A Journal of the Gesellschaft Deutscher Chemiker

Angewandte

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Chemie

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Accepted Article

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To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.201708197
Angew. Chem. 10.1002/ange.201708197

Link to VoR: http://dx.doi.org/10.1002/anie.201708197
http://dx.doi.org/10.1002/ange.201708197

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10.1002/anie.201708197

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Selective Radical Fluorination of Tertiary Alkyl Halides at Room Temperature

He Chen,[a] Zhonglin Liu,[a] Ying Lv,[b] Xinqiang Tan,[a] Haigen Shen,[a] Hai-Zhu Yu,*, [b] and Chaozhong Li*, [a], [c]

Abstract: *Direct fluorination of tertiary alkyl bromides and iodides with Selectfluor reagent is described. The halogen-exchange fluorination proceeds efficiently in acetonitrile at room temperature under metal-free conditions and exhibits a wide range of functional group compatibility. Furthermore, the reactions are highly selective in that alkyl chlorides and primary and secondary alkyl bromides remain intact. A radical mechanism is proposed for this selective fluorination.*

The prominent roles of organofluorine compounds in various disciplines such as pharmaceuticals and agrochemicals have spurred a considerable interest in the development of new methods for C–F bond formations, especially in site-specific manner.[1] In this regard, the halogen-exchange fluorination of alkyl halides is particularly attractive because of the easy availability of organohalides.[2–7] A number of methods have been developed for these site-specific C(sp^3)–F bond formations, including nucleophilic fluorination of allylic,[2] primary[3] and secondary[3] alkyl halides. Furthermore, Doyle et al. successfully introduced the palladium-catalyzed enantioselective fluorination of allylic chlorides and bromides.[2b, 2c, 2f] However, the fluorination of tertiary alkyl halides remains a formidable challenge.[4–7] The halogen-exchange fluorination with Cu_2O-HF-THF[4] or AgF[5], and the oxidative deiodinative fluorination[6] with F_2,[6a] XeF_2,[6c–6e] *p*-iodotoluene difluorides[6b, 6f] or iodonium fluoride[6g], were reported for tertiary alkyl halides. These reactions proceed via carbocationic intermediacy (Figure 1), and thus suffer from the competing solvolysis, elimination or rearrangement reactions (also vide infra). As a consequence, their applications are mainly limited to bridgehead halides in which the side reactions can be suppressed. More recently, Nishikata et al. reported the copper-catalyzed fluorination of α-bromo-*N*-arylamides with CsF.[7] However, this method is not applicable to ordinary tertiary alkyl halides. Herein we report the selective fluorination of tertiary alkyl halides with Selectfluor reagent (1-chloromethyl-4-fluoro-diazoniabicyclo[2,2,2]octane bis(tetrafluoroborate))[8] via the intermediacy of alkyl radicals[1c, 9, 10] (Figure 1).

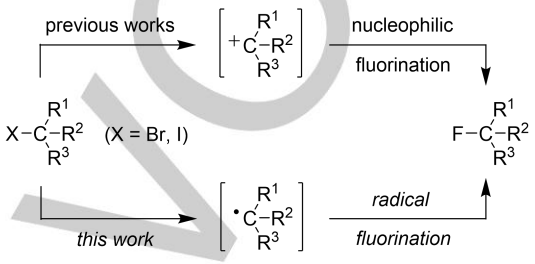
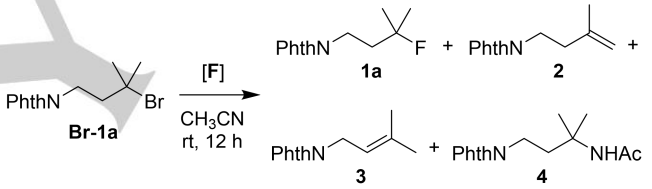


Figure 1. Fluorination of tertiary alkyl halides.

