

REACTION OF *exo*-2-NORBORNYL AND 1-ADAMANTYL *p*-TOLUENESULFONATES WITH
SODIUM PHENOXIDE IN TETRAHYDROFURAN. IONIZATION OF THE SUBSTRATES
UNDER "APPARENTLY-S_N2" CONDITIONS

Ken'ichi TAKEUCHI, Yukari KATO, Takamasa MORIYAMA, and Kunio OKAMOTO*
Department of Hydrocarbon Chemistry, Faculty of Engineering,
Kyoto University, Sakyo-ku, Kyoto 606

exo-2-Norbornyl and 1-adamantyl tosylates react with sodium phenoxide in tetrahydrofuran *via* ionization, most probably through a cyclic transition state. The results call for attention in interpreting substitution reactions under "apparently-S_N2" conditions.

It is well known that some salts, such as lithium perchlorate, promote ionization of various organic substrates in less polar solvents, especially in ethereal ones.¹⁾ In their pioneering work on salt-promoted ionization of organic substrates, Winstein and his coworkers examined the effects of various salts composed of Li⁺, Na⁺, Bu₄N⁺, and ClO₄⁻, Br⁻, *p*-nitrobenzoate anion on the rates of ionization of 2,2-dimethyl-2-(*p*-methoxyphenyl)ethyl tosylate²⁾ and spiro[4.5]deca-6,9-dien-8-yl *p*-nitrobenzoate³⁾ in less polar solvents. However, no mention has been made of the products from the former substrate; the latter substrate has been reported to give only tetrahydronaphthalene, no substitution products being formed.

Here we wish to report on the unique behavior of sodium phenoxide (NaOPh) in tetrahydrofuran (THF) that the salt not only promotes ionization of *exo*-2-norbornyl and 1-adamantyl tosylates (1 and 2, respectively), but affords substitution products. Notably, it has been shown that the reaction obeys good second-order kinetics, but actually it proceeds with rate-determining ionization. The present findings suggest that one must be careful in interpreting the mechanism of the reactions which are conducted under "apparently-S_N2" conditions.

Kinetic Studies — The tosylates 1 and 2 are essentially intact in THF at 75°C in the absence of added salts. However, when the reaction of 1 and 2 with NaOPh in THF at 75.0 and 100.0°C is followed titrimetrically, it obeys good second-order kinetics (Fig. 1 and 2 for the reactions at 100.0°C). In addition, the pseudo first-order rate constant determined at 75.0°C by use of excess NaOPh increases linearly with the NaOPh concentration (Fig. 3). Thus the reaction appears to proceed as if it followed an S_N2 mechanism. However, it has been found that the ionization of these tosylates is enormously accelerated by LiClO₄ (Fig. 3). This suggested that NaOPh actually accelerates ionization of the tosylates in the manner similar to LiClO₄. Consequently, with a view to obtaining evidence for the ionization, the products of the reaction and the deuterium scrambling in the products from *exo*-2-norbornyl-*exo*-3-*d* tosylate (1-3-*d*) have been examined as follows.

Product Studies — The reactions of 1 and 2 with NaOPh in THF at 100°C for ten

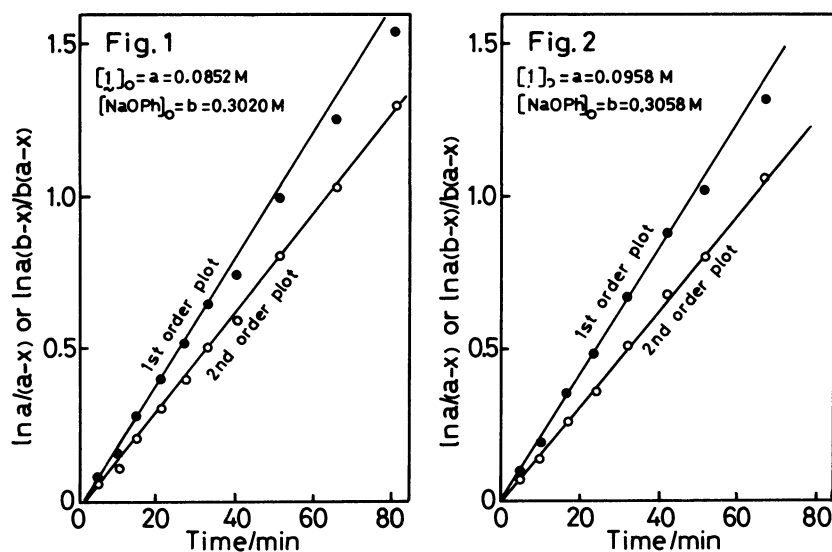


Fig. 1, 2. First- and second-order plots for the reaction of 1 (Fig. 1) and 2 (Fig. 2) with NaOPh in THF at 100.0 °C.

