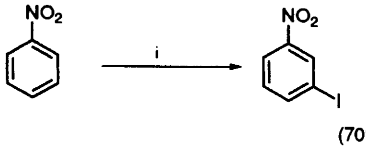
Elemental Fluorine as an 'Enabler' for Generation of Powerful Electrophiles from Other Halogens

Richard D. Chambers,[*a] **Christopher J. Skinner,**[a] **Malcolm Atherton**[b] **and John S. Moilliet**[b]

[a] *Department of Chemistry, University Science Laboratories, South Road, Durham, UK DH1 3LE*
[b] *BNFL Fluorochemicals Ltd., Bldg. 619, Salwick, Preston, UK PR4 0XJ*

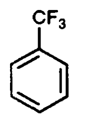
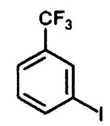
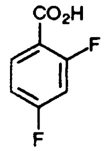
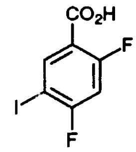
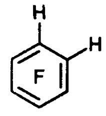
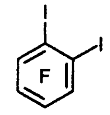
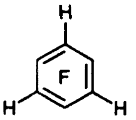
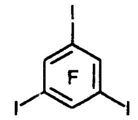
A new direct iodination procedure for aromatic systems involves iodine, substrate, sulfuric acid, and elemental fluorine at room temperature.

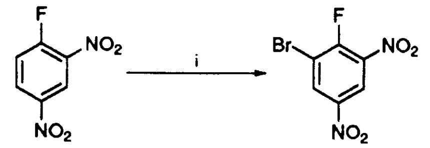
Direct iodination of aromatic compounds is very difficult, especially for deactivated systems, and current methodology is either of limited reactivity or involves relatively harsh conditions.[1]



Scheme 1 *Reagents and conditions*: i, I_2, C_6F_{12}, H_2SO_4, 10% F_2–N_2, room temp., 70%

Table 1 Iodination and polyiodination of aromatic systems, induced by fluorine (10% F_2–N_2)

Substrate	Product	Conditions	Conversion (%)	Yield (%)
		Room temp. H_2SO_4, CF_2ClCCl_2F, I_2	100	83
		Room temp. H_2SO_4, CF_2ClCCl_2F, I_2	100	77
		Room temp. H_2SO_4, CF_2ClCCl_2F, I_2	100	76
		Room temp. H_2SO_4, CF_2ClCCl_2F, I_2	100	63



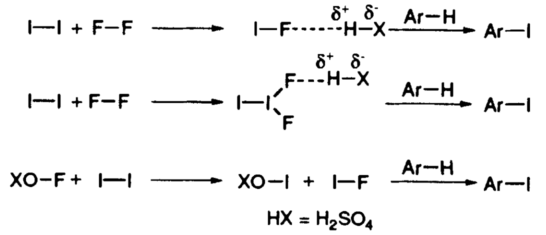
Scheme 2 *Reagents and conditions*: i, Br_2, H_2SO_4, 10% F_2–N_2, room temp., 60%

An accompanying paper describes the remarkable influence of concentrated acid on the reactivity of elemental fluorine as an electrophile and we here describe a development of this technique for a very simple and versatile method for iodination of aromatic systems. This procedure involves using a mixture containing iodine, concentrated sulfuric acid and the substrate and then simply passing fluorine diluted with nitrogen into this mixture at room temperature. For example, nitrobenzene is converted to 3-iodonitrobenzene (100% conversion, 70% isolated yield) under these conditions (Scheme 1). If required, sulfuric acid can be used alone or in combination with inert solvents like perfluorodecalin or CF_2ClCCl_2F. Other examples are shown in Table 1.

The orientation of substitution is obviously that anticipated for electrophilic attack. It is quite remarkable however, that polyiodination may be achieved simply by altering the ratio of iodine to substrate (Table 1) and quite clearly, 'hyper reactivity' is induced by the combination of iodine and sulfuric acid in this system.

We have also demonstrated that the use of bromine in the analagous system is even more reactive, as illustrated by bromination of 2,4-dinitrofluorobenzene, which does not react with the iodination system (Scheme 2).

The mechanism of the process is by no means certain: we could have *in situ* formation and immediate reaction of iodine fluoride which is unstable except at low temperatures,[2] [eqn. (1)]. Alternatively, formation of a hypervalent species [eqn. (2)] is possible and the *in situ* formation of a hypofluorite derived from sulfuric acid [eqn. (3)] could also occur. It is not easy to distinguish between these very short-lived possibilities but the procedure that we have described above is an extremely useful development in methodology.



$$\text{I–I} + \text{F–F} \longrightarrow \text{I–}\overset{\delta^+}{\text{F}}\cdots\cdots\overset{\delta^-}{\text{H–X}} \xrightarrow{\text{Ar–H}} \text{Ar–I} \tag{1}$$

$$\text{I–I} + \text{F–F} \longrightarrow \text{I–I}\begin{smallmatrix}\overset{\delta^+}{\text{F}}\text{---}\overset{\delta^-}{\text{H–X}}\\ \text{F}\end{smallmatrix} \xrightarrow{\text{Ar–H}} \text{Ar–I} \tag{2}$$

$$\text{XO–F} + \text{I–I} \longrightarrow \text{XO–I} + \text{I–F} \xrightarrow{\text{Ar–H}} \text{Ar–I} \tag{3}$$

$$\text{HX} = H_2SO_4$$

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References

1 E. B. Merkushev, *Synthesis*, 1988, 923.
2 S. Rozen and M. J. Brand, *J. Org. Chem.*, 1985, **50**, 3342.