Effect of Acetonitrile–Water Mixtures on the Reaction of Dinitrochlorobenzene and Dinitrochlorobenzotrifluoride with Hydroxide Ion

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ABSTRACT: The kinetics of alkaline hydrolysis of 2-chloro-3,5-dinitrobenzotrifluoride **1** and 1-chloro-2,4-dinitrobenzene **2** were studied in various acetonitrile–water (AN–H$_2$O) mixtures (10–90% w/w) at different temperatures. Thermodynamic parameters $\Delta H^{\#}$ and $\Delta S^{\#}$ show great variation, whereas $\Delta G^{\#}$ appears to vary little with the solvent composition presumably due to compensating variations. The results are discussed in terms of the solvent parameters such as preferential solvation, dielectric constant, polarity/polarizability, and hydrogen bond donor and acceptor parameters. It has been found that the factors controlling the reaction rates are the desolvation of OH$^-$, the solvophobicity of the medium, and free water molecules in rich AN mixed solvent. The data showed that the solvatochromic parameters of (AN–H$_2$O) mixed solvent are destroyed in the presence of excess OH$^-$. © 2010 Wiley Periodicals, Inc. Int J Chem Kinet 42: 453–463, 2010

INTRODUCTION

The rate of chemical reactions in solutions can be affected by two solvent effect types: nonspecific and specific. Nonspecific solvent effects denote the electrostatic interaction of the solvent molecules with the ionic substances, whereas specific solvent effects denote the chemical interaction due to the presence of

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electron-donating and/or electron-accepting centers in the solvent molecules. Several factors influence these solvent effects on chemical reaction rates; their relative importance seems to be a function of substrate, detailed mechanism of reaction, and experimental conditions [1]. A solvent would not only provide a background for the reaction to occur but also stabilize the reactants and activated complex by solvating them [2–6]. According to Gholami and Habibi [7], solvent–solute interactions are much more complex in reactions involving a neutral molecule and strongly solvated species, in particular, the alkoxide and hydroxide ions, may be partially or

completely dominated by the mixed solvents than by pure solvents because of preferential solvation by any of the components present in the solvent mixture. Because of this, the local composition of the solvent shell must be different from that of the bulk [8–9]. Another factor is the energetic desolvation barrier of the base accompanied by the introduction of the neutral reagent into its solvation shell [10].

The preferential solvation in a binary solvents mixture has an important role in solution chemistry for explaining spectroscopic, equilibrium, and kinetic data [11–13]. Chatterjee and Bagchi [14] studied the role of solvent–solvent interaction, specifically investigated the preferential solvation of N-ethyl-4-cyanopyridinium iodide (4CN-NEPI) in mixed binary solvents containing acetone and alcohols. They found that the solute showed no preference for methanol or ethanol in the alcohol-rich regions.

Since electrostatic interactions with hydrogen bonding exist in a wide range of solute–solvent and solvent–solvent interactions, empirical scales have been introduced to represent the solvent polarities because of a lack of theoretical expression for the calculation of solvent effect. These scales include Dimroth and Reichardt's $E_{T(30)}$ value (derived from solvent-sensitive standard compounds such as dye number 30) [15,16], Kamlet–Taft solvatochromic parameters [17,18], dielectric constants [19], solubility parameters, ionizing power, and the Kovats index.

The reactivity of nucleophilic aromatic substitution (S_NAr) reactions is notably affected by the solvent polarity. Different reported contributions show how extensive and complex interactions of the substrate and/or the intermediate(s) are with solvent molecules [7,8a]. Interactions, both nonspecific, such as Coulombic, inductive, and dispersion interactions, and specific, such as hydrogen bond, electron-pair donor/electron-pair acceptor, and solvophobic interactions, may all play a part [8b].

For the reactions of nitroaryl halides with nucleophilic anions, the two-step mechanism is fully established and the breakdown of the Meisenheimer intermediate occurs spontaneously. The transition state leading to the Meisenheimer intermediate is expected to be favored by increasing solvent polarity. Solvent effects in S_NAr involving nitrohalobenzenes with amines, including organic solvents [2–7] and binary aqueous–organic mixtures [20], were reported earlier.

In continuation with our studies in the field of S_NAr reactions [21], we report here solvent-dependent properties in binary solvent mixtures such as different mixed solutions of acetonitrile–water (AN–H_2O). To get an idea about intersolvent interactions, these solvent–solvent and solvent–solute inter-

actions have been estimated by a detailed study of the rates and mechanism of the alkaline substitution of 2-chloro-3,5-dinitrobenzotrifluoride **1** and 1-chloro-2,4-dinitrobenzene **2** in different mixed (AN–H_2O) solutions to test various theories of solvent effect on chemical reactions.

EXPERIMENTAL

Acetonitrile with high purity (>99.%) (BDH) was used. 3,5-Dinitro-2-chlorobenzotrifluoride (DNCBTF) **1** was commercially available (Aldrich). 1-Chloro-2,4-dinitrochlorobenzene (DNCB) **2** was purified by crystallization three times from aqueous methanol and obtained as yellow crystals (m.p. = 53°C). Its purity was checked by thin layer chromatography. Fresh water was redistilled using an all Pyrex apparatus from which carbon-free distilled water was obtained by double distillation over alkaline permanganate solution.

REACTION PRODUCTS

General Procedure

A solution of 2-chloro-3,5-dinitrobenzotrifluoride **1** (3.69×10^{-3} mole) was treated with sodium hydroxide (0.037 mole) in 10 mL of 50% aqueous AN. The reaction mixture was refluxed for 1 h, cooled, and then poured into an aqueous solution of HCl (5%) to remove the excess sodium hydroxide and turn the product to free phenol derivatives. The separated solid was filtered, washed thoroughly with H_2O, dried, and then crystallized from petroleum ether as brownish yellow crystals.

