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Specific and non-specific solvent effects on aromatic nucleophilic substitution. Kinetics of the reaction of 1-fluoro-2,6-dinitrobenzene and homopiperidine in binary solvent mixtures

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ABSTRACT: This paper presents a comparative study of the solvent effects on the kinetics of the reactions between 1-fluoro-2,6-dinitrobenzene and hexahydro-1*H*-azepine in ethyl acetate + chloroform or acetonitrile and acetonitrile + chloroform binary solvent mixtures. The purpose was to asses the contribution of each molecular-microscopic solvent property to the overall solvation effect of the reaction critical state. The influence of the dipolarity/polarizability, hydrogen-bond donor acidity and hydrogen-bond acceptor basicity of the solvent mixtures on the reaction rate was analyzed by the application of the multiparametric approach of Kamlet, Abboud and Taft. The evaluation of the correlation coefficients shows that the solvation effects are dominated by the non-specific interactions. Moreover, the incidence of the hydrogen-bond acceptor solvent ability is more important than that corresponding to the hydrogen-bond donor character, except for the reactions that manifest kinetic retarding effects. The influence of the solvation effects on the base catalysis was analyzed, describing the response patterns of the partial rate coefficients to the mixture composition and also to each solvent property. The application of a preferential solvation model to the kinetic results yields information on the preferential solvation of the reaction critical state by any of the pure solvents, or by the hydrogen-bonded complexed media.

KEYWORDS: solvent effects; preferential solvation; aromatic nucleophilic substitution; correlations; base catalysis

INTRODUCTION

Binary mixtures of solvents are frequently used as media in many physical and chemical processes taking place in solution. It is known that the solvatochromic shifts of selected chemical solutes reflect the molecular-microscopic properties of the solvent. Selected probes have been used to establish empirical scales of microscopic parameters, which are able to provide a quantitative description of solvent characteristics. The $E_T(30)$ scale of Dimroth and Reichardt (which measures the polarity and the acidity of solvents mainly) and the π^*, β and α scales constructed by Kamlet, Abboud and Taft (KAT) (which quantify the solvent's dipolarity/polarizability, hydrogen-bond acceptor ability and hydrogen-bond donor ability) are the most widely used in the uniparametric and multiparametric approaches, respectively.[1–4]

It has long been recognized that the reactivity of aromatic nucleophilic substitution (S_NAr) reactions is notably affected by the solvent. Most of the analyses of solvent effects have been performed in pure solvents showing how extensive and complex the interactions of the substrate and/or the intermediate(s) with the solvent molecules can be.[5–7] Recently, we reported different studies aimed at the characterization of mixed solvents and at the determination of the kinetic data of S_NAr reactions, relating the solvatochromic response with the kinetic response. Correlations between the kinetic data and the molecular-microscopic solvent parameters, according to the general linear solvation energy relationships (LSER), have been investigated and discussed. In order to analyze the influence of preferential solvation on the two different solvent-dependent processes so as to understand solvation effects better, preferential solvation models have also been applied.[8] Here it was of interest to study the S_NAr reaction between 1-fluoro-2,6-dinitrobenzene (2,6-DNFB) and the secondary amine homopiperidine (HPIP; hexahydro-1*H*-azepine) in some binary

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mixtures of solvents. The mixed solvents chosen here are considered as representatives of the types we proposed for mixtures of polar aprotic solvents where both pure components are able to form complexes or cross-associated species,[9] which were grouped on the basis of the molecular-microscopic descriptors determined in earlier measurements: type A [hydrogen-bond acceptor (HBA) solvent + potential hydrogen-bond donor (HBD) cosolvent]; type B [HBA solvent + HBA/potential HBD cosolvent]; and type C [HBA/potential HBD solvent + potential HBD cosolvent].[10]

The aim of this work was to investigate the influence of solvent effects on the selected S_NAr process by comparison with information obtained by performing the same reaction in different mixed solvent systems. In this direction, the kinetic results for the reaction performed in binary mixtures of types A, B and C are analyzed and related through (i) the comparison of the kinetic response models which are reflected by the plots of the rate coefficient as a function of mixture composition and at each nucleophile concentration explored; (ii) a correlation analysis (according to the KAT multiparameter model) in order to quantify the contribution of each type of solvent property on the rate coefficient; (iii) the investigation of the response patterns corresponding to the partial rate coefficients as a function of the solvent composition and also as a function of each molecular-microscopic solvent property, in order to understand the influence of the solvent effects on the base catalysis; and (iv) the application of preferential solvation models with the object of inferring the preferential solvation order of the critical state of the reaction by the pure components or by the solvent formed as consequence of the interactions between them.

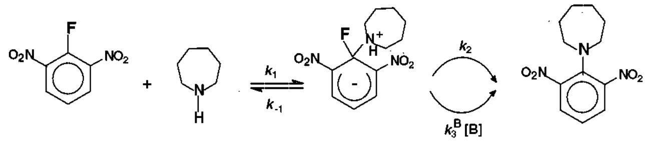
RESULTS AND DISCUSSION

Ethyl acetate (EAc) was selected as an aprotic HBA solvent, chloroform as a aprotic solvent with potential HBD ability and acetonitrile (AcN) as an HBA/potential HBD aprotic solvent. The molecular-microscopic solvent properties of the selected mixtures have been reported previously.[8a,c] The value $\beta = 0.10$ was used for pure chloroform. The binary mixtures explored were EAc + $CHCl_3$, EAc + AcN and AcN + $CHCl_3$, which were taken as representative of types A, B and C, respectively.

Kinetic results

The S_NAr reactions between halonitrobenzenes and primary and secondary amines have been investigated in polar and apolar solvents. As is known, a two-step mechanism is well established: either the first step (formation of the zwitterionic intermediate) or the second step (decomposition of the intermediate) can be rate-limiting, with the possibility of base catalysis (Scheme 1). The observation of base catalysis and the form of the catalysis law depend on the type of amine, the nucleofugal group, the nature and the degree of activation of the aromatic substrate, the relative position of activating substituent(s) and the solvent employed. The kinetic law which describes this phenomenon is represented by

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



Scheme 1

The kinetics of the S_NAr reaction between 2,6-DNFB and HPIP in EAc + $CHCl_3$, EAc + AcN and AcN + $CHCl_3$ solvent systems was determined at 25 °C. The reaction was explored by systematically varying the solvent composition, and the influence of amine concentration on the reaction rate was analyzed in all cases. The reaction was carried out under pseudo-first-order conditions. The formation of the expected product *N*-(2,6-dinitrophenyl)homopiperidine was quantitative and proved to be first order in the substrate. The second-order rate constants, k_A, were calculated from the experimental pseudo-first-order constants, k_φ, and the appropriate amine concentration.

Table 1 presents the k_A values for the reactions performed in the explored mixtures. The data in pure solvents are additionally presented.[8] For all solvent systems, the kinetic results reveal a satisfactory linear dependence of the rate on amine concentration, showing low k_A values at low amine concentrations.

