SOLVENT EFFECTS ON AROMATIC NUCLEOPHILIC SUBSTITUTION REACTIONS. PART 7. DETERMINATION OF THE EMPIRICAL POLARITY PARAMETER $E_T(30)$ FOR DIPOLAR HYDROGEN BOND ACCEPTOR–CO-SOLVENT (CHLOROFORM OR DICHLOROMETHANE) MIXTURES. KINETICS OF THE REACTIONS OF HALONITROBENZENES WITH ALIPHATIC AMINES

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Empirical solvent polarity parameters $E_T(30)$ were determined by UV/VIS spectroscopy, using Dimroth–Reichardt's betaine dye, as a function of composition, for several binary solvent mixtures [i.e. polar hydrogen bond acceptor (PHBA) solvents + chloroform or dichloromethane]. Each solvent system was analyzed according to its deviations from additivity due to preferential solvation of the chemical probe and also from complicated intermolecular interactions of the mixed solvents. The $E_T(30)$ parameter of many of these mixtures has presented synergism. The synergetic effects were more significant for those binary solvent systems in which chloroform is the co-solvent. These results were related to the solvent effects on some aromatic nucleophilic substitution reactions. The kinetics of the reactions between 1-halo-2,4-dinitrobenzenes and primary or secondary aliphatic amines were studied in three solvent systems (PHBA + chloroform) where the synergism for the $E_T(30)$ polarity parameter is the rule. In all the aminodehalogenation reactions discussed the formation of the intermediate is the rate-determining step. The kinetic data show a tendency to decrease with decrease in the overall solvation capability of the binary mixture. In general, the reaction rates presented a gradual decrease in the PHBA solvent-rich zone and a large decrease at high co-solvent concentrations. The $E_T(30)$ values corresponding to binary dipolar hydrogen bond acceptor–hydrogen bond donor mixtures may be not generally valid for interpreting solvation effects on the reactions under consideration. © 1997 John Wiley & Sons, Ltd.

INTRODUCTION

The considerable influence of solvents on chemical and physical processes (reaction rates, mechanisms, selectivity, chemical equilibria, position and intensity of spectral absorption bands, liquid chromatographic separations) has been well established.[1] Chemists have usually attempted to understand solvent effects in terms of *polarity*, defined as the overall solution capabilities that depend on all possible (specific and non-specific) intermolecular interactions between solute and solvent molecules. Numerous reports on solvent polarity scales have been published in the last few decades.[2] These scales have been based on single and multiple parameter approaches and they are mainly derived from spectroscopic measurements.[3–5] More recently, Abraham[6] has proposed scales of solute hydrogen bond acidity and solute hydrogen bond basicity, and has devised a general solvation equation.

Negatively and positively solvatochromic dyes are particularly suitable as standard substances for the determination of empirical solvent parameters. Among these, by virtue of the exceptionally large extent of its solvatochromism, the

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negatively solvatochromic 2,6-diphenyl-4-(2,4,6-triphenyl-1-pyridinio)phenolate (**I**) or $E_T(30)$ dye, proposed by Reichardt,[7] is the most widely used. The interpretation of the $E_T(30)$ values for a single solvent is different from that for mixed solvents.

The chemical characteristics of solvent mixtures are customarily determined in the same manner as those of neat solvents by means of solvatochromic indicators. However, 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. On the other hand, solvent–solvent interactions can also affect solute–solvent interactions. Preferential solvation leads to non-linear relationships between solvatochromic polarity and solvent composition. Dawber *et al.*[8] proposed the deviation from linearity of the $E_T(30)$ of binary solvent mixtures as a measure of the extent of preferential solvation and related it to several thermodynamic and kinetic properties.

Several equations that relate the transition energy of the $E_T(30)$ indicator with the solvent composition have been derived and compared. The parameters obtained explain the synergism observed for some of the mixtures with strong hydrogen bond donors. Skwierczynski and Connors[9] proposed two different solvent exchange models to describe the $E_T(30)$ values of binary aqueous mixtures. More recently, Bosch and co-workers[10] derived a more general model based on a two-step solvent exchange model that can be effectively applied to synergetic mixtures.

In the present study, the $E_T(30)$ values of completely non-aqueous binary mixtures of several dipolar hydrogen bond acceptor solvents (PHBA) with chloroform and dichloromethane, taken as hydrogen bond donor solvents (HBD), were measured and interpreted. The acidic hydrogen atom in chloroform and dichloromethane can readily form complexes, via hydrogen bonding, with the oxygen atoms of the PHBA solvent molecules. Hence these mixtures are an interesting set of solvent systems where the possibility of synergetic effects on the indicator is present.

Additionally, it was of interest to evaluate the influence of solvent mixtures, in which the two solvents interact to form a hydrogen-bonded complex with polarity and $E_T(30)$ values higher than those of the two pure solvents, on the kinetics of some aromatic nucleophilic substitution reactions.

RESULTS AND DISCUSSION

Determination of $E_T(30)$ values

The binary mixtures between solvents that have a strong hydrogen bond acceptor and poor hydrogen bond capabilities with strong hydrogen bond donor solvents often present a synergetic effect for the $E_T(30)$ parameters. It has been reported that in these systems a 1:1 complex is formed by means of intermolecular hydrogen bonding. Mixtures of trialkyl phosphates with chloroform are a good example of such synergetic mixtures.[11,12]

The empirical solvent polarity parameter $E_T(30)$ was determined at 25°C for completely non-aqueous mixtures of dimethyl sulfoxide (DMSO), *N,N*-dimethylformamide (DMF), acetonitrile (AcN), nitromethane (NM), acetone (AC), butanone (BUT), cyclohexanone (CyH) and ethyl acetate (EAc) (PHBA solvents) with chloroform and dichloromethane (HBD co-solvents).

$E_T(30)$ is defined as the molar transition energy [kcal mol^{-1} (1 kcal=4.184 kJ)] derived from the longest wavelength solvatochromic UV/VIS absorption band of **I** (Reichardt's dye).[7a] This betaine dye presents a strongly negative solvatochromism owing to its highly dipolar electronic ground state relative to its less dipolar excited state. It exhibits a significant permanent dipole moment (suitable for dipole–dipole and dipole–induced dipole interactions), a large polarizable π-electron system (suitable for dispersion interactions), a substantial negative charge on the phenoxide oxygen [highly basic electron-pair donor center suitable for interactions with weak Brönsted acids (H-bonding) and Lewis acids (EPD/EPA bonding)] and a positive charge on the pyridinium nitrogen (sterically shielded). Therefore, the solvation effects of the betaine are more important for HBD and EPA solvents than for EPD solvents.[7b]

The longest wavelength UV/VIS absorption band of **I** was determined by varying the solvent composition systematically. Each binary system was studied at nine molar fractions of co-solvent.

