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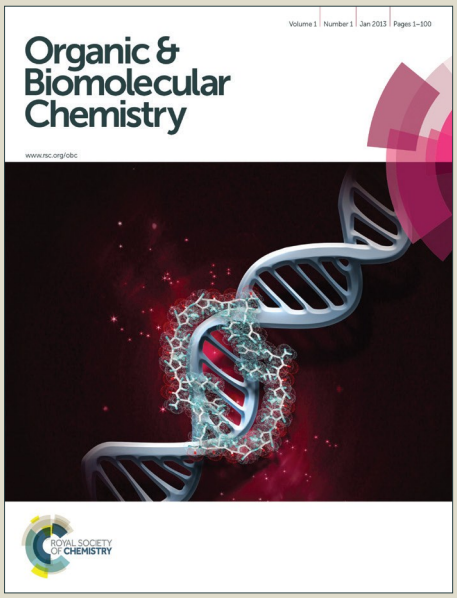

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Denitrogenative Hydrofluorination of Aromatic Aldehyde Hydrazones Using (Difluoroiodo)toluene

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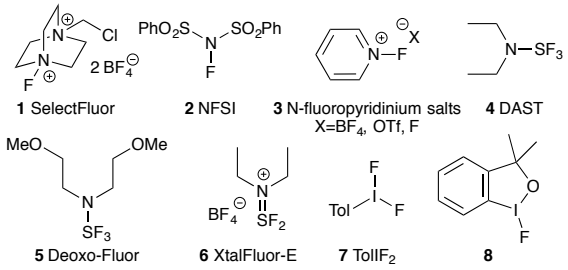
An operationally simple conversion of aromatic aldehyde hydrazones to monofluoromethylated arenes is reported. The hypervalent iodine reagent TolIF$_2$ serves as an oxidant, converting the hydrazone to the corresponding diazo compounds. The byproduct of the oxidation process, HF, is consumed in-situ by a denitrogenative hydrofluorination reaction of the diazo group.

Introduction

There are only a handful of naturally occurring fluorocarbons, so fluorine's use in medicinal chemistry might never have come to pass had chemists limited themselves to naturally-inspired pharmaceuticals.[1] As fluorine is small, univalent and makes very strong bonds to carbon, it is now routinely employed as a biostere for hydrogen.[2] Over the past few decades, site-specific fluorination has become an essential tool to medicinal chemists due to fluorine's ability to act as a biostere, and because of its desirable effects on the lipophilicity, metabolic stability and bioavailability of pharmaceutical and agrochemical agents.[3]

Given the breadth of biologically active fluorinated compounds,[4] the development of new fluorination strategies and reagents remain an important field of research.[5] As a complement to nucleophilic fluorination strategies, a large body of research developing electrophilic fluorinating reagents has been completed. While elemental fluorine is the simplest and most direct source of electrophilic fluorine, it is toxic, explosively reactive with organic compounds, and cannot be used without specialized laboratory equipment. To mitigate fluorine's reactivity, chemists have synthesized designer electrophilic fluorinating reagents based on N-F,[6] S-F,[7] and I-F bonds[8,9] (Figure 1). However, contrary to the N-F reagents (**1**-**3**) that serve as sources of electrophilic "F$^+$", the S-F and I-F compounds (**4**-**8**) have umpolung reactivity: attack of the hypervalent sulphur or iodine atom by a Lewis base expels fluoride, and generates an electrophilic adduct to be displaced by the fluoride anion.

Figure 1: Fluorine transfer reagents based on N-F, S-F or I-F bonds.



