Dual-Parameter Correlations on Rate of an Aromatic Nucleophilic Substitution Reaction in Aqueous Solutions of Methanol, Ethanol, and Propan-2-ol

M. R. GHOLAMI,* A. HABIBI YANGJEH

Department of Chemistry, Sharif University of Technology, Tehran, Iran, P. O. Box 11365-9516 Received 30 March 2000; accepted 15 August 2000

> ABSTRACT: Reaction kinetics of 1-chloro-2,4-dinitrobenzene with piperidine was studied spectrophotometrically in aqueous solutions of methanol, ethanol, and propan-2-ol at 25°C. The reaction in these solutions is not catalyzed by piperidine. The plots of second-order rate constants of the reaction vs. mole fraction of water show maxima in the all-aqueous solutions. Single-parameter correlations of log k_2 vs. π^* (dipolarity/polarizability), α (hydrogen-bond donor acidity), and E_{τ}^{N} (normalized polarity parameter) are very poor in the all solutions (for example, in aqueous solutions of ethanol, regression coefficients are 0.814, 0.113, and 0.486, respectively). Dual-parameter correlations of log k_2 vs. π^* and α in all cases represent significant improvement with regard to the single-parameter models (in aqueous solutions of ethanol: n = 11, r = 0.980, and s = 0.034). Dipolarity/polarizability and hydrogen-bond donor acidity (HBD) of media have opposite effects on the reaction rate. The activated complex leading to the zwitterionic intermediate is expected to be favored by increasing the solvent dipolarity/polarizability parameter. Increasing the hydrogen-bond donor acidity of solvent stabilizes piperidine and hence the reaction rate decreases. A dual-parameter equation of log k_2 vs. π^* and α was obtained in the all-aqueous solutions (n = 31, r = 0.956, s = 0.055) in which π^* and lpha have approximately equal and opposite effects on the reaction rate. © 2001 John Wiley & Sons, Inc. Int J Chem Kinet 33: 118-123, 2001

INTRODUCTION

That solvents have considerable influence on chemical and physical processes (reaction rates, selectivity, chemical equilibria, position and intensity of spectral absorption bands) has been well established [1]. Solvent effects are closely related to the nature and extent of solute-solvent interactions locally developed in the immediate vicinity of the solutes. Solute-solvent interactions are much more complex in mixed solvents than in pure solvents due to the possibility of prefer-

Correspondence to: M. R. Gholami (Gholami@Ch.Sharif.Ac.Ir) © 2001 John Wiley & Sons, Inc.

ential solvation by any of the solvents present in the mixtures. Moreover, the solvent–solvent interactions produced in solvent mixtures can affect the solute– solvent interactions and therefore they can also affect preferential solvations [2].

Modeling of solvent effects is one of the most useful methods used to obtain information about the mechanism of organic reactions [1]. Also, the complexity of the chemistry of life *in vivo*, which occurs primarily in an aqueous environment, should be encouraging chemists to investigate further the reactions in aqueous solutions. Water is considered an unusual and poorly understood liquid. The complexity of even the simplest reactions in aqueous solutions is significantly greater than that of reactions in organic solvents [3–7].

In addition to the nonspecific, columbic inductive and dispersion interactions, others such as specific hydrogen-bond, electron-pair donor-acceptor, and solvophobic interactions may play a part in the solvent effects. The problem is to identify and to assess the relative importance of these various factors on the solvent effects. The purpose of our work is to identify the medium effects in aromatic nucleophilic substitution reactions in aqueous solutions. Therefore, the kinetics of the reaction of 1-chloro-2,4-dinitrobenzene with piperidine was studied in aqueous solutions of methanol, ethanol, and propan-2-ol at 25°C.

The gross mechanism of aromatic nucleophilic substitution reactions is now well established when primary or secondary amines are the nucleophiles (Scheme I) [8].



