

## Reactions of Charged Substrates. 8. The Nucleophilic Substitution Reactions of (4-Methoxybenzyl)dimethylsulfonium Chloride

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Displacement reactions on the title compound (**1**) occur only for nucleophiles with intermediate hardness. Nucleophiles that react display a range of mechanisms. **1** reacts with the neutral nucleophile pyridine-*d*<sub>5</sub> through a mixed S<sub>N</sub>1/S<sub>N</sub>2 mechanism; salt added to control ionic strength affects the rate for the unimolecular process, but has no effect on the bimolecular rate constant. The mechanism of displacement by N<sub>3</sub><sup>-</sup> and SO<sub>3</sub><sup>2-</sup> depends on the presence or absence of exogenous salt. At constant ionic strength, the mechanism is mixed S<sub>N</sub>1/S<sub>N</sub>2 over most of the range of [Nu]. With nucleophile only present, plots of *k*<sub>obsd</sub> vs [Nu] exhibit severe breaks that are not the result of salt effects. Analysis of rate constants and product ratios suggests that at low [Nu] reaction occurs simultaneously through concerted Hughes–Ingold S<sub>N</sub>2 and preassociation-concerted mechanisms. At high [Nu], displacement occurs only through the preassociation-concerted mechanism. Comparison of these results with data for gas-phase dissociation of benzyl dimethylsulfoniums and with solution results for benzyl pyridiniums suggests that the intrinsic stability of the intermediate does not necessarily determine the mechanism.

### Introduction<sup>V1</sup>

Studies of the solvolysis and nucleophilic substitution reactions of neutral and charged benzyl derivatives have been central to the development of modern theories of physical organic chemistry.<sup>1</sup> Depending on a number of factors, including the nature of the leaving group and the “ionizing power” of the solvent, these substrates can exhibit a range of possible mechanisms. While there are clear examples of limiting S<sub>N</sub>1 and S<sub>N</sub>2 mechanisms for substitution reactions,<sup>2,3</sup> the commonly observed borderline kinetic behavior—kinetic order in nucleophile between 0 and 1—has been interpreted in terms of an ion-pair mechanism,<sup>4–6</sup> a simple mixed S<sub>N</sub>1/S<sub>N</sub>2 mechanism,<sup>2,7–9</sup> solvent nucleophilic participation,<sup>10,11</sup> or

a complex scheme proposed by Jencks,<sup>12</sup> part of which is shown in Scheme 1.

Reactions of 4-methoxybenzyl chloride are illustrative. Kohnstam<sup>7</sup> measured the kinetics and product distribution for the reaction of 4-methoxybenzyl chloride with azide and proposed that the mechanism was mixed S<sub>N</sub>1/S<sub>N</sub>2. In an attempt to extend the ion pair hypothesis for substitution reactions of secondary alkyl compounds,<sup>13</sup> Sneen and Larsen<sup>4</sup> reanalyzed Kohnstam's data with eq 1, in which *k*<sub>obsd</sub> is the rate constant in the presence of a

$$k_{\text{obsd}}/k_0 = \frac{(\{K_{-1}/K_W\} + 1)(1 + \{K'_N/K'_W\}[\text{Nu}])}{(1 + \{K_{-1}/K_W\} + \{K'_N/K'_W\}[\text{Nu}])} \quad (1)$$

given [Nu], *k*<sub>0</sub> is the rate constant in the absence of nucleophile, and the other rate constants are those for the ion pair mechanism shown in Scheme 1. Because of the good fits of rate constants and product ratios to eq 1, they argued that substitution involved attack on a contact ion pair. Studies of chlorine kinetic isotope effects were interpreted as proof for and against<sup>14</sup> the ion-pair mechanism. Friedberger and Thornton<sup>15</sup> argued that Sneen's mechanism was perfectly reasonable if it could be proven that no azide product arose from trapping of the free carbenium ion. In a recent study, Amyes and Richard<sup>2</sup> showed through a careful dissection of various kinetic quantities, including common ion suppression and product ratios, that the reaction was mixed S<sub>N</sub>1/S<sub>N</sub>2 in 80:20 and 70:30 acetone:water, but S<sub>N</sub>1 in 1:1 trifluoroethanol:water. They ruled out ion-pair and preassociation mech-

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(1) Amyes and Richard<sup>2</sup> provide a fairly complete list of references for the reactions of various benzyl substrates; we will not reproduce that list here.

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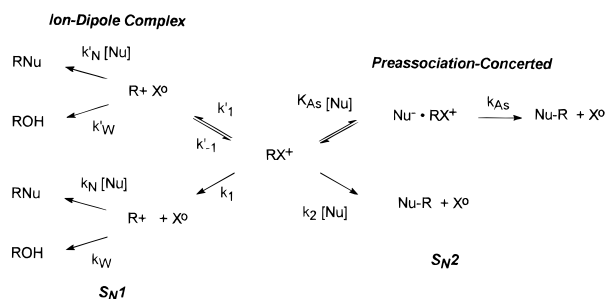
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Scheme 1



anisms. These excellent, definitive experiments seem to have resolved the issue of 4-methoxybenzyl chloride reaction mechanisms.

In an attempt to generalize his ion-pair hypothesis, Sneen<sup>5</sup> studied the nucleophilic substitution reactions of (4-methoxybenzyl)- and benzyldimethylsulfonium salts and, based on good fits of kinetic quantities to eq 1, argued that both substrates reacted through an ion-dipole complex (IDC), the intermediate for positively charged substrates analogous to the ion pair. This mechanism has been extended to other systems.<sup>6,16</sup>

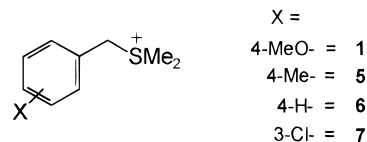
In contrast, Swain and his colleagues<sup>8</sup> reported that the bimolecular reactions (lyoxide,  $N_3^-$ ) of substituted benzyl dialkyl and alkyl/arylsulfonium salts are  $S_N2$  at constant ionic strength in water, and Richard and Jencks<sup>17</sup> later found that the reaction of (1-(4-methylphenyl)ethyl)dimethylsulfonium with azide is mixed  $S_N1/S_N2$  under conditions of constant ionic strength in trifluoroethanol-water. We recently suggested<sup>18</sup> that the hydrolysis of (4-methoxybenzyl)dimethylsulfonium chloride (**1**) in the presence or absence of exogenous salt does not occur through an IDC, which by microscopic reversibility would rule out the IDC mechanism for the azide substitution reaction as well. In their report of the hydrolysis of **1**, Kevill and colleagues<sup>9</sup> reanalyzed Sneen's data assuming a mixed  $S_N1/S_N2$  mechanism and based on better fits of the product data ruled out the IDC mechanism. In the gas phase, 4-substituted benzyldimethylsulfonium ions appear to dissociate directly and not through an ion-neutral complex (INC).<sup>19</sup>

It would be expected that benzyl compounds with other charged leaving groups might react through the IDC mechanism. Katritzky<sup>6</sup> has proposed that the reaction of benzyl 2,4,6-triphenylpyridinium ion substrates with amines in chlorobenzene occurs through an IDC mechanism. In a recent study,<sup>3</sup> we showed that the azide substitution and solvolysis reactions of benzyl 3'-substituted-pyridinium ions in  $D_2O$  under constant ionic strength occurs by direct displacement, with no evidence for either a stepwise or IDC mechanism. In the gas phase, however, these substrates appear to dissociate through a mixed ion-neutral complex/direct dissociation mechanism.<sup>19</sup>

In addition to conceptual challenges to Sneen's mechanism,<sup>10,11,15</sup> a major technical criticism was that his experiments were conducted with low, limited concentrations of added nucleophile with no exogenous salt added

to control ionic strength. Indeed, the majority of Sneen's studies were conducted with  $N_3^-$  as the only added nucleophile. Schleyer and his colleagues<sup>11</sup> proposed that the kinetics for neutral secondary alkyl substrates was the result of special  $NaN_3$  salt effects and not of an ion-pair mechanism, and Gregoriou<sup>20</sup> showed that an analysis of Sneen's data using activities of  $NaN_3$  rather than concentrations was not consistent with an ion-pair mechanism.

To resolve this dilemma, we studied the substitution reactions of **1** under Sneen's original conditions and at constant ionic strength with a wide range of nucleophiles.



A second-order reaction occurs only for nucleophiles with intermediate hard-soft-acid-base (HSAB) rank. While exogenous salt has no effect on the mechanism of the bimolecular reaction for the neutral nucleophile pyridine-*d*<sub>5</sub>, the mechanism of substitution for negatively charged nucleophiles depends strongly on the presence or absence of exogenous salt and is independent of any "normal" salt effect.

## Experimental Section

**General.** All chemicals and solvents were obtained from Aldrich and used without further purification. All rate constants were measured on a General Electric QE-300 NMR spectrometer with a variable temperature probe rated at  $\pm 0.1$  °C; the temperature of the probe was calibrated by measuring water relaxation times and comparing them with known values at various temperatures. (Exact correspondence between the NMR rate constants for the reaction of **1** with  $NaN_3$ , reported by Sneen,<sup>5</sup> and the hydrolysis of **1** measured by Kevill<sup>9</sup> at various temperatures and by us<sup>18</sup> using different methods to control temperature, shows that the NMR rate constants are accurate at the reported temperatures.) FT IR spectra were obtained on a Nicolet DX spectrophotometer. Positive- and negative-ion liquid secondary ion mass spectra (LSIMS) were obtained in the UCSF Mass Spectrometry Facility using a 4-sector Kratos Concept II HH mass spectrometer fitted with an optically coupled 4% diode array detector. Microanalysis was performed in the Microanalytical Laboratory, College of Chemistry, University of California, Berkeley. Plots were made and regression analysis and curve fitting were performed on Origin V. 2.8.

**Syntheses. (4-Methoxybenzyl)dimethylsulfonium (1).** The synthesis has been reported.<sup>18</sup>

**Trimethylsulfonium Iodide.** A chloroform solution of 1 equiv of iodomethane and 1 equiv of methyl sulfide was shaken for 5–10 min at ambient temperature; the thin white crystals formed were collected and washed with chloroform repeatedly. The yield was essentially quantitative.

