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Nonafluoro-*tert*-butoxylation of Diaryliodonium Salts

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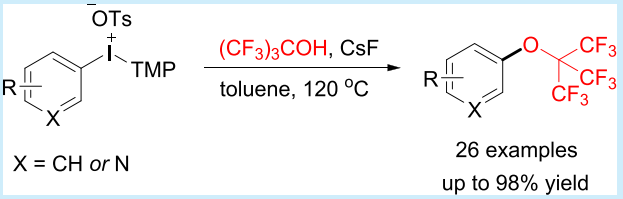
Supporting Information

ABSTRACT: A highly efficient method to incorporate the nonafluoro-*tert*-butoxy group into various arenes is developed. This C−O cross-coupling reaction proceeds smoothly in the absence of transition-metal catalyst with good functional group tolerance and scalability. In comparison with the conventional approach, this method avoids the use of nonafluoro-*tert*-butyl alcohol as the reaction solvent and does not require handling of hazardous diazonium salts. A series of $OC(CF_3)_3$-containing analogues of ^{19}F NMR-based probes targeting various biologically relevant analytes are prepared.



Fluorine-containing molecules have attracted increasing attention owing to their unique biological functions and superior physical properties.[1] In addition to being extensively explored in the pharmaceutical industry and material sciences, fluorine-containing molecules also have striking applications in molecular sensing and imaging.[2] For instance, the ^{18}F-labeled radiotracers have been widely employed in positron emission tomography (PET) to identify the abnormal metabolism in biological processes.[3] On the other hand, the ^{19}F-labeled molecular probes have enabled the investigation of recognition processes and conformational changes of biomolecules, such as DNAs, RNAs, peptides, and proteins, under physiologically relevant conditions.[4] In addition, the activity of an enzyme is readily determined by monitoring the enzymatic reaction using ^{19}F-decorated substrates.[2a−c,5] On the basis of the characteristic recognition-induced perturbation of ^{19}F chemical shifts, various cations, anions, and neutral organic analytes can be unambiguously identified in complex mixtures.[2a−c,6] It is noteworthy that the scarcity of naturally occurring ^{19}F NMR signals and the high penetration of the harmless radio frequency irradiation to large and opaque objects make the ^{19}F NMR-based sensing techniques well suited for the noninvasive detection of biological systems with high fidelity.[2a,b] Despite their robust sensory power, one limitation still hampering the wide application of many NMR-based techniques is their relatively low sensitivity.[2a,b] Routine NMR analysis often requires samples in the millimolar concentration range, which is significantly higher than that of unenriched real-world samples. The incorporation of multiple magnetically equivalent fluorine atoms is an efficient way to increase the sensitivity of ^{19}F NMR-based detection. In this regard, the nonafluoro-*tert*-butoxy group $[OC(CF_3)_3]$ is a privileged moiety owing to its large number of equivalent fluorine atoms and the intense singlet ^{19}F NMR signal. For instance, the α-(nonafluoro-*tert*-butoxy)carboxylic acids have been used as sensitive ^{19}F NMR-based solvating agents for the discrimination of chiral amines.[7] The S_N2 substitution of aliphatic halides or tosylates with nonafluoro-*tert*-butyl alcohol is most frequently used to incorporate the $OC(CF_3)_3$ group, where a flexible methylene unit $(-CH_2-)$ usually serves as the linkage.[8] This approach has successfully led to tracer agents for sensitive ^{19}F MRI applications (Scheme 1, a).[9] Unlike molecular tracers, many ^{19}F-labeled probes, especially those used in the chemical-shift based sensing scheme, require the installation of fluorinated moieties on arenes because the precise positioning of ^{19}F and the effective electron transmission between ^{19}F and the recognitive moiety are crucial to the success of the detection.[6] Unfortunately, methods to access the nonafluoro-*tert*-butyl aryl ether are scarce. The only known approach relies on the thermal decomposition of aryl diazonium salts.[10] The use of expensive nonafluoro-*tert*-butyl alcohol as the solvent and the need to handle hazardous chemicals hampers its wide adaptation (Scheme 1, b). Herein, we report an efficient method to introduce the nonafluoro-*tert*-butoxy group onto various arenes (Scheme 1c), which gives access to sensitive ^{19}F NMR probes targeting diverse biologically relevant analytes.

