mL) was heated at reflux for 4 h. The reaction mixtures was cooled, basified with Na_2CO_3, and extracted with CH_2Cl_2 to provide quinolizidinone 7 (38 mg, 95%) after flash chromatography (CH_2Cl_2–MeOH (95:5)), which was identified by comparison of its TLC and spectral data with those already obtained.

Acknowledgment. This work was supported by the DGICYT (Spain) through Grant PB-88/0316 and by the Acción Integrada Hispano-Francesa HF-078 (1991). Thanks are also due to the "Departament d'Ensenyament", Generalitat de Catalunya, for a fellowship given to one of us (C.V.).

Registry No. 1, 132113-29-2; 2, 55854-97-2; 6, 130179-28-1; 11, 130179-30-5; 12, 136061-54-6; 13, 136061-55-7; 14, 130627-35-9; 15, 132113-30-5; 15 (de-(phenylsulfonyl) derivative), 136061-57-9; 16, 80360-20-9; 17, 62240-37-3; 18, 130179-18-9; 19, 130627-33-7; 20, 132113-31-6; 21, 130627-34-8; 22, 132113-33-8; 23, 132113-32-7; 24, 130627-38-2; 25, 130627-37-1; 26, 132200-44-3; 27, 132200-45-4; 28, 132113-34-9; 29, 136061-56-8; 30, 92579-46-9; 31, 130627-39-3; 33, 130627-40-6; 35, 132113-35-0.

Supplementary Material Available: 2D NMR spectra of pertinent compounds (4 pages). Ordering information is given on any current masthead page.

Utilizing Acetyl Hypofluorite for Chlorination, Bromination, and Etherification of the Pyridine System

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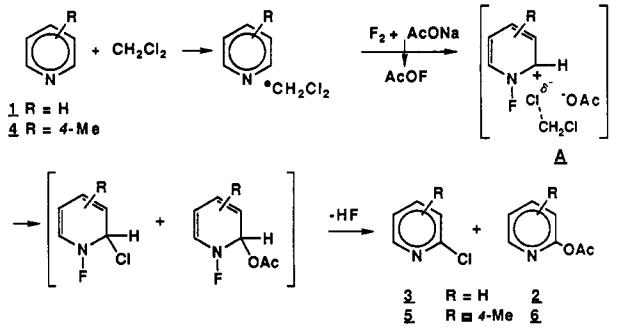
Acetyl hypofluorite, which is easily made from F_2, possesses a strong electrophilic fluorine. This electrophile is able to attach itself to the nitrogen atom of pyridine and activate the ring toward nucleophilic attacks. The ultimate elimination of HF results in an overall easy nucleophilic displacement of the hydrogen of the important 2-position. The nucleophiles used; $Cl^{\delta-}$, $Br^{\delta-}$, and $RO^{\delta-}$, originate from solvents such as CH_2Cl_2, CH_2Br_2, and various primary alcohols. Thus, 2-halo- or 2-alkoxypyridines were formed. The reaction conditions (room temperature, very short reaction times, and good yields) transform the task of direct substitution of the pyridine ring from an extremely difficult to a very easy procedure.

During the last few years we have demonstrated that, apart from its more obvious function as a fluorinating agent, F_2 can be used for an array of processes leading eventually to difficult to obtain, fluorine-free compounds. We have utilized reagents directly prepared from fluorine for introducing double bonds in deactivated saturated sites,[1] for bromination and iodination of aromatic compounds,[2,3] for hydroxylation of saturated tertiary C–H bonds,[4] and for efficient epoxidation of many types of olefins.[5]

The pyridine system is of course very important in organic and pharmaceutical chemistry. Despite numerous research reports dealing with this system, reactions aimed specifically at direct substitution of the parent hydrogen at the important 2-position are very rare. Hydroxylations through arrangements of the appropriate *N*-oxide[6] and Chichibabin's amination[7] are practically the only routes for activating this position. Direct regiospecific halogenation of the pyridine ring is extremely difficult and usually unsatisfactory, and yet, examination of the literature leads to the conclusion that halopyridines constitute a very large part of this heterocycle's chemistry.[8] Recently we have discovered that acetyl hypofluorite (AcOF), made from F_2,[9] can be used for direct acetoxylation of the pyridine ring by utilizing the strong electrophilicity of the oxygen-bound fluorine coupled with the formation of the very strong HF bond.[10] We present here a somewhat unexpected,[11] yet