The properties [$E_T(30)$ and Kamlet–Taft solvatochromic parameters][1a,13] of the pure solvents used to prepare the binary mixtures in this work are given in Table 1. DMSO, DMF, AC, BUT, CyH and EAc are in general strong PHBA and poor HBD solvents, whereas AcN and NM are dipolar, relatively strong HBA solvents with weak HBD properties. Chloroform and dichloromethane are polyhalogenated solvents, weak HBD and highly polarizable species. The $E_T(30)$ values of the pure solvents determined at 25°C are in good agreement with those reported in the literature. Tables

Table 1. Empirical parameters of pure solvents: polarity [$E_T(30)$ in kcal mol^{-1}], dipolarity/polarizability (π^*) and HBD and HBA abilities (α,β) (at 25°C)[1a,7b,13]

Solvent type	Solvent	$E_T(30)$	π^*	α	β
PHBA	EAc	38·1	0·55	0·00	0·45
	CyH	40·3[a]	0·76	0·00	0·53
	BUT	41·3	0·67	0·06	0·48
	AC	42·2	0·71	0·08	0·48
	DMF	43·8	0·88	0·00	0·69
	DMSO	45·0	1·00	0·00	0·76
	AcN	46·0	0·75	0·19	0·40
	NM	46·3	0·85	0·22	0·37
HBD	Chloroform	39·1	0·58	0·20	0·10
	Dichloromethane	40·9	0·82	0·13	0·00

[a] This work.

2 (co-solvent chloroform) and 3 (co-solvent dichloromethane) give the measured $E_T(30)$ values for all non-aqueous solvent mixtures studied over the full composition range from $X_{CoS}=0$ to $X_{CoS}=1$. Some of these binary systems [(DMSO+chloroform), (AC+chloroform) and (AC+dichloromethane)] have also been studied by other workers.[8a,11,12]

The interpretation of the $E_T(30)$ values as a function of the composition for the mixtures cited above suggests different behaviors. The data set can be divided into two general groups of binary mixtures according to the preferential solvation models for describing the $E_T(30)$ polarity parameter: (a) synergetic mixtures and (b) mixtures clearly not synergetic. The first group can be subdivided into (a′) mixtures with a high synergetic effect and (a″) mixtures with a moderate synergetic effect (including those that are on the verge of synergism).

Synergetic mixtures

These mixtures have $E_T(30)$ values higher than those of the two pure mixed solvents. The synergetic effects are observed in such solvent mixtures which form hydrogen bond complexes that are more polar than any one of the pure solvents. It has been suggested that mixtures of chloroform or dichloromethane with alkyl phosphates, dimethyl sulfoxide or acetone present a synergetic effect. This effect is also observed in mixtures of alcohols with acetonitrile or dimethyl sulfoxide.[14] These mixtures should be taken as ternary (or higher) solvent systems (solvent 1, solvent 2 and solvent 1–solvent 2 complexes). We considered the difference between the maximal $E_T(30)$ value of the binary mixture and the highest $E_T(30)$ value of the two pure solvents mixed as measurement of the synergetic effect (SE_{max}).

Mixtures with high synergetic effect. We have included in this set those binary mixtures that present $SE_{max} \geq 1.5$ kcal-mol^{-1}. Figure 1 shows the plots of $E_T(30)$ values as a function of the co-solvent mole fraction for (EAc+chloroform), (CyH+chloroform) and (BUT+chloroform) binary solvent mixtures. Each mixture exhibits a maximum in the curve. In all cases the maximum synergism is observed at lower chloroform concentration ($X_{Cl_3CH} \approx 0.3$) (region rich in PHBA solvent). Ethyl acetate, cyclohexanone and butanone

Table 2. $E_T(30)$ values (kcal mol^{-1}) for (PHBA solvent+chloroform) systems at 25°C

| PHBA solvent | Chloroform | mole | fraction | | | | | | |
	0·10	0·20	0·30	0·40	0·50	0·60	0·70	0·80	0·90
EAc	40·7	41·0	41·3	41·2	41·0	40·7	40·3	40·0	39·5
CyH	41·5	42·0	42·2	42·3	42·2	41·9	41·3	40·8	40·1
BUT	42·4	42·7	42·9	42·8	42·6	42·2	41·6	41·0	40·3
AC[a]	42·9	43·1	43·0	42·7	42·2	41·6	40·9	40·2	39·6
DMF	44·3	44·5	44·7	44·3	43·9	43·4	42·8	41·8	40·7
DMSO[b]	45·3	45·3	45·1	44·9	44·6	44·1	43·5	42·6	41·4
AcN	46·2	46·3	45·9	45·1	44·4	43·8	42·9	42·0	41·0
NM	46·0	45·8	45·4	44·9	44·4	43·9	43·1	42·2	41·3

[a]Data from Refs 11–13.
[b]Data from Ref. 11.

Table 3. $E_T(30)$ values (kcal mol^{-1}) for (PHBA solvent+dichloromethane) systems at 25°C

| PHBA solvent | Dichloromethane | mole | fraction | | | | | | |
	0·10	0·20	0·30	0·40	0·50	0·60	0·70	0·80	0·90
EAc	39·3	40·0	40·3	40·5	40·7	40·8	40·9	41·0	40·9
CyH	41·1	41·5	41·6	41·7	41·8	41·8	41·7	41·5	41·3
BUT	41·6	41·9	42·0	42·0	42·0	41·9	41·8	41·6	41·4
AC[a]	42·8	42·9	42·9	42·9	42·8	42·6	42·4	42·2	41·8
DMF	43·9	43·9	43·8	43·6	43·4	43·2	42·5	41·7	
DMSO	45·2	45·2	44·9	44·7	44·3	43·8	43·2	42·7	42·0
AcN	45·7	45·4	45·0	44·7	44·3	43·8	43·2	42·7	42·0
NM	45·9	45·5	45·1	44·7	44·3	43·8	43·2	42·6	41·9

[a]Data from Ref. 12.
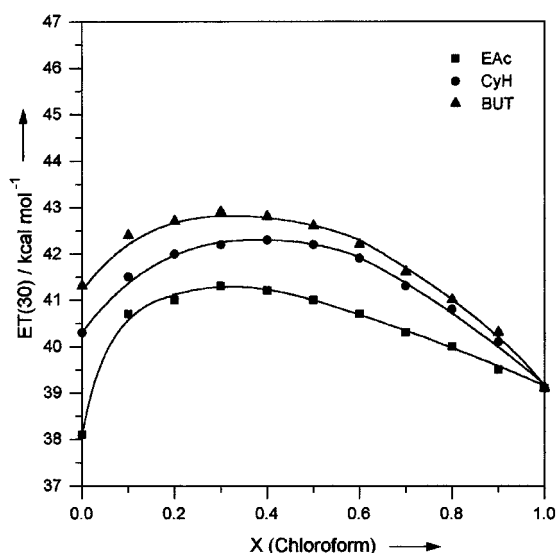
Figure 1. Plot of $E_T(30)$ *vs* co-solvent mole fraction for (EAc+chloroform), (CyH+chloroform) and (BUT+chloroform) solvent systems at 25°C

