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Solvent effects on aromatic nucleophilic substitution reactions. Part 9. Special kinetic synergistic behavior in binary solvent mixtures

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ABSTRACT: The kinetics of the reactions of 1-fluoro-2,4-dinitrobenzene with morpholine and piperidine were studied at 25 °C in several binary solvent mixtures of the polar aprotic hydrogen bond acceptor solvent + chloroform or dichloromethane type, which, in some cases, exhibit synergism for the $E_T(30)$ solvent polarity parameter. In each case, the kinetic response model was analyzed as a function both of the amine concentration and of the solvent mixture composition. The kinetic data show that for some reaction systems under certain experimental conditions, the reactions are faster in binary solvent mixtures than in the corresponding pure solvents, manifesting a special kinetic synergetic behavior. This kinetic effect was attributed to a complex combination of factors related to the variations of the influence of base catalysis with the solvent composition, and to the consequence of specific solvent effects. The kinetic results were related to the $E_T(30)$ solvent polarity parameter, analyzing the general validity of the chemical probe for interpreting the solvent effects in the aromatic nucleophilic substitution reactions explored. The applicability of the preferential solvation model allowed the special behavior observed to be attributed to the influence of preferential solvation phenomena. Copyright © 1999 John Wiley & Sons, Ltd.

KEYWORDS: kinetic synergistic behavior; binary solvents; aromatic nucleophilic substitution reactions; solvent effects

INTRODUCTION

Organic liquids are characterized by several properties that make them suitable for dissolving and for providing reaction media for various types of solutes.[1,2] Solvent effects are closely related to the nature and extent of solute–solvent interactions locally developed in the inmediate vicinity of the solutes.

Solute–solvent interactions are much more complex in mixed solvents than in pure solvents owing to the possibility of preferential solvation by any of the solvents present in the mixture. Moreover, the solvent–solvent interactions produced in solvent mixtures can affect the solute–solvent interactions and, therefore, they can also affect preferential solvation.[3]

We have recently determined[4] the empirical solvent polarity parameter, $E_T(30)$, which is assumed to reflect a combination of dipolarity and hydrogen bond donor (HBD) capability, for binary mixtures of solvents selected with different structural characteristics and an extensive range of polarity in which preferential solvation is the rule. Among these, binary mixtures of a dipolar hydrogen bond acceptor solvent with chloroform or dichloromethane often show synergetic effects for the $E_T(30)$ value. We have also pointed out that this synergism is more significant for those binary solvent systems in which chloroform is the cosolvent. These results were related to the solvent effects on simple models of aromatic nucleophilic substitution (S_NAr) reactions.

The S_NAr reactions between halonitrobenzenes and primary or secondary amines have been investigated in both polar and apolar solvents. The rate of these reactions is notably affected by the solvent properties and the solvent effects have often been studied in recent decades. These studies show how extensive and complex are the interactions of the substrate and/or the intermediate(s) with the solvent molecules. However, few systematic studies on pure solvents, and even less on mixed solvents, have been carried out.[5,6]

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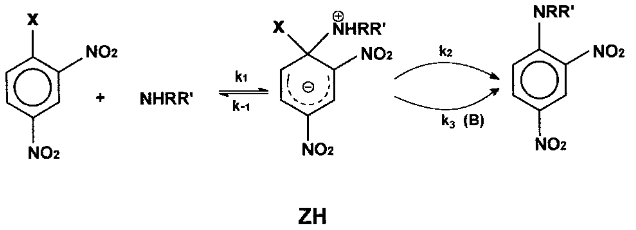

Scheme 1

In a first attempt to systematize the study of the solvent effects,[7] we reported that the second-order-rate coefficients, k_A, for the reactions of 1-chloro-2,4-dinitrobenzene (CDNB) with piperidine (PIP) in several aprotic solvents are well correlated with the Dimroth–Reichardt solvent polarity scale $E_T(30)$ according to the relationship log k_A vs $E_T(30)$. The correlation is remarkably good if the HBD solvents are excluded (taking into account that the reactivity in hydroxylic solvents is inversely proportional to the hydrogen-bond donating ability of the solvents).[8a] Also, the kinetics of the reaction between 1-fluoro-2,4-dinitrobenzene (FDNB) and PIP were determined in several polar and apolar aprotic solvents.[8b] Except for HBD solvents, the second-order rate coefficients in the rest of the solvents explored were sensitive to an increase in amine concentration, indicating base catalysis. These results were interpreted as an indication that in this reaction the detachment of the nucleofuge is the rate-limiting step in most aprotic solvents; in those solvents with HBD ability, the intermediate formation is the rate-determining step. A simple linear energy solvation correlation was found between the $E_T(30)$ parameter and the second-order rate coefficient obtained at [nucleophile] $\leq 10^{-1}$ M. For higher amine contents increasing deviations were found.

In addition, we have studied the CDNB + PIP reaction in two different systems of completely non-aqueous binary mixtures in which preferential solvation is the rule, but without synergetic effects for the $E_T(30)$ parameter.[4a] Moreover, we have studied the reaction between 1-halo-2,4-dinitrobenzenes and primary and secondary aliphatic amines in which the formation of the intermediate is the rate-determining step CDNB + *n*-butylamine or PIP and FDNB + *n*-butylamine in synergetic mixtures for $E_T(30)$, showing that the synergism is not reproduced in the kinetic data.[4b]

In this connection, it was of interest to evaluate the solvent effects of some of the reported synergetic mixtures for $E_T(30)$ on other simple models of S_NAr reactions in which base catalysis is possible. Taking into account that, in general, base catalysis is more often observed with secondary than with primary amines and with poor leaving groups, we studied here the kinetics of the reactions between FDNB and two aliphatic secondary amines of different basicity, PIP and morpholine (Mo), in binary mixtures of a dipolar HBA solvent with chloroform or dichloromethane that yield high, moderate and non-synergetic effects on $E_T(30)$ polarity. The purpose of this work was to contribute to our understanding on how solvent effects modify a given chemical process. Also, this approach was intended to relate the extent of the preferential solvation of a chemical probe to the kinetic properties of S_NAr reactions in the same binary solvent systems. Further, this work was aimed at making a contribution to the concept of 'property of a solvent mixture' and to whether such a property can be defined by means of chemical probes or other solvent-dependent processes.