Previous investigations on copper-based reactions for C−O bond formation have revealed that the couplings between aryl iodides and alcohols proceed smoothly in the presence of suitable ligands, such as 1,10-phenanthroline (Table 1, **L1**) and ethyl 2-cyclohexanonecarboxylate (Table 1, **L4**).[11] Similar ligands also effectively promote the copper-mediated or

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Scheme 1. Methods To Introduce the Nonafluoro-*tert*-butoxy Group

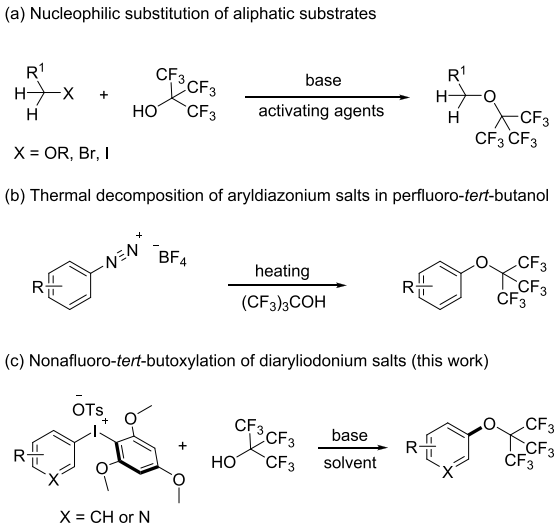
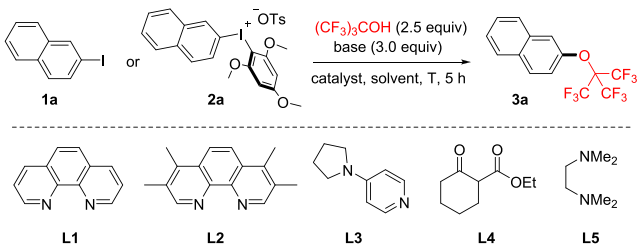


Table 1. Survey of Reaction Conditions



entry	substrate	catalyst	base	solvent	T (°C)	yield[a] (%)
1[b]	**1a**	CuI/**L1**	Cs_2CO_3	toluene	120	ND
2[b]	**1a**	CuI/**L2**	Cs_2CO_3	toluene	120	ND
3[c]	**1a**	CuI/**L3**	Cs_2CO_3	toluene	120	ND
4[b]	**1a**	CuI/**L4**	Cs_2CO_3	toluene	120	ND
5[b]	**1a**	CuI/**L5**	Cs_2CO_3	toluene	120	ND
6[b]	**1a**	CuI/**L1**	Cs_2CO_3	toluene	180	ND
7[b]	**2a**	CuI/**L1**	Cs_2CO_3	toluene	120	51
8	**2a**		Cs_2CO_3	toluene	120	82
9	**2a**		K_2CO_3	toluene	120	79
10	**2a**		K_3PO_4	toluene	120	39
11	**2a**		CsF	toluene	120	95
12	**2a**		CsF	dioxane	120	78
13	**2a**		CsF	CH_3CN	120	47
14	**2a**		CsF	DMF	120	34
15	**2a**		CsF	toluene	60	11
16	**2a**		CsF	toluene	80	52
17[d]	**2a**		**CsF**	**toluene**	**120**	**99 (94)**[e]

[a]Reactions were conducted on 0.17 mmol scale. Yields were determined by ^{19}F NMR analysis using $PhCF_3$ as an internal standard. [b]CuI (0.1 equiv) and ligand (0.2 equiv) were employed. [c]CuI (0.1 equiv) and **L3** (1.2 equiv) were employed. [d]Reaction time = 12 h. [e]Isolated yield. ND denotes not detected.

catalyzed trifluoroethoxylation of aryl bromides and iodides.[12] In the light of these advances, we commenced our investigation by screening various ligands and bases for the copper-catalyzed C−O coupling reaction between 2-iodonaphthalene (**1a**) and nonafluoro-*tert*-butyl alcohol. However, no desired product was observed when the reaction was carried out in the presence of copper iodide and various ligands at 120 °C (Table 1, entries 1−5) or under more forcing conditions (Table 1, entry 6). Mechanistically, the oxidative addition of the CuOR (R = aryl, alkyl) species to aryl iodide to form ArCu(III)ORI is often involved in the copper-catalyzed C−O couplings.[12] We envisioned that this crucial step might become sluggish due to the low electron-donating ability of the $OC(CF_3)_3$ group. Therefore, diaryliodonium salt **2a**, which has a much higher reduction potential compared to that of **1a**, was attempted with the aim of facilitating the oxidative addition.[13] To our delight, the use of **2a** as the substrate furnished the desired product **3a** in 51% yield (Table 1, entry 7). Nevertheless, control experiments disclosed that the reaction proceeded even better in the absence of both copper and ligand (Table 1, entry 8), which indicated that a transition-metal-free coupling between **2a** and nonafluoro-*tert*-butyl alcohol occurred. It is noteworthy that the couplings between diaryliodonium salts and alcohols are known;[14] however, the nonafluoro-*tert*-butoxylation has not been achieved.

