JOURNAL OF PHYSICAL ORGANIC CHEMISTRY
J. Phys. Org. Chem. 2001; **14:** 123–130

Concurrent S_N1 and S_N2 reactions in the benzylation of pyridines

Soo-Dong Yoh,[1] Duk-Young Cheong,[1] Chung-Heun Lee,[1] Sung-Hong Kim,[1] Jong-Hwan Park,[1] Mizue Fujio[2]* and Yuho Tsuno[2]

[1]Department of Chemistry Education, Kyungpook National University, Taegu 702-701, Korea
[2]Institute for Fundamental Research of Organic Chemistry, Kyushu University, Hakozaki, Fukuoka 812-8581, Japan

Received 20 June 2000; revised 18 September 2000; accepted 9 November 2000

ABSTRACT: The Menschutkin reactions of 3,4-methylenedioxybenzyl and 3,4-dimethoxybenzyl bromides and also *p*-methoxybenzyl bromide with Y-substituted pyridines were kinetically studied for a range of amine concentration in acetonitrile. The strongly activated benzyl bromides showed a significant positive intercept in the plot of the pseudo-first-order rate constants against the concentrations of nucleophiles, while less activated benzyl bromides did not give such significant intercepts. The rate data for respective substrates were fitted to the equation $k_{obs} = k_1 + k_2[Nu]$. The first-order rate constant, k_1, is unaffected by the nature of the nucleophile, whereas the second-order rate constant, k_2, increased with increasing nucleophilicity. This was ascribed to the simultaneous occurrence of S_N1 and S_N2 reactions without an intermediate mechanism. These results are taken as evidence for the duality of S_N1 and S_N2 mechanisms in the Menschutkin reaction in the non-solvolyzing solvent acetonitrile. Copyright © 2001 John Wiley & Sons, Ltd.

KEYWORDS: Menschutkin reaction; benzyl bromides; duality of S_N1–S_N2 mechanisms

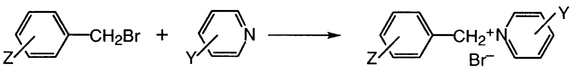
INTRODUCTION

The solvolytic and nucleophilic substitution reactions of benzylic substrates with nucleophiles have long been a target of world-wide studies.[1-6] Various sophisticated mechanisms other than the classical Ingold S_N1 and S_N2 mechanisms[1] were proposed for displacement reactions in the so-called borderline case.[3,5-7] Especially the mechanistic transition from S_N2 to S_N1 in the displacement reaction has still been the subject of considerable controversy. Sneen proposed a unification of the S_N1 and S_N2 mechanisms in which all nucleophilic substitutions involve the formation of ion pairs.[6] Bentley and co-workers proposed the concept of continuous spectrum of S_N1–S_N2 mechanisms, involving a continuity of solvolytic mechanisms from S_N1, via S_N2 (intermediate), to the conventional S_N2 mechanism.[7]

We have been also involved in the investigations by means of the substituent effect analysis on the mechanism of the Menschutkin reactions of benzylic systems with various nucleophiles.[8–19] In previous studies on the Menschutkin reaction of Z-substituted benzyl X-benzenesulfonates with Y-substituted *N*, *N*-dimethylanilines in acetone or acetonitrile,[8,10,13,14] the substituent effect analysis in terms of the correlation interaction coefficients, ρ_{ij}, led to the conclusion that the reaction proceeded through the S_N2 mechanism in which the transition state coordinate moved to the tight-loose direction with benzyl Z-substituents and to the early-late direction with nucleophile Y-substituents.[10,11a]

During the course of our continuing studies, we in the IFOC laboratory found the surprising fact in the above Menschutkin reaction of benzyl tosylates[15] that the strongly activated benzyl tosylates showed a significant positive intercept in the plot of the pseudo-first-order rate constants against the concentrations of nucleophiles, while less activated benzyl tosylates did not give such significant intercepts. This was ascribed to the simultaneous and independent occurrence of S_N1 and S_N2 reactions without an intermediate mechanism in non-solvolyzing solvents. These results led to the conclusion of the duality of displacement mechanism, the S_N1 and S_N2 mechanisms, in the borderline region.

Later, we extended our substituent effect studies on reaction mechanisms to the Menschutkin reactions of substituted benzyl bromides with substituted pyridines and the related nucleophiles in aprotic solvents. Here also the concurrent S_N1 mechanism will be the case.



(1)

Z = *p*-MeO (**1**); 3,4-$(CH_3O)_2$ (**2**); 3,4-methylenedioxy (**3**)
Y = 4-NH_2, 3-NH_2, 4-Me, H and 3-Cl

**Correspondence to:* M. Fujio, Institute for Fundamental Research of Organic Chemistry, Kyushu University, Hakozaki, Fukuoka 812-8581, Japan.

Contract/grant sponsor: KOSEF; *Contract/grant number:* BSRI - 1998–1999.