Scheme I



general, reaction derived from the action of AcOF on the pyridine ring leading to chlorination, bromination, and alkoxylation of this relatively inactive heterocycle.[12] The mild conditions of this reaction and its efficiency (a few seconds at room temperature and usually high yields) are unparalleled for this type of chemistry.[13]

We found that the outcome of applying AcOF to pyridine (1) depends on the solvent system used. As we have already reported,[10] use of apolar solvents such as $CFCl_3$ resulted in 2-acetoxypyridine (2) in excellent yield. With CH_2Cl_2, however, the reaction course is altered and the major product, formed in 70% yield, is 2-chloropyridine

(1) Rozen, S.; Gal, C. *J. Org. Chem.* **1987**, *52*, 2769.
(2) Rozen, S.; Brand, M.; Lidor, R. *J. Org. Chem.* **1988**, *53*, 5545.
(3) Rozen, S.; Zamir, D. *J. Org. Chem.* **1990**, *55*, 3552.
(4) Rozen, S.; Brand, M.; Kol, M. *J. Am. Chem. Soc.* **1989**, *111*, 8325.
(5) Rozen, S.; Kol, M. *J. Org. Chem.* **1990**, *55*, 5155.
(6) Yamamoto, J.; Imagawa, M.; Yamauchi, S.; Nakazawa, O.; Umezu, M.; Matsuura, T. *Tetrahedron* **1981**, *37*, 1871.
(7) Chichibabin, A. E. *Chem. Ber.* **1923**, *56*, 1879.
(8) Scriven, E. F. In *Comprehensive Heterocyclic Chemistry*; Boulton, A. J., McKillop, A., Eds.; Pergamon Press: New York, 1984; Vol. 2, p 198.
(9) Rozen, S.; Lerman, O.; Kol, M. *J. Chem. Soc., Chem. Commun.* **1981**, 443.
(10) Rozen, S.; Hebel, D. *Heterocycles* **1989**, *28*, 249.
(11) It is worth mentioning in this respect Umemoto's and Zupan's work, which, although different from ours, still bears some similarities: (a) Umemoto, T.; Tomizawa, G. *Tetrahedron Lett.* **1987**, *28*, 2705. (b) Stavber, S.; Zupan, M. *Tetrahedron Lett.* **1990**, *31*, 775.
(12) For a preliminary communication, see: Hebel, D.; Rozen, S. *J. Org. Chem.* **1988**, *53*, 1123.
(13) In many cases, substitution of the 2-hydrogen with some other group proceeds very slowly at very high temperatures, and in poor yields. Thus a reaction with KOH yields only traces of 2(1*H*)-pyridone, while autoclave treatment with $CuSO_4$ of some substituted derivatives, such as 3-picoline at 300 °C, gives the corresponding pyridones in less than 7% yield. Tomasik, P.; Woszczyk, A. *Tetrahedron Lett.* **1977**, 2193.

0022-3263/91/1956-6298$02.50/0

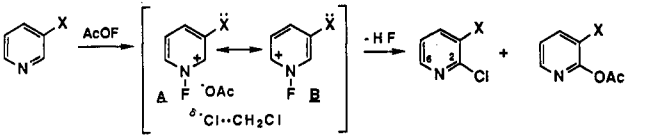
(3), accompanied by an addtional 15% of 2. Similar chlorination at the 2-position was also observed with 4-methylpyridine (4), where 2-chloro-4-methylpyridine (5) was formed, again with a small amount of the corresponding 2-acetoxy derivative (6).