We next tested the influence of other reaction parameters on this reaction. Bases such as K_2CO_3 and K_3PO_4 could also promote the current reaction, albeit with lower efficiency (Table 1, entries 9 and 10). The best yield was achieved in the reaction using CsF as the base, despite the fear of the competitive fluorination reaction (Table 1, entries 11 and 17).[15] No fluoroarenes were produced in these reactions, which indicates that the nucleophilicity of the fluoride ion is significantly weakened due to the hydrogen bonding with nonafluoro-*tert*-butyl alcohol. Yields were substantially diminished when the reactions were performed at lower temperatures (Table 1, entries 15 and 16) or in polar solvents such as dimethylformamide and acetonitrile (Table 1, entries 13 and 14). When the reaction time was extended to 12 h, a quantitative yield of **3a** was obtained. Having identified the suitable reaction conditions (Table 1, entry 17), we next explored the scope of this nonafluoro-*tert*-butoxylation reaction. Unsymmetrical iodonium salts **2** bearing the dummy 1,3,5-trimethoxyphenyl (TMP) group were used as the substrates to achieve a chemoselective coupling of the desired aryl moiety.[16] As summarized in Scheme 2, the $OC(CF_3)_3$ group can be readily incorporated into a variety of arenes in good to excellent yields. Common functionalities, such as ester, nitrile, ketone, and nitro, are compatible. The reaction is also amenable to substrates (**2f**, **2i−k**, and **2o−q**) containing a carbon−bromine bond, providing opportunities for further structural elaborations. The heterocyclic iodonium salts were smoothly converted to the corresponding $OC(CF_3)_3$-substituted products (**3d**, **3v**, **3x**) under the same conditions. Azide-containing building block **3y** can be obtained through the current method, which is useful for the rapid access to $OC(CF_3)_3$-labeled molecules through a click reaction.[17] Highly sterically congested substrate **2o** could participate in the reaction as well, furnishing product **3o** in excellent yield. The nonafluoro-*tert*-butoxy group was readily introduced to the protected tyrosine, which could serve as a sensitive ^{19}F-labeled unit to study the function of proteins.[10c] The reaction is readily scaled up, providing more than 1 g of products **3q** and **3u** in 78% and 90% yields, respectively. Notably, other highly fluorinated tertiary alcohols (Scheme 3, **4**, **6**, and **8**) are also suitable substrates for this C−O coupling, affording structurally diversified fluoroalkyl aryl ethers (Scheme 3, **5**, **7**, and **9**), which are otherwise difficult to access.

To gain more insights into the reaction mechanism, the diaryliodonium nonafluoro-*tert*-butoxide 2-BrC_6H_4(TMP)-