RESULTS AND DISCUSSION

Kinetic determinations

The kinetics of the FDNB + Mo and FDNB + PIP reactions were determined at 25 °C in ethyl acetate (EAc) + chloroform or dichloromethane and acetonitrile (AcN) + chloroform or dichloromethane solvent mixtures. Chloroform and dichloromethane are taken as HBD species (chloroform being the strongest). The acidic hydrogen atom of these solvents can readily form complexes with the oxygen atoms of the dipolar HBA solvent molecules.

The gross mechanism of these reactions in all solvents is given in Scheme 1:[5b,9] the breakdown of the zwitterionic σ intermediate, ZH, can occur spontaneously or by a base-catalyzed mechanism. The transition state leading to the ZH intermediate is expected to be favored by increasing solvent polarity. In aprotic polar solvents, the S_NA reactions followed second-order kinetics (first order in both reagents), whereas in apolar solvents the order in amine was in the range 1–3, depending on the nature of the solvent and the nature of the amine.[10] The evidence for mechanisms proposed for the S_NAr reactions with primary or secondary amines in aprotic solvents of low relative permittivity has recently been reviewed.[11] Each kind of reaction was explored at different solvent compositions, and the influence of amine concentration was studied in all cases. The reactions were carried out under pseudo-first-order conditions; they yielded the expected product in quantitative yield [*N*-(2,4-dinitrophenyl)piperidine and *N*-(2,4-dinitrophenyl)morpholine], and proved to be first order in the corresponding substrate. The second-order rate constants, k_A, calculated from the experimental pseudo-first-order rate constants, k_φ, are listed in Tables 1 and 2 for the amines Mo and PIP, respectively, in EAc + $CHCl_3$ or CH_2Cl_2. For the AcN + $CHCl_3$ or CH_2Cl_2 solvent systems the k_A values are presented in Tables 3 and 4. The k_A values for the reactions in the corresponding pure solvents are additionally presented.

The application of the steady-state hypothesis to the gross mechanism shown in Scheme 1 gives the following

Table 1. Second-order rate constants, k_A (1 mol^{-1} s^{-1}), for the reaction of 5 × 10^{-5} M FDNB with piperidine in EAc + CHCl$_3$ or CH$_2$Cl$_2$, including the data in pure solvents

		[PIP] × 10^{-4} (M)							
Solvent	Concentration[a]	6.25	12.5	25	50	75	100	125	150
EAc + CHCl$_3$	0	6.25	8.76	10.6	21.8	25.7	31.4	39.3	45.8
	0.1	10.6	13.1	16.8	18.9	26.5	28.3	32.0	33.2
	0.3	20.5	23.6	24.8	25.8	29.0	30.7	31.3	32.7
	0.5	23.9	25.2	25.2	26.8	30.5	30.9	31.4	32.9
	0.7	23.6	24.0	24.5	26.4	27.8	28.6	29.0	29.6
	0.9	21.1	21.5	22.0	22.8	23.5	24.5	24.9	25.2
	1	20.0	19.7	19.0	19.0	19.2	19.3	20.1	20.6
EAc + CH$_2$Cl$_2$	0.1	9.30	10.3	14.8	18.2	24.2	29.5	31.2	34.3
	0.3	14.3	15.2	17.7	23.3	31.1	33.1	37.6	41.7
	0.5	21.3	22.9	25.5	30.4	35.7	39.5	41.2	43.5
	0.7	28.7	30.0	31.4	37.6	42.1	45.5	46.5	48.6
	0.9	33.1	34.2	38.7	43.8	47.9	48.3	50.7	53.3
	1	36.5	37.9	42.4	47.5	52.5	58.0	58.5	59.6

[a] The concentrations of the binary mixtures are in cosolvent mole fraction.

Table 2. Second-order rate constants, k_A (1 mol^{-1} s^{-1}), for the reaction of 5 × 10^{-5} M FDNB with morpholine in EAc + CHCl$_3$ or CH$_2$Cl$_2$, including the data in pure solvents

		[Mo] (M)							
Solvent	Concentration[a]	0.002	0.004	0.008	0.01	0.016	0.02	0.04	0.08
EAc + CHCl$_3$	0	0.110	0.201	0.331	0.392	0.473	0.630	1.33	2.52
	0.1	0.234	0.295	0.378	0.388	0.571	0.650	1.11	2.12
	0.3	0.315	0.306	0.419	0.422	0.459	0.597	0.841	1.35
	0.5	0.279	0.316	0.346	0.368	0.403	0.421	0.601	0.870
	0.7	0.184	0.198	0.232	0.238	0.252	0.265	0.326	0.439
	0.9	0.094	0.106	0.116	0.113	0.119	0.138	0.161	0.210
	1	0.0701	0.0604	0.0787	0.0760	0.0874	0.0860	0.0985	0.132
EAc + CH$_2$Cl$_2$	0.1	0.172	0.230	0.371	0.494	0.595	0.735	1.22	1.88
	0.3	0.190	0.233	0.351	0.372	0.539	0.677	1.05	1.72
	0.5	0.224	0.305	0.336	0.354	0.500	0.597	0.938	1.45
	0.7	0.195	0.205	0.225	0.258	0.357	0.411	0.621	1.02
	0.9	0.109	0.125	0.162	0.203	0.221	0.227	0.365	0.640
	1	0.111	0.116	0.138	0.154	0.222	0.222	0.336	0.602

[a] The concentrations of the binary mixtures are in cosolvent mole fraction.

Table 3. Second-order rate constants, k_A (1 mol^{-1} s^{-1}), for the reaction of 5 × 10^{-5} M FDNB with morpholine in AcN + CHCl$_3$ or CH$_2$Cl$_2$, including the data in pure solvents

		[Mo] (M)							
Solvent	Concentration[a]	0.002	0.004	0.008	0.01	0.016	0.02	0.04	0.08
AcN + CHCl$_3$	0	0.800	1.11	1.40	1.74	2.10	2.72	4.05	5.53
	0.1	0.774	0.906	1.22	1.35	1.67	2.09	2.94	3.94
	0.3	0.753	0.786	0.884	1.05	1.21	1.52	1.91	2.55
	0.5	0.484	0.517	0.636	0.688	0.767	0.787	1.05	1.53
	0.7	0.337	0.354	0.386	0.397	0.418	0.462	0.585	0.857
	0.9	0.131	0.135	0.136	0.139	0.160	0.174	0.200	0.260
	1	0.070	0.060	0.0787	0.0760	0.0874	0.086	0.0985	0.132
AcN + CH$_2$Cl$_2$	0.1	0.795	0.853	1.32	1.45	1.95	2.54	3.61	5.38
	0.3	0.549	0.649	0.927	1.11	1.38	1.67	2.28	3.88
	0.5	0.519	0.500	0.626	0.723	0.915	1.00	1.47	2.30
	0.7	0.305	0.329	0.437	0.519	0.650	0.810	1.09	1.93
	0.9	0.189	0.188	0.224	0.258	0.313	0.376	0.503	0.850
	1	0.111	0.116	0.138	0.154	0.222	0.222	0.336	0.602

[a] The concentrations of the binary mixtures are in cosolvent mole fraction.