Table 1: Halogen-exchange fluorination of tertiary alkyl bromide **Br-1a**.[a]



Entry	[F]	Yield (%)[b] 1a	2	3	4
1	Selectfluor	93	0	0	0
2	AgF	23	37	21	10
3	*p*-Me-$C_6H_4IF_2$	35	trace	trace	55
4	NFSI	No reaction			

[a] Reagents and conditions: **Br-1a** (0.2 mmol), **[F]** (0.6 mmol), CH_3CN (2 mL), rt, 12 h. [b] Isolated yield based on **Br-1a**. Phth = phthalyl; Selectfluor = 1-chloromethyl-4-fluorodiazoniabicyclo[2,2,2]octane bis(tetrafluoroborate); NFSI = *N*-fluorobis(benzenesulfonyl)imide.

We recently reported the Ag(I)-catalyzed decarboxylative radical fluorination of aliphatic carboxylic acids with Selectfluor.[11] This method was successfully extended to the deboronofluorination of alkylboronates and to the fluorofunctionalization of unactivated alkenes.[12] These results urged us to test whether alkyl halides could also undergo radical fluorination with Ag(I)/Selectfluor. Thus, *N*-(3-bromo-3-methylbutyl)phthalimide (**Br-1a**) was selected as the model substrate to explore this possibility. However, after a careful screening of reaction conditions (see Table S1 in the Supporting Information (SI) for details), we were surprised to find that direct treatment of **Br-1a** with a stoichiometric amount of Selectfluor in acetonitrile at room temperature for 36 hours led to the clean formation of the corresponding alkyl fluoride **1a** in 86% yield. No silver catalyst was required. Use of excess (3 equiv) Selectfluor speeded up the fluorination, and **1a** was isolated in 93% yield

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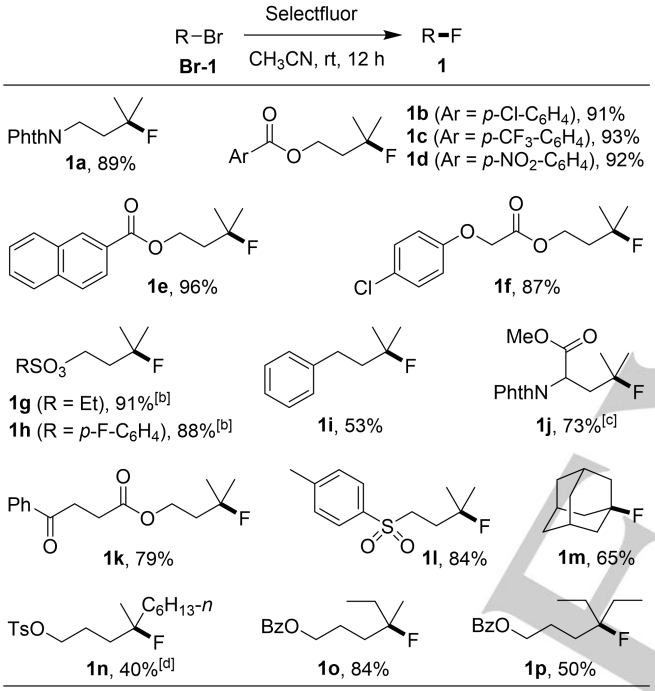
within 12 hours (entry 1, Table 1). As a comparison, the reaction of **Br-1a** with dry AgF in acetonitrile gave the mixture of fluoride **1a** (23%), alkenes **2** (37%) and **3** (21%), and amide **4** (10%) (entry 2, Table 1). The oxidative fluorination of **Br-1a** with *p*-iodotoluene difluoride afforded the mixture of **1a** (35%), **4** (55%) and traces of **2** and **3** (entry 3, Table 1). In contrast, no reaction occurred between **Br-1a** and NFSI (*N*-fluorobis(benzenesulfonyl)imide)[13] (entry 4, Table1). These experiments clearly indicate that the reaction of **Br-1a** with Selectfluor proceeds via a mechanism different from that with AgF or *p*-iodotoluene difluoride.

