Aromatic Substitution. XXVII.[1] Kinetics of Nucleophilic Substitution of Some Fluoropyridines and -picolines with Methoxide, Thiomethoxide, and Thiophenoxide Ions

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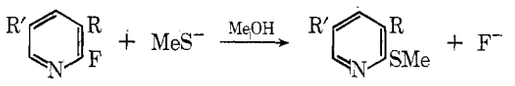
The rates and activation parameters were determined for the reactions of KSMe and KOMe in methanol with 2-fluoro-, 2-fluoro-3-methyl-, and 2-fluoro-5-methylpyridine, and of KOMe, KOPh, and KSPh with 2-fluoropyridine in hexamethylphosphoramide. The F/Br mobility ratios for 2-halogenopyridines with MeO^-, MeS^-, and PhS^- in methanol were compared with those in HMPA and the results are discussed.

Quantitative studies[2,3] on the reactivity of thiomethoxide ion with halogenonitrobenzenes in methanol revealed a high value of the ratio F/I, similar to that observed for nucleophiles of low polarizability such as methoxide. With the iodo derivatives an increase in the free energy was associated with low $\Delta S^\dagger$ values which were regarded as steric in origin, reflecting interaction between the bulky leaving group and the sulfur nucleophile.

In order to determine if the halogen mobility in the pyridine series would reflect such a heavy (sulfur) nucleophile effect, the kinetics of the reaction of 2-fluoropyridines (1) with thiomethoxide ion in methanol to give **2** were studied;



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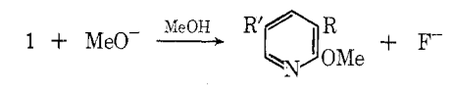
the kinetic data for the reactions with 2-bromopyridines were reported earlier.[1] The rate data and Arrhenius parameters are summarized in Table I. An examination of the specific rate constants shows that the order of reactivities was 2-fluoro > 2-fluoro-3-methyl- > 2-fluoro-5-methylpyridine and follows the order of energies of activation. The lesser deactivation of the ortho than of the para position by a 3-methyl group parallels that reported earlier for the 2-bromopyridines with MeS^- [4] and MeO^- [4] in methanol. Unlike the 2-bromopyridines with PhS^- in methanol,[5] an *o*-methyl group does not activate the 2 position in 2-fluoropyridine toward attack by MeS^- in methanol.

In order to compare the F/Br ratios obtained with MeS^- in methanol with those for MeO^-, it was necessary to study the kinetics of the reaction of fluoropyridines with MeO^- in methanol. The reaction of 2-fluoropyridine with MeO^- was reported earlier.[4] The rate data and activation parameters are summarized in Table II. The order of reactivities was again the same as that reported earlier[4] for the bromo-



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pyridines with methoxide ion, *i.e.*, 2-F > 2-F-3-Me > 2-F-5-Me-pyridine, and was dependent upon E_{act}.

For the reaction of CH_3O^- with halogenopyridine derivatives in methanol the typical[2,6-9] leaving group pattern [F > Br (Table III)] was observed. This pattern is a result of the electronegativity (α) effect, which lowers E_{act} by *ca.* 3 kcal/mol for the reactions of the fluoro- (Table II) compared with the bromopyridines.[4]

With thiomethoxide in methanol the F/Br ratio (Table III), although slightly greater than unity, cannot be attributed to a lower E_{act} for the fluoro isomer; in fact, the E_{act} is consistently larger (1–2 kcal/mol) for the fluoro (Table I) than for the bromo derivatives.[4] The E_{act} value is probably best looked upon as being normal for the fluoro compounds while the lower values for the bromo analogs are most likely a result of attractive dispersion forces between the polarizable nucleophile and the leaving group.[10] Although this reduction in E_{act} for the bromo compounds is not large enough to counterbalance the heavy (sulfur) nucleophile steric interaction between entering and leaving groups, and thus not large enough to reverse the observed mobility pattern (F > Br), the F/Br mobility ratio is reduced substantially compared with that observed with MeO^-.