Benzylic fluorides, represented by the $ArCH_2F$, $ArCF_2H$ and $ArCF_3$ groups,[10] are common synthetic targets and strategies towards the $ArCH_2F$ and $ArCF_2H$ functional groups have received considerable attention in the literature.[5a,5j,11] General strategies towards their synthesis include deoxygenative fluorination of benzyl alcohol (using **4**-**6**),[12] substitution reactions of benzyl halides,[13] metal-catalyzed cross-coupling of fluorine-containing units,[3a,14] or radical-based fluorination reactions.[15] The $ArCH_2F$ group might also be synthesized by the hydrofluorination reaction of diazo compounds, simply by treating them with HF sources (Et_3N•3HF, Py•HF, HBF_4, etc).[16] This reaction is highly effective for stabilized diazo compounds (eg. flanked by two Ar, carbonyl, CF_3 groups); however, the aryldiazomethanes required to synthesize benzylic monofluorides are unstable, rarely isolable, and cannot easily serve as hydrofluorination precursors. Nonetheless, development of this methodology could offer a mild, rapid, operationally-simple and metal-free approach to benzylic monofluorides from simple starting materials.

Recently Yadav and co-workers reported a novel reaction where tosylhydrazone derivatives of aromatic aldehydes were converted to diazo intermediates in situ, and then treated with

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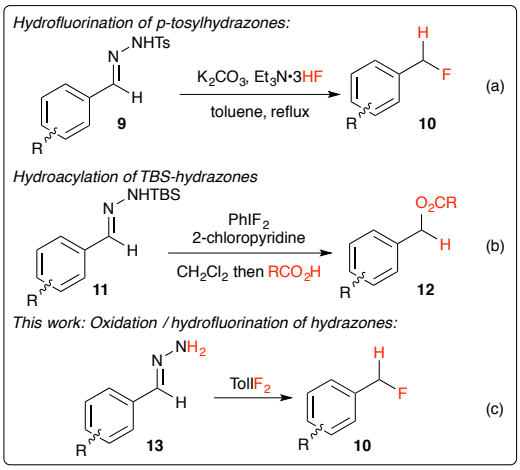
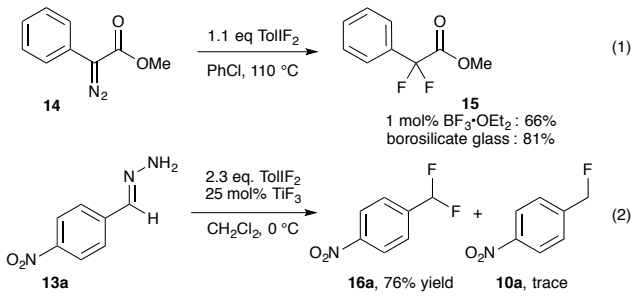
$Et_3N\bullet 3HF$ to produce hydrofluorination products **10** (Figure 2, a).[17] In an earlier study, Myers reported the oxidation of TBS-hydrazones to aryldiazomethanes using (difluoroiodo)benzene, and their subsequent hydroacylation with carboxylic acids (Scheme 1, b).[18] By combining these two concepts, we have developed the first synthesis of benzyl fluorides where the hypervalent iodine reagent, $TolIF_2$, acts as both an oxidant and as the fluoride source, and gives **10** under mild and operationally simple reaction conditions (Scheme 1, c).

Figure 2: In situ synthesis of aryldiazomethanes with subsequent hydrofunctionalization by acidic nucleophiles.



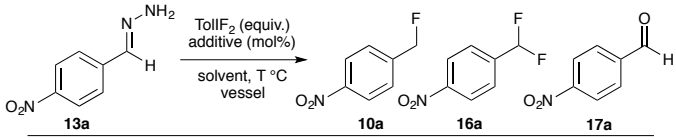
Results and Discussion

Our studies of halogenation reactions using $PhICl_2$ or $TolIF_2$ as halogen sources have led to the *gem*-dihalogenation of diazocarbonyl compounds[19] and the oxidative dichlorination of isatin-3-hydrazones.[20] The *gem*-difluorination reactions of diazoesters proceeded best using Lewis acid activation of $TolIF_2$ with $BF_3\bullet OEt_2$[19c] or borosilicate glass[21] (eq. 1). Similarly, the oxidative difluorination reactions of benzaldehyde hydrazone **13a** proceeded best with TiF_3 activation of the iodane (eq. 2).[22] During these latter studies, we observed for the first time traces of hydrofluorination by-product **10a**, which we attributed to the HF generated during the oxidation[23] competing with $TolIF_2$ as an electrophilic partner for the diazo intermediate. We believed that this intermediate could be induced to react preferentially to give **10a** by undertaking chemoselectivity-guided modification of the reaction conditions.