Application of the steady-state approximation derives Eq. (1), in which k_A is the observed second-order rate constant and B can be either a second molecule of the nucleophile or an added base:

$$k_{\rm A} = \{k_1(k_2 + k_3^{\rm B}[{\rm B}])\}/\{k_{-1} + k_2 + k_3^{\rm B}[{\rm B}])\} \quad (1)$$

The main situations of interest with respect to the reaction shown in Scheme I are as follows:

a. $k_2 + k_3^{B}[B] \gg k_{-1}$. In this case, base catalysis is not possible and Eq. (1) simplifies to $k_A = k_1$, and formation of the intermediate is the ratedetermining step of the reaction. b. k₂ + k₃^B[B] ≪ k₋₁. This situation corresponds to rapid formation of the intermediate followed by its rate-determining decomposition to products. In this case, Eq. (1) reduces to Eq. (2), which predicts base catalysis with a linear dependence of k_A on [B]:

$$k_{\rm A} = k_1 k_2 / k_{-1} + (k_1 k_3^{\rm B} / k_{-1}) [{\rm B}]$$
 (2)

c. $k_2 + k_3^{B}[B] \sim k_{-1}$. In this intermediate situation, Eq. (1) indicates that base catalysis should be observed with a curvilinear dependence of k_A on [B].

The reaction of 1-chloro-2,4-dinitrobenzene with piperidine is not catalyzed by base (situation (a)) [9–11] in aprotic and protic solvents. The second-order rate constants of the reaction, k_A , are well correlated by the Dimroth-Reichardt solvent polarity scale $E_T(30)$ in several aprotic solvents. In some alcohols, the values of rate constants of the reaction are not well correlated by $E_T(30)$ parameters, but the reactivity is inversely proportional to the hydrogen-bond donor acidity (HBD) of the solvents [9–11].

EXPERIMENTAL

Reagents and Solvents

1-chloro-2,4-dinitrobenzene was prepared from 4-nitro-1-chlorobenzene as follow: 16 g nitric acid (65%) was added gradually into a solution of 4-nitrochlorobenzene (16 g) in 70 ml sulphuric acid (98%). The reaction mixture was heated on the water-bath, then cooled to room temperature and poured on ice, and the precipitate was washed with water. Recrystallization was carried out in aqueous solution of ethanol. All solvents were of the highest quality available and were purified as usual. Water was redistilled in a quartz distillation unit.

Kinetic Procedures

The kinetics of the reaction was studied spectrophotometrically. The spectrophotometer was coupled to a PC with an interface that allows absorbance measurements vs. time (four readings per second). Absorbance was recorded at wavelengths from 370 (in propan-2ol) to 400 nm (in water) at 25°C. Pseudo-first-order (k_{obs}) conditions were used in all cases. Infinity values of absorbance (A_{∞}) were experimentally determined for each run. All the kinetic runs were carried out at least in triplicate. Concentration of 1-chloro-2,4-dini-

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[Piperidine] (mol dm ⁻³)	Methanol k_2 *10 ² /dm ³ mol ⁻¹ sec ⁻¹	Ethanol $k_2^*10^2/\mathrm{dm^3mol^{-1}sec^{-1}}$	Propan-2-ol k_2 *10 ² /dm ³ mol ⁻¹ sec ⁻¹
0.00462	3.52 ± 0.04	5.10 ± 0.06	7.19 ± 0.08
0.00712	3.48 ± 0.04	5.13 ± 0.04	7.26 ± 0.06
0.01245	3.50 ± 0.05	5.06 ± 0.04	7.25 ± 0.06
0.02790	3.49 ± 0.03	5.02 ± 0.05	7.29 ± 0.09
0.05650	3.49 ± 0.04	5.14 ± 0.07	7.20 ± 0.10
0.07480	3.50 ± 0.05	5.15 ± 0.06	7.25 ± 0.10

Table I Search for Piperidine Catalysis. Second-Order Rate Constants in Reaction of 1-Chloro-2,4-Dinitrobenzene with Piperidine in Aqueous Solutions of Methanol, Ethanol, and Propan-2-ol at 25°C.^a

^a Mole fractions of water in aqueous solutions of methanol, ethanol, and propan-2-ol are 0.839, 0.884, and 0.908, respectively.

trobenzene was 10^{-4} M, and those of piperidine were between 5×10^{-3} M to 10^{-1} M. Regression coefficients of plots of $\ln(A_{\infty} - A_i)$ vs. time were at least 0.9900. Thermostated water was circulated around the cell of the spectrophotometer, and the temperature was maintained at 25 ± 0.1 °C.