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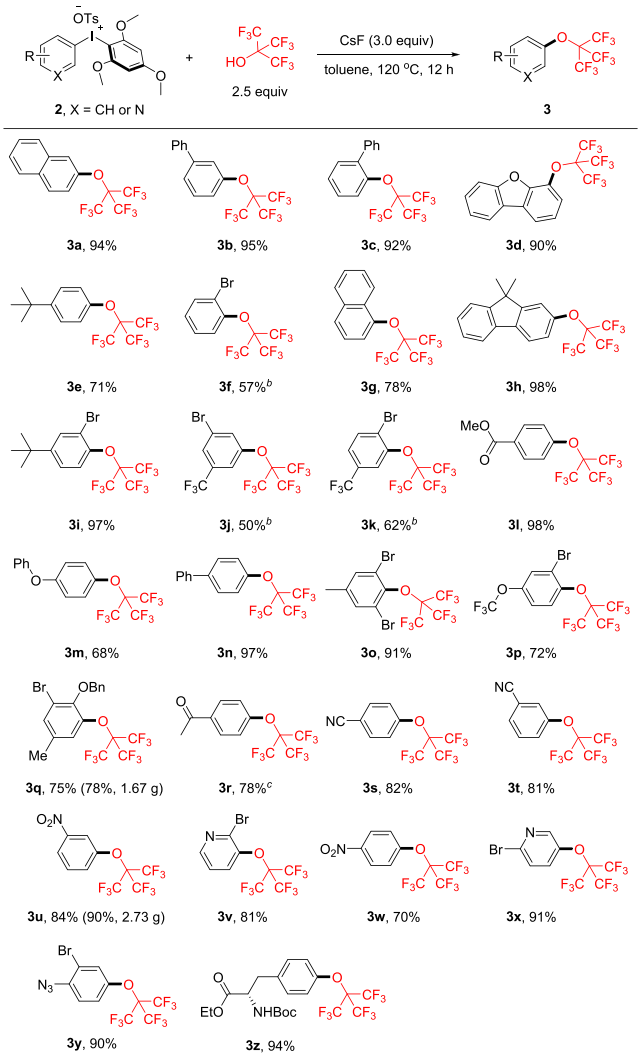
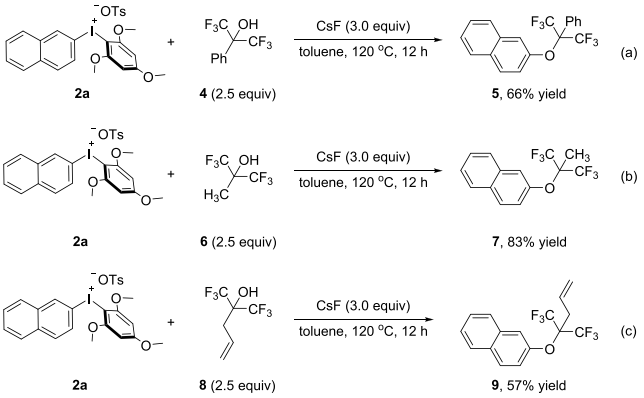
Scheme 2. Substrate Scope[a]



[a]With 200 mg of **2**. Yields of isolated products are given. [b]The low yields are partially due to the high volatility of the products. [c]The reaction was carried out at 80 °C for 20 h.

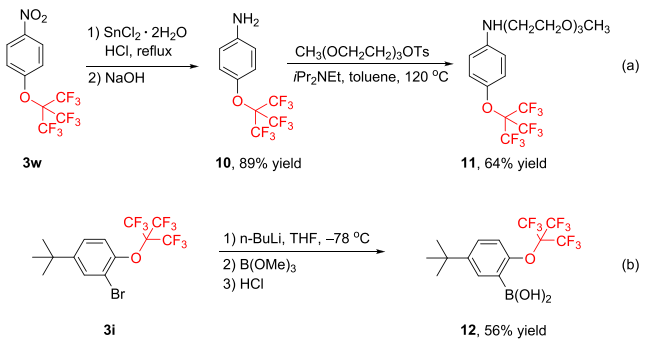
Scheme 3. Reactions with Other Highly Fluorinated Tertiary Alcohols



IOC_4F_9 (**2f′**) was prepared through ion exchange of **2f** with potassium nonafluoro-*tert*-butoxide. Thermal decomposition of **2f′** in toluene at 80 °C for 4 h gave the expected coupling product **3f** in 95% yield (for details, see Figure S1). This result suggests the reaction pathway is similar to what was observed in other C−O couplings with diaryliodonium salts, which involves a ligand exchange followed by a reductive elimination-like ligand coupling.[14]

To illustrate the application of the current method for the construction of sensitive ^{19}F NMR-based probes, we selected a series of previously reported probes targeting diverse biologically relevant analytes and decorated them with the $OC(CF_3)_3$ moiety for enhanced sensitivity. Sando and coworkers have shown that *p*-aminophenyl trifluoroethyl ether reacted selectively with hypochlorite ion (^-OCl) through *ipso*-substitution.[18] This highly specific reactivity was utilized to create a hypochlorite ion responsive ^{19}F MRI agent.[18] The structural analogue of this probe with the replacement of the OCH_2CF_3 group by a more sensitive $OC(CF_3)_3$ was readily obtained by a simple reduction of **3w**, followed by alkylation to increase its solubility in aqueous solution (Scheme 4, a). The