These and other results, described below, indicate that the reaction is governed by the nature of both the pyridine derivative and the solvent. The main demands on the latter are high polarity, ease of approach to the reacting center, and a relatively weak C–X bond. None of these will be of much help, however, if the pyridine derivative is unsuitable. The fact that pyridine reacts, albeit slowly, with CH_2Cl_2[14] indicates that there is always some degree of complexation between these compounds. The basicity of the nitrogen atom and steric effects are the main factors for the ease of complexation. Scheme I outlines the reaction mode that leads to either the 2-chloro or 2-acetoxy derivative.[15]

Solvents with lower polarity such as $CHCl_3$ or CCl_4 or with strong C–Cl bonding as in *n*-BuCl either cannot form as strong a complex as CH_2Cl_2 or are unable to offer the necessary chloride ion eventually needed (intermediate A, Scheme I). As a result, only the corresponding acetoxy derivatives are formed and isolated in higher than 80% yield. On the other hand, the polar *t*-BuCl will donate its chloride atom quite readily, but the approach to the reacting center is hampered by its bulkiness. These two opposite effects are responsible in this latter case for the formation of a 1:2.5 mixture of **3**:**2** in an overall yield of 85%.

Methylene chloride also proved to be an efficient chlorinating agent for many other pyridine derivatives. It was interesting, for example, to find out how pyridines substituted at the 3-position would behave, since two possible sites for chlorination, at 2 and 6, are available. Examination of the results from the reaction of 3-methylpyridine (**7**) with AcOF in CH_2Cl_2 showed that these positions were equally attacked by both chloride and acetoxy moieties (**8**–**11**). The results, however, were different with other types of substituents at the 3-position. Thus 3-chloropyridine (**12**) and 3-benzoylpyridine (**13**) gave only the corresponding 2-chloro compounds (**14** and **15**) in 80% yield. Similar results were observed with methyl nicotinate (**16**) and 3-fluoropyridine (**17**) forming the 2-chloro derivatives (**18** and **19**) along with small amounts of the corresponding 2-acetoxypyridines (**20** and **21**). We believe that the stability of the carbocation intermediate has a major role in governing the outcome of the reaction both in terms of regiospecificity and ratio of chlorination to acetoxylation. It is clear that in the case of 3-methylpyridine the intermediates A and B (Scheme II) do not have a considerable advantage one over the other, leaving sites C-2 and C-6 equally reactive. Since these charged intermediates are quite unstable on account of the fluorine atom at the α position, and since C-2 is also partially hindered by the methyl group, they react quickly with the closest available negative species, which is the small oxygen atom of the acetoxy group rather than the bulky, only partially charged chlorine atom in dichloromethane. Other X groups at the 3-position, however, can enhance the resonance stabilization of the intermediates through extended conjugation (form A). This offers a chance for the acetate to diffuse out of the ion pair cage, direct the substitution exclusively to the 2-position, and encourage a higher proportion of 2-Cl:2-OAc formation. It should be noted that the other resonance form (B) offers only a cross-conjugated π arrangement and therefore is of lesser importance.

Scheme II



7	X = Me	8	10
		9 (2-H,6-Cl)	11 (2-H,6-OAc)
12	X = Cl	14	
13	X = COPh	15	
16	X = COOMe	18	20
17	X = F	19	21

The basicity of the heterocyclic ring has an important role in this reaction. Compounds with very low basicity such as 2-cyano-, 2-chloro-, or 3,5-dichloropyridine cannot interact with the electrophilic fluorine of the acetyl hypofluorite, and only the starting material is eventually isolated. With somewhat stronger bases such as 1,4-pyrazine, the complexation step with the solvent cannot be accomplished and only the acetoxy derivative is obtained.[10] With still stronger bases, there is a clear hierarchy based upon the nucleophilicity of the lone pair of the nitrogen. Thus, it is easy to see that when an equimolar mixture of pyridine (**1**) and 3-chloropyridine (**12**) was reacted with an excess of AcOF in CH_2Cl_2, only after a full conversion of **1** to **3** was achieved did the much weaker base **12** start to react, producing the expected 2,3-dichloropyridine (**14**).