IR spectra were recorded on Perkin Elmer FT-IR Spectrum BX. UV spectra measurements were carried out in methanol with Shimadzu 160 A instrument. ^{1}H NMR spectra were recorded on (JEOL 500 MHZ) instrument, using $CDCl_3$ as the solvent. Microanalysis was performed at the Cairo University Microanalytical Laboratory.

2,4-DINITRO-6-TRIFLUOROMETHYL PHENOL

Yield = 77%, m.p. = 60°C. UV (MeOH): λ_{max} = 342 nm (ε = 22,053). IR (KBr): ν cm^{-1} = 3246 (OH$^-$ phenolic), 1626 (C=C aromatic), 1556 and 1342 (asymmetric and symmetric NO_2). ^{1}H NMR ($CDCl_3$) δ ppm: 12.00 (OH proton disappears in D_2O), 9.26 (1H, s, $J_{3,5}$ = 3.0 Hz, a proton flanks between two nitro groups), 8.80 (1H, s, $J_{5,3}$ = 3.0 Hz, a proton flanks between nitro and trifluoromethyl groups). Analytical

calculation for $C_7H_3F_3N_2O_5$: Calculated: C, 33.30%; N, 11.10%; H, 1.19%; 5O; 31.74%. Found: C, 33.29%; N, 10.87%; H, 1.02%.

2,4-DINITROPHENOL

The same procedure was followed for the reaction of 1-chloro-2,4-dinitrobenzene with NaOH. On workup, the reaction gave a yellow solid that gave yellow needles by crystallization from dilute methanol (yield 97%, m.p. 108°C).

KINETIC PROCEDURE

All reactions were followed spectrophotometrically on a Shimadzu UV-160A spectrophotometer connected to a water bath in which temperature can be adjusted within an uncertainty of ±0.01°C. The hydrolysis was followed under pseudo-first-order reaction conditions, using sodium hydroxide in large excess. The change in absorbance was monitored at a suitable wavelength, $\lambda = 400$ and 370 nm, for the two reactions containing substrate **1** and substrate **2**, respectively, as a function of time. The observed first-order rate constants were obtained from the slopes of plot $\log(A_\infty - A_t)$ versus time (min), where A_∞ and A_t were the values of absorbance at the end of the reaction and at time t, respectively. All rate constants were obtained from linear plots with correlation coefficients of .9995 or more.

The reaction was started by preparing a stock solution of the substrate (1×10^{-3} mol dm^3) in a suitable volume of AN (the substrate was insoluble in pure water) and then transferring 1 mL of this stock solution into a 10-mL measuring flask to reach a final concentration of the substrate to 1×10^{-4} mol dm^3. The rest of the water and AN was added to reach the desired mole fraction (X_{AN}). Then, the solution was lifted to stand for about 15 min in the water bath in order to reach thermal equilibrium. Finally, we added a given volume of the NaOH solution, with a concentration range from 0.002 to 0.02 mol dm^3. This solution was then transferred quickly into a stoppered cuvette to start the reaction.

RESULTS AND DISCUSSION

The reaction of 2-chloro-3,5-dinitrobenzotrifluoride **1** and 1-chloro-2,4-dinitrobenzene **2** with OH⁻ in 0.00–90.11 wt% AN as co-solvent with water under the same conditions of kinetic runs gave 2,4-dinitro-6-trifluoromethyl phenoxide **3** and 2,4-dinitrophenoxide **4**, respectively, in quantitative yields (Scheme 1). Elemen-

tal analysis, UV, IR, and ¹H NMR spectra indicated the formation of the substitution compounds **3** and **4**.

Kinetic measurements of the reaction were made spectrophotometrically, with [OH⁻] in large excess. The first-order rate constants k_{obs} were found to increase linearly with [OH⁻] at all range of applied temperatures, indicating that the initial nucleophilic attack is the rate-limiting step (k_1 step, Scheme 1). Alternatively, on division of the pseudo-first-order k_{obs} by the corresponding [OH⁻] gave nearly equal values as those obtained from the plot of k_{obs} versus [OH⁻] (Tables I and II). By applying the steady state to Scheme 1, we can obtain the following relationship:

$$\text{Rate} = dP/dt = k_2[I] \tag{1}$$

where P is the product and [I] is the concentration of intermediate I.

$$k_1[\text{sub}][OH^-] = k_{-1}[I] + k_2[I]$$
$$[I] = (k_1[\text{sub}][OH^-])/(k_{-1} + k_2) \tag{2}$$

By substitution in Eq. (1), we obtain Eq. (3):

$$\frac{\text{Rate}}{[\text{sub}][OH^-]k_A} = \frac{k_2 k_1}{k_{-1} + k_2} \tag{3}$$

when $k_2 > k_{-1}$, so $k_A = k_1 = k_{obs}/[OH^-]$, that is, the first step is the rate-determining step, where k_A is the apparent second-order rate constant. Thus, the formation of Meisenheimer intermediate I is rate limiting and its decomposition is spontaneous [20,22]. The rate constant k_A values cannot be obtained in more than 90 wt% AN in (AN–H_2O) mixtures because of high turbidity of these media.