Scheme 4. Preparation of $OC(CF_3)_3$-Containing Analogues of ^{19}F NMR-Based Probes



fluorinated aryl boronic acids have been widely utilized as selective sensors for hydrogen peroxide and various carbohydrates.[6d,e,19] These sensors usually suffer from low sensitivity due to the quite limited amounts of equivalent fluorine atoms appended to the probe. The $OC(CF_3)_3$-containing boronic acid is therefore of interest for achieving superior sensitivity. It was found that the $OC(CF_3)_3$ group is robust under the lithium bromide exchange conditions, thereby allowing the desirable boronic acid **12** to be quickly prepared through the synthetic route depicted in Scheme 4b.

In summary, we have developed an efficient method for the installation of the $OC(CF_3)_3$ group onto various arenes. A variety of functional groups are tolerated, and the reaction gives access to the $OC(CF_3)_3$-containing version of NMR probes targeting diverse biologically relevant analytes. We expect this method will significantly promote the creation of novel sensitive ^{19}F-labeled probes and widen the scope of NMR-based detection. A systematic exploration of the application of $OC(CF_3)_3$-containing probes is currently underway in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b01813.

Experimental details, characterization of new compounds, and NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) Kirsch, P. *Modern Organofluorine Chemistry*; Wiley-VCH: Weinheim, 2004. Uneyama, K. *Organofluorine Chemistry*; Wiley: Hoboken, 2008. (b) Kirk, K. L. *Org. Process Res. Dev.* **2008**, *12*, 305. (c) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320−330. (d) Müller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881−1886. (e) Weber, E.; Hulliger, J.; Resnati, G.; Berger, R.; Metrangolo, P. *Chem. Soc. Rev.* **2011**, *40*, 3496−3508.

(2) (a) Xu, Z.; Liu, C.; Zhao, S.; Chen, S.; Zhao, Y. *Chem. Rev.* **2019**, *119*, 195−230. (b) Yu, J. X.; Hallac, R. R.; Chiguru, S.; Mason, R. P. *Prog. Nucl. Magn. Reson. Spectrosc.* **2013**, *70*, 25−49. (c) Swager, T. M. *Angew. Chem., Int. Ed.* **2018**, *57*, 4248−4257. (d) Yu, J.; Kodibagkar, V. D.; Cui, W.; Mason, R. P. *Curr. Med. Chem.* **2005**, *12*, 819−848. (e) Cobb, S. L.; Murphy, C. D. *J. Fluorine Chem.* **2009**, *130*, 132−143. (f) Knight, J. C.; Edwards, P. G.; Paisey, S. J. *RSC Adv.* **2011**, *1*, 1415−1425. (g) Ruiz-Cabello, J.; Barnett, B. P.; Bottomley, P. A.; Bulte, J. W. M. *NMR Biomed.* **2011**, *24*, 114−129.

(3) (a) Deng, X.; Rong, J.; Wang, L.; Zhang, L.; Liang, S. H.; Josephson, L.; Vasdev, N. *Angew. Chem., Int. Ed.* **2019**, *58*, 2580−2605. (b) Preshlock, S.; Tredwell, M.; Gouverneur, V. *Chem. Rev.* **2016**, *116*, 719−766. (c) Campbell, M. G.; Mercier, J.; Genicot, C.; Gouverneur, V.; Hooker, J. M.; Ritter, T. *Nat. Chem.* **2017**, *9*, 1−3. (d) Van Der Born, D.; Pees, A.; Poot, A. J.; Orru, R. V. A.; Windhorst, A. D.; Vugts, D. *Chem. Soc. Rev.* **2017**, *46*, 4709−4773.