**4-Methoxybenzyl 4'-Sulfobenzoate (4).** The general method given by Feiser and Feiser<sup>21</sup> was used. An anhydrous pyridine solution containing 1 equiv of 4-methoxybenzyl alcohol and 1.1 equiv of 4-carboxybenzenesulfonyl chloride was heated gently and then stored at 0 °C overnight. A white precipitate formed when this solution was poured into ice-cold 0.1 M HCl. The solid was collected by filtration and dried *in vacuo*. This product, which gave reasonable NMR (DMSO-*d*<sub>6</sub>, >98% purity), FTIR (KBr pellet), and negative-ion LSIMS spectra, was assumed initially to be the sulfonate ester **2** (Scheme 2). Rate constants for solvolysis were many orders of magnitude lower than expected based on Tsuno's estimate

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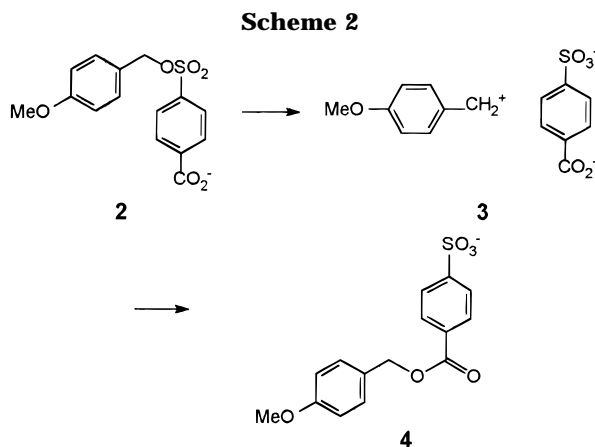
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for the corresponding tosylate,<sup>22</sup> however, but were close to values for 4-methoxybenzyl benzoate esters reported by Aymes and Richard.<sup>2,23</sup> Indeed, hydrolysis was so slow that we subsequently found the solid could be recrystallized by dissolving it in a small amount of boiling water and immediately quenching in iced brine, a maneuver completely incompatible with the very reactive sulfonate ester **2**.

Because of this disparity, we ran the reaction in pyridine-*d*<sub>5</sub> and directly observed its progress by NMR at 25 °C. After 10–15 min, signals for 4-methoxybenzyl alcohol had fallen to a low, steady level, and a complex pattern of peaks appeared, none of which corresponded to the isolated product. A portion of this solution was hydrolyzed (D<sub>2</sub>O, 80 °C, 20 min). The NMR spectrum of the residue showed the sulfonic acid, 4-methoxybenzyl alcohol, and (4-methoxybenzyl)pyridinium-*d*<sub>5</sub> (from the benzyl AA'BB' signal), a compound known to hydrolyze very slowly at 80 °C.<sup>3</sup> After standing at ambient temperatures for several days, the pyridine-*d*<sub>5</sub> solution was reduced carefully to an oil. The NMR spectrum of the residue in DMSO-*d*<sub>6</sub> showed the solid product as the major component; the only other product was (4-methoxybenzyl)pyridinium-*d*<sub>5</sub>. These results suggest that the initially formed sulfonate ester **2** ionizes to the ion pair **3** that collapses to the benzoate ester **4** (Scheme 2). The relatively low yield (15–20%) of (4-methoxybenzyl)pyridinium-*d*<sub>5</sub> suggests that internal return is faster than either direct displacement by pyridine-*d*<sub>5</sub> on **2** or **3** or trapping of any carbenium ion that may leak out of the contact ion pair. Because of these complications, we did not attempt to isolate **2**.

Benzoate ester **4**: mp (sealed tube) > 250 °C. FTIR (KBr pellet): 1713, 1511, 1273, 1234, 1176 cm<sup>-1</sup>. <sup>1</sup>H NMR: pyridine-*d*<sub>5</sub> (δ 0 = TMS) δ 8.42 (d, *J* = 8 Hz, 2H, benzoate AA'), 8.18 (d, *J* = 8 Hz, 2H, benzoate BB'), 7.52 (d, *J* = 8.4 Hz, 2H, benzyl AA'), 7.06 (d, *J* = 8.4 Hz, 2H, benzyl BB'), 5.42 (s, 2H, -CH<sub>2</sub>-), 3.72 (s, 3H, MeO); DMSO-*d*<sub>6</sub> (anhydrous; δ 0 = TMS) δ 7.93 (d, *J* = 8 Hz, 2H, benzoate AA'), 7.73 (d, *J* = 8 Hz, 2H, benzoate BB'), 7.43 (d, *J* = 8.4 Hz, 2H, benzyl AA'), 6.97 (d, *J* = 8.4 Hz, 2H, benzyl BB'), 5.27 (s, 2H, CH<sub>2</sub>), 3.76 (s, 3H, MeO), 3.36 (s, 6H, H<sub>2</sub>O). <sup>13</sup>C NMR: DMSO-*d*<sub>6</sub> δ 165.30, 159.26, 152.64, 130.09, 129.51, 128.91, 127.93, 125.91, 113.93, 66.15, 55.13. Negative-ion LSIMS (%): *m/z* 321.1 (100), M<sup>-</sup>, calcd 321.2; 201 (18) [M<sup>-</sup> - O<sub>2</sub>CC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub><sup>-</sup>]; 156 (20) [O<sub>2</sub>CC<sub>6</sub>H<sub>4</sub>-SO<sub>3</sub><sup>-</sup> - CO<sub>2</sub>]. Anal. Calcd for C<sub>15</sub>H<sub>14</sub>O<sub>6</sub>S·3H<sub>2</sub>O: C, 48.0; H, 5.3. Found: C, 48.7; H, 4.2.

**NMR Kinetics.** Pseudo-first-order rate constants for reactions with the nucleophiles and salts listed in Table 1 were measured by observing the loss of the SMe<sub>2</sub><sup>+</sup> signal in the <sup>1</sup>H-NMR spectra in D<sub>2</sub>O either at constant ionic strength or without salt added. (For ND<sub>3</sub> and NaOD, the benzyl AB pattern was followed because the benzyl methylene and sulfonium methyl protons exchanged instantaneously.) The

typical concentration of substrate was ca. 10 mM, which allowed spectra with good signal-to-noise ratios to be collected in a single 90° pulse experiment. Solutions were preheated in the probe (60–80 °C), removed, added to the substrate, and returned to the probe, the spectrometer was reshimmed (ca. 1–1.5 min), and the appropriate peak was integrated at various timed intervals.

**Product Ratios.** Reactions in D<sub>2</sub>O or H<sub>2</sub>O (as a control for exchange of benzyl methylenes) were run in NMR tubes; in some instances, solutions from kinetic runs were used and in others fresh solutions were made. At least three batches of substrate were used, and the concentrations of substrate at each [Nu] were varied. After heating at 80 °C for > 10 half-lives, the aqueous layers were extracted with CDCl<sub>3</sub>, which was dried by filtration through a short column of anhydrous sodium sulfate. Spectra of the remaining D<sub>2</sub>O layers showed that complete extraction was achieved. Product ratios were obtained by integrating the benzyl methylene peaks of products (4-methoxybenzyl alcohol [δ = 4.62] or 4-methoxybenzyl azide [δ = 4.26]). Spectra were obtained under identical conditions at 25 °C. In samples with low concentrations of alcohol, both peaks were integrated in pairs three to five times, with the slope and curvature of the integration adjusted each time, and the readings were averaged. With the exceptions noted below, the product ratios obtained in either D<sub>2</sub>O or H<sub>2</sub>O were the same, which showed that exchange did not take place on the time scale of the experiments.

For the pyridine-*d*<sub>5</sub> reactions, the extraction method could not be used because the pyridinium ion product is not soluble in CDCl<sub>3</sub>. The benzyl proton ratios were read directly from dilute reaction mixtures in D<sub>2</sub>O. To assure that accurate readings for 4-methoxybenzyl alcohol had been obtained, some samples were read and diluted with DMSO-*d*<sub>6</sub>, and the determination was repeated; the same results were obtained by both methods. This method was used to obtain a crude estimate of *k<sub>N</sub>/k<sub>W</sub>* for the reaction of **4** with a 1.0 M solution of pyridine-*d*<sub>5</sub> in D<sub>2</sub>O at 80 °C with no added salt.

## Results

**Kinetics.** Pseudo-first-order constants were calculated by linear regression from plots of ln(*C<sub>t</sub>/C<sub>0</sub>*) vs time and are reported in min<sup>-1</sup> as the mean ± SE. (At the request of a referee, all *k<sub>obsd</sub>* used to construct the various plots are tabulated in the supporting information.) Plots were linear over two to five half-lives, and all had *r* ≥ 0.996; SE were 1–9%. Because reactions with all nucleophiles that display a kinetic order, except NaSCN (see below),<sup>24</sup> go to completion, no infinity term is included explicitly in the equations. (These nucleophiles also buffer the reaction solutions, and the hydronium-catalyzed equilibrium among **1** and the products<sup>18</sup> is not a factor.) Second-order rate constants were calculated by linear regression from plots of *k<sub>obsd</sub>* vs [Nu] and are reported in M<sup>-1</sup> min<sup>-1</sup> as the mean ± SE. Second-order rate plots are shown below with the appropriate nucleophile.

**Reaction of 1 with Nucleophiles.** A summary of the reactions of **1** with the 14 nucleophiles and salts that cover the HSAB range is given in Table 1.

**HSAB Dependence.** **1** reacts with intermediate but not with hard or soft nucleophiles<sup>25</sup> (Table 1). In contrast, Swain and his colleagues found that 4-Me (**5**), 4-H (**6**), and 3-Cl (**7**) benzyldimethylsulfonium ions react with the intermediate nucleophile N<sub>3</sub><sup>-</sup> and the hard nucleophiles HO<sup>-</sup> and PhO<sup>-</sup> in water,<sup>8a,b,d</sup> and Snee found that **6**

(22) Fujio, M.; Goto, M.; Susuki, T.; Akasaka, I.; Mishima, M.; Tsuno, Y. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1146–1153. These authors estimated the rate constant for solvolysis of *p*-methoxybenzyl tosylate at 25 °C in 80% aqueous acetone to be 0.83 s<sup>-1</sup>; extrapolation to 25 °C for the white insoluble solid gives *k* = 2.9 × 10<sup>-6</sup> s<sup>-1</sup>.

(23) We thank John Richard for calling this to our attention.

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(25) Pearson, R. G. In *Advances in Free Energy Relationships*; Chapman, N. B., Shorter, J., Eds.; Plenum Press: New York, 1972; pp 281–319.

**Table 1. Reactions of Nucleophiles with (4-Methoxybenzyl)dimethylsulfonium, 80 °C, D<sub>2</sub>O**

nucleophile	HSAB	100% reaction	order in Nu	products	$k_{\text{Nu}}/k_{\text{W}}^b$
OH <sup>-</sup>	H	yes	0	ROH	0.43
ND <sub>3</sub>	H	yes	0	ROH, RND <sub>3</sub>	
OCN <sup>-</sup>	H	yes	0	ROH, ROCN, RNCO	
F <sup>-</sup>	H	yes	0	ROH	1.3
SO <sub>4</sub> <sup>2-</sup>	H	yes	0	ROH	
Cl <sup>-</sup>	H	no	0	ROH	
ClO <sub>4</sub> <sup>-</sup>	H	no	0	ROH	
CN <sup>-</sup>	S	yes	0	ROH, RCN	7.5
I <sup>-</sup>	S	no	0	ROH	
Br <sup>-</sup>	I	no	0	ROH	55.5
SCN <sup>-</sup>	I	yes	yes	ROH, RSCN, RNCS	
N <sub>3</sub> <sup>-</sup>	I	yes	yes	ROH, RN <sub>3</sub>	1.0
Py- <i>d</i> <sub>5</sub>	I	yes	yes	ROH, R-Py- <i>d</i> <sub>5</sub> <sup>+</sup>	
SO <sub>3</sub> <sup>2-</sup>	I	yes	yes	RSO <sub>3</sub> H, ROH	

<sup>a</sup> H = hard; S = soft; I = intermediate. R = 4-MeO-benzyl.

<sup>b</sup> Averages of the slopes of plots of [RNU]/[ROH] vs. [Nu] for salt and no salt. ROCN and RNCO hydrolyze and give a complex mixture of products.