The rate constant k_A is larger for 2-chloro-3,5-dinitrobenzotrifluoride **1** than for 1-chloro-2,4-dinitrobenzene **2** (Tables I and II). The dependence of the pseudo-first-order rate constant upon [OH⁻] and faster rates for 2-chloro-3,5-dinitrobenzotrifluoride **1** than for 1-chloro-2,4-dinitrobenzene **2** clearly suggested that the rate of reaction of each substrate with OH⁻ is determined by the bond-forming step [17,22]. It must be mentioned here that the increase in stability of the Meisenheimer intermediate (**I**) led to an increase in the rate constants since it is the rate-limiting step. This stabilization in the present investigation arises from the solvation of this intermediate and depends on solvent properties, namely, preferential solvation $E_{T(30)}$, permittivity (dielectric constant D), the polarity/polarizability π^*, hydrogen bond donor (HBD) α, and hydrogen bond acceptor (HBA) β parameters. The values of $E_{T(30)}$ in various (AN–H_2O) mixtures for
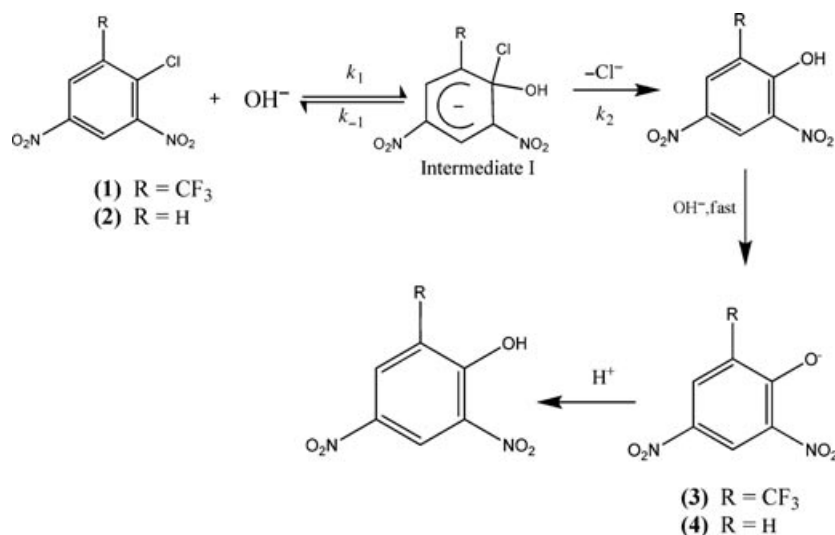
Scheme 1

Table I The Second-Order Rate Constant k_2 for the Reaction of 2-Chloro-3,5-dinitrobenzotrifluoride **1** with Sodium Hydroxide at Different Temperatures and (CH_3CN–H_2O) Mixed Solvent and Their Related Thermodynamic Parameters

wt%	$10^2 k_2$ (dm^3 mol^{-1} s^{-1})					$\Delta H^{\#}$	$\Delta S^{\#}$	$\Delta G^{\#}$	$\delta\Delta G^{\#}$
(CH_3CN)	25°C	30°C	35°C	40°C	45°C	(kJ/mol)	(J mol^{-1} K^{-1})	(kJ mol^{-1})	(kJ mol^{-1})
0.000	0.592	1.066	1.861	2.975	4.625	77.544	−27.217	85.654	0.000
10.000	0.959	1.420	2.558	3.934	6.525	75.462	−30.195	84.460	−1.194
30.000	1.305	2.015	3.435	5.133	8.471	74.323	−31.461	83.698	−1.956
36.300	1.420	2.370	3.880	5.500	9.660	70.685	−42.968	83.489	−2.165
40.000	1.804	2.601	4.734	6.424	10.043	64.822	−60.656	82.897	−2.757
50.000	2.053	2.750	3.915	6.237	10.427	63.202	−65.019	82.577	−3.077
60.320	2.600	3.570	6.140	9.125	13.000	60.866	−70.898	81.993	−3.661
70.000	5.395	6.570	12.354	16.148	23.797	55.720	−82.108	80.188	−5.466
77.370	13.286	18.571	28.660	37.000	60.000	51.563	−88.578	77.959	−7.695
80.000	14.585	22.902	33.905	42.221	61.605	47.403	−101.764	77.728	−7.926
90.110	177.33	257.14	307.69	366.66	475.00	29.986	−139.478	71.550	−14.104

Table II The Second-Order Rate Constant k_2 for the Reaction of 1-Chloro-2,4-dinitrobenzene **2** with Sodium Hydroxide at Different Temperatures and (CH_3CN–H_2O) Mixed Solvent and Their Related Thermodynamic Parameters

wt%	$10^2 k_2$ (dm^3 mol^{-1} s^{-1})						$\Delta H^{\#}$	$\Delta S^{\#}$	$\Delta G^{\#}$	$\delta\Delta G^{\#}$
(CH_3CN)	25°C	35°C	40°C	45°C	50°C	55°C	(kJ mol^{-1})	(J mol^{-1} K^{-1})	(kJ mol^{-1})	(kJ mol)
0.000	0.011	0.040	0.063	0.107	0.168	0.261	83.987	−38.660	95.507	0.000
10.000	0.019	0.058	0.088	0.142	0.211	0.361	77.336	−56.366	94.133	−1.374
30.000	0.023	0.069	0.096	0.172	0.237	0.468	75.672	−60.451	93.686	−1.821
36.300	0.027	0.073	0.098	0.175	0.250	0.470	74.002	−64.786	93.308	−2.199
40.000	0.034	0.077	0.115	0.180	0.261	0.491	68.182	−82.390	92.734	−2.773
50.000	0.038	0.084	0.118	0.192	0.276	0.526	65.696	−89.695	92.425	−3.082
60.320	0.062	0.127	0.214	0.280	0.437	0.750	61.955	−98.251	91.233	−4.274
70.000	0.067	0.172	0.287	0.422	0.461	0.959	57.798	−111.550	91.041	−4.466
77.370	0.220	0.416	0.742	1.162	1.540	2.500	53.641	−115.639	88.101	−7.406
80.000	0.350	0.652	0.978	1.305	1.823	2.936	51.563	−118.759	86.953	−8.554
90.110	2.480	4.090	4.500	6.800	9.400	10.00	40.755	−138.780	82.111	−13.396

Table III Solvatochromic Parameters and Dielectric Constants [26] at Various (CH$_3$CN–H$_2$O) Mixtures at 25°C