(4) For selected examples, see: (a) Kiviniemi, A.; Virta, P. *J. Am. Chem. Soc.* **2010**, *132*, 8560−8562. (b) Granqvist, L.; Virta, P. *J. Org. Chem.* **2015**, *80*, 7961−7970. (c) Lombès, T.; Moumné, R.; Larue, V.; Prost, E.; Catala, M.; Lecourt, T.; Dardel, F.; Micouin, L.; Tisné, C. *Angew. Chem., Int. Ed.* **2012**, *51*, 9530−9534. (d) Kreutz, C.; Kählig, H.; Konrat, R.; Micura, R. *Angew. Chem., Int. Ed.* **2006**, *45*, 3450−3453. (e) Graber, D.; Moroder, H.; Micura, R. *J. Am. Chem. Soc.* **2008**, *130*, 17230−17231. (f) Fauster, K.; Kreutz, C.; Micura, R. *Angew. Chem., Int. Ed.* **2012**, *51*, 13080−13084. (g) Michurin, O. M.; Afonin, S.; Berditsch, M.; Daniliuc, C. G.; Ulrich, A. S.; Komarov, I. V.; Radchenko, D. S. *Angew. Chem., Int. Ed.* **2016**, *55*, 14595−14599. (h) Takaoka, Y.; Kioi, Y.; Morito, A.; Otani, J.; Arita, K.; Ashihara, E.; Ariyoshi, M.; Tochio, H.; Shirakawa, M.; Hamachi, I. *Chem. Commun.* **2013**, *49*, 2801−2803.

(5) For selected recent examples, see: (a) Yu, J.-X.; Kodibagkar, V. D.; Liu, L.; Zhang, Z.; Liu, L.; Magnusson, J.; Liu, Y. *Chem. Sci.* **2013**, *4*, 2132−2142. (b) Baranowski, M. R.; Nowicka, A.; Rydzik, A. M.; Warminski, M.; Kasprzyk, R.; Wojtczak, B. A.; Wojcik, J.; Claridge, T. D. W.; Kowalska, J.; Jemielity, J. *J. Org. Chem.* **2015**, *80*, 3982−3997. (c) Stockman, B. J. *J. Am. Chem. Soc.* **2008**, *130*, 5870−5871. (d) Yamaguchi, K.; Ueki, R.; Nonaka, H.; Sugihara, F.; Matsuda, T.; Sando, S. *J. Am. Chem. Soc.* **2011**, *133*, 14208−14211. (e) Dalvit, C.; Ardini, E.; Flocco, M.; Fogliatto, G. P.; Mongelli, N.; Veronesi, M. *J. Am. Chem. Soc.* **2003**, *125*, 14620−14625.

(6) For selected recent examples, see: (a) Zhao, Y.; Chen, L.; Swager, T. M. *Angew. Chem., Int. Ed.* **2016**, *55*, 917−921. (b) Zhao, Y.; Swager, T. M. *J. Am. Chem. Soc.* **2015**, *137*, 3221−3224. (c) Gan, H.; Oliver, A. G.; Smith, B. D. *Chem. Commun.* **2013**, *49*, 5070−5072. (d) Axthelm, J.; Askes, S. H. C.; Elstner, M.; Upendar Reddy, G.; Görls, H.; Bellstedt, P.; Schiller, A. *J. Am. Chem. Soc.* **2017**, *139*, 11413−11420. (e) Axthelm, J.; Görls, H.; Schubert, U. S.; Schiller, A. *J. Am. Chem. Soc.* **2015**, *137*, 15402−15405. (f) Guo, L. E.; Hong, Y.; Zhang, S. Y.; Zhang, M.; Yan, X. S.; Cao, J. L.; Li, Z.; James, T. D.; Jiang, Y. B. *J. Org. Chem.* **2018**, *83*, 15128−15135. (g) Yang, S.; Zeng, Q.; Guo, Q.; Chen, S.; Liu, H.; Liu, M.; McMahon, M. T.; Zhou, X. *Talanta* **2018**, *184*, 513−519. (h) Bar-Shir, A.; Gilad, A. A.; Chan, K. W. Y.; Liu, G.; Van Zijl, P. C. M.; Bulte, J. W. M. M.; McMahon, T. *J. Am. Chem. Soc.* **2013**, *135*, 12164−12167. (i) Bar-Shir, A.; Yadav, N. N.; Gilad, A. A.; Van Zijl, P. C. M.; McMahon, M. T.; Bulte, J. W. M. *J. Am. Chem. Soc.* **2015**, *137*, 78−81. (j) Zhao, Y.; Swager, T. M. *J. Am. Chem. Soc.* **2013**, *135*, 18770−18773. (k) Zhao, Y.; Markopoulos, G.; Swager, T. M. *J. Am. Chem. Soc.* **2014**, *136*, 10683−10690. (l) Peng, Q.; Yuan, Y.; Zhang, H.; Bo, S.; Li, Y.; Chen, S.; Yang, Z.; Zhou, X.; Jiang, Z.-X. *Org. Biomol. Chem.* **2017**, *15*, 6441−6446.