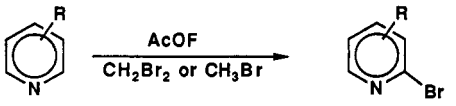
Chlorination was not the only reaction that could be achieved by this method. Replacing methylene chloride with either methylene bromide or methyl bromide presented a rare opportunity for substituting the hydrogen at the 2-position with bromine. As far as we know, there is not a single method for such direct regiospecific bromination of the pyridine ring. Thus, when pyridine (**1**) reacted with acetyl hypofluorite in the presence of either CH_2Br_2 or CH_3Br, 2-bromopyridine (**22**) was obtained in about 60% yield along with an additional 20% of the acetoxy derivative (**2**). Similar results were obtained with 4-methyl- and 4-acetylpyridine (**4** and **23**), which yielded, correspondingly, 2-bromo-4-methylpyridine (**24**) and 2-bromo-4-acetylpyridine (**25**), again accompanied by some minor amounts of the corresponding acetates, **6** and **26**. No surprises were reocrded with 3-substituted pyridines concerning the regioselectivity. Thus, for example, 3-chloropyridine (**12**) was converted in high yield to 2-bromo-3-chloropyridine (**27**) with no detectable formation of the 6-bromo derivative.

It was of interest to compare the efficiency of dichloromethane vs dibromomethane in this reaction. On one hand, CH_2Cl_2 should give a better complex with the pyridine ring because it is both smaller and more polar than CH_2Br_2. On the other hand, the C–Br bond is weaker than the C–Cl one, a fact that should facilitate the bromination process. Thus when pyridine was reacted with AcOF in an equimolar mixture of CH_2Cl_2 and CH_2Br_2 as solvent, the two opposite factors canceled each other and 2-chloro- and 2-bromopyridine (**3** and **22**) were obtained in approximately equal amounts. However, when CH_2BrCl

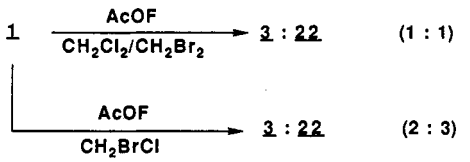
(14) Nevstad, G. O.; Songstad, J. *Acta Chem. Scand., Ser. B* **1984**, *38*, 469.

(15) We have not found any significant amount of 4-substitution. This is in agreement with the fact that the most strongly polarized solvent molecules are electrostatically bonded to the region between the nitrogen atom and the 2-position.

was used as the solvent, the bond strength factor predominated and the ratio of **3** to **22** was found to be 2:3.



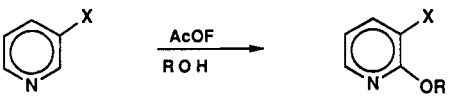
1	R = H	22	+	2
4	R = 4-Me	24	+	6
23	R = 4-Ac	25	+	26
12	R = 3-Cl	27		



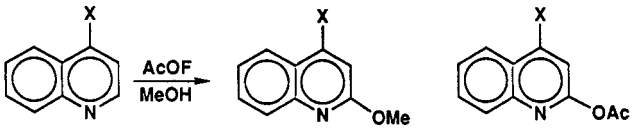
Naturally the next step was an attempt to introduce iodine into the pyridine ring by employing CH_3I or CH_2I_2. However, these solvents were immediately oxidized by the AcOF to produce only iodine. This result directed us to search for solvents that are not rapidly oxidized by the AcOF, but still possess a highly nucleophilic moiety. Primary alcohols seem to satisfy both conditions.[16]

Although direct halogenation of the pyridine system is difficult, inefficient, and rarely described in the literature, there are still some methods devised for this purpose. Direct alkoxylation of this heterocycle, however, is without a precedent. The strong electrophilic fluorine of the acetyl hypofluorite opens new possibilities in this field. Adding AcOF to a methanolic solution of pyridine results in a fast reaction, with formation of two products easily identified as 2-methoxypyridine (**28**, 70% yield) and a small amount of the acetoxy derivative **2**. It is important not to use a large excess of AcOF in this case since 2-methoxypyridine can further react with AcOF, and the corresponding *N*-fluoro intermediate thus formed cannot eliminate HF, a fact that leads eventually to tar formation. Since, however, 2-methoxypyridine is considerably less basic than pyridine, it is easy to monitor the reaction and stop it when a full conversion is achieved. Other primary alcohols gave very similar results. Ethanol, butanol, and 1,1,1-trifluoroethanol were all reacted with pyridine to yield about 70% of the corresponding ethers (**29–31**). Some competitive reactions clearly showed that the more polar solvent forms a stronger complex with the pyridine ring, leading to a higher yield of the appropriate ether. When AcOF was reacted with pyridine dissolved in an equimolar mixture of EtOH and CF_3CH_2OH, **29** and **31** were formed in a ratio of 1:2. Similar competitive reactions with MeOH/EtOH and MeOH/CF_3CH_2OH were also performed, resulting, in the first case, in a higher proportion of 2-methoxypyridine, while the second mixture yielded practically equal amounts of **28** and **31**. Not surprisingly, when such a competition was set up between MeOH and CH_2Cl_2, most of the product proved to be the ether **28** and only a trace of the chloro derivative **3** was formed.

