# Substitution at a Saturated Carbon Atom. XIII. Demonstration of the Operation of the Ion-Pair Mechanism in Substitutions into α-Phenylethyl Bromide, α-p-Tolylethyl Chloride, and α-p-Tolylethyl Bromide[1]

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**Abstract:** Product distributions and rates of reaction as a function of nucleophile concentration have been measured for the competitive substitutions by solvent ethanol and added nucleophile (azide and thiocyanate ion) into three α-arylethyl halides (α-phenylethyl bromide (I), α-p-tolylethyl chloride (II), and α-p-tolylethyl bromide (III)) in ethanol at 50.0°. The data conform to the predictions of the ion-pair mechanism of nucleophilic substitution for these reactions (Scheme I). The use of two nucleophiles of differing nucleophilicities ($m = k_N/k_s$), azide and thiocyanate ion, provides the basis for an independent test of the ion-pair mechanism: if it is operative the ratio of rate constants $x = k_{-1}/k_s$, defined by Scheme I, should be independent of the nature of the nucleophile. This prediction has been verified. It is shown that the data are consistent with the view that, for these three related substrates, the apparent changes in kinetic order from ∼second (I) to borderline (II) to ∼first (III) results not from any fundamental change in mechanism (*e.g.*, SN2 to SN1) but rather reflects a gradual change in the relative energies of the transition states for formation and destruction of the ion-pair intermediate of Scheme I ($k_{-1}/k_s = x = 8.50$ for I, $x = 3.30$ for II, $x \simeq 0$ for III). Finally, the manuscript is concluded with a discussion of two recent, independent publications which had separately questioned the uniqueness of our ion-pair interpretation of the substitution reactions of 2-octyl sulfonates.

In our continuing search for additional examples of substrates which can be shown experimentally to undergo substitution reactions *via* the ion-pair mechanism[3,4] of nucleophilic substitution we were led to investigate reactions of three related α-arylethyl halides,[5] α-phenylethyl bromide (I, PEB), α-p-tolylethyl chloride (II, TEC), and α-p-tolylethyl bromide (III, TEB). Before discussing some of the ancillary reasons prompting this investigation it may be well to reset the stage by reviewing briefly the basic features of the ion-pair mechanism.

Experiments by Weiner[6] and Larsen[3,7] initially with 2-octyl mesylate had led us to suggest that the competitive substitutions which this substrate undergoes with solvent water and added azide ion (in aqueous dioxane mixtures) share a common, reversibly formed asymmetric intermediate, an intimate ion pair ($R^+$-$X^-$).

**Scheme I**
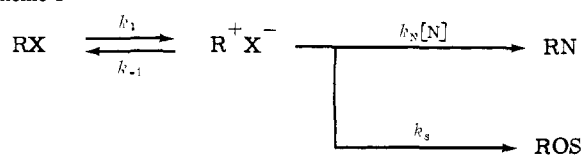


Such a mechanistic scheme[3] differs in its predictions in several significant ways from other conceivable mechanisms (SN1 and/or SN2). In particular it makes different predictions about the interrelations among rates, product distributions, and nucleophile concentration. These fundamental quantitative predictions of the ion-pair mechanism are given below as eq 1 and 2.

These most fundamental differences between the ion-pair mechanism and alternatives have been tested experimentally, with results that have led us to conclude that the ion-pair mechanism is operative during the solvolysis of 2-octyl mesylate[3,8] (25 and 30% aqueous dioxane), benzoyl chloride[4,11] (50 wt % acetone), p-methoxybenzyl chloride[4,12] (70% aqueous acetone), and α,γ-dimethylallyl chloride[13] (absolute and 90% aqueous ethanol). In this work we wished to subject these α-arylethyl halides (I, II, and III) to these same fundamental experiments which had been applied successfully in our earlier studies to establish the ion-pair mechanism.

But in addition there remain other differences between the ion-pair mechanism and others which can be subjected to experimental test, differences of a more subtle type than those we have so far dealt with in print.[14–16] It was these latter that we hoped especially to pursue in the present study.

(1) Supported in part by the National Science Foundation.

(2) David Ross Predoctoral Fellow of the Purdue Research Foundation, 1967–1969.

(3) R. A. Sneen and J. W. Larsen, *J. Amer. Chem. Soc.*, **91**, 362 (1969).

(4 R. A. Sneen and J. W. Larsen, *ibid.*, **91**, 6031 (1969).

(5) For a summary of earlier studies of these substrates see, *e.g.*, C. K. Ingold, "Structure and Mechanism in Organic Chemistry," 2nd ed, Cornell University Press, Ithaca, N. Y., 1969, Chapter VII.

(6) H. Weiner and R. A. Sneen, *J. Amer. Chem. Soc.*, **87**, 287, 292 (1965).

(7) R. A. Sneen and J. W. Larsen, *ibid.*, **88**, 2593 (1966).

(8) At the suggestion of a referee and at the request of the Editor, we have appended to this manuscript a discussion of two recent, independent publications which had separately questioned the uniqueness of our ion-pair interpretation of these reactions.[9, 10]

(9) B. J. Gregory, G. Kohnstam, M. Paddon-Row, and A. Queen, *Chem. Commun.*, 1032 (1970).

(10) D. J. Raber, J. M. Harris, R. E. Hall, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **93**, 4821 (1971).

(11) V. Gold, J. Hilton, and E. G. Jefferson, *J. Chem. Soc.*, 2756 (1954).

(12) G. Kohnstam, A. Queen, and B. Shillaker, *Proc. Chem. Soc.*, 157 (1959).

(13) R. A. Sneen and W. A. Bradley, *J. Amer. Chem. Soc.*, **94**, 6975 (1972).

(14) See, however, ref 13, 15, and 16.

(15) R. A. Sneen and H. M. Robbins, *J. Amer. Chem. Soc.*, **91**, 3100 (1969).

(16) R. A. Sneen, submitted for publication in *Accounts Chem. Res.*

The basic reasons for undertaking this work then, in addition to establishing the ion-pair mechanism for substitution reactions of the $\alpha$-arylethyl halides by the more routine, if fundamental, tests, were the following. (1) Reaction of $\alpha$-phenylethyl bromide (PEB (I)) in solvent ethanol in the presence of ethoxide ion had been reported to undergo elimination to furnish styrene, competitively, with substitution.[17] We hypothesized that this competitive elimination was related to the substitution processes *via* a common ion-pair intermediate, thus linking together the four basic mechanisms, SN1, SN2, E1, and E2, through a common intermediate. This hypothesis has been confirmed and has earlier been communicated.[15,18] We will not discuss it further here. (2) A feature of the ion-pair mechanism which suggests an experimental test for it is that the rate constants defined in Scheme I as $k_{-1}$ and $k_s$ and therefore their ratio, $k_{-1}/k_s$, should be independent of the nature of the nucleophile (N).[13,16] In this manuscript we report our study of the competitive reactions of both PEB (I) and TEC (II) with solvent, and, on the one hand, azide ion, $N_3^-$, and on the other, thiocyanate ion, $CNS^-$, to determine whether in fact the common ratio, $k_{-1}/k_s$, is independent of nucleophile; it is. (3) Another goal of the present investigation was to study the effects of changes in structure on the various energy quantities of the ion-pair mechanism. In particular we wanted information on certain free-energy changes ($k_{exptl}$, $k_{-1}/k_s = x$, $k_N/k_s = m$; see eq 1 and 2) accompanying a change in leaving group (Cl $\rightarrow$ Br or $CH_3$-$C_6H_4CHClCH_3$ (II) $\rightarrow$ $CH_3C_6H_4CHBrCH_3$ (III)) as well as para substituent of the aryl ring ($p$-H $\rightarrow$ $p$-$CH_3$ or $HC_6H_4CHBrCH_3$ (I) $\rightarrow$ $p$-$CH_3C_6H_4CHBrCH_3$ (III)). (4) The most aesthetically satisfying feature of the ion-pair mechanism is that it accommodates not only borderline behavior ($k_{-1} \simeq k_s$) but also "SN1" ($k_s \gg k_{-1}$) and "SN2" ($k_{-1} \gg k_s$) as well.[3] We had hoped to establish (and we have succeeded) that by making modest changes in structure (($I$)$p$-H,Br$\rightarrow$ (II)$p$-Me,Cl$\rightarrow$ (III) $p$-Me,Br) we could accomplish *apparent* mechanism changes from SN2-like $\rightarrow$ borderline $\rightarrow$ SN1-like. The continuity of the various measurable quantities within this series of compounds will be shown to be consistent only with the operation of a single basic mechanism, since a fundamental change in mechanism (*e.g.*, SN2 $\rightarrow$ SN1) might well be expected to show abrupt discontinuities in these quantities. The differences in kinetic order arise, we believe, as a result of gradual alterations in the relative energies of the formation and destruction of the ion-pair intermediate, not from a fundamental change in mechanism.