(7) Nemes, A.; Csóka, T.; Béni, S.; Farkas, V.; Rábai, J.; Szabó, D. *J. Org. Chem.* **2015**, *80*, 6267−6274.

(8) (a) Tressler, C. M.; Zondlo, N. J. *J. Org. Chem.* **2014**, *79*, 5880−5886. (b) Tressler, C. M.; Zondlo, N. J. *Biochemistry* **2017**, *56*, 1062−1074. (c) Buer, B. C.; Levin, B. J.; Marsh, E. N. G. *J. Pept. Sci.* **2013**, *19*, 308−314. (d) Tanabe, K.; Harada, H.; Narazaki, M.; Tanaka, K.; Inafuku, K.; Komatsu, H.; Ito, T.; Yamada, H.; Chujo, Y.; Matsuda, T.; Hiraoka, M.; Nishimoto, S. *J. Am. Chem. Soc.* **2009**, *131*, 15982−15983. (e) Taraban, M. B.; Deredge, D. J.; Smith, M. E.; Briggs, K. T.; Li, Y.; Jiang, Z.-X.; Wintrode, J. P.; Yu, L. Y. B. *Magn. Reson. Chem.* **2019**, 1−12. (f) Jiang, Z.-X.; Feng, Y.; Yu, Y. B. *Chem. Commun.* **2011**, *47*, 7233−7235. (g) Yue, X.; Taraban, M. B.; Hyland, L. L.; Yu, Y. B. *J. Org. Chem.* **2012**, *77*, 8879−8887. (h) Yue, X.; Feng, Y.; Yu, Y. B. *J. Fluorine Chem.* **2013**, *152*, 173−181.

(9) (a) Jiang, Z. X.; Liu, X.; Jeong, E. K.; Yu, Y. B. *Angew. Chem., Int. Ed.* **2009**, *48*, 4755−4758. (b) Liu, X.; Jiang, Z.-X.; Yu, B. Y.; Jeong, E.-K. *MAGMA* **2019**, *32*, 97−103. (c) Chen, X.; Niu, G.; Rong, P.; Ma, Y.; Kiesewetter, D. O.; Wang, Z.; Lizak, M.; Yue, X.; Wang, Y.; Wang, F.; Huang, P.; Qian, C. *Adv. Healthcare Mater.* **2014**, *3*, 1326−1333. (d) Tirotta, I.; Mastropietro, A.; Cordiglieri, C.; Gazzera, L.; Baggi, F.; Baselli, G.; Grazia Bruzzone, M.; Zucca, I.; Cavallo, G.; Terraneo, G.; Baldelli Bombelli, F.; Metrangolo, P.; Resnati, G. A. *J. Am. Chem. Soc.* **2014**, *136*, 8524−8527. (e) Huynh, A. M.; Müller, A.; Kessler, S. M.; Henrikus, S.; Hoffmann, C.; Kiemer, A. K.; Bücker, A.; Jung, G. *ChemMedChem* **2016**, *11*, 1568−1575. (f) Tirotta, I.; Dichiarante, V.; Pigliacelli, C.; Cavallo, G.; Terraneo, G.; Bombelli, F. B.; Metrangolo, P.; Resnati, G. *Chem. Rev.* **2015**, *115*, 1106−1129.

(10) (a) Nabuurs, R. J. A.; Kapoerchan, V. V.; Metaxas, A.; De Jongh, S.; De Backer, M.; Welling, M. M.; Jiskoot, W.; Windhorst, A. D.; Overkleeft, H. S.; Van Buchem, M. A.; Overhand, M.; Van Der Weerd, L. *Bioorg. Med. Chem.* **2014**, *22*, 2469−2481. (b) Canning, P. S. J.; Maskill, H.; McCrudden, K.; Sexton, B. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 789−800. (c) Tressler, C. M.; Zondlo, N. J. *Org. Lett.* **2016**, *18*, 6240−6243.

