium effects. It follows that the studied reactions can be considered to be genuine base catalysed in *n*-hexane.

These are surprising results, since chloride ion is such a good leaving group, and genuine base catalysis has previously been detected in only a very few cases.[14,21] Also, it is generally accepted that base catalysis should not be expected when chloride is the leaving group. Nevertheless, the base catalysis observed in these cases can be justified considering the highly non-polar character of the solvent, *n*-hexane $(\pi^* = -0\cdot08)$[22] and its consequently non-existent ionizing power.

Also, in view of the non-polar character of this solvent we can propose a mechanism of catalysis in which the second molecule of amine acts as a bifunctional catalyst within aggregates of conveniently charged dipolar species.[10,23]

On the other hand, EDA complex formation between the aromatic substrates and the amines, although it seems to occur as inferred by the lack of additivity of the absorbances of the reaction mixtures at zero times of reaction, its role in the mechanism is not kinetically distinguishable.

Reactions in aromatic solvents and *n*-hexane–aromatic solvent mixtures

Reactions with primary amines

The kinetics of the reactions of *n*-BA with CDNB and CNTFB were also studied in benzene. The results are shown in Table 6.

As can be seen, the reactions in this solvent have very low values of k''/k' and they may not be regarded as base catalysed, as considered in previous kinetic studies on CDNB-amines.[24] On the other hand, these reactions with primary amines in benzene seem to be much slower than in *n*-hexane $[k_\psi\ (\text{benzene})/k_\psi\ (\text{hexane}) < 0\cdot67]$.

Thus, as in the reactions of 1,2-DNB with primary amines, we find a remarkable difference in reactivity when using benzene instead of hexane as solvent, even though the former is considered to be a typical non-polar solvent. We also investigated the effect of mesitylene as solvent, since it is a stronger donor[25] and also

Table 6. Kinetic results for the reactions of *n*-BA with CDNB and CNTFB in benzene at 26 °C

Substrate	Parameter	Values							
CDNB[a]	[*n*-BA] (M)	0·05	0·10	0·15	0·25	0·30			
	10^5k_ψ (s^{-1})	2·25	5·27	8·52	17·40	22·65			
	k''/k' ($l\,mol^{-1}$)	3·28							
CNTFB[b]	[*n*-BA] (M)	0·15	0·25	0·37	0·51	0·63	0·76	1·00	1·27
	10^6k_ψ(s^{-1})	1·02	1·73	3·05	5·93	7·45	11·10	17·76	28·49
	k''/k' ($l\,mol^{-1}$)	4·88							

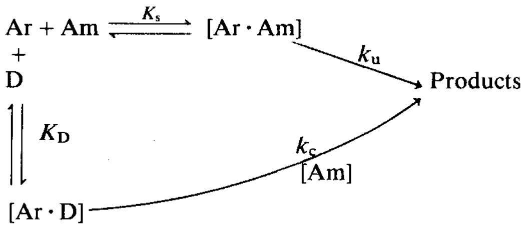
[a] $[CDNB]_0 = 6 \times 10^{-4}$ M.
[b] $[CNTFB]_0 = 5 \times 10^{-4}$ M.

slightly less polar ($\pi^* = 0·41$) than benzene ($\pi^* = 0·59$). The results are shown in Table 7. For both substrates the reactions show similar behaviour to that in benzene and completely different to that with hexane. The difference in reactivity may be explained[12,13] by considering an EDA interaction between the aromatic substrate and the aromatic solvent. The nitro-substituted aromatic substrates are typical π-electron acceptors[1,25] and benzene and mesitylene are good π-electron donors.[25] Moreover, since this solvent has a low dielectric constant, EDA interactions are favoured.

To evaluate these effects, the reaction can be studied in *n*-hexane–donor aromatic solvent mixtures. Then, as shown in Scheme 1, one can expect that the S_NAr reactions may occur either with the 'free' aromatic substrate (k_u, pseudo-first-order coefficient in *n*-hexane) or through the EDA complex (k_c) with the donor solvent, D.[13]

Accordingly, k_ψ can be expressed by

$$k_\psi = \frac{k_u + k_c K_D[D]}{1 + K_s[Am] + K_D[D]} \tag{6}$$



Scheme 1

In the limiting case where $K_s \ll K_D$, equation (6) reduces to

$$k_\psi = \frac{k_u + k_c K_D[D]}{1 + K_D[D]} \tag{7}$$

If $k_c < k_u$, the reaction is partially inhibited[26] by complexation of the substrate by the donor solvent in the solvent mixture and the plot of k_ψ vs [D] will be non-linear (downward curvature).