X_{H_2O}	X_{CH_3CN}	wt% (CH$_3$CN)	$E_{T(30)}$	1/D	log[H$_2$O]	Π*	α	β
1.000	0.000	0.000	1.000	0.013	1.744	1.140	1.130	0.470
0.953	0.047	10.000	0.930	0.013	1.699	1.100	1.030	0.590
0.842	0.158	30.000	0.840	0.015	1.589	1.010	0.920	0.610
0.799	0.201	36.300	–	0.016	1.551	0.970	0.900	0.610
0.774	0.226	40.000	0.810	0.017	1.523	0.970	0.910	0.610
0.695	0.305	50.000	0.790	0.018	1.443	0.920	0.900	0.610
0.603	0.397	60.320	0.750	0.020	1.343	0.870	0.900	0.600
0.495	0.505	70.000	0.730	0.021	1.222	0.840	0.890	0.590
0.402	0.598	77.370	–	0.023	1.098	0.820	0.870	0.590
0.370	0.630	80.000	0.700	0.024	1.046	0.810	0.850	0.590
0.202	0.798	90.110	0.640	0.027	0.735	0.770	0.750	0.570

our work were obtained from the solvation of betaine [13,23,24] and are depicted in Table III.

The Correlation of Rate Constant Values k_A with Preferential Solvation $E_{T(30)}$ Values, 1/D, and Mole Fraction of (AN–H$_2$O) Mixed Solvent

The effects of preferential solvation $E_{T(30)}$, which is sensitive to solvent–solvent interaction, on the rate of nucleophilic substitution reaction involving anions in binary mixed solvents have been examined [25–28]. In binary solvent mixtures, the solvent–solvent interactions dominate the solute–solvent interactions since the solvent is present in large excess compared with the solute [25]. These solvent–solvent interactions may be due to either hydrogen bond formation or polarizability effects that would affect the property under consideration. Therefore, (AN–H$_2$O) mixtures are very useful for studying the solvent effect upon the title reaction since the properties of various mixed solvents can be adjusted continuously by changing the composition of the mixtures.

It is found that the plot of log k_A versus $E_{T(30)}$ for both reactions 1 and 2 is nonlinear, consisting of two slopes and intersecting at about $E_{T(30)} = 0.75$ in (AN–H$_2$O) mixtures (Fig. 1). It is observed that intermediate I is preferentially solvated by AN, consistent with the inverse relationship between $E_{T(30)}$ values with X_{AN} and the increase in k_A values by progressive addition of AN (Fig. 2). On the other hand, the strong self-association interactions between the water molecules make them less available for solvation. However, once dipolar aprotic solvent (AN) is gradually added, it breaks the self-associated structure of water and the releasing "free" water molecules go on
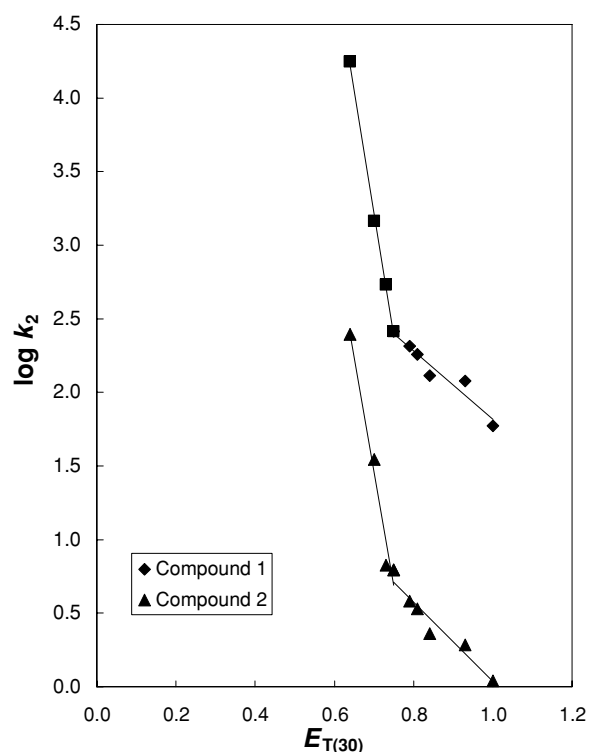

Figure 1 Variation in log k_2 vs. $E_{T(30)}$ at 25°C.

to solvate intermediate **I**. Actually, it is preferentially solvated by water in the AN-rich region. The correlation between log k_A and the mole fraction of AN (X_{AN}) shows an increase in rates of the studied reactions and gives breakup line correlation on going from water to AN. This leads us to suggest that the reaction rates are promoted by progressive addition of AN and probably associated with nonspecific solvation of the medium [29]. In other words, in an aqueous region with about $X_{AN} > 0.2$, Eq. (4) can be written for a monobasic
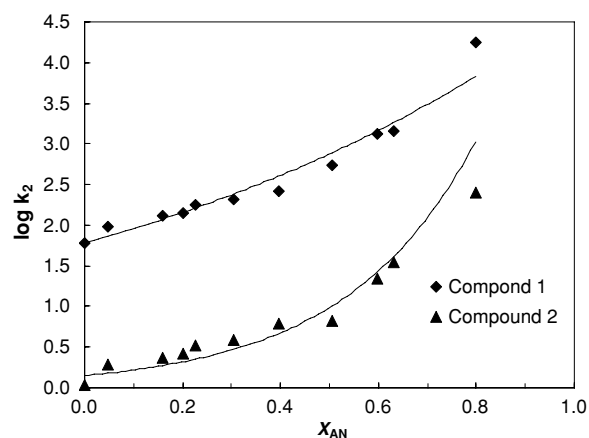
Figure 2 Variation in log k_2 vs. mole fraction of acetonitrile (AN) X_{AN} at 25°C.

co-solvent, where $(H_2O)_{free}$ is produced, as follows:

$$(H_2O)_{bulk} + CH_3CN = CH_3CN \cdots HOH$$
$$+ (H_2O)_{free} \qquad (4)$$
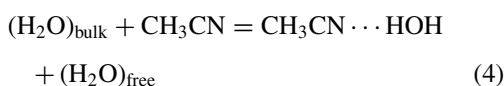
These free molecules of water seem to be of prime importance in their interactions with intermediate I.