Figure 2. Plot of $E_T(30)$ *vs* co-solvent mole fraction for (AC+chloroform), (DMF+chloroform), (DMSO+chloroform) and (AcN+chloroform) solvent systems at 25°C

interact with the HBD solvent chloroform forming hydrogen-bonded complexes with a high dipole moment. The properties for this binary solvent system are best correlated using the ideal association model (A2B), and 1:1 and 1:2 complexes would be present in the solution.[15] The polarities of the pure solvent mixed do not differ too much, and the betaine dye can be preferentially solvated by the complex, yielding $E_T(30)$ values higher than the $E_T(30)$ values of the pure solvent mixed. The synergetic effect is more important for the (EAc+chloroform) system ($SE_{max} \approx 2 \cdot 2$ kcal mol^{-1}) than for (CyH+chloroform) and (BUT+chloroform) solvent mixtures ($SE_{max} \approx 2 \cdot 0$ and $1 \cdot 6$ kcalmol^{-1}, respectively). This is probably due to the fact that EAc–chloroform interactions are stronger than CyH–chloroform and BUT–chloroform interactions. These systems also exhibit a large positive deviation from linearity ($> 2 \cdot 5$ kcal mol^{-1}), indicating a strong preferential solvation effect by the '*mixed solvent*' obtained. It seems that in order to account for the variation in composition of $E_T(30)$ values of these mixtures, the formation 1:1 and 1:2 complexes and self-association of chloroform molecules need to be considered. Then, the preferential solvation order of the solvatochromic indicator would be 'PHBA solvent–chloroform complex' > 'chloroform' > 'PHBA solvent.'

Mixtures with moderate or weak synergetic effect. We have included in this set those binary mixtures that present $SE_{max} \lesssim 1$ kcal mol^{-1}.

Figures 2 (co-solvent chloroform and 3 (co-solvent dichloromethane) show shifts in the molar transition energy $E_T(30)$ with an increase in co-solvent concentration for the binary solvent systems (AC+chloroform), DMF+chloroform), (DMSO+chloroform) and (AcN+chloroform)
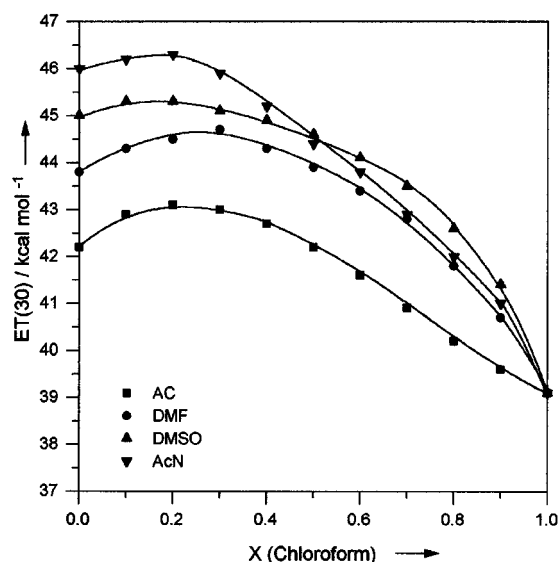
(Figure 2) and (EAc+dichloromethane), (CyH+dichloromethane), (BUT+dichloromethane), (AC+dichloromethane), (DMF+dichloromethane) and (DMSO+dichloromethane) (Figure 3). These systems exhibit a moderate or very low synergetic effect, and the general trends observed are detailed as follows. The synergetic
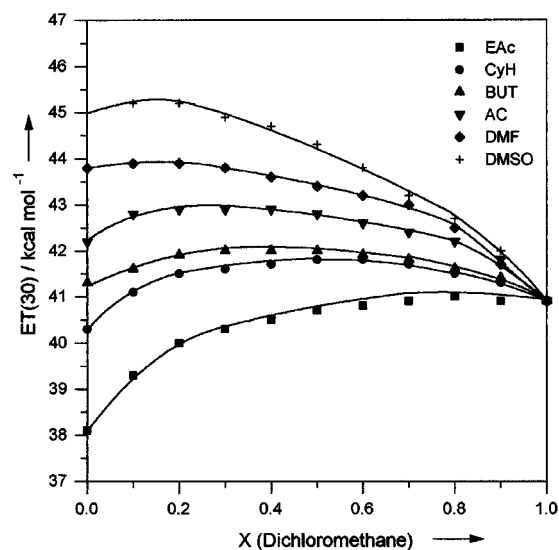

Figure 3. Plot of $E_T(30)$ *vs* co-solvent mole fraction for (EAc+dichloromethane), (CyH+dichloromethane), (AC+dichloromethane), (DMF+dichloromethane) and (DMSO+dichloromethane) solvent systems at 25°C

effects for the mixtures in which the co-solvent is dichloromethane are slightly lower than those with chloroform as co-solvent, probably because that PHBA solvent–chloroform interactions are stronger than PHBA solvent–dichloromethane interactions. In general, for both types of systems these effects decrease when the polarity of the HBA solvent increases. In all cases, the betaine dye is preferentially solvated by the solvent–solvent complex rather than by pure solvents.

The properties of (PHBA solvent+chloroform) systems are similar to those binary mixtures cited before (high synergetic effect). All systems exhibit the maximum synergism at lower chloroform concentrations; the $E_T(30)$ values increase the mole fraction, $X_{Cl_3CH} \approx 0.2$–0.3 and then decrease to a constant value for pure chloroform. Once again, the ideal association model (A2B) would be applicable.[15] It can be seen that the synergism is inversely proportional to the difference in $E_T(30)$ of the pure solvents [SE_{max} vs $\Delta E_T(30)$] (Figure 4).

For the (PHBA solvent+dichloromethane) systems, the relationship between SE_{max} and $\Delta E_T(30)$ is given in Figure 5. The behavior of the (EAc+dichloromethane) binary mixture is striking, probably owing to the difference in the $E_T(30)$ values corresponding to the pure solvents [$\Delta E_T(30)=2.8$ kcal mol^{-1}, with dichloromethane having the higher value]. In this case, the SE_{max} is observed in the zone rich in HBD solvent, whereas in the other solvent mixtures the maxima are moved towards the PHBA solvent-rich region.