Table 2: Fluorination of tertiary alkyl bromides **Br-1**.[a]

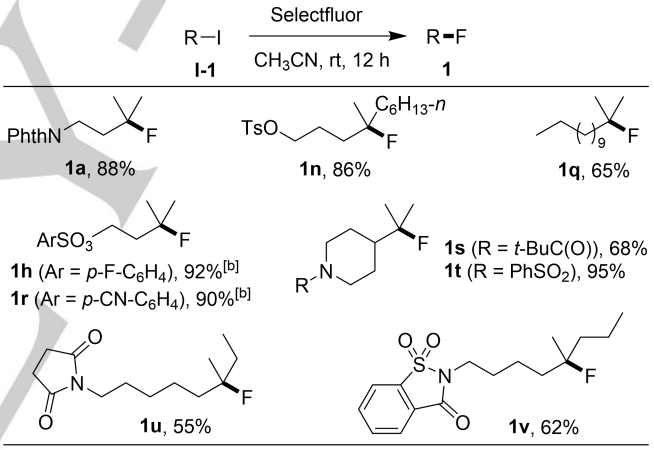


[a] Reagents and conditions: **Br-1** (0.2 mmol), Selectfluor (0.6 mmol), CH_3CN (2 mL), rt, 12 h. Yields of isolated products are given. [b] Reaction time: 48 h. [c] Reaction time: 24 h. [d] **Br-1n** was recovered in 55% yield. Ts = *p*-toluenesulfonyl; Bz = benzoyl.

We then aimed to define the scope of this metal-free fluorination method. As shown in Table 2, a wide range of differentially substituted tertiary alkyl bromides were readily converted to the corresponding tertiary alkyl fluorides **1a–1p** in good to excellent yield. The reaction was tolerant of a number of functional groups such as ether, ketone, ester, amide, imide, nitro, sulfone, and sulfonate. Notably, fluorinated amino acid **1j**, a key building block for the synthesis of the drug odanacatib,[5a] was achieved in 73% yield from the corresponding bromide **Br-1j** by this method. In contrast, the reaction of **Br-1j** with AgF under various conditions gave **1j** in no more than 30% yield, and byproducts such as alkenes and γ-lactone were also formed in significant amounts, as reported by Otting and Easton et al.[5a] Of particular note, fluorinated sulfonates **1g** and **1h** were obtained in excellent yield, while further nucleophilic fluorination or bromination of these sulfonates that is hardly avoidable under nucleophilic fluorination conditions,[7] was not observed at all. Given that tertiary alkyl bromides are easily prepared by conventional methods[14] such as bromination of tertiary alkyl alcohols,[14a] bromofunctionalization[14b] or hydrobromination[14c] of alkenes (see also SI), this method nicely complements the available fluorination methods. It is worth mentioning that direct hydrofluorination of alkenes suffer from either harsh reaction conditions or limited substrate scope,[15] while direct deoxy-fluorination of tertiary alkyl alcohols, unlike that of primary or secondary alkyl alcohols, is challenging.[16] Also note that the method is site-specific compared to the recently developed C–H fluorination.[17]

We next extended the above method to the fluorination of tertiary alkyl iodides, and the results are summarized in Table 3. As for the reaction of alkyl bromides, tertiary alkyl iodides **I-1** also underwent smooth halogen-exchange fluorination with Selectfluor and gave the corresponding products **1** in satisfactory yield.

Table 3: Fluorination of tertiary alkyl iodides **I-1**.[a]



[a] Reagents and conditions: **I-1** (0.2 mmol), Selectfluor (0.6 mmol), CH_3CN (2 mL), rt, 12 h. Yields of isolated products are given. [b] Reaction time: 24 h.

