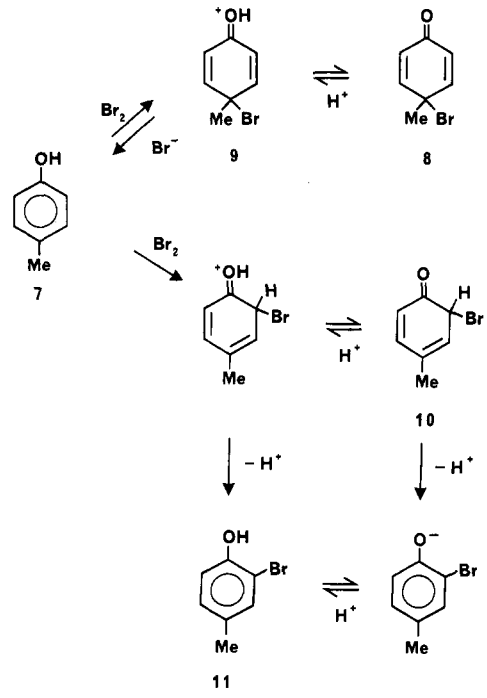
Scheme II



might occur ipso to the substituent. Support for this idea comes from the work of Fischer and Henderson who have isolated 4-chloro-2,5-cyclohexadienones resulting from ipso chlorine attack upon *p*-alkylphenols in nonaqueous solvents.[16] Using *p*-cresol (7) as substrate in aqueous bromination, we find that we can indeed observe an intermediate at about 250 nm. However, the absorbance change associated with its disappearance is small (only 10% of that found for 4 or its dimethyl analogue), and the major portion of the product appears before the intermediate disappears. The first-order decay of the intermediate, presumed to be the 2,5-cyclohexadienone 8, shows acid catalysis (Figure 1) *and* is linearly dependent upon bromide ion concentration.

Our observations for *p*-cresol are rationalized by Scheme II. The substrate is mainly attacked by bromine at an ortho position to give a 2,4-cyclohexadienone **10**, which is converted through to product fairly quickly.[17] A minor amount (~10%) of bromine attack occurs ipso to give the observed intermediate 8. This undergoes debromination by bromide ion attack upon the protonated form **9** to give back *p*-cresol and bromine and so is eventually converted to the ortho bromo product 11.

In summary, we have observed the formation and decay of intermediates in the aqueous bromination of phenol, 2,6-dimethylphenol, and *p*-cresol. They exhibit kinetic and spectral properties[19] that are consistent with them being 4-bromo-2,5-cyclohexadienones.

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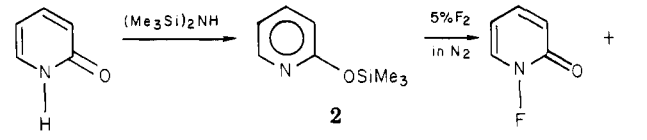
1-Fluoro-2-pyridone: A Useful Fluorinating Reagent

Summary: 1-Fluoro-2-pyridone (mp 50–53 °C) has been prepared by reaction of 5% fluorine in nitrogen and 2-(trimethylsiloxy)pyridine in $FCCl_3$ at −78 °C. After sublimation, the pyridone is used as a selective fluorinating agent in the preparation of some fluoromalonates.

Sir: Since many organic compounds acquire interesting new properties on the introduction of a fluorine atom, methods of selectively introducing fluorine into organic molecules are of interest. Many of the procedures now used to prepare fluorinated molecules employ extremely reactive, corrosive, toxic, and often gaseous materials that require specialized equipment. We wish to report the synthesis of a solid organic molecule, 1-fluoro-2-pyridone, that shows potential as a fluorine transfer agent. 1-Fluoro-2-pyridone (1) was chosen as a potentially selective fluorinating reagent[1] because of several attractive features: (1) the labile N–F linkage, (2) the aromatizability of the pyridone nucleus after fluorination (a driving force for reaction), (3) the likelihood that the compound would be solid, and (4) the absence of toxic or explosive reaction byproducts. Furthermore, a synthetic route to 1 was readily envisioned. Because of the affinity of silicon for fluorine as well as a low-energy six-membered transition state available for reaction, 2-(trimethylsiloxy)pyridine[3] (2) was chosen for treatment with 5% fluorine in nitrogen[4] (eq 1). Furthermore, use of the siloxypyridine eliminated the possibility of interference by HF that might occur during fluorination of the unsubstituted pyridone, 3.