In order to understand the influence of the solvent effects on the explored reaction with changes in the composition of the mixtures, plots of k_A vs X_{CoS} at each amine concentration are presented in Fig. 1. The shapes of the curves for the reaction performed in EAc + $CHCl_3$ mixtures clearly reveal two different kinetic response patterns depending on the nucleophile concentration. At higher amine concentrations the k_A values decrease as a non-linear function of the cosolvent mole fraction: the highest decrease takes place in the HBD solvent-poor mixtures. At [HPIP] ≤ 0.05 M the second-order rate constant values in the mixtures are lower than those in the pure individual solvents (in which the k_A values are very similar) exhibiting a kinetic retarding effect. The magnitude of this special effect on the reaction rate,

Table 1. Second-order rate coefficient, k_A (l mol^{-1} seg^{-1}), for the reaction between 1-fluoro-2,6-dinitrobenzene (5×10^{-4} M) and homopiperidine in binary solvent mixtures (including the pure solvents), measured at 25 °C

		[HPIP] (M)							
Solvent	X_{CoS}[a]	0.01	0.03	0.05	0.07	0.09	0.1	0.125	0.150
EAc	0.0	0.012	0.038	0.064	0.095	0.114	0.133	0.136	0.180
AcN		0.038	0.077	0.133	0.176	0.215	0.240	0.760	0.220
$CHCl_3$			0.037	0.053	0.061	0.067	0.071	0.850	0.960
EAc + $CHCl_3$	0.1		0.028	0.056	0.089	0.105	0.123	0.144	0.169
EAc + AcN		0.013	0.039	0.066	0.097	0.12	0.136	0.162	0.194
AcN + $CHCl_3$			0.067	0.110	0.146	0.173	0.200	0.240	0.275
EAc + $CHCl_3$	0.2		0.026	0.052	0.083	0.100	0.113	0.138	0.157
EAc + AcN		0.014	0.039	0.067	0.099	0.122	0.139	0.167	0.195
AcN + $CHCl_3$			0.053	0.091	0.116	0.143	0.158	0.193	0.218
EAc + $CHCl_3$	0.3		0.023	0.043	0.078	0.093	0.105	0.123	0.140
EAc + AcN		0.015	0.04	0.068	0.103	0.125	0.14	0.173	0.207
AcN + $CHCl_3$			0.048	0.08	0.095	0.119	0.129	0.151	0.175
EAc + $CHCl_3$	0.4		0.021	0.044	0.076	0.091	0.100	0.121	0.137
EAc + AcN		0.015	0.042	0.074	0.106	0.130	0.147	0.177	0.214
AcN + $CHCl_3$			0.046	0.069	0.083	0.104	0.114	0.132	0.158
EAc + $CHCl_3$	0.5		0.024	0.045	0.074	0.086	0.094	0.113	0.125
EAc + AcN		0.017	0.046	0.084	0.115	0.136	0.153	0.180	0.221
AcN + $CHCl_3$			0.044	0.066	0.080	0.098	0.109	0.122	0.145
EAc + $CHCl_3$	0.6		0.024	0.044	0.073	0.085	0.091	0.110	0.124
EAc + AcN		0.02	0.049	0.090	0.121	0.150	0.169	0.196	0.237
AcN + $CHCl_3$			0.037	0.055	0.071	0.086	0.091	0.105	0.124
EAc + $CHCl_3$	0.7		0.024	0.048	0.070	0.085	0.089	0.107	0.120
EAc + AcN		0.024	0.056	0.103	0.129	0.166	0.188	0.217	0.261
AcN + $CHCl_3$			0.035	0.051	0.068	0.080	0.086	0.095	0.113
EAc + $CHCl_3$	0.8		0.028	0.047	0.070	0.080	0.083	0.120	0.115
EAc + AcN		0.025	0.060	0.108	0.140	0.180	0.200	0.236	0.279
AcN + $CHCl_3$			0.030	0.045	0.058	0.068	0.075	0.089	0.100
EAc + $CHCl_3$	0.9		0.032	0.049	0.068	0.077	0.080	0.096	0.109
EAc + AcN		0.026	0.068	0.122	0.153	0.195	0.213	0.254	0.299
AcN + $CHCl_3$			0.029	0.045	0.055	0.064	0.071	0.086	0.098

[a] X_{CoS} = mole fraction of the cosolvent.

which is quantified by the maximum decrease (expressed as a percentage) of k_A values in the mixtures with respect to the lowest one in the pure solvents, is 19% at [amine] = 0.05 M and 43% at [amine] = 0.03 M.

With respect to the reaction carried out in EAc + AcN mixtures, the plots manifest a unique pattern of kinetic response: k_A increases with increase in the HBA/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 concentrations is markedly higher for pure AcN and at AcN-rich mixtures than for EAc-rich mixtures.

On the other hand, the reaction carried out in AcN + $CHCl_3$ also exhibits a unique kinetic response pattern: as in the case of EAc + $CHCl_3$ mixtures, k_A decreases with increase in the $CHCl_3$ mole fraction, reflecting that the influence of amine concentration is higher in AcN-rich mixtures than in $CHCl_3$-rich mixtures. Moreover, a tendency for incipient retarding effects on k_A is revealed at low amine concentrations.

Table 2 presents the partial rate relations k_1k_2/k_{-1}, k_1k_3/k_{-1}, and k_3/k_2 obtained by linear regression treatment of the kinetic data. The results in the pure solvents indicate that the reaction is clearly base-catalyzed in EAc, it is less influenced by catalysis in AcN and it is uncatalyzed in $CHCl_3$. In EAc + $CHCl_3$ mixtures, the reaction is base-catalyzed until $X_{CoS} = 0.7$, decreasing the incidence of the catalysis with increase in $CHCl_3$ mole fraction. In EAc + AcN mixtures, the k_3/k_2 values reveal that the reaction is base-catalyzed over the whole range of mixed solvent composition, exhibiting a particular behavior: small increments in AcN strongly increase the influence of the base catalysis until $X_{CoS} = 0.4$ Subsequent additions of AcN decrease the incidence of the catalysis. In AcN + $CHCl_3$ mixtures the reaction is base catalyzed at $X_{CoS} = 0.1$–0.2.

As can be observed from the results, the explored reaction is susceptible to be base-catalyzed when it is performed in pure solvents with HBA properties (EAc and AcN), in their mixtures (EAc + AcN) and also in mixtures of those solvents with an HBD solvent (EAc or AcN + $CHCl_3$) (in the last case only in the HBA solvent-rich zone). These results can be related to the influence of the solvents with HBD properties on the base catalysis in similar S_NAr reactions.[11a] The solvents in which no base catalysis was detected are those that exhibit hydrogen-