## Results and Discussion

The criteria which have been established as sufficient[3] to ensure the operation of the ion-pair mechanism of Scheme I, during the competitive substitutions by solvent and added nucleophile into a given substrate, are that products be formed in accordance with eq 1[19]

(17) E. D. Hughes, C. K. Ingold, S. Masterman, and B. J. McNulty, *J. Chem. Soc.*, 899 (1940).

(18) See, however, D. J. McLennan, *Tetrahedron Lett.*, 2317 (1971). We will postpone for now a discussion of this publication.

(19) In theory, competitive SN1 and SN2 processes would give products in accordance with the linear eq 1 only if the ratio of second-order rate constants, $k_{2N}/k_{2s}$ were equal to the corresponding ratio of first-order constants, $k_{1N}/k_{1s}$.[20] In practice caution must be exercised in the use of this criterion[9] since eq 1 is not particularly sensitive

$$\frac{[RN]}{[ROS]} = \frac{k_N[N]}{k_s} = m[N] \qquad (1)$$

and that rates be determined in accordance with eq 2,

$$\frac{k_{exptl}}{k_{NS}} = \frac{[(k_{-1}/k_s) + 1][1 + (k_N[N]/k_s)]}{[(k_{-1}/k_s) + 1 + (k_N[N]/k_s)]} = \frac{(x + 1)(1 + m[N])}{(x + 1 + m[N])} \qquad (2)$$

where $k_{exptl}$ is the experimentally determined pseudo-first-order rate constant, $k_{NS}$ is the solvolysis rate constant in the absence of nucleophile (N) but after correction for a normal salt effect,[21] $m = k_N/k_s$ and is available from product data and eq 1, and $x = k_{-1}/k_s$.[22]

Our fundamental approach, then, involved a study of both rates and product distributions of the competitive reactions of the three $\alpha$-arylethyl halides mentioned in the title, $\alpha$-phenylethyl bromide (PEB (I)), $\alpha$-$p$-tolylethyl chloride (TEC (II)), and $\alpha$-$p$-tolylethyl bromide (TEB (III)), with solvent ethanol and added nucleophile (tetra-$n$-propylammonium azide and sodium thiocyanate) in absolute ethanol at 50.0°. Rates were followed by measuring the change in acid titer with time and are reported as pseudo-first-order constants. Product distributions were obtained by titrating infinity solutions for liberated acid (since thiocyanate or azide ion incorporation does not result in the liberation of acid) and, in some cases, by vapor phase chromatographic analysis.

Product and rate data for the competitive reactions of $\alpha$-phenylethyl bromide (PEB (I)) with solvent ethanol and tetra-$n$-propylammonium azide are given in Table I, while data for the reactions of this same substrate, I, with added sodium thiocyanate in ethanol are given in Table II. Similar data for $\alpha$-$p$-tolylethyl chloride (TEC (II)) with tetra-$n$-propylammonium azide[23] and sodium thiocyanate are given in Tables III

unless either these rate ratios are significantly different or unless data over a rather wide range of nucleophile concentrations are available.

(20) See Appendix of ref 3.

(21) It will be appropriate here to comment briefly on our treatment of salt effects. The quantity $k_{NS}$ of eq 2, the expected solvolytic rate constant in the absence of nucleophile but after correction for a normal salt effect, has been estimated from the linear equation, $k_{NS} = k_{NS}^0(1 + b[N])$, whose validity has been established in independent experiments with model salts (*vide infra* and Table VI). To a very good approximation salt effects on ethanolysis of the $\alpha$-arylethyl halides, I, II, III, are linear in concentration and independent of the nature of the salt. Of the remaining quantities of eq 2, $x$ and $m[N]$, salt effects on only the former, $x$, need be of concern since the linearity of a plot of product data *vs.* [N] (eq 1) assures that the use of the term, $m[N]$, in eq 2 is tantamount to the use of the experimental quantity [RN]/[ROS]; *vide infra*. Furthermore, the linearity of the product plots[20] suggests that the ratio of rate constants, $m = k_N/k_s$, is independent of salt concentration; that is, $k_N$ and $k_s$ are apparently affected similarly by salt effects. This is very probably associated with the fact that the two reactions in question are relatively unselective processes, both emanating from a relatively unstable, high-energy intermediate, $R^+X^-$. If so it follows that the quantity $x = k_{-1}/k_s$ ought also to be relatively insensitive to salt effects. We have here assumed it to be constant, independent (to a first approximation) of salt concentration. Finally, it should be noted that the linearity of product plots serves one other important and useful function; it establishes that, at the concentration levels of salt employed in these studies ($\leq 0.113$ $M$), concentrations must be proportional to activities.

(22) Note that in the borderline region ($0.1 \leq x \leq 10$) eq 2 predicts a nonlinear plot of $k_{exptl}/k_{NS}$ *vs.* [N] whereas mechanism SN1 ($x = 0$) and mechanism SN2 ($x = \infty$) predict linear plots with slopes = 0.0 and $m$, respectively, while linear combinations of mechanisms SN1 and SN2 also predict linear plots.

(23) Levorotatory $\alpha$-$p$-tolylethyl chloride, $[\alpha]^{27}D$ $-1.15°$, gave, under ethanolysis conditions (0.102 $M$ tetra-$n$-propylammonium azide, 50°, 8 half-lives), dextrorotatory ethyl $\alpha$-$p$-tolylethyl ether, $[\alpha]^{25}D$ $+0.47°$, and dextrorotatory $\alpha$-$p$-tolylethyl azide, $[\alpha]^{25}D$ $+0.74°$ (J. R. Ellis, Ph.D. Thesis, Purdue University, 1969).

**Table I.** Comparison of Observed and Predicted Product Distributions and Rate Constants for the Reactions of $\alpha$-Phenylethyl Bromide (PEB (I)) with Ethanol and Tetra-$n$-propylammonium Azide in Ethanol at 50.0°

| [($n$-Pr)$_4$NN$_3$], $M \times 10^2$ | % RN$_3$, exptl | % RN$_3$,[a] calcd | $k_{exptl} \times 10^4$, sec$^{-1}$ | $k_{ip}{}^b \times 10^4$, sec$^{-1}$ | $k_{SN2}{}^c \times 10^4$, sec$^{-1}$ |
|---|---|---|---|---|---|
| | | | 1.13 ± 0.03 | | |
| 1.14 | 59.5 | 59.7 | 2.34 ± 0.10 | 2.54 | 2.94 |
| 2.06 | | | 3.45 ± 0.15 | 3.55 | 4.55 |
| 2.08 | | | 3.52 ± 0.07 | 3.55 | 4.55 |
| 2.27 | 73.7 | 74.6 | | | |
| 3.06 | 79.4 | 79.8 | 4.58 ± 0.20 | 4.48 | 6.35 |
| 3.13 | 80.1 | 80.0 | 4.54 ± 0.05 | 4.52 | 6.49 |
| 3.42 | 82.3 | 81.6 | 5.24 ± 0.15 | 4.77 | 7.00 |
| 3.45 | 81.7 | 81.6 | | | |

[a] Calculated from eq 1 with $m = k_N/k_s = 130.5$; see Figure 1. [b] Calculated from eq 2 with $m = 130.5$, $x = k_{-1}/k_s = 8.50$, $k_{NS} = 1.13 \times 10^{-4}(1 + 4.00[N_3^-])$. [c] Calculated from eq 2 with $m = 130.5$, $x = \infty$, $k_{NS} = 1.13 \times 10^{-4}(1 + 4.00[N_3^-])$.