RESULTS AND DISCUSSION

Although no base catalysis is expected for the reaction of 1-chloro-2,4-dinitrobenzene with piperidine, to confirm this the influence of piperidine concentration on the reaction rate with different mole fractions of water was studied in aqueous solutions of methanol, ethanol, and propan-2-ol. For instance, three experimental data are shown in Table I. As can be observed, no significant acceleration in the reaction rate occurs with increasing concentration of piperidine. This in-

Table II Second-Order Rate Constants of the Reaction in Aqueous Solutions of Methanol at 25°C. E_{T}^{N} , π^{*} , and α are Normalized Polarity Parameter, Dipolarity/Polarizability and Hydrogen-Bond Donocity of Solvent.^a

Xw	$k_2 * 10^2 / \text{dm}^3 \text{mol}^{-1} \text{sec}^{-1}$	$E_{\mathrm{T}}^{\mathrm{N}}$	π^*	α
0.000	1.17 ± 0.01	0.762	0.58	1.14
0.200	1.54 ± 0.02	0.779	0.70	1.09
0.360	1.88 ± 0.02	0.791	0.79	1.04
0.491	2.27 ± 0.04	0.794	0.88	1.03
0.599	2.90 ± 0.05	0.823	0.95	1.01
0.692	3.20 ± 0.04	0.838	1.01	1.01
0.771	3.44 ± 0.03	0.870	1.05	1.04
0.839	3.49 ± 0.04	0.896	1.09	1.08
0.900	3.24 ± 0.04	0.925	1.11	1.13
0.953	3.26 ± 0.03	0.964	1.12	1.19
1.00	3.46 ± 0.05	1.00	1.14	1.26

^a At least three runs were averaged.

dicates that rate of the reaction was not catalyzed by bases in the all-aqueous solutions. Hence, it can be concluded that the formation of zwitterionic intermediate is the rate-determining step of the reaction [5]. Similar results have been reported for this reaction in aprotic and protic solutions. The second-order rate constants of the reaction, k_A , in aqueous solutions of methanol, ethanol, and propan-2-ol were obtained at 25°C (Tables II, III, and IV). In all cases, the rate constants of the reaction increase with the increasing mole fraction of water (approximately up to $X_{\rm w} = 0.85$), then it starts to decrease. In fact, in these aqueous solutions, rate constants of the reaction vs. $X_{\rm W}$ show maxima (Fig. 1). The results show that this increase of the reaction rate in aqueous solutions of propan-2ol is higher than those of ethanol and methanol.

The normalized polarity parameter (E_T^N) of media increases with the mole fraction of water in aqueous solutions of the alcohols. In the same mole fraction of water, E_T^N of aqueous solutions of methanol > ethanol > propan-2-ol. If the E_T^N of media was the



Figure 1 Plot of second-order rate constants of the reaction vs. mole fraction of water in aqueous solutions of methanol (\bigcirc) , ethanol (+), and propan-2-ol(*) at 25°C.