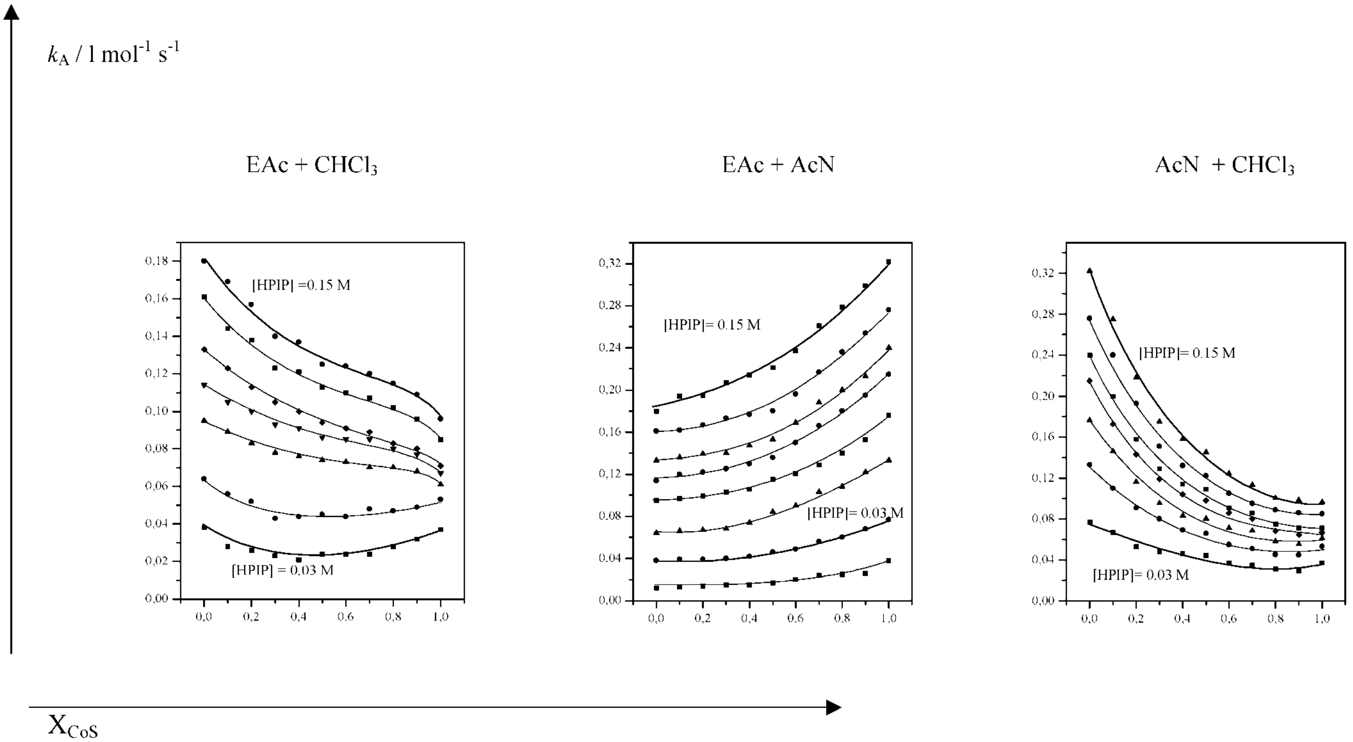


Figure 1. Plots of k_A vs X_{CoS} for the reaction of 2,6-DNFB with HPIP in EAc + $CHCl_3$ or AcN and AcN + $CHCl_3$ mixtures, at each amine concentration

bond donor abilities (chloroform, acetonitrile, nitromethane), especially in protic solvents[11b] (methanol), and also in some binary solvent mixtures in which at least one component exhibits HBD capacity. All these results were attributed to the fact that the solvents with HBD abilities can effectively assist fluoride detachment.

Correlation analysis of kinetic data with molecular-microscopic solvent properties: solvent effects on the second-order rate coefficient k_A

In order to interpret the influence of the solvent effects on the explored S_NAr reaction, we made a correlation analysis between the kinetic data and the molecular-microscopic solvent properties. In order to determine the incidence of each type of solvent property on the kinetics of the reaction, we applied a quantitative treatment of the solvent effects by means of the multiparametric approach developed by Kamlet, Abboud and Taft.[12] The data derived from the equation

$$\log k_A = Y + s\pi^* + a\alpha + b\beta \qquad (2)$$

(where *s, a* and *b* measure the relative susceptibilities of the explored reaction to the solvent properties dipolarity/polarizability, HBD and HBA ability, respectively) are presented in Table 3. The good correlations obtained by multiple regression analysis, based on least squares over the whole range of solvent compositions allow an interpretation of the influence of any mixed solvent property on the kinetic process.

For the explored systems, the order of incidence of each solvent property on k_A evaluated by the absolute values of the correlation coefficients *s, a* and *b* is dipolarity/polarizability > HBD ability > HBA ability for mixtures with $CHCl_3$, and dipolarity/polarizability > HBA ability > HBD ability for mixtures without $CHCl_3$. For the reaction performed in the EAc + $CHCl_3$ system at [HPIP] = 0.030 and 0.050 M the order of incidence is HBD ability > dipolarity/polarizability > HBA ability and HBD ability ≈ dipolarity/polarizability > HBA ability, respectively.

It can be pointed out that these reactions exhibit kinetic retarding effects on k_A, which at first sight could be related with the detected incidence of the specific solvation effects on the critical state of the reaction attributed to the HBD character of the medium, and also on the nucleophile.[13]

Response patterns of the partial rate coefficients k_1k_3/k_{-1} and k_1k_2/k_{-1} to the molecular-microscopic solvent properties: solvent effects on base catalysis

The chemical properties of the mixed solvent in which the explored reaction is carried out determine whether the

Table 2. Partial rate constants for the reaction of 2,6-DNFB with HPIP in binary solvent mixtures (including the data in the pure solvents)

Solvent	X_{CoS}	$10^3 k_1 k_2/k_{-1}$ ($\text{l mol}^{-1}\text{s}^{-1}$)	$k_1 k_3/k_{-1}$ ($\text{l}^2\text{mol}^{-2}\text{s}^{-1}$)	k_3/k_2 (l mol^{-1})	r[a]	SD[a]	n[a]
EAc	0.0	3.09	1.23	400	0.996	0.005	8
AcN		24.3	2.05	84	0.996	0.009	8
$CHCl_3$		26.2	0.466	18	0.993	0.002	7
EAc + $CHCl_3$	0.1	5.72	1.17	204	0.993	0.060	7
EAc + AcN		1.79	1.30	726	0.999	0.003	8
AcN + $CHCl_3$		21.0	1.73	82	0.998	0.005	7
EAc + $CHCl_3$	0.2	5.32	1.09	205	0.994	0.006	7
EAc + AcN		2.46	1.32	536	0.998	0.004	8
AcN + $CHCl_3$		18.4	1.37	74	0.997	0.005	7
EAc + $CHCl_3$	0.3	7.07	0.990	140	0.986	0.007	7
EAc + AcN		1.63	1.38	850	0.999	0.002	8
AcN + $CHCl_3$		23.4	1.03	44	0.996	0.004	7
EAc + $CHCl_3$	0.4	6.59	0.969	147	0.988	0.007	7
EAc + AcN		2.32	1.42	612	0.999	0.004	8
AcN + $CHCl_3$		20.7	0.91	44	0.998	0.002	7
EAc + $CHCl_3$	0.5	5.81	0.846	146	0.985	0.007	7
EAc + AcN		6.79	1.43	210	0.997	0.005	8
AcN + $CHCl_3$		22.8	0.820	36	0.997	0.003	7
EAc + $CHCl_3$	0.6	5.19	0.834	160	0.987	0.006	7
EAc + AcN		8.01	1.55	193	0.998	0.005	8
AcN + $CHCl_3$		19.3	0.706	37	0.996	0.003	7
EAc + $CHCl_3$	0.7	8.59	0.785	91	0.986	0.006	7
EAc + AcN		10.7	1.69	156	0.998	0.006	8
AcN + $CHCl_3$		20.2	0.629	31	0.992	0.004	7
EAc + $CHCl_3$	0.8	14.0	0.685	49	0.983	0.006	7
EAc + AcN		10.7	1.83	171	0.998	0.002	8
AcN + $CHCl_3$		20.2	0.576	36	0.998	0.006	7
EAc + $CHCl_3$	0.9	18.1	0.625	34	0.991	0.004	7
EAc + AcN		14.6	1.94	133	0.997	0.007	8
AcN + $CHCl_3$		14.5	0.564	39	0.998	0.002	7

[a] r = Correlation coefficient; SD = standard deviation; n = number of data points.

formation or the decomposition of the zwitterionic intermediate is the rate-limiting step. In order to contribute to the interpretation of the mechanism in relation with the solvent effects, we analyzed the influence of the microscopic solvent properties on the base catalysis through the response patterns of the partial rate coefficients k_1k_3/k_{-1} (related to the catalyzed step) and k_1k_2/k_{-1} (related to the uncatalyzed step) as a function of the composition of the mixtures and also as a function of π^*, α and β solvatochromic parameters. The results are presented in Figs 2–7.

