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<tbody>
<tr>
<td>Title</td>
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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, alkynes, carbonyl compounds, sulfur compounds, and iodoalkanes. Generally, the Carpenter method has been used for the preparation of 1a, because dangerous \( \text{F}_2 \), \( \text{SF}_4 \) or expensive \( \text{XeF}_2 \) is not necessary. A drawback to this method is the use of a large quantity of harmful \( \text{HgO} \) 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 \( \text{F}_2 \) gas nor harmful \( \text{Hg} \) salts, had been desired.

\[
\begin{array}{ccc}
\text{Cl}_2 & \text{HgO} & \text{aq HF} \\
\text{CH}_3 & \text{CH}_2\text{Cl}_2 & \text{F}_2 \\
\text{2a} & \text{1a} & \text{HgCl}_2
\end{array}
\]

Scheme 1
In classical methods, 1a was prepared from an 4-iodosotoluene (3a) without Hg salts. 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, XeF₂, SF₄, or F₂. 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 ones⁷ (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 (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Yield of 3 (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Yield of 1 (%)&lt;sup&gt;a&lt;/sup&gt;</th>
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<tr>
<td>1</td>
<td>CH₃</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>NO₂</td>
<td>90</td>
<td>81</td>
<td>85&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
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</table>

<sup>a</sup> Isolated yield. <sup>b</sup> As 1d is insoluble in hexane, it was isolated without recrystallization.
4-Iodotoluene Dichloride (2a)<sup>10</sup>

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<sub>2</sub>Cl<sub>2</sub> (15 mL). To the mixture, Cl<sub>2</sub> gas, generated from MnO<sub>2</sub> (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<sub>2</sub> 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-Iodosolotoluene (3a)<sup>11</sup>

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<sub>2</sub>O (50 mL). The solid was separated by suction filtration and washed again with H<sub>2</sub>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™ PFA was charged with freshly prepared 3a (9.1 g, 33.4 mmol) and CH<sub>2</sub>Cl<sub>2</sub> (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<sub>2</sub>Cl<sub>2</sub> (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.<sup>9a</sup> 107-109 °C).
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 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$_3$): $\delta$ = 142.3, 132.1, 130.2, 120.8, 21.1.
$^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ = -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$_3$): $\delta$ = 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$_3$): $\delta$ = 131.3, 130.9, 129.9, 123.8.
$^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ = -177.8 (s, 2F) (lit. 7b –175.9).

$p$-Chloriodobenzene Difluoride (1c)
White solid; mp 101 °C (lit. 9a 99 °C).
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.86 (d, $J$ = 8.9 Hz, 2H), 7.58 (d, $J$ = 8.9 Hz, 2H).
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 138.1, 131.5, 130.9, 120.5.
$^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ = -177.0 (s, 2F) (lit. 7b –178.2).

$p$-Nitoriodobenzene Difluoride (1d)
White solid; mp 162 °C {lit. 7b 155 °C (decomposed)}.
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 8.45 (d, $J$ = 9.2 Hz, 2H), 8.15 (d, $J$ = 9.2 Hz, 2H).
$^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ = -176.1 (s, 2F) (lit. 7b –172.8).

References