Unlike tertiary alkyl bromides and iodides, primary and secondary alkyl chlorides and bromides were unreactive towards Selectfluor. This difference in reactivity allowed the implementation of chemoselective fluorination of alkyl halides. Thus, tertiary alkyl bromides **5a–5i** containing another alkyl halide moiety, were subjected to the treatment with Selectfluor in CH_3CN at room temperature. The results are grouped in Table 4. The reactions of tertiary alkyl bromides bearing a primary, secondary or tertiary alkyl chloride moiety afforded the corresponding tertiary alkyl fluorides **6a–6d** in high yield while the chloride moiety remained intact. Dibromides **5e–5g** and even tribromide **5h** underwent chemoselective monofluorination to provide tertiary alkyl fluorides **6e–6h** in excellent yield. Furthermore, for substrate **5i** having two different tertiary alkyl bromide motifs, the fluorination occurred exclusively at the all-alkyl-substituted carbon to give product **6i** in 82% yield whereas the α-carbamoyl bromide moiety remained unchanged. This

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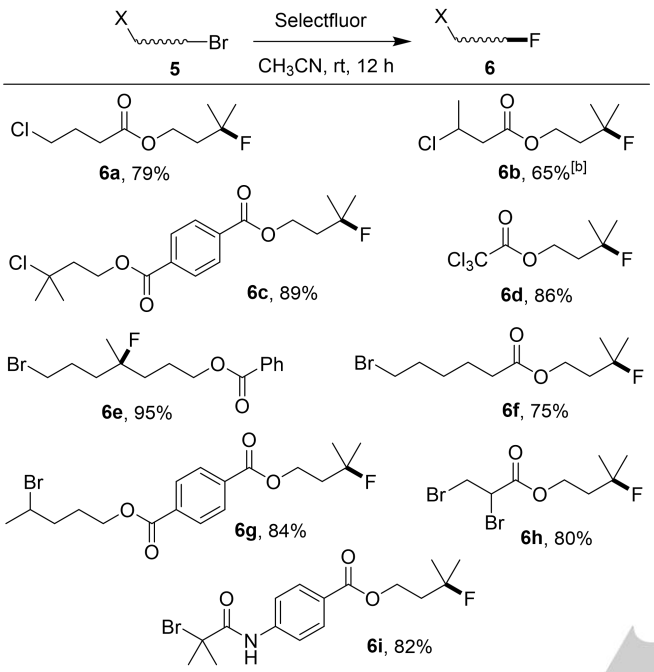
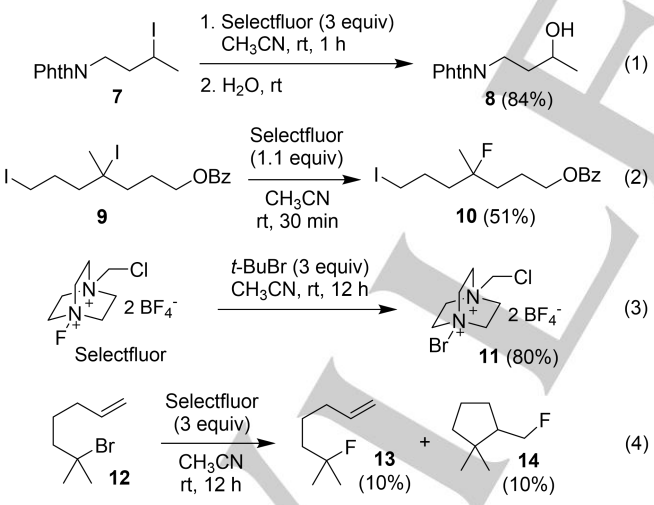
selectivity is opposite to that in the copper-catalyzed fluorination with CsF.[7]

Table 4: Selective fluorination of tertiary alkyl bromides **5**.[a]



[a] Reagents and conditions: **5** (0.2 mmol), Selectfluor (0.6 mmol), CH_3CN (2 mL), rt, 12 h. Yields of isolated products are given. [b] Reaction time: 24 h.



The reactivity of primary and secondary alkyl iodides towards Selectfluor was also tested. Secondary alkyl iodide **7** underwent fast reaction with Selectfluor at room temperature. However, no expected fluorination product could be observed. Instead, alcohol **8** was obtained in 84% yield after the quenching of the reaction with H_2O (Eq. 1). Primary alkyl iodides underwent slow decomposition on treatment with Selectfluor, and no desired alkyl fluorides were observed. In another case, the reaction of diiodide **9** with a slightly excess amount of Selectfluor at room temperature for 30 minutes provided the chemoselective monofluorination product **10** in 51% yield (Eq. 2).