The previous findings are explained on the basis that the composition of the immediate surroundings of intermediate **I** may be different from the composition of the bulk mixture. Preferential solvation is attributable to an excess or deficiency of one of the solvents in these surroundings. If intermediate **I** has no preference for the solvent molecules, the solvent composition in the cytotatic zone, in the immediate neighborhood of intermediate **I**, is the same as that in the bulk. For such cases, Eq. (5) can be represented as follows:

$$k_A = X_{H_2O}(k_A)_{H_2O} + X_{AN}(k_A)_{AN} \qquad (5)$$

where $(k_A)_{H_2O}$ and $(k_A)_{AN}$ represent the k_A values in solvents H_2O and AN, respectively.

Another view is the relevance of $E_{T(30)}$ for the dependence of k_A on medium composition for reactions carried out in binary mixtures; the greater the response of the reaction to the microheterogeneity of

the medium, the larger the difference in dipolarity between the reactants and the corresponding activated complex is.

It is notable that water (protic solvent) has not only hydrogen atoms that can form a hydrogen bond but also lone pair electrons on the oxygen atom that allow hydrogen atoms from another water molecule to be accepted. Acetonitrile affects water structure by intercomponent hydrogen bonding due to basicity difference in the solvent structure. (AN–H$_2$O) mixtures contain a large number of monomeric water molecules and are effectively more basic than water. Other studies showed that the basicity of AN may lead to the formation of intercomponent hydrogen-bonded complexes as shown in Fig. 3, resulting in an increased basicity of the hydroxyl oxygen atoms of water molecules.

These properties of both solvents are in agreement with the formation of Meisenheimer complex intermediate **I** in the rate-determining step where the effect of medium is presumably nonspecific and consistent with the decrease in the dielectric constant of the medium [19,29]. The polarity of the bulk phase is not an adequate parameter to account for the changes in k_A values, and finally the strong electrostatic forces developed in the activated state restrict the freedom of motion of the solvent molecules in the neighborhood of the activated species [30–32].

The dependence of log k_A values on the reciprocal of dielectric constants $(1/D)$ (not shown), of (AN–H$_2$O) mixtures for the two reactions is also nonlinear because AN molecules disrupted water structure over the whole range of the composition and this shifted the cluster-size distribution of water into smaller configurations.

The first addition of small amounts of AN to water leads to moderate acceleration, where dramatic change is observed for up to 80 wt% AN, which is in agreement with AN hydrophobicity. Numerous studies have shown that although co-solvents are monomeric molecules at low concentrations [30], their presence in water enhances the interaction between hydrophobic species. The co-solvents have the same competing effect on interactions between reactant **1** or **2** and OH$^-$, which leads to the additional rate enhancement. At higher concentrations, organic solvent molecules start to associate and form hydrophobic domains [30,33,34],
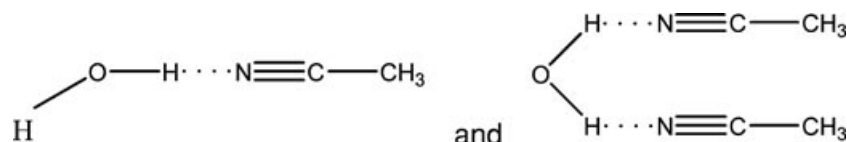
Figure 3 Types of intercomponent hydrogen-bonding complexes of AN–H$_2$O mixture.

which leads to preferential solvation of reactants by the co-solvent. Therefore, one would conclude that the dielectric theory medium effects do not particularly apply to water-rich solutions, and for the lower dielectric constant of a binary solvent mixture, higher k_A values are in agreement with the observed values.

Another deviation from the ideal dependence on the composition of the mixture gives a nonlinear plot of log k_A versus X_{H_2O} (not shown), which indicates that the solvent composition in the neighborhood of the intermediate may differ from that in the bulk.

This can be explained by assuming that there exist three regions in (AN–H_2O) mixtures [23,35]. On the water-rich side, the first region exists where the water structure remains more or less intact with the AN molecules without disrupting the water structure [8,23], whereas in the second region, k_A values vary linearly with X_{AN} or X_{H_2O} with an inflection point at about 0.48 and $\approx$.52 for the reactions of **1** and **2**, respectively. In the third region (middle range of composition), preferential solvation of intermediate **I** is increased leading to an increase in rate constant because the number of water clusters is low and (AN–H_2O) interactions that could be discounted in the middle range become important.

The trends of reaction rates with solvent composition can also be observed in light of the log k_A versus log[H_2O] correlation (Fig. 4), where two linear portions were obtained for each solvent system separated by a sharp boundary at a water concentration of about 1.2–1.4 mol dm^3. The slope of each linear portion gave the number of water molecules in the transition state (n). Some reactions have shown that the (n) value decreases or increases when [H_2O] increases depending on the type of reaction [35–41]. The (n) value reflects not only the number of water molecules in the transition state but also the susceptibility of the reaction

to the microstructure of the medium [42]. This behavior indicates that the internal structure of the medium suffers serious changes with the addition of organic solvent [43]. Therefore, the formation of two regions of different internal structure media explains their different behavior toward S_NAr [35–43].

