

The Duality of S_N1 and S_N2 Mechanisms for the Reaction of *p*-Methoxybenzyl Bromide with *N,N*-Dimethylanilines

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Menschutkin reaction of benzylic systems¹⁻⁷ with tertiary amines has long been regarded as one of the best examples of mechanistic studies of borderline reaction (S_N1 & S_N2). In previous works,⁸⁻¹² we studied kinetics and mechanism for the Menschutkin reaction of benzylic systems with pyridine and *N,N*-dimethylanilines, in which the cationic transition state from S_N1 (looser) to S_N2 (tighter) was reached on going from electron-donating to electron-withdrawing substituents in the benzyl substrate. Recently we reported¹³ the results that the Menschutkin reaction of benzylic systems with aromatic tertiary amines proceeds simultaneously by the independent S_N1 and S_N2 mechanisms. In this work, we study the precise kinetic analysis for the benzylation of *N,N*-dimethylanilines in acetonitrile to get detailed information for the reaction mechanism.

Results and Discussion

The rate constants for the quarternization of various concentration of substituted *N,N*-dimethylaniline with *p*-methoxybenzyl bromide are listed in Table 1, in which the rate constants were measured by the increasing conductance of the quarternary ammonium salt produced in the reaction medium. The reaction was carried out in the condition of 5×10^{-4} M of substrate with 10^{-2} - 3×10^{-1} M of nucleophile in acetonitrile at 50 °C. The plots of the pseudo-first order rate constants, k_{obs} , vs concentrations of nucleophiles in non-solvolyzing solvent, acetonitrile at 50 °C are shown in Figure 1. Positive intercept was found in zero concentration of all of the nucleophiles, indicating the intercept is independent of the concentration or nature of nucleophiles. These results can be fitted to a kinetic equation as the sum of zero and first-order terms in nucleophile concentration:

$$k_{\text{obs}} = k_1 + k_2[\text{Nu}] \quad (1)$$

On the other hand, the Menschutkin reaction of *N,N*-dimethylanilines with less activated benzyl bromides than *p*-methoxybenzyl bromide proceeds entirely by a second-order process (S_N2 reaction) as eq. 2.

$$k_{\text{obs}} = k_2'[\text{Nu}] \quad (2)$$

The second-order rate constants, k_2' , obtained from the slope of the linear parts of plots in Figure 1, increase with increasing nucleophilicity of Y-substituted *N,N*-dimethyl-

Table 1. Pseudo-first Order Rate Constants (k_{obs}) for the Reaction of *p*-MeO-Benzyl Bromide with (Y)-Substituted-*N,N*-Dimethylanilines in Acetonitrile at 50 °C

Nu (Y)	[Nu](M)	$k_{\text{obs}} 10^2$ (s ⁻¹)
<i>p</i> -Me	0.010	60.68
	0.020	119.4
	0.040	218.8
	0.060	316.2
	0.080	414.4
	0.10	514.8
<i>m</i> -Me	0.01	47.27
	0.02	92.20
	0.04	164.8
	0.06	239.8
	0.08	321.2
	0.10	384.1
H	0.01	32.65
	0.05	133.7
	0.10	246.9
	0.15	359.9
	0.20	472.9
<i>p</i> -Br	0.01	16.38
	0.02	27.90
	0.04	49.08
	0.06	70.31
	0.08	86.84
	0.10	103.5
<i>m</i> -NO ₂	0.01	4.340
	0.05	21.37
	0.10	40.67
	0.15	59.40
	0.20	77.03
	0.25	90.97
	0.30	105.0

anilines in this order: Y = *p*-Me > H > *p*-Br > *m*-NO₂. From the above results, the reaction can be expressed by eq. 1 and depicted by the Scheme 1.

From the Scheme 1, the reaction rate expressed by eq. 3, where Nu is *N,N*-dimethylaniline (DMA).

$$k_{\text{obs}} = \frac{k_1 k_2' [\text{DMA}]}{k_{-1} + k_2' [\text{DMA}]} + k_2 [\text{DMA}] \quad (3)$$

