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The Menschutkin Reaction of 1-Arylethyl Bromides with Pyridine: Evidence for the Duality of Clean S_N1 and S_N2 Mechanisms

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Abstract: 1-Arylethyl bromides react with pyridine in acetonitrile by unimolecular and bimolecular processes. These processes are quite distinct and this fact affords clear evidence for the duality of clean S_N1 and S_N2 mechanisms, occurrence of independent S_N1 and S_N2 reaction processes without an intermediate mechanism.

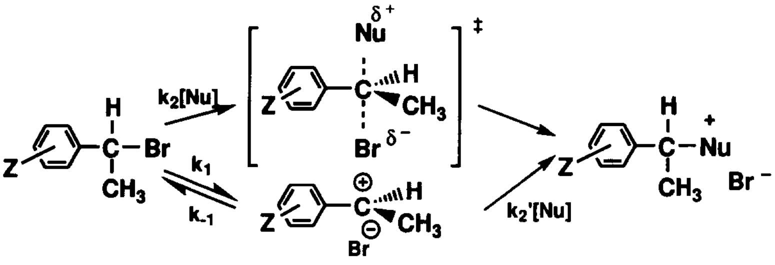
The nucleophilic displacement reaction of 1-phenylethyl precursors has long been of particular interest, primarily because of the mechanistic complexity that the electron-attracting aryl substituent brings about, by the destabilization of the carbocationic transition state and enhancement of nucleophilic attack, which leads to S_N1-S_N2 mechanistic changeover.1,2) Thus, the exalted r value of 1.15 in substituent effect correlations for solvolytic reactions of 1-phenylethyl precursors in terms of Yukawa-Tsuno Eq. (1) 3,4)

$$\log (k/k_0) = \rho\ (\sigma^0 + r\Delta\bar{\sigma}_R^+) \qquad (1)$$

has been interpreted in terms of the changeover of mechanism from S_N1 for electron-donating substituent region to S_N2 for electron-attracting one in a high nucleophilic solvent such as 80% aq. acetone.5) Whereas there remains a fundamental question concerning the molecularity of the rate-determining step, there is no way to solve this problem by kinetics under the solvolytic conditions. In the present paper, we have chosen a typical S_N2 reaction, namely, the Menschutkin reaction of such a borderline system and carried out precise examination of the kinetic dependence of the rate on the nucleophile pyridine concentration [Nu] for a wide range of substituents in 1-arylethyl bromides in the nonsolvolyzing solvent acetonitrile at 35°C.

Observed rate constants, k_{obs}, were determined under pseudo-first-order condition at various concentrations [Nu] of pyridine (0.01-0.3M) and bromides (0.0005M) by following the conductance changes of the pyridinium salt produced in a similar way to that in previous relevant studies.6) For all derivatives more deactivated than the unsubstituted one, the reaction clearly proceeds almost entirely by a second-order process (bimolecular S_N2 mechanism); the plot of k_{obs} vs. [Nu] passes through the origin within experimental uncertainty, indicating that the reaction is accurately first-order in pyridine concentration. On the other hand, there is a significant intercept in these plots for the electron-donating substituents, while there is a significant first-order component, indicating concurrence of a zeroth-order reaction in pyridine. These results can be fitted to an experimental kinetic equation (2) and depicted by the mechanistic scheme 1.

$$k_{obs} = k_1 + k_2[\mathrm{Nu}] \qquad (2)$$



Scheme 1

There is a zeroth-order component (k_1), which is independent of the amount and nature of the nucleophile. In other words, we clearly have the S_N1 component alongside of the S_N2 one. Since the reaction was studied in inert solvent there is no doubt that the solvent is acting truly as a solvent and not as a nucleophile.

The k_1 and k_2 values were calculated by Eq. (2) and are listed in Table 1. The dependence of the S_N1 rate on the aryl substituents is clearly far greater than that of the S_N2 rate. While the S_N1 rates can be obtained only for the limited range of substituted derivatives which are more electron-donating than H, the substituent effect of this unimolecular process can be described in terms of Eq. (1) with a ρ value of -5.0 and an exalted r value of 1.15 (correlation coefficient=0.999 and SD=±0.07) as shown by the excellent linear plot in Fig. 1. The correlation parameters are the same as those obtained for the corresponding 1-phenylethyl chloride solvolyses in solvolyzing solvents proceeding through pure S_N1 carbocationic transition state.[3)]

On the other hand, the plot of log k_2 vs. $\bar{\sigma}$ (r=1.15) for the bimolecular process gives a smooth curvature as shown in Fig. 1. The curved plot is interpreted in terms of a gradual change in ρ value associated with the so-called S_N2-S_N1 mechanistic shift as the substituent changes from strongly deactivated (Z=3,5-$(CF_3)_2$) to highly activated (Z=*p*-MeO) substituents. The negative ρ value should indicate the positive charge accumulated at the central carbon in the transition state, implying a significant imbalance between the bond formation and

Table 1. Rate data (cf., Eq. (2)) for the unimolecular (k_1) and bimolecular (k_2) reactions of 1-arylethyl bromides with pyridine in MeCN at 35°C