Table 4. Second-order rate constants, k_A (1 mol^{-1} s^{-1}), for the reaction of 5×10^{-5} M FDNB with piperidine in AcN + $CHCl_3$ or CH_2Cl_2, including the data in pure solvents

		[PIP] × 10^{-4} (M)							
Solvent	Concentration[a]	6.25	12.5	25	50	75	100	125	150
AcN + $CHCl_3$	0	77.5	107	131	161	167	174	181	
	0.1	108	122	130	136	140	142	145	
	0.3	79.4	88.7	97.7	100	104	99.2	103	101
	0.5	71.6	79.8	80.7	80.4	85.3	83.0	84.3	84.3
	0.7	60.2	62.1	63.6	66.7	66.4	64.2	65.2	62.8
	0.9	32.9	34.4	35.9	36.1	35.9	35.3	36.9	36.2
	1	20.0	19.7	19.0	19.0	19.2	19.3	20.1	20.6
AcN + CH_2Cl_2	0.1	84.8	109	110	119	130	132	134	
	0.3	89.2	102	114	119	120	129	130	131
	0.5	81.5	82.9	93.7	99.8	99.0	103	105	107
	0.7	70.1	74.7	79.5	82.7	90.6	95.2	100	102
	0.9	53.7	54.5	63.1	69.3	70.5	78.8	79.8	84.4
	1	36.5	37.9	42.4	47.5	52.5	58	58.5	59.6

[a] The concentrations of the binary mixtures are in cosolvent mole fraction.

equation, where k_A is the observed second-order rate constant and B is a second molecules of the nucleophile:

$$k_A = \frac{k_1\left(k_2 + k_3^B[B]\right)}{k_{-1} + k_2 + k_3^B[B]} \tag{1}$$

Either the formation of the intermediate ZH or its decomposition to products can be rate-limiting. If $k_{-1} \ll k_2 + k_3[B]$ then $k_1 = k_A$, the reaction is not base catalyzed and the formation of the intermediate is the rate-limiting step. If this condition does not hold, the decomposition to products is rate limiting and the reaction is base catalyzed. Two forms of base catalysis have been observed in protic and dipolar aprotic solvents: (a) when the condition $k_{-1} \gg k_2 + k_3[B]$ holds, Eqn. (1) reduces to

$$k_A = k' + k''[B] \tag{2}$$

and there is a linear dependence of k_A on the catalyst concentration. This situation corresponds to the rapid formation of the intermediate ZH, followed by its rate-determining decomposition; (b) when $k_{-1} \approx k_2 + k_3[B]$, Eqn. (1) cannot be simplified and the plots of k_A vs [B] are curvilinear downwards. At low [B], the plot of k_A vs [B] should be a straight line which will change to a plateau at high [B], where the formation of the intermediate becomes rate limiting. However, in aprotic solvents, a new situation has recently been discovered: for several S_NAr reactions with amines an upward curvature has been found in the plots of k_A vs [B] which corresponds to a parabolic dependence of k_A on [B], and a fourth-order kinetic law. Several alternative mechanisms have been proposed to account for this new kinetic finding.[11,12]

The variation of the rate constant with the change in amine in all solvent systems explored follows the usual pattern found in S_NAr reactions:[13] the rate constant values decrease from PIP to Mo. For both amines the statistical parameters reveal a satisfactory linear dependence of the rate constant on the change in amine concentration for EAc + $CHCl_3$ or CH_2Cl_2 mixtures. A similar behavior is observed for the mixtures of AcN with both cosolvents at $X_{AcN} \leq 0.50$. For AcN-rich mixtures a curvilinear relationship can be seen in the plots of k_A vs [B]. This type of tendency was recently observed for the same reaction in mixtures of EAc + AcN.[4c] According to the reported results, base catalysis in EAc and absence of catalysis in $CHCl_3$ is noted for both amines. Hydrogen bond complexes between chloroform and amines have long been known. For AcN and CH_2Cl_2, a borderline condition in the evaluation of the base catalysis can be considered.

Tables 5 and 6 present the partial rate constants for both amines in EAc + $CHCl_3$ or CH_2Cl_2. In EAc + $CHCl_3$ mixtures, both amines show a striking behavior: the general trend shows that the reaction is strongly accelerated on increasing the amine concentration in pure EAc, and that the incidence of the base catalysis markedly decreases on increasing the HBD solvent concentration; for $X_{CoS} > 0.3$, the reaction could be considered non-catalyzed. In EAc + CH_2Cl_2 mixtures, the incidence of base catalysis also decreases with increase in the mole fraction of the HBD solvent. For the PIP amine, the incidence of base catalysis decreases slowly from pure EAc to pure CH_2Cl_2. Otherwise, for Mo the influence of base catalysis decreases strongly from EAc to $X_{CoS} \approx 0.1$ and then decreases mildly.