The types of plots obtained are shown in Figures 2

Table 7. Kinetic results for the reactions of *n*-BA and PIP with CDNB and CNTFB in mesitylene at 26 °C

Substrate	Parameter	Values			
CDNB[a]	[*n*-BA] (M)	0·10	0·16	0·25	0·30
	10^5k_ψ (s^{-1})	3·76	6·79	12·14	15·59
	k''/k' ($l\,mol^{-1}$)	2·19			
	[PIP] (M)	0·01	0·05	0·10	0·15
	10^3k_ψ (s^{-1})	0·21	1·24	2·86	4·84
	k''/k' ($l\,mol^{-1}$)	3·53			
CNTFB[b]	[*n*-BA] (M)	0·25	0·51	0·81	1·21
	10^6k_ψ (s^{-1})	1·53	4·67	10·82	22·19
	k''/k' ($l\,mol^{-1}$)	4·38			
	[PIP] (M)	0·10	0·15	0·20	0·25
	10^5k_ψ (s^{-1})	3·31	7·36	9·35	13·26
	k''/k' ($l\,mol^{-1}$)	3·01			

[a] $[CDNB]_0 = 2 \times 10^{-4}$ M.
[b] $[CNTFB]_0 = 5 \times 10^{-4}$ M.

and 3. They present the expected dependence in equation (7) for the reactions of CDNB and CNTFB with *n*-BA. As can be seen, mesitylene exerts a greater inhibition than benzene, as would be expected as it is a stronger donor.

Also, by fitting equation (7) with the experimental data the values of K_D were obtained for the following systems: CDNB–benzene = 0·76 ± 0·02, CNTFB–benzene = 0·26 ± 0·02, CDNB–mesitylene = 0·96 ± 0·02 and CNTFB–mesitylene = 0·48 ± 0·02 l mol^{-1}. These are reasonable values considering that K_D increases with increasing donor strength of the aromatic solvents.[25] Moreover, the fact that the values of K_D for the CDNB complexes are higher than those of the CNTFB complexes is well justified, since NO_2 is a more electron-withdrawing group ($\sigma_p = 0{\cdot}81$) than CF_3 ($\sigma_p = 0{\cdot}53$), and consequently CDNB is a better acceptor.[27]

When the rate coefficients are compared for both substrates, the same effect is observed, thus k_ψ follows

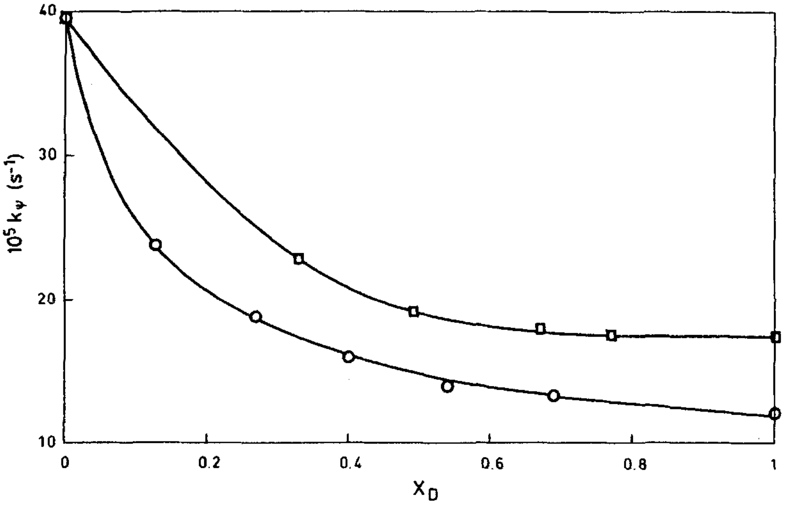


Figure 2. Plots of k_ψ against the molar fraction (X_D) of the donor solvent for the reaction of CNDB with *n*-BA in hexane–aromatic solvent mixtures. (□) Benzene; (○) mesytilene. Temperature, 27·0 ± 0·5 °C; [CDNB] = 2×10^{-4} M; [*n*-BA] = 0·25 M