On going from 2-bromo- to 2-fluoropyridine the polarizability of the leaving group is reduced.[11] This permits a more useful comparison of the *o*-Me:*p*-Me rate ratios for MeO^- and MeS^- with the fluoro- than with the bromopyridine derivatives. An examination of these rate ratios, given in Table IV, suggests once again[1] that more than just ion–dipole attractive interactions between the 3-methyl group and MeS^- are involved. If only ion–dipole effects were im-

Table I
Kinetic Data and Activation Parameters for the Reaction of 2-Fluoropyridines with Potassium Thiomethoxide in Methanol

	Pyridine		
	2-Fluoro	2-Fluoro-3-methyl	2-Fluoro-5-methyl
10^4k_2, M^{-1} sec^{-1} (temp, °C)	3.07(90), 7.11(100), 17.3(108), 28.9(115), 42.6(120)	0.985(90.3), 2.61(100.2), 6.34(110), 9.85(114.9), 16.5(120)	0.373(100.4), 0.973(110), 2.35(120), 6.32(130)
10^4k_2, M^{-1} sec^{-1} (at 110°)	19.1	6.34	0.97
E_{act}, kcal/mol[a]	25.3	26.6	28.3
$\Delta S\dagger$, eu	−7.4	−6.1	−5.3
$\Delta F\dagger$, kcal/mol (at 100°)	27.3	28.1	29.6

[a] Experimental errors are ±0.2 kcal in E_a and ±0.4 eu in $\Delta S^\dagger$.

Table II
Kinetic Data and Activation Parameters for the Reaction of 2-Fluoropyridines with Potassium Methoxide in Methanol

	Pyridine		
	2-Fluoro[b]	2-Fluoro-3-methyl	2-Fluoro-5-methyl
10^4k_2, M^{-1} sec^{-1} (temp, °C)[a]	11.8(100), 33.5(113.0), 72.0(123.2), 135(131.2)	3.32(100), 8.09(110.2), 11.8(115), 18.6(120), 33.7(128)	2.69(100), 4.01(105), 9.34(115), 14.1(120), 25.7(128)
10^4k_2, M^{-1} sec^{-1} (at 110°)[a]	26.9	7.85	6.08
E_{act},[c] kcal/mol	23.3	24.7	25.3
$\Delta S\dagger$, eu	−11.9	−10.8	−9.5
$\Delta F\dagger$, kcal/mol (at 110°)	27.0	27.9	28.1

[a] [MeO$^-$] = [fluoropyridine] = 0.0959 N = 0.00480 mol of reactants. [b] Taken from ref 4. [c] Experimental errors are ±0.2 kcal in E_{act} and ±0.4 eu in $\Delta S\dagger$.

Table III
Halogen Mobility and Nucleophilic Rate Ratios in Reactions of Potassium Methoxide and Potassium Thiomethoxide with Halogenopyridine Derivatives in Methanol at 110°

Substituent	F/Br mobility ratio MeO$^-$	F/Br mobility ratio MeS$^-$	Rate ratios MeS$^-$/MeO$^-$
2-F			0.71
	28.5	4.3	
2-Br			4.7
2-F-3-Me			0.81
	32.8	1.43	
2-Br-3-Me			11.2
2-F-5-Me			0.16
	39.4	1.40	
2-Br-5-Me			4.5

portant one might have expected methoxide ion to yield a higher *o*-Me:*p*-Me ratio than would the larger thiomethoxide ion. The results summarized in Table IV show that, not only is the ortho:para ratio in fluoride ion displacement by methoxide (1.3) lower than that for thiomethoxide (6.5), but also that the latter ratio is larger than the ratio (3.9) observed when bromide ion is displaced by thiomethoxide.[1] Since London interactions between methoxide and an *o*-methyl group are small,[11] the $k_{o\text{-Me}}/k_{p\text{-Me}}$ ratio being greater than unity with both bromo and fluoro compounds must represent contributions from an ion–dipole[12,13] attractive interaction. With thiomethoxide, however, London dispersion forces between the nucleophile and the ortho substituent become more important and larger $k_{o\text{-Me}}/k_{c}p$-Me rate ratios result.

Di Nunno and Todesco[14] have suggested that the reactivity of a nucleophile represents both the aptitude to bind a positive group as well as polarizability effects.[15] On comparing CH_3O^- with CH_3S^- (Tables I and III) we see that for 2-fluoropyridine, where polarizability effects are minimal, CH_3O^- is a better nucleophile since it reacts with 2-fluoropyridine faster than does thiomethoxide (k_{MeS^-}/k_{MeO^-} = 0.71), *i.e.*, nucleophilicity follows the order of relative carbon basicities. This basicity difference is manifested in the E_a term which is *ca.* 2 kcal/mol lower for the reaction of CH_3O^- than for the reactions of CH_3S^- with the 2-fluoropyridine derivatives.