Due to the increased stability of the putative intermediate diazo compound, hydrazone **13a** was used as our model substrate during the reaction optimization. We first studied the effects of Lewis acid activators on the reaction, in both laboratory glassware and PFA vials, using the optimal conditions previously determined in our *gem*-difluorination reactions.[19c,21,22] Treating **13a** with $TolIF_2$ and 1 mol% $BF_3\bullet OEt_2$ generally failed in both types of reaction vessel, and gave aldehyde **17a** as the major product (Table 1, entries 1,2). The reactions were repeated using TiF_3 as the activator, and while the reaction in glassware was very low yielding, the reaction in PFA gave **10a** in 48% yield, along with 25% of aldehyde **17a** (Table 1, entries 3,4). The experiment conducted in glassware without a Lewis acidic activator was also very low yielding,[21] but the analogous reaction in a PFA vial proceeded in 47% yield (Table 1, entries 5, 6).

Table 1: Optimization of the denitrogenative hydrofluorination reaction.



entry	vessel	$TolIF_2$ (equiv.)	additive (mol%)	solvent	temp °C	yield[a] **10a**	yield[a] **16a**	yield[a] **17a**
1	glass[b]	1.1	1% $BF_3\bullet OEt_2$	PhCl	110	5%	18%	71%
2	PFA[c]	1.1	1% $BF_3\bullet OEt_2$	DCM	40	22%	–	55%
3	glass	1.1	25% TiF_3	DCM	40	10%	19%	34%
4	PFA	1.1	25% TiF_3	DCM	40	48%	–	25%
5	glass	1.1	–	PhCl	110	22%	10%	44%
6	PFA	1.1	–	DCM	40	47%	–	6%
7[d]	PFA	1.1	25% TiF_3	DCM	40	48%	–	19%
8[d]	PFA	1.1	–	DCM	40	60%	5%	12%
9[d]	PFA	1.5	–	DCM	40	61%	10%	15%
10[d]	PFA	1.7	–	DCM	40	74%	11%	12%
11[d]	PFA	2.1	–	DCM	40	71%	15%	11%

[a]Isolated yields. [b]Reaction carried out in a borosilicate round bottom flask. [c]Reaction carried out in a 4 mL PFA vial. [d]Reverse addition of hydrazone to $TolIF_2$.

Mass spectrometry analysis of the crude reaction mixtures of these preliminary trials by revealed the occasional occurrence of a hydrofluorinated dimerization product. To preclude dimer formation by minimizing the concentration of substrate relative to electrophile, the two most promising trial reactions (entries 4 and 6) were repeated using reverse addition of the hydrazone. The reaction using TiF_3 was unchanged (entry 7), but the reaction without a Lewis acid activator gave **10a** in 60% yield (entry 8). These two trials (entries 6,8) were to first examples of fluorination reactions occurring in a PFA vessel in the absence of a Lewis-acidic activator. Presumably this is due to $TolIF_2$ acting solely as an oxidant, instead of as an electrophilic fluorine source, for which Lewis acid activation is unnecessary.[18] We completed our reaction optimization by varying the loading of the $TolIF_2$ (entries 9-11). While the production of the aldehyde by-product **17a** was unchanged with increasing $TolIF_2$ loading, the amount of benzylic difluoride (**16a**) increased with increasing $TolIF_2$ loading. This is consistent with our expectation that