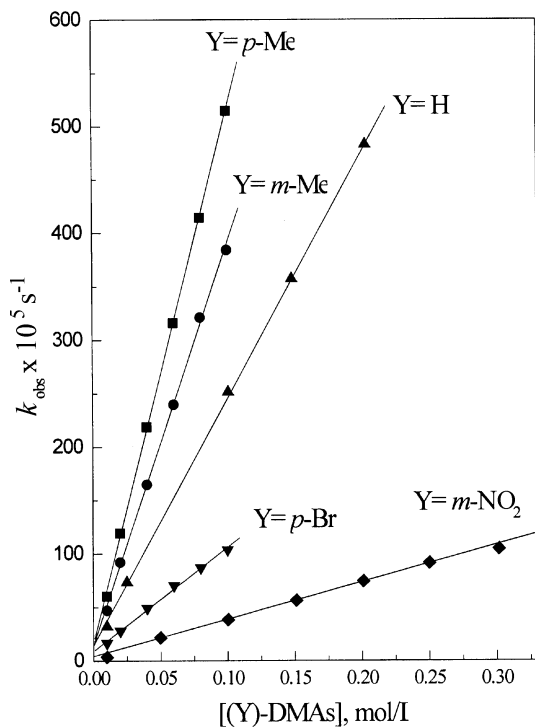
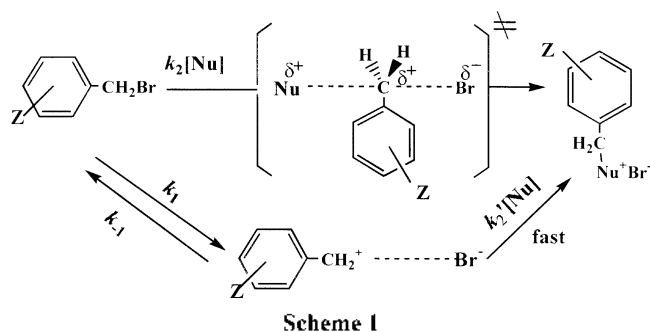


Figure 1. Plot of pseudo-first order rate constants (k_{obs}) vs nucleophile concentration for reactions of *p*-MeO-benzyl bromide with (Y)-substituted *N,N*-dimethylanilines in acetonitrile at 50 °C.



Scheme 1

when $k_2[\text{DMA}] \gg k_1$, which is given by simple eq. 4.

$$k_{\text{obs}} = k_1 + k_2[\text{DMA}] \quad (4)$$

The k_1 and k_2 values are determined from the intercept and the slope of the linear part of k_{obs} vs $[\text{DMA}]$ plots, respectively. The k_1 and k_2 values for the two kinds of nucleophiles, pyridine and DMA, are listed in Table 2, in which k_1 values are independent on the nucleophilicity of pyridine^{13d} and DMA, about same value of $(20.6 \pm 0.5)10^{-5}$ (s^{-1}) within the experimental uncertainty. The k_2 values, however, are dependence of nucleophilicities of two kinds of nucleophiles.

The percentage (%) contribution of S_N1 process at 0.1 M concentration of Y-pyridine and Y-DMA are listed in Table 2, calculated from the eq. 5.

$$S_N1\% = 100k_1/(k_1 + k_2[\text{Nu}]) \quad (5)$$

The percentages of S_N1 in this reaction of *p*-methoxybenzyl bromide with two kinds of nucleophiles are from 51.4%

Table 2. First-order (k_1) and Second-order (k_2) Rate Constants for the Reaction of *p*-MeO-Benzyl Bromides with (Y)-Pyridines^{13d} and (Y)-Dimethylanilines in Acetonitrile at 50 °C

Nucleophile	N ^a	r ^b	Slope $10^5 k_2 (\text{s}^{-1} \text{M}^{-1})$	Intercept $10^5 k_1 (\text{s}^{-1})$	$100k_1^c$ $0.1k_2 + k_1$
4-NH ₂ -Pyd.	5	0.9999	547.8	20.8	3.7
4-Me-Pyd.	4	0.9999	236.6	20.4	7.9
11-Pyd.	4	0.9999	135.1	20.3	13.0
3-Br-Pyd.	2		19.70	20.8	51.4
3-Cl-Pyd.			15.00		
4-Me-DMA	5	0.9999	493.1	20.8	4.1
3-Me-DMA	4	0.9999	365.3	19.5	5.1
11-DMA	4	0.9999	226.1	20.7	8.4
4-Br-DMA	3	0.9999	80.90	20.6	20.3
3-NO ₂ -DMA	3	0.9999	28.00	21.1	43.0

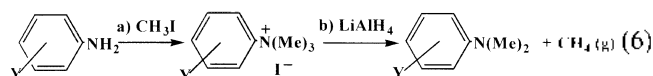
^a Number of runs. ^b Correlation coefficient. ^c Percent reaction by S_N1 route at $[\text{Y-DMA}] = 0.1 \text{ M}$.

to 3.7% for Y-pyridines and from 43.0% to 4.1% for Y-DMA. In any cases of nucleophiles, the S_N1 ratio increased for the weaker nucleophile, indicating the less nucleophilic pyridine and DMA derivatives bring the higher activation energy for bimolecular process. One example of the plots of k_{obs} for the reaction of *p*-methoxybenzyl bromide with H-DMA vs various $[\text{H-DMA}]$ in acetonitrile at 50 °C are represented with Figure 2.