In the case of the 2-bromopyridine derivatives, where polarizability factors should be more important, the relative carbon nucleophilicities of CH_3O^- and CH_3S^- ions are in the reverse order of their basicities, *i.e.*, $k_{MeS^-} > k_{MeO^-}$. This reactivity order reflects significant involvement of polarizability between attacking and departing groups, which contributes to the lowering of E_a for CH_3S^- by *ca.* 3 kcal/mol. These results are consistent with those reported by Di Nunno and Todesco[14] who found that the rate ratio k_Z/k_N (where k_Z is the rate constant for a polarizable nucleophile and k_N for a nonpolarizable one) varied linearly with the polarizability of the leaving group. For example, the relative nucleophilic abilities of PhS^- and CH_3O^- are in the reverse order of their basicities, *i.e.*, $k_{PhS^-} > k_{MeO^-}$, for the reactions with 2-halo-6-nitrobenzothiazoles, 2,4-dinitrohalobenzenes, and *p*-halogenonitrobenzenes.[14] On the other hand, with 2-fluorobenzothiazole,[14] 2-chloroquinoline,[16] and 2-bromopyridine[4,5] the rate ratio $k_{PhS^-}/k_{MeO^-} < 1$. In the case of 2-bromopyridine, polarizability attractive interactions between PhS^- and the bromine substituent are probably operative,[14] but these alone are not of sufficient magnitude to overcome the greater basicity of MeO^- (or MeS^-) and any steric repulsion in the transition state involving the bulky sulfur nucleophile (PhS^- is less basic than MeS^- due to delocalization of the negative charge in PhS^-).

Table IV
Rate Ratios for Reactions of 2-Fluoro-3- or 2-Fluoro-5-methylpyridine with Potassium Thiomethoxide and Potassium Methoxide in Methanol at 110°

R	$k_{o\text{-R}}/k_{p\text{-R}}$	$(k_{MeS^-}/k_{MeO^-})_R/(k_{MeS^-}/k_{MeO^-})_H$	$(k_{MeS^-}/k_{MeO^-})_{o\text{-R}}/(k_{MeS^-}/k_{MeO^-})_{p\text{-R}}$
CH_3	6.5 (MeS^-) 1.3 (MeO^-)	1.14 (*o*-Me), 0.226 (*p*-Me)	5.05

Our attention was directed next to the reactions of 2-fluoropyridine in hexamethylphosphoramide (HMPA) with MeO^-, MeS^-, and PhS^-. The rate constants and activation parameters are summarized in Table V. In order to facilitate the comparison of solvent effect upon halogen mobility, kinetic data for the reactions of these same nucleophiles in methanol with 2-fluoro- and 2-bromopyridine[1,4,5] are also included in Table V.

In both HMPA and methanol the order of reactivity with 2-fluoropyridine, $MeO^- > MeS^- > PhS^-$, followed the order of the proton basicity of the nucleophiles; with 2-bromopyridine where entering–leaving group polarizability factors are more important, the order of reactivity was $MeS^- > MeO^- > PhS^-$. It appears that the activating entering–leaving group interaction between thiophenoxide and bromine is not large enough (perhaps due to unfavorable steric effects[3]) to overcome the lower nucleophilicity of PhS^- compared with both MeO^- and MeS^-.

A comparison of F/Br mobility ratios in methanol and HMPA is given in Table VI. Except for thiomethoxide in HMPA, the nucleophiles in both HMPA and methanol reacted faster on going from 2-bromo- to 2-fluoropyridine, *i.e.*, $k_F/k_{Br} > 1$, which rate increase was dependent upon E_a [$E_{a(2\text{-F})} < E_{a(2\text{-Br})}$].

In the halogenonitrobenzene series a correlation of halide mobility or magnitude of F/I ratio with which of the two transition states is rate determining is often difficult.

Table V
Rate Constants and Activation Parameters for the Reaction of 2-Fluoropyridine with MeO^-, MeS^-, PhS^- Ions in HMPA. Comparison with 2-Bromopyridine[a] and with Kinetics in Methanol