To gain further insight into the fluorination, the following experiments were carried out. When Selectfluor was treated with excess *t*-BuBr in CH_3CN at room temperature overnight, a white precipitate was observed. After the usual workup, *N*-bromoaminium salt **11** was obtained in 80% yield (Eq. 3). The reaction of optically pure (-)-**5e** led to racemic product (±)-**6e**. Finally, the fluorination of radical probe **12** was performed (Eq. 4). Both uncyclized (**13**) and cyclized (**14**) products were observed, albeit in low yield, probably due to the competition of allylic C–H fluorination[17] and the bromination of the alkene with **11**.

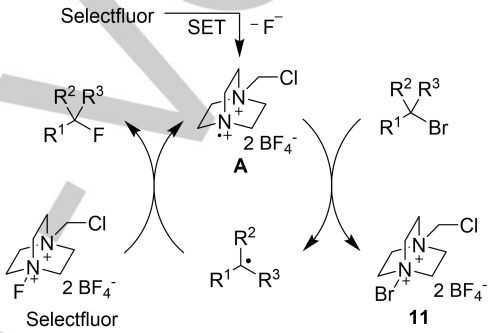


Figure 2. Proposed mechanism.

A plausible mechanism for the fluorination is shown in Figure 2. First, aminium radical cation **A** is generated by single electron reduction of Selectfluor[18] (presumably by tertiary alkyl bromide). The intermediate **A** then abstracts a bromine atom from tertiary alkyl bromide to produce *N*-bromoaminium salt **11** and the corresponding alkyl radical. Subsequent fluorine transfer[10] from Selectfluor to the alkyl radical affords the fluorination product and regenerates an aminium radical cation **A**. Theoretical calculations at M062X/6-31G(d) level showed that the bromine atom transfer from *t*-BuBr to **A** is endergonic by 20.7 kcal/mol. For comparison, the incorporation of a solution phase single point energy calculation at M06-2X/6-311++G(2df,2p) level (with IEFPCM model and CH_3CN solvent) reveals a higher energy demand of 27.8 kcal/mol. Meanwhile, the subsequent fluorine transfer (from Selectfluor to *t*-butyl radical) is highly exergonic by 48.1 and 51.8 kcal/mol for the gas phase and solution phase calculations, respectively. These calculations suggest that the Br-transfer is the rate-determining step in the overall transformation. Our kinetic experiments on the fluorination of **Br-1a** indicated that the rate of product formation has a first-order dependence on the substrate, in support of this assumption (see Figure S1 in the SI). Electron-rich alkyl bromides facilitate the Br-transfer because of the electrophilic nature of aminium radical cation **A**. This accounts for the chemoselectivity of fluorination illustrated in Table 4.

The fluorination of tertiary alkyl iodides can also be explained by the mechanism depicted in Figure 2. In contrast, secondary alkyl iodides are less reactive, and their reaction with

Selectfluor produces the corresponding alkyl iodine(III) difluorides, which decompose in water to give the hydroxylation products (e.g., **8**) via carbocationic intermediates.[6] This analysis is supported by the fact that the oxidation of aryl iodides with Selectfluor provides aryl iodine(III) dilfuorides.[19]

In conclusion, we have developed a practical protocol for the highly selective fluorination of tertiary alkyl bromides and iodides. As the procedure is operationally simple, free from metal ions, broad in scope, and tolerant of sensitive functional groups, the method should find application in the synthesis of important fluorinated molecules.

Acknowledgements

This project was supported by the 973 Program (Grant 2015CB931900), by the NFSC (Grants 21421002, 21472220, 21532008, 21672001, and 21602239), and by the Strategic Priority Research Program of the Chinese Academy of Sciences (Grant XDB20020000).

