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Communications

Direct Aromatic Iodination Using IF Prepared from I_2 and F_2

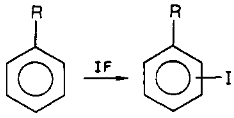
Summary: IF, made directly from the corresponding elements, may be used without any catalyst as an electrophilic iodinating agent in its reactions with activated and deactivated aromatic rings.

Sir: Of all aromatic halogenations, iodination suffers most from lack of versatility in methods of preparation. Direct iodination requires the presence of oxidizing agents such as HNO_3, which first oxidizes the iodine, while the more popular indirect method starts with an appropriate aniline derivative which is converted to the corresponding diazonium salt and quenched with iodine or KI.

As part of our goal to demonstrate that F_2 can serve as a unique reagent, even for the preparation of fluorine free products,[1] we report a method for the direct iodination of activated and deactivated aromatic rings.

A cold (−78 °C) suspension of iodine in $CFCl_3$ reacts with F_2 to produce yet another suspension proved to be IF.[2] This reagent seems to be less reactive then ClF or BrF, since it is apparently a cluster compound with molecules interconnected through $I \cdots F$ bridges.[3] Still, the difference in electronegativity of the atoms enables ionic reactions to occur with various organic substrates.[2a,b] This inherent polarity is the basis of our belief that this compound can serve as a source for electrophilic iodine strong enough to react with most types of aromatic compounds without the help of any external Friedel–Crafts catalyst.[4]

Toluene reacts with IF at −78 °C to produce a 1:1 mixture of *o*- and *p*-iodotoluene in a combined yield of 65%. Raising the temperature to −20 °C enables the introduction of an additional iodine atom and 2,4-diiodotoluene is formed in about 50% yield. Similar behavior was observed with benzene, where *p*-diiodobenzene could be obtained in greater than 70% yield. More weakly activated compounds like phenyl acetate are iodinated at the para position in 40% yield. When the aromatic ring is strongly activated, as in the case of anisole, only tars are produced, even at −78 °C. However, from 4-nitroanisole, 2-iodo-4-nitroanisole was isolated in 80% yield.[5]



Perhaps the most important feature of this reaction is the ability of this reagent to iodinate deactivated aromatic rings. Although nitrobenzene failed to react, benzonitrile produced *m*-iodobenzonitrile in good yield, but only in moderate conversion, even after 16 h. Ethyl benzoate and benzaldehyde however were fully converted to the corresponding *m*-iodo derivatives, each in 85% yield, although a relatively long reaction time, up to 16 h, was required for ethyl benzoate.

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Registry No. IF, 13873-84-2; PhMe, 108-88-3; *o*-IC_6H_4Me, 615-37-2; *p*-IC_6H_4Me, 624-31-7; 2,4-$(I)_2$-MeC_6H_3, 32704-08-8; PhH, 71-43-2; PhI, 591-50-4; *p*-IC_6H_4I, 624-38-4; PhOAc, 122-79-2; *p*-IC_6H_4OAc, 33527-94-5; *p*-$NO_2C_6H_4OMe$, 100-17-4; 1-OMe-2-I-4-$NO_2C_6H_3$, 5399-03-1; PhCN, 100-47-0; *m*-IC_6H_4CN, 69113-59-3; $PhCO_2Et$, 93-89-0; *m*-$IC_6H_4CO_2Et$, 58313-23-8; PhCHO, 100-52-7; *m*-IC_6H_4CHO, 696-41-3; PhOMe, 100-66-3; $PhNO_2$, 98-95-3.

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(2) (a) Rozen, S.; Brand, M. *J. Org. Chem.* **1985**, *50*, 3342. (b) Rozen, S.; Brand, M. *J. Org. Chem.* **1986**, *51*, 222. (c) Schmeisser, M.; Sartori, P.; Naumann, D. *Chem. Ber.* **1970**, *103*, 880.

(3) Lehmann, E.; Naumann, D.; Schmeisser, M. *J. Fluorine Chem.* **1976**, *7*, 135.

(4) The same reasoning led us to explore first the possibility of using the much more reactive BrF for similar purposes. Rozen, S.; Brand, M. *J. Chem. Soc., Chem. Commun.* **1987**, 752.

(5) Experimental details for IF preparation at −78 °C can be found in ref 2a. A cold (−78 °C) $CHCl_3$ solution of the aromatic substrate was added to the IF suspension. The reaction was vigorously agitated with a Vibromixer (ref 2a) and monitored by GC. In the case of deactivated aromatic substrates the cooling bath was removed after 1 h and the reaction temperature was allowed to increase gradually to room temperature (about 2 h). Most of the aromatic iodination took place at that time although agitating for a longer period at room temperature increased the yields somewhat. The reaction mixture was then poured into a thiosulfate solution to cause complete reduction of excess I_2 and IF. The organic layer was washed with carbonate until neutral and the products were purified either by chromatography or crystallization. They were fully characterized and were shown to be identical with authentic samples or their spectral data were in excellent agreement with those reported in the literature.

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Chlorination, Bromination, and Oxygenation of the Pyridine Ring Using AcOF Made from F_2

Summary: Acetyl hypofluorite reacts with pyridines in halogenated solvents or alcohols to give the corresponding 2-halo- or 2-alkoxypyridines.

Sir: Regiospecific halogenation of a pyridine is a formidable task. The reactions are usually carried out at several hundred degrees and in many cases require reagents such as oleum. Since the nature of the halogenating agent is sensitive to changes in conditions it is difficult to define the precise nature of the reacting species, resulting usually in mixtures of several halogenated products in low to moderate yields. Regiospecific substitution of pyridinic hydrogen by an alkoxy group has not yet been achieved. Despite these limiting factors these reactions have been dominant in the recent pyridine related chemical literature.[1]

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