Table 1. Pseudo-first-order rate constants (k_{obs}) for the reactions of strongly activated benzyl bromides **1, 2** and **3** with unsubstituted pyridine in acetonitrile at 50 °C[a]

	p-MeO (**1**)		3,4-(MeO)$_2$ (**2**)		4-OCH$_2$O-3 (**3**)	
[Nu] (mol l^{-1})	10^5k_{obs} (s^{-1})	10^4k_2* (lmol^{-1}s^{-1})	10^5k_{obs} (s^{-1})	10^4k_2* (lmol^{-1} s^{-1})	10^5k_{obs} (s^{-1})	10^4k_2* (lmol^{-1}s^{-1})
0.01	17.01	170.1	20.3	203	13.18	131.8
0.03	48.8	162.6	53.0	176.6	37.2	123.9
0.05	80.2	160.4	84.7	169.4	61.8	123.6
0.10	158.9	158.9	162	161.9	119.7	119.7
0.15	235	156.6	242	161.0	180	120.2
0.20	309	154.6	318	158.8	238	119.1
0.25	383	153.1	396	158.3	296	118.5
0.30	455	151.8	472	157.4	353	117.7
0.35	528	151.0				

[a] k_2* values were evaluated using Eqn. (2); k_2* = k_{obs}/[Nu].

Katritzky and co-workers[5] studied extensively the substitution reactions of *N*-alkyl- and -aralkyl-2,4, 6-triphenylpyridinium salts with neutral amine nucleophiles in non-polar solvents. They also found that the substitution reactions of the *N*- (*m*, *p*-substituted benzyl) salts with neutral amine nucleophiles in non-polar solvents occurred by a competition mechanism of concurrent first- and second-order substitution reactions. Through detailed discussions with Professor Katritzky, the authors arrived at the common consensus in their opinion on the generality of the competitive occurrence of the concurrent S_N1 and S_N2 mechanisms. Our special interest was therefore strongly focused on the duality of displacement mechanisms, in the borderline region.

In the present study, in order to ascertain the duality of S_N1 and S_N2 mechanisms, we undertook precise kinetic studies on the reactions of strongly activated benzyl bromides **1**–**3** with pyridines in acetonitrile, based on a detailed analysis of the dependence of rate on the concentration of nucleophiles.

RESULTS AND DISCUSSION

The apparent rate constants k_{obs} were determined under the pseudo-first-order conditions at the concentration (0.0005 M) of substituted benzyl bromides with various concentrations of Y-substituted pyridines (0.01–0.3 M). Apparent second-order rate constants (k_2*) were derived in the usual manner by dividing k_{obs} by nucleophile concentrations:

$$k_{obs} = k_2^*[\mathrm{Nu}] \qquad (2)$$

In Table 1 are summarized the rate constants for the reactions in acetonitrile at 50 °C of *p*-methoxybenzyl (**1**), 3,4-dimethoxybenzyl (**2**) and piperonyl (3,4-methylenedioxybenzyl) (**3**) bromides with the nucleophile pyridine (Y = H). The plots of the pseudo-first-order rate constants, k_{obs}, versus nucleophile concentrations for these substrates are illustrated in Fig. 1, in which there seem to be detectable non-zero intercepts at zero concentration of the nucleophile.

Apparent second-order rate constants k_2* are not a constant of the substrate bromide for varying pyridine concentrations but decrease with increasing pyridine concentration to approach a constant value at higher concentrations as shown in Tables 1 and 2.

The apparent rate constants k_{obs} for 2 and 3 with a series of Y-substituted pyridines all exhibit linear relations against nucleophile concentrations with different slopes (k_2*) significantly depending on the nucleo-

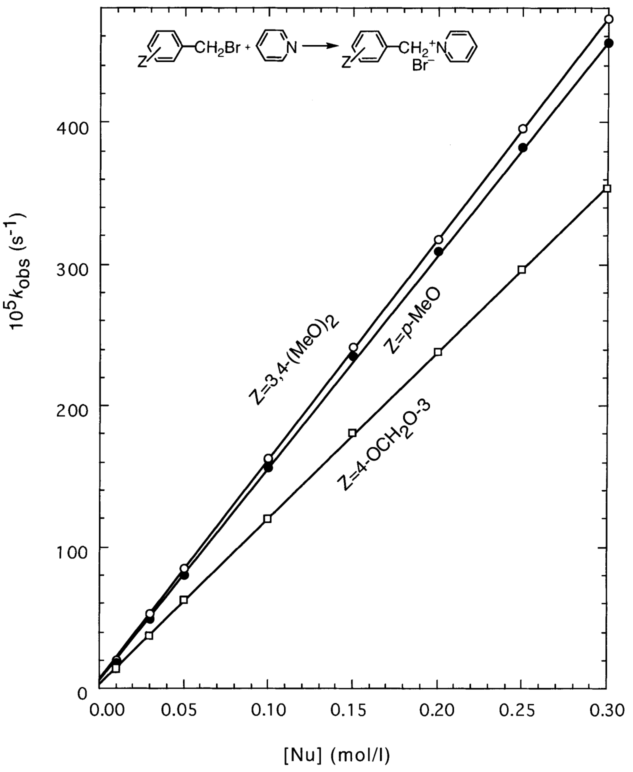


Figure 1. Plots of pseudo-first-order rate constants (k_{obs}) vs pyridine concentrations for the reactions of strongly activated benzyl bromides, **1, 2** and **3**, with unsubstituted pyridine in acetonitrile at 50 °C

Table 2. Pseudo-first-order rate constants (k_{obs}) for the reactions of benzyl bromides **2** and **3** with Y-substituted pyridines in acetonitrile at 50 °C[a]