The $k_3/k_2(k''/k')$ values determined for the reaction system FDNB + Mo in AcN + $CHCl_3$ or CH_2Cl_2 also indicated that the influence of the base catalysis decreases

Table 5. Partial rate constants[a] for FDNB + PIP and FDNB + Mo reactions in EAc + $CHCl_3$ solvent mixtures, including values in pure EAc

X_{CoS}	Amine	k_1k_2/k_{-1} (M^{-1} s^{-1})	k_1k_3/k_{-1} (M^{-2} s^{-1})	k_3/k_2 (M^{-1})	r[b]	s[c]	n[d]
0.0	PIP	5.23	2718	520	0.996	1.441	8
	Mo	0.053	30.87	582	0.999	0.0430	8
0.1	PIP	11.61	1590	137	0.980	1.869	8
	Mo	0.176	24.09	137	0.999	0.0218	8
0.3	PIP	22.10	771	35	0.967	1.183	8
	Mo	0.286	13.3	47	0.997	0.0310	8
0.5	PIP	24.1	625	26	0.971	0.8825	8
	Mo	0.283	7.45	26	0.998	0.0135	8
0.7	PIP	23.7	437	18	0.975	0.5717	8
	Mo	0.197	3.10	16	0.991	0.0117	8
0.9	PIP	21.2	292	14	0.988	0.2620	8
	Mo	0.100	1.42	14	0.988	0.00629	8

[a] Calculated values from Eqn. (2).
[b] Regression coefficient.
[c] Standard deviation.
[d] Number of data points.

Table 6. Partial rate constants[a] for FDNB + PIP and FDNB + Mo reactions in EAc + CH_2Cl_2 solvent mixtures including the pure solvents

X_{CoS}	Amine	k_1k_2/k_{-1} (M^{-1} s^{-1})	k_1k_3/k_{-1} (M^{-2} s^{-1})	k_3/k_2 (M^{-1})	r[b]	s[c]	n[d]
0.0	PIP	5.23	2718	520	0.996	1.441	8
	Mo	0.053	30.87	582	0.999	0.043	8
0.1	PIP	9.31	1790	192	0.989	1.578	8
	Mo	0.220	21.82	99	0.988	0.0898	8
0.3	PIP	13.44	1958	146	0.993	1.366	8
	Mo	0.1993	19.65	99	0.995	0.0572	8
0.5	PIP	21.66	1595	74	0.985	1.602	8
	Mo	0.233	15.76	68	0.994	0.04775	8
0.7	PIP	28.89	1458	50	0.978	1.7965	8
	Mo	0.1677	10.83	64	0.997	0.0217	8
0.9	PIP	34.4	1371	40	0.963	2.214	8
	Mo	0.1074	6.63	62	0.997	0.0151	8
1	PIP	34.4	1371	40	0.986	0.6287	8
	Mo	0.096	6.29	66	0.997	0.01232	8

[a] Calculated values from Eqn. (2).
[b] Regression coefficient.
[c] Standard deviation.
[d] Number of data points.

with increase in the mole fraction of the HBD cosolvent. The same behavior can be expected for PIP. Hydrogen bond interactions in AcN are possibly weaker than in EAc, because of the important dielectric effects of AcN.

Description of kinetic response models as a function of nucleophile concentration and solvent mixture composition

The results in Tables 1–4 indicate that in some intermediate binary mixtures and for certain nucleophile concentrations ([Mo] ≤ 0.020 M and [PIP] ≤ 0.0075 M) the k_A values are higher than those in the pure solvents, part of the mixtures indicating a special synergistic behavior. The term ‘synergetic’ was proposed by Koppel and Koppel[14] to describe the behavior shown by some binary mixtures that have $E_T(30)$ values higher than those of the pure solvents mixed. This effect was observed[15a] for binary mixtures between solvents that have strong HBA and poor HBD capabilities with strong HBD donor solvents: in these cases the synergism was explained by the formation of hydrogen-bonded complexes of higher ‘polarity’ than those of the pure components. More recently, Bosch, *et al.*[15b] extended the use of the term ‘synergism’ to other microscopic solvent properties. By analogy we refer to the observed special enhancement effect of the reaction rate at some intermediate compositions of the mixtures as a ‘kinetic synergetic effect’, which in our opinion is concerned with a special

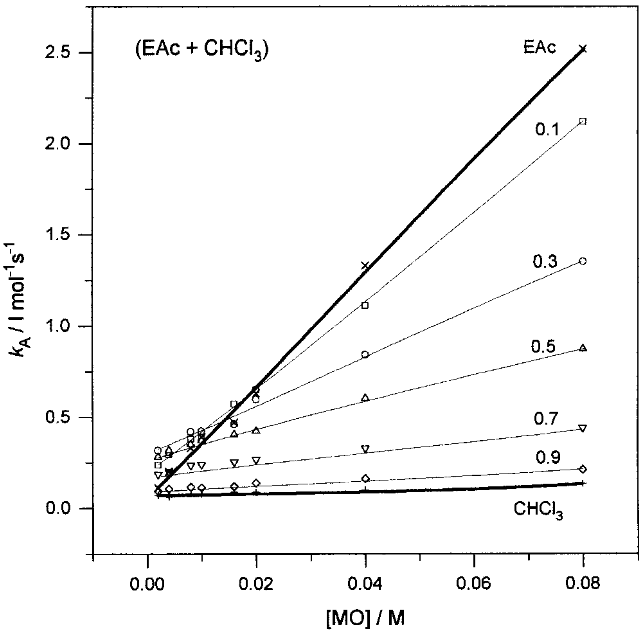

Figure 1. Plots of k_A vs [Mo] for FDNB + Mo reaction in EAc + $CHCl_3$ solvent mixtures at different amine concentrations

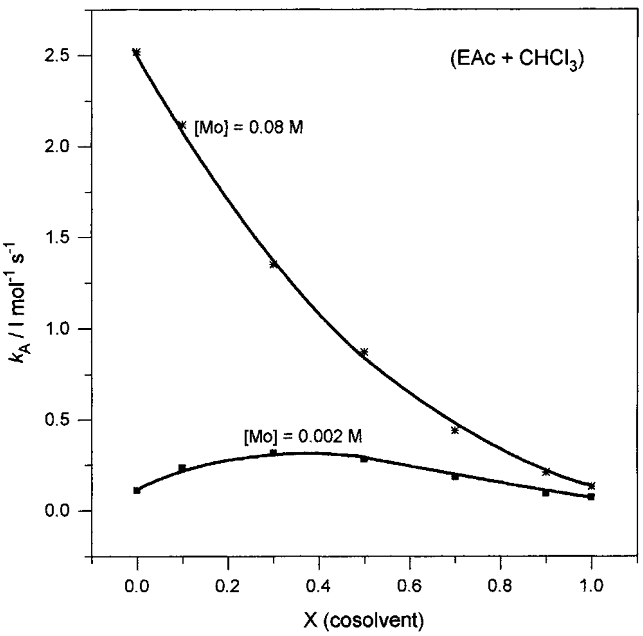

Figure 2. Plots of k_A vs X_{CoS} for FDNB + Mo reaction in EAc + $CHCl_3$ solvent mixtures at [Mo] = 0.002 and 0.08 M

combination of base catalysis and specific solvent effects, particularly hydrogen bond interactions.

