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Reaction of 2,4-dinitrochlorobenzene with aniline. Solvent effects and molecular complex formation

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The kinetics of the reaction of aniline with 2,4-dinitrochlorobenzene (2,4-DNClB) were studied in several benzene–*n*-hexane mixtures at 40 °C in the presence of variable amounts of aniline. A linear dependence of the second-order rate coefficients, k_A, with [B] is observed, with a null intercept. Taking into account the non-polar character of the solvent, and the excellent nucleofugacity of chlorine, this kinetic behaviour is interpreted as evidence of the aggregation of aniline, the hydrogen-bonded dimer acting as the nucleophile. Consistent with this interpretation, when the solvent is changed to THF, a good hydrogen-bond acceptor (HBA), the k_A is no longer dependent on [B]. Electron donor–acceptor (EDA) molecular complexes of 2,4-DNClB with benzene and with aniline, and also between aniline and the product, were clearly recognized and the stability constants of each one of these complexes were determined.

Introduction

The ever-increasing knowledge of the structures of aggregates in organic solvents of low permittivity is stimulating research into the role that the different possible aggregates play in defining the reaction mechanisms in solution.[1,2] Nucleophilic aromatic substitutions by amines in non-polar aprotic solvents are especially sensitive to the degree of aggregation of both the substrate and the nucleophile, and the role of these complexes is increasingly being recognized.[3]

The mechanism by which $\mathrm{S_NAr}$ by amines in protic solvents occurs is well established, but the mechanism in aprotic solvents is still controversial.[4] Due to the dipolar character of the reactants and the zwitterionic structure of the reaction intermediate, in a solvent of low permittivity several types of "molecular complexes" could, in principle, be formed and, in fact, most of them have been observed, each one under special reaction conditions (throughout this work, as in previous papers, the generic term "molecular complex" (MC) would involve any type of non-covalent interactions, *e.g.* charge-transfer, hydrogen-bonding, electron donor–acceptor (EDA) complexes, *etc.*). One of the most fundamental pieces of evidence for the role of MCs in the mechanism of $\mathrm{S_NAr}$ by amines is the observation of a third order in amine, which was reported for the first time in 1981.[5] This feature was interpreted as being due to the *dimer* of the amine (a hydrogen-bonded molecular complex) acting as the true nucleophile and additional observations such as negative entropies of activation, inverse solvent effects, effects of hydrogen-bond acceptor (HBA) additives, *etc.* supported this interpretation.[6,7]

Further research on $\mathrm{S_NAr}$ by amines in non-polar aprotic solvents reported the observation of EDA complexes between the nitro-activated substrates and benzene (which was used as the solvent);[8,9] of "mono-heteroconjugates" between the nucleophile and a HBA additive;[10,11] of a MC between the nitro-activated substrate and the nucleophile;[12–14] of a MC between the nucleophile and any other tertiary non-nucleophilic amine;[7,15–17] and, recently, a charge-transfer complex between 1,3,5-trinitrobenzene and indole-3-carboxylate has been isolated.[18]

Table 1 Reaction of 2,4-dinitrochlorobenzene (2,4-DNClB)[a] with aniline in hexane–benzene (4:1) at 40 °C. Pseudo-first-order, k_ψ, and second-order, k_A, rate coefficients[a]

[Aniline]/M	$k_\psi/10^{-6}\ \mathrm{s^{-1}}$	$k_A/10^{-6}\ \mathrm{M^{-1}\ s^{-1}}$
0.5	0.92	1.84
1.0	4.6	4.6
1.5	9.5	6.3
2.0	17	8.5

[a] [2,4-DNClB] = 2 × 10^{-4} M.

The present paper describes a kinetic and spectroscopic study of the reactions between 2,4-dinitrochlorobenzene (2,4-DNClB) and aniline in aromatic pure solvents and in binary mixtures of any of these solvents with *n*-hexane. Formation of various types of electron donor–acceptor complexes and also of hydrogen bonded aggregates was clearly recognized and the stability constants of several of those MCs were determined. The observed results afford new evidence concerning the critical role that complexation plays in the kinetic behaviour of these reactions.

