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

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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_2^9e 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.

\[
\begin{align*}
\text{Cl}_2 
+ \text{HgO} & \rightarrow \text{aq HF} \\
\text{CH}_3 & \rightarrow \text{HgCl}_2
\end{align*}
\]

Scheme 1
In classical methods, 1a was prepared from an 4-iodosotoluene (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](image)

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

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>Yield of 2 (%)(^a)</th>
<th>Yield of 3 (%)(^a)</th>
<th>Yield of 1 (%)(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH(_3)</td>
<td>96</td>
<td>81</td>
<td>86</td>
</tr>
<tr>
<td>2</td>
<td>H</td>
<td>98</td>
<td>73</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>Cl</td>
<td>92</td>
<td>61</td>
<td>79</td>
</tr>
<tr>
<td>4</td>
<td>NO(_2)</td>
<td>90</td>
<td>81</td>
<td>85(^b)</td>
</tr>
</tbody>
</table>

\(^a\) Isolated yield.  \(^b\) As 1d is insoluble in hexane, it was isolated without recrystallization.
4-Iodotoluene Dichloride (2a)\textsuperscript{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\textsubscript{2}Cl\textsubscript{2} (15 mL). To the mixture, Cl\textsubscript{2} gas, generated from MnO\textsubscript{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\textsubscript{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)\textsuperscript{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\textsubscript{2}O (50 mL). The solid was separated by suction filtration and washed again with H\textsubscript{2}O (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\textsuperscript{TM} PFA was charged with freshly prepared 3a (9.1 g, 33.4 mmol) and CH\textsubscript{2}Cl\textsubscript{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\textsubscript{2}Cl\textsubscript{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\textsuperscript{TM} apparatuses and storage of 1a in a Teflon\textsuperscript{TM} bottle is recommended; white needles; mp 98 °C (lit.\textsuperscript{9a} 107-109 °C).
1H NMR (400 MHz, CDCl₃): δ = 7.84 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 2.47 (s, 3H).

13C NMR (100 MHz, CDCl₃): δ = 142.3, 132.1, 130.2, 120.8, 21.1.

19F NMR (376 MHz, CDCl₃): δ = -177.3 (s, 2F) (lit. 7b –174.3).

4-Iodobenzene Difluoride (1b)
White solid; mp 34 °C (lit. 7b 36 °C).

1H NMR (400 MHz, CDCl₃): δ = 7.94 (d, J = 8.3 Hz, 2H), 7.61-7.57 (m, 2H), 7.51 (t, J = 7.3 Hz, 1H).

13C NMR (100 MHz, CDCl₃): δ = 131.3, 130.9, 129.9, 123.8.

19F NMR (376 MHz, CDCl₃): δ = -177.8 (s, 2F) (lit. 7b –175.9).

p-Chloriodobenzene Difluoride (1c)
White solid; mp 101 °C (lit. 9a 99 °C).

1H NMR (400 MHz, CDCl₃): δ = 7.86 (d, J = 8.9 Hz, 2H), 7.58 (d, J = 8.9 Hz, 2H).

13C NMR (100 MHz, CDCl₃): δ = 138.1, 131.5, 130.9, 120.5.

19F NMR (376 MHz, CDCl₃): δ = -177.0 (s, 2F) (lit. 7b –178.2).

p-Nitroiodobenzene Difluoride (1d)
White solid; mp 162 °C {lit. 7b 155 °C (decomposed)}.

1H NMR (400 MHz, CDCl₃): δ = 8.45 (d, J = 9.2 Hz, 2H), 8.15 (d, J = 9.2 Hz, 2H).

19F NMR (376 MHz, CDCl₃): δ = -176.1 (s, 2F) (lit. 7b –172.8).

References