A quick view of the first region with higher water content (Fig. 4) shows that the rate increases with the progressive addition of AN. This can be explained by the gradual breakdown of the tetrahedral structure of water and the strong hydrogen bonding between the water and dipolar aprotic AN molecules [42], along with an increase in the hydroxide ion affinity of the medium. The slope of the line in this region is 1.64, and the net result is that there is an increased rate of reaction.

In the last region of smaller water concentration, the increase in reaction rate becomes more pronounced and the slope of the line increases to 3.11. This increase in reaction rate may be due to the fact that the tetrahedral structure of water has been largely broken, releasing more free water molecules that preferentially solvate the activated complex **I**. Hence, the availability of free water molecules in this range of solvent composition is greater than that in the previous region. Meanwhile, the hydroxide ion affinity will be increased because of its association with the free water molecules. These two reasons cumulate the effect because of the decrease in water concentration, and the net increase in rate becomes more than that in the previous range.

The nonlinear behavior of the previous correlations could be explained in terms of the structural features of the (AN–H_2O) mixtures. The structure of mixtures of water and AN was explored by Marcus et al. [8]. They concluded that a strong microheterogeneity exists in the middle range of compositions in mixtures of water and AN. Thus, for a given mixture, a preference exists for water molecules rather than for AN molecules [13]. It has been reported that many binary mixtures are microheterogeneous; there exist microdomains [42–44] composed of organic solvents surrounded by water and of water solvated by organic solvent molecules. The onset and composition of microdomains depend on the nature of paired solvents. There exists the possibility of solvation of the reacting species and/or the activated complex by one of the two microdomains [42–44].

Another factor that cannot be neglected is the increase in desolvation of OH^- by the progressive addition of AN. In binary solvent mixtures, the composition of the solvation shell of the species of internal reagent and/or activated complexes differs from that of bulk medium. This difference may be exploited in S_N2 and acyl transfer reactions, where desolvation of the attacking nucleophile enhances the reaction rate [10,45,46].
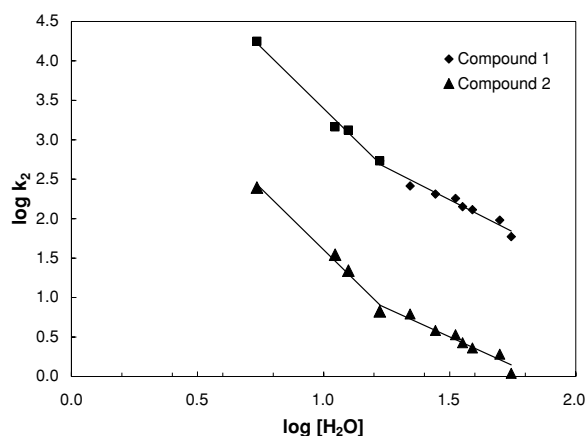

Figure 4   Plots of log k_2 vs. log[H_2O].

Variation in Thermodynamic Parameters of Activation with Solvent Compositions

The thermodynamic properties of the activated complex are usually taken as a measure of the solvation effects. These effects have been investigated by changing the mole fraction of the co-solvent. The thermodynamic parameters $\Delta H^{\#}$, $\Delta S^{\#}$, and $\Delta G^{\#}$ were calculated for each solvent composition by using all the values of the second-order rate constants (Tables I and II). The negative $\Delta S^{\#}$ values in both systems 1 and 2 at all ranges of X_{AN} indicated nonrandom distribution of the solvent molecules in the activated state, that is, the reaction passes through an ordered transition state. The $\Delta H^{\#}$ and $\Delta S^{\#}$ values showed great variations, whereas that of $\Delta G^{\#}$ appears to vary little with solvent composition. There are compensating variations for $\Delta H^{\#}$ and $\Delta S^{\#}$ for each substrate used, as they showed a well extremum for a water–co-solvent mixtures in such a way that $\Delta H^{\#}$ and $\Delta S^{\#}$ have a maximum and minimum that are mirror images to give a simple variation in $\Delta G^{\#}$ (Figs. 5a and 5b).

The type of solvent interaction could be deduced from the plot of $\Delta H^{\#}$ versus $\Delta S^{\#}$ for different X_{AN} at 25°C, which gives rise to a linear relationship (not shown) for the reaction of **1** and **2** with OH$^-$ in all binary solvents used, indicating similar mechanisms. Also, the isokinetic temperatures 138.1 and 139°C for the reactions of **1** and **2**, respectively, are far from temperature ranges used in the kinetic runs and suggested that the title reactions are entropy controlled.

