Solvent Interactions in the Allylation of Piperidine

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ABSTRACT: The reaction between allylbromide and piperidine has been studied in different protic and aprotic solvents. The reaction is first order with respect to [allylbromide] and [piperidine]. A correlation analysis of the rate data with solvent properties shows that polarity (Y), polarizability (P), and electrophilicity (E) of the solvent simultaneously influence the rate of reaction. From the regression analysis, information regarding the relative solvation of the reactants and the activated complex is obtained and a solvation model is proposed. © 2009 Wiley Periodicals, Inc. Int J Chem Kinet 41: 421–425, 2009

INTRODUCTION

In any reaction, the interactions of reactants and activated complex with the solvent molecules are extensive and complex. The solvent-solute interactions are of two types, namely specific and nonspecific [1]. All solvents interact with substances nonspecifically. The intensities of these interactions are measured in terms of polarity (Y) [2] and polarizability (P) [2] of the solvent. The specific solvent-solute interactions are short-range forces and are chemical in nature. Specific solvation of the substance primarily occurs when the solvent interacts with a specific charged atom or group in a molecule. The intensities of these interactions are measured in terms of electrophilicity (E) [3], nucleophilicity (B) [3], hydrogen-bond donor ability (α) [4], hydrogen-bond acceptor ability (β) [4], and specific polarizability and dipolarity parameter (π^*) [4] of the solvent. So the general-term polarity of the solvent means the overall solvation ability of the solvent due to either all or some of these properties. Hence the effect of solvent on the reaction rate has to be presented not by a single parameter equation but by a multiparametric equation introduced by Koppel and Palm [5] as

$$\log k = \log ko + yY + pP + bB + eE + \cdots$$
(1)

In the above equation, k is the rate constant of the reaction in any solvent and ko is the rate constant in an inert solvent that does not solvate at all, taken as a reference state. Y, P, B, and E are different solvation parameters of the solvent under consideration. The coefficients y, p, b, and e are the susceptibilities of kto the respective solvent-solute interaction parameters. These coefficients indicate the differential solvation of the reactants and the activated complex and the mode of solvation. The results on such studies have been reported earlier [6-14] using different nucleophiles and substrates. Similar studies of solvent effects on the kinetics of the allylation reactions are limited. Hence, the reaction between allylbromide and piperidine has been studied in 16 different protic and aprotic solvents and the results are presented.

EXPERIMENTAL

Allyl bromide (Merck, Mumbai, India) and piperidine (Sd-fine, Mumbai, India) were used without further purification. Methanol, ethanol, *n*-propanol, *n*-butanol,

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sec-butanol, *i*-butanol, *t*-butanol, and cyclochexanone were Sd-fine samples of AR grade. Acetone, ethyl methyl ketone, *N*,*N*-dimethylformamide, dimethyl-sulfoxide, formamide, acetonitrile, *i*-propanol, and benzyl alcohol are Merck samples. These solvents were purified if necessary after checking their boiling points.

The solutions of the reactants of required concentrations were prepared by dissolving known volumes of allylbromide and the nucleophile piperidine in a known volume of the solvent. The reactions were initiated by mixing the thermally equilibrated solutions of allylbromide and the nucleophile at required temperature. Preliminary studies indicated that HBr is one of the products of the reaction. Hence, the course of the reaction was followed by measuring the conductance of the reaction mixture at different time intervals using a conductivity bridge (Century make) in the temperature range 303–318 K. The temperature was maintained constant within $\pm 0.5^{\circ}$ using an Insref thermostat.

The conductance of the reaction mixture was measured at the beginning of the reaction (C_0) , at different known time intervals (C_t) , and also after completion of the reaction (C_{∞}) . The order of the reaction was established by studying the reaction at 0.02 mol dm⁻³ allylbromide and 0.1, 0.2, and 0.4 mol dm⁻³ piperidine concentrations. In each set, the plot of $\log((C_{\infty} - C_t)/C_t)$ against time was linear, suggesting the first-order nature of the reaction with respect to allylbromide. The first-order rate constants determined from the slopes of the above linear plots are 1.65, 3.36, and 6.67 \times 10^{-2} s⁻¹, respectively, in methanol at 303 K. These data suggest that the order with respect to the nucleophile is also one. Since the overall order is two, the present reactions were conducted at [allylbromide] = [piperidine] = $0.02 \text{ mol } \text{dm}^{-3}$ and the second-order rate constants k were calculated using the relation [15]

$$k = \frac{1}{at} \frac{C_t}{C_\infty - C_t} \tag{2}$$

where a is the initial concentration of the reactants.