Results and discussion

Reactions in aromatic solvent and *n*-hexane–aromatic solvent mixtures. Molecular complex formation

The kinetics of the reaction of aniline with 2,4-dinitrochlorobenzene were studied in benzene and in a binary solvent *n*-hexane–benzene (Hx–Bz) at 40 °C in the presence of variable amounts of the nucleophile under pseudo-first order conditions. The pseudo-first, k_ψ and the second order rate coefficients, k_A, of the reaction of 2,4-dinitrochlorobenzene with aniline in Hx:Bz (4:1) are shown in Table 1. The plot of k_A *vs.* [B] exhibits a linear response to the nucleophile concentration, B.

A linear dependence on [B] is characteristic of most base-catalyzed reactions, it has been widely observed in $\mathrm{S_NAr}$ with

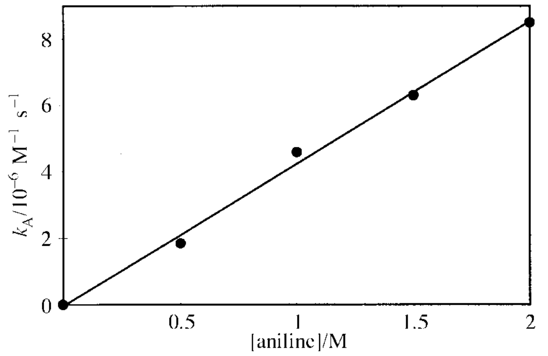


Fig. 1 Overall second-order rate coefficients, k_A, for the reaction of 2,4-dinitrochlorobenzene with aniline in hexane–benzene (4:1) at 40 °C.

Table 2 Reaction of 2,4-dinitrochlorobenzene, 2,4-DNClB,[a] with aniline in binary solvents hexane–benzene at 40 °C. Second-order rate coefficients $k_A/10^{-6}$ s^{-1} M^{-1}, at different aniline concentrations

	[Aniline]		
% Hexane	0.5 M	1.0 M	2.0 M
0	0.36	0.71	1.25
20	0.66	0.85	1.75
40	0.88	1.50	2.50
50	0.86	1.80	3.25
60	1.08	2.40	4.35
80	1.84	4.60	8.50

[a] [2,4-DNClB] = 2 × 10^{-4} M.

amines when the second step is rate determining, the second order reaction rate coefficients obey eqn. (1).[3,4,19]

$$k_A = \frac{k_1 k_2}{k_{-1}} + \frac{k_1 k_3 [\mathrm{B}]}{k_{-1}} \qquad (1)$$

The intercept represents the uncatalysed reaction and the slope measures the base catalysis. In some cases, with very poor nucleofugues in aprotic solvents, only the base catalysed mechanism is observed.[3] Nevertheless, when chlorine is the nucleofugue, usually formation of the zwitterionic intermediate, k_1, is the rds and no base catalysis is observed, but instead a spontaneous decomposition of the intermediate to products is seen.[4]

In the present case, taking into account the non-polar character of *n*-hexane ($\pi^* = -0.088$),[20] aggregation of the nucleophile is expected and a mechanism in which the nucleophile is the dimer of the amine is proposed. In the plot of the second order rate coefficient, k_A, as a function of [aniline], (Fig. 1) a null intercept is found. A kinetic law consistent with the observed results is eqn. (2), where $K = [\mathrm{B:B}]/[\mathrm{B_o}]^2$ represents the amine auto-association. The null intercept observed with this good nucleofugue, together with the linear dependence of k_A on [B], clearly indicates that eqn. (2) applies to the present case.

$$k_A = \frac{k_1 k_2 K [\mathrm{B}]}{k_{-1}} \qquad (2)$$

The reaction was then carried out in other Hx–Bz mixtures at three aniline concentrations, and the results are shown in Table 2. The reactions are less sensitive to [B] in the presence of aromatic solvent, and the null intercept is again observed. Only when the hexane content is high (80%) are the rates comparable to pure hexane. The plot of k_A *vs.* % hexane (not shown) exhibits an upward curvature which strongly increases with [B]. The different behavior of the reactions in the presence of an aromatic solvent in comparison with pure hexane can be explained by the specific solvent effect, which solvates preferentially the aromatic reactant, by virtue of its electron donor properties, through EDA complex formation. The formation of EDA complexes has been earlier considered either as a side-reaction[21] or as a pre-equilibrium to the formation of the σ-intermediate.[8,22] The nitro-substituted aromatic substrate is a typical π-electron acceptor and benzene can be a good π-electron donor. The stability constant between benzene and 2,4-dinitrochlorobenzene, K_D, has been reported to be 0.076 ± 0.02.[23]