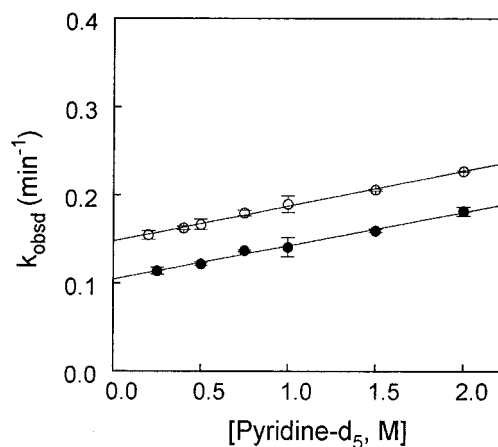
reacts with the soft nucleophile I<sup>-</sup> in water.<sup>5</sup> While nucleophile/leaving group HSAB symbiosis is well documented, these results suggest that a direct resonance interaction of a substituent with the reaction center is sufficient to cause the effect.

Because kinetics alone was not sufficient to explain the HSAB dependence, it was examined computationally using semiempirical methods. The results, which will be published in detail elsewhere, show that for **1** and **6** the rate constants for the solution reactions correlate well with the HOMO–LUMO gap between nucleophile and electrophile and with  $E_{\text{HOMO}}$  for the activated complexes. The difference in reactivity between **1** and **6** is apparently related to differences in HOMO orbital symmetries and energies between the ground state and activated complexes. Differences in HSAB rank are apparently related to the orbital symmetries of the activated complexes.

#### Reactions Zero Order in Nucleophile. Halides.

The four halide salts used span the HSAB range. If direct displacement occurred, the disappearance of **1** should have a dependence on [halide]; none does. The observed rate constants for disappearance of **1** in the presence of the halide salts is equal to the first-order rate constant in the presence of equivalent concentrations of NaCl and NaClO<sub>4</sub> as the exogenous salts, consistent with an S<sub>N</sub>1 reaction. In fact, reaction with NaI and NaBr show the same pattern of incomplete hydrolysis documented for the S<sub>N</sub>1 reaction **1** in the presence of NaCl and NaClO<sub>4</sub>, and with no added salt.<sup>18</sup> The reaction with NaF goes to completion because under the reaction conditions the high [F<sup>-</sup>] would buffer the solution. Products are not diagnostic of a displacement or trapping reaction. It would be expected that any 4-methoxybenzyl halide formed would immediately hydrolyze.<sup>5</sup> 4-Methoxybenzyl alcohol was the only product detected for reactions with the four halides.

**NaOD and ND<sub>3</sub>.** Rate constants did not depend on the concentration of either of these hard nucleophiles (Figure S1 for NaOD; ND<sub>3</sub> not shown). Benzyl methylene and sulfonium hydrogens exchange rapidly for deuterons, and the lower rate constants are the result of a benzyl α deuterium secondary isotope effect.<sup>26</sup> Values of  $k_{\text{obsd}}$  for ND<sub>3</sub> were 1.56-fold lower than the first-order rate constants in D<sub>2</sub>O, which yields  $k_{\text{H}}/k_{\text{D}} = 1.26$  per deuterium



**Figure 1.** Second-order rate plots for the reaction of **1** with pyridine-*d*<sub>5</sub> with (●) and without (○) NaCl added to control ionic strength. Error bars are ± S.E. The two regression lines are parallel.

for the secondary isotope effect for hydrolysis of **1**, consistent with a limiting S<sub>N</sub>1 reaction.<sup>26</sup>

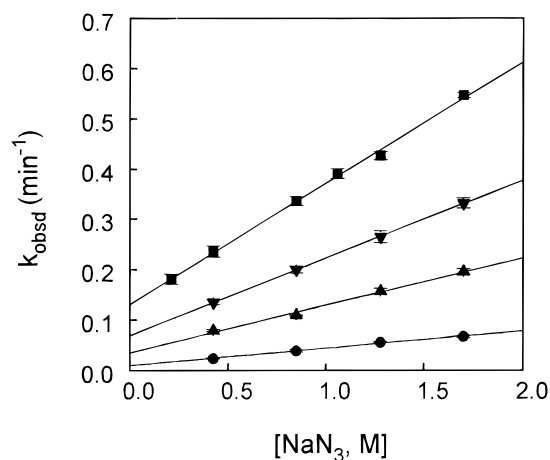
Rate constants for the reaction of NaOD and **1** at various ionic strengths were in the same limited range within error (Figure S1). Dividing the hydrolysis rate constants for diprotio **1** at  $\mu = 0$  and 1.7 by 1.56 gives expected rate constants of 0.096 and 0.079, respectively, which are within the values, including error, of 0.085–0.090 ± 0.003–0.010 found for NaOD reaction at the same ionic strengths.

**NaCN and NaOCN.** The second-order rate plot for NaCN (HSAB = soft) under constant ionic strength ( $\mu = 1.7$ , NaCl) at 80 °C shows no dependence on [NaCN] (Figure S1). The measured rate constant, 0.106 min<sup>-1</sup>, is in excellent agreement with the measured or extrapolated value for hydrolysis alone at this ionic strength.<sup>18</sup> Measured rate constants for NaOCN (HSAB = hard) alone at 1.7 M (0.109 min<sup>-1</sup>) and 0.85 M (0.129 min<sup>-1</sup>) increase with a decrease in ionic strength and are in excellent agreement with the hydrolysis rate constants at these ionic strengths with either NaCl or NaClO<sub>4</sub> used to control ionic strength. NaCN gives 4-methoxybenzyl cyanide as the sole product. NaOCN gives a complex mixture of products that form by hydrolysis of the initial products 4-methoxybenzyl cyanate and isocyanate; the mixture was not characterized.

**Na<sub>2</sub>SO<sub>4</sub>.** Values of  $k_{\text{obsd}}$  decrease with increasing concentration of salt; at [Na<sub>2</sub>SO<sub>4</sub>] = 1 M,  $k_{\text{obsd}} = 0.085$  min<sup>-1</sup> and at [Na<sub>2</sub>SO<sub>4</sub>] = 2 M,  $k_{\text{obsd}} = 0.048$  min<sup>-1</sup>, which are about half the values for the corresponding concentrations of NaCl or NaClO<sub>4</sub> and are consistent with the values obtained as the intercept of plots of  $k_{\text{obsd}}$  vs [Na<sub>2</sub>SO<sub>3</sub>] obtained with Na<sub>2</sub>SO<sub>4</sub> used to control ionic strength (see Figure 6). The rate constants are the result of the effect of anion charge and size and of the higher values of  $\mu$  for the dianions as a function of molarity. 4-Methoxybenzyl alcohol is the sole product.

**Reactions with an Order in Nucleophile. Reaction of 1 with Pyridine-*d*<sub>5</sub> at Constant Ionic Strength and with No Added Salt.** Plots of  $k_{\text{obsd}}$  vs [pyridine-*d*<sub>5</sub>] (Figure 1), based on the means of three or more separate determinations, are linear. At  $\mu = 2$  (NaCl),  $k_2 = 0.038 \pm 0.001$  M<sup>-1</sup> min<sup>-1</sup> and  $k_1 = 0.104 \pm 0.001$  min<sup>-1</sup>

(26) Shiner, V. J. In *Isotope Effects in Chemical Reactions*; Collins, C. J.; Bowman, N. S., Eds; Van Nostrand Reinhold: New York, 1970; pp 91–159.



**Figure 2.** Second-order rate plots for the reaction of **1** with  $\text{NaN}_3$  at 60 °C (●,  $r = 0.997$ ), 70 °C (▲,  $r = 0.997$ ), 75 °C (▼,  $r = 0.9999$ ), and 80 °C (◆,  $r = 0.999$ ) with NaCl used to hold the ionic strength constant at  $\mu = 1.7$ . Error bars are  $\pm$  S.E. (For the 80 °C line with  $\text{NaClO}_4$  used to control ionic strength, see Figure 8.)

**Table 2.** First- and Second-Order Rate Constants for the Overall Reaction of **1** with  $\text{NaN}_3$  in  $\text{D}_2\text{O}$  at Constant Ionic Strength (NaCl)<sup>a</sup>

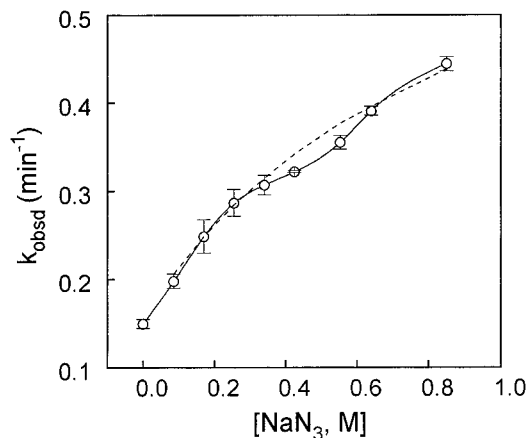
$T$ (°C)	$k_1$ ( $\text{min}^{-1}$ )	$k_2$ ( $\text{M}^{-1} \text{min}^{-1}$ )	$r$
$\mu = 0.85$			
80	$0.138 \pm 0.005$	$0.354 \pm 0.008$	0.999
$\mu = 1.7$			
60	$0.010 \pm 0.001$	$0.034 \pm 0.001$	0.997
70	$0.035 \pm 0.003$	$0.094 \pm 0.003$	0.996
75	$0.069 \pm 0.001$	$0.154 \pm 0.001$	0.9999
80	$0.110 \pm 0.002$	$0.239 \pm 0.002$	0.999
80 ( $\text{NaClO}_4$ )	$0.109 \pm 0.002$	$0.249 \pm 0.005$	0.996
$\mu = 5$			
80	$0.103 \pm 0.008$	$0.197 \pm 0.004$	0.999

<sup>a</sup> Values are the mean  $\pm$ SE obtained by linear regression.

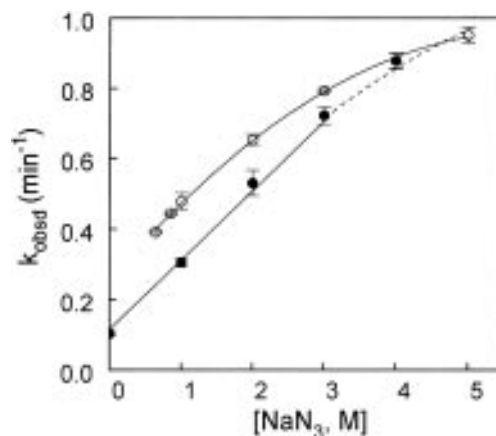
( $r = 0.996$ ); at  $\mu = 0$ ,  $k_2 = 0.040 \pm 0.001 \text{ M}^{-1} \text{ min}^{-1}$  and  $k_1 = 0.148 \pm 0.001 \text{ min}^{-1}$  ( $r = 0.998$ ). Values of  $k_1$  are within experimental error of the values obtained with  $\text{N}_3^-$  as the nucleophile or the values measured in water only.<sup>18</sup> Kevill and colleagues<sup>9</sup> found a similar dependence on pyridine concentration. The fact that the two lines are parallel shows that there is no salt effect on the rate of the bimolecular reaction. The pyridine only line does not have the curvature observed for  $\text{NaN}_3$  or  $\text{Na}_2\text{SO}_3$  alone (see below).