Reaction in EAc + $CHCl_3$ solvent system. The plot k_1k_3/k_{-1} vs X_{CoS} presented in Fig. 2 shows that the addition of the HBD cosolvent produces a continuous, nearly linear decrease in k_1k_3/k_{-1} values from pure EAc (in which the base catalysis is operative) to pure $CHCl_3$ (in which the absence of base catalysis is detected). The plot k_1k_2/k_{-1} vs X_{CoS} presented in Fig. 3 reveals that the k_1k_2/k_{-1} ratio remains nearly constant with the addition of the HBD solvent until $X_{CoS} \approx 0.7$, then markedly increasing to the value in pure $CHCl_3$. These results could be related to the influence of the base catalysis evaluated by the k_3/k_2 ratio (Table 2): at those solvent mixtures in which k_1k_2/k_{-1} is lower and tend to be constant the reaction is base-catalyzed, being uncatalyzed in very rich mixtures in HBD cosolvent in which k_1k_3/k_{-1} is low and k_1k_2/k_{-1} is strongly increased. Moreover, the k_1k_3/k_{-1} ratio decreases 0.58 times and the k_1k_2/k_{-1} ratio increases 0.24 times from pure EAc up to $X_{CoS} = 0.7$ (taking the corresponding changes from EAc to $CHCl_3$ as reference). These results suggest that the decrease in the incidence of base catalysis is principally due to the decrease in k_3 values.

The influence of the solvent effects related to each kind of solvent properties on k_1k_3/k_{-1} and k_1k_2/k_{-1} is reflected by the shape of the corresponding curves presented in Figs 2 and 3, respectively. The plots show decreases in k_1k_3/k_{-1} and increases in k_1k_2/k_{-1} with increments in the dipolarity/polarizability and decreases in the HBA ability of the mixed solvent. The same tendency is observed as a function of the HBD character from EAc to $CHCl_3$. As a consequence, the reaction is base catalyzed in the mixtures that do not have high $CHCl_3$ concentrations.

The decrease in the incidence of base catalysis from

Table 3. Correlation coefficient (*r* and r^2), standard deviation (SD), intercept (*Y*) and the parameters *s*, *a* and *b* (and their standard errors) and the number of data points (*n*) corresponding to $\log k_A = Y + s\pi^* + a\alpha + b\beta$ for the reaction between 2,6-DNFB and HPIP in binary mixtures (including the data in pure solvents)

[HPIP] (M)	r (r^2)	SD	Y (s_Y)	s (s_s)	a (s_a)	b (s_b)	n
($EAc + CHCl_3$)							
0.03	0.962	0.028	−0.741	−0.814	−1.04	−0.474	11
	(0.926)		(0.237)	(0.273)	(0.136)	(0.193)	
0.05	0.932	0.021	−0.399	−0.601	−0.618	−0.423	11
	(0.887)		(0.180)	(0.208)	(0.103)	(0.147)	
0.07	0.970	0.016	−0.370	−1.06	−0.249	−0.128	11
	(0.940)		(0.137)	(0.158)	(0.078)	(0.112)	
0.09	0.983	0.014	−0.259	−1.16	−0.241	−0.081	11
	(0.966)		(0.120)	(0.138)	(0.068)	(0.098)	
0.1	0.978	0.020	0.159	−1.64	−0.280	−0.263	11
	(0.957)		(0.174)	(0.200)	(0.099)	(0.141)	
0.125	0.977	0.021	0.182	−1.57	−0.301	−0.216	11
	(0.954)		(0.176)	(0.202)	(0.101)	(0.143)	
0.150	0.970	0.026	0.337	−1.70	−0.273	−0.285	11
	(0.934)		(0.221)	(0.255)	(0.127)	(0.180)	
(EAc + AcN)							
0.03	0.986	0.021	−1.88	+1.56	−0.132	−0.874	11
	(0.972)		(0.533)	(0.497)	(0.283)	(0.591)	
0.05	0.985	0.023	−1.22	+1.23	+0.222	−1.31	11
	(0.971)		(0.580)	(0.542)	(0.308)	(0.643)	
0.07	0.991	0.014	−1.38	+1.34	−0.070	−1.31	11
	(0.983)		(0.344)	(0.322)	(0.183)	(0.643)	
0.09	0.988	0.017	−1.41	+1.27	−0.080	−0.687	11
	(0.977)		(0.428)	(0.400)	(0.228)	(0.475)	
0.1	0.985	0.018	−1.18	+1.20	−0.045	−0.793	11
	(0.971)		(0.455)	(0.424)	(0.241)	(0.504)	
0.125	0.988	0.015	−1.26	+1.31	−0.155	−0.563	11
	(0.977)		(0.378)	(0.353)	(0.201)	(0.419)	
0.150	0.990	0.014	−1.07	+1.05	+0.054	−0.555	11
	(0.980)		(0.356)	(0.332)	(0.189)	(0.3950	
($AcN + CHCl_3$)							
0.03	0.973	0.036	0.775	−2.92	+0.665	+0.188	11
	(0.947)		(0.637)	(0.801)	(0.190)	(0.149)	
0.05	0.988	0.029	1.52	−3.68	+0.747	+0.287	11
	(0.976)		(0.510)	(0.641)	(0.152)	(0.119)	
0.07	0.978	0.012	1.32	−1.62	+0.085	+0.194	11
	(0.957)		(0.209)	(0.263)	(0.062)	(0.049)	
0.09	0.988	0.036	1.89	−4.04	+0.706	+0.523	11
	(0.971)		(0.622)	(0.782)	(0.185)	(0.146)	
0.1	0.988	0.034	2.27	−4.48	+0.655	+0.605	11
	(0.976)		(0.589)	(0.741)	(0.174)	(0.138)	
0.125	0.992	0.026	2.56	−4.74	+0.644	+0.589	11
	(0.985)		(0.452)	(0.567)	(0.134)	(0.106)	
0.150	0.991	0.029	2.40	−4.47	+0.685	+0.591	11
	(0.982)		(0.509)	(0.64)	(0.152)	(0.119)	

EAc to $CHCl_3$ can be related to previous results reported for S_NAr reactions between 1-fluoro-2,4-dinitrobenzene and piperidine or morpholine in pure HBA, HBD and protic solvents, and also in EAc + $CHCl_3$ or CH_2Cl_2 solvent mixtures: the solvents in which no base catalysis was detected are those which exhibit hydrogen-bond donor abilities.[8b,11] Only those pure aprotic solvents or mixtures of solvents with HBD capability can assist fluoride detachment and in these cases the decomposition of the intermediate ZH is not rate limiting and its formation is the slow step.

Reaction in EAc + AcN solvent system. The plot of k_1k_3/k_{-1} vs X_{CoS} presented in Fig. 4 shows that the addition of the HBA/HBD cosolvent to EAc produces a nearly linear increase in k_1k_3/k_{-1} from EAc to AcN: the reaction is base catalyzed in both pure solvents and in the binary mixtures. The plot of k_1k_2/k_{-1} vs X_{CoS} presented in Fig. 5 reveals a particular behavior: the plot shows a region with small decreases in k_1k_2/k_{-1} (until $X_{\mathrm{CoS}} = 0.4$) followed by large increases leading to the value in pure AcN. These results can be related to the special effect observed on the base catalysis reflected by the relation $k_3/$