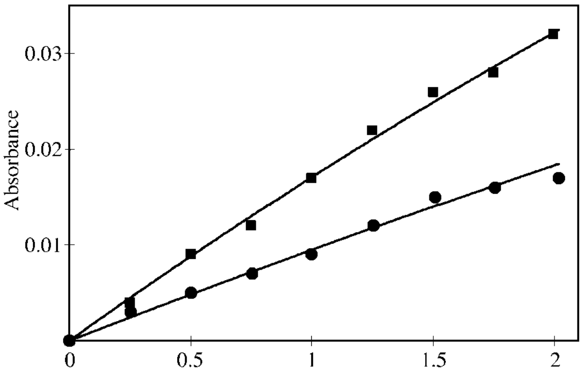
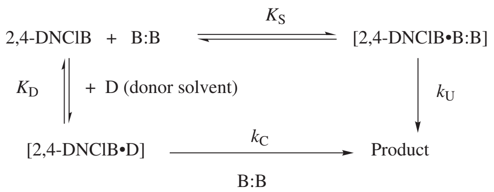


Fig. 2 "*Excess*" optical densities of the reaction mixtures of 2,4-dinitrochlorobenzene with aniline at 450 nm, extrapolated at $t = 0$ as a function of aniline concentration. ■ hexane–benzene (4:1), ● benzene.

The lack of additivity in the absorbances of the reaction mixtures extrapolated at zero time, observed in the present work, suggests formation of EDA complexes also between the aromatic substrate and the amine. Fig. 2 shows the values of absorbances *vs.* [aniline] at $t = 0$. To examine the possible formation of an EDA complex prior to substitution, the stability constants, K_S, between 2,4-DNClB and aniline were calculated by a method previously described[9,24] and the values are 0.066 ± 0.010 in *n*-hexane–benzene (4:1) and 0.035 ± 0.01 in pure benzene. In view of the observed result, it is proposed that, for reactions in a solvent mixture in which a complexing agent is present (*i.e.* benzene), the substrate may undergo two parallel reactions: a) proceeding from the free aromatic substrate, or b) through an EDA complex with the donor solvent, D; a competition between the nucleophile (monomer and dimer) and the donor solvent as complexing agents may be established in the solvent mixtures. This situation is depicted in Scheme 1 where



Scheme 1

k_U and k_C represent the pseudo-first order rate coefficients for the free substrate (uncomplexed) and the complexed substrate, respectively, and D represents the complexing solvent. A similar scheme, but with a monomer nucleophile, has been reported by Silber and co-workers for the reaction of dinitrobenzene with *n*-butylamine.[25] Complexation with the monomer nucleophile is also possible under the present reaction conditions but, since reaction with the dimer is faster, it is omitted in Scheme 1 for the sake of simplicity.

An inhibitory effect of the donor solvent is observed whenever the substrate–solvent complex constant is greater than the substrate–nucleophile stability constant. Under the experimental conditions the absorbances at "infinite" reaction time are higher than expected from standard solutions of *N*-(2,4-dinitrophenyl)aniline and aniline, assuming a quantitative

Table 3 "*Excess*" in the absorbances of the mixture of *N*-(dinitrophenyl)aniline, DNPA,[a] with aniline in benzene and in binary solvents hexane–benzene (Hx–Bz). Stability constants of the complexes, K_s, and extinction coefficients, ε (in brackets)

	Absorbance		
[Aniline]	Hx–Bz (4 : 1)	Hx–Bz (1 : 1)	Bz
0.00	0.000	0.000	0.000
0.248	0.051	0.015	0.011
0.500	0.085	0.033	0.039
0.748	0.113	0.057	0.041
1.000	0.143	0.078	0.060
1.248	0.173	0.099	0.080
1.500	0.192	0.116	0.085
1.748	0.224	0.136	0.099
2.000	0.242	0.150	0.110
K_s	0.257 ± 0.02 (3553)	0.130 ± 0.03 (3500)	0.109 ± 0.01 (3090)

[a] [DNPA] = 2 × 10^{-4} M, wavelength = 450 nm.