Subst. Z	$10^5k_1(s^{-1})$	$10^5k_2(M^{-1}s^{-1})$	Subst. Z	$10^5k_1(s^{-1})$	$10^5k_2(M^{-1}s^{-1})$
p-MeO	1660	2820	2-Naph	0.28	11.6
p-MeS	103	215	*m*-Me	0.055	7.29
p-PhO	41.5	119	H	0.032	5.54
p-MeO-*m*-Cl	21.2	79.0	*p*-Cl	—	4.37
2-Fluorenyl (2-Fl)	18.3	59.5	*m*-Cl	—	2.085
3,4,5-Me_3	8.56	41.1	*m*-CF_3	—	1.77
3,4-Me_2	3.67	28.3	*m*-NO_2	—	1.21
p-Me	1.46	19.2	*p*-NO_2	—	1.19
p-*t*-Bu	0.81	15.2	3,5-$(CF_3)_2$	—	0.651

bond cleavage, i.e., the preferential bond breaking over bond formation in the pentavalent displacement structure of the S_N2 transition state. Similarly, a curved correlation of the substituent effect has been observed in the Menschutkin reaction of substituted benzyl tosylates with a nucleophile and has been elegantly interpreted by the perpendicular shift of the transition state coordinate for the bimolecular displacement mechanism from neutral (tight) to carbocationic transition state (loose) with the substituent Z.[6] The transition state should become more S_N1-like (loose) as the aryl substituent becomes more electron-donative.

The concave plot of log k_2 against $\bar{\sigma}$ (r=1.15) for the bimolecular process can well be analyzed in terms of regressional power series expression, log $(k_Z/k_H) = -1.54\bar{\sigma} + 0.74(\bar{\sigma})^2$ (*p*-MeO excluded), with correlation coefficient = 0.995 and SD = ±0.08 (n=17).[7] The apparent ρ_Z values for the bimolecular process are estimated to be -2.9 ~ -2.6 for Z=*p*-MeO ~ 2-Fluorenyl and -0.1 for Z=3,5-(CF_3)$_2$ from the tangent value of the

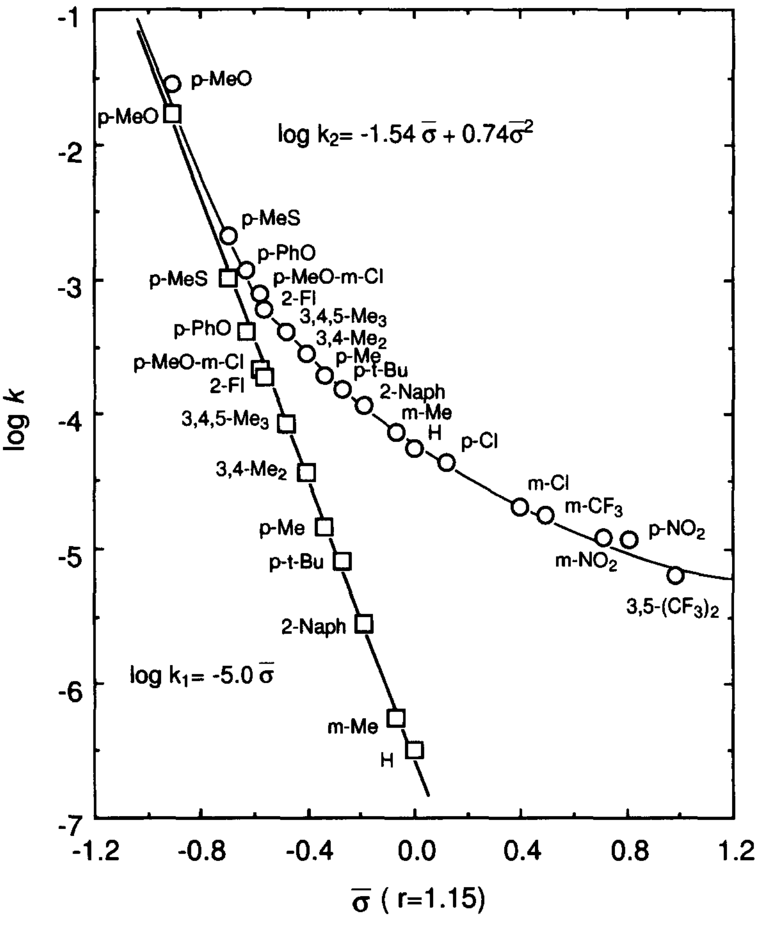


Fig. 1. The substituent effect in the Menschutkin reaction of 1-arylethyl bromides with pyridine in acetonitrile at 35°C; circles represent k_2 for the bimolecular process and squares k_1 for unimolecular process.

correlation curve. The resonance-exalted substituent dependence with an appreciably high negative ρ value will indicate the near limiting (S_N1) nature of the S_N2 mechanism for strongly electron-donating substituents. While the reaction of strongly rate-enhancing *p*-MeO derivative appears to proceed through an appreciably cationic transition state, it should still be characterized as a bimolecular displacement mechanism of the so-called S_N2 category. For the deactivated derivatives ranging from *m*-Cl to 3,5-$(CF_3)_2$, the significantly small $|\rho|$ value should be related to a tight transition state in the present S_N2 reaction.

The recognition by Ingold of distinct S_N1 and S_N2 reaction mechanisms for nucleophilic substitution at saturated carbon atoms was a milestone in the development of organic chemistry.8) Although the reality of these distinct reaction types is now universally recognized,9) the fundamental question of whether S_N1 and S_N2 reactions remain distinct at the borderline or gradually merge is still very controversial. Bentley and Schleyer proposed the concept of a continuous spectrum of S_N1-S_N2 solvolytic mechanisms, from S_N1 through S_N2(intermediate) to the conventional S_N2 mechanism.10) This is in contrast with the present experimental evidence. Indeed, we believe that we have provided here a clear and unambiguous evidence which solves this controversy, namely, that S_N1 and S_N2 reactions can indeed remain distinct and that at a mechanistic borderline, as well as at a most electron-donating end of the substrate series, the reaction occurs by both reaction pathways proceeding independently and simultaneously. In conclusion, S_N1 and S_N2 reaction pathways constitute different channels and the energetically unfavored channel still exists even when only the favorable one is experimentally observed.

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