# Nucleophilic Substitution Reactions of Meta- and Para-Substituted Benzylamines with Benzyl Bromide in Methanol Medium

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ABSTRACT: The rates of reactions of para- and meta-substituted benzylamines with benzyl bromide were measured using conductivity technique in methanol medium. The reaction followed a total second-order path. The end product of the reaction is identified as dibenzylamine (X-C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>NHCH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>) (where X = 4-OCH<sub>3</sub>, 4-CH<sub>3</sub>, H, 4-Cl, 4-CF<sub>3</sub>, 3-CF<sub>3</sub>, 4-NO<sub>2</sub>). Electron-withdrawing groups such as chloro, trifluoromethyl, and nitro in the benzylamine moiety decrease the rate of the reaction, whereas the electron-donating groups, such as methoxy and methyl, increase the rate compared to the unsubstituted compound. A mechanism involving formation of an S<sub>N</sub>2-type transition state between the amine nucleophiles and the benzyl bromide and its subsequent decomposition is proposed. Hammett's reaction constant  $\rho$  of the reaction decreases with an increase in temperature. Activation parameters were calculated and discussed. © 2014 Wiley Periodicals, Inc. Int J Chem Kinet 47: 36–41, 2015

## INTRODUCTION

The Hammett equation [1,2] had received a successful application in reaction mechanisms in physical organic chemistry. Nucleophilic substitution at the benzylic carbon is of broad synthetic utility and has received considerable attention from organic chemists. Literature survey shows that applications of the Hammett equation on different nucleophilic substitution reactions involving nucleophiles, namely thiourea [3], thiobenzamide [4], pyridines [5], quinolines [6], different aliphatic and aromatic primary and secondary amines [7], and 2-mercapto benzimidazole [8] have been reported. In continuation of our earlier work on

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Figure 1 Order in [benzyl bromide], plot of log [benzyl bromide] versus time [benzyl bromide] = 0.01 M, [benzylamine] = 0.1 M, temp. = 303 K.



Figure 2 Order in [benzylamine], plot of log  $K_{obsd}$  versus log[benzylamine] [benzyl bromide] = 0.01 M, temperature = 303 K.

the benzylation of N-substituted benzylamines with benzyl bromide [9], we are reporting herein the effect of substituents attached to the benzene ring of benzylamine on the reaction rates.

# **EXPERIMENTAL**

All the chemicals and solvents used in the present work were purchased from Aldrich (Bangalore, India) and used as received. The conductivity meter and the conductivity cell used were obtained from Digison Electronics (Hyderabad, India) with an accuracy of  $\pm 0.01$  mho. The constant temperature bath was purchased from Biotech Electronics (New Delhi, India) and maintained at constant temperature with an accuracy of  $\pm 0.1^{\circ}$ C. All other experimental details are similar to that reported in our previous publication [9].

# **PRODUCT ANALYSIS**

Benzyl bromide (0.1 M) was reacted with benzylamine (0.1 M) in a methanol medium at 30°C. After more

		$k_2 (\mathrm{dm}^3 (\mathrm{mol}\mathrm{min})^{-1}) T(\mathrm{K})$						
Substituent (X)	σ	298	303	308	313	$E_{\rm a}$ (kJ mol <sup>-1</sup> )	$^{*}\Delta H^{\#}$ (kJ mol $^{-1}$ )	$^{*}\Delta S^{\#} (J \pmod{K})^{-1})$
4-OMe	-0.27	0.0880	0.1272	0.2090	0.3860	74.2	71.7	-25.3
4-Me	-0.17	0.0616	0.0911	0.1757	0.3321	86.5	83.9	12.9
Н	0.00	0.0576	0.0851	0.1350	0.3040	82.6	79.8	-1.69
4-Cl	0.23	0.0424	0.0621	0.1010	0.1957	76.6	74.2	-22.8
3-CF <sub>3</sub>	0.43	_	0.0520	0.0941	0.1537	81.5	78.9	-9.01
4-CF <sub>3</sub>	0.54	0.0296	0.0434	0.0620	0.1206	69.3	66.7	-50.7
4-NO <sub>2</sub>	0.78	0.0163	0.0324	0.0420	0.0708	70.8	68.3	-49.5