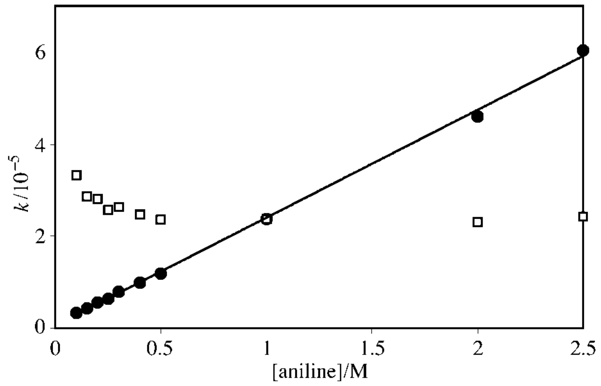


Fig. 3 Pseudo-first-order, k_ψ, and overall second-order, k_A, rate coefficients for the reaction of 2,4-dinitrochlorobenzene with aniline in tetrahydrofurane at 40 °C. ● k_ψ (s^{-1}), □ k_A (s^{-1} M^{-1}).

conversion of 2,4-dinitrochlorobenzene to product (see data in Table 3). An almost linear dependence (not shown) was observed between the "excess" in absorbances of the product and the [aniline] indicating formation of MC. The stability constants, K_S, between *N*-(2,4-dinitrophenyl)aniline and aniline were determined in Hx–Bz (4 : 1), (1 : 1) and pure benzene. The data gathered in Table 3 show that the K_s values are higher than those with DNClB and increase with the hexane proportion in the solvent, conditions that favour EDA complex formation. The EDA complexes between the reaction products and aniline do not affect the reaction mechanism, although they must be included in the rate coefficient calculation (eqn. (3)).

$$k_A = \frac{k_1 k_2 K K_s [B]}{k_{-1}} \tag{3}$$

Reactions in electron-donor solvents

Likewise, the reactions of 2,4-dinitrochlorobenzene with aniline were carried out in tetrahydrofuran (THF) and in binary solvent mixtures toluene–THF at 40 °C. The reactions in THF show a peculiar kinetic behavior in which dependence of the second-order rate coefficients, k_A, on the amine concentration is not observed. The results are shown in Fig. 3. It can be observed that k_A slightly diminishes on increasing [aniline] in the range 0.1–0.5 M and then remains almost constant. The pseudo-first order rate coefficients are linearly related to [aniline] in the whole range studied. These results can be interpreted as competition between THF and aniline to be the proton acceptor at low [aniline] up to a value with higher THF contents after which the rate is insensitive to [B].

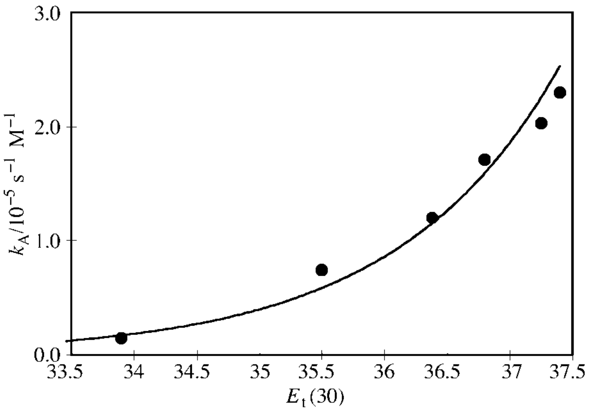


Fig. 4 Solvent effects on the second-order rate coefficients, k_A, for the reaction of 2,4-dinitrochlorobenzene with 2 M aniline in THF–toluene as a function of $E_T(30)$ values (see ref. 26).