**Reaction of **1** with  $\text{NaN}_3$  at Constant Ionic Strength.** Plots of  $k_{\text{obsd}}$  vs  $[\text{NaN}_3]$  at  $\mu = 1.7$  with NaCl (Figure 2) or  $\text{NaClO}_4$  (see Figure 8) are linear with  $r \geq 0.996$ . Values for the slopes ( $k_2$ ) and intercepts ( $k_1$ ) are listed in Table 2. Rate constants are the same with either exogenous salt. As expected,<sup>27</sup>  $k_2$  increases with a decrease in ionic strength. The plot of  $k_{\text{obsd}}$  vs.  $[\text{NaN}_3]$  at  $\mu = 5$  is linear ( $r = 0.999$ ) over most of the concentration of nucleophile, but is slightly curved above  $[\text{NaN}_3] = 3.0 \text{ M}$  (see Figure 4).

**Reaction of **1** with  $\text{NaN}_3$  with No Added Salt.** A plot of  $k_{\text{obsd}}$  vs.  $[\text{NaN}_3]$  at 80 °C for 0–0.85 M  $\text{NaN}_3$  is shown in Figure 3. There is a distinct break in the plot at ca. 0.50 M  $\text{NaN}_3$ . The standard errors for three to ten separate determinations made with at least two separate batches of solvent at 0.42, 0.55, and 0.64 M  $\text{NaN}_3$  are



**Figure 3.** Plot of  $k_{\text{obsd}}$  vs  $[\text{NaN}_3]$  with no exogenous salt used to hold the ionic strength constant at 80 °C. Error bars are  $\pm$  S.E. The dashed line was computed using  $k'_1$  and  $k'_2$  as described in the text and ref 35 assuming a simple mixed  $\text{S}_{\text{N}}1/\text{S}_{\text{N}}2$  mechanism. The full upper portion of the curve (from 0.65 to 5 M) is shown in Figure 4.



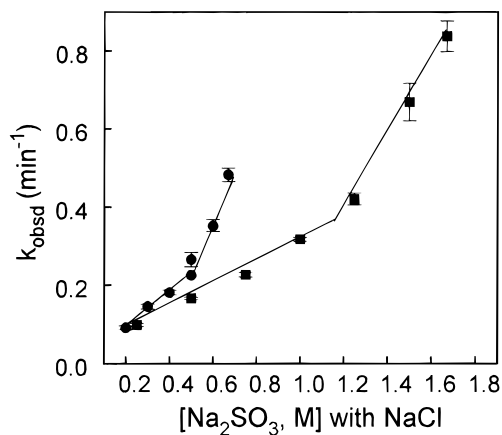
**Figure 4.** Plot of  $k_{\text{obsd}}$  vs  $[\text{NaN}_3]$  with no exogenous salt used to hold the ionic strength constant at 80 °C (○). Error bars are  $\pm$  S.E. For reference, the values for  $\mu = 5$  with NaCl are included (●); the plot is linear up to 3 M  $\text{NaN}_3$  ( $r = 0.999$ ), after which curvature is apparent (dashed line).

1%, 2%, and 1%, respectively; the break is not the result of experimental error in the determinations. Above 0.64 M  $\text{NaN}_3$ , the points describe a smooth curve that appears to be approaching a limiting value for  $k_{\text{obsd}}$  (Figure 4). Because 5.0 M  $\text{NaN}_3$  is approaching saturation in  $\text{D}_2\text{O}$  and because determination of  $k_{\text{obsd}}$  was near the technically feasible limit, we could not evaluate  $k_{\text{obsd}}$  at higher  $\text{NaN}_3$  concentrations.

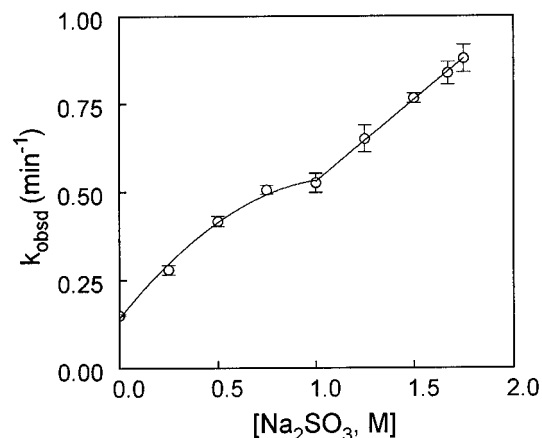
**Reaction of **1** with  $\text{Na}_2\text{SO}_3$  at Constant Ionic Strength.** The shape of plots of  $k_{\text{obsd}}$  vs.  $[\text{Na}_2\text{SO}_3]$  depended dramatically on the salt used to control ionic strength (Figures 5 and 6). As expected,<sup>27</sup> the rate constants are lower for the higher ionic strength. For NaCl at  $\mu = 2$  and 5, the plots appear to consist of two intersecting straight lines (Figure 5). For  $\text{Na}_2\text{SO}_4$  as the added salt, however, the plots are linear at  $\mu = 2$  and 5 (Figure 6;  $r = 0.9991$  and 0.9993, respectively). Values of the various rate constants are summarized in Table 3.

**Reaction of **1** with  $\text{Na}_2\text{SO}_4$  with no Control of Ionic Strength.** The plot of  $k_{\text{obsd}}$  vs.  $[\text{Na}_2\text{SO}_3]$  shown in Figure 7 has the same break found for the reaction of  $\text{NaN}_3$  with **1** with no control of ionic strength (Figure 3).

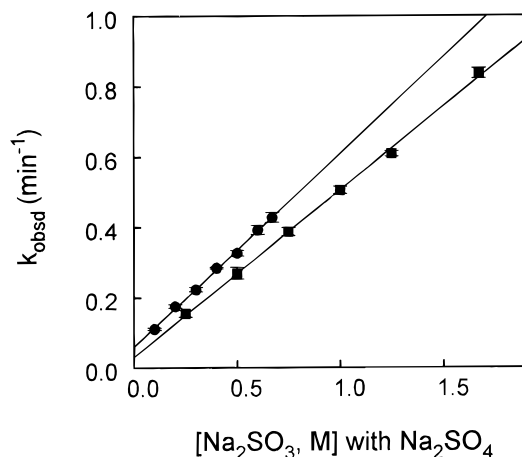
(27) Ingold, C. K. *Structure and Mechanism in Organic Chemistry*; Cornell: Ithaca, NY, 1953; pp 306–408.



**Figure 5.** Plots of  $k_{\text{obsd}}$  vs  $[\text{Na}_2\text{SO}_3]$  with NaCl used to hold the ionic strength constant at  $\mu = 2$  (●) and  $\mu = 5$  (■) at 80 °C. Error bars are  $\pm$  S.E.



**Figure 7.** Plot of  $k_{\text{obsd}}$  vs  $[\text{Na}_2\text{SO}_3]$  with no exogenous salt used to hold the ionic strength constant at 80 °C. Error bars are  $\pm$  S.E.



**Figure 6.** Plots of  $k_{\text{obsd}}$  vs  $[\text{Na}_2\text{SO}_3]$  with  $\text{Na}_2\text{SO}_4$  used to hold the ionic strength constant at  $\mu = 2$  (●) and  $\mu = 5$  (■) at 80 °C. Plots are linear with  $r = 0.9990$  and  $0.9993$ , respectively.

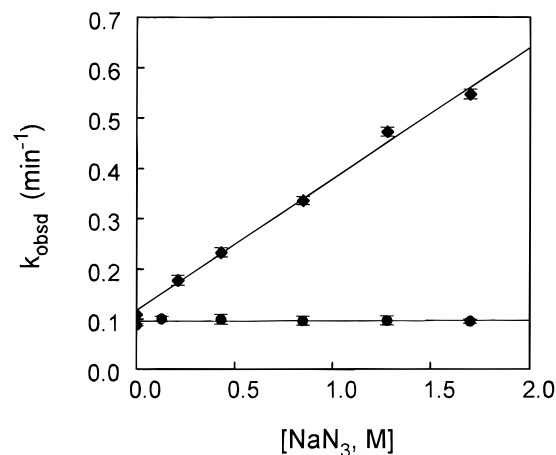
**Table 3. First- and Second-Order Rate Constants for the Overall Reaction of 1 with  $\text{Na}_2\text{SO}_3$  in  $\text{D}_2\text{O}$  at 80 °C under Constant Ionic Strength with NaCl or  $\text{Na}_2\text{SO}_4$ <sup>a</sup>**

conditions	$k_1$ ( $\text{min}^{-1}$ )	$k_2$ ( $\text{M}^{-1} \text{min}^{-1}$ )	$r$
$\mu = 2$ , NaCl			
0–0.5 M $\text{Na}_2\text{SO}_3$		$0.438 \pm 0.012$	0.9970
0.5–0.75 M $\text{Na}_2\text{SO}_3$		$1.49 \pm 0.080$	0.9940
$\mu = 5$ , NaCl			
0–1.0 M $\text{Na}_2\text{SO}_3$		$0.286 \pm 0.008$	0.9960
1.25–1.67 M $\text{Na}_2\text{SO}_3$		$0.993 \pm 0.001$	1.000
$\mu = 2$ , $\text{Na}_2\text{SO}_4$			
0.1–0.67 M $\text{Na}_2\text{SO}_3$	$0.059 \pm 0.003$	$0.550 \pm 0.005$	0.9990
$\mu = 5$ , $\text{Na}_2\text{SO}_4$			
0.25–1.67 M $\text{Na}_2\text{SO}_3$	$0.030 \pm 0.005$	$0.496 \pm 0.004$	0.9993

<sup>a</sup> Values are the mean  $\pm$ SE obtained by linear regression.

Unlike the  $\text{N}_3^-$  results, however, the upper portion of the curve appears to be linear.