		4-OCH$_2$O-3 (**3**)		3,4-(MeO)$_2$ (**2**)	
Pyridine Y	[Nu] (mol 1^{-1})	10^5k_{obs} (s^{-1})	10^4k_2* ($lmol^{-1}s^{-1}$)	10^5k_{obs} (s^{-1})	10^4k_2* ($lmol^{-1}s^{-1}$)
4-NH$_2$	0.01	164.4	1644	197.6	1976
	0.03	478	1593	574	1913
	0.05	791	1582	948	1895
	0.08	1280	1600	1520	1900
	0.10	1590	1590	1900	1900
3-NH$_2$	0.01	51.2	512.1	68.7	687
	0.03	149.0	497	197.2	657
	0.05	244	487	322	644
	0.10	483	483	631	631
	0.15	729	486	940	626
	0.20	977	489	1250	625
	0.25	1210	484	1570	628
	0.30	1450	483	1890	630
4-Me	0.01	22.8	228	33.1	331
	0.03	65.6	219	88.4	295
	0.05	107.4	215	142.5	285
	0.10	212	212	277	277
	0.15	312	208	413	275
	0.20	418	209	548	274
	0.25	528	211	682	273
	0.30	626	209	822	274
3-Cl	0.01	3.76	37.6	7.77	77.7
	0.03	6.49	21.6	12.94	43.1
	0.05	9.79	19.6	17.92	35.8
	0.10	16.82	16.8	29.8	29.8
	0.15	23.9	15.9	41.6	27.8
	0.20	30.9	15.5	53.7	26.9
	0.25	38.5	15.4	65.4	26.2
	0.30	45.9	15.3	77.0	25.7

[a] k_2* values were evaluated using Eqn. (2); k_2* = k_{obs}/ [Nu].

philicity of Y-substituted pyridines, i.e. Y: 4-NH$_2$ > 3-NH$_2$ > 4-Me > H > 3-Cl (Table 2).

In Fig. 2, k_{obs} values for **2** are plotted against the concentrations of a series of substituted pyridines. The k_{obs} vs [Nu] plots are all linear with different slopes characteristic of Y-pyridines, and all the linear plots converge to an identical positive intercept at [Nu] = 0. In practice, as shown in Fig. 3, the Y = 3-Cl and also Y = H runs should give a more accurate k_{obs} value of the intercept, because of distinctly lower slopes of their k_{obs} vs [Nu] plots.

The slopes of the linear plots should correspond to the second-order rate constants, k_2, for the bimolecular reactions of the respective bromide with pyridines, and the intercept is independent of the nucleophiles and their concentrations, that is, zeroth order in the nucleophile and first order in the substrate (bromide).

These kinetic results can be fitted into a kinetic equation as the sum of zero- and first-order terms to the nucleophile concentration [Nu]:

$$k_{obs} = k_1 + k_2[\mathrm{Nu}] \tag{3}$$

The k_2 and k_1 values for the reactions of benzyl bromides with pyridines are determined from the slope and intercept of the linear plot of k_{obs} versus concentration of pyridines with Eqn. (3), as shown in Table 3. In the last column in Table 3 are given the compositions (%) of the unimolecular reaction in the overall reaction at [Y-pyridine] = 0.1 M derived based on Eqn. (3).

In the reaction of less activated benzyl bromides[17] of which the substituents Z are less electron-donating than *p*-Me, the reaction was accurately first-order in pyridine concentration following the second-order kinetics of the equation

$$k_{obs} = k_2[\mathrm{Nu}] \tag{4}$$

Experimentally, the plots of pseudo-first-order rate constants k_{obs} vs [Nu] were found to be precisely linear and all to pass through the origin within the experimental uncertainty, as generally observed for typical S_N2 displacement reactions. It is therefore remarkable that the strongly electron-donating bromides **1**–**3** appeared to give significant positive intercepts in the k_{obs} vs [Nu] plots, suggesting a competition of unimolecular reaction. Their k_2 values exhibit a significant dependence upon the nucleophilicity of pyridines and the electron-donating

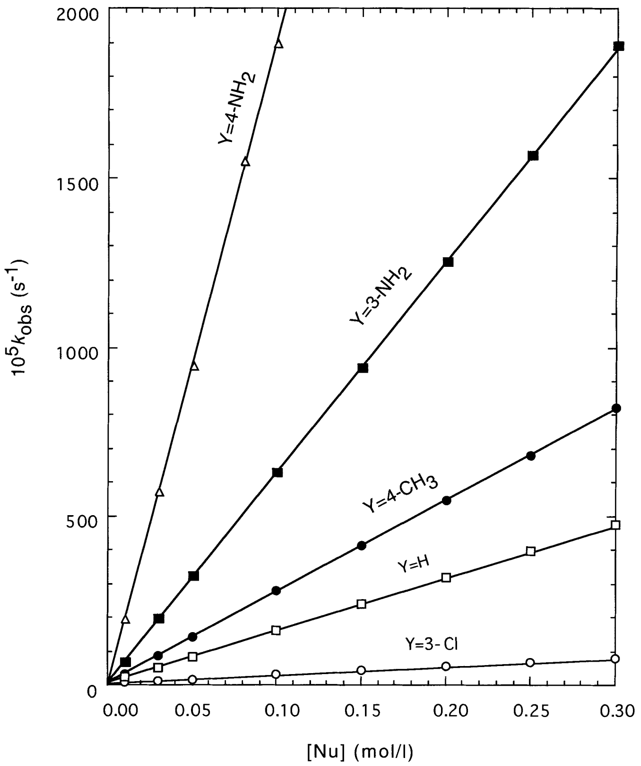


Figure 2. Plots of pseudo-first-order rate constants (k_{obs}) vs nucleophile concentrations for the reactions of 3,4-dimethoxybenzyl bromide with Y-substituted pyridines in acetonitrile at 50 °C