Nucleophile	Solvent	10^3k_2, M^{-1} sec^{-1} (°C)	10^5k_2 at 110°	E_{act},[b] kcal/mol	$\Delta S^\dagger$, eu	$\Delta F^\dagger$ (100°)
CH_3O^-	HMPA	23.8 (40.4)	33100	16.3	−15.8	21.6
		5.5 (24)	[3390][a]	[14.8][a]	[−24.0][a]	
		1.42 (10)				
	MeOH[c]		27.0	23.3	−11.8	
			[0.94]	[26.8]	[−9.2]	
CH_3S^-	HMPA	0.65 (24)	692	12.0	−34.6	24.36
		1.85 (40)	[17400]	[13.6]	[−24.1]	
		4.14 (54)				
	MeOH		19.1	25.3	−7.4	
			[4.4]	[24.3]	[−12.9]	
PhS^-	HMPA	1.98 (70)	490	19.0	−17.9	24.9
		4.17 (80)	[202]	[19.2]	[−18.5]	
		18.7 (100.2)				
	MeOH		0.34			
			[0.214][d]	−[25.6][d]	−[15.6][d]	

[a] Values in brackets are the corresponding values for 2-bromopyridine.[1] [b] Experimental errors are ±0.4 kcal in E_{act} and ±0.8 eu in $\Delta S^\dagger$. [c] Reference 4. [d] Reference 1, footnote 16, and ref 5.

Table VI
Comparison of Halogen Mobility in Reactions of 2-Halogenopyridines with MeO^-, MeS^-, and PhS^- in Methanol and in HMPA at 110°

Solvent	F/Br mobility ratio		
	CH_3O^-	CH_3S^-	PhS^-
MeOH	28.5[a]	4.3	1.6
HMPA	9.8	0.039	2.4

[a] See ref 4.

For example, the F/I ratio is <1 for the less reactive nucleophiles SCN^-,[17,18] $PhNHCH_3$,[19] and I^-,[20] while the formation of the second transition state is rate limiting with the fluoro derivatives; however, with the more reactive thiomethoxide ion[2,9] the F/I ratio is 3.7×10^3 compared with a value of 2.3 for thiophenoxide.[3] Calculations of the transition state energies for reactions of both PhS^- and MeS^- with fluoronitrobenzenes showed the second transition state to be rate limiting.[3,21] Miller[21] pointed out that for anionic nucleophiles in which the nucleophilic atom is in the first horizontal row of the Periodic Table, the characteristic mobility pattern is F ≫ Cl > Br > I. With heavy nucleophiles (those whose nucleophilic atom is in the second or lower horizontal row of the Periodic Table) the mobility of fluorine relative to the other halogens is typically reversed due to the second transition state formation being rate limiting. Whereas thiocyanate ion behaves as a nucleophile as do heavy halide ions in relation to the halogen mobility order, the more typical second row reagent, thiomethoxide ion, appears to be borderline with respect to its influence on the mobility order of displace groups; PhS^- ion behaves much more typically as a heavy nucleophile.[21]

The borderline behavior of MeS^- with respect to its influence on halogen mobility is displayed in its reactions with fluoro- and bromopyridines (Table VI). Whereas the F/Br ratio is >1 in methanol for the reaction of 2-halogenopyridine with MeS^-, it is reduced by a factor of approximately 10^3 in HMPA (from 4.3 to 0.039). In the 2-halogenonitropyridine series, as with the halogenonitrobenzene series, we do not observe a direct correlation of the magnitude of F/Br ratio with which transition state is rate determining. The second transition state is probably rate limiting for the reactions of MeS^- and PhS^- with 2-fluoropyridine[21] and yet the F/Br ratio is <1 for MeS^- in HMPA and >1 for MeS^- in MeOH and for PhS^- in both MeOH and HMPA. With 2-fluoropyridine in HMPA we observed a substantial difference in the E_a values for the two sulfur nucleophiles, $\Delta E_{(PhS^- - MeS^-)} = 7$ kcal/mol. A low F/Br ratio (0.039) as is observed for MeS^- in HMPA, in which $E_{a(2\text{-F})} < E_{a(2\text{-Br})}$, but $\Delta\Delta S^\dagger$ (= $\Delta S^\dagger_{2\text{-Br}} - \Delta S^\dagger_{2\text{-F}}$) = 10.5 eu, is not without precedent in the literature. Hammond and Parks[19] found that in the reaction of $PhNHCH_3$ with 1-halogeno-2,4-dinitrobenzenes in $PhNO_2$, the F/Br ratio of 0.0205 reflected the lower $\Delta S^\dagger$ for the fluoro compound ($\Delta\Delta S^\dagger$ = 12 eu), although E_a for the fluoro compound (10 kcal/mol) was lower than that for the bromo analog (11 kcal/mol).