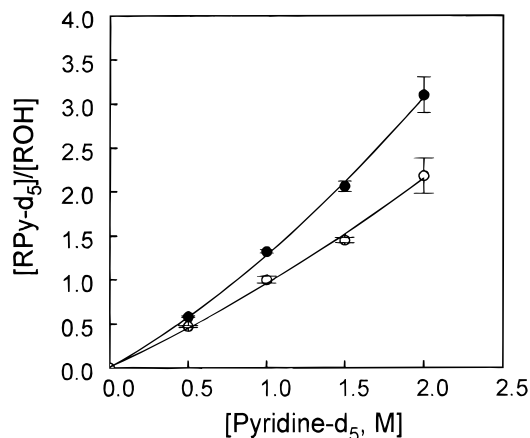
**Reaction of 1 with NaSCN.** Rate plots for NCS<sup>-</sup> with or without added salt were approximately linear for the first half-life, after which the lines exhibited severe curvature (see Figure 1 of ref 24). A detailed analysis of this phenomenon has been reported.<sup>24</sup> In brief, an equilibrium is set up among all products and the starting material; the primary initial product RSCN is converted to RNCS by displacement under the reaction conditions and by some concomitant trapping of the carbenium ion. Because of this, the rate constants cannot be obtained



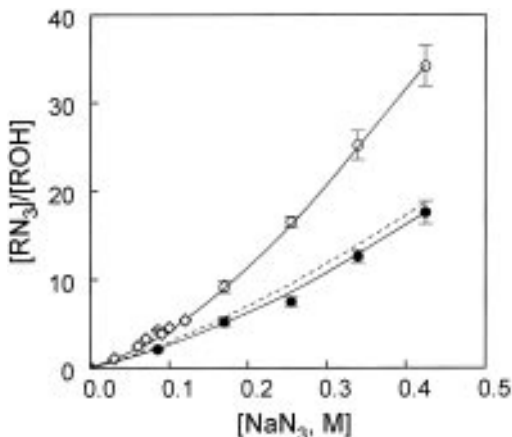
**Figure 8.** Plot of  $k_{\text{obsd}}$  vs  $[\text{NaN}_3]$  for the benzoate ester **4** at 80 °C,  $\mu = 1.7$  with NaCl (●). Within error ( $\pm$ S.E.), there is no dependence on  $[\text{NaN}_3]$ . For reference, data for the reaction of  $\text{NaN}_3$  and **1** with  $\text{NaClO}_4$  used to control ionic strength at  $\mu = 1.7$  are included (◆); the slope and intercept are essentially the same as found for the NaCl conditions (Figure 2 and Table 2).

accurately. The general pattern in reactivity seen with the other nucleophiles is found for  $\text{SCN}^-$ , however.

**Hydrolysis and Azide Reactions of 4-Methoxybenzyl-4'-Sulfobenzoate (4).** In order to calculate the ratio  $[\text{RN}_3]/[\text{ROH}]$  for **1** at constant ionic strength, it was necessary to have the value of the partitioning ratio,  $k_N/k_W$ , for capture by nucleophile and water of the 4-methoxybenzyl carbenium ion under our reaction conditions. We measured  $k_{\text{obsd}}$  for the benzoate **4** in pure  $\text{D}_2\text{O}$ , 1.7 M NaCl and  $\text{NaClO}_4$ , and 0.05–1.7 M  $\text{NaN}_3$  solutions by following the loss of the benzoate ester AA'BB' pattern in  $^1\text{H}$  NMR spectra. This method of analysis is not as accurate as that used for **1**, and errors and scatter are larger than found for **1**. Rate constants are zero order in  $\text{N}_3^-$  at  $\mu = 1.7$  with NaCl or  $\text{NaClO}_4$  used to control ionic strength and are ca. 2-fold higher than in  $\text{D}_2\text{O}$  only (Figure 8; for reference, data are shown for the reaction of **1** and  $\text{NaN}_3$  with  $\text{NaClO}_4$  used to control ionic strength). This pattern is consistent with the ionization of **4** to the solvent-equilibrated carbenium ion with subsequent partitioning between  $\text{N}_3^-$  and  $\text{D}_2\text{O}$ , with no  $\text{RN}_3$  formed by direct displacement on substrate.<sup>15</sup>



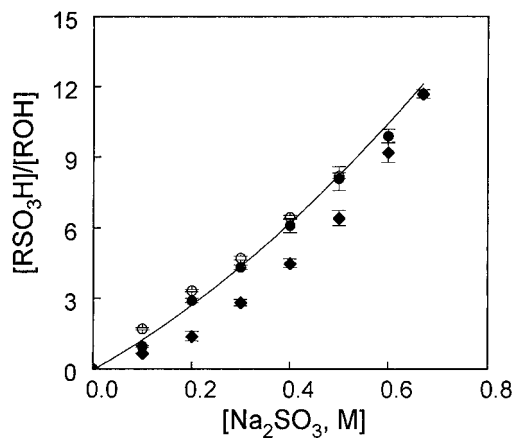
**Figure 9.** Plots of  $[RPy-d_5]/[ROH]$  vs  $[Py-d_5]$  with NaCl added to control ionic strength ( $\bullet$ ) and without any added salt ( $\circ$ ). R = 4-methoxybenzyl. (Results with  $NaClO_4$  as the added salt are the same as those for NaCl.) The lines are best fits to eq 2 using the appropriate  $k_2/k_1$  ratios. From these fits values of  $k_N/k_W$  of 0.8 ( $\mu = 1.7$ ) and 0.42 ( $\mu = 0$ ) were obtained for pyridine- $d_5$  trapping of the (4-methoxybenzyl)carbenium ion.



**Figure 10.** Plots of  $[RN_3]/[ROH]$  vs  $[NaN_3]$  for the reaction of **1** at 80 °C with ( $\bullet$ ) and without ( $\circ$ ) control of ionic strength. R = 4-methoxybenzyl. Error bars are  $\pm$  S.E. The ratios are the same if the added salt is NaCl or  $NaClO_4$ . The line through the solid circles was computed using eq 2 and the appropriate experimental rate constants, and the line through the open circles was computed using eq 4 with the appropriate experimental rate constants and the estimated rate constants  $k'_1$  and  $k'_2$  (ref 35). The dashed line was computed with eq 2 using  $k'_1$  and  $k'_2$  as described in the text. Product ratios reported by Sneen (ref 5) for no salt conditions at 60 °C are included for reference ( $\diamond$ ); the fit to the line computed with eq 4 is apparent.

**Product Ratios for 1 under Constant Ionic Strength and with No Added Salt. Pyridine- $d_5$ .** Plots of  $[RPy-d_5]/[ROH]$  vs.  $[pyridine-d_5]$  for these two sets of conditions, determined at 80 °C, are shown in Figure 9. The fit of these points to an equation derived assuming a simple mixed  $S_N1/S_N2$  mechanism is discussed below.

**NaN<sub>3</sub>.** Plots of  $[RN_3]/[ROH]$  vs.  $[NaN_3]$  (up to 0.5 M  $NaN_3$ , which is near the limit of NMR detection for the low concentrations of alcohol produced) for constant ionic strength (Figure 10, closed circles) and for  $NaN_3$  only (Figure 10, open circles) are curved up. The slope of a regression line through the first several points (0–0.2 M) of the no salt plot is linear (not shown;  $r = 0.999$ ) with a



**Figure 11.** Plots of  $[RSO_3H]/[ROH]$  for the reaction of **1** at 80 °C with ( $\bullet$ ) and without ( $\circ$ ) control of ionic strength with  $Na_2SO_4$ . R = 4-methoxybenzyl. Error bars are  $\pm$  S.E. The ratios for NaCl as the added salt are included ( $\blacklozenge$ ). The line was computed using eq 4 and the appropriate experimental rate constants.

slope of 46  $M^{-1}$ . The slope reported by Sneen<sup>5</sup> for reaction at 60 °C with 0–0.12 M  $NaN_3$  is 48  $M^{-1}$ ; indeed, Sneen's experimental points (open diamonds) fit nicely on the line for the nucleophile only conditions. The fit of these data to two equations derived assuming different mechanisms is discussed below.

**Na<sub>2</sub>SO<sub>3</sub>.** Plots of  $[RSO_3H]/[ROH]$  vs.  $[Na_2SO_3]$ , shown in Figure 11, are very similar for constant ionic strength with  $Na_2SO_4$  (closed circles) and nucleophile only (open circles) conditions. The plot for constant ionic strength with NaCl (closed diamonds) are significantly lower, the result of the much higher rate constant for hydrolysis with NaCl. The fit of these data to two equations derived assuming different mechanisms is discussed below.

**NaSCN.** The product ratios yield no quantitative insight because of the equilibria among all products (see above). The major initial product, however, was the thiocyanate formed by displacement by the soft end of this ambident nucleophile.<sup>24</sup>

**Product Ratios for 4 Under Constant Ionic Strength and with No Added Salt.** Product ratios for  $N_3^-$  trapping of the 4-methoxybenzyl carbenium ion were measured as described above for **1** in  $H_2O$  solutions with either NaCl or  $NaClO_4$  used to control ionic strength or with  $NaN_3$  only present. Plots of  $[RN_3]/[ROH]$  vs.  $[NaN_3]$  for both salts are linear (not shown;  $r = 0.990$ ) with the same slope,  $k_N/k_W$ , of  $20.5 \pm 1.1 M^{-1}$ . With nucleophile only,  $k_N/k_W$  is  $17.3 \pm 0.9 M^{-1}$  ( $r = 0.998$ ). Each plot is based on averages of three to eight determinations per point. The product ratios for  $Na_2SO_3$  were determined in the same way;  $k_N/k_W$  is  $0.62 M^{-1}$ .

**Solvolysis of Trimethylsulfonium Iodide.** Under conditions used for **1**, there was no detectable solvolysis after 24 h, but almost complete exchange of the methyl protons was observed. Rate constants reported by Swain and colleagues<sup>8d</sup> for this substrate at 158 °C are ca.  $3 \times 10^3$  lower than rate constants we obtain for **1** at 80 °C. Thus, unlike the benzyl and methyl pyridinium substrates that react with  $N_3^-$  and water at essentially the same rates,<sup>3</sup> methyl dimethylsulfonium is very resistant to reaction, despite the fact that the  $pK_a$  of methyl sulfide is ca. 6 pK units more favorable than the  $pK_a$  for 3-cyanopyridine.

**Table 4. Eyring Activation Values for the Hydrolysis ( $k_1$ ) and Azide Substitution Reactions ( $k_2$ ) of 4-Methoxybenzyl Derivatives at Constant Ionic Strength  $\mu = 1.7$  (NaCl)<sup>a</sup>**

rate constants	$\Delta H^\ddagger$ (kcal/mol)	$\Delta S^\ddagger$ (gibbs/mol)	$\Delta G_{80}^\ddagger$ (kcal/mol)
dimethylsulfonium			
$k_1$	$27.7 \pm 1.0$	$7.1 \pm 1.0$	25.2
$k_2$	$22.2 \pm 1.8$	$-6.7 \pm 0.8$	24.6
3'-cyanopyridinium ( $k_2$ )	$17.6 \pm 0.8$	$-21.6 \pm 2.0$	25.3

<sup>a</sup> Values determined from 4-point Eyring plots with  $r > 0.998$ .

**Activation Values.** The Eyring activation values<sup>28</sup> for **1** were determined from a four-point plot in the range 60–80 °C ( $r = 0.998$ ). Values are listed in Table 4 with those for the 4-methoxybenzyl-3'-cyanopyridinium ion.<sup>3</sup>

## Discussion

### Mechanisms for the Substitution Reactions of **1**.

The kinetics and product ratios for reaction of **1** with neutral and negative nucleophiles show an astonishing range of behavior that depends on the presence or absence of exogenous salt and the nature of the salt anion. Despite this complexity, it is possible to define with reasonable certainty the range of mechanisms in this system.

**Mechanism for the Neutral Nucleophile.** The fact that plots of  $k_{\text{obsd}}$  vs. [pyridine-*d*<sub>5</sub>] are linear and parallel with and without exogenous salt (Figure 1) shows that there is no salt effect on the displacement reaction, either because of a "salting-out" effect on the neutral nucleophile<sup>29</sup> or because of a change in the activity of the charged reactant. (While it is possible that the activities of both nucleophile and substrate change in a completely compensatory manner, this seems highly unlikely because of the difference in charge of the two reactants.) The fact that the values of  $k_1$  obtained as intercepts are the same as those found for hydrolysis with and without exogenous salt suggests that the mechanism is merely mixed S<sub>N</sub>1/S<sub>N</sub>2.