In order to analyze the experimental results from this point of view, the data set can be divided into two general groups according to the kinetic behavior of the studied reactions: (a) reaction systems that exhibit kinetic synergetic effects on k_A values, and (b) reaction systems without synergism on the reaction rate. Moreover, the first group can be divided into (a′) reaction systems with high kinetic synergism and (a″) systems with moderate kinetic synergism.

Synergetic effects on the reaction rate. These reaction systems exhibit, in some binary mixtures and for certain amine concentrations, k_A values higher than those in the pure individual solvents. We measured this special effect on the reaction rate by the maximum increment (expressed as a percentage) of the second-order rate coefficient with respect to the highest one in the pure solvents (k_{SEmax}).

Systems with high kinetic synergetic effect. We included in this case the FDNB + Mo reaction in EAc + $CHCl_3$ or CH_2Cl_2 solvent mixtures, which present k_{SEmax} >100% on k_A values. Here we are concerned with a reaction carried out in binary mixtures of solvents that, each one individually, affect the possibility of base catalysis in a different way: the reaction is clearly base catalyzed in EAc, it is less influenced by catalysis in CH_2Cl_2 and it is uncatalyzed in $CHCl_3$. These reaction systems exhibit two different behaviors depending on the nucleophile concentrations. At low amine concentration range ([Mo] $\leq$ 0.02 M), the k_A values increase from pure EAc (in which base catalysis is observed) on increasing the HBD solvent concentration until a maximum, and then decrease to the corresponding value in the cosolvent. k_{SEmax} (EAc + $CHCl_3$) = 186% (X_{CoS} = 0.3; [Mo] = 0.002 M; k_3/k_2 = 47) and k_{SEmax} (EAc + CH_2Cl_2) = 108% (X_{CoS} = 0.5; [Mo] = 0.002 M; k_3/k_2 = 74) referred to the k_A values in EAc. On the other hand, at higher amine concentrations ([Mo] $\geq$ 0.04 M), the k_A values decrease continuously with increasing amount of HBD solvent.

Taking into account that the two reaction systems exhibit similar kinetic behavior under the explored conditions and in order to show the results, we selected the reaction in EAc + $CHCl_3$ solvent mixtures as a representative model. Figure 1 presents the plots of k_A vs [Mo] for the binary mixtures and the pure solvents. It can be clearly seen that the increase in k_A values on increasing the nucleophile concentration is the highest in pure EAc and decreases with increase in amount of chloroform. In order to compare the variation of the reaction rate with the composition of the solvent mixtures, the plots of k_A vs X_{CoS} at constant nucleophile concentrations are presented in Fig. 2 for the lowest ([Mo] = 0.002 M) and the highest ([Mo] = 0.08 M) amine concentration. The shape of the curves clearly reflects the two different kinetic response models depending on the nucleophile concentration, and as a function of the composition of the mixtures. At low amine concentration and for $X_{CoS} \leq 0.5$, the improved k_A values indicate a synergetic behavior. The results indicate that the bulk dielectric effects, although important, are clearly unable

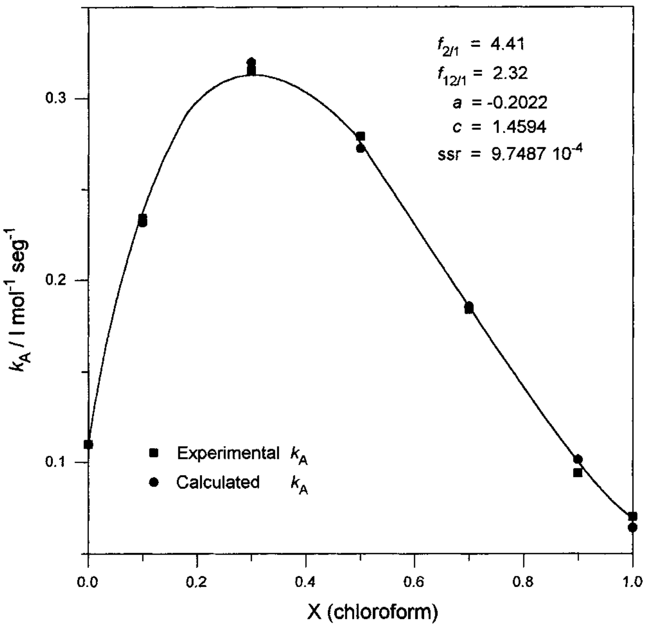

Figure 3. Application of the preferential solvation model to FDNB + Mo reaction in EAc + $CHCl_3$ solvent mixtures at [Mo] = 0.002 M; ssr = sum of square of residuals; $f_{2/1}$ and $f_{12/1}$ measure the tendency of the critical states of the reaction to be solvated with $CHCl_3$ and EAc–$CHCl_3$ complex, respectively, with reference to EAc

Table 7. Values of k_A^{Cl} and k_A^F/k_A^{Cl} for the reactions of FDNB and CDNB with Mo

Solvent	Concentration[a]	k_A^{Cl}	k_A^F/k_A^{Cl}
EAc + $CHCl_3$	0	0.0266	94.7
	0.1	0.0236	89.8
	0.3	0.0204	66.2
	0.5	0.0161	54.0
	0.7	0.00804	54.6
	0.9	0.00415	50.6
	1	0.00283	46.6
EAc + CH_2Cl_2	0.1	0.0242	77.7
	0.3	0.0221	77.8
	0.5	0.0175	82.8
	0.7	0.0122	83.6
	0.9	0.00824	77.7
	1	0.00584	46.6

[a] The concentrations of the binary mixtures are in cosolvent mole fraction.

to account for the observed phenomenon. Even at low cosolvent concentration, same mechanism is at work that is a fundamental contributor to the overall bulk "solvent effects" on reaction rate.[16]