The PHBA solvents–dichloromethane association models are different from those corresponding to PHBA solvents–chloroform interactions. In (PHBA solvent–dichloromethane) systems, the probable presence
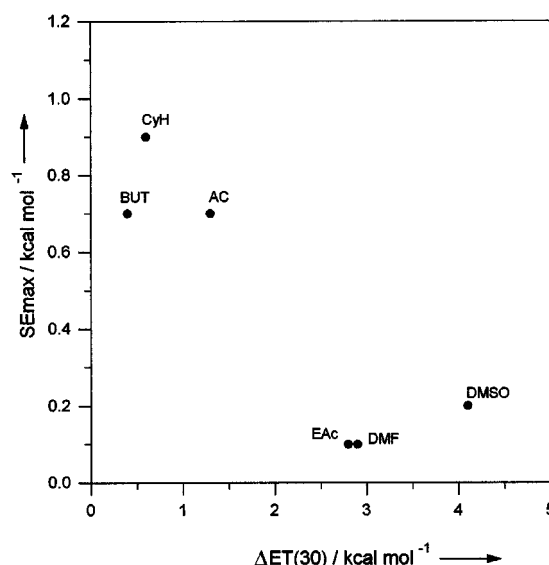
Figure 5. Plot of SE_{max} vs $\Delta E_T(30)$ of the pure solvent mixed for (PHBA solvent+dichloromethane) systems at 25°C

of an intermolecular complex of at least two different stoichiometries (2:1 and 1:2 complexes, with the absence of a 1:1 complex) has been reported.[12]

Non-synergetic mixtures

If the two mixed solvents have very different polarities, the polarity of the solvent–solvent complex is intermediate between those of the pure solvents. Alternatively, a maximum is not obtained when the non-associated component, having a low value of the property, does not interact appreciably with the associated component but only dilutes it. Then, the mixture attains a considerable value of $E_T(30)$, even when only a small amount of the latter is added and the curve shows a steep portion, followed by another of much lower slope.[16]

Figure 6 shows a plot of $E_T(30)$ values as a function of co-solvent mole fraction for the (NM+chloroform) solvent system. This binary mixture does not exhibit a synergetic effect. A gradual decrease in $E_T(30)$ values in the zone rich in NM and a large decrease at high chloroform concentrations can be observed. The shape of the curve indicates that the preferential solvation of the solvatochromic indicator would be more important with nitromethane than with chloroform. Nitromethane is a very polar solvent with hydrogen bond donor ability ($\alpha=0.22$). Consequently, it competes with the co-solvent for the betaine phenoxide oxygen. In this case, the difference in polarity between the two mixed solvents is substantial.

Figures 7 show the plots of $E_T(30)$ values as a function of the co-solvent mole fraction for (AcN+dichloromethane) and (NM+dichloromethane) solvent mixtures. In both cases, the polarities of the pure solvents are different. These
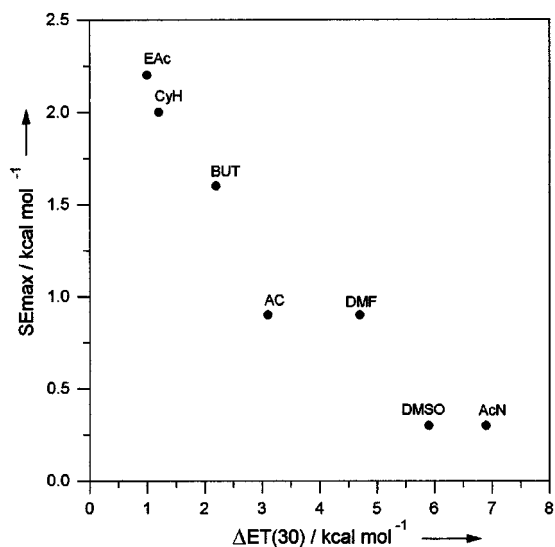
Figure 4. Plot of SE_{max} vs $\Delta E_T(30)$ of the pure solvents mixed for (PHBA solvent+chloroform) systems at 25°C
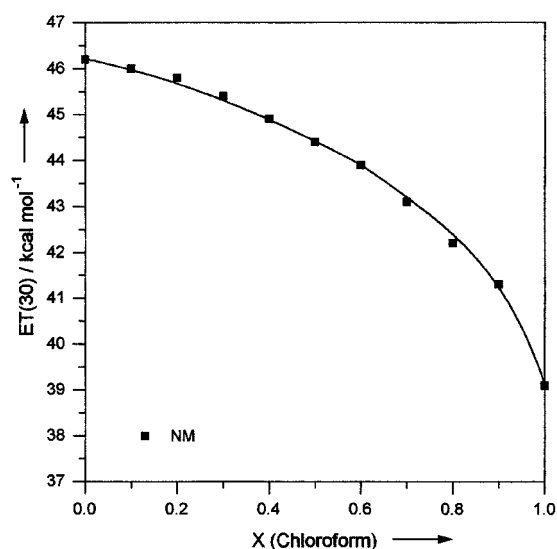
Figure 6. Plot of $E_T(30)$ *vs* co-solvent mole fraction for (NM + chloroform) solvent system at 25°C

systems exhibit similar behavior, giving nearly linear curves [indicating a gradual decrease in $E_T(30)$ values with an increase of dichloromethane concentration], small deviations from additivity and the absence of synergetic effects. Nearly linear curves are obtained when the mixed solvents are associated to nearly the same extent and interact mutually to form similar associates. In fact, acetonitrile and nitromethane have very similar polarities and hydrogen-

bond capabilities.[17] Nitromethane and acetonitrile have lower hydrogen bond acceptor capabilities than the rest of the PHBA solvents treated in this work, and their hydrogen bond donor ability competes with dichloromethane in the solvation of the betaine dye.

Thermo-solvatochromism

It is known that solvent polarity is temperature dependent. In addition to its negative solvatochromism, pyridinium *N*-phenoxide betaine dyes also exhibit negative thermosolvatochromism caused by the increased differential stabilization of the betaine ground state, relative to its less dipolar excited state, with a decrease in temperature.[2,18] It was therefore of interest to determine the $E_T(30)$ values for (EAc + chloroform) and (AC + chloroform) binary mixtures at different temperatures, because these systems present synergetic effects at 25°C. The former binary mixture under consideration has the highest synergism in the series explored and the latter corresponds to a mixture with a negligible synergetic effect.

In addition to the $E_T(30)$ values at 25°C corresponding to the cited binary solvent systems given in Table 2, further measurements were made at 15 and 40°C. Figures 8 and 9 show the shifts in molar transition energy $E_T(30)$ with increase in chloroform concentration for (EAc + chloroform) and (AcN + chloroform), respectively, at 15, 25 and 40°C. In each system the $E_T(30)$ values decrease with increase in temperature, which is in agreement with the expected temperature effects.