Plots of the product ratio [RPy-*d*<sub>5</sub>]/[ROH] for the constant ionic strength and nucleophile alone conditions are shown in Figure 9. For the mixed S<sub>N</sub>1/S<sub>N</sub>2 mechanism, the equation

$$\frac{[\text{RNu}]/[\text{ROH}]}{[\text{Nu}](k_{\text{N}}/k_{\text{W}}) \{1 + (k_2/k_1)[\text{Nu}]\} + (k_2/k_1)[\text{Nu}]} \quad (2)$$

is obtained using the steady-state approximation for the appearance of products. The various rate constants refer to Scheme 1. A best fit of points to eq 2 using the experimental  $k_2/k_1$  gives  $k_{\text{N}}/k_{\text{W}} = 0.80 \text{ M}^{-1}$  for constant ionic strength and  $k_{\text{N}}/k_{\text{W}} = 0.42 \text{ M}^{-1}$  for nucleophile only. In agreement with the best fits, a crude estimated value of  $k_{\text{N}}/k_{\text{W}} = 0.48 \text{ M}^{-1}$  was obtained for the reaction with **4** with no added salt (see Experimental Section). These values show the same trends measured directly for NaN<sub>3</sub>: higher for constant ionic strength than for nucleophile alone. Conversely, the product ratios [RPy-*d*<sub>5</sub>]/[ROH] are larger for the constant ionic strength conditions, a consequence of the fact that  $k_1$  is lower than  $k_2$  with no added salt (Table 2). The plots are relatively

shallow and close because  $k_2$  is much lower than  $k_1$  and is constant for both conditions. These results are also consistent with a mixed S<sub>N</sub>1/S<sub>N</sub>2 mechanism for the neutral nucleophile.

**Mechanism for NaN<sub>3</sub> and Na<sub>2</sub>SO<sub>3</sub>.** It is clear from the plots of  $k_{\text{obsd}}$  vs. [Nu] for the reactions of **1** with the intermediate HSAB anionic nucleophiles that there is a dramatic difference between reactions under constant ionic strength (Figures 2 and 6) and with the nucleophile alone (Figures 3, 4, and 7). These differences may be the result either of salt effects or of different mechanisms.

**Mechanism with Control of Ionic Strength. NaN<sub>3</sub>.** All the results are consistent with a simple mixed S<sub>N</sub>1/S<sub>N</sub>2 mechanism at constant ionic strength. The second-order rate plots are linear over most of the concentration range of NaN<sub>3</sub>; deviation from linearity is most apparent at the higher ionic strengths (compare Figures 2 and 4). Values of  $k_1$  from extrapolation of the second-order plots match almost precisely the values obtained from hydrolysis in the absence of nucleophile (for  $\mu = 0.5, 1.0, 1.7$ ). Results for the reaction of N<sub>3</sub><sup>-</sup> and **1** with either NaCl (Figure 2) or NaClO<sub>4</sub> (Figure 8) used to control ionic strength show that the nature of the univalent added salt does not affect the bi- or unimolecular reactions.

The product ratio [RN<sub>3</sub>]/[ROH] should conform to the mechanism of substitution. The line through the data (solid circles) in Figure 10 was calculated with eq 2 using the measured first- and second-order rate constants for the reaction at  $\mu = 1.7$  and the ratio  $k_{\text{N}}/k_{\text{W}} = 20.5 \text{ M}^{-1}$  obtained for **4** under identical conditions. The correspondence is excellent<sup>30</sup> and strongly suggests that the simple mixed mechanism operates under conditions of constant ionic strength.

**Na<sub>2</sub>SO<sub>3</sub>.** Second-order rate plots for the SO<sub>3</sub><sup>2-</sup> reaction under constant ionic strength depend dramatically on the use of either NaCl or Na<sub>2</sub>SO<sub>4</sub> as the added salt. The SO<sub>3</sub><sup>2-</sup>/NaCl plots (Figure 5) have severe breaks, while the SO<sub>3</sub><sup>2-</sup>/Na<sub>2</sub>SO<sub>4</sub> plots are linear over a large range of nucleophile concentration (Figure 6). The charge and volume of an anion can change the activity of a second anion in solution,<sup>31</sup> and the effects are more severe for larger ions. This appears to be the effect seen in Figure 5: the activity of SO<sub>3</sub><sup>2-</sup>, which will affect the rate constants for the second order reaction, is lowered by the presence of NaCl and increases as NaCl is diluted out with addition of nucleophile. In the presence of Na<sub>2</sub>SO<sub>4</sub>, however, which has the same charge and essentially the same ionic volume as the nucleophile, the activity of SO<sub>3</sub><sup>2-</sup> is constant over the entire range of nucleophile concentration, and the rate constants increase linearly with an increase in Na<sub>2</sub>SO<sub>3</sub> (Figure 6). The fact that Cl<sup>-</sup>, ClO<sub>4</sub><sup>-</sup>, CN<sup>-</sup>, and OCN<sup>-</sup>, which have the same charge but different ionic volumes and shapes, have the same effect on the hydrolysis rate constant while SO<sub>4</sub><sup>2-</sup> has a dramatic effect on both first- and second-order rate constants suggests that the charge of the salt anion is more important than volume for both the hydrolysis and substitution reactions.

Despite these salt effects, the mechanism appears to be mixed S<sub>N</sub>1/S<sub>N</sub>2 for the SO<sub>3</sub><sup>2-</sup>/Na<sub>2</sub>SO<sub>4</sub> combination: the

(28) Maskill, H. *The Physical Basis of Organic Chemistry*, Oxford: New York, 1985; p 450.

(29) Gould, E. S. *Mechanism and Structure in Organic Chemistry*, Holt, Rinehart and Winston: New York, 1959; pp 185–187.

(30) The [RN<sub>3</sub>]/[ROH] obtained for 4-methoxybenzyl chloride in 80% aqueous acetone by Aymes and Richard<sup>2</sup> are excellently fit by eq 2 (not shown). Fitting the data to eq 2 with the Marquardt–Levenberg nonlinear least-squares algorithm with  $k_{\text{N}}/k_{\text{W}}$  allowed to float gives  $k_{\text{N}}/k_{\text{W}} = 8.04 \text{ M}^{-1}$ , precisely the partitioning value obtained by Aymes and Richard using a different approach.



second-order rate plots are linear, show the expected effect of ionic strength on the rate constant,<sup>27</sup> and extrapolate almost precisely to the values obtained for hydrolysis in the absence of nucleophile with Na<sub>2</sub>SO<sub>4</sub> as the added salt. As discussed below, the plot of [RSO<sub>3</sub>H]/[ROH] vs. [Na<sub>2</sub>SO<sub>3</sub>] is fit well by eq 2 for the mixed S<sub>N</sub>1/S<sub>N</sub>2 mechanism.

#### Mechanism with No Control of Ionic Strength.

The reactions of both N<sub>3</sub><sup>-</sup> and SO<sub>3</sub><sup>2-</sup> alone with **1** are quite different than the reactions with exogenous salt present. Both nucleophiles show breaks in plots of  $k_{\text{obsd}}$  vs. [Nu] with no added salt, which are much more dramatic for Na<sub>2</sub>SO<sub>3</sub> (Figure 7) than for NaN<sub>3</sub> (Figure 3). These effects may be the result of salt effects on the S<sub>N</sub>2 mechanism or of a change to an alternative bimolecular substitution mechanism.

**NaN<sub>3</sub>.** There are a variety of possible salt effects that could cause the break in the plot. Assuming a "normal" primary kinetic salt effect<sup>29</sup> in the region 0–0.3 M NaN<sub>3</sub> gives a Winstein–Fainberg  $b$  value<sup>32</sup> of ca. +3.5, the sign and magnitude of which are inconsistent with "normal" salt effects in this region of nucleophile concentration. In fact, the  $b$  value computed for the second-order reaction under different ionic strengths is –0.1. It should also be noted that in the case of the SO<sub>3</sub><sup>2-</sup>/NaCl salt effects (Figure 5), the curve is concave up, while with NaN<sub>3</sub> and Na<sub>2</sub>SO<sub>3</sub> alone, the curve is concave down, which suggests that the break is not the result of a salt effect.

A second possibility is that the break is the result of a special salt effect. This seems unlikely for several reasons. In the classic profile for solvolysis described by Winstein and Fainberg,<sup>32</sup> there is an initial sharp increase in rate followed by a linear increase with increasing salt concentration. As shown in Figure 4, however, the plot of  $k_{\text{obsd}}$  vs. [NaN<sub>3</sub>] between 0.65 M and 5 M NaN<sub>3</sub> is a smooth curve (concave down). Moreover, the special salt effect arises because a solvent-separated ion pair is trapped by exogenous salt. Our results,<sup>18</sup> Kevill's analysis of the S<sub>N</sub>1 mechanism,<sup>9</sup> and the Friedberger–Thornton<sup>15</sup> sulfur kinetic isotope effects all suggest that **1** does not react through an IDC mechanism. This alternative is not viable.

Third, if the break is the result of a change in activity with increasing amounts of nucleophile, a plot of  $k_{\text{obsd}}$  vs. the activity for the nucleophile would be linear.<sup>20</sup> Measured activity coefficients ( $\gamma$ ) are available for NaN<sub>3</sub> in water.<sup>33</sup> A plot of  $k_{\text{obsd}}$  vs. the activity ( $\alpha$ ) computed from these  $\gamma$ s (Figure S2) shows the same breaks as the concentration plots,<sup>34</sup> which is incompatible with a specific salt effect for NaN<sub>3</sub> in this concentration range of nucleophile.

A fourth possibility is that the curve is merely the result of a decrease in both  $k_2$  and  $k_1$  with an increase in ionic strength with increasing concentration of NaN<sub>3</sub>. Estimated first ( $k'_1$ )- and second ( $k'_2$ )-order rate constants<sup>35</sup> can be used to calculate an estimated overall rate

constant  $k'_{\text{obsd}} = k'_1 + k'_2 [\text{NaN}_3]$  at each ionic strength corresponding to the concentration of added nucleophile. As shown in Figure 3 (dashed line), a plot of  $k'_{\text{obsd}}$  vs. [NaN<sub>3</sub>] provides a fairly good match for the experimentally determined rate constants at each [NaN<sub>3</sub>]. Thus a "normal" Hughes–Ingold S<sub>N</sub>2 reaction with smoothly decreasing rate constants could account for the shape of the curve.

If this were so, the plot of [RN<sub>3</sub>]/[ROH] vs. [NaN<sub>3</sub>] for the nucleophile only conditions should be fit by eq 2 using the variable ratio  $k'_2/k'_1$  at each point and the constant ratio  $k_{\text{N}}/k_{\text{W}} = 17.3 \text{ M}^{-1}$  measured for the reaction of **4** with nucleophile only. The calculated line, however, does not match the points for [RN<sub>3</sub>]/[ROH] with no control of ionic strength; indeed, the line falls very close to the points for constant ionic strength conditions (dashed line, Figure 10). This failure of the rate constants to fit the product data suggests that another mechanism is operative.