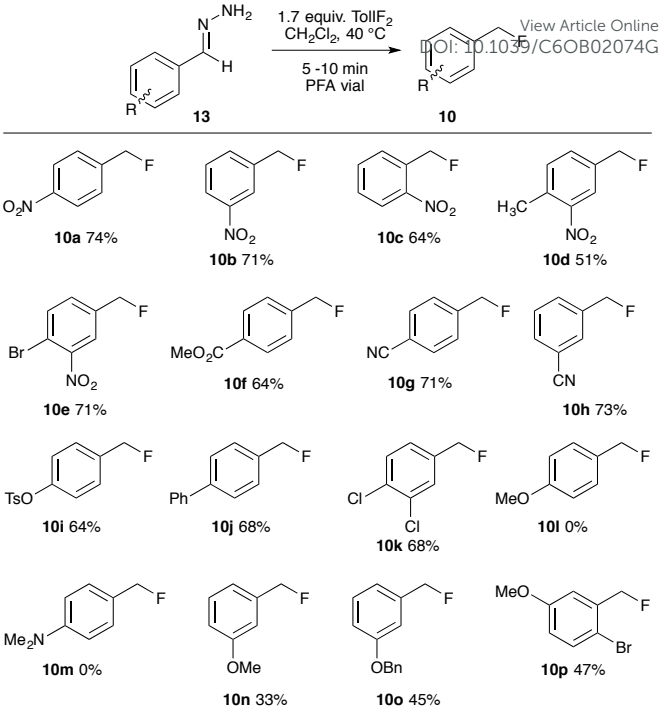
the *gem*-difluorination reaction should compete with hydrofluorination in the presence of excess $TolIF_2$. The highest yield (74%) of the desired benzylic fluoride **10a** was achieved when 1.7 equivalents of iodane was used.

Having demonstrated that benzaldehyde hydrazones could be induced to react selectively via the denitrogenative hydrofluorination reaction, we next investigated the reaction efficacy on a variety of substituted benzaldehyde hydrazone derivatives. The *para*-, *meta*- and *ortho*-nitro substituted substrates all performed well, as did the di-substituted derivatives having a *meta*-NO_2 substituent, giving the products **10a**-**e** in 51-74% yield. The *para*-carbomethoxy and *para*- or *meta*-cyano substituted benzylic fluorides (**10f**-**h**) were isolated in good yield, as were the benzylic fluorides of the *para*-tosylate, *para*-phenyl and 3,4-dichloro substrates (**10i**-**k**). The *para*-methoxy and *para*-dimethylamino benzaldehyde hydrazones substrates were consumed by the action of $TolIF_2$; however, no traces of the benzylic fluorides (**10l**,**m**) were observed. Interestingly, when the electron-releasing -OMe functional group was in the *meta*-position, the hydrofluorination reaction gave **10n** in 45% NMR yield, and 33% isolated yield. Presuming the volatility of **10n** to be problematic, we investigated the bulkier substrates **13o** and **13p**, which also possessed electron releasing -OBn and -OMe groups in their respective *meta*- positions, and in both cases, the products **10o**,**p** were recovered in moderate yield.[24]

These experiments indicate that substrates bearing electron-neutral or electron-withdrawing substituents are well-tolerated in the hydrofluorination reaction. And while substrates with electron-releasing substituents at the *para*- position were not compatible, substrates with the same electron-donating groups in the *meta*- position were moderately effective in the reaction. We attribute this trend to the destabilizing effect of electron-donating groups on the aryldiazomethane intermediates, and the decreased stability of the benzyl fluoride products that bear an electron-donating group at the *para*- position. Our experimental observations, coupled with the unlikelihood of free carbene formation at this low reaction temperature, led us to propose an ionic mechanism for the oxidative hydrofluorination reaction (Figure 3). Upon oxidation of hydrazone **13** to aryldiazomethane intermediate **A**, iodotoluene and HF (excess) would be generated as by-products. Protonation of the diazo group would give diazonium ion **B**, from which N_2 gas could be expelled upon fluoride attack, leading to benzylic fluoride **10**.

