and 2-chloro-6-isopropyl-4-methylimidazo[1,5-*a*]pyrimidine (**7b**) in 22% and 47% yield, respectively. **7b**: mp 88–89 °C (hexane); ^{1}H NMR ($CDCl_3$) δ 2.82 (s, 3, 4-CH_3). Heating of **4b** for 18 h gave **7b** in 67% yield.

Compound **6b**, on treatment with phosphorus oxychloride at 90 °C for 50 h, was transformed to **7b** in 65% yield.[9]

When **3a–c** were heated with phosphorus oxychloride at 90 °C for 3 h, compounds **7a–c** were obtained in good yields: **7a** (73%), **7b** (75%), **7c** (75%). **7c**: mp 189–190 °C (benzene); ^{1}H NMR ($CDCl_3$) δ 2.14 (s, 3, 4-CH_3).[10]

Although a number of purine analogues have been synthesized, only few references are available concerning the synthesis of imidazo[1,5-*a*]pyrimidines.[4,11,12] All of them have been synthesized from imidazole derivatives. The merit of our method is that appropriate substituents can be introduced at the 6- and 8-positions of imidazo-[1,5-*a*]pyrimidines by using various N-acylated amino acid esters, and further investigations are in progress.[13]

Acknowledgment. A part of the expense for this work was defrayed by the Grant-in-Aid for Scientific Research of the Ministry of Education, which is gratefully acknowledged. Thanks are also due to Mrs. C. Koyanagi of the Central Analyses Room of this institute for elemental analyses.

Registry No. 1, 15846-25-0; **2a**, 1906-82-7; **2b**, 31766-30-0; **2c**, 1499-53-2; **3a**, 79898-99-0; **3b**, 79899-00-6; **3c**, 50850-18-5; **4a**, 79899-01-7; **4b**, 79899-02-8; **5a**, 79899-03-9; **5b**, 79899-04-0; **5c**, 79899-05-1; **6a**, 79899-06-2; **6b**, 79899-07-3; **7a**, 79899-08-4; **7b**, 79899-09-5; **7c**, 79899-10-8.

(9) The formation of **7a,b** from **6a,b** involves the ring transformation; that is, the first stage might be the bond cleavage between the nitrogen (N_5) and carbon (C_8) of **6a,b** to give the 2-substituted pyrimidine intermediate which recyclizes to **7a,b**. Details of the reaction mechanism will be discussed in our future report.

(10) The signal due to methyl group at the 4-position is shifted at higher field owing to benzene ring.

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(13) We have observed that ester of *N*-acylalanine (or phenylalanine) reacts with 1 to give the pyrimidine-4(3*H*)-one which, on treatment with PPA or phosphorus oxychloride, is transformed to imidazo[1,5-*a*]pyrimidine.

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The Nucleophilicity of Nitranions

Summary: The nucleophilicities of carbazole, phenothiazine, and diphenylamine nitranions toward benzyl and *n*-butyl halides in dimethyl sulfoxide solution have been found to be 30–500 times less than those of carbanions of similar structure and equal basicity, depending on the substrate.

Sir: Although the alkylation of nitranions is important in synthetic chemistry and biochemistry, quantitative measurement of the nucleophilicity of these anions appears to be limited to a study of the reactions of the conjugate bases of succinimide, phthalimide, benzenesulfonamide, and *N*-methyl- and *N*-phenylbenzenesulfonamides toward methyl iodide in methanol.[1] It was concluded from this study that methoxide ion in methanol has a nucleophilicity about 50-fold less than a nitranion of the same basicity. On the other hand, comparison of the rate data for phthalimide ion with that for phenoxide ion, which have about the same basicity in MeOH (the pK_a values of their conjugate acids are 14.5[1] and 14.2,[2] respectively, in MeOH), indicates that the nitranion is slightly *less* reactive. (The n_{MeI} values are 5.4 and 5.75, respectively.[3]) Recently we have used Brønsted-type plots to compare the nucleophilicity of thianions, oxanions, and carbanions of the same basicity reacting by S_N2 pathways with alkyl halides in dimethyl sulfoxide solution.[4] This investigation has now been extended to nitranions.