The smooth curve above 0.65 M NaN<sub>3</sub> (Figure 4) is reminiscent of the shape of the curve for a preassociation-concerted mechanism (Scheme 1) governed by

$$k_{\text{obsd}} = k_{2\text{As}}K_{\text{As}}[\text{Nu}]/(1 + K_{\text{As}}[\text{Nu}]) \quad (3)$$

A double reciprocal plot of  $1/k_{\text{obsd}}$  vs.  $1/[\text{NaN}_3]$  for the data from Figure 5 is linear (Figure S3,  $r = 0.9965$ ). Using eq 3 to analyze this plot gives  $k_{2\text{As}} = 1.18 \text{ min}^{-1}$  and  $K_{\text{As}} = 0.70 \text{ M}^{-1}$ . When the experimental points in Figure 4 were fitted to eq 3 using the Marquardt–Levenberg nonlinear least-squares algorithm with the parameters allowed to float, values of  $k_{2\text{As}} = 1.21 \pm 0.04 \text{ min}^{-1}$  and  $K_{\text{As}} = 0.66 \pm 0.06 \text{ M}^{-1}$  ( $\chi^2 = 5.8 \times 10^{-4}$ ) were obtained, in excellent agreement with the values obtained from the double reciprocal plot.

For the case with no exogenous salt, the S<sub>N</sub>1, Hughes–Ingold S<sub>N</sub>2, and preassociation-concerted mechanisms should operate simultaneously below the break point in Figure 3. Using the steady-state approximation the equation

$$\begin{aligned} [\text{RNu}]/[\text{ROH}] = & [\text{Nu}](k_{\text{N}}/k_{\text{W}})\{1 + (k_2/k_1)[\text{Nu}] + \\ & (k_{2\text{As}}/k_1)(K_{\text{As}}/\{1 + K_{\text{As}}[\text{Nu}]\})[\text{Nu}]\} + \{(k_2/k_1)[\text{Nu}] + \\ & (k_{2\text{As}}/k_1)(K_{\text{As}}/\{1 + K_{\text{As}}[\text{Nu}]\})[\text{Nu}]\} \quad (4) \end{aligned}$$

is obtained for the three-component mechanism. The line through the open circles in Figure 11 was calculated with eq 4 using  $k_{2\text{As}}$ ,  $K_{\text{As}}$ , the appropriate estimated rate constants  $k'_1$  and  $k'_2$  for the ionic strength at the give point,<sup>35</sup> and  $k_{\text{N}}/k_{\text{W}} = 17.3 \text{ M}^{-1}$ . This correspondence, too, is excellent, which strongly suggests that the substitution reaction with N<sub>3</sub><sup>-</sup> alone follows stepwise, concerted Hughes–Ingold S<sub>N</sub>2, and preassociation-concerted mechanisms. As Ritchie points out,<sup>12c</sup> the Hughes–Ingold concerted mechanism, in which the encounter complex is not an intermediate, and the preassociation-concerted mechanism, in which Nu·RSMe<sub>2</sub><sup>+</sup> is an intermediate, will have different reaction profiles and kinetics. Note that for the pyridine-*d*<sub>5</sub> reaction, which is unambiguously mixed S<sub>N</sub>1/S<sub>N</sub>2, the values of [RPy-*d*<sub>5</sub>]/[ROH] at constant ionic strength are larger than the nucleophile alone

(31) Meissner, H. P.; Kusik, C. L. *Am. Inst. Chem. Eng. J.* **1972**, *18*, 294–298. Meissner, H. P.; Kusik, C. L. *Ind. Eng. Chem. Process Des. Develop.* **1973**, *12*, 205–208. Harned, H. S.; Robinson, R. A. *Multicomponent Electrolyte Solutions*; Pergamon: New York, 1963.

(32) Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc.* **1956**, *78*, 2763–2767.

(33) Maiorova, T. N.; Karpenko, G. V.; Poltoratskii, G. M.; Goverdovskii, B. A.; Krauklis, I. Deposited Document in the Soviet Archive VINITI 3433-77, 193–7, 1977.

(34) Double reciprocal plots of  $1/k_{\text{obsd}}$  vs.  $1/\alpha$  for both N<sub>3</sub><sup>-</sup> and SO<sub>3</sub><sup>2-</sup> above the break point are linear (not shown).

(35) Values of  $k'_1$  were estimated using the Winstein–Fainberg  $b$  values<sup>32</sup> for the solvolysis reaction<sup>18</sup> and vary only slightly between 0 and 0.5 M salt (between 0.148 and 0.144 min<sup>-1</sup>). Values of  $k'_2$  were estimated either from plots of  $k_{\text{obsd}}$  vs. [Nu] or log  $k_{\text{obsd}}$  vs.  $\mu^{1/2}$  for reactions at constant ionic strength. The two methods give reasonable agreement.

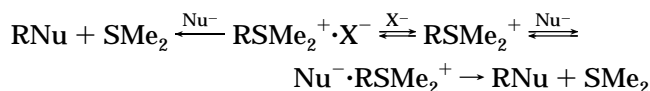
values, the reverse of the pattern for  $\text{NaN}_3$ . This is not a result of a difference in partitioning of the carbenium ion because  $k_N/k_W$  for salt and no salt conditions for both nucleophiles show the same trends, higher for constant ionic strength. Thus the difference in the product ratios probably is the result of differences in the concerted displacement mechanism.

**$\text{Na}_2\text{SO}_3$ .** Treatment of the data for  $\text{Na}_2\text{SO}_3$  alone gives the same patterns found for  $\text{NaN}_3$  alone. Measured  $\gamma$ s are available for  $\text{Na}_2\text{SO}_3$  in water.<sup>36</sup> A plot of  $k_{\text{obsd}}$  vs.  $\alpha$  computed from these  $\gamma$ s (Figure S4) show the same breaks as the concentration plots,<sup>34</sup> which is incompatible with a specific salt effect for  $\text{Na}_2\text{SO}_3$  in this region of nucleophile concentration.

A double reciprocal plot of the data for the upper portion for the sulfite curve from Figure 7 yields an excellent straight line (Figure S3;  $r = 0.9999$ ) from which values of  $k_{2\text{As}} = 7.87 \text{ min}^{-1}$  and  $K_{\text{As}} = 0.070 \text{ M}^{-1}$  can be obtained as described above. When the data from the upper, linear portion were fit to eq 3, values of  $k_{2\text{As}} = 7.34 \pm 0.90 \text{ min}^{-1}$  and  $K_{\text{As}} = 0.078 \pm 0.01 \text{ M}^{-1}$  ( $\chi^2 = 1.24 \times 10^{-5}$ ) are obtained by successive fitting, in good agreement with the values obtained from the double reciprocal plot. The later break for  $\text{Na}_2\text{SO}_3$  (1 M) compared with  $\text{NaN}_3$  (0.65 M) is consistent both with the lower value of  $K_{\text{As}}$  and the higher ionic strength for the dianion.

For  $\text{SO}_3^{2-}$ , a fit of the product ratio data is more complex than for the other nucleophiles for several reasons. First, the change in the first-order rate constant is much more severe than for the  $\text{N}_3^-$  case, as shown by the effect of  $\text{Na}_2\text{SO}_4$  on the hydrolysis reaction (see Results section). Second, as shown in Figure 6, the difference in second-order rate constants between  $\mu = 2$  and 5 (Table 3) is much less than the  $\text{N}_3^-$  case (Table 2). Third, the different effects of  $\text{NaCl}$  and  $\text{Na}_2\text{SO}_4$  as the added salt makes fitting the product ratios for  $\text{NaCl}$  conditions much more complex (Figure 5). Given all these caveats, however, as shown in Figure 11 the product ratios for no added salt are fit very well by the values calculated using eq 4 for the three pathway mechanism. It will be appreciated that because of the low value of both  $K_{\text{As}}$  (0.07) and  $k_N/k_W$  (0.62, determined from reaction of **4** with  $\text{Na}_2\text{SO}_3$ ), the fit for the constant ionic strength portion of the curve will be approximately the same as for the no salt case.

The question remains why the preassociation-concerted mechanism does not operate under conditions of ionic strength over most of the range of nucleophile. Cations in the presence of several anions undergo rapid exchange to form all possible ion pairs.<sup>37</sup> In the presence of a large excess of an unreactive anion, formation and reaction of productive complexes are disfavored. Thus in our system,  $\text{X}^-$  ( $\text{Cl}^-$ ,  $\text{ClO}_4^-$ , or  $\text{SO}_4^{2-}$ ) competes with nucleophile ( $\text{N}_3^-$



or  $\text{SO}_3^{2-}$ ) for formation of the productive ion pairs  $\text{Nu}^- \cdot \text{RSM}_2^+$ , with the equilibrium far to the left under conditions of constant ionic strength with  $[\text{X}^-] > [\text{Nu}^-]$ ; the preassociation-concerted mechanism should be suppressed relative to the  $\text{S}_{\text{N}}2$  mechanism. The  $\text{S}_{\text{N}}1$  com-

ponent is independent of complexation. (Note that even under conditions of constant ionic strength the preassociation-concerted mechanism can operate; as shown in Figure 4, the correlation line for the constant ionic strength reaction does not extrapolate linearly to the  $\text{NaN}_3 = 5 \text{ M}$  point; some curvature above 3 M  $\text{NaN}_3$  is evident [dashed line], at which point  $\text{N}_3^-$  may compete with salt for substrate and react by the preassociation-concerted pathway.) In this sense, these are salt effects, but not those associated with the passive effects of salt on activities.

In their study of the solvolysis of trimethyl sulfonium and tribenzyl sulfonium salts, Swain and Kaiser<sup>38</sup> argued against formation and subsequent displacement reactions of  $\text{Nu}^- \cdot \text{RSM}_2^+$  based on conductance studies, the results of which did not agree with ion-pair formation. We examined this possibility by looking for changes in the chemical shifts of  $\text{SMe}_2$  and benzyl methylene protons in the presence of various concentrations of salt and nucleophile and found no effect. While the high ionic strengths used in our study favors the formation of simple ion aggregates,<sup>37</sup> these species would be transient intermediates.

**The Snee Mechanism.** None of the results reported here, or those from the earlier work on the hydrolysis,<sup>9,18</sup> is consistent with Snee's IDC mechanism for the reaction of **1** with nucleophiles. Friedberger and Thornton's<sup>15</sup> argument that Snee's mechanism fails if benzyl azide arises from trapping of the solvent-equilibrated carbenium ion is borne out by the fits of the product ratio plots (Figures 9–11). In their analysis of the kinetics of the Snee mechanism, Kevill and colleagues<sup>9</sup> show that product ratios calculated assuming a mixed  $\text{S}_{\text{N}}1/\text{S}_{\text{N}}2$  mechanism with a  $k_N/k_W = 21.1 \text{ M}^{-1}$ , obtained by a fitting procedure, are closer to the experimental values than those obtained with Snee's equation (eq 1); our measured value of  $k_N/k_W = 20.5 \text{ M}^{-1}$  is in excellent agreement with the Kevill value. It seems reasonable that at the low  $[\text{NaN}_3]$  Snee used, 0.03–0.12 M, the plot of  $[\text{RN}_3]/[\text{ROH}]$  vs.  $[\text{NaN}_3]$  would appear to be linear and would be consistent with the IDC mechanism. In fact, Snee's experimental values for  $[\text{RN}_3]/[\text{ROH}]$  (open diamonds, Figure 10) fit nicely on the lower portion of our experimental curve for  $\text{NaN}_3$  alone and the computed curve for the three-pathway mechanism. In this initial region, the three-pathway curve is essentially indistinguishable, within error, from the line computed assuming the mixed  $\text{S}_{\text{N}}1/\text{S}_{\text{N}}2$  mechanism (dashed line, Figure 10), which may account for the good fits obtained by Kevill assuming a simple mixed mechanism.<sup>9</sup> As our results show, the product ratios and mechanism are a function of the presence of exogenous salt, and an examination of one set of conditions is not sufficient to either reject or accept a mechanism.