Table III Second-Order Rate Constants of the
Reaction in Aqueous Solutions of Ethanol at 25°C. E_T^N ,
π^* , and $lpha$ are Normalized Polarity Parameter,
Dipolarity/Polarizability, and Hydrogen-Bond Donocity
of Solvent.ª

$X_{\rm W}$	$k_2 * 10^2 / \text{dm}^3 \text{mol}^{-1} \text{sec}^{-1}$	$E_{\mathrm{T}}^{\mathrm{N}}$	π^*	α
0.000	1.76 ± 0.04	0.648	0.51	0.98
0.266	2.26 ± 0.04	0.673	0.66	0.93
0.449	2.75 ± 0.05	0.702	0.75	0.89
0.583	2.87 ± 0.06	0.717	0.81	0.89
0.685	3.96 ± 0.04	0.731	0.88	0.88
0.765	4.88 ± 0.12	0.761	0.96	0.86
0.830	5.25 ± 0.09	0.784	1.03	0.87
0.884	5.10 ± 0.08	0.842	1.10	0.92
0.929	4.24 ± 0.06	0.907	1.12	1.05
0.967	3.43 ± 0.06	0.959	1.13	1.17
1.00	3.46 ± 0.05	1.00	1.14	1.26

Table IV Second-Order Rate Constants of the Reaction in Aqueous Solutions of Propan-2-ol at 25°C. $E_{\rm N}^{\rm N}$, π^* , and α are Normalized Polarity Parameter, Dipolarity/Polarizability, and Hydrogen-Bond Donocity of Solvent.^a

$X_{\rm W}$	$k_2 * 10^2 / \text{dm}^3 \text{mol}^{-1} \text{sec}^{-1}$	$E_{\mathrm{T}}^{\mathrm{N}}$	π^*	α
0.000	2.53 ± 0.03	0.552	0.49	0.76
0.320	2.62 ± 0.04	0.583	0.65	0.78
0.514	3.14 ± 0.03	0.639	0.72	0.81
0.645	3.50 ± 0.04	0.667	0.77	0.80
0.738	4.18 ± 0.04	0.685	0.81	0.82
0.809	5.42 ± 0.04	0.714	0.87	0.82
0.864	6.25 ± 0.11	0.740	0.95	0.82
0.908	7.24 ± 0.09	0.790	1.06	0.85
0.944	6.65 ± 0.10	0.901	1.14	0.96
0.974	3.91 ± 0.07	0.957	1.15	1.12
1.000	3.46 ± 0.05	1.00	1.14	1.26

^a At least three runs were averaged.

only factor for the solvent effects on the reaction rate, it may be expected that the reaction rate in water should be higher than those of all the aqueous solutions of methanol, ethanol, and propan-2-ol.

Single-parameter correlations of log k_2 vs. E_T^N do not give good results in three type of the aqueous solutions (Table V). The rate of the reaction in some protic solvents decreases with hydrogen-bond donor acidity of solvent. HBD of water is higher than those of methanol, ethanol, and propan-2-ol. HBD of media first decreases and then increases with the increasing mole fraction of water in aqueous solutions of meth^a At least three runs were averaged.

anol and ethanol. This quantity increases continuously with X_w in aqueous solutions of propan-2-ol. If HBD of media were the only factor for solvent effects on the reaction rate, one would expect that the secondorder rate constant of the reaction in water similar to protic solvents should be less than those of methanol, ethanol, and propan-2-ol [9–11]. Single-parameter correlations of log k_2 vs. α do not give good results in the three types of the aqueous solutions (Table V).

The normalized polarity parameter is a blend of dipolarity/polarizability and HBD of media. Linear correlations of log k_2 vs. π^* do not give good results in

Table V Regression Coefficients and Slopes of Solvent Parameters in Aqueous Solutions of Methanol, Ethanol, Propan-2-ol and the All-Aqueous Solutions at 25°C

Aqueous Solutions	$E_{\mathrm{T}}^{\mathrm{N}}$	π^*	α	Intercept	r
of Methanol	1.612			-2.975	0.779
	_	0.856	_	-2.402	0.979
	_	_	0.152	-1.758	0.074
		0.897	-0.381	-2.025	0.995
of Ethanol	0.624	_	_	-1.958	0.486
	_	0.580	_	-1.994	0.814
		_	0.130	-1.336	0.113
		0.778	-0.698	-1.497	0.980
of Propan-2-ol	0.474	_	_	-1.734	0.438
		0.482	_	-1.807	0.665
			0.056	-1.432	0.058
		1.061	-1.061	-1.374	0.955
the All-Aqueous Solutions	0.384		_	-1.782	0.244
		0.596	_	-2.017	0.654
			0.438	-1.055	0.327
	_	0.918	-1.048	-1.293	0.956

all three types of solutions (Table V) [12,13]. So, we decided to correlate log k_2 vs. both π^* and α in aqueous solutions of methanol, ethanol, and propan-2-ol. Dual-parameter correlations of log k_2 vs. π^* and α in the three all types of solutions give interesting results:

