SYNLETT
Spotlight 205A Fluorinating Hypervalent Iodine(III)
Reagent: 4-Iodotoluene Difluoride

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This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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Introduction

There is a great interest of organic chemists in hypervalent iodine reagents because a wide range of reactions can be performed selectively under mild conditions and, in some cases, catalytically.¹ Fluorinated molecules are highly valuable due to the unique characteristics displayed by the fluorine atom.²

4-Iodotoluene difluoride (*p*-TolIF₂, **1**) is a hypervalent iodine reagent that promotes chemoselective fluorinations avoiding the use of fluorine gas, as well as the expensive xenon difluoride. Several N-fluoro compounds have been developed as stable and effective fluorinating reagents; their preparation, however, generally demands the use of fluorine gas. Compound **1** is usually preferred over its iodobenzene difluoride analogue because of easier preparation, purification, and handling.

Preparation

Compound **1** is commercially available. However, it can be prepared in different ways from 4-iodotoluene.³ In one of them, the use of harmful gases or mercury salts is avoided (Scheme 1).⁴

Scheme 1

Abstracts

(A) Reacting α -phenylsulfanylated esters⁵ and amides⁶ with 1 equiv of **1** led to α -monofluoro sulfides via a fluoro-Pummerer reaction. α -Selenocarboxylic acid derivatives could be easily α -monofluorinated via a similar Pummerer reaction.⁴

(B) Hara and co-workers achieved α -fluorinated monoketones using the corresponding silyl enol ethers as substrates.⁷

(C) The α -monofluorination of β -keto esters, amides, and ketones was easily accomplished using **1**, overcoming the problematic use of amine-HF complexes.⁸ However, the fluorination under these conditions is slower than that using an acid medium.⁹

(D) The preparation of vicinal difluoroalkanes was achieved reacting aliphatic alkenes with **1**.

(E) The behavior of cyclic alkenes towards **1** can be different from the acyclic variant because a fluorinative and diastereoselective ring-contraction reaction may take place.¹⁰

(F) Unsaturated alcohols and acids are fluorocyclized when treated with **1** in the presence of amine-HF complexes and afford cyclic ethers and lactones with poor or no stereoselectivity, respectively.¹¹

(G) (*E*)-β-Fluoroalkenylidonium salts were prepared regio- and stereoselectively by Hara and co-workers from the corresponding terminal alkynes and **1** without using 5HF·Et₃N.¹² These compounds could be subsequently used in Pd-catalyzed cross-coupling reactions^{12,13} or Pd-catalyzed carbomethoxylation.¹⁴

(H) Alkynes and alkenes undergo phenylselenofluorination in the presence of **1** and PhSeSePh in high stereo- and regioselectivity.¹⁵ Analogously, when iodine instead of PhSeSePh is employed, iodo-fluorination of alkenes and alkynes affords fluoroiodoalkanes and fluoroiodoalkenes.¹⁶

(I) Iodoalkanes give the corresponding alkyl fluoride when treated with **1** in the presence of amine-HF complexes, via an iodonium intermediate.¹⁷

(J) Stereoselective ring expansion of iodine-containing 4-, 5-, and 6-membered cyclic ethers took place using **1**, affording 5-, 6-, and 7-membered cyclic fluoro ethers.¹⁸

References

- (a) Stang, P. J. *J. Org. Chem.* **2003**, *68*, 2997. (b) Wirth, T. *Angew. Chem. Int. Ed.* **2005**, *44*, 3656. (c) Moriarty, R. M. *J. Org. Chem.* **2005**, *70*, 2893. (d) Silva, L. F. Jr. *Molecules* **2006**, *11*, 421. (e) Richardson, R. D.; Wirth, T. *Angew. Chem. Int. Ed.* **2006**, *45*, 4402.
- Dolbier, W. R. Jr. *J. Fluorine Chem.* **2005**, *126*, 157.
- (a) Carpenter, W. J. *J. Org. Chem.* **1966**, *31*, 2688. (b) Fuchigami, T.; Fujita, T. *J. Org. Chem.* **1994**, *59*, 7190. (c) Sawaguchi, M.; Ayuba, S.; Hara, S. *Synthesis* **2002**, 1802. (d) Ye, C.; Twamley, B.; Shreeve, J. M. *Org. Lett.* **2005**, *7*, 3961.
- Arrica, M. A.; Wirth, T. *Eur. J. Org. Chem.* **2005**, 395.
- Greaney, M. F.; Motherwell, W. B. *Tetrahedron Lett.* **2000**, *41*, 4463.
- Greaney, M. F.; Motherwell, W. B. *Tetrahedron Lett.* **2000**, *41*, 4467.
- Sato, S.; Yoshida, M.; Hara, S. *Synthesis* **2005**, 2602.
- Yoshida, M.; Fujikawa, K.; Sato, S.; Hara, S. *ARKIVOC* **2003**, (vi), 36.
- Hara, S.; Sekiguchi, M.; Ohmori, A.; Fukuhara, T.; Yoneda, N. *Chem. Commun.* **1996**, 1899.
- Hara, S.; Nakahigashi, J.; Ishi-i, K.; Fukuhara, T.; Yoneda, N. *Tetrahedron Lett.* **1998**, *39*, 2589.
- Sawaguchi, M.; Hara, S.; Fukuhara, T.; Yoneda, N. *J. Fluorine Chem.* **2000**, *104*, 277.
- Yoshida, M.; Kawakami, K.; Hara, S. *Synthesis* **2004**, 2821.
- (a) Yoshida, M.; Nagahara, D.; Fukuhara, T.; Yoneda, N.; Hara, S. *J. Chem. Soc., Perkin Trans. 1* **2001**, *1*, 2283. (b) Yoshida, M.; Yoshikawa, S.; Fukuhara, T.; Yoneda, N.; Hara, S. *Tetrahedron* **2001**, *57*, 7143.
- Yoshida, M.; Komata, A.; Hara, S. *J. Fluorine Chem.* **2004**, *125*, 527.
- Panunzi, B.; Picardi, A.; Tingoli, M. *Synlett* **2004**, 2339.
- (a) Conte, P.; Panunzi, B.; Tingoli, M. *Tetrahedron Lett.* **2006**, *47*, 273. (b) Conte, P.; Panunzi, B.; Tingoli, M. *Tetrahedron Lett.* **2006**, *47*, 3325.
- Sawaguchi, M.; Hara, S.; Nakamura, Y.; Ayuba, S.; Fukuhara, T.; Yoneda, N. *Tetrahedron* **2001**, *57*, 3315.
- Inagaki, T.; Nakamura, Y.; Sawaguchi, M.; Yoneda, N.; Ayuba, S.; Hara, S. *Tetrahedron Lett.* **2003**, *44*, 4117.