Keywords: fluorination • radicals • halogen-exchange • alkyl halides • metal-free

[1] For reviews, see: a) D. E. Yerien, S. Bonesi, A. Postigo, *Org. Biomol. Chem.* **2016**, *14*, 9398–8427; b) P. A. Champagne, J. Desroches, J.-D. Hamel, M. Vandamme, J.-F. Paquin, *Chem. Rev.* **2015**, *115*, 9073–9174; c) C. Chatalova-Sazepin, R. Hemelaere, J.-F. Paquin, G. M. Sammis, *Synthesis* **2015**, *47*, 2554–2569; d) J. Wu, *Tetrahedron Lett.* **2014**, *55*, 4289–4294; e) T. Liang, C. N. Neumann, T. Ritter, *Angew. Chem., Int. Ed.* **2013**, *52*, 8214–8264; *Angew. Chem.* **2013**, *125*, 8372–8423; f) C. Hollingworth, V. Gouverneur, *Chem. Commun.* **2012**, *48*, 2929–2942; g) T. Furuya, A. S. Kamlet, T. Ritter, *Nature* **2011**, *473*, 470–477; h) T. Furuya, J. E. M. N. Klein, T. Ritter, *Synthesis* **2010**, *42*, 1804–1821; i) J. A. Wilkinson, *Chem. Rev.* **1992**, *92*, 505–519.

[2] For recent examples, see: a) J. A. B. Laurenson, S. Meiries, J. M. Percy, R. Roig, *Tetrahedron Lett.* **2009**, *50*, 3571–3573; b) M. H. Katcher, A. G. Doyle, *J. Am. Chem. Soc.* **2010**, *132*, 17402–17404; c) M. H. Katcher, A. Sha, A. G. Doyle, *J. Am. Chem. Soc.* **2011**, *133*, 15902–15905; d) Z. Zhang, F. Wang, X. Mu, P. Chen, G. Liu, *Angew. Chem. Int. Ed.* **2013**, *52*, 7549–7553; *Angew. Chem.* **2013**, *125*, 7697–7701; e) J. M. Larsson, S. R. Pathipati, K. J. Szabo, *J. Org. Chem.* **2013**, *78*, 7330–7336; f) M. H. Katcher, P.-O. Norrby, A. G. Doyle, *Organometallics* **2014**, *33*, 2121–2133.

[3] For recent examples, see: a) H. Sun, S. G. DiMagno, *J. Am. Chem. Soc.* **2005**, *127*, 2050–2051; b) C. B. Murray, G. Sanford, S. R. Korn, D. S. Yufit, J. A. K. Howard, *J. Fluorine Chem.* **2005**, *126*, 571–576; c) D. W. Kim, H.-J. Jeong, S. T. Lim, M.-H. Sohn, D. Y. Chi, *Tetrahedron* **2008**, *64*, 4209–4214; d) D. W. Kim, H.-J. Jeong, S. T. Lim, M.-H. Sohn, *Tetrahedron Lett.* **2010**, *51*, 432–434; e) H. Zhao, F. P. Gabbai, *Org. Lett.* **2011**, *13*, 1444–1446; f) G. Ung, G. Bertrand, *Chem. Eur. J.* **2012**, *18*, 12955–12957; g) Y. He, X. Zhang, N. Shen, X. Fan, *J. Fluorine Chem.* **2013**, *156*, 9–14; h) Y. Liu, C. Chen, H. Li, K.-W. Huang, J. Tan, Z. Weng, *Organometallics* **2013**, *32*, 6587–6592; i) S. Bouvet, B. Pegot, J. Marrot, E. Magnier, *Tetrahedron Lett.* **2014**, *55*, 826–829.

[4] a) N. Yoneda, T. Fukuhara, S. Nagata, A. Suzuki, *Chem. Lett.* **1985**, 1693–1694; b) G. A. Olah, J. G. Shih, B. P. Singh, B. G. B. Gupta, *Synthesis* **1983**, 713–715; c) G. A. Olah, J. M. Bollinger, *J. Am. Chem. Soc.* **1968**, *90*, 947–953.