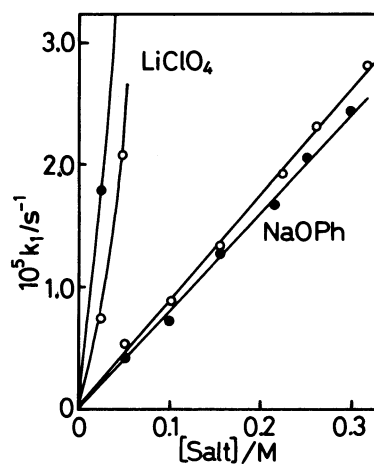


Fig. 3. Effects of added salts on the rates of reaction of 1 and 2 in THF at 75.0 °C; open circle, 1; closed circle, 2.

half-lives afforded the corresponding alkyl phenyl ethers (O-alkylation) and alkylphenols (C-alkylation) as main substitution products,⁴⁾ the latter being predominantly composed of *o*-alkylphenols. Besides these expected products, substantial amounts of 2-(4-phenoxybutoxy)norbornane (3) and 1-(4-phenoxybutoxy)adamantane (4), which are apparently formed by the ring-opening of THF, were isolated.⁵⁾ In the case of 1 considerable amounts of elimination products (58.0%) were produced.⁶⁾ The results are shown in the Table.

Table. Substitution products in the reaction of *exo*-2-norbornyl and 1-adamantyl tosylates (0.1 M) with NaOPh (0.3 M) in THF at 100.0 °C

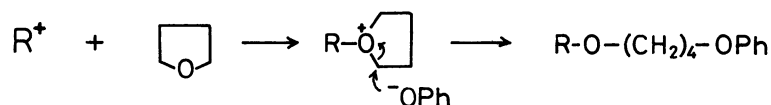
ROTs	Time/h	Substitution products/% ^a			
		ROPh	<i>o</i> -RC ₆ H ₄ OH	<i>p</i> -RC ₆ H ₄ OH	RO(CH ₂) ₄ OPh
<i>exo</i> -2-Norbornyl tosylate (<u>1</u>)	4.0	12.7 ^b	19.4 ^c	0.4	9.5 ^d
1-Adamantyl tosylate (<u>2</u>)	5.0	35.7	37.1	0.0	27.2

a) The percentages are relative to GLPC internal standard and normalized. b) *exo:endo* = 97:3. c) *exo:endo* = 96:4. d) *exo* > 91%

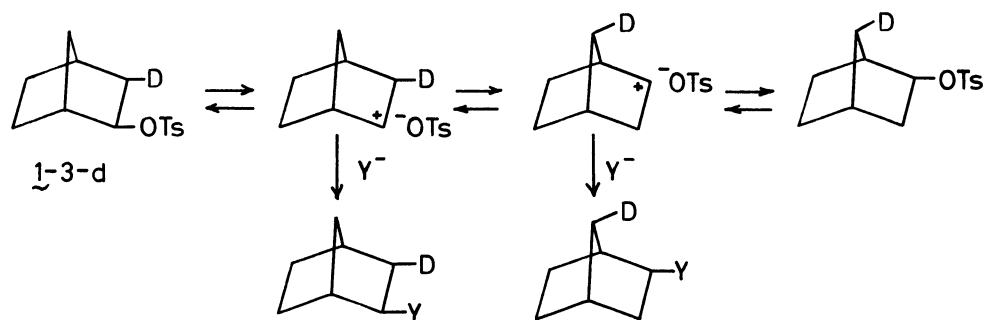
The *exo:endo* product ratios in 2-phenoxy-norbornane and in *o*-(2-norbornyl)phenol from *exo*-2-norbornyl tosylate 1 are 97:3 and 96:4, respectively. The predominance of the *exo* substitution is in harmony with the predominant *exo* substitution generally observed in the solvolytic reactions,⁷⁾ suggesting that 1 reacts with NaOPh in THF via 2-norbornyl cation.