As is known, in solvent mixtures the solutes can interact to a different degree with the components of the mixture, and this difference in the interactions is reflected in the composition of the microsphere of solvation. Several equations based on solvent exchange models that relate the transition energy of the Dimroth–Reichardt $E_T(30)$ indicator to the solvent composition have been derived and compared.[15a] Moreover, a more general model based on a two-step solvent exchange process can be effectively applied to synergetic mixtures for any solvatochromic solutes (solvent parameters).[17] In this connection, the following equation has been used to relate the transition energy of a solvatochromic indicator to the solvent composition:

$$Y = Y_1 + \frac{a(x_2^0)^2 + c(1 - x_2^0)x_2^0}{(1 - x_2^0)^2 + f_{2/1}(x_2^0)^2 + f_{12/1}(1 - x_2^0)x_2^0} \quad (3)$$

where Y is an appropriate solvatochromic property, $a = f_{2/1}(Y_2 - Y_1)$ and $c = f_{12/1}(Y_{12} - Y_1)$. The constants of these processes are defined by the preferential solvation parameters $f_{2/1}$ and $f_{12/1}$ that relate the ratio of the mole fractions of solvents S1, S2 and S12 (which represents a solvent formed by the interactions of solvents S1 and S2) solvating the indicator (x_1^s, x_2^s and x_{12}^s, respectively) to the ratio of the mole fractions of the two solvents in the bulk mixed solvent (x_1^0 and x_2^0, respectively). The constants $f_{2/1}$ and $f_{12/1}$ measure the tendency of the indicator to be solvated with S2 and S12, respectively, with reference to S1.

Here, we extended this preferential solvation model when the solutes are the reagents and/or the intermediates of the S_NAr reactions that exhibit high synergism in order to analyze the relative preferential solvation abilities and compare the correspondence between the synergistic behaviors for the two solvent-dependent processes. The results obtained for the application of the equation to k_A vs X_{CoS} for the reaction FDNB + Mo in EAc + $CHCl_3$ at [B] = 0.002 M are presented in Fig. 3. As can be observed, there is a good convergence of the model at low amine concentrations (to [B] < 0.01 M) and the order of preferential solvation of the critical state of the present reaction (measured by the preferential solvation parameters) is $CHCl_3$ >EAc–$CHCl_3$ complex > EAc.

At higher amine concentrations the k_A values decrease as a non-linear function of the cosolvent mole fraction: the higher decreases take place in the HBD solvent-poor mixtures.

For these systems, the sensitivity of the reaction rates to small amounts of the HBD solvent is very different at low nucleophile concentrations with respect to higher corcentrations. Probably this behavior is mainly related to the influence of base catalysis on this type of reaction. The kinetics of the CDNB + Mo reaction, which is known not to present base catalysis, was determined at 25 °C in EAc + $CHCl_3$ or CH_2Cl_2 in order to confirm these results. Each reaction system was explored at different solvent compositions. The experimental data are reported in Table 7. In both solvent systems we observed the same kinetic response model with the composition of the mixtures: the k_A values decrease as a non-linear function of cosolvent mole fraction, without kinetic synergism.

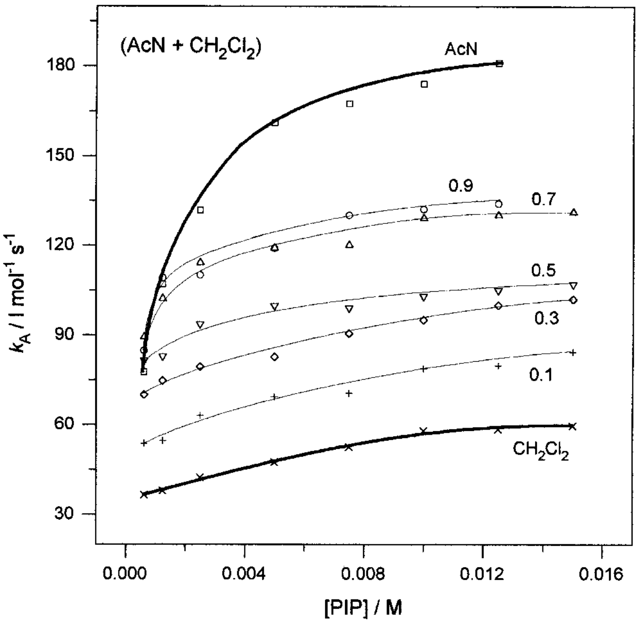

Figure 4. Plots of k_A vs [PIP] for FDNB + PIP reaction in AcN + CH_2Cl_2 solvent mixtures at different amine concentrations

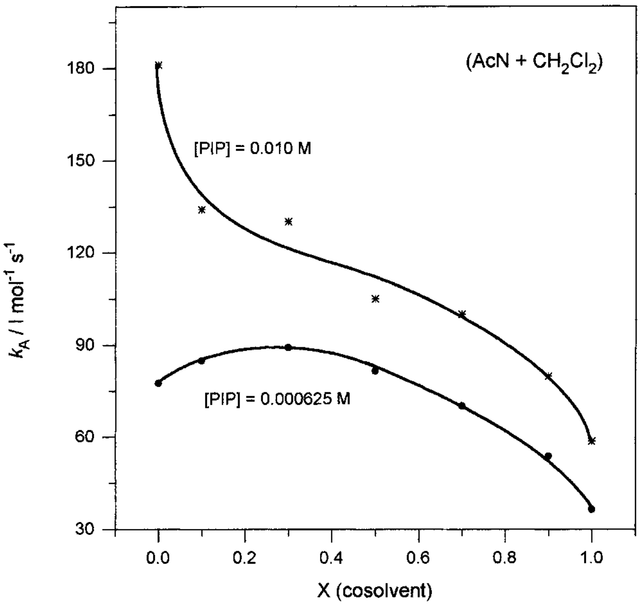

Figure 5. Plots of k_A vs X_{CoS} for FDNB + PIP reaction in AcN + CH_2Cl_2 solvent mixtures at [PIP] = 0.000625 and 0.010 M

Systems with moderate kinetic synergetic effects. We considered that those reaction systems that present k_{SEmax} <100% (with respect to the cosolvent) could be included in this set: FDNB + PIP in EAc + $CHCl_3$ and AcN + $CHCl_3$ or CH_2Cl_2. For the reaction in EAc + $CHCl_3$, the k_A values in pure EAc are lower than those in pure chloroform at the lower piperidine concentrations, but are higher for the rest. On the other hand, for the reaction in the mixtures of AcN with both cosolvents, the k_A values in pure $CHCl_3$ are the smallest over the whole range of amine concentration.