Of course, pyridine is not the only compound that successfully reacts with the AcOF/ROH combination. Other examples include 3-chloropyridine, which was converted to 2-methoxy-3-chloropyridine (**32**), while quinoline (**33**)



X = H; R = Me	28	+	2	
X = H; R = Et	29	+	2	
X = H; R = Bu	30	+	2	
X = H; R = CF_3CH_2	31	+	2	
X = Cl; R = Me	32			



33	X = H	34	35
36	X = Me	37	38

and 4-methylquinoline (**36**) were methoxylated in higher than 60% yield. This is in contrast to quinoline's behavior with methylene chloride and bromide, where only acetoxylation, but not halogenation, was observed. We attribute this difference to the fact that quinoline is a weaker base than pyridine and can form complexes only with the more polar alcohols.

In conclusion, it has been shown that fluorine can be used, directly or through some in situ prepared agent, to accomplish chemical transformations even on unreactive systems such as the pyridine family, employing extremely mild conditions. In a broader sense, we hope chemists will begin to consider this element as a "legitimate" tool not only to perform reactions aimed at introducing this atom into various molecules but also for a broad spectrum of organic syntheses.

Experimental Section

^1H NMR spectra were recorded with a Bruker WH-360 spectrometer with $CDCl_3$ as the solvent. They are reported in parts per million downfield from Me_4Si serving as an internal standard. Mass spectra were measured with a Du Pont 21-491B spectrometer. IR spectra were recorded as neat films, in $CHCl_3$ solution, or in KBr pellets on a Perkin–Elmer 177 spectrometer, and the wavelengths are reported in cm^{-1} units.

General Procedure for Work with Fluorine. Fluorine is of course a strong oxidizer and a very corrosive material. An appropriate vacuum line made from copper or Monel in a well-ventilated area should be constructed for working with this element. Variations of such vacuum lines are described, for example, in Matheson Report No. G-115B or in Vyplel's review.[17] Although we have never had an emergency situation, traps filled with either soda lime or alumina should be attached to the vacuum line as a safety device in case the primary or secondary fluorine tank should be evacuated. The fluorine mixtures with N_2 are prepared in a secondary container,[18] and the composition can be monitored by controlling the partial pressure of each gas with pressure gauges deactivated for work with fluorine (Matheson, Air Products, and others). The reactions themselves can be carried out in glass vessels. Efficient mixing, which is an especially important factor for obtaining higher yields, is achieved by using a vibromixer (Chemapec), which also ensures a fine dispersion of the gas bubbles. If elementary precautions are taken, work with fluorine

(16) Secondary alcohols have also been tried, but like the iodine-containing solvents, they were rapidly oxidized by the AcOF.

(17) Vyplel, H. *Chimia* **1985**, *39*, 305.

(18) Various mixtures of fluorine in inert gases such as N_2 or He are commerically available.