The formation of the ring-opening products [RO(CH₂)₄OPh] from THF can be best

explained in terms of the mechanism involving the nucleophilic attack of THF to the carbocations followed by the S_N2 attack of a phenoxide ion to the oxonium ion. Therefore, this also provides strong evidence for ionization of 1 and 2.



Deuterium Scrambling in the Substitution Products — In order to obtain conclusive evidence for the ionization of the tosylates, the reaction of *exo*-2-norbornyl-*exo*-3-*d* tosylate (1-3-*d*) with NaOPh in THF has been conducted at 100.0°C, and the deuterium distribution in the substitution products determined with ^{13}C NMR. The deuterium has been found to scramble completely to the C-3 and C-7 positions in each of the three kinds of substitution products. In addition, the deuterium in the re-claimed tosylate has been found to distribute to the 3- and 7-positions. Clearly the phenoxide and THF trap the "symmetric" (bridged or rapidly equilibrating) norbornyl cation (Scheme).⁸⁾

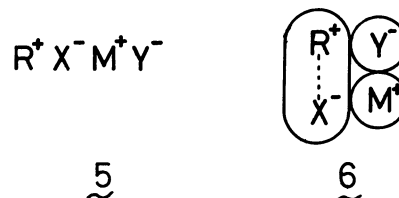


Scheme

As to the reaction of 1-adamantyl tosylate 2, direct evidence for ionization such as ^{18}O scrambling, has not been obtained; however, it must be safely concluded from the aforementioned product study that this also reacts *via* ionization.

The acceleration of ionization of organic substrates by added salts (M^+Y^-) in less polar solvents has been interpreted in two different manners. Winstein²⁾ and Pocker⁹⁾ proposed a linear quadruple ion intermediate 5, whereas Perrin and Pressing¹⁰⁾ postulated cyclic, electrostatic dipole-dipole interaction between the salt and the transition state as illustrated by 6. Although it is premature to conclude which of the two models be more likely, the present kinetic studies appear to support the cyclic model 6 on the basis of the following findings. The rate ratio (2/1) dramatically changes depending on the kind of salt. In the presence of LiClO_4 , 1-adamantyl tosylate 2 reacts twice as fast as *exo*-2-norbornyl tosylate 1 at 75.0°C (Fig. 3).¹¹⁾

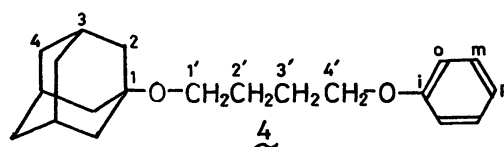
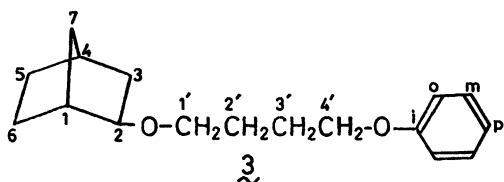
On the other hand, in the reaction with NaOPh the order of reactivity is reversed, and 2 reacts slightly more slowly than 1, with the rate ratio (2/1) being 0.8 - 0.9 (Fig. 3). This dependence of the rate ratio on the kind of salt seems to be explicable by postulating the interaction of the counter anion of the salt ion-pair with the cationic



center at the transition state.¹²⁾ Presumably, the phenoxide anion interacts with the secondary center of 1 more intimately than with the tertiary center of 2 for steric reasons. Further mechanistic implication of the salt effects will be discussed in detail in a full paper by including the results of 2,2-dimethyl-2-(*p*-methoxyphenyl)-ethyl and *endo*-2-norbornyl tosylates as additional substrates.