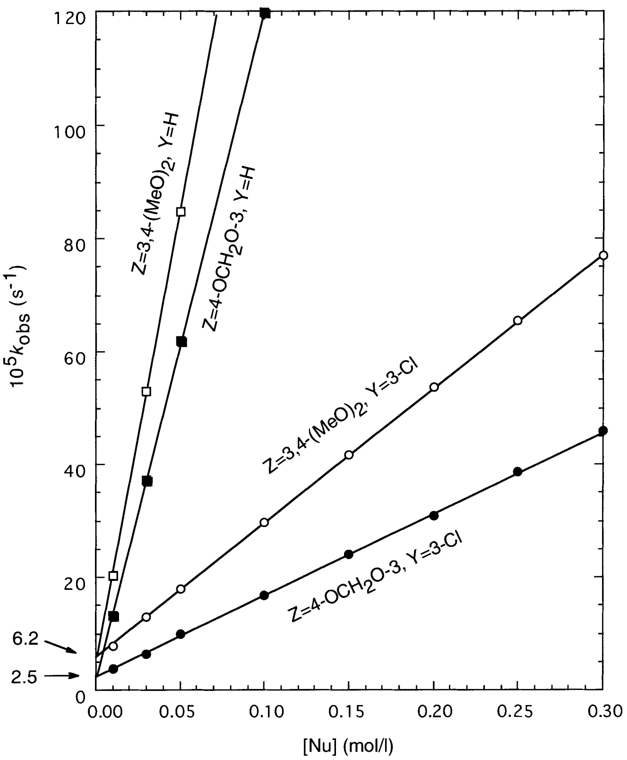


Figure 3. Dependence of k_{obs} on concentrations of 3-chloro- and unsubstituted pyridines in the Menschutkin reactions of benzyl bromides, **2** and **3**, in acetonitrile at 50 °C

ability of substituents Z. The first-order rate constant, k_1, remains a constant irrespective of nucleophiles and is zeroth order in the nucleophile, converging to the same intercept at [Nu] = 0 as shown in Figs 2 and 3.

In the Menschutkin reactions of relevant benzylic precursors, as summarized in Table 4, the competition of the unimolecular mechanism (S_N1 reaction) appeared to be more important in the reactions of the benzyl tosylates than in the corresponding bromides,[15] and the unimolecular mechanism is even more significant for secondary benzylic systems.[16] In the case of 1-phenylethyl bromides, the unimolecular k_1 term was observed for the whole range of electron-donating substituents $\bar{\sigma}_Z{}^+ \leq 0$.[16]

The kinetic Eqn. (3) is compatible with the simultaneous and competitive occurrence of independent S_N1 and S_N2 processes, and the overall reaction can be depicted by the mechanistic Scheme **1**.

Both the unimolecular and bimolecular rate constants k_1 and k_2 should show different susceptibilities to the

Table 3. First-order (k_1) and second-order (k_2) rate constants for the reactions of Z-substituted benzyl bromides with Y-pyridines in acetonitrile at 50 °C

Z	Y	n^a	R^b	Slope 10^4k_2 (lmol^{-1}s^{-1})	Intercept, 10^5k_1 (s^{-1})	$100k_1/(0.1k_2 + k_1)^c$
4-OCH$_2$O-3 (**3**)	4-NH$_2$	5	0.9999	1587	2.6	0.2
	3-NH$_2$	8	0.9999	484	2.6	0.5
	4-Me	8	0.9999	208	2.6	1.2
	H	8	0.9999	117.4	2.5	2.1
	3-Cl	8	0.9999	14.46	2.3	13.8
p-MeO (**1**)	H	9	0.9999	150.4	5.6	3.6
3,4-(MeO)$_2$ (**2**)	4-NH$_2$	5	0.9999	1891	6.5	0.3
	3-NH$_2$	8	0.9999	625	6.4	1.0
	4-Me	8	0.9999	272	6.4	2.3
	H	8	0.9999	155.7	6.2	3.9
	3-Cl	8	0.9999	23.8	5.8	19.5

[a] The number of data.
[b] Correlation coefficient.
[c] Percent reaction by S_N1 route at [Y-pyridine] = 0.1 M.