(11) (a) Bhunia, S.; Pawar, G. G.; Kumar, S. V.; Jiang, Y.; Ma, D. *Angew. Chem., Int. Ed.* **2017**, *56*, 16136−16179. (b) Wolter, M.; Nordmann, G.; Job, G. E.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 973−976. (c) Altman, R. A.; Shafir, A.; Choi, A.; Lichtor, P. A.; Buchwald, S. L. *J. Org. Chem.* **2008**, *73*, 284−286. (d) Sugata, H.; Tsubogo, T.; Kino, Y.; Uchiro, H. *Tetrahedron Lett.* **2017**, *58*, 1015−1019. (e) Shafir, A.; Lichtor, P. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 3490−3491. (f) Niu, J.; Zhou, H.; Li, Z.; Xu, J.; Hu, S. *J. Org. Chem.* **2008**, *73*, 7814−7817. (g) Niu, J.; Guo, P.; Kang, J.; Li, Z.; Xu, J.; Hu, S. *J. Org. Chem.* **2009**, *74*, 5075−5078. (h) Yu, H. Z.; Jiang, Y. Y.; Fu, Y.; Liu, L. *J. Am. Chem. Soc.* **2010**, *132*, 18078−18091. (i) Chen, Z.; Zhang, L.; Jiang, Y.; Ma, D.; Guo, Y.-L. *J. Am. Chem. Soc.* **2019**, *141*, 3541−3549.

(12) (a) Huang, Y.; Huang, R.; Weng, Z. *Synlett* **2015**, *26*, 2327−2331. (b) Zhang, K.; Xu, X. H.; Qing, F. L. *J. Fluorine Chem.* **2017**, *196*, 24−31. (c) Vuluga, D.; Legros, J.; Crousse, B.; Bonnet-Delpon, D. *Eur. J. Org. Chem.* **2009**, *2009*, 3513−3518. (d) Pethő, B.; Novák,

DOI: 10.1021/acs.orglett.9b01813
Org. Lett. XXXX, XXX, XXX−XXX

Z. *Asian J. Org. Chem.* **2018**, 1−8, DOI: 10.1002/ajoc.201800414. (e) Ding, J.; You, Y.; Weng, Z. *Tetrahedron Lett.* **2016**, *57*, 1724−1727. (f) Huang, R.; Huang, Y.; Lin, X.; Rong, M.; Weng, Z. *Angew. Chem., Int. Ed.* **2015**, *54*, 5736−5739.

(13) Ghosh, I.; Marzo, L.; Das, A.; Shaikh, R.; König, B. *Acc. Chem. Res.* **2016**, *49*, 1566−1577.

(14) For selected examples, see: (a) Sundalam, S. K.; Stuart, D. R. *J. Org. Chem.* **2015**, *80*, 6456−6466. (b) Lindstedt, E.; Ghosh, R.; Olofsson, B. *Org. Lett.* **2013**, *15*, 6070−6073. (c) Ghosh, R.; Lindstedt, E.; Jalalian, N.; Olofsson, B. *ChemistryOpen* **2014**, *3*, 54−57. (d) Lindstedt, E.; Stridfeldt, E.; Olofsson, B. *Org. Lett.* **2016**, *18*, 4234−4237. (e) Yoshimura, A.; Zhdankin, V. V. *Chem. Rev.* **2016**, *116*, 3328−3435.

(15) (a) Pike, V. W.; Aigbirhio, F. I. *J. Chem. Soc., Chem. Commun.* **1995**, *27*, 2215−2216. (b) Chun, J. H.; Lu, S.; Lee, Y. S.; Pike, V. W. *J. Org. Chem.* **2010**, *75*, 3332−3338. (c) Ross, T. L.; Ermert, J.; Hocke, C.; Coenen, H. H. *J. Am. Chem. Soc.* **2007**, *129*, 8018−8025.

(16) (a) Seidl, T. L.; Sundalam, S. K.; McCullough, B.; Stuart, D. R. *J. Org. Chem.* **2016**, *81*, 1998−2009. (b) Sandtorv, A. H.; Stuart, D. R. *Angew. Chem., Int. Ed.* **2016**, *55*, 15812−15815. (c) Malmgren, J.; Santoro, S.; Jalalian, N.; Himo, F.; Olofsson, B. *Chem. - Eur. J.* **2013**, *19*, 10334−10342.

(17) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004−2021.

(18) Doura, T.; An, Q.; Sugihara, F.; Matsuda, T.; Sando, S. *Chem. Lett.* **2011**, *40*, 1357−1359.

(19) Nonaka, H.; An, Q.; Sugihara, F.; Doura, T.; Tsuchiya, A.; Yoshioka, Y.; Sando, S. *Anal. Sci.* **2015**, *31*, 331−335.

DOI: 10.1021/acs.orglett.9b01813
Org. Lett. XXXX, XXX, XXX−XXX