**Table II.** Comparison of Observed and Predicted Product Distributions and Rate Constants for the Reactions of $\alpha$-Phenylethyl Bromide (PEB (I)) with Ethanol and Sodium Thiocyanate in Ethanol at 50.0°

| [NaSCN], $M \times 10^2$ | % RSCN, exptl | % RSCN,[a] calcd | $k_{exptl} \times 10^4$, sec$^{-1}$ | $k_{ip}{}^b \times 10^4$, sec$^{-1}$ | $k_{SN2}{}^c \times 10^4$, sec$^{-1}$ |
|---|---|---|---|---|---|
| | | | 1.13 ± 0.03 | | |
| 2.73 | 42.6 | 42.5 | 2.02 ± 0.09 | 2.04 | 2.19 |
| 3.81 | 50.1 | 50.6 | 2.47 ± 0.08 | 2.41 | 2.66 |
| 4.82 | | | 2.67 ± 0.09 | 2.75 | 3.14 |
| 5.02 | 57.3 | 57.6 | 2.88 ± 0.09 | 2.82 | 3.21 |
| 5.64 | | | 3.07 ± 0.08 | 3.04 | 3.47 |
| 6.67 | | | 3.40 ± 0.06 | 3.40 | 4.05 |
| 7.16 | 66.0 | 65.8 | | | |
| 7.18 | | | 3.54 ± 0.03 | 3.59 | 4.29 |
| 7.44 | | | 3.65 ± 0.06 | 3.68 | 4.43 |

[a] Calculated from eq 1 with $m = k_N/k_s = 27.0$; see Figure 3. [b] Calculated from eq 2 with $m = 27.0$, $x = k_{-1}/k_s = 8.50$, $k_{NS} = 1.13 \times 10^{-4}(1 + 4.00[SCN^-])$. [c] Calculated from eq 2 with $m = 27.0$, $x = \infty$, $k_{NS} = 1.13 \times 10^{-4}(1 + 4.00[SCN^-])$.

**Table III.** Comparison of Observed and Predicted Product Distributions and Rate Constants for the Reactions of $\alpha$-$p$-Tolylethyl Chloride (TEC (II)) with Ethanol and Tetra-$n$-propylammonium Azide in Ethanol at 50.0°

| [($n$-Pr)$_4$NN$_3$], $M \times 10^2$ | % RN$_3$, exptl | % RN$_3$,[a] calcd | $k_{exptl} \times 10^4$, sec$^{-1}$ | $k_{ip}{}^b \times 10^4$, sec$^{-1}$ | $k_{SN2}{}^c \times 10^4$, sec$^{-1}$ |
|---|---|---|---|---|---|
| | | | 1.67 ± 0.04 | | |
| 1.82 | 14.8 | 16.5 | 2.04 ± 0.06 | 2.06 | 2.16 |
| 2.86 | 19.7 | 24.1 | | | |
| 3.04 | 24.6 | 25.2 | 2.25 ± 0.11 | 2.32 | 2.51 |
| 3.85 | | | 2.36 ± 0.07 | 2.50 | 2.74 |
| 4.95 | | | 2.58 ± 0.08 | 2.75 | 3.10 |
| 6.38 | 43.3 | 41.5 | | | |
| 6.57 | 40.5 | 42.2 | 2.88 ± 0.03 | 3.12 | 3.65 |
| 7.53 | 46.0 | 45.5 | | | |
| 8.39 | | | 3.19 ± 0.05 | 3.54 | 4.30 |
| 11.03 | 54.4 | 55.0 | | | |
| 11.30 | 56.3 | 55.6 | | | |

[a] Calculated from eq 1 with $m = k_N/k_s = 11.1$. [b] Calculated from eq 2 with $m = 11.1$, $x = k_{-1}/k_s = 3.30$, $k_{NS} = 1.67 \times 10^{-4}(1 + 4.00[N_3^-])$. [c] Calculated from eq 2 with $m = 11.1$, $x = \infty$, $k_{NS} = 1.67 \times 10^{-4}(1 + 4.00[N_3^-])$.

and IV, respectively. A limited number of data for reactions of $\alpha$-$p$-tolylethyl bromide (III) with both tetra-$n$-propylammonium azide and sodium thiocyanate are given in Table V. Table VI summarizes experiments designed to assess the ability of the salt effect equation of ref 21 to correct for normal salt effects. Figures 1 and 2 demonstrate graphically the ability of eq 1 and 2 to correlate product and rate data, respectively, for the reactions of PEB (I) with tetra-$n$-propylammonium azide, while Figures 3 and 4 graph the same type of data for this substrate, PEB (I), with

sodium thiocyanate. Finally, the pertinent kinetic parameters for the three substrates are compared in Table VII.

Careful inspection of Tables I–IV will reveal that the competitive substitutions effected with either azide or thiocyanate ion, with both $\alpha$-phenylethyl bromide (I) and $\alpha$-$p$-tolylethyl chloride (II), conform beautifully to the predictions of the ion-pair mechanism. Not only are products for each of these four studies formed in accordance with eq 1 (columns 2 and 3 of Tables I–IV) and rates in accordance with eq 2 (columns 4 and 5),

**Table IV.** Comparison of Observed and Predicted Product Distributions and Rate Constants for the Reactions of α-p-Tolylethyl Chloride (TEC (II)) with Ethanol and Sodium Thiocyanate in Ethanol at 50.0°

| [NaSCN], $M \times 10^2$ | % RSCN, exptl | % RSCN,[a] calcd | $k_{\text{exptl}} \times 10^4$, sec$^{-1}$ | $k_{\text{ip}}{}^b \times 10^4$, sec$^{-1}$ | $k_{\text{SN}_2}{}^c \times 10^4$, sec$^{-1}$ |
|---|---|---|---|---|---|
| | | | $1.67 \pm 0.04$ | | |
| 4.16 | 15.8 | 15.5 | $2.28 \pm 0.09$ | 2.27 | 2.31 |
| 6.00 | 21.7 | 20.9 | $2.58 \pm 0.09$ | 2.56 | 2.72 |
| 8.28 | 25.4 | 26.7 | $2.83 \pm 0.06$ | 2.82 | 3.06 |
| 10.00 | 31.2 | 30.6 | $3.02 \pm 0.10$ | 3.06 | 3.39 |

[a] Calculated from eq 1 with $m = k_N/k_s = 4.40$. [b] Calculated from eq 2 with $m = 4.40$, $x = k_{-1}/k_s = 3.30$, $k_{NS} = 1.67 \times 10^{-4}(1 + 4.00[\text{SCN}^-])$. [c] Calculated from eq 2 with $m = 4.40$, $x = \infty$, $k_{NS} = 1.67 \times 10^{-4}(1 + 4.00[\text{SCN}^-])$.

**Table V.** Product Distribution, Rate, and Salt Effect Data for Some Substitution Reactions of α-p-Tolylethyl Bromide (TEB (III)) in Ethanol at 50.0°

| Salt | [Salt], $M \times 10^2$ | $k_{\text{exptl}} \times 10^3$, sec$^{-1}$ | % RN[a] | $m^b = k_N/k_s$ |
|---|---|---|---|---|
| | | $2.65 \pm 0.05$ | | |
| NaSCN | 5.09 | $2.90 \pm 0.10$ | 26.1 | |
| NaSCN | 7.78 | | 38.4 | 7.56[c] |
| NaClO₄ | 5.47 | $2.89 \pm 0.06$ | | |
| (n-Pr)₄NN₃ | 5.46 | | 55.4 | 22.7 |

[a] Percentage of nucleophilic product. [b] Calculated from eq 1. [c] Average.