Ho, Miller, and Wong[3] ascribed the high MeS^-/MeO^- rate ratios in protic solvents to solvation factors; for example, in reactions with halogenonitrobenzenes the higher reactivity of thiomethoxide over methoxide ion was attributed to the lower heat of solvation of the former more than compensating for unfavorable differences in strengths of the bonds formed and of electron affinities. On this basis, a reversal or leveling out of this order in nonprotic solvents (such as HMPA) where both nucleophiles are poorly solvated was predicted.[3] The solvent clearly plays a key role in these reactions, since with thiomethoxide ion in methanol, the expected (on the basis of a heavy nucleophile effect) order, $\Delta S^\dagger_{2\text{-Br}} < \Delta S^\dagger_{2\text{-F}}$ is observed. This appears to rule out ground-state solvation of MeS^- as the determining factor since this is the same in the reaction with both 2-fluoro- and 2-bromopyridine. If ground-state solvation of the two pyridines had been the key factor the same pattern would have been observed with both MeO^- and PhS^-. Any secondary steric effects between the entering heavy nucleophile and leaving group would have led to $\Delta S^\dagger$ being lower for reaction with 2-bromo- than with 2-fluoropyridine. This leaves solvation of the transition state as a possible explanation of the abnormally low value of $\Delta S^\dagger_{MeS^-(2\text{-F})}$.

On going from methanol to HMPA there is a reduction in the F/Br rate ratio (from 28.5 to 9.8) when methoxide ion is used. This ratio is probably a reflection of the increased reactivity of methoxide in HMPA due to reduced solvation of the small anion, resulting in a reduction of the selectivity of MeO^- for the two halogenopyridines. In the case of MeS^-, the reduction in F/Br mobility ratio (from 4.3 to 0.039) may, in addition, be due to solvation of the 2-F-MeS^- transition state in HMPA, as discussed above. With PhS^- the activation parameters are similar to each other in HMPA for 2-fluoro- and 2-bromopyridine.

The rate of the reaction of MeS^- with 2-bromopyridine[1] increases by a factor of *ca.* 3950 at 110° on going from

Table VII
Comparison of Nucleophilic Rate Ratios in Methanol and in HMPA

Pyridine	MeS^-/MeO^- rate ratios[a] In MeOH	MeS^-/MeO^- rate ratios[a] In HMPA	PhS^-/MeO^- rate ratios[a] In MeOH	PhS^-/MeO^- rate ratios[a] In HMPA
2-F	0.71	0.021	0.013	0.015
2-Br	4.7	5.14	0.23	0.059
2-F-3-CH_3	0.81			
2-Br-3-CH_3	11.2	3.4	1.26	0.13
2-F-5-CH_3	0.16			
2-Br-5-CH_3	4.5	2.9	0.40	0.028

[a] Also reported in Table III.

methanol to HMPA as a result of a reduction in E_a: $\Delta E_{a(MeOH-HMPA)} = 10.7$ kcal/mol, in spite of a smaller $\Delta S^\dagger$ value in HMPA (Table V), $\Delta\Delta S^\dagger_{(MeOH-HMPA)} \simeq 11$ eu. In the reaction of MeS^- with 2-fluoropyridine the rate increases by a factor of 36 at 110° on going from methanol to HMPA; despite a reduction in E_a[$\Delta E_{a(MeOH-HMPA)} \simeq 13$ kcal/mol], the much smaller value of $\Delta S^\dagger$ in HMPA than in methanol results in the smaller rate increase for 2-fluoro- compared with 2-bromopyridine in HMPA. Only one example which might support the prediction[3] that, in those cases in which $k_{MeS^-}/k_{MeO^-} > 1$ in a protic solvent, owing to the greater heat of solvation of the smaller more basic Me^- ion, on going to an aprotic solvent $k_{MeS^-}/k_{MeO^-} < 1$ should be observed was found (Table VII). This is the case in which k_{PhS^-}/k_{MeO^-} for 2-bromo-3-picoline is 1.26 in MeOH and 0.13 in HMPA. This is not valid support, however, for two reasons: (i) it is not really fair to compare PhS^- with MeO^-; it would have been better to compare PhS^- with PhO^-, but this is not possible;[1] (ii) the reason that $k_{PhS^-}/k_{MeO^-} > 1$ in methanol is due to the polarizability attractive interaction between the 3-methyl group in 2-bromo-3-picoline and PhS^- in the transition state, which does not obtain with MeO^-.[1,5] Of more interest is the fact that $k_{MeS^-}/k_{MeO^-} > 1$ in MeOH and, though somewhat reduced in magnitude, this ratio did not become less than unity on going from methanol to HMPA for any of the bromo compounds. The higher reactivity of MeS^- than MeO^- with the bromopyridines in MeOH, therefore, is most likely not just a reflection of the lower heat of solvation of the thiomethoxide ion[3] but probably mirrors the contribution from an attractive interaction between the polarizable entering MeS^- ion and the polarizable leaving bromine atom.