Table 4. First-order (k_1) and second-order (k_2) rate constants for the Menschutkin reactions of benzylic substrates

Substrate	Z	Nucleophile Nu[a] and solvent[b]	Slope, 10^4k_2 ($\mathrm{lmol^{-1}\ s^{-1}}$)	Intercept, 10^5k_1 ($\mathrm{s^{-1}}$)	$100k_1/(0.1k_2 + k_1)$[c]
Benzyl bromide	*p*-MeO[d]	Py, AN	150.4	5.6	3.6
	p-MeO[e]	Py, AN	68.8	<2	
Benzyl tosylates[e]	*p*-MeS	DMA, AN	137	203	60
	p-MeO	DMA, AN	330[f]	1700[f]	
1-Phenylethyl bromides[e,g]	*p*-MeO	Py, AN	282	1660	85
	H	Py, AN	0.554	0.03	5.5
1-Phenylethyl tosylate[e,h]	H	Py, AN	4.53	10.8	70
	H	DMA, AN	7.98	10.7	58

[a] Nucleophiles, Nu; Py = pyridine; DMA = *N*, *N*-dimethylaniline.
[b] Solvent; AN = acetonitrile.
[c] Percent reaction by S_N1 route at [Y-pyridine] = 0.1 M.
[d] At 50 °C.
[e] At 35 °C.
[f] Estimated by means of the Yukawa-Tsuno correlations for the k_1 and k_2 processes; Ref. 15.
[g] Ref. 16.
[h] Y. Tsuno and M. Fujio, unpublished work data taken from C. Lim, *PhD Dissertation*, Kyushu University, Fukuoka, 1998.

benzyl Z-substituents reflecting the nature of two competing mechanistic processes. For the benzyl Z-substituent effects, the resonance-enhanced scale $\overline{\sigma}^{+}$ appears perhaps to be appropriate. The apparent $\overline{\sigma}^{+}$ values for *p*-methoxy and 3,4-methylenedioxy groups were available from the solvolysis of 1-phenylethyl chlorides, by means of the Yukawa–Tsuno equation:[20]

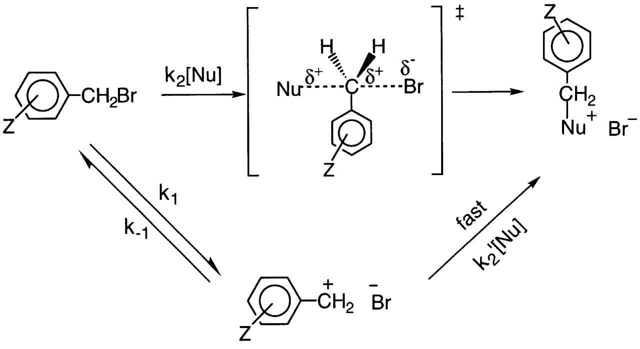
$$\log(k/k_0) = \rho(\sigma^0 + r\Delta\overline{\sigma}_{\mathrm{R}}^{+}) \tag{5}$$

In the solvolysis of 1-phenylethyl chlorides, the apparent $\overline{\sigma}^{+}$ values at $r = 1.14$ were given as -0.923 for *p*-MeO and -0.845 for 3,4-methylenedioxy substituents; the difference $(\overline{\sigma}_1^{+} - \overline{\sigma}_3^{+})$ should be constant at -0.078 irrespective of minor changes in the *r* parameter of the system (Y. Tsuno and M. Fujio, unpublished work). The $\overline{\sigma}^{+}$ value of 3,4-dimethoxy substituent in the present system appears to be slightly more negative than the value for the *p*-methoxy group; this is reasonable for the σ^{+}-type reactions in aprotic acetonitrile solution.

Hence the unimolecular reaction of which the reactivity difference of log $(k_1)_{\mathbf{1}}/(k_1)_{\mathbf{3}} = 0.40$ between **1** and **3** gives a ρ^{+} value of ca. -5, for the difference -0.08 in $\overline{\sigma}^{+}$ for **1** and **3**. On the other hand, the corresponding reactivity difference log $(k_2)_{\mathbf{1}}/(k_2)_{\mathbf{3}} \approx 0.1$ for this σ^{+} range gives a small ρ^{+} of -1 and also a lower ρ value of -0.5 for electron-withdrawing substituents from previously reported data.[17]

The ρ^{+} value of -5 for the unimolecular reaction is comparable to those for typical S_N1 solvolyses of benzylic substrates. The curved σ^{+} plot with smaller varying ρ^{+} for the bimolecular reaction is characteristic of the S_N2 mechanism, involving the tight–loose coordinate shift of the transition state with Z-substituents.

The ionizing power of the solvent will render it possible to distinguish between the unimolecular S_N1 and the bimolecular S_N2 mechanisms. The apparent k_{obs} for 3,4-dimethoxybenzyl bromide (**2**) with pyridine increases with increasing content of TFE in the range 0–5% (v/v) in binary acetonitrile–2,2,2-trifluoroethanol (TFE) mixtures at 50 °C (Table 5). In Fig. 4, the plot of log k_{obs} vs [Nu] for **2** in neat acetonitrile solution moves upwards in a



Scheme 1

Table 5. Pseudo-first-order rate constants (k_{obs}) for the reactions of 3,4-dimethoxybenzyl bromide with pyridine in TFE–acetonitrile mixtures at 50 °C

	$10^5k_{\mathrm{obs}}/(\mathrm{s^{-1}})$	
[Pyridine] ($\mathrm{mol\ 1^{-1}}$)	2% (v/v) TFE	5% (v/v) TFE
0.01	30.0	54.6
0.03	63.1	89.8
0.05	93.8	120.6
0.10	173.7	197.5
0.15	253	279
0.20	328	357
0.25	405	434
0.30	485	511
10^5k_1 ($\mathrm{s^{-1}}$)	16.1	41.4
10^4k_2 ($\mathrm{l\,mol^{-1}\ s^{-1}}$)	156.2	157.1