Despite this difference, the behavior is similar: at low amine concentration ([PIP] $\leq$ 0.0075 M), the reaction rate increases from pure EAc (base catalysis, $k_3/k_2 = 520$) with increase in HBD solvent concentration up to a maximum. k_{SEmax} (EAc + $CHCl_3$) = 28%, k_{SEmax} (AcN + $CHCl_3$) = 39% and k_{SEmax} (AcN + CH_2Cl_2) = 15%, referred to k_A values in EAc and AcN, respectively. Figure 4 presents the plots of k_A vs [PIP] for the binary mixtures and the pure solvents for the reaction carried out in AcN + CH_2Cl_2, taken here as a representative model system. In order to understand the characteristics of this reaction with the change in the composition of the mixtures, the plots of k_A vs X_{CoS} at constant nucleophile concentrations are presented in Fig. 5 for the lowest ([PIP] = 0.000625 M) and the highest ([PIP] = 0.010 M) amine concentrations. The shape of the curves reflects kinetic response models similar to those described for systems with high kinetic synergism, but the synergistic behavior is minimized, probably owing to the greater reactivity and smaller susceptibility to base catalysis of PIP with respect to Mo.

Non-synergetic reaction systems. In contrast to the reaction systems analyzed previously, FDNB + Mo in AcN + $CHCl_3$ or CH_2Cl_2 do not exhibit synergetic effects on the reaction rates at any nucleophile concentration. We selected the reaction in AcN + $CHCl_3$ mixtures as a model to analyze the results. Figure 6 presents the plots of k_A vs [Mo] for the binary mixtures and the pure solvents and Fig. 7 those of k_A vs X_{CoS} for the lowest ([Mo] = 0.002 M) and the highest ([Mo] = 0.08 M) amine concentrations. The shape of the curves reflects a unique model of kinetic response: k_A values decrease with increase in the HBD solvent mole fraction over the whole range of amine concentration. It can be clearly seen that the increase in k_A values with increase in nucleophile concentration is markedly higher for pure AcN and at low cosolvent mole fraction than for the cosolvent-rich mixtures.

On the other hand, the reaction system FDNB + PIP in EAc + CH_2Cl_2 exhibits a particular behavior. In this case the k_A values in CH_2Cl_2 ($k_3/k_2 = 40$) are higher than those in EAc ($k_3/k_2 = 520$) and in the explored range of amine concentrations they tend to approximate to higher nucleophilic concentrations.

Correlation of kinetic data with $E_T(30)$ empirical solvent parameter

The often linear correlation between empirical solvent parameters and other dependent properties (e.g. logarithms of rate and equilibrium constants, absorption energies) can be considered as manifestations of general linear free-energy relationships.[18,19] In this sense it is

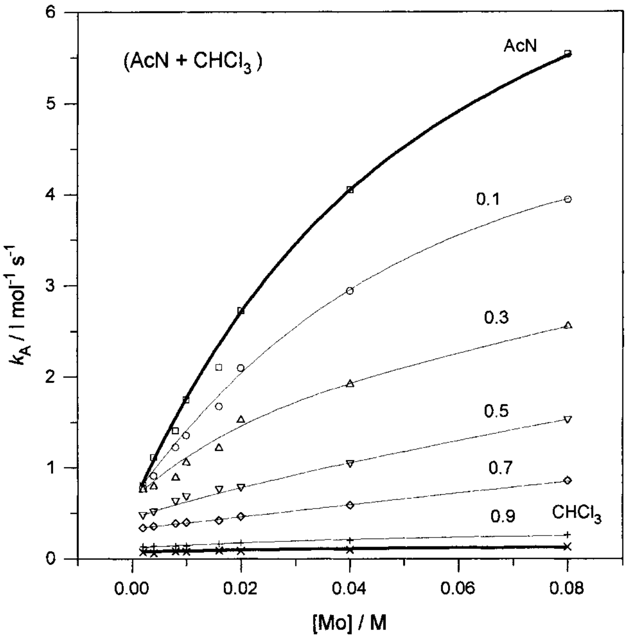

Figure 6. Plots of k_A vs [Mo] for FDNB + Mo reaction in AcN + $CHCl_3$ solvent mixtures at different amine concentrations

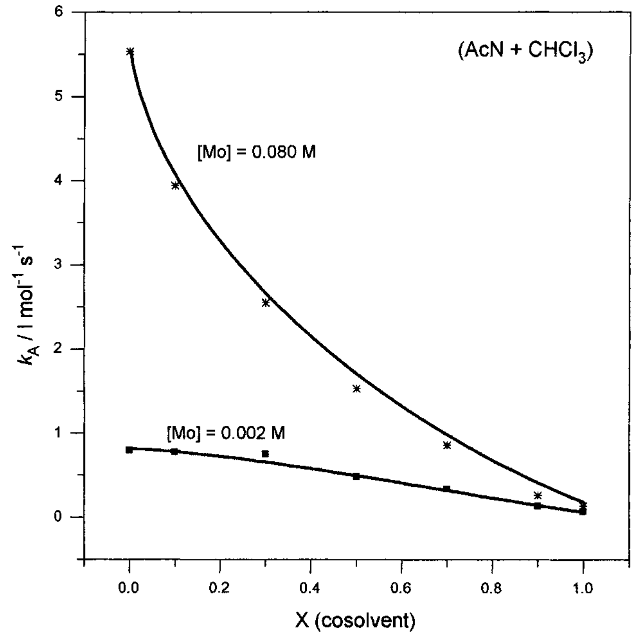

Figure 7. Plots of k_A vs X_{Cos} for FDNB + Mo reaction in AcN + $CHCl_3$ solvent mixtures at [Mo] = 0.002 and 0.08 M

possible to interpret the solvent effects with the aid of a model process yielding the same or similar effects.