3 2 1

Me_3SiF (1)

1-Fluoro-2-pyridone (1) is particularly notable because no unusual safety precautions are required for either its preparation or its use. The fluorination system was constructed entirely from glass vessels and Tygon tubing; Kel-F was used to lubricate the joints. The diluted fluorine[4] was passed through solid NaF and into the reactor,

(16) Fischer, A.; Henderson, G. N. *Can. J. Chem.* **1979**, *57*, 552.
(17) 2,4-Cyclohexadienones (e.g., **10**) are kinetically much less stable than the 2,5-isomers.[16,18]
(18) Miller, B. *Acc. Chem. Res.* **1975**, *8*, 245.
(19) The absorption maxima for 4, 2,6-dimethyl-substituted 4, and 8 are about 240, 250, and 250 nm, respectively. In the first two cases the extinction coefficients are about 10 000, as found for isolable 2,5-cyclohexadienones (see ref 2, 3, 10 and references therein). In contrast, the isomeric 2,4-cyclohexadienones have maxima around 310 nm and somewhat smaller extinction coefficients.[20]
(20) Miller, B. *J. Am. Chem. Soc.* **1970**, *92*, 6246, 6252. Quinkert, G.; Durner, G.; Kleiner, E.; Haupt, E.; Leibfritz, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 556. Lasne, M. C.; Ripoli, J. L. *Tetrahedron Lett.* **1980**, *21*, 463.

(1) Attempts to prepare *N*-fluorosuccinimide from succinimide or one of its salts (potassium, sodium, calcium, or silver) and various fluorinating agents (fluorine, trifluoromethyl hypofluorite, or perchloryl fluoride) in a variety of solvents (water, freon, chloroform, acetonitrile, methylene chloride, or trifluoroacetic acid) at temperatures ranging from −78 °C to room temperature were unsuccessful. Recently, *N*-fluoroperfluorosuccinimide has been prepared,[2] however its chemistry was not reported.
(2) Yagupol'skii, Ya. L.; Savina, T. I. *Zh. Org. Khim.* **1981**, *17*, 1330.
(3) Buchanan, M. J.; Cragg, R. H.; Steltner, A. *J. Organomet. Chem.* **1976**, *120*, 189.
(4) Available from Air Products. Although other fluorinating agents such as CF_3OF might have produced a higher yield of **3**, these reagents generally generate toxic gaseous products (e.g., COF_2) and are more expensive than fluorine diluted with nitrogen.

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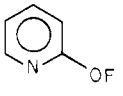
Table I. Preparation of Fluoromalonates Using 1-Fluoro-2-pyridone

$RCH(CO_2Et)_2$, R =	moles pyridone / moles malonate	time, h	fluorinated product	yield,[a] %	^{19}F NMR data,[b] ppm
Ph	1.0	1	$PhCF(CO_2Et)_2$	20	160 (s)
Ph	2.0	16	$PhCF(CO_2Et)_2$	39	162 (s)
			$PhCHFCO_2Et$	5	181 (d)[d]
$PhCH_2$	1.0	1	$PhCH_2CF(CO_2Et)_2$	30	166 (t)
$PhCH_2$	2.0	16	$PhCH_2CF(CO_2Et)_2$	33	165 (t)
CH_3	2.0	1.7	$CH_3CF(CO_2Et)_2$	17	158 (q)
H	2.0	16	$F_2C(CO_2Et)_2$	5	113 (s)[e]
			$HCF(CO_2Et)_2$[c]	9	196 (d)

[a] Recovered unreacted malonate accounts for the remainder of product. [b] ppm downfield from $FCCl_3$. [c] Two other signals were observed in the ^{19}F NMR spectrum, at 74 and 144 ppm. [d] Fraisse-Jullien et al. (Fraisse-Jullien, R.; Thoi-Lai, N. *Bull. Soc. Chim. Fr.* **1967**, 3904) report a signal 182 ppm upfield from $FCCl_3$ for the methyl ester. [e] Bloshchitsa et al. (Bloshchitsa, F. A.; Burmakov, A. I.; Kunshenko, B. V.; Alekseeva, L. A.; Bel'ferman, A. L.; Pazderskii, Yu. A.; Yagupol'skii, L. M. *Zh. Org. Khim.* **1981**, *17*, 1417) reported an ^{19}F shift 34.6 ppm upfield from CF_3CO_2H (equivalent to 111 ppm upfield from $FCCl_3$).