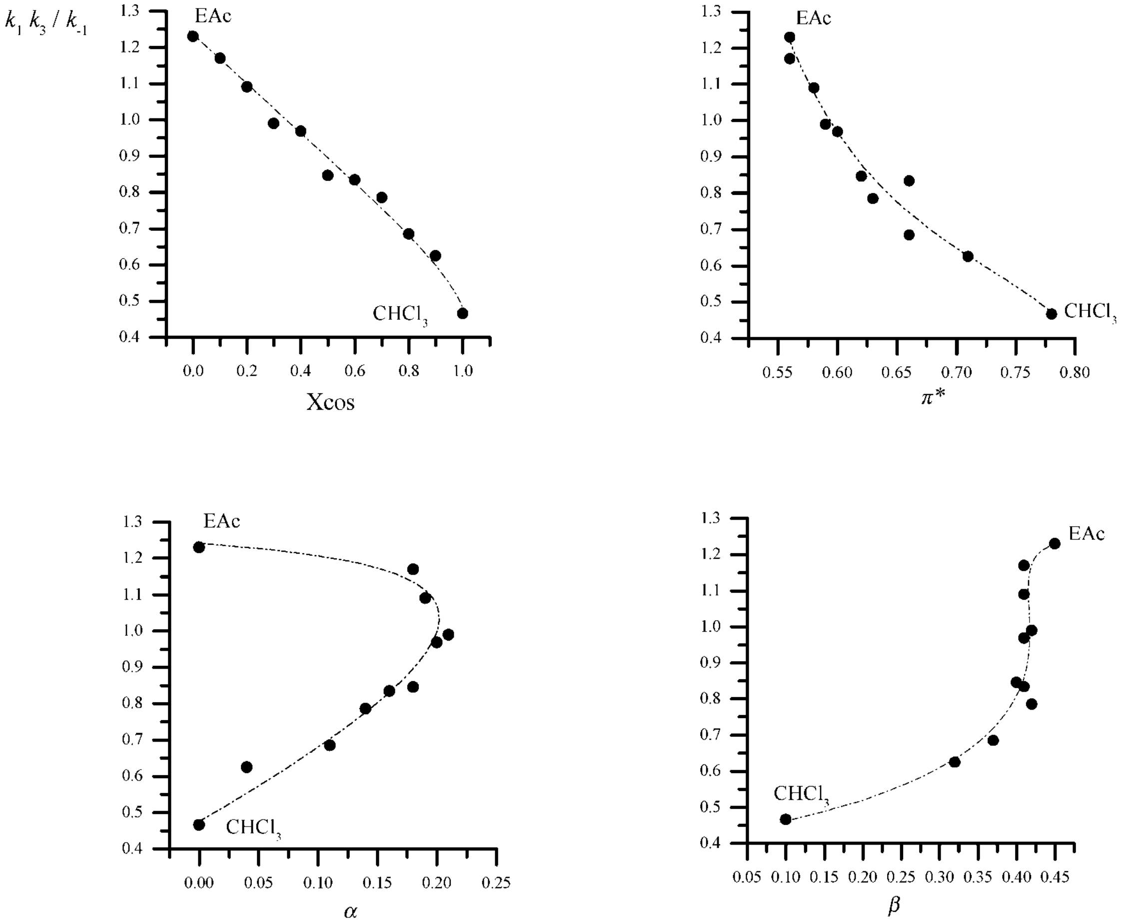


Figure 2. Plots of k_1k_3/k_{-1} vs X_{CoS} or π^* or α or β for the reaction performed in EAc + CHCl$_3$ mixtures

k_2 (Table 2): the reaction (which is base catalyzed over the whole range of solvent composition) exhibits incremented base catalysis with respect that one corresponding to the pure solvents, in those mixtures that manifest diminished k_1k_2/k_{-1} values. The k_3/k_2 ratio corresponding to $X_{\text{AcN}} = 0.3$ is 2.13 times higher than the value in pure EAc. The shapes of the curves corresponding to the partial rate coefficients as a function of π^*, α and β presented in Figs 4 and 5 reveal that (i) the k_1k_3/k_{-1} ratio increases in a continuous non-linear manner with dipolarity/polarizability, and it also increases with the HBD ability of the solvent; (ii) low k_1k_3/k_{-1} values are observed at those β values higher than the rest (and also pure EAc); and (iii) the shapes of the curves corresponding to the k_1k_2/k_{-1} ratio show a similar general tendency to that observed for the k_1k_3/k_{-1} ratio: the remarkable difference is the diminished k_1k_2/k_{-1} values observed at $X_{\text{AcN}} = 0.1$–0.4.

The particular behavior observed on the base catalysis can be related to the HBA ability of AcN, which would play a role in maximizing the solvation effects attributed to the HBA characteristics of the media and minimizing the effects related to its HBD ability.

Reaction in AcN + CHCl$_3$ solvent system. The plot of k_1k_3/k_{-1} vs X_{CoS} presented in Fig. 6 shows a continuous non-linear decrease in k_1k_3/k_{-1} with the increase in CHCl$_3$ concentration from pure AcN (base-catalyzed reaction) to pure CHCl$_3$ (uncatalyzed reaction). It can be pointed out that small variations in k_1k_2/k_{-1} values are observed with changes in mixed solvent composition (Fig. 7). These results suggest that the tendency detected on base catalysis up to $X_{\text{CoS}} = 0.2$ (k_3/k_2 ratio, Table 2) is mainly dependent on k_1k_3/k_{-1}.

From the plots of k_1k_3/k_{-1} as a function of the solvent properties, it can be inferred that HBD and, above all, the HBA ability of the mixed solvent have a strong positive influence on the base-catalyzed step in AcN-rich solvent mixtures.

The behavior observed with respect to the influence of solvent effects on the decrease in the incidence of the base catalysis is similar to that detected for EAc + CHCl$_3$ mixtures. The reaction carried out in EAc + CHCl$_3$ is base catalyzed up to $X_{\text{CoS}} = 0.7$, whereas in AcN + CHCl$_3$ mixtures it is base-catalyzed up to $X_{\text{CoS}} = 0.2$. This can be related with the HBD ability that AcN manifests, which would play a role in encouraging the

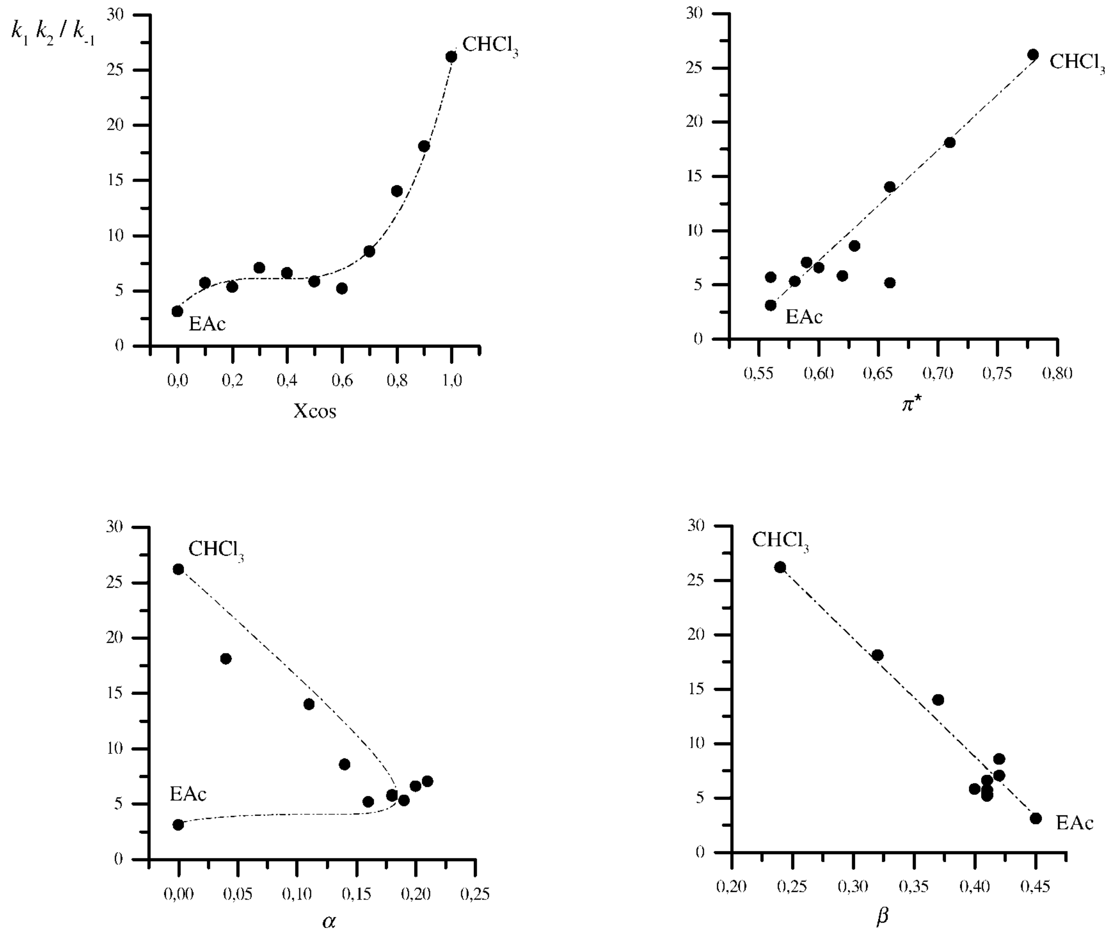


Figure 3. Plots of k_1k_2/k_{-1} vs X_{CoS} or π^* or α or β for the reaction performed in EAc + CHCl$_3$ mixtures

solvation effects attributed to the HBD characteristics of the cosolvent.