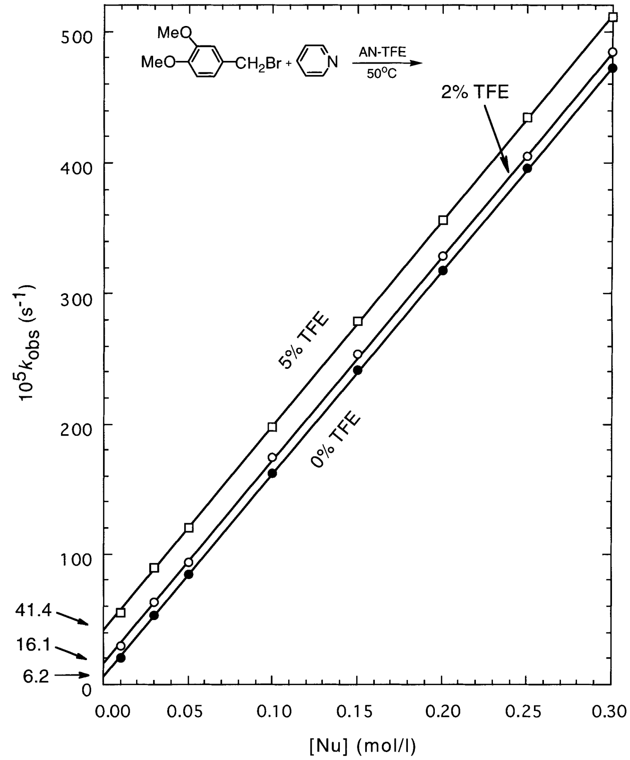


Figure 4. Plots of pseudo-first-order rate constants (k_{obs}) vs nucleophile concentrations for the reactions of 3,4-dimethoxybenzyl bromide with pyridine in TFE–acetonitrile mixtures at 50 °C

parallel manner with increasing TFE content in solvent; the increasing TFE content brings about higher intercepts, i.e. enhanced k_1 values, without a change in the slope of the plot, i.e. no change in k_2. These results imply that the unimolecular process should have a highly carbocationic transition state (most plausibly referred to as an S_N1 mechanism) but the bimolecular process an essentially neutral or uncharged transition state (S_N2 mechanism). Essentially the same solvent effect has been observed in the reaction of 1-phenylethyl arenesulfonates.[21]

The S_N1 mechanism can be evidenced by the detection of the return (k_{-1}) process from the intermediate to the reactant. In the Menschutkin reaction of benzyl tosylate, the ^{18}O scrambling of the alkoxy oxygen within the sulfonyl-O labeled tosylates-$S(^{18}O)_2$ was detected with or without *N*,*N*-dimethylanilines in acetonitrile.[22] These findings provide strong support for the concurrent k_1 ionization process of an S_N1 mechanism.

We have taken the present results as convincing evidence for the occurrence of simultaneous S_N1 and S_N2 mechanisms but against the mechanism with a single process involving either a common intermediate or a transition state, in the reaction of activated benzyl bromides with amines.

For the so-called S_N1 mechanism, the apparent reaction rate constant k_{S_N1*} can be expressed by

$$k_{S_N1*} = k_1 k'_2[\mathrm{Nu}]/(k_{-1} + k'_2[\mathrm{Nu}]) \tag{6}$$

Hence, when k'_2 [Nu] $\gg$ k_{-1}, Eqn. (6) should be reduced to the simple unimolecular rate equation, whereas Eqn. (6) corresponds to the bimolecular rate equation [Eqn. (4)] when $k_{-1} \gg k'_2$ [Nu]. This constitutes the basis of the Sneen unified ion-pair merged mechanism[6] of nucleophilic substitution. Nevertheless, whereas this merged mechanism may describe either the S_N1 or the S_N2 mechanism in terms of whether $k_{-1} \ll k'_2$ [Nu] or $k_{-1} \gg k'_2$ [Nu], it does not interpret the concurrent S_N1 and S_N2 mechanisms, i.e. Eqn. (3).

The present results are not compatible with the Sneen merged mechanism,[6] and the simplest scheme of the whole reaction should be described by Eqn. (3) or Eqn. (7) with $k_{-1} \ll k'_2$ [Nu]:

$$\begin{aligned} k_{obs} &= k_1 + k_2[\mathrm{Nu}] \\ &= k_1 k'_2[\mathrm{Nu}]/(k_{-1} + k'_2[\mathrm{Nu}]) + k_2[\mathrm{Nu}] \end{aligned} \tag{7}$$

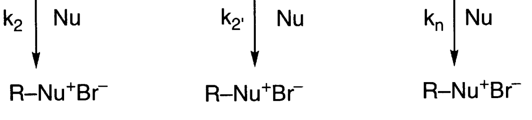
Both terms are exactly referred to the classical S_N1 and S_N2 mechanisms by the Ingold definition.[1] We believe that the results provide evidence for the duality of mechanisms at least for highly activated benzyl bromides even in the presence of a good nucleophile in acetonitrile. However, if $k_{-1} \gg k'_2$ [Nu], the S_N1 mechanism does not compete with the S_N2 mechanism from this simplest Scheme **1**.