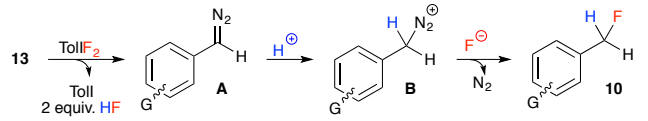
Conclusions

In conclusion, we have developed the first use of a hypervalent iodine reagent ($TolIF_2$) as both an oxidant and source of fluorine in the hydrofluorination of aromatic aldehyde hydrazones. The one-pot reaction made use of the oxidative potential of the iodane, converting the hydrazone to a diazo group, and generated an excess of the HF by-product which was consumed by a denitrogenative hydrofluorination reaction. The reaction proceeded best with electron-neutral or -withdrawing substituents, and failed with electron-donating groups capable of destabilizing the diazo intermediate. This reaction is a mild, rapid, metal-free and operationally simple alternative to the use of alternative deoxygenative fluorinating strategies in the synthesis of benzyl fluorides. Further exploration of this reaction, including expanding the substrate and functional group scope, is underway and will be disclosed in due course.



Scheme 1: Denitrogenative hydrofluorination of benzaldehyde hydrazone derivatives.

Figure 3: Plausible mechanistic pathway for the conversion of hydrazones to benzylic fluorides.



Experimental

A 4 mL PFA vial containing (difluoroiodo)toluene (1.7 equiv) was placed under nitrogen and immersed in a pre-heated 40 °C bath. To this was added a pre-made solution of hydrazone **13a** (50 mg, 1.0 equiv) in CH_2Cl_2 (1.5 mL) via a syringe pump over ~10 minutes. The reaction was monitored by TLC analysis, and upon consumption of the hydrazone (5-10 min), the reaction mixture was cooled to RT and concentrated by rotary evaporation. The resulting crude reaction mixture was purified by flash silica gel chromatography (10% EtOAc in hexanes) to provide benzyl fluoride **10a** (35 mg) in 74% yield.