In contrast to the conclusion that follows upon careful scrutiny of the data for PEB (I) and TEC (II), that these substrates undergo competitive substitution *via* the ion-pair mechanism, data for substitutions into α-p-tolylethyl bromide (III) do not distinguish for this substrate between a classical S$_N$1 mechanism and the ion-pair mechanism with $x = k_{-1}/k_s \simeq 0$. Inspection of Table V will reveal that normal salt effects on ethanolysis, effected by sodium perchlorate, can readily account for the rate enhancement observed with sodium thiocyanate. Other parallels in behavior, how-

**Table VI.** Salt Effects on Ethanolysis of α-Phenylethyl Bromide (I) and α-p-Tolylethyl Chloride (II) in Absolute Ethanol at 50.0°

| Substrate | Salt | [Salt], $M$ | $k_{\text{exptl}} \times 10^4$, sec$^{-1}$ | $b^a$ | $b,^a$ av |
|---|---|---|---|---|---|
| PEB (I) | | | $1.13 \pm 0.03$ | | |
| | NaClO₄ | 0.251 | $2.26 \pm 0.05$ | 3.99 | |
| | | 0.495 | $3.36 \pm 0.10$ | 4.00 | 4.00 |
| | KOAc | 0.111 | $1.64 \pm 0.04$ | 4.05 | |
| | | 0.206 | $2.05 \pm 0.06$ | 3.94 | 4.00 |
| | (n-Bu)₄NClO₄ | 0.0205 | $1.25 \pm 0.02$ | 4.82 | |
| | | 0.0505 | $1.40 \pm 0.03$ | 4.72 | 4.77 |
| TEC (II) | | | $1.67 \pm 0.04$ | | |
| | NaClO₄ | 0.0250 | $1.85 \pm 0.06$ | 4.33 | |
| | | 0.0513 | $2.06 \pm 0.04$ | 4.53 | 4.43 |
| | NaOAc | 0.0388 | $1.92 \pm 0.05$ | 3.87 | |
| | (n-Bu)₄NClO₄ | 0.0295 | $1.81 \pm 0.02$ | 2.84 | |

[a] Calculated from the equation $k_{\text{NS}} = k_{\text{NS}}{}^0(1 + b[\text{N}])$; see text and ref 21.

but deviations from predicted S$_N$2 behavior, in all four cases, are significant, as evidenced by a comparison of columns 4 and 6 of Tables I–IV.[24]

(24) An instructive way to assess the inconsistency of the data with either a traditional S$_N$2 or S$_N$1 reaction is to calculate the salt effect $b$ values[21] that would need to obtain if either of these classical mechanisms were solely operative. As an example, assuming an S$_N$2 mechanism for the azide substitution into PEB (I), the data at 0.0342 $M$ salt furnish $5.24/\{1.13[1 + b(0.0342)]\} = 1 + 131(0.0342)$ and $b = -4.8$ or a *negative* salt effect would be required.[25] Similarly, assuming an S$_N$1 mechanism for this substrate, a positive salt effect, $b = +120$, would obtain. For the same substrate (I) and sodium thiocyanate, $b$ values of $+1.0$ and $+30$ would be required for a pure S$_N$2 and pure S$_N$1 reaction, respectively. Since three model salts gave $b$ values of $+4.00$ to $+4.77$ (Table VI) it is apparent that the data are completely inconsistent with these assumed classical mechanisms. As a corollary the use of a single $b$ value, obtained independently from model salts, to correlate data for both nucleophiles with a single value of the parameter $x$ (for a given substrate) is gratifying corroboration of the ion-pair mechanism (vide infra).

(25) Note that the calculation does *not* require any assumptions about differing salt effects on $k_s$ and $k_N$. This can perhaps be most readily seen as follows: assume bimolecular displacements by solvent and nucleophile to be solely operative. Then
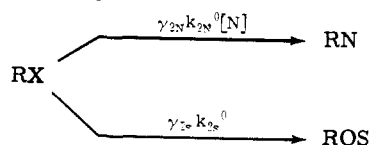
ever (Table VII), between III and substrates I and II suggest strongly that p-tolylethyl bromide (III) also undergoes reaction *via* the ion-pair mechanism with $x \simeq 0$ (vide infra).

where $k_{2N}{}^0$ and $k_{2s}{}^0$ are true thermodynamic rate constants and $\gamma_{2N}$ and $\gamma_{2s}$ are the corresponding activity coefficients. $k_{\text{exptl}} = \gamma_{2s}k_{2s}{}^0 + \gamma_{2N}k_{2N}{}^0[\text{N}]$; $k_{\text{NS}} = \gamma_{2s}k_{2s}{}^0$; $[\text{RN}]/[\text{ROS}] = \gamma_{2N}k_{2N}{}^0[\text{N}]/\gamma_{2s}k_{2s}{}^0$; $k_{\text{exptl}}/k_{\text{NS}} = 1 + (\gamma_{2N}k_{2N}{}^0[\text{N}]/\gamma_{2s}k_{2s}{}^0) = ([\text{ROS}] + [\text{RN}])/[\text{ROS}] = 1/f_s$, where $f_s = $ fraction of solvolysis. In words, by virtue of the necessary relation between product distribution and rates of reaction inherent in this assumed mechanism, it suffices to measure the salt effect only on solvolysis, $k_{2s}$; that on $k_{2N}$ *does not explicitly find itself in the expression*. Accordingly it cannot legitimately be argued (as some have in private communications) that a presumed *positive* salt effect on $k_{2s}$, together with a presumed *negative* salt effect on $k_{2N}$, can adequately force our data into an S$_N$2 picture.

It should also be realized that the direct relationship between rate constants and product distributions established above obviates the necessity for the independent measure of activity coefficients of any rate constants (e.g., $k_{2N}$) or concentration terms (e.g., [N]) except that on the $k_{2s}$ (= $k_{\text{NS}}$) process (see ref 21).

A similarly rigorous derivation utilizing activity coefficients, assuming the ion-pair mechanism (Scheme I), gives

$$\frac{k_{\text{exptl}}}{k_{\text{NS}}} = \frac{(\gamma_z x^0 + 1)([\text{ROH}] + [\text{RN}])/[\text{ROS}]}{\gamma_z x^0 + ([\text{ROH}] + [\text{RN}])/[\text{ROS}]} = \frac{(\gamma_z x^0 + 1)}{f_s \gamma_z x^0 + 1}$$

It will be apparent that the only activity coefficients which occur in the final expression are those on the rate ratio, $(k_{-1}/k_s) = x$, and on $k_{\text{NS}}$.

**Table VII.** Summary of Various Rate Constants and Rate Ratios for the Competitive Substitution Reactions of Three $\alpha$-Arylethyl Halides (I, II, III) with Solvent and Added Nucleophiles in Ethanol at 50.0° [a]

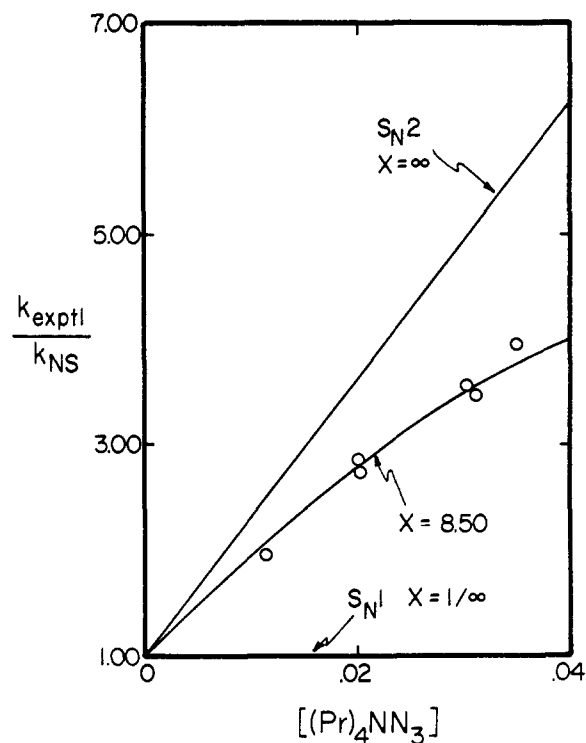| Substrate | $k_{NS}^0 \times 10^4$, sec$^{-1}$ | $x = k_{-1}/k_s$ | $(m)_{N_3^-} = (k_N/k_s)_{N_3^-}$ | $(m)_{SCN^-} = (k_N/k_s)_{SCN^-}$ | $k_{N_3^-}/k_{SCN^-}$ |
|---|---|---|---|---|---|
| $\alpha$-Phenylethyl bromide (I) | $1.13 \pm 0.03$ | 8.50 | 131 | 27.0 | 4.85 |
| $\alpha$-p-Tolylethyl chloride (II) | $1.67 \pm 0.04$ | 3.30 | 11.1 | 4.4 | 2.52 |
| $\alpha$-p-Tolylethyl bromide (III) | $26.5 \pm 0.5$ | $\sim 0$ | 22.7 | 7.6 | 2.98 |