[5] a) D. Padmakshan, S. A. Bennett, G. Otting, C. J. Easton, *Synlett* **2007**, 1083–1084; b) H. Schwertfeger, C. Würtele, H. Hausmann, J. E. P. Dahl, R. M. K. Carlson, A. A. Fokin, P. R. Schreiner, *Adv. Synth. Catal.* **2009**, *351*, 1041–1054; c) R. Hittich, H. Mach, K. Griesbaum, *Chem. Ber.* **1983**, *116*, 2738–2747.

[6] a) S. Rozen, M. Brand, *J. Org. Chem.* **1981**, *46*, 733–736; b) T. L. Macdonald, N. Narasimhan, *J. Org. Chem.* **1985**, *50*, 5000–5001; c) E. W. Della, N. J. Head, *J. Org. Chem.* **1992**, *57*, 2850–2855; d) E. W. Della, N. J. Head, W. K. Janowski, C. H. Schiesser, *J. Org. Chem.* **1993**, *58*, 7876–7882; e) T. B. Patrick, L. Zhang, *Tetrahedron Lett.* **1997**, *38*, 8925–8928; f) T. B. Patrick, L. Zhang, Q. Li, *J. Fluorine Chem.* **2000**, *102*, 11–15; g) F. Leroux, L. Garamszegi, M. Schlosser, *J. Fluorine Chem.* **2002**, *117*, 177–180.

[7] T. Nishikata, S. Ishida, R. Fujimoto, *Angew. Chem. Int. Ed.* **2016**, 55, 10008–10012; *Angew. Chem.* **2016**, *128*, 10162–10166.

[8] a) R. E. Banks, S. N. Mohialdin-Khaffaf, G. S. Lal, I. Sharif, R. G. Syvret, *J. Chem. Soc. Chem. Commun.* **1992**, 595–596; b) R. P. Singh, J. M. Shreeve, *Acc. Chem. Res.* **2004**, *37*, 31–44; c) P. T. Nyffeler, S. G. Durón, M. D. Burkart, S. P. Vincent, C.-H. Wong, *Angew. Chem. Int. Ed.* **2005**, *44*, 192–212; *Angew. Chem.* **2005**, *117*, 196–217.

[9] M. P. Sibi, Y. Landais, *Angew. Chem. Int. Ed.* **2013**, *52*, 3570–3572; *Angew. Chem.* **2013**, *125*, 3654–3656.

[10] For a seminal work on radical fluorination, see: M. Rueda-Becerril, C. C. Sazepin, J. C. T. Leung, T. Okbinoglu, P. Kennepohl, J.-F. Paquin, G. M. Sammis, *J. Am. Chem. Soc.* **2012**, *134*, 4026–4029.

[11] F. Yin, Z. Wang, Z. Li, C. Li, *J. Am. Chem. Soc.* **2012**, *134*, 10401–10404.

[12] a) Z. Li, Z. Wang, L. Zhu, X. Tan, C. Li, *J. Am. Chem. Soc.* **2014**, *136*, 16439–16443; b) Z. Li, L. Song, C. Li, *J. Am. Chem. Soc.* **2013**, *135*, 4640–4643; c) C. Zhang, Z. Li, L. Zhu, L. Yu, Z. Wang, C. Li, *J. Am. Chem. Soc.* **2013**, *135*, 14082–14085; d) L. Zhu, H. Chen, Z. Wang, C. Li, *Org. Chem. Front.* **2014**, *1*, 1299–1305; e) H. Chen, L. Zhu, C. Li, *Org. Chem. Front.* **2017**, 4, 565–568.

[13] E. Differding, H. Ofner, *Synlett* **1991**, 187–189.

[14] a) A. S. Dudnik, G. C. Fu, *J. Am. Chem. Soc.* **2012**, *134*, 10693–10697; b) L. Song, S. Luo, J.-P. Cheng, *Org. Lett.* **2013**, *15*, 5702–5705; c) J. Cossy, S. BouzBouz, A. Hakiki, *Tetrahedron Lett.* **1997**, *38*, 8853–8854.