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References

1. K. L. Kirk, *Org. Process. Res. Dev.*, 2008, **12**, 305.
2. K. Müller, C. Faeh and F. Diederich, *Science*, 2007, **317**, 1881.
3. a) J. Hu, B. Gao, L. Li, C. Ni and J. Hu, *Org. Lett.,* 2015, **17**, 3086; b) T. Fujiwara and D. O'Hagan, *J. Fluorine Chem.*, 2014, **167**, 16; c) J. Wang, M. Sanchez-Rosello, J. L. Acena, C. del Pozo, A. E. Sorochinsky, S. Fustero, V. A. Soloshonok and H. Liu, *Chem. Rev.*, 2014, **114**, 2432; d) S. Purser, P. R. Moore, S. Swallow and V. Gouverneur, *Chem. Soc. Rev.*, 2008, **37**, 320.
4. a) Y. Zhou, J. Wang, Z. N. Gu, S. N. Wang, W. Zhu, J. L. Acena, V. A. Soloshonok, K. Izawa and H. Liu, *Chem. Rev.*, 2016, **116**, 422; b) K. V. Turcheniuk, V. P. Kukhar, G. V. Roschenthaler, J. L. Acena, V. A. Soloshonok and A. E. Sorochinsky, *RSC Adv.*, 2013, **3**, 6693; c) B. Manteau, S. Pazenok, J. P. Vors and F. R. Leroux, *J. Fluorine Chem.*, 2010, **131**, 140; d) S. Fustero, J. F. Sanz-Cervera, J. L. Acena and M. Sanchez-Rosello, *Synlett*, 2009, **4**, 525.
5. For recent reviews of various fluorination strategies see a) P. A. Champagne, J. Desroches, J. D. Hamel, M. Vandamme and J. F. Paquin, *Chem. Rev.*, 2015, **115**, 9073; b) C. Chatalova-Sazepin, R. Hemelaere, J. F. Paquin and G. M. Sammis, *Synthesis*, 2015, **47**, 2554; c) M. G. Campbell and T. Ritter, *Chem. Rev.*, 2015, **115**, 612; d) X. Liu, C. Xu, M. Wang and Q. Liu, *Chem. Rev.*, 2015, **115**, 683; e) S. Barata-Vallejo, S. M. Bonesi and A. Postigo, *Org. Biomol. Chem.*, 2015, **13**, 11153; f) F. Toulgoat, S. Alazet and T. Billard, *Eur. J. Org. Chem.*, 2014, **2014**, 2415; g) Y. B. Dudkina, M. N. Khrizanforov, T. V. Gryaznova and Y. H. Budnikova, *J. Organomet. Chem.*, 2014, **751**, 301; h) T. Liang, C. N. Neumann and T. Ritter, *Angew. Chem., Int. Ed.*, 2013, **52**, 8214.
6. NFSI: a) E. Differding and H. Ofner, *Synlett*, 1991, 187; Selectfluor b) R. E. Banks, S. N. Mohialdinkhaffaf, G. S. Lal, I. Sharif and R. G. Syvret, *J. Chem. Soc., Chem. Commun.*, 1992, 595; c) R. E. Banks, *J. Fluorine Chem.*, 1998, **87**, 1; N-fluoropyridinium salts d) T. Umemoto and K. Tomita, *Tetrahedron Lett.*, 1986, **27**, 3271; e) T. Umemoto, K. Kawada and K. Tomita, *Tetrahedron Lett.*, 1986, **27**, 4465; For reviews of N-F reagents see f) X.-S. Xue, Y. Wang, M. Li and J.-P. Cheng, *J. Org. Chem.*, 2016, **81**, 4280; g) G. S. Lal, G. P. Pez and R. G. Syvret, *Chem. Rev.*, 1996, **96**, 1737.
7. C. F. Ni, M. Y. Hu and J. B. Hu, *Chem. Rev.*, 2015, **115**, 765.
8. For $TolIF_2$ see a) R. F. Weinland and W. Stille, *Liebigs Ann. Chem.*, 1903, **328**, 132; b) M. A. Arrica and T. Wirth, *Eur. J. Org. Chem.*, 2005, 395; c) P. Conte, B. Panunzi and M. Tingoli, *Tetrahedron Lett.*, 2006, **47**, 273; d) T. Inagaki, Y. Nakamura, M. Sawaguchi, N. Yoneda, S. Ayuba and S. Hara, *Tetrahedron Lett.*, 2003, **44**, 4117; e) J. Yu, J. Tian and C. Zhang, *Adv. Synth. Catal.*, 2010, **352**, 531; f) W. B. Motherwell, M. F. Greaney and D. A. Tocher, *J. Chem. Soc., Perkin Trans. 1*, 2002, 2809.
9. For fluoro iodoxole **8** see a) C. Y. Legault and J. Prevost, *Acta Crystallographica Section E*, 2012, **68**, 1238; b) G. C. Geary, E. G. Hope, K. Singh and A. M. Stuart, *Chem. Commun.*, 2013, **49**, 9263; c) V. Matoušek, E. Pietrasiak, R. Schwenk and A. Togni, *J. Org. Chem.*, 2013, **78**, 6763; d) G. C. Geary, E. G. Hope and A. M. Stuart, *Angew. Chem., Int. Ed.*, 2015, **54**, 14911; e) N. O. Ilchenko, B. O. A. Tasch and K. J. Szabo, *Angew. Chem., Int. Ed.*, 2014, **53**, 12897; f) A. Ulmer, C. Brunner, A. M. Arnold, A. Pothig and T. Gulder, *Chem. Eur. J.*, 2016, **22**, 3660.