Preferential solvation effects on kinetic results: application of preferential solvation models

As is known, in mixed solvents the solutes can interact to different extents with the components of the mixture, and this difference in the interactions is reflected in the composition of the microsphere of solvation. The general equation

$$Y = Y_1 + \frac{f_{2/1}(Y_2 - Y_1)\left(x_2^0\right)^2 + f_{12/1}(Y_{12} - Y_1)\left(1 - x_2^0\right)x_2^0}{\left(1 - x_2^0\right)^2 + f_{2/1}\left(x_2^0\right)^2 + f_{12/1}\left(1 - x_2^0\right)x_2^0} \qquad (3)$$

(based on the solvent exchange theory)[14] has been proposed in order to relate any solvatochromic solvent property linearly related to the transition energy (measured by means of solvatochromic solutes) to the solvent composition.[15] The preferential solvation parameters $f_{2/1}$ and $f_{12/1}$ measure the tendency of the solute to be solvated by cosolvent S2 and by the ‘mixed solvent’ S12 (structure attributed to the formation of intersolvent complexes or associates by hydrogen-bond interactions) with reference to solvent S1.

In order to obtain information about the solvation effects when the solutes are the reagents and/or intermediates of the explored S_NAr reaction, here we extended the application of the preferential solvation model to the kinetic data. The results obtained by the application of Eqn. (3) to k_A vs X_{CoS} are presented in Table 4.

For the reaction performed in EAc + CHCl$_3$ mixtures, it can be seen that (i) $f_{2/1} > 1$ at [HPIP] = 0.03–0.05 M, indicating that the preferential solvation is produced by CHCl$_3$ in preference to EAc; (ii) $f_{2/1} < 1$ at [HPIP] >0.05 M, which means that the solvation is by EAc with preference to CHCl$_3$; and (iii) $f_{12/1} > 1$ at all amine concentrations, suggesting preferential solvation by S12 in preference to EAc and CHCl$_3$. As a consequence, at [HPIP] ≤0.05 M the preferential solvation order is intersolvent complex > CHCl$_3$ > EAc, and at [HPIP] >0.05 M it is intersolvent complex > EAc > CHCl$_3$. It

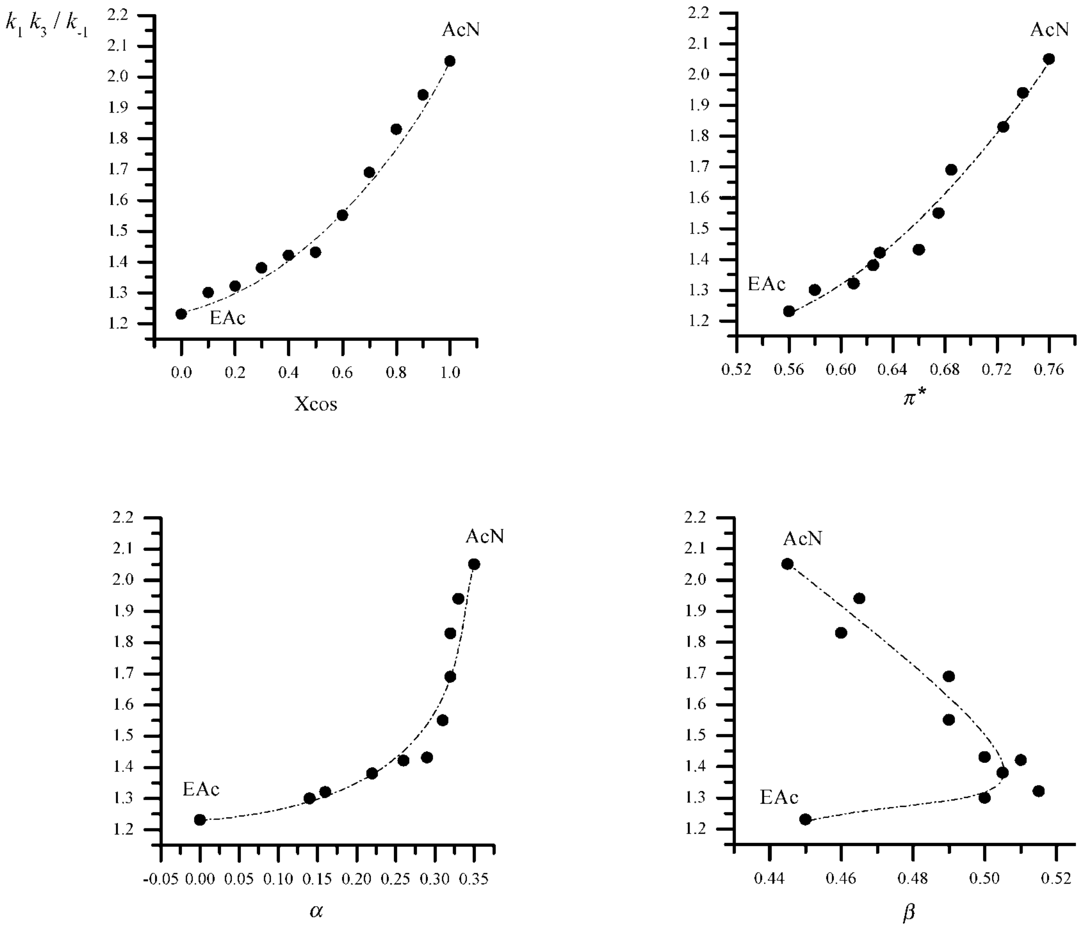


Figure 4. Plots of k_1k_3/k_{-1} vs X_{CoS} or π^* or α or β for the reaction performed in EAc + AcN mixtures

Table 4. Preferential solvation parameters calculated from the data in Table 1 and Eqn. (3)

[HPIP] (M)	Solvent	$f_{2/1}$	$f_{12/1}$	*ssr*
0.03	EAc + $CHCl_3$	1.12	2.93	7.1×10^{-6}
	EAc + AcN	0.642	1.52	4.2×10^{-6}
	AcN + $CHCl_3$	0.108	2.68	4.1×10^{-5}
0.05	EAc + $CHCl_3$	4.08	0.750	2.0×10^{-5}
	EAc + AcN	0.998	1.53	2.7×10^{-5}
	AcN + $CHCl_3$	0.0735	3.01	2.2×10^{-5}
0.07	EAc + $CHCl_3$	0.0113	3.02	4.5×10^{-6}
	EAc + AcN	4.62	14.3	1.2×10^{-5}
	AcN + $CHCl_3$	167	25.9	7.7×10^{-5}
0.090	EAc + $CHCl_3$	0.179	3.35	1.1×10^{-5}
	EAc + AcN	0.253	0.629	3.9×10^{-5}
	AcN + $CHCl_3$	0.0477	3.52	4.9×10^{-5}
0.10	EAc + $CHCl_3$	0.262	3.25	3.1×10^{-5}
	EAc + AcN	0.615	1.22	8.3×10^{-5}
	AcN + $CHCl_3$	2.68	0.505	8.6×10^{-5}
0.125	EAc + $CHCl_3$	0.0278	2.15	6.9×10^{-5}
	EAc + AcN	0.443	1.13	1.8×10^{-4}
	AcN + $CHCl_3$	27.8	4.88	7.2×10^{-5}
0.15	EAc + $CHCl_3$	0.002	2.10	0.0011
	EAc + AcN	0.0695	0.531	1.1×10^{-4}
	AcN + $CHCl_3$	2.66	0.475	1.3×10^{-4}

can be pointed out that a kinetic retarding effect was detected at [HPIP] $\leq$0.05 M and moreover, the correlation analysis reveals the highest order of incidence of the HBD ability. The behavior observed in EAc + AcN mixtures is similar to that observed for EAc + $CHCl_3$ mixtures at [HPIP] >0.05 M: the critical state of the reaction is preferentially solvated by the hydrogen-bonded complex solvent, AcN (the cosolvent with HBD ability) being the least preferred solvent. On the other hand, an undefined preferential solvation order is observed when the reaction is performed in AcN + $CHCl_3$ mixtures.