The rate constants thus determined were found to be reproducible within $\pm 5\%$ error. The possibility of the

substrate allylbromide undergoing solvolysis in the solvents used in the present study was checked by studying the conductance of the solution of allylbromide in each solvent in the absence of the nucleophile. There was a slow change in the conductance due to liberation of HBr. Estimation of the rate constants of this process indicated that the solvolysis rate constants are more than 100 times less than the substitution reaction rate constants under similar experimental conditions. Hence the solvolysis rates are neglected while calculating the substitution rate constants. The package data analysis that is part of MS Excel was used to carry out the linear multiple regression analysis. The *F*-test and *t*-test [16] were used to test the validity of the multiparametric equation.

The product separated at the end of the reaction was identified as the corresponding allyl piperidine from its IR spectral analysis. Its IR spectrum does not show any sharp absorption band around 3300 cm^{-1} due to the N–H bond, while this band is observed in the reactant. Furthermore, the IR absorption around 2800 cm⁻¹ confirms the presence of a N–CH₂ group [17].

RESULTS AND DISCUSSION

The second-order rate constants determined in 16 different solvents are presented in Table I. A glance at these values indicates that the rate constants are highly dependent on the nature of the solvent. To know the influence of the solvent on the rate, these rate constants are correlated individually with the solvent parameters Y, P, E, and B as well as α , β , and π^* . The corresponding correlation coefficients (r) obtained are 0.77, 0.55, 0.63, 0.32, 0.49, 0.25, and 0.07, respectively. These correlations are not satisfactory, suggesting that the variation in the rate due to change in the nature of the solvent cannot be described by a single property of the solvent. Hence, the data are analyzed by taking two parameters each time. Some of the successful correlations obtained with meaningful correlation coefficients are given below.

$$\log k = -8.33 + 14.37Y - 5.89 \times 10^{-4}B; \quad R = 0.77 \tag{3}$$

$$(1.73) \quad (3.57) \quad (13.69 \times 10^{-4}) \qquad (0.19)$$

$$\log k = -7.77 + 12.98Y - 1.40 \times 10^{-3}P; \quad R = 0.78$$
(4)
(1.88) (4.06) (1.70 × 10^{-3}) (0.19)

$$\log k = -7.26 - 2.70 \times 10^{-2}E + 12.31Y; \quad R = 0.88$$
(5)
(1.25) (0.83 × 10⁻²) (2.60) (0.15)

Solvent	$k \times 10^3 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}/(\text{K})$				E	$\wedge H^{\neq}$	∆S≠	ΔG^{\neq}	
	303	308	313	314	$(kJ mol^{-1})$	$(kJ mol^{-1})^a$	$(J K^{-1} mol^{-1})^a$	$(kJ mol^{-1})^a$	$\delta \Delta G^{\neq a}$
Methanol	11.67	16.21	25.00	34.61	57.44	54.92	-101	85.51	0.00
Ethanol	14.16	33.11	66.66	134.89	95.73	93.21	27	84.97	-0.54
n-Propanol	16.67	23.44	31.66	42.65	47.87	45.35	-129	84.57	-0.94
i-Propanol	10.01	19.95	35.00	63.09	76.54	74.02	-39	85.83	0.32
n-Butanol	10.06	17.85	27.83	42.68	71.80	69.28	-47	83.52	-1.99
Sec-Butanol	9.13	19.05	33.33	60.35	79.65	77.13	-29	86.08	0.57
<i>i</i> -Butanol	20.01	26.91	35.83	46.88	43.46	40.94	-142	84.10	-1.41
t-Butanol	10.23	16.21	24.15	36.30	63.82	61.30	-81	85.84	0.33
Benzyl alcohol	16.43	23.98	34.20	49.07	57.44	54.92	-98	84.61	-0.90
Dimethylformamide	31.26	40.73	50.01	60.25	31.78	29.26	-177	82.96	-2.55
Dimethylsulfoxide	59.42	87.09	108.82	141.25	38.29	35.77	-151	81.52	-3.99
Acetone	26.61	32.35	41.05	51.28	31.91	29.39	-170	80.90	-4.61
Acetonitrile	45.39	86.86	99.59	141.25	57.44	54.92	-90	82.19	-3.32
Ethylmethyl ketone	16.48	22.38	30.66	40.73	47.86	45.34	-130	84.73	-0.78
Cyclohexanone	16.66	22.35	27.50	33.11	38.29	35.77	-161	84.55	-0.96
Formamide	77.06	97.72	110.85	144.54	31.91	29.39	-169	80.59	-4.92

Table I Second-Order Rate Constants and Activation Parameters in the Reaction between Allyl Bromide and Piperidine in 16 Different Solvents

[Allyl bromide] = [piperidine] = $0.02 \text{ mol } \text{dm}^{-3}$.

^a At 303 K.