10. a) X. Y. Yang, T. Wu, R. J. Phipps and F. D. Toste, *Chem. Rev.*, 2015, **115**, 826; b) G. Landelle, A. Panossian, S. Pazenok, J. P. Vors and F. R. Leroux, *Beilstein J. Org. Chem.*, 2013, **9**, 2476; c) X. F. Wu, H. Neumann and M. Beller, *Chem. Asian. J.*, 2012, **7**, 1744; d) F. L. Qing, *Chin. J. Org. Chem.*, 2012, **32**, 815; e) O. A. Tomashenko and V. V. Grushin, *Chem. Rev.*, 2011, **111**, 4475.
11. a) A. Koperniku, H. Q. Liu and P. B. Hurley, *Eur. J. Org. Chem.*, 2016, **5**, 871; b) A. J. Lin, C. B. Huehls and J. Yang, *Org. Chem. Front.*, 2014, **1**, 434; c) T. Besset, T. Poisson and X. Pannecoucke, *Chem. Eur. J.*, 2014, **20**, 16830; d) M. C. Belhomme, T. Besset, T. Poisson and X. Pannecoucke, *Chem. Eur. J.*, 2015, **21**, 12836; e) J. B. Hu, W. Zhang and F. Wang, *Chem. Commun.*, 2009, **48**, 7465.
12. a) G. S. Lal, G. P. Pez, R. J. Pesaresi, F. M. Prozonic and H. Cheng, *J. Org. Chem.*, 1999, **64**, 7048; b) M. J. Koen, F. Le Guyader and W. B. Motherwell, *J. Chem. Soc., Chem. Commun.*, 1995, 1241; c) H. Koroniak, J. Walkowiak, K. Grys, A. Rajchel, A. Alty and R. Du Boisson, *J. Fluorine Chem.*, 2006, **127**, 1245; d) D. Obermayer, M. Damm and C. O. Kappe, *Chem. Eur. J.*, 2013, **19**, 15827; e) H. Zhao and F. P. Gabbaï, *Org. Lett.*, 2011, **13**, 1444; f) G. Ung and G. Bertrand, *Chem. Eur. J.*, 2012, **18**, 12955.
13. a) S. Bouvet, B. Pégot, J. Marrot and E. Magnier, *Tetrahedron Lett.*, 2014, **55**, 826; b) M. E. Hirschberg, N. V. Ignat'ev, A. Wenda and H. Willner, *J. Fluorine Chem.*, 2012, **137**, 50; c) R. Mirabdolbaghi, T. Dudding and T. Stamatatos, *Org. Lett.*, 2014, **16**, 2790; d) T. Sawamura, S. Kuribayashi, S. Inagi and T. Fuchigami, *Adv. Synth. Catal.*, 2010, **352**, 2757; e) T. Kitazume and T. Ebata, *J. Fluorine Chem.*, 2004, **125**, 1509; f) M. Mąkosza and R. Bujok, *Tetrahedron Lett.*, 2004, **45**, 1385; g) H. Sun and S. G. DiMagno, *J. Am. Chem. Soc.*, 2005, **127**, 2050.
14. a) H. Doi, I. Ban, A. Nonoyama, K. Sumi, C. Kuang, T. Hosoya, H. Tsukada and M. Suzuki, *Chem. Eur. J.*, 2009, **15**, 4165. For an example of coupling between benzyl carbanion and carbonyl compounds, see b) Y. Arroyo, M. A. Sanz-Tejedor, A. Parra and J. L. García Ruano, *Chem. Eur. J.*, 2012, **18**, 5314.
15. a) J.-J. Ma, W.-B. Yi, G.-P. Lu and C. Cai, *Org. Biomol. Chem.*, 2015, **13**, 2890; b) J. B. Xia, C. Zhu and C. Chen, *J. Am. Chem. Soc.*, 2013, **135**, 17494; c) P. Xu, S. Guo, L. Wang and P. Tang, *Angew. Chem., Int. Ed.*, 2014, **53**, 5955; d) S. Bloom, M. McCann and T. Lectka, *Org. Lett.*, 2014, **16**, 6338; e) J. C. T. Leung, C. Chatalova-Sazepin, J. G. West, M. Rueda-Becerril, J.-F. Paquin and G. M. Sammis, *Angew. Chem., Int. Ed.*, 2012, **51**, 10804.
16. a) E. Emer, J. Twilton, M. Tredwell, S. Calderwood, T. L. Collier, B. Liegault, M. Taillefer and V. Gouverneur, *Org. Lett.*, 2014, **16**, 6004; b) R. Pasceri, H. E. Bartrum, C. J. Hayes and C. J. Moody, *Chem. Commum.*, 2012, **48**, 12077; c) C. Qin and H. M. L. Davies, *Org. Lett.*, 2013, **15**, 6152.
17. A. K. Yadav, V. P. Srivastava and L. D. S. Yadav, *Chem. Commun.*, 2013, **49**, 2154.
18. M. E. Furrow and A. G. Myers, *J. Am. Chem. Soc.*, 2004, **126**, 12222.
19. a) K. E. Coffey and G. K. Murphy, *Synlett*, 2015, **26**, 1003; b) G. K. Murphy, F. Z. Abbas and A. V. Poulton, *Adv. Synth. Catal.*, 2014, **356**, 2919; c) J. Tao, R. Tran and G. K. Murphy, *J. Am. Chem. Soc.*, 2013, **135**, 16312.
20. a) K. E. Coffey, R. Moreira, F. Z. Abbas and G. K. Murphy, *Org. Biomol. Chem.*, 2015, **13**, 682; b) C. Hepples and G. K. Murphy, *Tetrahedron Lett.*, 2015, **56**, 4971.
21. G. S. Sinclair, R. Tran, J. Tao, W. S. Hopkins and G. K. Murphy, *Eur. J. Org. Chem.*, 2016, **27**, 4603.
22. Murphy lab, unpublished results.
23. a) M. E. Furrow and A. G. Myers, *J. Am. Chem. Soc.*, 2004, **126**, 5436; b) D. H. R. Barton, J. C. Jaszberenyi, W. S. Liu and T. Shinada,