The evaluation of the solvation parameters corresponding to the solvent systems selected as representatives of types A and B manifests, in these cases, similar preferred solvent order for the solvation of the critical state of the reaction; these results can be related to the HBA ability of EAc to form intersolvent complexes via hydrogen bonding. The mixtures of type C show a particular solvation behavior that could be attributed to the characteristics of AcN which can act as an HBA solvent but it is also able to compete with the cosolvent to donate a hydrogen atom.

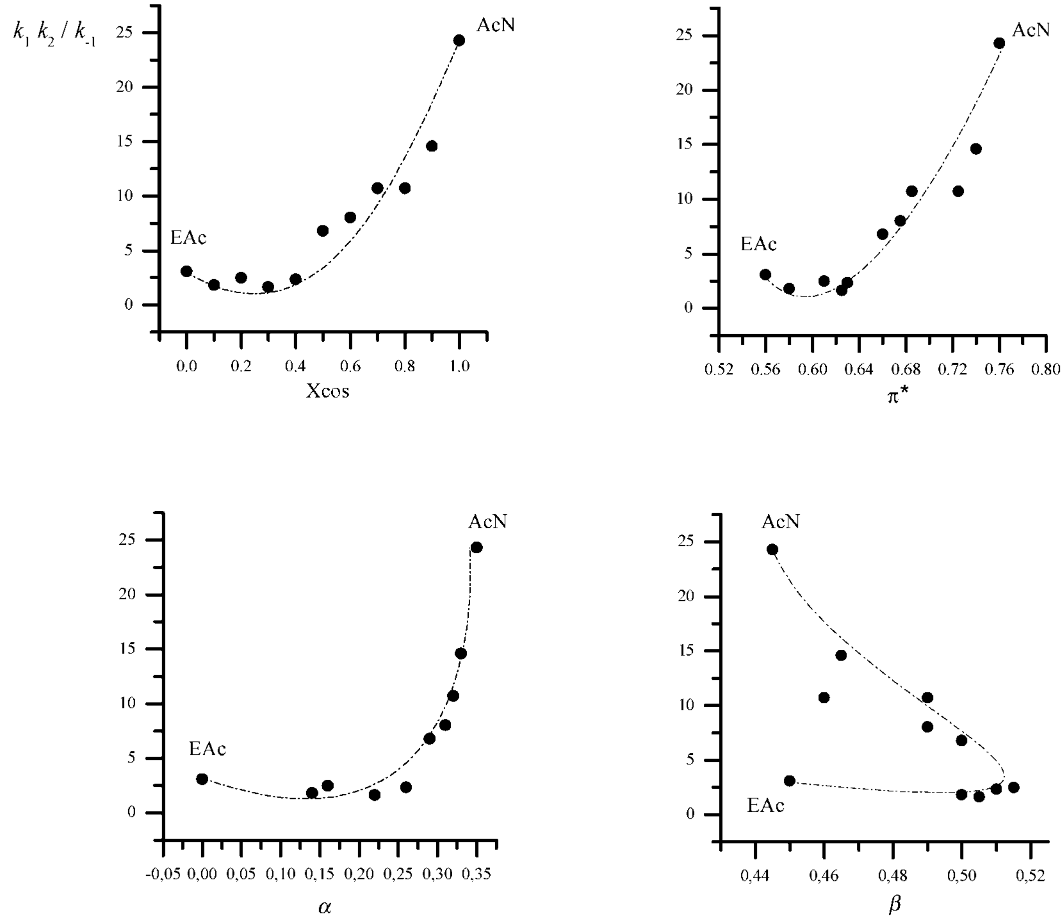


Figure 5. Plots of k_1k_2/k_{-1} vs X_{COS} or π^* or α or β for the reaction performed in EAc + AcN mixtures

Remarks on non-specific and specific solvation effects on kinetic results

The comparative study of the solvent effects on the reaction of 2,6-DNFB and HPIP in EAc + $CHCl_3$ or AcN and AcN + $CHCl_3$ binary mixtures clearly reveals the following:

(i) The solvation effects are dominated by the non-specific interactions. The rate constant is more influenced by the solvent effects attributed to dipole and induced-dipole interactions than those due to the hydrogen-bond interactions. Moreover, the incidence of the solvation effects ascribed to the HBA solvent properties are more important than those corresponding to the HBD solvent character. Exception are reactions for which kinetic retarding effects occur.

(ii) In the cases of the solvent mixtures with $CHCl_3$, the solvation effects attributed to the dipole and induced-dipole interactions manifest negative influence on k_A values whereas the incidence of solvation effects ascribed to the HBA ability is positive. In contrast, opposite effects are observed for the mixtures without $CHCl_3$.

(iii) The incidence of solvation effects related to the solvent HBD capability has little significance in all cases, except for the reactions that manifest retarding effects on k_A.

(iv) The base-catalyzed step is favored by the HBA ability of the media. When the reaction is carried out in mixtures of types A and C, base catalysis is operative in the HBA solvent, in the HBA/HBD solvent and also in mixtures at certain HBD cosolvent concentrations. The compositions of the solvent mixtures in which the reaction is not base catalyzed are related to their HBD ability: the mixtures with HBD ability can assist fluoride detachment and the decomposition of the intermediate could not be rate limiting. This capacity is increased when the pure solvents part of the mixture exhibit HBD ability: the solvation effects attributed to the HBD capacities seem to be reinforced. When the reaction is carried out in mixtures of type B, base catalysis is operative in both pure solvents and also over the whole range of cosolvent concentration. Moreover, an increased base catalysis was observed at certain cosolvent concentrations. This behavior can be attributed to the HBA ability that the cosolvent exhibits in addition to the HBD ability,