consisting of a three-necked round-bottom flask equipped with a gas dispersion tube (gas inlet), a magnetic stirring bar, and an adapter that allowed the exit gases to be vented through two slightly acidic KI traps. In a typical preparation, 1.896 g of 2-(trimethylsiloxy)pyridine (**2**, 11.35 mmol) was dissolved in 25 mL of $FCCl_3$ and cooled to −78 °C before the diluted fluorine was introduced at a rate such that the flow in the second trap was about 15–25 mL per min. After approximately 7 h, the second trap started to darken noticeably and the fluorination was discontinued. Nitrogen was bubbled through the apparatus for about 1 h to purge the system of residual fluorine. While the solvent was being rotary evaporated from the yellow solution containing precipitate at 0 °C, the mixture turned dark brown. The dark oily residue, 1.326 g, was chromatographed on silica gel (Merck 60 extra pure) with ethyl acetate to give 0.804 g of 1-fluoro-2-pyridone (63% yield). This was then sublimed at 40 °C (0.2 mm).[5] The product, a waxy white solid, mp 50–53 °C, gave multiplets between 6.0 and 8.0 ppm in the proton NMR spectrum. Infrared absorption was observed at 1660, 1675, and 880 cm^{-1}. Since the ^{19}F NMR signal for fluorine adjacent to oxygen is generally downfield from $FCCl_3$,[6] the single peak at 33 ppm upfield from $FCCl_3$ is consistent with structure **1**.

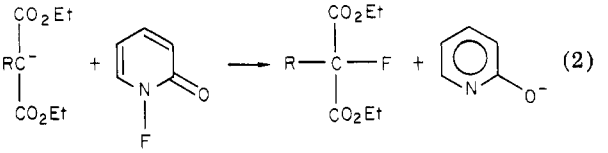
Other spectral data also support structure **1** for the fluoropyridone. The infrared and ultraviolet spectral information for **1** as well as the proton and ^{13}C NMR spectra allow the conclusion that compound **1**, not its aromatic tautomer **4**, is the product of the fluorination reaction.



4

This spectral data is available as supplementary material (see paragraph at the end of paper about supplementary material).

Fluorination of a series of substituted malonates[7] with 1-fluoro-2-pyridone illustrates the effectiveness of this reagent (eq 2). In a typical experiment, the sodium salt



(2)

of diethyl malonate in toluene was treated with the fluoropyridone at room temperature. The following day the reaction mixture was extracted with 10% HCl and water and dried over magnesium sulfate. After removal of solvent, the residue was analyzed by gas chromatography on a 30-m OV-17 column with a flame ionization detector (Hewlett-Packard 5880A Series GC). The results, assuming equal response factors, are shown in Table I along with the ^{19}F NMR shifts.

Although this is not the first report of the transfer of a fluorine from nitrogen to carbon,[8] it is the most practical. The Banks'[8a] and Knunyants'[8b] procedures both use *N*-fluoroperfluoropiperidine, which, while relatively stable, is formed in poor yield by electrofluorination in anhydrous HF.[9] Since 1-fluoro-2-pyridone is readily prepared and since it is an effective fluorine transfer agent, we are continuing to explore the scope of reactions involving the pyridone. In order to avoid problems due to the instability of **1**, in situ generation of the reagent is also being investigated.

Acknowledgment. We are grateful for support of this investigation from NIH Biomedical Research Support Grant RR07071.

Supplementary Material Available: Full ^1H and ^{13}C NMR data as well as UV and IR data for compounds **1–3** (2 pages). Ordering information is given on any current masthead page.

(5) Anal. Calcd for C_5H_4NOF: C, 53.10; H, 3.57; N, 12.39. Found: C, 51.99; H, 3.21; N, 11.99. Mass spectrum (70 eV), *m/z* 113 (M^+). The pyridone is kept in the freezer as it darkens and decomposes slowly; however, it maintains its effectiveness as a fluorine transfer agent for at least a week.

(6) Dungan, C. H.; Van Wazer, J. R. "Compilation of Reported F^{19} NMR Chemical Shifts (1951 to Mid-1967)"; Wiley-Interscience: New York, 1970.

(7) Dialkyl fluoromalonates have also been prepared by fluorination with perchloryl fluoride. Gershon, H.; Renwick, J. A. A.; Wynn, W. K.; D'Ascoli, R. *J. Org. Chem.* **1966**, *31*, 916.

(8) (a) Banks, R. E.; Williamson, G. E. *Chem. Ind. (London)* **1964**, *1864*. (b) Polishchuk, V. R.; Medvedev, B. Ya.; Bubnov, N. N.; German, L. S.; Knunyants, I. L. *Bull. Acad. Sci. USSR Div. Chem. Sci. (Engl. Transl.)* **1973**, *21*, 2736.

(9) Simmons, T. C.; Hoffmann, F. W.; Beck, R. B.; Holler, H. V.; Katz, T.; Koshar, R. J.; Larsen, E. R.; Mulvaney, J. E.; Paulson, K. E.; Rogers, F. E.; Singleton, B.; Sparks, R. E. *J. Am. Chem. Soc.* **1957**, *79*, 3429.

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