**Table I** Second-order rate constants ( $k_2$ ) for the Reaction of Substituted Benzylamines with Benzyl Bromide at Different Temperatures, BA = 0.2 mol dm<sup>-3</sup>, BB = 0.01 mol dm<sup>-3</sup>, Solvent: Methanol

\*T = 303 K.

than 15 half-lives, a product was isolated by a solvent extraction process using an ethyl acetate (50 mL) and water (10 mL) mixture after several attempts. The ethyl acetate solution was dried over anhydrous NaSO<sub>4</sub> and filtered and concentrated under vacuum to get the compound, which was subjected to column chromatography using ethyl acetate/*n*-hexane (1:9) as an eluent. The solvent was removed under reduced pressure, and a light yellow oily product was found. Analysis of the product gave the following results:

*N*,*N*-*Dibenzylamine*: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 1.65 (s, H, N-H), 3.8 (s, 4H, (PhCH<sub>2</sub>)<sub>2</sub>N), 7.25– 7.39 (m,10H, aromatic protons); IR (KBr): 3269, 3060, 3026, 2921, 2835, 1953, 1872, 1809, 1742, 1714, 1602, 1581, 1556, 1521, 1490, 1452, 1331, 1268, 1217, 1143, 1108, 1027, 1000, 980, 948, 906, 802, 729, 695 cm<sup>-1</sup>; mass spectrum (*m*/*z*): 198 (M – H)<sup>+</sup>.

### **RESULTS AND DISCUSSION**

The conductivity of the reaction mixture increases with time as the reaction produces HBr as one of the end products. Under the conditions [benzylamine]  $\gg$ [benzyl bromide], the plot of log ( $C_{\infty} - C_t$ ) versus time was linear until three half-lives with a correlation coefficient of 0.999 (Fig. 1), indicating the order in [benzyl bromide] was unity.

Here  $C_{\infty}$  and  $C_t$  are the conductivities of the reaction mixture at infinite time and at regular intervals of time, respectively. From such plots, the pseudo–first-order rate constants ( $k_{obsd}$ /min) were calculated for all the benzylamines. The plot of log ( $k_{obsd}$ /min) versus log [benzylamine] was again found to be linear with a correlation coefficient of 0.995 (Fig. 2), indicating the order in [benzylamine] was unity.

The pseudo-first-order rate constants  $(k_{obsd})$  for all reactions obeyed Eq. (1) with negligible  $k_0 ~(\approx 0)$  in

methanol. The second-order rate constants,  $k_2$ , were obtained as the slope of the plot of  $k_{obsd}$  against the benzylamine concentration. The second-order rate constants [ $k_2$  (dm<sup>3</sup> mol<sup>-1</sup> min<sup>-1</sup>)] are summarized in Table I.

$$k_{\text{obsd}} = k_0 + k_2 \left[ \text{benzylamine} \right] \tag{1}$$

Therefore, the simple rate equation would be

Rate = 
$$k_2$$
 [benzylamine] [benzyl bromide] (2)

where  $k_2$  is the second-order rate constant. Under otherwise similar conditions, the solvolysis reaction of benzyl bromide in the absence of benzylamine was checked and the rate was found to be 10 times less than the rate of the second-order reaction. Hence the rates of background reaction of benzyl bromide were neglected in these studies.