[a] See text for definitions.
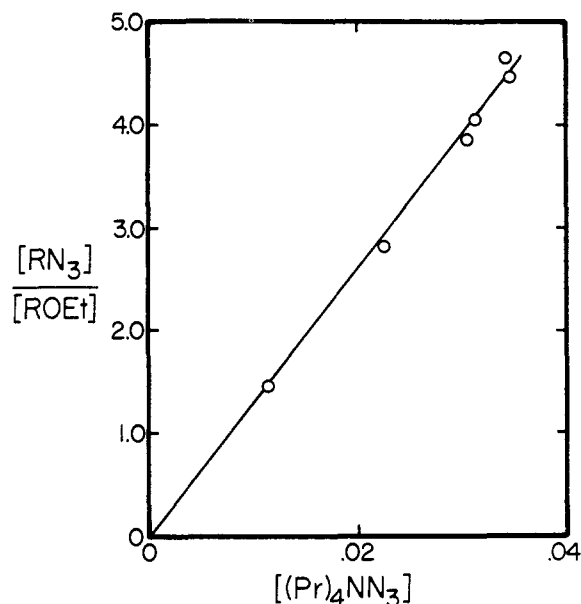


**Figure 1.** Plot of [RN$_3$]/[ROEt] vs. [(Pr)$_4$NN$_3$] for the reaction of $\alpha$-phenylethyl bromide (1) with tetra-$n$-propylammonium azide and ethanol in absolute ethanol at 50°. The solid line is a theoretical plot of eq 1 with slope $= m = k_N/k_s = 131$. Experimental points are encircled.



**Figure 2.** Plot of $k_{exptl}/k_{NS}$ vs. [(Pr)$_4$NN$_3$] for the reaction of $\alpha$-phenylethyl bromide (I) with tetra-$n$-propylammonium azide and ethanol in absolute ethanol at 50°. The curved line is a theoretical plot from eq 2 with $k_N/k_s = 131$ and $x = k_{-1}/k_s = 8.5$. The experimental points are encircled.

In the introductory section of this paper it was pointed out that the ion-pair scheme predicts that the rate ratio, $x = k_{-1}/k_s$, should be independent of nucleophile. This prediction is beautifully borne out by the data for both PEB (I) and TEC (II) with the two nucleophiles, azide and thiocyanate ion. A common value of $x = 8.5$ correlates data for I with both anions while a common value of $x = 3.30$ correlates data for II with these same two anions.

Note that this technique of using two different nucleophiles imposes an extra condition on the equations (1 and 2) describing the system. The quantity $x$ ceases to be an adjustable parameter; no degrees of freedom remain.[26]

A consideration of the data of Table VII, compiled from Tables I–VI, reveals several additional features of interest. Of greatest interest perhaps is the change in the ratio, $x = k_{-1}/k_s$, with structure. For example, with the introduction of a para methyl substituent into

$\alpha$-phenylethyl bromide (I) to give III, the *apparent* kinetic order (with respect to [N]) changes from nearly first ($x = 8.50$)[27] to ca. zero ($x \simeq 0$); that is, the reaction passes from "SN2-like" with I to "SN1-like" with III. Yet the mechanism is basically unchanged, the apparent change in kinetic order resulting from a change in the relative energies of the transition states

(26) Note also that implicit in the ability of a single value of $x$ to correlate data for two nucleophiles is a test of the appropriateness of salt effect corrections. Since azide ion is a more effective nucleophile than is thiocyanate ion (by a factor of $\sim$2.5–5.0, see Table VII), a concentration of sodium thiocyanate larger by this same factor than that of azide is needed to accomplish the same percentage incorporation. Salt effect corrections for thiocyanate are consequently 2.5–5.0 times greater than for azide. The required internal consistencies are not inconsequential.

(27) It has been suggested (ref 3 and ref 22) that for substrates reacting via the ion-pair mechanism only those with the rate ratio $k_{-1}/k_s = x \leq 10$ might be operationally distinguishable from a traditional SN2 mechanism ($x = \infty$). This is really an oversimplification. With substrates such as PEB (I) which show a relatively large $m = k_N/k_s$ ratio, a larger value of $x$ can be tolerated. To clarify this it is instructive to define the quantity, [N]$_{1/2}$, as the concentration of nucleophile, N, at which the rate constant predicted for a traditional SN2 mechanism is just twice the rate constant for an ion-pair mechanism. It can readily be shown[28] that [N]$_{1/2} = (x + 1)/m$. Thus, if both $x$ and $m$ for a particular substrate-nucleophile combination are relatively large or, conversely, if both are relatively small, a moderate concentration of [N]$_{1/2}$ will result. With PEB (I), both $x$ (= 8.5) and $m_{N_3^-}$ (= 131) are relatively large and yet [N]$_{1/2}$ = 0.073 suffices to give a significant difference between the SN2 and ion-pair pictures.
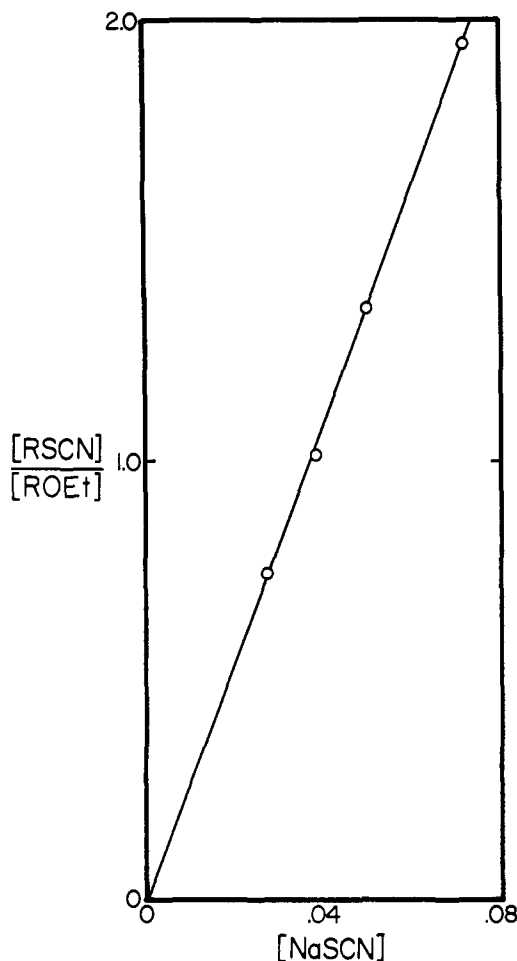
(28) W. A. Bradley, Ph.D. Thesis, Purdue University, 1970.

Figure 3. Plot of [RSCN]/[ROEt] vs. [NaSCN] for the reaction of α-phenylethyl bromide (I) with sodium thiocyanate and ethanol in absolute ethanol at 50°. The solid line is a theoretical plot of eq 1 with slope $= m = k_N/k_s = 27.0$. Experimental points are encircled.

Figure 4. Plot of $k_{exptl}/k_{NS}$ vs. [NaSCN] for the reaction of α-phenylethyl bromide (I) with sodium thiocyanate and ethanol in absolute ethanol at 50°. The curved line is a theoretical plot from eq 2 with $k_N/k_s = 27.0$ and $x = k_{-1}/k_s = 8.5$. The experimental points are encircled.

for formation and destruction of the ion-pair intermediate.[29]

Finally, with the assembled data from Table VII one can construct very approximate energy diagrams for the substitution reactions of the α-arylethyl halides (I, II, and III).[31] Several interesting observations emerge, but we will postpone a detailed discussion until our conclusions can be considerably less speculative. Especially interesting, however, and worthy of mention at this time, is the possibility that since the ratios $m = k_N/k_s$ (or, less equivocally, $k_{N_3^-}/k_{SCN^-}$ ratios) do show

(29) That a basic change in mechanism is not here involved is also suggested by the fact that the selectivities or $m$ values for the two substrates, I and III, are of comparable magnitude (differing by factors of 4–6). It would be difficult indeed to understand why substrates of fundamentally different kinds, e.g., covalent RX and carbonium ion, should give such comparable selectivities. An example of how divergent selectivity ratios, $k_N/k_s = m$, might be expected to be for attack on two fundamentally different types of substrates can be gleaned from data collected in our 1966 report[30] of a semiquantitative free-energy relationship between solvolysis rates and azide selectivity ratios for a series of substrates thought to be reacting at a dissociated carbonium ion stage. In that report 2-octyl mesylate and α-methylallyl chloride were found to have $k_N/k_s$ ratios too large by factors of 1250 and 6130, respectively, to be correlated by the relationship, presumably because these two substrates were undergoing reaction at an ion-pair stage. Two such different substrates as covalent RX and carbonium ion should not in general give such similar selectivities.