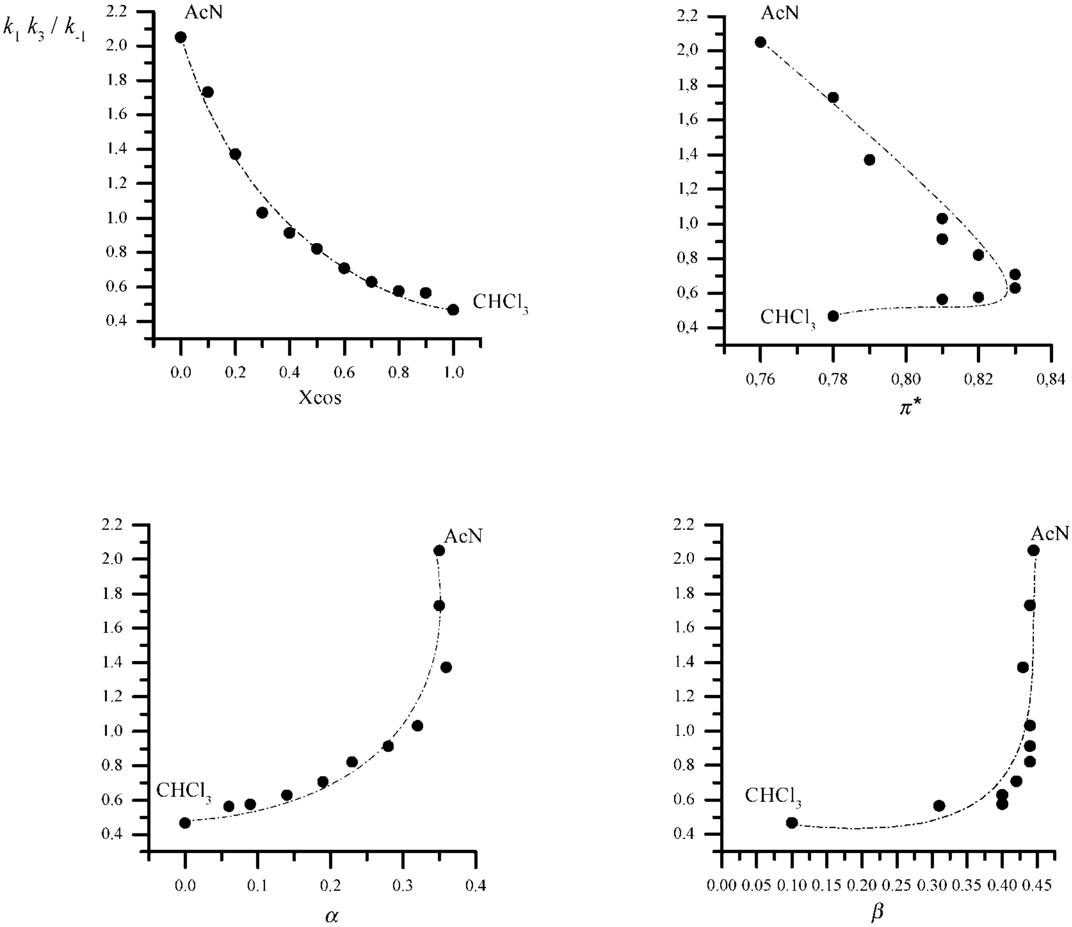


Figure 6. Plots of k_1k_3/k_{-1} vs X_{CoS} or π^* or α or β for the reaction performed in AcN + CHCl$_3$ mixtures

which would play a role in reinforcing the solvation effects attributed to the HBA characteristics of the media and minimizing the effects related to its HBD ability.

(v) The preferential solvation parameter data corresponding to mixtures of types A and B indicate that the critical state of the reaction is preferentially solvated by the structure formed by intersolvent hydrogen-bonded species: these results can be related to the HBA ability of EAc to form intersolvent complexes via hydrogen bonding with the cosolvent (CHCl$_3$ or AcN). The mixtures of type C show a particular solvation behavior that could be attributed to the characteristics of AcN forming self-associated species and also cross-associated species with the cosolvent.

(vi) The solvation effects are dominated by the specific interactions when the reactions show evidence of retarding effects on the rate constant. This special kinetic behavior detected for reactions performed in EAc + CHCl$_3$ (and mixtures of similar characteristics) at [HPIP] = 0.030–0.050 M can be attributed to (a) the higher incidence of the HBD ability with respect to the other solvent properties reflected by the correlation coefficients; (b) the preferential solvation of the critical state of the reaction by the 'mixed solvent'; (c) the negative deviations from the linear response for k_A vs X_{CoS}, principally in CHCl$_3$-poor mixtures; and (d) the fact that at [HPIP] = 0.030–0.050 M the k_A values in the pure solvents do not differ considerably, producing the said negative deviation brings up a kinetic retarding effect.

EXPERIMENTAL

2,6-DNFB was synthesized from 1-chloro-2,6-dinitrobenzene and was recrystallized from ethanol.[14] HPIP was refluxed for 3 h and then fractionated over sodium. The solvents were purified as reported previously[8] and all of them were kept over 4 Å molecular sieves and stored in special vessels that allow delivery without air contamination. All binary solvent mixtures were prepared prior to use and stored under anhydrous conditions.

The kinetics of the reactions were studied by UV–Vis spectrophotometry. A Perkin-Elmer Model 124 spectrophotometer was used, equipped with a data-acquisition

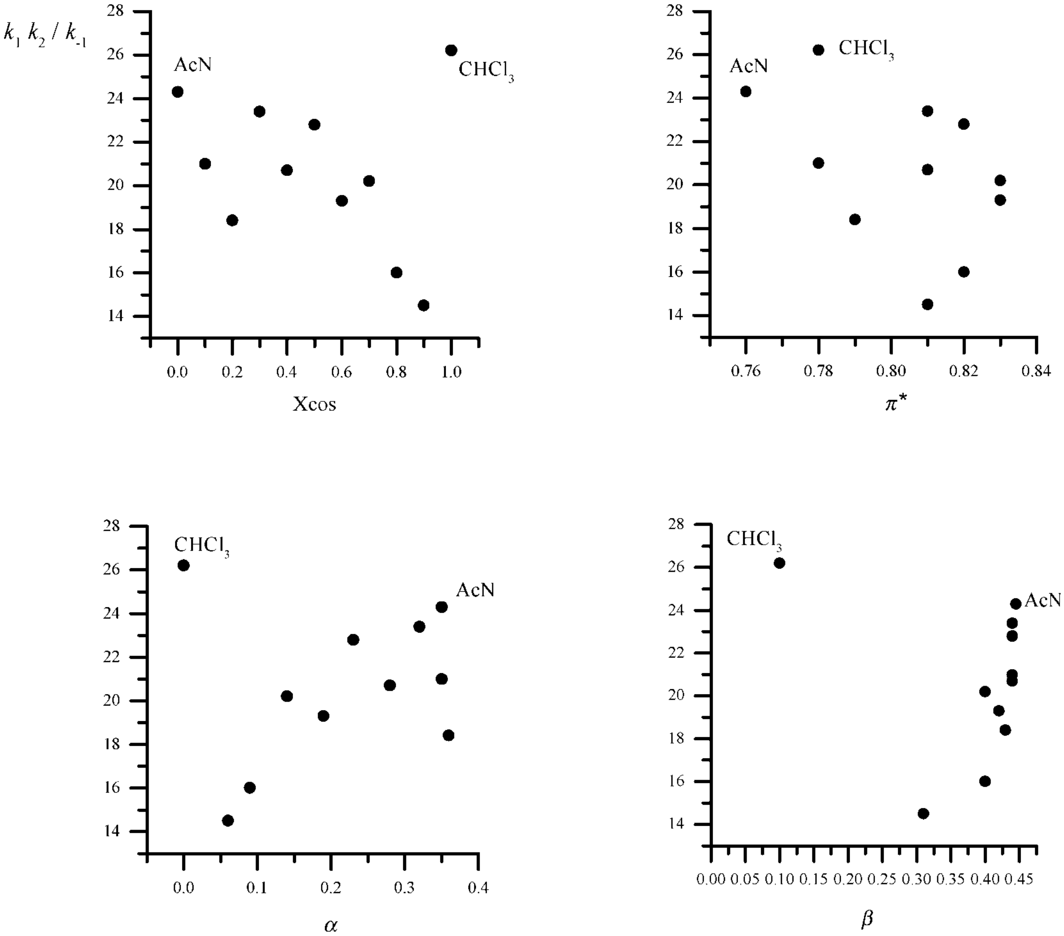


Figure 7. Plots of k_1k_2/k_{-1} vs X_{CoS} or π^* or α or β for the reaction performed in AcN + CHCl$_3$ mixtures

system. The parameters of solvation which minimize the square residuals of the k_A values were computed by non-linear regressions.

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