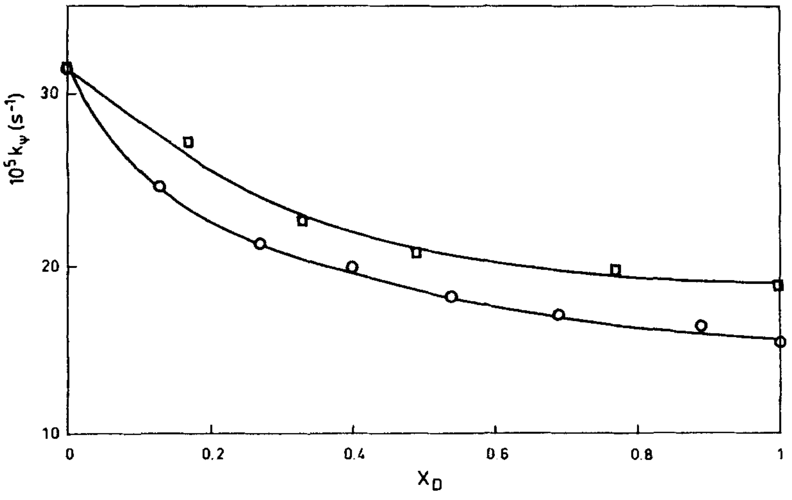


Figure 3. Plots of k_ψ against the molar fraction (X_D) of the donor solvent for the reaction of CNTFB with *n*-BA in hexane–aromatic solvent mixtures. (□) Benzene; (○) mesitylene. Temperature, 27·0 ± 0·5 °C; [CNTFB] = 3×10^{-4} M; [*n*-BA] = 0·25 M

the order CDNB > CNTFB, reflecting the decreasing electron-withdrawing power of the substituent.[28]

Reactions with secondary amines

On the other hand, for the reaction of the substrates with PIP, the effect of the donor solvent seems not to inhibit the reaction compared with *n*-hexane. (Figures 4 and 5). Actually, in benzene there is an accelerating effect [i.e. k_ψ(benzene)/k_ψ(hexane) > 0·24].

This can be easily explained by the increasing polarity of the media when the molar fraction of the aromatic solvent is increased. We have previously observed a similar behaviour for the reaction of 1,2-DNB–PIP. In such a case we were able to measure K_s for the EDA complex 1,2-DNB–PIP, which turns out to be $K_S \approx K_D$.[13] The same can be assumed in the systems CDNB–PIP and CNTFB–PIP, although K_S cannot be calculated by independent methods. Moreover, it is observed (Figures 4 and 5) that mesitylene, even though

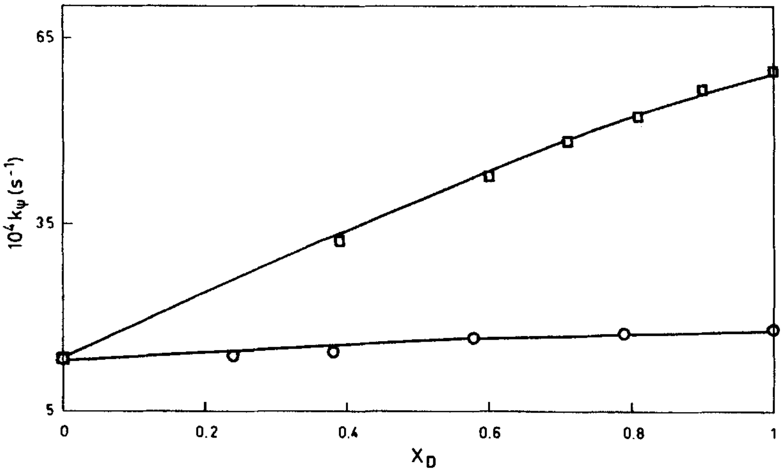


Figure 4. Plots of k_ψ against the molar fraction (X_D) of the donor solvent for the reaction of CDNB with PIP in hexane–aromatic solvent mixtures. (□) Benzene; (○) Mesitylene. Temperature, 27·0 ± 0·5 °C; [CDNB] = 2×10^{-4} M; [PIP] = 0·05 M. Solid lines, mathematical fit by equation (6)