(30) R. A. Sneen, J. V. Carter, and P. S. Kay, J. Amer. Chem. Soc., 88, 2594 (1966); see also ref 10.
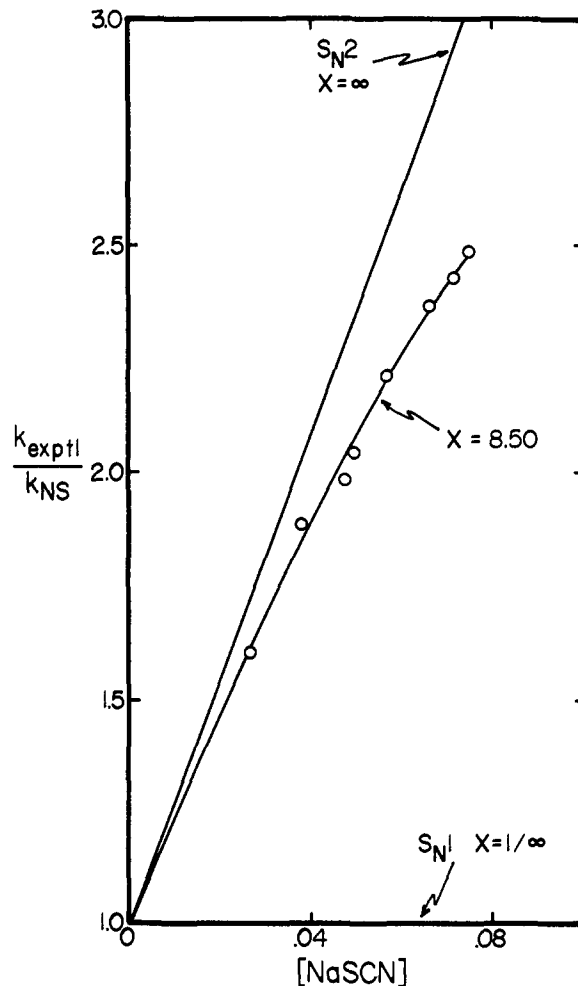
(31) H. M. Robbins, Ph.D. Thesis, Purdue University, 1969.

considerable variation, and since this ratio should be a measure of the selectivities and hence of the energies[30] of the corresponding product precursors (ion pairs), it suggests that a semiquantitative correlation may exist between these selectivities and the energies of the corresponding ion pairs.[32] We intend to pursue this possibility.

## Experimental Section[33]

**Preparation and Purification of Chemicals.** α-Phenylethyl Bromide. Commercial material (Eastman) was vacuum distilled (bp 86.5–87° (5 mm)) through a 6-in. Vigreux column and stored over Dry Ice. Purity was established by the ethanolysis infinity acid titer and was generally greater than 98%.

α-p-Tolylethyl Chloride. This material was prepared (greater than 85% yield) by the reaction of α-p-tolylethanol with thionyl chloride in dry chloroform at room temperature. Final purifica-

(32) A rather good linear free-energy relationship exists between the $k_{N_3^-}/k_s$ ratios (these ratios of Table VII have been corrected to include the concentration of solvent, ca. 17 M) and the $k_{N_3^-}/k_{SCN^-}$ ratios for the three investigated α-aryl halides. Thus (log $(17k_{N_3^-}/k_s))/(\log (k_{N_3^-}/k_{SCN^-})) = 4.9$ for PEB (I), 5.5 for TEC (II), and 5.5 for TEB (III).

(33) Boiling points are uncorrected. Infrared spectra were obtained with a Perkin-Elmer Model 137B Infracord spectrophotometer with sodium chloride optics. Nuclear magnetic resonance spectra were determined on a Varian Model A-60 spectrometer using tetramethylsilane as the internal standard.

tion was effected by vacuum distillation from anhydrous potassium carbonate through a 6-in. Vigreux column. The purity of the chloride thus prepared was generally better than 98%, as established by acid infinity titer upon ethanolysis. The material was stored over Dry Ice. α-p-Tolylethyl chloride had $n^{26.5}$D 1.5222, bp 70° (2 mm).

**α-p-Tolylethyl Bromide.** To 70 ml of anhydrous ether in a 300-ml three-necked flask fitted with a reflux condenser and drying tube was added ca. 50 g of α-p-tolylethanol. The solution was stirred and cooled to 0° in an ice bath. Hydrogen bromide was bubbled in slowly for 1 hr through a gas diffusion tube. Stirring and cooling were continued for another hour. The ethereal phase was then separated from the water formed during the reaction, washed several times with water and then 10% potassium carbonate, and finally dried over magnesium sulfate. Ether was removed on a water aspirator and the residual viscous oil was vacuum distilled through a 6-in. Vigreux column, bp 88–90° (2.3 mm). Nmr and ir data were consistent with the structural assignment and ethanolysis indicated the purity to be greater than 98%. The compound was stored over Dry Ice.

**Ethyl α-Phenylethyl Ether and Ethyl α-p-Tolylethyl Ether.** These ethers were prepared from their respective alcohols, silver oxide, and ethyl iodide according to the method of Mislow.[34] Final purification was effected by gas chromatography on a 6 ft × ¼ in., 10% FFAP on Chromosorb W-HMDS column at 160°. Structural assignments were consistent with nmr and ir data.

**α-Phenylethyl Azide and α-p-Tolylethyl Azide.** These compounds were prepared from their corresponding chloride by the method of Levene, Rothen, and Kuna.[35] Final purification was effected by gas chromatography on a 6 ft × ¼ in., 23% SE-30 on gas Chromosorb Q column at 165°. Both compounds exhibited a sharp peak at 2170 cm⁻¹ in their infrared spectra, characteristic of organic azides.[36] The nmr and ir spectra were consistent with the assigned structures. These compounds were stored over Dry Ice.

**Ethanol.** Three-liter batches of commercial 99.5% ethanol were dried by employing the diethyl phthalate method described by Wiberg.[37] New material was prepared each month.

**Salts.** Sodium perchlorate (G. Fredrich Smith Chemical Co.), potassium acetate (Baker), and sodium acetate (Baker) were stored over Drierite. Sodium thiocyanate (Baker) was stored over Drierite after drying over Drierite in vacuo. Tetra-n-butylammonium perchlorate (Southwestern Analytical Chemicals) was dried over phosphorus pentoxide in vacuo at 100° for 24 hr prior to use. Tetra-n-propylammonium azide was prepared according to the method of Seel and Nógrádi.[38] Since it is very hygroscopic the salt was stored over phosphorus pentoxide and prior to use was dried for 24 hr at 100° in vacuo.

*Anal.* Calcd for $C_{12}H_{28}N_4$: C, 63.10; H, 12.36; N, 24.53. Found: C, 62.42; H, 12.38; N, 24.35.

**Kinetic Procedures. Glassware.** All glassware was cleaned with a 5% hydrogen fluoride solution, rinsed with copious amounts of distilled water, and dried in an oven at 110°.

**Preparation of Solutions.** The ampoule technique was employed for the majority of the kinetic studies. Solutions were prepared by weighing an appropriate amount of the desired salt and substrate into a 100-ml volumetric flask and adding sufficient absolute ethanol to bring the volume to 100 ml. Precooled, nitrogen-flushed ampoules (constricted 6-in. test tubes) were then charged with ca. 6 ml of the resulting solution, sealed, and introduced into the constant temperature bath. At specific times, an ampoule was removed, cooled to 0° in an ice bath, and broken open. A specific volume of the reaction mixture was then pipetted into a quench and titrated.

Another technique was employed for reactions which were too fast to be followed by the use of ampoules. Solutions were prepared as above except that the substrate was not added. The 100-ml volumetric flask was then stoppered and placed in the rate bath to attain temperature, usually for 10–15 min. The flask was then removed from the bath, a predetermined amount of substrate was added, and the flask was sealed with a serum stopper and replaced

in the rate bath. At specific times a syringe was used to remove a standard volume of the reaction mixture for titration.