In general, it is found that synergism increases with decrease in temperature because the change in temperature has a large effect on the equilibrium constant for hydrogen bond formation. This can be observed in Figure 8 for ethyl

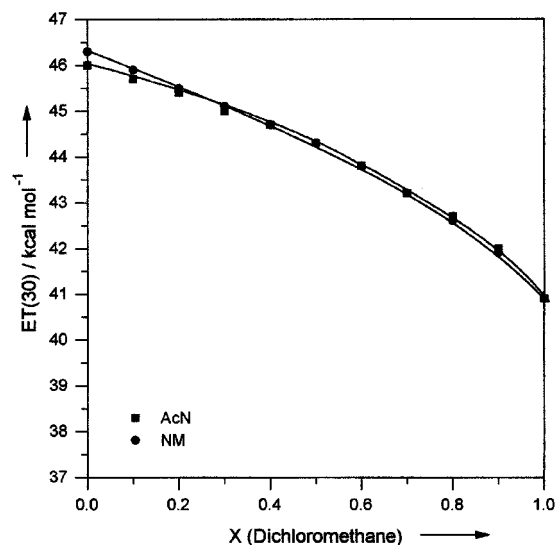Figure 7. Plot of $E_T(30)$ *vs* co-solvent mole fraction for (AcN + dichloromethane) and (NM + dichloromethane) solvent systems at 25°C
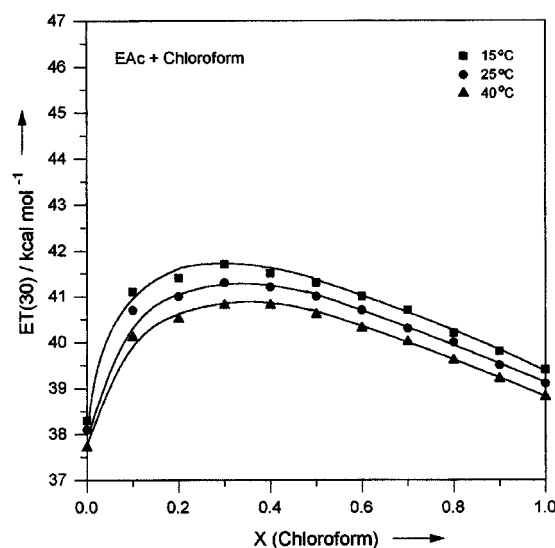

Figure 8. Plot of $E_T(30)$ *vs* co-solvent mole fraction for (EAc + chloroform) solvent system at 15, 25 and 40°C
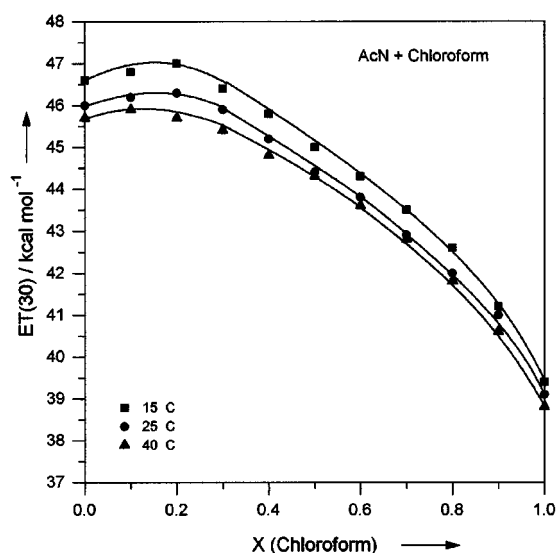
Figure 9. Plot of $E_T(30)$ vs co-solvent mole fraction for (AcN + chloroform) solvent system at 25, 25 and 40°C

Scheme 1

acetate–chloroform mixtures $[\Delta E_T(30)_{max} = 2\cdot3 \text{ kcal mol}^{-1}$ at 15°C, $2\cdot2$ kcal mol^{-1} at 25°C and $2\cdot0$ kcal mol^{-1} at 40°C] and in Figure 9 for acetonitrile–chloroform mixtures $[\Delta E_T(30)_{max} = 0\cdot4$ kcal mol^{-1} at 15°C, $0\cdot3$ kcalmol^{-1} at 25°C and $0\cdot2$ kcal mol^{-1} at 40°C]. This would also be connected with the different variations of the $E_T(30)$ values of the hydrogen bond complex with temperature.[19] In the two cases explored it is possible to note that the solvent systems support the model of preferential solvation for the chemical probe with independence of temperature. We observed only for the (AcN + chloroform) system a slight shift of SE_{max} towards the PHBA solvent-rich zone with an increase in temperature.

Synergetic binary mixtures for $E_T(30)$: Solvent effects on aromatic nucleophilic substitution reactions

Solvent effects on aromatic nucleophilic substitution (ANS) reactions involving halonitrobenzenes with amines were reported in the 1960s, including mixed solvents.[20] The rate of ANS reactions is notably affected by the solvent properties. Since the first pioneering studies,[21] different contributions have been reported to show how extensive and complex the interactions of the substrate and/or the intermediates with the solvent molecules are.[22]

The gross mechanism of ANS reactions in all solvents when either primary or secondary amines are the nucleophiles is represented in Scheme 1: 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.
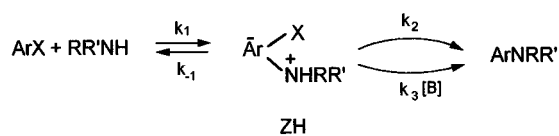
The reactions between 1-halo-2,4-dinitrobenzenes and aliphatic amines were extensively investigated in both polar and apolar solvents. In polar solvents the reactions followed a second-order kinetic law (first in both reagents), while in apolar solvents the experimental order in amine was in the range 1–3, depending on the nature of the solvent and the nature of the amine.[23,24] Recently, the evidence for the mechanisms proposed for ANS reactions by primary or secondary amines in aprotic solvents of low relative permittivity has been reviewed.[25] The reaction order >1 in nucleophiles was explained by the presence of base catalysis (usual two-step mechanism), and the catalysis can be performed by the reacting amine (autocatalysis). When catalysis is observed, the spontaneous breakdown of the ZH intermediate becomes the rate-limiting step and this prefers to evolve towards the products via a catalyzed pathway. This interpretation is generally accepted but it does not explain some experimental kinetic results (e.g. the kinetic behavior of the primary aliphatic amines in comparison with the kinetic behavior of the secondary aliphatic amines).[26] As an alternative interpretation, a different reaction pathway has been proposed to explain the enhancement of the reaction rate by increasing the initial amount of the nucleophile. This explanation agrees with the presence in the reaction mixture of interactions between the substrate and the amine yielding molecular complexes. An n–π donor–acceptor interaction was reported for interactions between nitroaromatic compounds and aliphatic amines, and the fact that fluoro derivatives are more prone to interact than the chloro derivatives confirms the possibility that hydrogen bonding would be an important additional interaction.[27]