We have recently[4a] analyzed the correspondence between $E_T(30)$ values and the logarithm of the rate constants for the reaction CDNB + PIP in aprotic solvent + toluene mixtures which have no synergetic effects for the chemical probe. Moreover,[4b] we have performed a similar correlation analysis for CDNB + PIP or *n*-butylamine and FDNB + *n*-butylamine in PAHBA solvent + $CHCl_3$ mixtures which in some cases present synergetic effects for $E_T(30)$. In general, there are satisfactory or relatively good correlations between $E_T(30)$ values and the logarithms of the rate constants, except for the reactions carried out in EAc + $CHCl_3$ mixtures in which the correlations are very poor. This behavior was related to the influence and extension of the synergism for the $E_T(30)$ polarity promoted by these mixtures.

Here we extended the preceding correlation analysis to the reaction systems explored in this work. The relationships were calculated for all solvent mixtures including the data corresponding to the pure solvents, at each amine concentration. The correlations were assessed by the evaluation of the correlation coefficient (r) and the standard deviation (s). The results are given in Table 8. For both reactions the correlations are satisfactory or relatively good when the solvents are AcN + $CHCl_3$ or CH_2Cl_2. However, when the reactions are carried out in EAc + $CHCl_3$ or CH_2Cl_2 solvent mixtures the correlations are poor or very poor. Therefore, the chemical probe under consideration is not generally valid to interpret the solvation effects produced by these kinds of solvent

Table 8. Correlation coefficients (r) standard deviations (s) and number of data points (n) of log k_A vs $E_T(30)$ for S_NAr reactions in solvent mixtures, including the data in pure solvents[a]

Reaction	Solvent mixture	r	s	n
FDNB + Mo	EAc + $CHCl_3$	$r \le 0.86$	<0.331	7
		$0.91 \le r \le 0.995$	0.0289–0.2202	6[b]
		$0.97 \le r \le 0.995$	0.0289–0.0804	6[c]
	AcN + $CHCl_3$	$0.99 \le r \le 0.994$	0.0498–0.1096	7
	AcN + CH_2Cl_2	$0.99 \le r \le 0.994$	0.0223–0.0529	7
FDNB + PIP	EAc + $CHCl_3$	$r \le 0.768$	0.0625–0.1985	7
	EAc + CH_2Cl_2	$0.49 \le r \le 0.949$	0.0741–0.1123	7
	AcN + $CHCl_3$	$0.945 \le r \le 0.988$	0.0526–0.1162	7
	AcN + CH_2Cl_2	$0.94 \le r \le 0.989$	0.0298–0.0685	7

[a] The statistical values indicate the maximum range for all [B].
[b] Kinetic data in pure EAc are excluded.
[c] Kinetic data for [B] ≤0.010 M, excluding the values in pure EAc.

mixtures on the reactions. The present situation could be related to the mechanisms of the preferential solvation observed. At first, the application of the Kamlet–Taft multiparametric approach,[20] dealt with in a forthcoming paper, is consistent with a more optimistic point of view in this sense.

CONCLUSIONS

For the reaction systems developed in the binary solvent mixtures explored in this work, we observed a special kinetic synergism which is not an exclusive consequence of the enhanced polarity of the mixed solvent. It shows differences with the known synergetic behavior promoted by polar aprotic HBA solvent + HBD solvent mixtures on solvatochromic indicators, which is assumed to be due to the hydrogen-bonded complex that has a higher polarity than the pure individual solvents.

We conclude that this kinetic synergism, which depends on the amine concentration, is concerned with a complex combination of factors related to the variation of the influence of base catalysis (with changes with solvent composition) and to specific solvent effects, particularly hydrogen-bond interactions. The higher kinetic synergetic effects are observed with the least reactive and most susceptible to base catalysis of the explored amines; they are also observed at low amine concentrations and in mixtures of solvents ($X_{\mathrm{CoS}} \leq 0.5$) which, individually, show large differences in the influence of the base catalysis.

On the other hand, the results obtained in the application of the preferential solvation model indicate that the behavior in this direction is clearly different between both solvent-dependent processes. It would seem that in the S_NAr reactions the critical states tend to be preferentially influenced by the HBD solvent, whereas the $E_T(30)$ solvatochromic indicator is preferentially solvated by the EAc–$CHCl_3$ complex (the results obtained in the fit of the solvent polarity parameter values to the model are $f_{12/1} = 14$ and $f_{12/2} = 1.56$). This restricts the convergence between the solvent effects on the compared processes, which is improved only when the synergetic effects are minimized.

EXPERIMENTAL

Reagents and solvents. 1-Chloro-2,4-dinitrobenzene, 1-fluoro-2,4-dinitrobenzene, piperidine and morpholine were purified as described previously.[4b,c] *N*-(2,4-Dinitrophenyl)piperidine, and *N*-(2,4-dinitrophenyl)morpholine were prepared and purified by methods reported previously.[4c] The solvents were purified as reported previously[8] and all of them were kept over 4 Å molecular sieves and stored in special vessels which allowed delivery without air contamination. All binary solvent mixtures were prepared prior to use and stored under anhydrous conditions.

Kinetic procedures. The kinetics of the reactions were studied spectrophotometrically.[4b] A Perkin-Elmer Model 124 spectrophotometer was used, with a data-acquisition system based on a microprocessor. This set-up has a 12-bit analog-to-digital converter, which allows absorbance measurements with an error of <0.1% at a maximum of 12 readings per second. The microprocessor controls data acquisition and also measures time through a quartz crystal-controller oscillator. Once data acquisition is completed, data can be read in the system display and/or transferred to a computer through an interface. In all cases, pseudo-first-order kinetics were observed.

Standard solutions of 1-halo-2,4-dinitrobenzene and the corresponding secondary amine were prepared in the desired binary solvent mixture at room temperature. The reactions were run by mixing known amounts of each solution in the thermostated cells of the spectrophotometer, recording the absorbances at *ca* 400 nm. The pseudo-first-order (k_φ) and second-order (k_A), rate constants were obtained as described previously.[4b] In all cases, the 'infinity' absorbance value, A_∞, was experimentally determined for each run at the working temperature. Within the experimental error, this value agreed with the 'theoretical' value calculated from application of Beer's law to a corresponding solution of *N*-(2,4-dinitrophenyl)amine in the working binary solvent mixture. All the kinetic runs were carried out at least in duplicate; the error in k_A is ≤2–3% for all the solvent mixtures examined.

Computational methods. The parameters of solvation which minimize the square residuals of the k_A and the $E_T(30)$ values for the binary solvent systems were computed by non-linear regression using the MATLAB version 4.2 c.1 program (MathWorks).

Acknowledgments

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