**Titrimetric Methods.** Rate constants were obtained by following the liberation of either acid or halide ion. The acid titer of a point was determined by titration of the quenched reaction aliquot with standard sodium hydroxide (ca. 0.01 M) using Bromothymol Blue-Phenol Red (1:1) mixed indicator. Quenches employed in acid titrimetry were either 90% acetone–10% distilled water or spectral grade chloroform (Baker) at 0°.

Halide ion was determined by potentiometric titration using a Fisher Titrimeter equipped with silver and calomel electrodes. An aliquot of the reaction mixture was quenched in a two-phase mixture of diethyl ether and 1 M nitric acid and titrated with standard silver nitrate (ca. 0.01 M).

**Calculations.** Pseudo-first-order rate constants were calculated by the relationship

$$k = \left( \ln \frac{V_\infty - V_0}{V_\infty - V_t} \right) \frac{1}{t}$$

where $V_\infty$ is the experimental infinity titer ($\geq$10 half-lives), $V_0$ is the initial titer ($t = 0$), and $V_t$ is the titer at any time $t$.

## Appendix

Since the publication[3] of our detailed kinetic study of the competitive substitutions by solvent and added azide ion into 2-octyl mesylate and of its interpretation in terms of the ion-pair mechanism, reports from two laboratories[9,10] have appeared on which it seems appropriate here to comment. While each of these reports acknowledges the ability of the ion-pair mechanism to accommodate our published data each suggests an alternate rationalization. Let us here deal with each of these two publications in turn.

Kohnstam, et al.,[9] would argue that the available data for the 2-octyl system, which we had interpreted in terms of the ion-pair mechanism, "are equally consistent with concurrent unimolecular and bimolecular processes." And they in fact establish that one of the criteria on which we had relied to eliminate this competitive SN1–SN2 possibility, the linearity of a plot of [RN]/[ROH] vs. [N], while correct in theory, is not, in practice, particularly sensitive.[19]

However, these authors appear to be unaware of the significance of our stereochemical studies of solvolyses of 2-octyl sulfonates.[6] Weiner had found that solvolysis of optically active 2-octyl mesylate in 25% aqueous dioxane furnishes optically active 2-octanol, 94.5% optically pure. And even this apparent 5.5% racemization could be ascribed to dioxane intervention as a nucleophile competitive with water since solvolysis of the active ester in pure water gave, within experimental error, 100% optically pure 2-octanol.

Unless one assumes that the presumed SN1 intermediate, the 2-octyl carbonium ion, unencumbered with its counteranion, can preserve its asymmetry one must conclude that, at most, 5.5% (and probably 0%) of 2-octyl mesylate can solvolyze via an SN1 pathway. Forced to accommodate these facts (in Kohnstam's terminology, $(k_s^B/k_1^B) \geq (94.5/5.5) = 17.2$, whereas his fits of our data assume $0 \leq (k_s^B/k_1^B) \leq 1.0$),[39] Kohnstam's scheme reduces toward a pure SN2 mechanism.[40]

Schleyer, et al.,[10] have published a well-reasoned analysis of our proposed ion-pair mechanism and of the data which we have reported to support our contention that 2-octyl mesylate undergoes substitution, in 25 and

(34) K. Mislow, *J. Amer. Chem. Soc.*, 73, 4043 (1951).
(35) P. A. Levene, A. Rothen, and M. Kuna, *J. Biol. Chem.*, 120, 777 (1937).
(36) N. B. Colthrup, L. H. Daly, and S. E. Wiberly, "Introduction to Infrared and Raman Spectroscopy," Academic Press, New York, N. Y., 1964.
(37) K. Wiberg, "Laboratory Techniques in Organic Chemistry," McGraw-Hill, New York, N. Y., 1960, p 243.
(38) F. Seel and J. Nógrádi, *Z. Anorg. Allgem. Chem.*, 264, 317 (1951).

(39) These limits correspond to predictions of optical purity of derived 2-octanol of 0–50%.
(40) See ref 22 of ref 10 for independent criticisms of Kohnstam's treatment.

30% aqueous dioxane, *via* that mechanism. They conclude that, while the available data are consistent with the ion-pair mechanism, "we cannot accept the view that "...the operation of this [ion pair] mechanism was demonstrated unequivocally"[41] for 2-octyl mesylate in these two solvent systems."

These authors suggest,[10] quite correctly, that if a *negative* (rate-retarding) normal salt effect of added azide ion ($b = -0.3$ for 25% dioxane and $b = -1.0$ for 30% dioxane) on solvolysis rates of 2-octyl mesylate in 25 and 30% aqueous dioxane is assumed (rather than the positive salt effect of $b = +1.04$ to $+1.08$ used in our analysis)[3] the available data can be interpreted in terms of traditional competitive SN2 reactions of solvent and azide ion; in other words, kinetic behavior would cease to be borderline.[42]

The critical issue, then, is the sign of the normal salt effect exerted by added azide ion on the solvolysis processes of 2-octyl mesylate in 25 and 30% aqueous dioxane.

Our original approach to an estimate of this salt effect had been to carry out the solvolyses of 2-octyl mesylate in the presence of the model salts, NaBr, NaNO$_3$, and LiClO$_4$, and these data have been published.[3] In all cases solvolysis rates were accelerated and to an extent reasonably independent of the nature of the salt and linear in its concentration; the solvolysis rate constant, corrected for a normal salt effect, $k_{NA}$ (no azide), could be reasonably approximated for all model salts by the empirical linear expression $k_{NA} = k^0(1 + b[\text{salt}])$, where $k^0$ is the rate constant in the absence of any salts and, in 30% aqueous dioxane, $b = 0.73$ for NaBr, $b = 0.73$ for NaNO$_3$, and $b = 1.04$ for LiClO$_4$.

The possibility remains of course that our chosen model salts are not, for whatever the reason, appropriate models to estimate the normal salt effect exerted by sodium azide in our system. Schleyer[10] suggests, for example, that these salts may introduce a bimolecular component into the rate, a possibility that we find remote, especially with LiClO$_4$. He also calls attention to two literature reports[44,45] which, he argues, support the possibility that normal salt effects may be negative. One of these, Frost and Pearson's discussion of salt effects on hydrolysis of $\gamma$-butyrolactone,[44] we consider irrelevant to the question at hand as that process is acid catalyzed and therefore of a charge type fundamentally different from that of hydrolysis of 2-octyl mesylate. Whether the second report alluded to by Schleyer, that of Grunwald, *et al.*,[45] which reports salt effects on solvolysis of neophyl tosylate, (C$_6$H$_5$)(CH$_3$)$_2$CCH$_2$OTs, in 50 wt % (~49 vol %) aqueous dioxane, is relevant to the question at hand is problematical since the products are, presumably, rearranged alkenes[46] in whose formation solvent

water obviously cannot function as a nucleophile. In any event the authors[45] report that of those seven salts investigated, NaCl, LiCl, NaBr, NaNO$_3$, NaI, NaClO$_4$, and 2-C$_{10}$H$_7$SO$_3$Na, only NaCl exerted a negative salt effect ($b = -0.22$ at 0.1 $M$ and $b = -0.37$ at 0.2 $M$).

In our own experiences we have yet to encounter an example of an uncomplicated negative salt effect on solvolysis and positive salt effects have been noted in each of the following systems: (1) cyclopropylcarbinyl $\beta$-naphthalenesulfonate (LiOAc, LiClO$_4$, NaOBz in 90% aqueous dioxane);[47] (2) cyclobutyl $\beta$-naphthalenesulfonate (NaOBz in 90% dioxane);[47] (3) *threo*-3-phenyl-2-butyl tosylate (LiClO$_4$, NaN$_3$[48] in 75% dioxane);[49] (4) $\alpha$-methylallyl chloride (LiClO$_4$ in 50% dioxane);[50] (5) $\gamma$-methylallyl chloride (NaClO$_4$ in 60% dioxane);[50] (6) neomenthyl brosylate (NaN$_3$[48] in 80% acetone);[51] (7) menthyl brosylate (NaN$_3$[48] in 80% acetone);[51] (8) bicyclo[2.2.2]octyl-2-brosylate (NaN$_3$[48] in 80% acetone);[52] (9) $\alpha$-phenyl-$\gamma$-methylallyl $p$-nitrobenzoate (NaOAc in MeOH);[53] (10) $\alpha$-methyl-$\gamma$-phenylallyl $p$-nitrobenzoate (NaOAc in MeOH);[53] (11) $\alpha$-methyl-$\gamma$-$p$-tolylallyl $p$-nitrobenzoate (NaOAc in MeOH);[53] (12) $\alpha$-methyl-$\gamma$-phenylallyl 2,6-dichlorobenzoate (NaClO$_4$ in MeOH and LiClO$_4$ in 50% methanolic dioxane)[54]; (13) $\alpha,\gamma$-dimethylallyl chloride (NaClO$_4$, NaCl, Bu$_4$NClO$_4$, NaSCN[48] in ethanol and 90% ethanol);[13] and (14) the three $\alpha$-arylethyl halides (NaClO$_4$, KOAc, NaSCN,[48] ($n$-Bu)$_4$NClO$_4$, NaOAc in ethanol) of this manuscript.