In previous studies, we have reported the influence of solvent effects on the reactions of 1-halo-2,4-dinitrobenzenes with piperidine in an attempt to produce a more systematic analysis of the ways in which solvent may affect reaction rates, especially in connection with the employment of the empirical solvent polarity parameter $E_T(30)$. Particularly detailed studies of solvent effects have been carried out with one of the simplest systems of ANS: the reaction of 1-chloro-2,4-dinitrobenzene (DNCB) with piperidine (PIP).[28] The kinetic data in several aprotic solvents are well correlated by the Dimroth–Reichardt solvent polarity scale $E_T(30)$, and the correlation is remarkably good if HBD solvents are excluded. On the other hand, the second-order rate coefficients for the reaction development in different alcohols are not well correlated by $E_T(30)$ parameters. The reactivity in hydroxylic solvents is inversely proportional to the hydrogen bond donating ability of the solvents. In addition, the kinetics of

the reaction between 1-fluoro-2,4-dinitrobenzene (FDNB) and PIP were determined in several polar and apolar aprotic solvents with different structural characteristics.[29] Except for the HBD solvents (chloroform, acetonitrile and nitromethane), the second-order rate coefficients in the rest of the solvents explored were sensitive to an increase in amine concentration, indicating neat 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 of the aprotic solvents; those solvents which are HBD assist the departure of fluorine with the formation of the intermediate being 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 $[B] \leqslant 10^{-2}$ M. For higher amine contents increasing deviations were found.

More recently, we have studied the CDNB + PIP reaction in two different models of completely non-aqueous binary mixtures on which preferential solvation is the rule, but without synergetic effects for the $E_T(30)$ parameter.[30] For (aprotic solvent + toluene) mixtures a property of mixed solvents would be defined by means of $E_T(30)$ values. In this kind of mixture the solvent effects on the reaction were similar to those of pure aprotic solvents. For (aprotic solvent + methanol) systems the presence of the protic solvent in the mixture strongly determines the solvent effects on the reaction and the chemical probe under consideration may not be valid to interpret the reaction solvation model.

Kinetic determinations

In the first part of this work, we have characterized several completely non-aqueous binary mixtures [(HBA aprotic solvent + chloroform or dichloromethane)] that present a synergetic effect for the $E_T(30)$ parameter. In this connection, the kinetics of the reactions (CDNB + piperidine), (CDNB + *n*-butylamine) and (FDNB + *n*-butylamine) were studied at 25°C in three of those mixtures: (EAc + chloroform), (AcN + chloroform) and (DMSO + chloroform). The first one shows the highest synergetic effect among all the mixtures explored, and the other two were classified as moderately (or scarcely) synergetic.

Each binary mixture was explored at different compositions and the influence of amine concentration was studied in the three kinds of reactions. 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)-butylamine, respectively], and proved to be first order in the corresponding substrate. The second-order rate coefficients, k_A, calculated from the experimental pseudo-first-order rate coefficients, k_ψ, are listed in Tables 4 (CDNB + piperidine reaction), 5 (CDNB + *n*-butylamine reaction) and 6 (FDNB + *n*-butylamine reaction). The kinetic data show a general tendency for a decrease in k_A values and an increase in co-solvent concentration due to the decrease in the

Table 4. Second-order rate coefficients, k_A (l mol^{-1} s^{-1}), for the reaction of 10^{-4} M 1-chloro-2,4-dinitrobenzene (**I**) with piperidine at 25°C

	[Piperidine] (M)			
Solvent[a]	0·02	0·04	0·08	0·16
EAc + chloroform				
0·10	0·232	0·225	0·229	0·231
0·30	0·203	0·209	0·209	0·203
0·50	0·162	0·163	0·162	0·165
0·70	0·131	0·147	0·128	0·135
0·90	0·104	0·111	0·104	0·118
AcN + chloroform				
0·10	0·530	0·547	0·537	0·530
0·30	0·384	0·399	0·405	0·393
0·50	0·322	0·334	0·330	0·320
0·70	0·231	0·236	0·237	0·238
0·90	0·184	0·192	0·193	0·188
DMSO + chloroform				
0·10	1·88	1·80	1·80	1·87
0·30	1·31	1·43	1·45	1·46
0·50	0·962	0·974	0·958	0·953
0·70	0·514	0·528	0·531	0·517
0·90	0·205	0·240	0·226	0·221

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

Table 5. Second-order rate coefficients, $10^2 k_A$ (l mol^{-1} s^{-1}), for the reaction of 10^{-4} M 1-chloro-2,4-dinitrobenzene (**I**) with *n*-butylamine at 25°C

[a]	[*n*-Butylamine] (M)			
Solvent	0·50	1·00	1·50	2·00
EAc + chloroform				
0·10	0·686	0·835	0·975	1·11
0·30	0·524	0·658	0·780	1·17
0·50	0·363	0·425	0·518	0·649
0·70	0·225	0·293	0·370	0·475
0·90	0·117	0·159	0·209	0·287
AcN + chloroform				
0·10	1·09	1·26	1·41	1·60
0·30	0·753	0·896	1·01	1·13
0·50	0·551	0·615	0·718	0·839
0·70	0·429	0·572	0·675	0·885
0·90	0·173	0·258	0·319	0·449
DMSO + chloroform				
0·10	13·47	13·68	11·16	14·71
0·30	8·68	11·72	10·80	11·64
0·50	3·86	3·94	4·77	5·15
0·70	2·07	2·51	2·64	3·03
0·90	0·361	0·438	0·586	0·668

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

overall solvation capability of the solvent mixture. As can be observed, no acceleration in rate is produced for an increasing amount of amine in the three solvent systems for (CDNB+piperidine) and (FDNB+n-butylamine) reactions. A slight acceleration in reaction rate with increase in amine concentration was verified for (CDNB+n-butylamine) reactions in almost all the binary mixtures explored. As the k_3/k_2 values are ≤3, we do not regard these reactions as being catalyzed and conclude that in all the amino-dehalogenation reactions studied the formation of the intermediate is rate-determining. Additionally, the (CDNB+PIP) reactions carried out in (EAc+chloroform) mixtures were examined

Table 6. Second-order rate coefficients, k_A (lmol^{-1} s^{-1}), for the reaction of 5×10^{-5} M 1-fluoro-2,4-dinitrobenzene (**I**) with n-butylamine at 25°C

Solvent[a]	[n-Butylamine] (M)			
	0.002	0.004	0.008	0.016
EAc+chloroform				
0.10	6.95	6.80	7.15	6.80
0.30	4.34	4.48	4.62	4.84
0.50	3.20	3.24	3.19	3.24
0.70	1.72	1.78	1.82	1.67
0.90	0.425	0.427	0.421	0.425
AcN+chloroform				
0.10	7.87	7.10	9.38	8.23
0.30	6.23	6.73	7.20	7.13
0.50	3.91	4.07	4.54	4.48
0.70	2.97	3.07	3.12	3.02
0.90	2.32	2.48	2.40	2.40
DMSO+chloroform				
0.10	74.5	81.5	98.7	95.0
0.30	79.1	60.1	80.3	74.0
0.50	38.4	41.5	46.3	49.4
0.70	11.0	10.8	11.2	11.2
0.90	2.61	2.72	2.53	2.71

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

at 15 and 40°C. Table 7 lists the second-order rate coefficients, k_A, and the calculated activation parameters.