Table I

compd no.	yield, % [mp, °C]	^{1}H NMR	IR, cm^{-1}; MS, m/e
3[a]	70		
5[20]	60 [oil]	8.0 (1 H, d, J = 4.8 Hz), 6.97 (1 H, d, J = 1.5 Hz), 6.88 (1 H, dd, J_1 = 4.8, J_2 = 1.5 Hz), 2.2 (3 H, s)	1580, 1560, 1370
8[20]	15[b] [oil]	8.19 (1 H, dd, J_1 = 4.8, J_2 = 2.1 Hz), 7.52 (1 H, dd, J_1 = 7.8, J_2 = 2.1 Hz), 7.07 (1 H, dd, J_1 = 7.8, J_2 = 2.1 Hz), 2.30 (3 H, s)	
9[20]	15[b] [oil]	8.17 (1 H, d, J = 2.5 Hz), 7.45 (1 H, dd, J_1 = 8.5, J_2 = 2.5 Hz), 7.14 (1 H, d, J = 8.5 Hz), 2.28 (3 H, s)	
14[a]	80 [65][c]		
15	80 [oil][d]	8.56 (1 H, dd, J_1 = 4.7, J_2 = 1.9 Hz), 7.81 (2 H, d, J = 7.5 Hz), 7.76 (1 H, dd, J_1 = 7.5, J_2 = 1.9 Hz), 7.65 (1 H, t, J = 7.5), 7.5 (2 H, d, J = 7.5 Hz), 7.4 (1 H, dd, J_1 = 7.5, J_2 = 4.7 Hz)	1670; 219, 217 (M)$^+$
18[21]	60 [102][e]	8.44 (1 H, dd, J_1 = 4.5, J_2 = 1.7 Hz), 8.25 (1 H, dd, J_1 = 7.5, J_2 = 1.7 Hz), 7.22 (1 H, dd, J_1 = 7.5, J_2 = 4.5 Hz), 3.92 (3 H, s)	
19[22]	40 [oil][f]	8.22 (1 H, br d, J = 4.6 Hz), 7.48 (1 H, dd, J_1 = 8.2, J_2 = 1.5 Hz), 7.26 (1 H, ddd, J_1 = 8.2, J_2 = 4.6, J_3 = 3.6 Hz); ^{19}F NMR −118 ppm (dd, J_1 = 10, J_2 = 3.4 Hz)	
22[a]	60 [oil]		
24[23]	55 [oil]	8.17 (1 H, d, J = 5 Hz), 7.27 (1 H, s), 7.03 (1 H, d, J = 5 Hz), 2.29 (3 H, s)	1575, 1560, 1360
25	60 [55][g]	8.56 (1 H, d, J = 4.9 Hz), 7.92 (1 H, d, J = 1.5 Hz), 7.69 (1 H, dd, J_1 = 4.9, J_2 = 1.5 Hz), 2.64 (3 H, s)	1650; 200, 198 (M)$^+$, 185, 183 (M − Me)$^+$
27	80 [59][h]	8.29 (1 H, dd, J_1 = 4.6, J_2 = 1.5 Hz), 7.76 (1 H, dd, J_1 = 8, J_2 = 1.5 Hz), 7.25 (1 H, dd, J_1 = 8, J_2 = 4.6 Hz)	−; 191, 193, 195 (M)$^+$
28[a]	70 [oil]		
29[11b]	70 [oil]	8.15 (1 H, dd, J_1 = 5.5, J_2 = 1.7 Hz), 7.49 (1 H, dt, J_1 = 8.5, J_2 = 1.7 Hz), 6.8 (1 H, dt, J_1 = 5.5, J_2 = 1.7 Hz), 6.7 (1 H, d, J = 8.5 Hz), 4.34 (2 H, q, J = 6.5 Hz), 1.55 (3 H, t, J = 6.5 Hz)	1630, 1450, 1260
30[a]	70 [oil]		
31	70 [oil][i]	8.14 (1 H, dd, J_1 = 5, J_2 = 1.5 Hz), 7.65 (1 H, dt, J_1 = 8, J_2 = 1.5 Hz), 6.8 (1 H, dt, J_1 = 5, J_2 = 1.5 Hz), 6.7 (1 H, d, J = 8 Hz), 4.72 (2 H, q, J = 9 Hz); ^{19}F NMR −74.4 ppm (t, J = 9 Hz)	1580, 1470, 1275
32[24]	75 [oil]	8.05 (1 H, dd, J_1 = 4.8, J_2 = 1.5 Hz), 7.62 (1 H, dd, J_1 = 7.7, J_2 = 1.5 Hz), 6.84 (1 H, dt, J_1 = 7.7, J_2 = 4.82 Hz), 4.02 (3 H, s)	1580, 1450, 1250
34[25]	60 [oil]	7.92 (1 H, d, J = 8 Hz), 7.85 (1 H, d, J = 8.3 Hz), 7.68 (1 H, dd, J_1 = 7, J_2 = 1 Hz), 7.6 (1 H, dt, J_1 = 7, J_2 = 1 Hz), 7.35 (1 H, dt, J_1 = 8, J_2 = 1 Hz), 6.87 (1 H, d, J = 8.3 Hz), 4.06 (3 H, s)	1610, 1480, 1210
37[25]	60 [oil]	7.84 (1 H, d, J = 8 Hz), 7.75 (1 H, d, J = 8 Hz), 7.56 (1 H, t, J = 8 Hz), 7.31 (1 H, d, J = 8 Hz), 6.67 (1 H, s), 4.02 (3 H, s), 2.49 (3 H, s)	1605, 1570, 1475, 1200