From the all of the results, the reaction of *p*-methoxybenzyl bromide with Y-substituted *N,N*-dimethylanilines proceeds simultaneously by the independent S_N1 and S_N2 mechanisms

Experimental Section

Materials. Acetonitrile was purified by the same method previously^{13a} described. *p*-Methoxybenzyl bromide was synthesized by the bromination¹⁴ of *p*-methoxybenzyl alcohol with hydrobromic acid. Liquid *N,N*-dimethylanilines dried over sodium hydroxide pellets were fractionated and solid ones recrystallized as usual method,¹² stored in a brown ampoule filled with nitrogen. The other substituted *N,N*-dimethylanilines (Y = *p*-methyl, *m*-methyl, 11, *p*-Br, *m*-NO₂) were synthesized as following methods. (eq. 6)



a) Synthesis of *p*-methyldimethylaniline methiodide

Dissolve 20 g of solid sodium carbonate in 200 mL of distilled water, then put 21 g (0.2 mole) of *p*-toluidine into above the solution, while stirring the solution at room temperature, 98 g of CH₃I (0.7 mole) was added gradually into it. After 24 hours reflux, cooled, filtration, and then recrystallization from ethanol. Yield 90%, mp 220 °C (lit.,¹⁵ 218 °C).

b) To freshly distilled, 200 mL of anhydrous tetrahydrofuran was added, with caution, 8 g (0.04 mol) of powdered

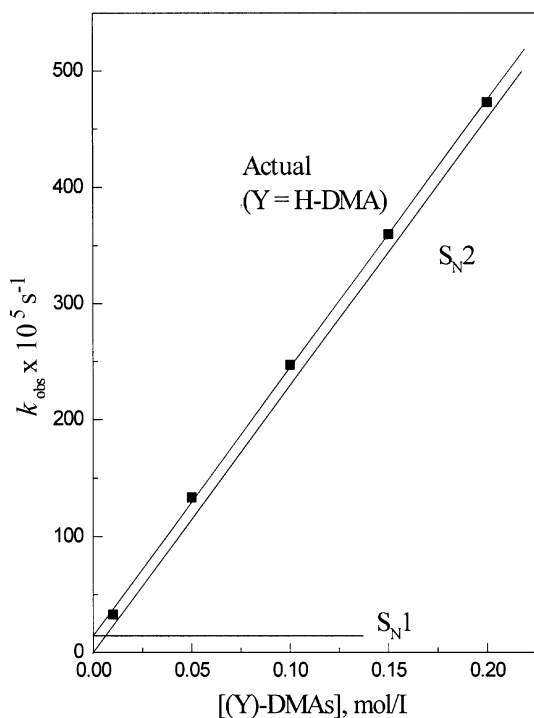


Figure 2. Schematic representation of the reactions of *p*-MeO-benzyl bromide with DMA in acetonitrile assuming that both S_N1 and S_N2 processes are occurring.

lithium aluminium hydride. The mixture was heated under reflux for 1 hour. Finely ground 11.0 g (0.04 mol) of *p*-methyl *N,N*-dimethylaniline methiodide was introduced in it and the mixture heated under reflux with stirring until evolution of methane ceased.

The mixture was cooled and cautiously hydrolysed by gradual addition of 200 mL of water. To isolate *N,N*-dimethyl *p*-toluidine, the mixture was extracted with ether (200 mL) and dried ($MgSO_4$). After removal of solvent by distillation, the residue was vacuum distilled as liquid. Yield 60–70%, bp 95 °C/30 mmHg (lit.¹⁶ 204–206 °C/740 mmHg).

Kinetic Measurement. Kinetic Measurement. Rates were measured conductometrically as described before.¹³ Conductance measurements were made in a 100 cm³ cell with Pt electrodes using approximately 30 cm³ solution at an initial concentration of 0.003–0.0004 mol/L of substrate in a thermostated water bath at appropriate temperature 50±0.01 °C.

Conductivity readings were taken by using a conductivity meter, CM-60S equipped with time interval unit and with a printer, (TOA Electric Ltd.).

The first order rate constants were determined by least squares computer program with correlation coefficient 0.999.

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