A Practical Synthetic Method for Iodoarene Difluorides without Fluorine Gas and Mercury Salts

Masanori Sawaguchi, Shinichi Ayuba, Shoji Hara*

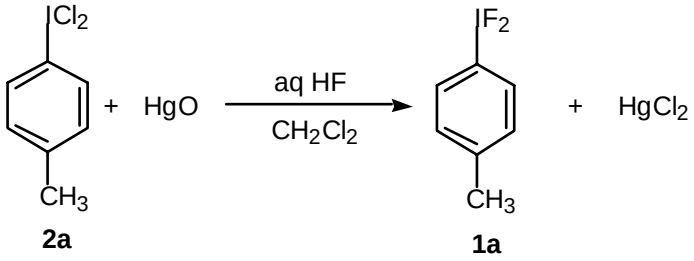
Division of Molecular Chemistry, Graduate School of Engineering, Hokkaido University, Sapporo 060-8628, Japan

Fax +81(11)7066556; E-mail: hara@org-mc.eng.hokudai.ac.jp

Abstract: Iodoarene difluorides were synthesized in three steps from the corresponding iodoarenes without the use of dangerous reagents such as fluorine gas or harmful mercury salts.

Key words: hypervalent iodine, iodosylarenes, fluorine compounds, iodoarene difluorides, hydrofluoric acid

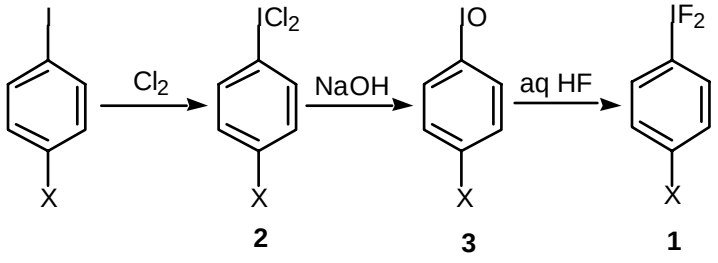
4-Iodotoluene difluoride (**1a**) has been used as a versatile fluorination reagent of alkenes,[1] alkynes,[2] carbonyl compounds,[3] sulfur compounds,[4] and iodoalkanes.[5] Generally, the Carpenter method[6] has been used for the preparation of **1a**, because dangerous F_2,[7] SF_4,[8] or expensive XeF_2[1e] is not necessary. A drawback to this method is the use of a large quantity of harmful HgO to remove the Cl ion when **1a** was prepared from 4-iodotoluene dichloride (**2a**) and HF (Scheme 1). A new method for preparation of **1a**, which needs neither dangerous reagents such as F_2 gas nor harmful Hg salts, had been desired.



2a **1a**

Scheme 1

In classical methods, **1a** was prepared from an 4-iodosoltoluene (**3a**) without Hg salts.[9] Carpenter noted that in the classical methods, the disproportionation of **3a** into 4-iodotoluene and 4-iodosotoluene caused the contamination and it is difficult to obtain pure **1a**. We wish to report here that pure **1a** can be prepared from **3a** without the Hg salt, XeF_2, SF_4, or F_2. 4-Iodosotoluene (**3a**) was prepared from iodotoluene in two steps by the modification of the Lucas procedure,[10,11] and then **3a** was treated with commercially available 46% aq HF. After recrystallization from hexane, pure **1a** could be obtained in 67% overall yield from iodotoluene and the spectra data of **1a** were in good agreement with the reported ones[7] (Scheme 2). The contamination of **1a** with 4-iodotoluene or 4-iodosotoluene could be avoided by using freshly prepared **3a**. This method is applicable to various iodoarene difluorides as shown in the Table 1.



Scheme 2

Table 1. Synthesis of Iodoarene Difluorides **1**

Entry	X	Yield of **2** (%)[a]	Yield of **3** (%)[a]	Yield of **1** (%)[a]
1	CH_3	96	81	86
2	H	98	73	86
3	Cl	92	61	79
4	NO_2	90	81	85[b]

a. Isolated yield. b. As **1d** is insoluble in hexane, it was isolated without recrestalization.

4-Iodotoluene Dichloride (2a)[10]

In a 50-ml two-necked flask equipped with a dry ice condenser and a gas inlet tube, were placed 4-iodotoluene (10.9 g, 50 mmol) and CH_2Cl_2 (15 mL). To the mixture, Cl_2 gas, generated from MnO_2 (30.5 g, 172 mmol) and concentrated HCl (40 mL), was bubbled through a gas inlet tube at 0 °C under stirring for 1h. After the introduction of Cl_2 gas, the mixture was stirred for 1 h at r.t. and then cooled again to 0 °C. The yellow solid formed was separated by filtration, washed with hexane, and dried in air on a filter paper to give **2a** (13.8 g, 48 mmol) in 96 % yield.

4-Iodosoltoluene (3a)[11]

To a THF solution (50 mL) of **2a** (13.8 g, 48 mmol) in a 200-ml round flask, was added an aq 3 M solution of NaOH (50 mL) and the flask was vigorously shaken for about 1 min. The crude **3a** was collected by suction, transferred to a beaker, and washed with H_2O (50 mL). The solid was separated by suction filtration and washed again with H_2O (50 mL). The wet **3a** was dried under vacuum, washed with hexane, suction filtrated, and dried under vacuum to give **3a** (9.1 g, 33.4 mmol) in 81% yield.

4-Iodotoluene Difluoride (1a); Typical Procedure

A 200 mL vessel made of Teflon™ PFA was charged with freshly prepared **3a** (9.1 g, 33.4 mmol) and CH_2Cl_2 (80 mL). To the heterogeneous mixture was added 46% aq HF (26 mL) and the flask was vigorously shaken for a few minutes to give a clear solution. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 X 10 mL). The combined organic phases were concentrated by gentle heating at atmospheric pressure to give a pale yellow solid, which was recrystallized from hexane to give white needles of **1a** (8.6 g, 33.4 mmol) in 86% yield. All operations should be carried out using Teflon™ apparatuses and storage of **1a** in a Teflon™ bottle is recommended; white needles; mp 98 °C (lit.[9a] 107-109 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 2.47 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.3, 132.1, 130.2, 120.8, 21.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ = -177.3 (s, 2F) (lit.[7b] –174.3).

4-Iodobenzene Difluoride (1b)

White solid; mp 34 °C (lit.[7b] 36 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 8.3 Hz, 2H), 7.61-7.57 (m, 2H), 7.51 (t, *J* = 7.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.3, 130.9, 129.9, 123.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ = -177.8 (s, 2F) (lit.[7b] –175.9).

***p*-Chloroiodobenzene Difluoride (1c)**

White solid; mp 101 °C (lit.[9a] 99 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.9 Hz, 2H), 7.58 (d, *J* = 8.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.1, 131.5, 130.9, 120.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ = -177.0 (s, 2F) (lit.[7b] –178.2).

***p*-Nitoroiodobenzene Difluoride (1d)**

White solid; mp 162 °C {lit.[7b] 155 °C (decomposed)}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.45 (d, *J* = 9.2 Hz, 2H), 8.15 (d, *J* = 9.2 Hz, 2H).

^{19}F NMR (376 MHz, $CDCl_3$): δ = -176.1 (s, 2F) (lit.[7b] –172.8).

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