[a] Commercially available. [b] About 30% of the corresponding acetate was also formed. [c] From cyclohexane. [d] Anal. Calcd for $C_{12}H_8ClNO$: C, 66.36; H, 3.69; Cl, 16.13. Found: C, 65.74; H, 3.92; Cl, 16.16. [e] From EtOAc. [f] About 40% of the corresponding acetate was also formed. [g] From petroleum ether. Anal. Calcd for C_7H_6BrNO: C, 42.00; H, 3.00. Found: C, 42.33; H, 3.08. [h] From ether. Anal. Calcd for C_5H_3BrClN: C, 31.17; H, 1.56; Cl, 18.44; Br, 41.56. Found: C, 30.93; H, 1.64; Cl, 17.69; Br, 40.96. [i] Anal. Calcd for $C_7H_6F_3NO$: C, 47.46; H, 3.39. Found: C, 48.01; H, 3.25.

is relatively simple, and we have never had an accident while working with it.

Preparation of AcOF and Its Reaction with Pyridines. A mixture of 15% F_2 in N_2 was bubbled into a cold (−75 °C) suspension of 8 g of AcONa in 400 mL of $CFCl_3$ and 50 mL of AcOH.[19] The amount of the AcOF thus obtained can be easily determined by reacting aliquots of the reaction mixture with aqueous KI solution and titrating the liberated iodine. After the desired concentration of AcOF is achieved (usually around 0.1–0.15 M), the oxidizing solution was added in portions of 10–20 mL each to the desired pyridine derivative, which was dissolved in the appropriate solvent (room temperature). The reactions were usually carried out on scales of 30–40 mmol using a 1.5–2-fold excess of AcOF, with conversions higher than 95%. They were usually monitored by GC, TLC, or NMR and in most cases were complete within a few minutes. The reaction was terminated by pouring it into 500 mL of thiosulfate solution, washing the organic layer with a $NaHCO_3$ solution followed by water until neutral, drying the organic layer over $MgSO_4$, and finally evaporating the solvent. The crude reaction mixture was usually subjected to vacuum flash chromatography using silica gel 60-H (Merck), with mixtures of EtOAc in petroleum ether serving as eluent. The halo and the alkoxy products were eluted first, followed by the more polar 2-acetoxy derivatives. Some of the compounds are not well characterized in the literature, so their physical data along with the appropriate references and yields are given in Table I.

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Registry No. 1, 110-86-1; 2, 3847-19-6; 3, 109-09-1; 4, 108-89-4; 5, 3678-62-4; 6, 108168-80-5; 7, 108-99-6; 8, 18368-76-8; 9, 18368-64-4; 10, 1006-97-9; 11, 1007-56-3; 12, 626-60-8; 13, 5424-19-1; 14, 2402-77-9; 15, 80099-81-6; 16, 93-60-7; 17, 372-47-4; 18, 40134-18-7; 19, 17282-04-1; 20, 135773-41-0; 21, 2267-37-0; 22, 109-04-6; 23, 1122-54-9; 24, 4926-28-7; 25, 111043-06-2; 26, 135773-42-1; 27, 96424-68-9; 28, 1628-89-3; 29, 14529-53-4; 30, 27361-16-6; 31, 113674-88-7; 32, 13472-84-9; 33, 91-22-5; 34, 6931-16-4; 35, 30074-79-4; 36, 491-35-0; 37, 15113-00-5; 38, 121607-59-8; 2-cyanopyridine, 100-70-9; 3,5-dichloropyridine, 2457-47-8; acetyl hypofluorite, 78948-09-1.

(19) Alternatively, 20 g of AcONa·AcOH dispersed in 450 mL of $CFCl_3$ can be used. The solvated salt can be made by leaving anhydrous AcONa over AcOH in a closed desiccator overnight.

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