The values in parentheses are standard errors of the corresponding coefficients. The analysis is further extended using three parameters as the correlation coefficients of the above biparametric equations are not satisfactory. The following are some of the results obtained:

(1.42)

 $(1 \ 13)$

(2 86)

correlation coefficient value of R = 0.91, the standard errors are higher than the coefficient of the parameter itself. Hence the above four-parameter equation (9) is rejected and only Eq. (8), in which the rate is simultaneously correlated with polarity (Y), polarizability

(0.17)

$$\log k = -8.76 + 4.26 \times 10^{-4}B - 18.82 \times 10^{-3}E + 15.33Y; \quad R = 0.83$$
(6)
(1.42) (18.17 × 10⁻⁴) (9.54 × 10⁻³) (3.14) (0.17)

$$\log k = -10.45 + 16.30Y + 6.89P - 1.52 \times 10^{-3}B; \quad R = 0.86$$
⁽⁷⁾

(3.14)

$$(1.43) \quad (2.86) \quad (2.46) \quad (1.80 \times 10^{-3}) \quad (0.15)$$
$$\log k = -10.26 + 16.24Y + 5.68P - 16.99 \times 10^{-3}E; \quad R = 0.91 \quad (8)$$

(1.20)(2.36)(1.95) (7.31×10^{-3}) (0.13)

(2.16)

Thus $\log k$ is better correlated with Y, P, and E. To know whether a fourth parameter would improve the strength of the correlation or not, the analysis is further extended using four parameters. The following result is obtained:

(P), and electrophilicity (E) of the solvent, is considered. This equation explains 83% of experimental data as indicated by the *R* value.

The applicability of Eq. (8) to the present system is confirmed by subjecting the data to the following tests:

$$\log k = -10.50 + 16.86Y + 6.46P - 1.46 \times 10^{-3}B - 16.78 \times 10^{-3}E; R = 0.91$$
(9)
(1.23) (2.47) (2.12) (1.57 × 10^{-3}) (7.31 × 10^{-3}) (0.13)

Although the rate constant data are correlated using the four parameters equation with the linear multiple 1. To apply the linear multiple regression analysis, the primary requirement is that the individual independent variables used in the analysis should not bear any meaningful relationship among themselves. This analysis results in the following correlation:

$$Y = -0.48 - 0.08P + 3.33 \times 10^{-3}E; R = 0.16$$

(0.04) (0.22) (0.85 × 10⁻³) (0.02)

A low correlation coefficient (0.16) among these three parameters used in Eq. (8) suggests that the above linear solvation energy relationship (LSER) is not a result of chance correlation.

 log k_{cal} using the above LSER for each solvent used in the present system is correlated with the experimentally determined k', i.e. log k_{obs}. This results in the following equation:

$$\log k_{obs} = 0.99 \log k_{cal}; r = 0.99$$

This excellent correlation is an indication of the applicability of the above equation (Eq. (8)) to the present system.

- 3. The calculated statistical *F* is compared with the table value. F_{cal} (18.43) is greater than the F_{table} (5.95) at 1% level of significance.
- 4. The significance of each independent variable used in the above LSER is confirmed by comparing the statistical *t*-values calculated for each parameter (t_{cal}) with the statistical table values (t_{table}), t_{cal} are 6.88, 2.92 and 2.32 for *Y*, *P*, and *E* terms. Comparison of these values with t_{table}

suggests that *Y* is significant at 99.95% confidence level, whereas *P* and *E* are significant at 95% confidence level. Thus, these tests confirm the applicability of the above LSER (Eq. (8)) to the present system. The contributions of these three parameters in this LSER are found to be Y = 53%, E = 21%, and P = 26%.

The following conclusions, regarding the mode of the differential solvation of the reactant and the activated complex, can be drawn from the above LSER:

- 1. The rate of the reaction is strongly influenced by the polarity of the solvent (*Y*). The positive value of the coefficient of *Y* in the above LSER suggests that the activated complex is more strongly solvated than the reactants due to the polarity of the solvent.
- 2. The rate of reaction is also influenced by polarizability (*P*) of the solvent. Positive value of the coefficient of *P* in the above LSER suggests that the activated complex is more strongly solvated than the reactants.
- 3. The reaction rate is influenced by the electrophilicity (E) of the solvent. The negative value of the coefficient of E in the LSER suggests that the reactants especially the nucleophilic center is more strongly solvated than the activated complex due to the electrophilic nature of the solvent.

In view of these observations, the following solvation model can be proposed in the reaction of allylbromide with piperidine.



From the temperature effect on the rate data, the energy of activation E_a , enthalpy, entropy and free energy of activation ΔH^{\neq} , ΔS^{\neq} and ΔG^{\neq} are computed and presented in Table I. The ΔS^{\neq} evaluated in different solvents indicate that these are highly dependent on the nature of the solvent. The ΔG^{\neq} computed is nearly constant (83.33 ± 2.74 kJ mol⁻¹), suggesting a unified reaction scheme in all the solvents. The differential free energy $\delta \Delta G^{\neq}$ values computed taking methanol as the reference solvent are all negative except in *i*-propanol and *t*-butanol, suggesting that the activated complex is more stabilized when it is changed from methanol to other solvents.

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