• In aqueous solutions of methanol:

$$\log k_{\rm A} = -2.025(\pm 0.080) + 0.897(\pm 0.032) \ \pi^* - 0.381(\pm 0.075) \ \alpha (n = 11, r = 0.995, s = 0.018, F_{2.8} = 396.30) (3)$$

• In aqueous solutions of ethanol:

$$log k_{\rm A} = -1.497(\pm 0.080) + 0.778(\pm 0.057) \pi^* - 0.698(\pm 0.091) \alpha (n = 11, r = 0.980, s = 0.034, F_{2.8} = 95.21)$$
(4)

• In aqueous solutions of propan-2-ol:

$$\log k_{\rm A} = -1.374(\pm 0.096) \\ + 1.061(\pm 0.117) \ \pi^* - 1.061(\pm 0.162) \ \alpha \\ (n = 11, r = 0.955, s = 0.053, F_{2.8} = 41.47)$$
 (5)

Regression coefficients and standard deviations of the equations are good. As can be seen, the dipolarity/ polarizability and HBD of the media have opposite effects on the reaction rate. The intermediate of the reaction has zwitterionic character: the activated complex of the reaction therefore, has higher polarity relative to those of the reactants of the reaction. The activated complex leading to the zwitterionic intermediate is expected to be favored by the increasing dipolarity/polarizability of media and hence the reaction rate increases. In the presence of piperidine, alcohols are known to act as HBD, and there is abundant evidence of strong hydrogen-bonding interactions between piperidine and alcohols [14,15]. Therefore, piperidine will be stabilized via hydrogen-bonding interactions with hydrogen-bond donors. Hence, the reaction rate decreases with the increasing HBD of the media. Because of the opposite effects of dipolarity/ polarizability and HBD of the media, maxima appear in plots of second-order rate constants of the reaction vs. mole fraction of water.

A dual-parameter correlation of log k_2 vs. π^* and α was obtained in the all-aqueous solutions of the alcohols:

$$\log k_{\rm A} = -1.293(\pm 0.074) \\ + 0.918(\pm 0.056) \ \pi^* - 1.048(\pm 0.083) \ \alpha$$

(n = 31, r = 0.956, s = 0.055, F_{2,28} = 150.67) (6)



Figure 2 Plot of experimental values of $\log k_2$ vs. the calculated values of it from Eq. (6) in the all-aqueous solutions at 25°C.

In Eq. (6), dipolarity/polarizability and hydrogen bond donor ability of the media have approximately equal but opposite effects on the reaction rate. In order to show the efficiency of suggested dual-parameter correlations, experimental values of log k_2 vs. its calculated values from Eq. (6) were plotted for different aqueous solutions of alcohols. As can be seen, the experimental and calculated values of log k_2 are in good agreement in the all-aqueous solutions (Fig. 2).

The rates of some organic reactions in water and several aqueous solutions are higher than those of organic solvents, and the reaction rate increases dramatically with the increasing mole fraction of water [16,17]. Hydrophobic interactions have important role in these conditions [18–21]. In these reactions, the rate of reaction in aqueous solutions of methanol is higher than that of ethanol, while in the reaction reported in this article, opposite observations were obtained. Also in this reaction, the increase of the reaction rate with $X_{\rm W}$ is very low. In fact, because of complete solubility of piperidine in water, hydrophobic interactions would not exist. This idea is established by dual-parameter correlations of log $k_{\rm A}$ vs. π^* and α in the all-aqueous solutions.

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