## Reaction Mechanism and Substituent Effects

Since the total order of the reaction is two, a bimolecular type of reaction scheme is proposed as shown in the following mechanism via an  $S_N$ 2-type transition state:

$$X = p - OCH_{3,p} - CH_3, H, p - Cl,$$
$$m - CF_3, p - CF_3, p - NO_2$$

Rate =  $k_2 [X - C_4 H_4 C H_2 N H_2] [C_6 H_5 C H_2 B r]$ 



**Figure 3** Plot of  $\Delta H^{\neq}$  versus  $\Delta S^{\neq}$  showing the isokinetic relationship.



**Figure 4** Exner plot of  $\log k_{303}$  versus  $\log k_{313}$ .

From the mechanism, one can predict a linear correlation would be observed between log  $k_2$  and Hammett's  $\sigma$  with a negative Hammett reaction constant ( $\rho$ ) because the rates would increase as the substituent (X) on the amine nitrogen becomes more and more electron donating, which facilitates the availability of the lone pair of electrons on nitrogen for the attack on the benzylic carbon of benzyl bromide (see Scheme 1).

The reaction between benzylamine and benzyl bromide has been studied at temperature 298–313 K in a methanol medium, and the rate constants were computed. Electron-withdrawing groups such as chloro, trifluoromethyl, trifluoromethy, and nitro in



**Figure 5** Hammett plot of log k against Hammett sigma ( $\sigma$ ) at 303 K.



**Figure 6** Brönsted plot of  $\log k$  versus  $pK_a$  of X-substituted benzylamines at 303 K.

X-C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>NH<sub>2</sub> decrease the rate of the reaction, whereas the electron-donating groups such as methyl and methoxy increase the rate compared to the unsubstituted compound. To verify the applicability of Hammett's linear free energy relationship, "log  $k_2$ " is correlated with Hammett's substituent constant in the temperature range 298–313K. Hammett's reaction constant  $\rho$  of the reaction decreases with an increase in the temperature.

## **Isokinetic Relationship**

An isokinetic plot is obtained in the present work (Fig. 3) when  $\Delta H^{\pm}$  is plotted against  $\Delta S^{\pm}$  according to the equation  $\Delta H^{\pm} = \beta \Delta S^{\pm}_{+}$  constant, the

slope of which corresponds to an isokinetic temperature  $\beta$  of 266 K, which is well below the experimental temperature range (298–313 K) used in the present reactions to study the effect of temperature on reaction rates. According to isokinetic theory [10], this means that the effect exerted by the meta- and para-substitution of benzylamines, both the processes, i.e., formation and the heterolysis of the transition state, are controlled predominantly by entropy.

It has been asserted that apparently linear correlations of  $\Delta H^{\pm}$  with  $\Delta S^{\#}$  are sometime misleading, and the evaluation of  $\beta$  by means of the equation  $\Delta H^{\pm}$  $= \beta \Delta S^{\pm}$  + constant lacks statistical validity [11]. Exner [12] describes an alternative method for the treatment of experimental data. If the rates of several reactions in a series have been measured at different temperatures and log  $k_2$  (at  $T_2$ ) is linearly related to log  $k_1$  (at  $T_1$ ), i.e., according to the equation, log  $k_2 = a + b \log k_1$ , so that  $\beta$  can be evaluated using the equation,  $\beta = T_1T_2 (b - 1)/(T_2b - T_1)$ . We have calculated the isokinetic temperature  $\beta$  as 270 K by plotting log  $k_2$  at 313 K versus log  $k_1$  at 303 K as shown in Fig. 4; the value of  $\beta$  (270 K) is lower than the experimental temperature 298 K. This indicates that the rate is governed by the entropy of activation [13].

The Brönsted  $\beta_X$  value was calculated by correlating log  $k_2$  with pKa [14]. The substituent effects (X) of the nucleophiles upon the aminolysis rates are compatible with those for a typical nucleophilic substitution reaction, and the stronger nucleophile leads to a faster rate with positive charge development at the nucleophilic N atom in the transition state, resulting in negative  $\rho_X$  (-0.526; Fig. 5) and positive  $\beta_X$  (0.52; Fig. 6) values at 30°C.

# CONCLUSION

The reactions of para- and meta-substituted benzylamines with benzyl bromide follow a  $S_N$ 2-type reaction. One of the authors (RR) is grateful to University Grants Commission, New Delhi, India, for providing financial assistance in the form of a fellowship.

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