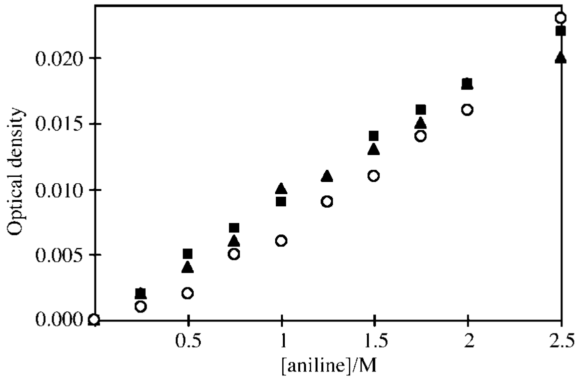


Fig. 5 "*Excess*" optical densities of the reaction mixtures of 2,4-dinitrochlorobenzene with aniline at 450 nm, extrapolated at $t = 0$, as a function of [aniline] in: ○ THF, ■ THF–toluene (1 : 1) and ▲ toluene at 40 °C.

In THF–toluene mixtures an increase in the rate was observed as a function of the THF content in the mixture. The plot of k_A *vs.* $E_T(30)$[26] (Fig. 4) is not linear, the upward curvature is consistent with an effect of THF greater than that expected from its polarity effect. Cooperation in the decomposition of the zwitterionic intermediate due to their known HBA properties is superimposed to the polarity effect. Consistent with this interpretation is the linear dependence of the second order rate coefficient with [THF]; this dependence indicates the significance of a [THF] term in the kinetic law related to the contribution of this HBA solvent in the second step of the reaction.

The absorbances of the reaction mixtures (measured at $\lambda = 450$ nm, where the reactants are transparent) extrapolated at $t = 0$ show a linear increase with the [aniline] in the three solvents studied (THF, THF–toluene (1 : 1) and toluene) (see Fig. 5). The null intercept and the excellent linear correspondence in the three solvent studied are also consistent with the formation of EDA complexes prior to the aromatic nucleophilic substitution.

Experimental

Reagents and solvents

Aniline (Fluka) was kept overnight over potassium hydroxide, distilled over zinc powder and then over sodium; both distillations were carried out under nitrogen at reduced pressure. 2,4-Dinitrochlorobenzene (Sigma) was crystallized twice from absolute ethanol (mp 52–53 °C, lit. 52–53 °C).[16] Toluene, benzene and hexane were kept over sodium wire for several days, and distilled twice over sodium. Tetrahydrofuran was treated successively with sodium sulfite, sodium hydroxide and sodium wire and then distilled, the fraction of bp 64 °C was collected. *N*-(2,4-Dinitrophenyl)aniline (mp 155–156 °C, lit. 155–156 °C)[27] was prepared from 2,4-dinitrochorobenzene and aniline following the procedure reported for *N*-(2,4-dinitrophenyl)-2-methoxyaniline[16] Solvents were stored in special vessels which allow delivery without air contamination.

Ancillary spectrophotometric measurements

UV-VIS spectra of the substrate, the product, and of different mixtures of both compounds with aniline at several concentrations were recorded in a Shimadzu spectrophotometer. UV spectra of control solutions of the substitution product in toluene containing different amounts of the amine were recorded, and the extinction coefficients determined at $\lambda = 450$ nm where the reagents are transparent under these conditions. All the solutions were found to obey Beer's law.

Determination of EDA complex formation constants, K_S. A UV spectrophotometric method previously described was used.[24,25] The solutions, prepared in the concentration range 0.5–2.0 M, were completely stable. The absorbances of the mixtures were measured at 450 nm. The increases in the absorbances of the mixtures at 450 nm with respect to the sum of the isolated components alone ("*excess*" in the absorbances) are interpreted as being due to the formation of MC; K_S were calculated in every case by an iterative procedure developed by Silber and co-workers.[24,25]

Kinetic procedures

Kinetic runs were performed by the methods previously reported[28] following the appearance of the reaction product at $\lambda = 450$ nm. In all cases pseudo-first order kinetics were observed. The pseudo-first order rate coefficients, k_ψ, were obtained by the least-squares method as the slope of the correlation ln $(A_\infty - A_t)/A_\infty$ against time, where A_∞ is the optical density of the reaction mixture measured at "infinity" (more than ten half-lives); the second order rate coefficients, k_A, were obtained by dividing k_ψ by the amine concentrations. Rate coefficients were reproducible to ±2%. No corrections for expansion coefficients were applied to the concentration values.

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