**Activation Values.** For **1**,  $\Delta G^\ddagger$  for the uni- and bimolecular reactions are very similar despite the large difference in  $-T\Delta S^\ddagger$ , and both reactions can occur simultaneously (Table 4). (Swain and Taylor<sup>38</sup> found very similar activation values for the bimolecular reactions of **6** and  $\text{SMe}_3^+$  with  $\text{OH}^-$  and  $\text{PhO}^-$ .) The pyridinium substrate has a  $\Delta G^\ddagger$  for the  $\text{S}_{\text{N}}2$  reaction in the same range as that for the sulfonium substrate, but this value is clearly dominated by an unfavorable  $-T\Delta S^\ddagger$  term and less so by differences in  $\Delta H^\ddagger$ . There is a large difference

(36) Morgan, R. S. *J. Chem. Eng. Data* **1961**, *6*, 21–23.

(37) Loupy, A.; Tchoubar, B.; Astruc, D. *Chem. Rev.* **1992**, *92*, 1141–1165.

(38) Swain, C. G.; Kaiser, L. E. *J. Am. Chem. Soc.* **1958**, *80*, 4089–4092.

in entropies for the  $\text{NaN}_3$  reaction between the sulfonium and pyridinium substrates ( $\Delta\Delta S^\ddagger = -15$  gibbs/mol). We interpret this difference to be the result of solvation of the leaving group at the transition state.<sup>18</sup> Introduction of  $\text{SMe}_2$ , which is hydrophobic, into solvent at the transition state would be expected to have little effect on the organization of solvent and thus on the entropy, while introduction of a very water soluble pyridine or sulfonic acid would be expected to cause reorganization of solvent at the transition state with a large loss in entropy.

**Hammett Plots.** There is a severe break in the Hammett plot for hydrolysis of 4-substituted benzyldimethylsulfoniums that is the result of a change from an  $\text{S}_{\text{N}}1$  mechanism for **1** to direct solvent displacement for substrates with less electron-donating substituents (see Figure 7A of ref 18).<sup>39</sup> The Hammett plot for the  $\text{N}_3^-$  reaction under constant ionic strength against  $\sigma^+$ , based on our data for **1** and data for **5–7** reported by Swain, Rees, and Taylor,<sup>16c</sup> is also curved (Figure S5), a shape often found for substitution reactions of both neutral<sup>40</sup> and charged<sup>41</sup> benzyl substrates. In this context the shape of the plot is unremarkable, given the clean  $\text{S}_{\text{N}}2$  reaction for **1** under constant ionic strength. The arguments made by Richard and Yeary<sup>42</sup> to account for these curves, cast in terms of the Pross–Shaik model,<sup>43</sup> seem entirely appropriate for this system as well. Certainly they are adequate to explain substituent effects for benzyldimethylsulfonium ion substrates.<sup>3</sup> On the other hand, the computational results for the benzyldimethylsulfonium ions (see above) suggest that the frontier orbital effects that control the rates are more subtle than can be accounted for by valence bond theories. Clarification of this issue awaits further study.

**Summary and Conclusions.** We have shown that the reactions of **1** occur only for nucleophiles with intermediate HSAB rank, apparently because of frontier orbital interactions between the substituent and the reaction center mediated in part by orbital symmetries. For pyridine-*d*<sub>5</sub>, the substitution reactions with exogenous salt and with nucleophile alone are mixed  $\text{S}_{\text{N}}1/\text{S}_{\text{N}}2$ . For  $\text{NaN}_3$  and  $\text{Na}_2\text{SO}_3$  over most of the range of nucleophile concentration in the presence of an equivalent exogenous salt, the reactions are also mixed  $\text{S}_{\text{N}}1/\text{S}_{\text{N}}2$ . The reactions with  $\text{NaN}_3$  and  $\text{Na}_2\text{SO}_3$  alone, however, occur by three pathways:  $\text{S}_{\text{N}}1$ , Hughes–Ingold  $\text{S}_{\text{N}}2$ , and preassociation-concerted at low concentrations of nucleophile, and primarily by the preassociation-concerted mechanism at high concentrations of nucleophile. These assignments of mechanism rest on the excellent correspondence between the experimental  $[\text{RNu}]/[\text{ROH}]$

value and the values calculated with eq 2 and eq 4 that relate rate constants for the various processes and the independently measured value of  $k_{\text{N}}/k_{\text{W}}$  for partitioning of the 4-methoxybenzyl carbenium ion between nucleophile and solvent under the reaction conditions. The values of  $k_{\text{N}}/k_{\text{W}}$  for trapping of the carbenium ion by pyridine-*d*<sub>5</sub> or  $\text{N}_3^-$  are both larger for salt present, a consequence of the lower  $\text{S}_{\text{N}}1$  rate constant at the higher ionic strength.<sup>44</sup> The fact that the values of  $[\text{RNu}]/[\text{ROH}]$  are larger for pyridine-*d*<sub>5</sub> in the presence of exogenous salt than for pyridine-*d*<sub>5</sub> alone, but are larger for nucleophile alone for  $\text{NaN}_3$  and  $\text{Na}_2\text{SO}_4$ , is compatible only with the intervention of a second faster bimolecular process in which  $\text{Nu}^- \cdot \text{RSM}_2^+$  is an intermediate. In the presence of a large excess of exogenous salt, ion pairs such as  $\text{Cl}^- \cdot \text{RSM}_2^+$  would be in equilibrium with and largely favored over the productive  $\text{Nu}^- \cdot \text{RSM}_2^+$  ion pair. The increased rate of the preassociation-concerted mechanism may be merely the result of Menger's spatio-temporal hypothesis<sup>45</sup> in an intermolecular reaction.

With the results reported here and our work on the (4-methoxybenzyl)-3'-cyanopyridinium ion substrate<sup>3</sup> we can evaluate Jencks's<sup>12</sup> arguments regarding the importance of the stability of an intermediate and its ability to become solvent equilibrated as determining factors for the particular mechanism a substrate "chooses." The boldest statement of the ramifications of this view was made by Knier and Jencks:<sup>46</sup> "All solvolysis and substitution reactions at saturated carbon that proceed through  $\text{S}_{\text{N}}2$  displacement mechanisms do so simply because the intermediate in the alternative  $\text{S}_{\text{N}}1$  mechanism is too unstable to exist [*italics added*]." For the  $\text{NaN}_3$  substitution reactions of **1**, **4**, and the (4-methoxybenzyl)-3'-cyanopyridinium ion, the putative carbenium ion, nucleophile, and solvent are the same, and there are no added cosolvents and therefore no chance of differential solvation, differential hydrogen bonding of the activated complex, or other manifestations of "solvent sorting". While the ground states will be solvated differently, the structure of the solvation shell about the putative carbenium ion will be the same. At constant ionic strength, **4** reacts through an  $\text{S}_{\text{N}}1$  mechanism and produces the carbenium ion as a stable, solvent-equilibrated species that can select between water and  $\text{N}_3^-$ ; **1** undergoes  $\text{N}_3^-$  substitution through a mixed  $\text{S}_{\text{N}}1/\text{S}_{\text{N}}2$  mechanism; and (4-methoxybenzyl)-3'-cyanopyridinium ion undergoes both hydrolysis and  $\text{N}_3^-$  substitution by direct displacement with a very "loose" activated complex for the  $\text{N}_3^-$  reaction ( $\beta_{\text{LG}} = -1.47$ ).<sup>3</sup> All of the activated complexes have significant "carbenium ion character",

(39) In contrast, the gas-phase relative rates for collisionally activated dissociation of a series of 4-substituted benzyldimethylsulfoniums<sup>19</sup> give linear Hammett plots against either  $\sigma^+$  or  $\delta\Delta G^\ddagger$ , a gas-phase scale for the equilibrium protonation of a series of 4-X-2-aryl propenes to the corresponding *tert*-cumyl carbenium ions (Taft, R. W.; Topsom, R. D. *Prog. Phys. Org. Chem.* **1987**, *16*, 2–83). While the mechanism of the gas-phase dissociation could not be ascertained with certainty, it appears to be a direct dissociation without the intervention of an ion-neutral complex, unlike the corresponding benzyldimethylsulfonium substrates that react through mixed ion-neutral complex/direct dissociation mechanisms.<sup>19</sup>

(40) Hudson, R. F.; Klopman, G. *J. Chem. Soc.* **1962**, 1062–1067.

(41) Lyoxide reactions of substituted benzyl dimethyl and phenylmethyl sulfoniums show V-shaped Hammett plots. Schowen, K. B. J. Doctoral Dissertation (MIT, 1964).

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(44) The fact that  $k_{\text{N}}/k_{\text{W}}$  is inverse for pyridine-*d*<sub>5</sub> (0.42  $\text{M}^{-1}$  and 0.80  $\text{M}^{-1}$  for no salt and salt present, respectively) but not for  $\text{NaN}_3$  (17.3  $\text{M}^{-1}$  and 20.5  $\text{M}^{-1}$  for no salt and salt present, respectively) is a consequence of the rates at which amines and  $\text{N}_3^-$  react with carbenium ions. McClelland and his colleagues (McClelland, R. A.; Kanagasabapathy, V. M.; Banait, N. S.; Steenken, S. *J. Am. Chem. Soc.* **1992**, *114*, 1816–1823) found that rates for the reaction of amines with stable carbenium ions decrease with increasing concentrations of water (in acetonitrile/water mixtures) because of the need for equilibrium desolvation of  $\text{RNH}_2 \cdots \text{OH}_2$  before trapping can occur. Because the rate constants for amines and water would be expected to be similar, mere stoichiometry favors water capture. These authors had previously shown (McClelland, R. A.; Kanagasabapathy, V. M.; Banait, N. S.; Steenken, S. *J. Am. Chem. Soc.* **1992**, *113*, 1009–1014) that carbenium ions such as the 4-methoxybenzyl ion react with  $\text{N}_3^-$  at the diffusion rate while water reacts more slowly, which greatly favors formation of  $\text{RN}_3$ .

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but the "choice" of mechanism appears to be related to the leaving group and not to the potential carbenium ion. Indeed, for reaction with  $\text{NaN}_3$ , differences between **1** and (4-methoxybenzyl)-3'-cyanopyridinium ion are related to a large, unfavorable  $\Delta S^\ddagger$  for the latter, a consequence of solvation of the leaving group. Given these factors, the intrinsic stability of the intermediate in the substitution reactions of these substrates is not a factor that influences the "choice" of mechanism.

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**Supporting Information Available:** Figures S1–S5 and tables of primary rate constants used to construct Figures 1–7 are available (7 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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