In all solvent systems, when the substrate is CDNB the variation of the rate constants with a change in amine follows the usual pattern found in ANS reactions.[31] Comparing amines of approximately the same basicity, piperidine is more nucleophilic than n-butylamine. Moreover, the experimental results indicate that FDNB is more reactive than CDNB.

In the three kinds of ANS reactions analyzed, the sequence of relative reactivities in (DMSO+chloroform), (AcN+chloroform) and (EAc+chloroform) systems is in agreement with the solvating power of the mixed solvents [polarity defined by $E_T(30)$ values]. The rate constants values decrease from (DMSO+chloroform) through (AcN+chloroform) to (EAc+chloroform) binary mixtures. The greatest change in rate occurs between (DMSO+chloroform) and (AcN+chloroform) solvent systems at low co-solvent concentration. It is well known that when amines are the nucleophiles, the transition state for bimolecular ANS reactions are hydrogen bond donors and are solvated more strongly by PHBA solvents (DMSO is the polar solvent with the highest β value in the series shown in Table 1; AcN and chloroform have HBD properties).

We observed no synergetic effect for the second-order rate coefficients in any binary solvent system employed to carry out the different ANS reactions. In relation to the $E_T(30)$ values of binary solvent systems, it is accepted that the synergetic effects are associated with the increase in 'polarity' of the mixture as a consequence of the 'PHBA solvent–HBD solvent' complex formation. This 'improved polarity' is not 'reflected' by the critical states of the ANS reactions analyzed. Figure 10 gives the profiles corresponding to the evolution in each case of log k_A as a function of the co-solvent concentration. In general, the shapes of the curves show a gradual decrease in log k_A in the zone rich in PHBA solvent and a large decrease at high chloroform concentration. This type of solvent effect is more intense for those reactions in which the nucleophile is a primary amine and it does not depend on the halogen involved. When the

Table 7. Second-order rate coefficients, $10^2 k_A$ (lmol^{-1} s^{-1}), for the reaction of 10^{-4} M 1-chloro-2,4-dinitrobenzene (**I**) with piperidine in (EAc+chloroform) binary mixtures at 15 and 40°C and the activation parameters

Solvent[a]	[Piperidine] (M)							
	15°C			40°C			$\Delta H^{\neq}$ (kJ mol^{-1})	$-\Delta S^{\neq}$ (J mol^{-1}K^{-1})
	0.02	0.08	0.16	0.02	0.08	0.16		
0.10	0.150	0.172	0.182	0.425	0.430	0.435	26.6	170.0
0.30	0.155	0.160	0.160	0.387	0.394	0.391	25.1	173.6
0.50	0.110	0.117	0.118	0.289	0.293	0.290	25.5	174.4
0.70	0.110	0.115	0.110	0.290	0.280	0.280	26.0	174.4
0.90	0.094	0.098	0.094	0.243	0.248	0.245	26.8	173.4

[a]The concentrations of the binary mixtures are in mole fraction of chloroform.
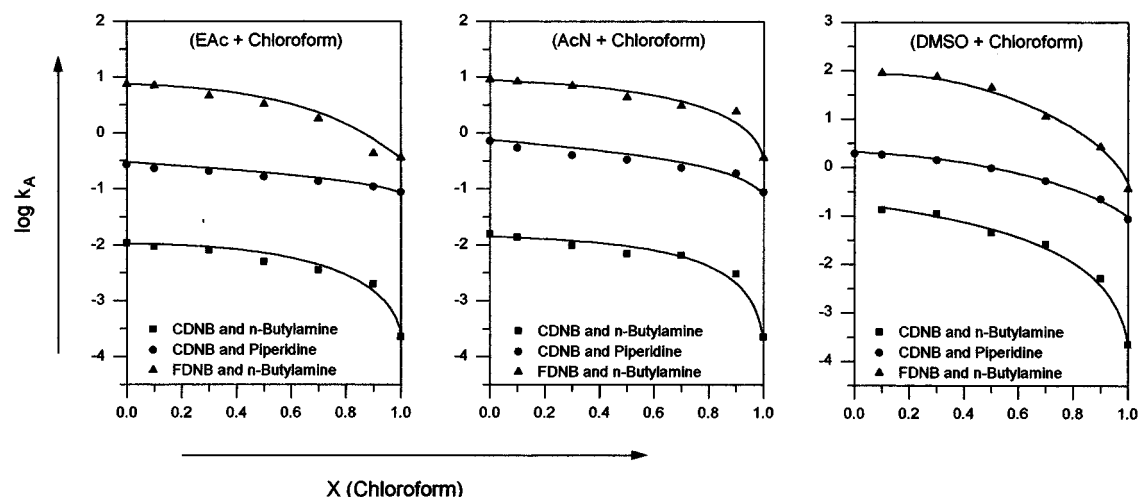
Figure 10. Plot of log k_A *vs* co-solvent mole fraction for the reaction of 1-halo-2,4-dinitrobenzenes with primary or secondary amines in (PHBA+chloroform) solvent systems at 25°C

substrate contains an *o*-nitro group, hydrogen bonding occurs in the intermediate between the ammonium hydrogen atoms and the oxygen atom of the nitro group. When the nucleophile is a secondary amine, there is only one ammonium hydrogen atoms which is involved in the 'built-in solvation.' When the nucleophile is a primary amine, a second hydrogen atom is available to interact with PHBA solvents and a more significant preferential solvation would occur.

Correlation analysis

The often linear correlation between empirical solvent parameters and other solvent-dependent properties (e.g. logarithms of rate and equilibrium constant, absorption energies) can be considered as manifestations of general linear free-energy relationships (LFERs).[7a,32] It is possible to interpret the solvent effects with the aid of model processes that yield the same or similar effects. However, the use of individual empirical solvent polarity parameters should be limited in a first approach to largely analogous processes. Through the analysis of solvent effects on the reaction of DNCB with PIP carried out in several (aprotic solvents +toluene) systems, we have recently demonstrated that there exists a satisfactory correlation between $E_T(30)$ values and the logarithms of the rate constants.[30a] These binary solvent mixtures have no synergetic effects for the chemical probe.