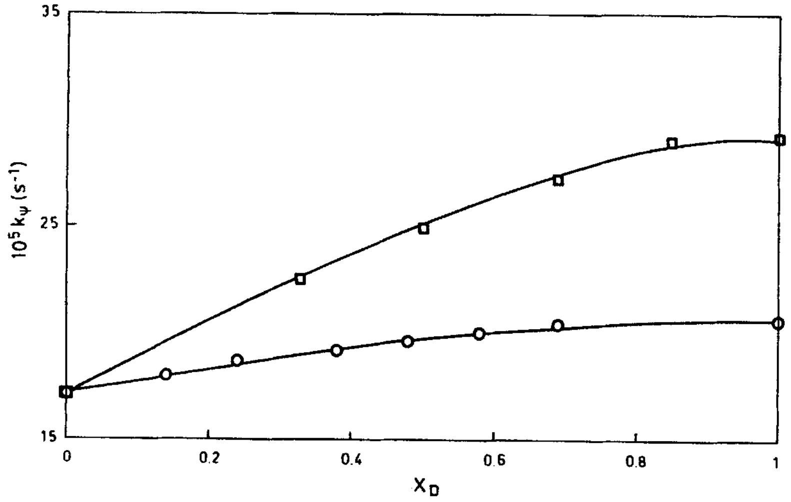


Figure 5. Plots of k_ψ against the molar fraction (X_D) of the donor solvent for the reaction of CNTFB with PIP in hexane–aromatic solvent mixtures. (□) Benzene; (○) mesitylene. Temperature, 27·0 ± 0·5 °C; [CNTFB] = 2×10^{-4} M; [PIP] = 0·40 M

having a similar polarity to benzene, does not exert any acceleration, as could be expected owing to its higher donor strength.

If in comparison with other systems[11] a value of $K_S = 0{\cdot}55\ \mathrm{l\,mol^{-1}}$ is assumed for the CDNB–PIP complex in hexane, and using the values of K_D calculated from the reactions with *n*-BA, a very good mathematical fit of the experimental data by equation (6) is obtained for the systems in Figure 4.

Hence, the proposal of the complexation of the substrates by the donor solvents seems to be plausible and explains all the solvent effects observed.

CONCLUSIONS

As was observed for 1,2-DNB as substrate, the reactions of *n*-BA and PIP with CDNB and CNTFB show a marked difference in reactivity when they are studied in hexane compared with aromatic solvents.

The reactions in hexane are wholly base catalysed, even when chlorine is the leaving group, owing to the highly non-polar character ($\pi^* = -0{\cdot}08$) of this solvent. However, in aromatic solvents only mild acceleration is observed even though these solvents are considered to be typical non-polar solvents for S_NAr reactions. Also, despite the fact that they can be considered more polarizable solvents than hexane, the reactions are usually slower than expected in aromatic solvents.

The preferential solvation that a donor solvent may exert through EDA complex formation with the substrate provides evidence to explain these effects, which seem to be common for S_NAr reactions of a variety of substrates at least when aliphatic amines are the nucleophiles. The inhibitory effects are observed whenever the substrate–solvent complex constant is greater than the substrate–nucleophile stability constant.

EXPERIMENTAL

1-Chloro-2,4-dinitrobenzene (CDNB) from Aldrich was recrystallized from anhydrous ethanol and then sublimed under vacuum (m.p. = 53 °C). 4-Chloro-3-nitrotrifluoromethylbenzene (CNTFB) from Aldrich was fractionally distilled in a dry nitrogen atmosphere. Its purity was determined by GLC [0V-225 S on Chromosorb W HP (80–100 mesh) column] and HPLC (Micropak M CH-10 column) and eluted with methanol-water (pH 7) (80 : 20, v/v).

n-Butylamine (*n*-BA) and piperidine (PIP) from BDH were purified as described previously.[9,11] *n*-Hexane and benzene (HPLC quality) from Sintorgan and mesitylene from Aldrich were used as received.

The reaction of the amines *n*-BA and PIP with the aromatic substrates in all the solvents showed quantitative chlorine atom substitution, giving the corresponding alkylanilines as shown by HPLC, TLC and UV–visible spectrometric analysis of the reaction mixtures.

The reactions were followed by the increase in the absorbance of the visible absorption maximum of the products. Thermostatically controlled cells on a Varian Cary 17 and Hewlett-Packard HP 8452 spectrophotometer were used.

The concentration of the nucleophile in all instances was at least 100 those of the substrates and the reactions were followed to a least three half-lifes. The GLC and HPLC measurements were performed on Varian Aerograph 2800 and Varian 5000/20 chromatographs, respectively.

ACKNOWLEDGEMENTS

Financial support from the Consejo Nacional de Investigaciones Cientificas y Técnicas (CONICET) and the Consejo de Investigaciones Científicas y Tecnológicas de la Provincia de Córdoba (CONICOR) is gratefully acknowledged. E.D. thanks the Secretaría de Ciencia y Técnica de la Universidad Nacional de Río Cuarto for a research fellowship.

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