Title	A Practical Synthetic Method for Iodoarene Difluorides without Fluorine Gas and Mercury Salts
Author(s)	Sawaguchi, Masanori; Ayuba, Shinichi; Hara, Shoji
Citation	Synthesis, 2002(13), 1802-1803
Issue Date	2002-09
Doc URL	http://www.thieme-chemistry.com/thieme-chemistry/journals/info/synthesis/index.shtml ; http://hdl.handle.net/2115/624
Type	article (author version)
File Information	Shoji Hara.pdf

[Instructions for use](#)

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 method⁶ has been used for the preparation of **1a**, because dangerous F₂,⁷ SF₄,⁸ or expensive XeF₂^{1c} 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 F₂ gas nor harmful Hg salts, had been desired.

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, 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

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 recrystallization.

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 CH₂Cl₂ (15 mL). To the mixture, Cl₂ gas, generated from MnO₂ (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 Cl₂ 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 H₂O (50 mL). The solid was separated by suction filtration and washed again with H₂O (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 CH₂Cl₂ (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 CH₂Cl₂ (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).

^1H 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).

^1H 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*-Chloriodobenzene Difluoride (1c)**

White solid; mp 101 °C (lit.^{9a} 99 °C).

^1H 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*-Nitoriodobenzene Difluoride (1d)**

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

^1H 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).

References

(1) (a) Bornstein, J.; Borden, M. R.; Nunes, F.; Tarlin, H. I. *J. Am. Chem. Soc.*, **1963**, 85, 1609. (b) Zupan, M.; Pollak, A. *Chem. Commun.*, **1975**, 715. (c) Gregorcic, A.; Zupan, M. *Bull. Chem. Soc. Jpn.*, **1976**, 50, 517. (d) Gregorcic, A.; Zupan, M. *J. Chem. Soc.*,

Perkin I, **1977**, 1446. (e) Zupan, M. *Collection Czechoslov. Chem. Commun.*, **1977**, 42, 266. (f) Patrick, T. B.; Scheibel, J. J.; Hall, W. E.; Lee, Y. H. *J. Org. Chem.*, **1980**, 45, 4492. (g) Shellhamer, D. F.; Conner, R. J.; Richardson, R. E.; Heasley, V. L.; Heasley, G. E. *J. Org. Chem.*, **1984**, 49, 5015. (h) Hara, S.; Nakahigashi, J.; Fukuhara, T.; Yoneda, N. *Tetrahedron Lett.*, **1998**, 39, 2589. (i) Hara, S.; Nakahigashi, J.; Ishi-i, K.; Sawaguchi, M.; Sakai, H.; Fukuhara, T.; Yoneda, N. *Synlett*, **1998**, 495. (j) Sawaguchi, M.; Hara, S.; Fukuhara, T.; Yoneda, N. *J. Fluorine Chem.*, **2000**, 104, 277. (k) Sawaguchi, M.; Hara, S.; Yoneda, N. *J. Fluorine Chem.*, **2000**, 105, 313.

(2) (a) Hara, S.; Yoshida, M.; Fukuhara, T.; Yoneda, N. *Chem. Commun.*, **1998**, 965. (b) Hara, S.; Yamamoto, K.; Yoshida, M.; Fukuhara, T.; Yoneda, N. *Tetrahedron Lett.*, **1999**, 40, 7815. (c) Yoshida, M.; Hara, S.; Fukuhara, T.; Yoneda, N. *Tetrahedron Lett.*, **2000**, 41, 3887.

(3) (a) Tsushima, T.; Kawada, K.; Tsuji, T. *Tetrahedron Lett.*, **1982**, 23, 1165. (b) Edmunds, J. J.; Motherwell, W. B. *Chem. Commun.*, **1989**, 881. (c) Hara, S.; Sekiguchi, M.; Ohmori, A.; Fukuhara, T.; Yoneda, N. *Chem. Commun.*, **1996**, 1899.

(4) (a) Edmunds, J. J.; Motherwell, W. B. *Chem. Commun.*, **1989**, 1348. (b) Motherwell, W. B.; Wilkinson, J. A. *Synlett*, **1991**, 191. (c) Caddick, S.; Motherwell, W. B.; Wilkinson, J. A. *Chem. Commun.*, **1991**, 674. (d) Koen, M. J.; Guyader, F. L.; Motherwell, W. B. *Chem. Commun.*, **1995**, 1241. (e) Caddick, S.; Gazzard, L.; Motherwell, W. B.; Wilkinson, J. A. *Tetrahedron*, **1996**, 52, 149. (f) Greaney, M. F.; Motherwell, W. B. *Tetrahedron Lett.*, **2000**, 41, 4463. (g) Greaney, M. F.; Motherwell, W. B. *Tetrahedron Lett.*, **2000**, 41, 4467. (h) Greaney, M. F.; Motherwell, W. B.; Tocher, D. A. *Tetrahedron Lett.*, **2001**, 42, 8523.

(5) Sawaguchi, M.; Hara, S.; Nakamura, Y.; Ayuba, S.; Fukuhara, T.; Yoneda, N. *Tetrahedron*, **2001**, 57, 3315.

- (6) Carpenter, W. *J. Org. Chem.*, **1966**, *31*, 2688.
- (7) (a) Ruppert, I. *J. Fluorine Chem.*, **1980**, *15*, 173. (b) Naumann, D.; Rüther, G. *J. Fluorine Chem.*, **1980**, *15*, 213.
- (8) Lyalin, V. V.; Orda, V. V.; Alekseeva, L. A.; Yagupol'skii, L. M. *Zh. Org. Khim.* **1970**, *6*, 329.
- (9) (a) Bockemüller, W. *Ber.*, **1931**, *64*, 522. (b) Garvey, Jr., B. S.; Halley, L. F.; Allen, C. F. H. *J. Am. Chem. Soc.*, **1937**, *59*, 1827.
- (10) Lucas, H. J.; Kennedy, E. R. *Org. Synth.*, **1955**, *Col. Vol. III*, 482.
- (11) Lucas, H. J.; Kennedy, E. R.; Formo, M. W. *Org. Synth.*, **1955**, *Col. Vol. III*, 483.