It has been reported that (AN–H$_2$O) mixtures induce maximum viscosity (η) at $X_{AN} = 0.15$, indicating the formation of 6H$_2$O:AN adduct complex where the cavities between the structured iceberg of water can contaminate the other organic solvent [47]. This associated formula belongs to the class of solutions possessing numerous solute–water bonds that are stronger than the hydrogen bonds between water molecules themselves. In this field, Hafez and Sadek [48] found that minimum (negative) at $X_{AN} = 0.15$ and maximum (positive) at $X_{AN} = 0.8$ could be obtained when plotting the difference in molar viscosity $\Delta \eta_{M12}$ between calculated and experimental values against X_{AN}. Harms et al. [49] attributed negative $\Delta \eta_{M12}$ in the light of the molecular theory on the internal friction due to mixing. On dilution of a polar component with a nonpolar component, association of molecules occurs. With further dilution, the equilibrium shifts toward the formation of simple molecules and viscosity decreases again for a given lubricant (positive deviation) where breakdown of the large units of water molecules occurs and new numbers of loose positions appear that enhance internal
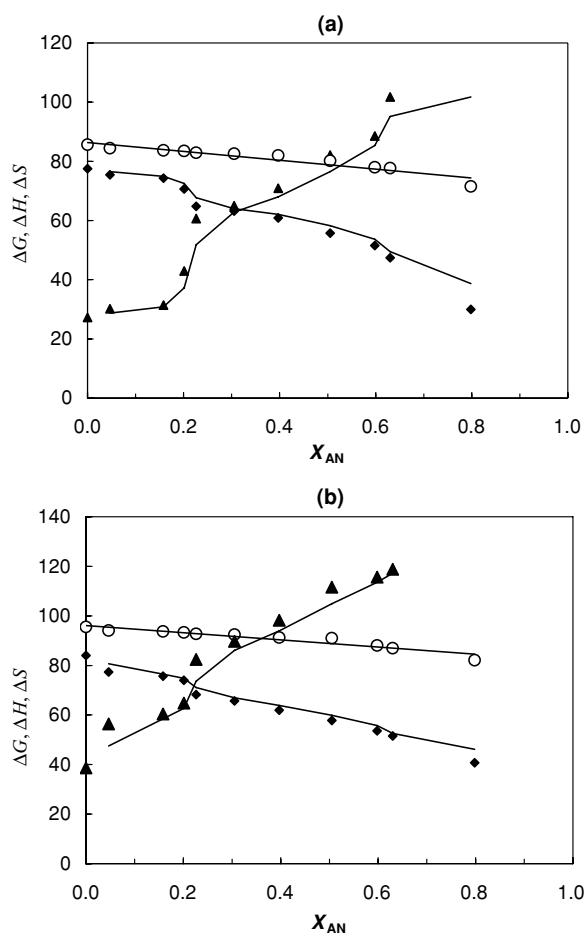
Figure 5   Variation in (○) $\Delta G^{\#}$, (■) $\Delta H^{\#}$, and (▲) $- \Delta S^{\#}$ for substrate **1** (a) and substrate **2** (b) vs. X_{AN} in (AN–H$_2$O) mixtures.

lubrication. Accordingly, $\Delta H^{\#}$ and $\Delta S^{\#}$ at about $X_{AN} = 0.15$ must be disordered because of a top-ordering process of solvation around ions and maximum conditions of enhancement of the reaction rate are present to move the product in a forward direction (i.e., $k_2 > k_{-1}$).

The concentration of our activation parameters values in (AN–H$_2$O) mixtures is an indication of the perturbation of the water and co-solvent components in the vicinity of the substrate, nucleophile, or the activated complex as the composition of the mixed solvent system is changed. The solvation is likely to be strongly influenced by the substrate size, ionic charge of the nucleophile, the size and charge of intermediate **I**, and the factors controlling steric hindrance to solvation around the previous species by the components of the binary solvent mixtures.

The differential free energies of solvation $\partial \Delta G^{\#}$ are evaluated [29] from the free energies of activation $\Delta G^{\#}$ at different X_{AN} (taking water as a reference) and

presented in Tables I and II. This differential solvation is a measure of the extent of charge on the stability of the transition state when the reaction system is changed from pure water to about $X_{AN} = 0.8$ in (AN–H$_2$O) mixtures. These values indicate that the transition state is more stabilized when the reactants are transferred in one direction ($k_1 > k_{-1}$). The differential free energy of solvation $\partial \Delta G^{\#}$ or both systems containing substrates **1** and **2** with OH$^-$ at a given X_{AN} suggested that Meisenheimer intermediate **I** developed from substrate **1** is more stable than that developed from substrate **2**. This result is probably due to the presence of the electron-withdrawing -CF$_3$ group in **1**, which stabilizes intermediate **I** by charge dispersion reflecting a faster rate for substrate **1** than for substrate **2**.

Correlation between $\Delta G^{\#}$ and Preferential Solvation $E_{T(30)}$ Values

The variations in reaction rate constants with solvent polarity are of considerable interest and their interpretation in terms of activation parameters has been reviewed by Blandamer and Burgess [50]. Now, we investigate a possible correlation between activated free energy in (AN–H$_2$O) mixtures and solvent polarity as indicated by $E_{T(30)}$ values and their possible interpretation in terms of preferential solvation.

Although the $E_{T(30)}$ scale of solvent polarity is measured from the solvation of betaine [24], a correlation between the activated parameters for the reaction of substrates **1** and **2** and OH$^-$ from H$_2$O of (AN–H$_2$O) mixtures was investigated. In Fig. 6, $\Delta G^{\#}$ values of the titled reactions for the (AN–H$_2$O) system are plotted against the related $E_{T(30)}$ values in mixed solvents (Table III). It can be seen that there is a linear correlation between two linear portions. In spite of the fact that $E_{T(30)}$ values change quite rapidly as an organic cosolvent is added to water, the behavior of the reaction
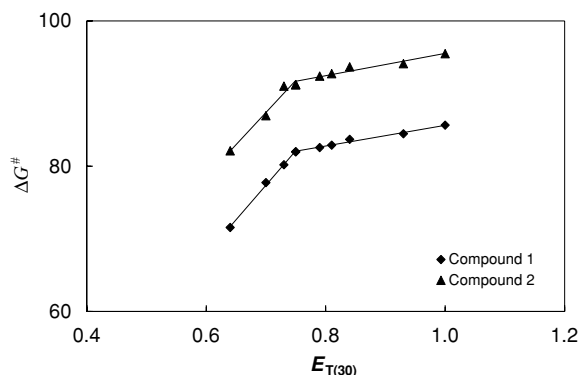

Figure 6 Plots of $\Delta G^{\#}$ vs. $E_{T(30)}$ values.

with regard to preferential solvation must be similar to that when betaine is used [33–35].

MULTIPARAMETRIC ANALYSIS

According to the previous discussion, there are factors that may control the reactions of **1** and **2** with OH$^-$ in 0.00–90 wt/% AN in (AN–H$_2$O) mixed solvents. Acceleration of rates is due to single or multiple factors: the increase in the hydrophobicity of the mixture, $E_{T(30)}$, decrease in the dielectric D, release of free water molecules as well as the polarity/polarizability π^* of the mixture, HBD α, HBA β, and finally the desolvation of the OH$^-$ base.