We have now extended the preceding correlation analysis to the kinetic data for the cited ANS reactions in (PHBA solvent+chloroform) systems. The correlations were assessed by the evaluation of the correlation coefficients (r) and the standard deviations (s). The results are presented in Table 8. The regression equations summarized in Table 8 are reasonably good for the (DMSO+chloroform) system in

all the reactions explored ($r \approx 0.99$, and $s \approx 0.09$–0.17). With the (AcN+chloroform) system the regression equations are relatively good ($r \geq 0.95$ and $s \approx 0.09$–0.17), except for (CDNB+*n*-butylamine) reaction data. However, the correlations are very poor for the (EAc+chloroform) system at the three temperatures explored (we have not included these results in Table 8) ($r < 0.3$ and $s \approx 0.6$). Therefore, the chemical probe under consideration is not generally valid for interpreting the solvation effects produced by this kind of solvent mixture on the reactions, and the present situation would be related to the influence and extension of synergism exhibited by the $E_T(30)$ polarity parameter.

Marcus's interesting point of view introduces the discussion of the notion of 'property of a mixed solvent' and whether such property can be defined by means of chemical probes.[33] Probes which interact with the components of the mixture less strongly than the complicated self- or mutual

Table 8. Correlation coefficient (r) standard error of the estimate (s) and number of data points (n) of log k_A vs $E_T(30)$ for ANS reactions in (PHBA solvent+chloroform) systems, including the pure solvents, at 25°C

Reaction	PHBA solvent	r	s	n
CDNB+piperidine	AcN	0·962	0·091	7[a]
	DMSO	0·986	0·094	7[a]
CDNB+*n*-butylamine	AcN	0·916	0·279	7[a]
	DMSO	0·989	0·170	6[b]
FDNB+*n*-butylamine	AcN	0·946	0·172	7[a]
	DMSO	0·989	0·170	6[b]

[a]The correlations were calculated for X_{Cl_3CH}=0·00, 0·10, 0·30, 0·50, 0·70, 0·90 and 1·00.
[b]The correlations were calculated for X_{Cl_3CH}=0·10, 0·30, 0·50, 0·70, 0·90 and 1·00.

interactions of the solvent would have similar environments and provide convergence with the expression employed for neat solvents.

Seemingly, it is possible to relate these concepts to the results of our studies of the solvent effects on ANS reactions. The influence of (aprotic solvent + aprotic non-HBD co-solvent) systems on simple models of ANS reactions is very similar to those of aprotic pure solvents; then, a chemical property (polarity) of 'mixed solvents' would be defined by means of the $E_T(30)$ parameter. In these cases, convergence exists with the expression employed for neat solvents. In contrast, for (aprotic solvent + protic co-solvent) systems or when the aprotic co-solvent (e.g. chloroform) has HBD ability, the mentioned convergence does not exist and preferential solvation precludes the practical use of $E_T(30)$ in these mixtures.

CONCLUSIONS

On the basis of the results obtained from the $E_T(30)$ and kinetic determinations using several (polar HBA solvent + chloroform or dichloromethane) binary systems, the following conclusions can be drawn.

Most of the binary solvent mixtures explored presented synergetic effects for the $E_T(30)$ polarity parameter, which is generally revealed in the PHBA solvent-rich zone. The extent of the synergism is related to the difference in polarities of the two solvents mixed and with their ability to form hydrogen-bonded complexes. If the PHBA solvent part of these types of mixtures also has some hydrogen-bond donor property, synergism is not observed. The synergetic effects are more significant in those systems in which chloroform is the co-solvent.

In the cases of synergetic mixtures, the preferential solvation models for the probe molecule and the complicated interactions of the solvent mixed are not confirmed when the solutes are the reagents and/or intermediates corresponding to ANS reactions between halodinitrobenzenes and primary or secondary amines. As can be expected, these solvent mixtures do not produce kinetic synergism, and consequently the $E_T(30)$ parameter is not appropriate to describe the solvent effects on these reactions when they are carried out in such binary mixtures. This situation is more expressive for solvent systems with strong synergism. Instead, in mixtures which have moderate (or negligible) synergetic effects for the indicator, the parameter–kinetics correspondence is better.

The preferential solvation model produced by these kinds of binary mixtures of solvents on all the ANS reactions studied seems to be similar. The reaction rates present a gradual decrease in the HBA solvent rich zone of the mixture and a large decrease at high co-solvent concentration (chloroform is a less polar HBD solvent). Apparently, the HBD character of mixtures play a role in the solvent effects on reaction rate (e.g. the reaction of FDNB with *n*-butylamine is not base catalyzed when it is developed in the three binary solvent systems cited above).

EXPERIMENTAL

Reagents and solvents. 1-Chloro-2,4-dinitrobenzene, 1-fluoro-2,4-dinitrobenzene and piperidine were purified as described previously.[28a] *n*-Butylamine (Aldrich, 99%, b.p. 78°C) was fractionally distilled from sodium. *N*-(2,4-Dinitrophenyl)piperidine and *N*-(2,4-dinitrophenyl)butylamine were prepared and purified by methods reported previously. 2,6-Diphenyl-4-(2,4,6-triphenyl-1-pyridinio)phenolate (Reichardt's dye, Aldrich, 95%, m.p. 271–275°C) was used without any further purification. Cyclohexanone and butanone were dried for several days over anhydrous sodium sulfate and fractionally distilled twice. The rest of the solvents were purified as reported previously[28,29] 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.

$E_T(30)$ measurements. The pure solvents were mixed in appropriate proportions by weight to give binary solvent mixtures of various compositions. 2,4-Diphenyl-4-(2,4,6-triphenyl-1-pyridinio)phenolate solutions were prepared just prior to use. Visible spectra of sample solutions in 10 mm cells were recorded at 15, 25 and 40°C by using a Perkin-Elmer Model 124 UV VIS spectrophotometer and a Zeiss PMQ 3 UV VIS spectrophotometer equipped with a data-acquisition system and a thermostated cell holder. Temperatures were measured in the cell and were accurate to within ±0·1°C. The $E_T(30)$ values were determined from the longest-wavelength UV VIS absorption band of Reichardt's betaine dye and were calculated according to the equation $E_T(30)$ [kcal-mol^{-1}] = $hcvN$ = $2·859 \times 10^{-3}$ ν [cm^{-1}].

Kinetic procedures. The kinetics of the reactions were studied spectrophotometrically.[28a] 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 primary or 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 coefficients were obtained as described previously. In all cases, the 'infinity' values, A_∞, was determined experimentally 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. Values of $\Delta H^{\neq}$ were accurate to $ca \pm 0.4$ kJ mol^{-1} and values of $\Delta S^{\neq}$ to ± 8 J mol^{-1} K^{-1}.

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