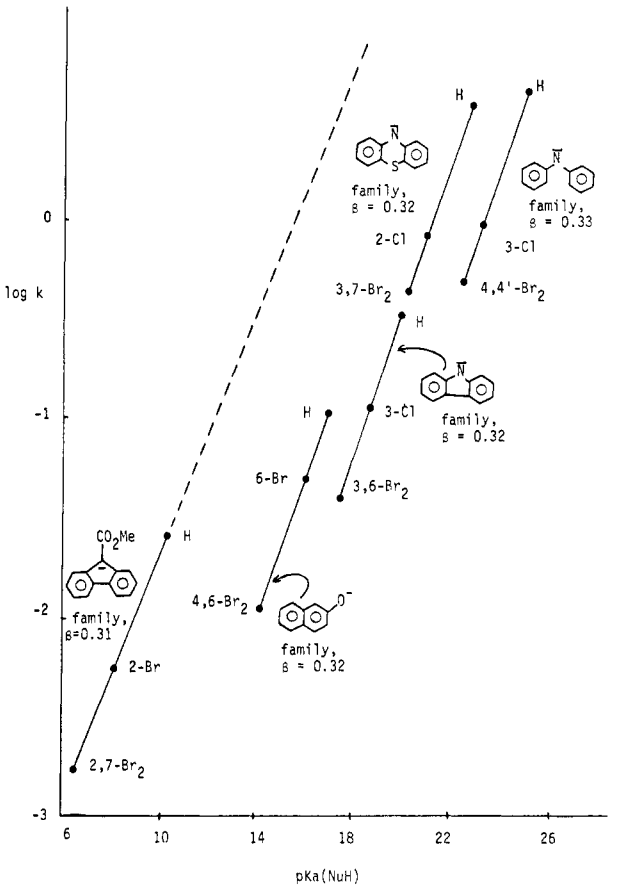

Figure 1. Plots of the log of the second-order rate constants for the reactions of substituted 9-(methoxycarbonyl)fluorenyl anions, 2-naphthoxide anions, carbazole anions, phenothiazine anions, and diphenylamine anions with benzyl chloride in Me_2SO at 25 °C vs. the pK_a values of their conjugate acids in Me_2SO.

Rates of reactions with benzyl chloride in Me_2SO solution were measured for nitranions derived from carbazoles, phenothiazines, and diphenylamines. The results are compared in Figure 1 with those for remotely substituted 9-(methoxycarbonyl)fluorenyl carbanions (9-CO_2Me-Fl$^-$) and 2-naphthoxide ions (NpO$^-$). Examination of Figure 1 reveals three noteworthy features: (1) the phenothiazine line is essentially an extension of the carbazole line, and the diphenylamine line is displaced to the right of the carbazole–phenothiazine line, (2) the slopes of the carbanion, oxanion, and nitranion lines are nearly the same, and (3) the nitranion lines are displaced to the right of the carbanion and oxanion lines.

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0022-3263/82/1947-0169$01.25/0

The lesser reactivity of nitranions than carbanions denoted by the displacement of the carbazole–phenothiazine line to the right of the (extended) 9-CO_2Me-Fl$^-$ line, which we have adopted as a model for the least sterically demanding of the 9-G-Fl$^-$ carbanions,[5] cannot be due to a steric effect since carbazole anions have *less* steric demands than fluorenyl anions. (They lack the 9-substituent.) On the other hand, the sixfold lower reactivity of a diphenylamine nitranion than a carbazole–phenothiazine nitranion of the same basicity probably *is* a steric effect since it parallels the fourfold lower reactivity of PhC(Ph)CN$^-$ carbanions, relative to the 9-CO_2Me-Fl$^-$ line.[6]

The near equality in β_{Nu} values for carbanions, oxanions, and nitranions suggests that the transition-state structures for these reactions are closely related, despite the different kinds of atoms that are being bonded to carbon. The near equality of slopes is a useful feature since it allows comparison of the nucleophilicity of different kinds of anions at constant basicity.[4]