[15] a) H. Shigehisa, E. Nishi, M. Fujisawa, K. Hiroya, *Org. Lett.* **2013**, *15*, 5158–5161; b) T. J. Barker, D. L. Boger, *J. Am. Chem. Soc.* **2012**, *134*, 13588–13591; c) S. Thibaudeau, A. Martin-Mingot, M.-P. Jouannetaud, O. Karam, F. Zunino, *Chem. Commun.* **2007**, 3198–3200; d) G. A. Olah, M. Nojima, I. Kerekes, *Synthesis* **1973**, 779–780.

[16] a) W. J. Middleton, *J. Org. Chem.* **1975**, *40*, 574–578; b) G. S. Lal, G. P. Pez, R. J. Pesaresi, F. M. Prozonic, H. Cheng, *J. Org. Chem.* **1999**, *64*, 7048–7054; c) I. Bucsi, B. Torok, A. I. Marco, G. Rasul, G. K. S. Prakash, G. A. Olah, *J. Am. Chem. Soc.* **2002**, *124*, 7728–7736; d) G. Bellavance, P. Dube, B. Nguyen, *Synlett* **2012**, *23*, 569–572; e) F. Sladojevich, S. I. Arlow, P. Tang, T. Ritter, *J. Am. Chem. Soc.* **2013**, *135*, 2470–2473; f) M. K. Nielsen, C. R. Ugaz, W. Li, A. G. Doyle, *J. Am. Chem. Soc.* **2015**, *137*, 9571–9574.

[17] For seminal works in C(sp^3)–H fluorination, see: a) W. Liu, X. Huang, M.-J. Cheng, R. J. Nielsen, W. A. Goddard, III, J. T. Groves, *Science* **2012**, *337*, 1322–1325; b) S. Bloom, C. R. Pitts, D. C. Miller, N. Haselton, M. G. Holl, E. Urheim, T. Lectka, *Angew. Chem. Int. Ed.* **2012**, *51*, 10580–10583; *Angew. Chem.* **2012**, *124*, 10732–10735; c) W. Liu, J. T. Groves, *Angew. Chem. Int. Ed.* **2013**, *52*, 6024–6027; *Angew. Chem.* **2013**, *125*, 6140–6143; d) S. D. Halperin, H. Fan, S. Chang, R. E. Martin, R. Britton, *Angew. Chem. Int. Ed.* **2014**, *53*, 4690–4693; *Angew. Chem.* **2014**, *126*, 4778–4781; e) C. R. Pitts, S. Bloom, R. Woltornist, D. J. Auvenshine, L. R. Ryzhkov, M. A. Siegler, T. Lectka, *J. Am. Chem. Soc.* **2014**, *136*, 9780–9791.

[18] a) S. Stavber, M. Jereb, M. Zupan, *J. Phys. Org. Chem.* **2002**, *15*, 56–61; b) Q. Michaudel, D. Thevenet, P. S. Baran, *J. Am. Chem. Soc.* **2012**, *134*, 2547–2550.

[19] C. Ye, B. Twamley, J. M. Shreeve, *Org. Lett.* **2005**, *7*, 3961–3964.

10.1002/anie.201708197

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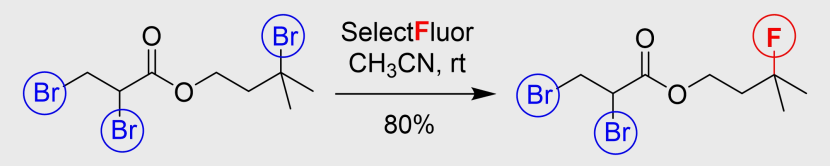

The reactions of tertiary alkyl bromides and iodides with Selectfluor proceed smoothly at room temperature to give the corresponding fluorination products in good yield. This metal-free method is highly selective in that alkyl chlorides and primary and secondary alkyl bromides remain intact.

He Chen, Zhonglin Liu, Ying Lv, Xinqiang Tan, Haigen Shen, Hai-Zhu Yu, Chaozhong Li**

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