According to the Winstein ion-pair scheme (Scheme **2**),[3] when $k_{-1} \gg k'_2$ [Nu], the S_N1 mechanism should operate at the second carbocation (or the final ion pair) intermediate, of which the foregoing transition state is essentially rate determining. Provided $k_{-C} \ll k_n$ [Nu], k_{obs} can be given by a kinetic equation:

$$k_{obs} \approx (k_2 + K_1 k'_2)[\mathrm{Nu}] + K_1 k_c \tag{8}$$

where $K_1 = k_1/k_{-1}$. The form of the equation does not depend on the number of intervening ion-pair intermediates; the term $K_1 k'_2$ [Nu] may be replaced by the sum of terms $[\mathrm{Nu}]\Sigma(K_1 k_2)_i$. Thus the S_N1 and S_N2 mechanisms remain distinct from their molecularity (or the kinetic order) in the present reaction.

The Bentley-Schleyer concept of a continuous spectrum of S_N1–S_N2 mechanisms[7] involves the S_N2 (inter-



Scheme 2

mediate) mechanism, given by the term $K_1k'_2$ [Nu] in Eqn. (8), which may correspond to the Sneen S_N2 mechanism. Whereas we see a continuous series of S_N2 mechanisms of varying tightness for the bimolecular process on changing the Z substituents, the S_N2 (intermediate) should be the loosest (most dissociative) limit of the S_N2 transition state. Nevertheless, this mechanism is still discernible from the unimolecular ionization mechanism, even though it closely resembles in structure the transition state of the S_N1 mechanism.[15,16]

Katritzky and co-workers' amine exchange of benzyl-2,4,6-triphenylpyridinium ion is virtually an identity reaction, which is conceivably an ideal system to be described by a continuous spectrum of S_N2 mechanisms of varying tightness.[5] The competition of the unimolecular reaction must be highly enhanced. The bulky leaving group should enhance the dissociation but retard the S_N2 reaction by steric hindrance to the approaching nucleophile. In addition, the aprotic solvent should be favorable for the S_N2 mechanism but not unfavorable for the S_N1 mechanism of the positively charged (or almost neutral) leaving groups. Nevertheless, the duality of S_N1–S_N2 mechanisms is in fact independent of the different natures of the leaving groups. Furthermore, the reactions of *p*-methoxybenzyl bromide (**1**) with pyridines or with thiourea in aqueous acetone solution were also found to proceed by simultaneous S_N1 and S_N2 mechanisms.[23] The simultaneous occurrence of independent S_N1 and S_N2 mechanisms is believed to be fairly general and not specific to the present Menschutkin system in aprotic solvents.

Finally, the nature of the Menschutkin reaction as a typical bimolecular mechanism can also be most clearly demonstrated by the substituent effects of nucleophiles by means of the Brønsted-type or the Hammett-type relationships.[4a] The ρ_y values in the log k_2 vs $\sigma_{\rho y}$ relationship[19] for the nucleophile substituent effects of these bromides **2** and **3** (in Tables 1 and 2) are -1.85 and -1.98. These ρ_y values refer to the Brønsted-type β values, 0.25 and 0.27. The magnitudes of these ρ_y and β values are very compatible with the bimolecular process of the dissociative S_N2 mechanism.[11] Detailed discussion on this point will be reported, including full data for electron-withdrawing Z-benzyl substrates, in separate papers.

EXPERIMENTAL

Materials. Purification of acetonitrile has been described previously.[15,17] Pyridines are commercially available and were further purified by distillation or recrystallization before use. Benzyl bromides were prepared from the corresponding benzyl alcohols commercially available by bromination with hydrobromic acid.

The typical method for preparing piperonyl bromide is as follows: HBr gas in 47% HBr solution was added using a connected glass tube to 10 ml of an ethereal solution of piperonyl alcohol (0.015 mol, 2.28 g), with stirring below 0 °C for several hours. The product was extracted with diethyl ether, washed twice, treated with 10% K_2CO_3 solution and then distilled under reduced pressure. The crude piperonyl bromide was purified by recrystallization from diethyl ether-hexane; m.p. 48 °C (lit.[24] 49 °C); ^1H NMR ($CDCl_3$), δ 4.71 (s, 2H, CH_2), 6.13 (s, 2H, —OCH_2O—), 6.90–7.24 (m, 3H, aromatic). *p*-MeO derivative; liquid; ^1H NMR ($CDCl_3$), δ 3.79 (s, 3H, CH_3O), 4.61 (s, 2H, CH_2), 6.83–7.49 (m, 4H, aromatic). 3,4-$(MeO)_2$ derivative; m.p. 39–41 °C; ^1H NMR ($CDCl_3$), δ 4.04 (s, 6H, $(CH_3O)_2$), 4.62 (s, 2H, CH_2), 7.14–7.48 (m, 3H, aromatic).

Kinetic measurements. The reaction rates of substituted benzyl bromides with pyridine in acetonitrile at 50 °C were measured using a conductimetric method[15] by following the conductance changes of the quaternary pyridinium salts formed in the reaction as shown in Eqn. (1).