The vertical gap between the 9-CO_2Me-Fl$^-$ and carbazole–phenothiazine family lines indicates that the carbanions are 80 times more nucleophilic than the corresponding nitranions of the same basicity.[7] When combined with data from earlier studies,[4] this result leads to the nucleophilicity order: $S^- \gg C^- > O^- > N^-$ for anions of similar structure and the same basicity.[9] Factors that may be important in determining this order include bond distance (average bond distances are as follows: S–C, 1.82; C–C, 1.54; O–C, 1.43; N–C, 1.47), bond strength (average bond strengths are 65, 83, 86, and 83 kcal/mol, respectively), and electronegativity (S, 2.5; C, 2.5; N, 3.0; O, 3.5). The much higher nucleophilicity of thianions[4] can be correlated with the longer S–C bond distance, together with the low electronegativity of sulfur. The higher nucleophilicity of carbanions, relative to oxanions and nitranions, can also be correlated with the longer C–C bond length and the low electronegativity of carbon. (The longer S–C and C–C bond distances could serve to decrease steric interactions in the transition state, TS.) The lower electronegativity of S and C could serve to decrease solvation and thus decrease the amount of solvent reorganization required in the TS; lower electronegativity can also be correlated with greater anion polarizability and with the availability of molecular orbitals of higher energy, which may provide the proper HOMO–LUMO combination to lower the energy of the TS. The greater nucleophilicity of oxanions than nitranions is not expected on any of these grounds, however.[9]

The size of Brønsted β values has generally been taken as a measure of the extent of bond formation in the TS.[10] Bell has pointed out that (for proton transfer) this could be related to (a) the geometrical position of the proton, (b) the orders of force constants of the two bonds holding the proton, (c) the distribution of charge, or (d) the free-energy change in the overall reaction.[11] In the S_N2 reactions under consideration here one would expect the geometries, force constants, and $\Delta G°$ values for the overall reaction to change appreciably as the kind of atom bonded to carbon is changed. We conclude from the near constancy of β_{Nu} values for S$^-$, C$^-$, O$^-$, and N$^-$, however, that these changes are not causing appreciable changes in TS structures for these anionic nucleophiles. Instead, the size of β_{Nu} in these reactions appears to be almost entirely substrate dependent.[7] If β_{Nu} values provide a measure of the fraction of charge transferred from the anion to the substrate in the transition state,[12] then our results show that, for a given substrate reacting with delocalized anions, the same fraction of charge is transferred from anions of different structure over a wide range of basicity.

Acknowledgment. This work was supported by the National Science Foundation.

Registry No. Benzyl chloride, 100-44-7; 9-(methoxycarbonyl)-fluorenyl anion, 12565-94-5; 2-bromo-9-(methoxycarbonyl)fluorenyl anion, 73838-71-8; 2,7-dibromo-9-(methoxycarbonyl)fluorenyl anion, 73838-70-7; 2-naphthoxide anion, 15147-55-4; 6-bromo-2-naphthoxide anion, 78232-03-8; 4,6-dibromo-2-naphthoxide anion, 78232-04-9; carbazole nitranion, 23560-25-0; 3-chlorocarbazole nitranion, 80010-03-3; 3,6-dibromocarbazole nitranion, 79990-92-4; phenothiazine nitranion, 76069-04-0; 2-chlorophenothiazine nitranion, 79990-93-5; 3,7-dibromophenothiazine nitranion, 79990-94-6; diphenylamine nitranion, 61057-05-4; *N*-(3-chlorophenyl)benzene amine nitranion, 78525-46-9; bis(4-bromophenyl)amine nitranion, 79990-95-7.

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(7) The C$^-$/N$^-$ ratio is sensitive to the structure of the substrate. It is only 30 for BuCl but 500 for BuI.[8]
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(9) In a later paper we will show that the size, extent of delocalization, and nature of delocalization of carbanions such as PhC(CN)$_2^-$, 9-CN-Fl$^-$, MeC(CN)$_2^-$, and the like do not affect the linear basicity–nucleophilicity correlation. This gives us confidence that the present comparison of carbanion and nitranion nucleophilicities is valid. On the other hand, the fact that the nucleophilic atom in thianions and oxanions is on the periphery of the anion, whereas that for carbanions and nitranions is more centrally located, may be a factor affecting their nucleophilicities.
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New Penem Synthesis via a Novel Pummerer Rearrangement Process

Summary: The olefinic group of the penem ring system has been introduced via a Pummerer rearrangement of the penam sulfoxide **11** by utilizing trifluoroacetic anhydride–lutidine.

Sir: The novel penem β-lactam ring system **2** has recently been described by the Woodward group and others.[1] In their sequence, the C-2 olefin was constructed by Wittig reaction of the phosphorane **1** (Chart I). Recently, conversion of clavulanic acid (**3**) and penicillanic acid (**4**) into the penem system has been reported by Cherry[2] and Beels[3]

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