To decide which factor(s) has a large contribution on the reaction rate, an examination of the can explain which microscopic parameters of the solvent are responsible. The phenomenon of $E_{T(30)}$ and the group formed by α, β, and π^* are the parameters that are mostly used in the uniparametric and multiparametric analyses [18]. Since the solvent effects on nucleophilic substitution reactions are very well established qualitatively, we attempt to examine quantitatively the correlation between rate constants of the titled reactions and single, dual, and multiple parameters of (AN–H$_2$O) mixed solvents under investigation. It is found that the correlation between rate constants k_A and single parameters of the (AN–H$_2$O) mixed solvents such as $E_{T(30)}$, D, π^*, α, and β is poor.

Therefore, the solvatochromic parameters of the media are not individually the main factor for determining solvent effects on the reaction rate. The Taft–Kamlet–Abboud equation [37] takes the form of Eq. (6):

$$SDP = Constant + a\,\alpha + b\,\beta + s\,\pi^{\#} \qquad (6)$$

where SDP, the solvent-dependent phenomenon, such as rate constant, equilibrium constant, and spectroscopic shift, is modeled as a linear combination of solvatochromic parameters $s\pi^*$, $a\alpha$, and $b\beta$. The contribution of the mixed-solvent properties to solvation can be extracted from the regression coefficients s, a, and b, respectively. These coefficients permit a comparison of the response of different substrates and activated complex with the same solvent property, that is, measure the relative susceptibility of the solvent-dependent solute property on rate. Furthermore, the coefficients give us a concept about which previous factor(s) should react in the titled reactions. Equation (6) can include additional terms, or some of its terms will be equal to zero, depending on the property of the reacting species. Values of the Kamlet–Taft solvatochromic parameters

α, β, and π^* for (AN–H$_2$O) mixtures over the entire range of composition are known [51] and give the relevant solvatochromic parameter values for studied mixtures. Accordingly, the multiparametric equation can be applied:

$$\log k_A = \text{Constant} + a\,\alpha + b\,\beta + s\,\pi^{\#} \qquad (7)$$

This equation gives satisfactory results as observed from the correlation coefficient, r, and standard deviation, SD.

$\log k_A = \text{Constant} - 7.54\alpha - 9.89\beta - 0.86\pi^*$, for substrate 1 ($n = 11$, $r = 0.92$, SD = 0.246).
$\log k_A = \text{Constant} - 6.86\alpha - 8.98\beta - 1.06\pi^*$, for substrate 2 ($n = 11$, $r = 0.90$, SD = 0.254).

where n is the number of points.

Since the reaction involves hydroxide ion as the reagent and nitroaryl chloride (electron-deficient nucleus) as the reactant, it was expected that the hydrogen-bonding capability of both would be relevant. The results indicate the following observations: (i) the smallest coefficient of the π^* parameter does not change significantly as the proportion of water in the mixed solvent is decreased. There is some confirmation that for the parameter concerned, π^* rules out the effect of polarity of the mixed solvents on rates in both reactions. (ii) The two largest coefficients (a and b) agree with one or all effects, namely: increases the solvophobicity of the mixtures, releases free water molecules that stabilize intermediate **I** by solvation, or may be partially or completely dominated by the desolvation barrier of OH$^-$. The sign and magnitudes of the two remaining coefficients indicated that these two major factors are of comparable importance. (iii) The significant dependence on the HBD parameter α is a site for any reaction involving the hydroxide ion [52]. (iv) The negative sign of coefficients α and β suggested that the specific interaction observed between the reactants and the solvent through HBD and HBA properties, respectively, is more than that between the activated complex and the solvent. However, the rate constant increases with a decrease in parameter α and an increase in parameter β. These results ruled out the effect of both parameters α and β to increase the stability of Meisenheimer intermediate I formed in the rate-determining step. This is explained by increasing the solvophobicity of the mixtures and the releasing free water molecules that stabilize the intermediate **I** by solvation or may be either partially or completely dominated by the desolvation barrier of OH$^-$, combined with destroying the solvatochromic parameters of the pure solvent or aqueous–organic solvent in the presence of excess OH$^-$ base in the case of S$_N$Ar.

CONCLUSION

The reaction rates increased by an increase in AN contents as a result of the selective solvation with the dipolar aprotic solvent AN. The correlations of k_A with $E_{T(30)}$ and $1/D$ indicated that solvent–solute interactions are important factors. The interaction observed from the plot of $\log k_A$ versus [H$_2$O] indicates that the formation of two internal different structural media where AN molecules break down the self-associated structure of water releasing free water molecules is capable of increasing the stability of intermediate I. The $\Delta S^{\#}$ values indicated a nonrandom distribution of the solvent molecules around the activated complex I, whereas the $\delta\Delta G^{\#}$ values indicated that -CF$_3$ group stabilizes intermediate I obtained from substrate **1** more than that obtained from substrate **2**. The plot of $\Delta G^{\#}$ versus $E_{T(30)}$ values indicated preferential solvation by AN similar to that of the betaine that is used to measure $E_{T(30)}$ values. The plots of k_A against single parameters of (AN–H$_2$O), such as $E_{T(30)}$, $1/D$, α, β, and π^*, gave poor correlations.

The application of the Kamlet–Taft–Abboud equation indicated that the polarity of the mixed solvents has no significant effect and there is a significant dependence on the HBD parameter α and HBA parameter β; however, the rate constants are in contrast with the effects of these parameters, suggesting that the rate of reaction is controlled by the solvophobicity of the medium, the release of free water molecules and the desolvation of OH$^-$ ions combined with the destruction of the solvatochromic parameters of the pure or binary solvent in the presence of excess base.

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