All kinetic runs were carried out under the pseudo-first-order conditions with initial concentrations of 0.01–0.30 M pyridine, which are 20–600 times larger than the initial concentration (0.0005 M) of the substrate, benzyl bromides.

The second- and first-order rate constants k_2 and k_1 in Eqn. (3) were determined by the least - squares method as the slope and intercept of the plot of pseudo-first-order rate constants k_{obs} vs [Nu]; correlation coefficients $R > 0.9999$.

Acknowledgements

This work was partially supported by the KOSEF through the Center for Biofunctional Molecules and the Basic Research Institute Program, Ministry of Education, Korea (BSRI - 1998–1999).

REFERENCES

1. Ingold CK. *Structure and Mechanism in Organic Chemistry* (2nd edn). Cornell University Press; London, 1969.
2. (a) McLennan DJ. *Acc. Chem. Res.* 1976; **9**: 281, and references cited therein; (b) Harris JM. *Prog. Phys. Org. Chem.* 1974; **11**: 89; (c) Richard JP. *Tetrahedron* 1995; **51**: 1535.
3. Winstein S, Appel B, Baker R, Diaz A. *Spec. Publ. Chem. Soc.* 1965; **(19)**: 109.
4. (a) Abboud J-LM, Notario R, Bertran J, Sola M. *Prog. Phys. Org. Chem.* 1993; **19**: 1; (b) Westaway KC, Waszczylo Z. *Can. J. Chem.* 1982; **60**: 2500; (c) Ballistreri FP, Maccarone E, Mamo A. *J. Org. Chem.* 1976; **41**: 3364; (d) Richard JP, Yeary PE. *J. Am. Chem. Soc.* 1993; **115**: 1739; Richard JP. *J. Org. Chem.* 1992; **57**: 625; Amyes TL, Stevens IW, Richard JP. *J. Org. Chem.* 1993; **58**: 6057.
5. (a) Katritzky AR, Musumarra G, Sakizadeh K, El-Shafie SMM, Jovanovic B. *Tetrahedron Lett.* 1980; **21**: 2697; (b) Katritzky AR, Musumarra G, Sakizadeh K. *J. Org. Chem.* 1981; **46**: 3831; (c) Katritzky AR, Brychi BE. *J. Phys. Org. Chem.* 1988; **1**: 1; (d) Katritzky AR, Brycki BE. *Chem. Soc. Rev.* 1990; **19**, 83.
6. Sneen RA. *Acc. Chem. Res.* 1973; **6**: 46.
7. (a) Bentley TW, Schleyer PvR. *J. Am. Chem. Soc.* 1976; **98**: 7658;

(b) Schadt FL, Bentley TW, Schleyer PvR. *J. Am. Chem. Soc.* 1976; **98**: 7667; (c) Bentley TW, Bowen CT, Morten DH, Schleyer PvR. *J. Am. Chem. Soc.* 1981; **103**: 5466.

8. Yoh S-D. *PhD Dissertation*, Osaka University, 1973.
9. Yoh S-D, Tsuno Y, Yukawa Y. *J. Korean Chem. Soc.* 1984; **28**: 433.
10. Yoh S-D, Tsuno Y, Fujio M, Sawada M, Yukawa Y. *J. Chem. Soc., Perkin Trans.* **2** 1989; 7.
11. (a) Yoh S-D, Cheong D-Y. *J. Phys. Org. Chem.* 1995; **8**: 442; (b) Yoh S-D, Cheong D-Y. *J. Phys. Org. Chem.* 1996; **9**: 701.
12. Yoh S-D, Cheong D-Y, Park J-H, Kim S-H, Howang K-H. *Bull. Korean Chem. Soc.* 1998; **19**: 434.
13. Kim S-H. *PhD Dissertation*, Kyungpook National University, Taegu, Korea, 1992.
14. Kim S-H, Yoh S-D, Fujio M, Imahori H, Mishima M, Tsuno Y. *Bull. Korean Chem. Soc.* 1995; **16**: 760.
15. Kim S-H, Yoh S-D, Lim C, Mishima M, Fujio M, Tsuno Y. *J. Phys. Org. Chem.* 1998; **11**, 254.
16. Lim C, Kim S-H, Yoh S-D, Fujio M, Tsuno Y. *Tetrahedron Lett.* 1997; **38**: 3243.
17. Cheong D-Y, Kim S-H, Lee M-H, Yoh S-D, Fujio M, Tsuno Y. *J. Korean Chem. Soc.* 1995; **39**: 643.
18. Yoh S-D, Kim H-R, Kim S-H, Park B-S. *J. Korean Chem. Soc.* 1988; **32**: 581.
19. Cheong D-Y, Yoh S-D. *Bull. Korean Chem. Soc.* 1995; **16**: 604.
20. Tsuno Y, Fujio M. *Adv. Phys. Org. Chem.* 1999; **32**: 267.
21. Howang KT. *PhD Dissertation.* Kyungpook National University, Taegu, Korea, 2000.
22. Tsuji Y, Saeki Y, Yatsugi K, Kim S-G, Fujio M, Tsuno Y. *Mem. Fac. Sci. Kyushu Univ., Ser. C* 1993; **19**: 47.
23. Queen A. *Can. J. Chem.* 1979; **57**: 2646.
24. Robinson GM, Robinson R. *J. Chem. Soc.* 1914; **105**: 1456.