References and notes

- 1) J. E. Gordon, "The Organic Chemistry of Electrolyte Solutions," Wiley-Interscience, New York (1975), Chap. 1.
- 2) S. Winstein, S. Smith, and D. Darwish, *J. Am. Chem. Soc.*, **81**, 5511 (1959).
- 3) S. Winstein, E. C. Friedrich, and S. Smith, *ibid.*, **86**, 305 (1964).
- 4) These products showed spectral and GLPC data identical with those of authentic samples; see, a) K. Okamoto, K. Matsubara, and T. Kinoshita, *Bull. Chem. Soc. Jpn.*, **45**, 1191 (1972); b) K. Okamoto, T. Kinoshita, and Y. Ito, *ibid.*, **46**, 2905 (1973).
- 5) 3 and 4 were isolated in the liquid state with TLC (silica gel). 3: ¹H NMR (CCl₄,



60 MHz) δ 0.9-2.0 (m, 12H), 2.2 (br, 2H), 3.2-3.5 (t and m overlap, 3H), 3.90 (t, 2H, $J=6$ Hz), and 6.6-7.3 (m, 5H); ¹³C NMR (CDCl₃, 25 MHz) δ 24.6 (C-6), 26.3 (C-2' or 3'), 26.6 (C-2' or 3'), 28.5 (C-5), 34.8 (C-4), 35.0 (C-7), 39.6 (C-3), 40.3 (C-1), 67.5 (C-1' or 4'), 67.6 (C-1' or 4'), 82.4 (C-2), 114.4 (C-o), 120.4 (C-p), 129.5 (C-m), and 159.1 (C-i). 4: ¹H NMR (CCl₄, 60 MHz) δ 1.6 (m, 16H), 2.1 (br, 3H), 3.27 (t, 2H, $J=6$ Hz), 3.80 (t, 2H, $J=6$ Hz), and 6.5-7.2 (m, 5H); ¹³C NMR (CDCl₃, 25 MHz) δ 26.2 (C-2' or 3'), 27.1 (C-2' or 3'), 30.4 (C-3), 36.5 (C-4), 41.6 (C-2), 59.2 (C-1'), 67.6 (C-4'), 71.7 (C-1), 114.4 (C-o), 120.3 (C-p), 129.2 (C-m), and 158.9 (C-i).

- 6) The elimination product (58.0%) was composed of norbornene and nortricyclene in a ratio 18:82. The ratio is similar to what is observed in solvolytic reactions, and E2 reaction would not be a predominant pathway; see, H. Kwart, T. Takeshita, and J. L. Nyce, *J. Am. Chem. Soc.*, **86**, 2606 (1964).
- 7) For a review, see; H. C. Brown, "Nonclassical Ion Problem," Plenum Press, New York (1977).
- 8) In this communication, we do not intend to clarify the structure of the 2-norbornyl cation generated as an intermediate. The structural formulas in the form of a "classical" ion are tentatively employed for convenience to understand the deuterium scrambling caused by the Wagner-Meerwein rearrangement.
- 9) Y. Pocker and R. F. Buchholz, *J. Am. Chem. Soc.*, **92**, 4033 (1970).
- 10) C. L. Perrin and J. Pressing, *ibid.*, **93**, 5705 (1971).
- 11) This is qualitatively compatible with the rate ratios (2/1) of 10 (EtOH, 25°C) or 22 (AcOH, 25°C) observed in solvolytic reactions, where the ionization is facilitated by the electrophilic nature of the hydroxylic solvents to the leaving group. The above rate ratios were calculated from the data in; a) H. C. Brown, M. Ravindranathan, F. J. Chloupek, and I. Rothberg, *J. Am. Chem. Soc.*, **100**, 3143 (1978); b) P. von R. Schleyer, M. M. Donaldson, and W. E. Watts, *ibid.*, **87**, 375 (1965); c) D. N. Kevill, K. C. Kolwyck, and F. L. Weitl, *ibid.*, **92**, 7300 (1970).
- 12) The mole fraction of dissociated NaOPh calculated from the dissociation constant (1.21×10^{-10} M) determined by conductivity measurement is only 0.3% for a 0.2 - 0.3 M solution in THF at 25°C. Our previous value (K. Okamoto, T. Kinoshita, T. Oishi, and T. Moriyama, *J. Chem. Soc. Perkin II*, **1978**, 453) is erroneous because of the difficulties encountered in determining electric conductance at low NaOPh concentrations.

(Received May 15, 1981)