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Tetrahedron, 1996, **52**, 14673; c) P. A. S. Smith and E. M. Bruckmann, *J. Org. Chem.*, 1974, **39**, 1047; d) A. Cnossen, J. C. M. Kistemaker, T. Kojima and B. L. Feringa, *J. Org. Chem.*, 2014, **79**, 927; e) L. Lapatsanis, G. Milias and S. Paraskewas, *Synthesis*, 1985, **1985**, 513.

24. Hydrazones of 1-naphthaldehyde, pentafluorobenzaldehyde and 3-bromo-4-methoxybenzaldehyde were also effective in the reaction, proceeding in 40-50% NMR yield. The products were not sufficiently purified to determine isolated yields.

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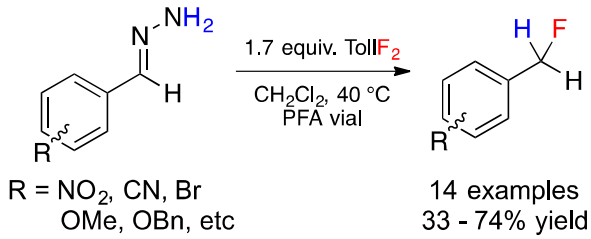

Tandem oxidation/denitrogenative hydrofluorination

(Difluoroiodo)toluene acts as both the oxidant and the fluoride source in this one-pot oxidation/denitrogenative hydrofluorination reaction.