Experimental Section

Materials. HMPA (Dow Chemical Co.) was fractionally distilled, the fraction of bp 65–66° (1 mm) being used. 2-Fluoropyridine was distilled, bp 123–124° (750 mm) [lit.[22] bp 124.8–125.4° (755 mm)].

2-Fluoro-3-methylpyridine. A vigorously stirred solution of 2-amino-3-picoline (40 g) in tetrafluoroboric acid (170 ml) was maintained below 10° while sodium nitrite (25.6 g) was added. After 1 hr at 10°, the solution was heated to 50° to complete decomposition of the tetrafluoroborate salt. The solution was cooled to 5°, neutralized (Na_2CO_3), and steam distilled. The aqueous phase was extracted with ether (4 × 75 ml). The ethereal layer was dried ($MgSO_4$) and concentrated to give a yellow liquid which was distilled to give 2-fluoro-3-methylpyridine as a colorless liquid (16.7 g, 40%), bp 149–151° (755 mm) [lit.[23] bp 150.5–151° (757 mm)]; nmr (CCl_4) δ 8.02 (d, 1, H_6), 7.79 (m, 1, H_4), 7.08 (m, 1, H_5), 2.28 (s, 3, CH_3).

2-Fluoro-5-methylpyridine. This was prepared as described above but starting from 2-amino-5-methylpyridine. The product was a colorless liquid (18.8 g, 45%), bp 154–155° (750 mm) [lit.[23] bp 155–156° (752 mm)]; nmr (CCl_4) δ 7.95 (br s, 1, H_6), 7.50 (m, 1, H_4), 6.73 (m, 1, H_3), and 2.22 (s, 3, CH_3).

Solutions of potassium thiomethoxide and potassium methoxide in methanol and of potassium methoxide, potassium thiomethoxide, and potassium thiophenoxide in HMPA were prepared as previously reported.[1,4]

Reaction Products. These were obtained by a preparative reaction of the appropriate 2-fluoropyridine with potassium thiomethoxide and potassium methoxide in methanol and with potassium methoxide, thiomethoxide, and thiophenoxide in HMPA under the conditions of the kinetic runs. 2-Thiomethoxypyridine had bp 54–55° (3 mm) [lit.[24] bp 197° (760 mm)]. 3-Methyl-2-thiomethoxypyridine had bp 61–62° (2.6 mm) (61%) [lit.[1] bp 61–62° (2.6 mm)]. 5-Methyl-2-thiomethoxypyridine had bp 70–71° (2.6 mm) (53%) [lit.[1] bp 70–71° (2.6 mm)]. 2-Methoxy-3-methylpyridine had bp 157–159° (750 mm) (65%) [lit.[4] bp 38° (6 mm)]. 2-Methoxy-5-methylpyridine had bp 39–40° (2 mm) (73%) [lit.[4] bp 52° (6 mm)]. 2-Methoxypyridine had bp 138–140° (755 mm) [lit.[4] bp 140–142° (740 mm)]. 2-Thiophenoxypyridine had bp 123–124° (1 mm) [lit.[25] bp 160–162° (8 mm)].

Kinetic Procedures. A. Potassium Thiomethoxide and Methoxide in Methanol. The procedure was identical with that reported earlier[1] for the reaction of potassium thiomethoxide with bromopyridines in methanol.

B. Potassium Methoxide, Thiomethoxide, and Thiophenoxide in HMPA. The procedures utilized here were the same as those reported earlier[1] for the 2-bromopyridines in HMPA.

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Registry No.—2-Fluoropyridine, 372-48-5; 2-bromopyridine, 109-04-6; 2-fluoro-3-methylpyridine, 2369-18-8; 2-bromo-3-methylpyridine, 3430-17-9; 2-fluoro-5-methylpyridine, 407-22-7; 2-bromo-5-methylpyridine, 3510-66-5; potassium methoxide, 865-33-8; potassium thiomethoxide, 26385-24-0; 2-amino-3-picoline, 1603-40-3; 2-amino-5-methylpyridine, 1824-81-3.

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