To this list of documented positive salt effects may be added: the extensive studies of Ingold and his coworkers with *tert*-butyl bromide (NaN$_3$, LiCl, and LiBr in 90% acetone)[55] benzhydryl chloride (LiBr in 80% acetone), benzyhydryl bromide (LiCl in 80% acetone),[56] and $p,p'$-dimethylbenzhydryl chloride (NaN$_3$, LiBr, NMe$_4$NO$_3$ in aqueous acetone);[57] the studies of Kohnstam and coworkers[58] with $p$-methoxybenzyl chloride (NaClO$_4$, NaBF$_4$, NaNO$_3$ in 70% acetone), with $p$-phenoxybenzyl chloride (NaClO$_4$, NaBF$_4$, NaNO$_3$ in 70% acetone), and with benzhydryl chloride (NaClO$_4$, NaBF$_4$, NaNO$_3$, NaBr, and NaN$_3$ in 70% acetone); and the study of Bordwell and Mecca[59] with $p$-MeC$_6$H$_4$SO$_2$CH=CH(CH$_3$)$_2$CBr (LiClO$_4$ in methanol and 60% methanol).

While Schleyer's conclusion,[10] that an assumed negative salt effect for NaN$_3$ ($b = -1.0$) for the solvolysis of 2-octyl mesylate in 30% aqueous dioxane (36.2°) can force our published data into an SN2 framework, is

(41) This inner quotation is ours from ref 3.

(42) They recognize,[10] quite correctly, that the only salt effect in question is that on the solvolysis process; questions of any salt effect(s) on other processes or deviations from ideality resulting from nonunit activity coefficients are irrelevant. In Schleyer's words,[43] "both Sneen's work and our own utilize the relationship between rate and product data; consideration of activity is implicit in these treatments."

(43) See ref 20 of ref 10. See also ref 25 of this manuscript.

(44) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, Wiley, New York, N. Y., 1961, pp 150–155.

(45) E. F. Duynstee, E. Grunwald, and M. L. Kaplan, *J. Amer. Chem. Soc.*, **82**, 5654 (1960).

(46) A. H. Fainberg and S. Winstein, *ibid.*, **78**, 2763 (1956).

(47) R. A. Sneen, K. M. Lewandowski, I. A. I. Taha, and B. R. Smith, *ibid.*, **83**, 4843 (1961).

(48) In these cases rate enhancements are greater than can be accounted for assuming all substitution product (RN$_3$ and RSCN) arises *via* a bimolecular pathway.

(49) M. Nieh, Ph.D. Thesis, Purdue University, 1970.

(50) R. A. Sneen and J. V. Carter, *J. Amer. Chem. Soc.*, **94**, 6990 (1972).

(51) M. A. Collins, Ph.D. Thesis, Purdue University, 1968.

(52) D. M. Roscher, Ph.D. Thesis, Purdue University, 1966.

(53) R. A. Sneen and A. M. Rosenberg, *J. Amer. Chem. Soc.*, **83**, 895 (1961).

(54) R. A. Sneen and P. S. Kay, *ibid.*, **94**, 6983 (1972).

(55) L. C. Bateman, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 960 (1940).

(56) O. T. Benfey, E. D. Hughes, and C. K. Ingold, *ibid.*, 2488 (1952).

(57) L. C. Bateman, E. D. Hughes, and C. K. Ingold, *ibid.*, 974 (1940).

(58) B. J. Gregory, G. Kohnstam, A. Queen, and D. J. Reid, *Chem. Commun.*, 797 (1971).

(59) F. G. Bordwell and T. G. Mecca, private communication.

correct in theory, there exists, to our knowledge, no example of a negative salt effect of this magnitude on solvolysis of *any* substrate in *any* solvent by *any* salt; and in fact there exists but one authenticated example (NaCl in 50 wt % aqueous dioxane with neophyl tosylate) of a relevant negative salt effect of *any* magnitude ($b = -0.22$ to $-0.37$).[45] We conclude that the available evidence is overwhelmingly opposed to an $S_N2$ interpretation of the 2-octyl mesylate data.

Finally, it should be recognized that the 2-octyl system, our first published example of the operation of the ion-pair mechanism, is now but one of several "borderline" systems which have been shown to conform to the predictions of the ion-pair mechanism.

Among them are *p*-methoxybenzyl chloride ($NaN_3$ in 70% acetone),[4,12] benzoyl chloride[4,11] (*o*-nitroaniline in 50 wt % aqueous acetone), two of the substrates considered in this manuscript (*α*-phenylethyl bromide and *α*-*p*-tolylethyl chloride with $N_3^-$ and $SCN^-$ in ethanol), and *α*,*γ*-dimethylallyl chloride ($N_3^-$ and $SCN^-$ in ethanol and 90% ethanol).[13] The evidence in each case against mechanistic alternatives has been presented and argued. While the case for the operation of the ion-pair mechanism with any one of these substrates singly might not be completely convincing as an isolated example to all observers it is difficult for us to see how the cumulative weight of all of these studies can be denied.

# Solvolytic Chemistry of 1,4-Dimethylbenzene Oxide. A New and Novel Mechanism for the NIH Shift

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**Abstract:** The kinetics of the aromatization of 1,4-dimethylbenzene oxide (I) into 2,5-dimethylphenol (II) and 2,4-dimethylphenol (III), the latter arising *via* the NIH shift of a methyl group, were measured over the pH range of 1–12, in 50% aqueous dioxane, $\mu = 0.1$ (KCl), and follow the equation $-d[I]/dt = [I][k_0 + (k_H^1 + k_H^2)a_H]$ (where $k_0 = 4.8 \times 10^{-3}$ sec$^{-1}$; $k_H^1 = 7.3 \times 10^2$ $M^{-1}$ sec$^{-1}$; and $k_H^2 = 5.3 \times 10^2$ $M^{-1}$ sec$^{-1}$). In this equation, $k_0$ is a spontaneous rate giving rise to a 13:87 ratio of II:III and $k_H^1$ and $k_H^2$ are acid-catalyzed terms giving rise to a 54:46 ratio of II:III. The reaction proceeding through the $k_H^1$ path does not involve detectable intermediates, whereas that through the $k_H^2$ path proceeds *via* the intermediate 1,4-dimethyl-2,5-cyclohexadiene-2,4-diol (IV). The $k_H^2$ path represents a new mechanism for the NIH shift. The mechanistic details of these reactions are discussed.

**W**ith the recent demonstration that arene oxides function as the initial intermediates in the enzymatic formation of phenols and other metabolites of the aromatic nucleus,[3] considerable interest has developed in the chemical and biological fate of these labile compounds. In particular, arene oxides have been implicated as agents in the toxicity,[4] mutagenicity,[5] and carcinogenicity[3,6] of mono- and polycyclic aromatics. These adverse reactions have been speculated to be the consequence of covalent binding of arene oxides to cellular nucleophiles. Thus, an understanding of the mechanisms by which arene oxides

isomerize to phenols and react with nucleophiles acquires considerable significance.

A characteristic of the mixed function oxidase-catalyzed formation of phenols is the migration and subsequent retention of ring substituents originally present at the position of hydroxylation, the NIH shift.[7] Evidence that arene oxides are intermediates compatible with the NIH shift is found in the isomerizations of 1-$^2H$-4-methylbenzene oxide[8] and 1-$^2H$-naphthalene oxide[9] to the corresponding phenols. The magnitude of deuterium retention was found to be a function of pH in each case. Kinetics of the isomerization of benzene and naphthalene 1,2-oxide[10] have shown that different mechanisms are operative at high and low pH. In the neutral to basic region, an un-

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