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Room-temperature base-free copper-catalyzed trifluoromethylation of organotrifluoroborates to trifluoromethylarenes

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ABSTRACT

An efficient room temperature copper-catalyzed trifluoromethylation of organotrifluoroborates under the base free condition using an electrophilic trifluoromethylating reagent is demonstrated. The corresponding trifluoromethylarenes were obtained in good to excellent yields and the reaction tolerates a wide range of functional groups.

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1. Introduction

The incorporation of a trifluoromethyl group to a molecule often results in the improvement of desirable characteristics such as binding selectivity, high lipophilicity, and excellent metabolic stability.[1] The direct introduction of a CF_3 group into the desired position in the drug-like molecules has become a powerful strategy in the new drug design. In particular, the trifluoromethylarenes are widely used as active ingredients, which are present in several top-selling pharmaceuticals, including Januvia (Sitagliptin), Celebrex (Celecoxib), Prozac (Fluoxetine), and Avodart (Dutasteride). It has attracted intensive attention to the development of practical methods to synthesize such molecules due to the widespread importance of trifluoromethylarenes units in medicinal and materials chemistry.

Recent reports of transition metal-mediated or catalyzed trifluoromethylation reactions have proved to be an efficient strategy to construct the $ArCF_3$ motifs.[2,3] For example, Amii and co-workers have reported Cu(I)-diamine complexes -catalyzed aromatic trifluoromethylation of aryl iodides with CF_3SiEt_3 and fluoral derivatives as the trifluoromethyl source;[4] Gooßen et al. reported a similar reaction with potassium (trifluoromethyl)trimethoxyborate as CF_3 sources;[5] Buchwald et al. reported a remarkable breakthroughs of Pd-catalyzed trifluoromethylation of aryl chlorides with CF_3SiEt_3;[6] Shen and Liu's group independently reported copper-catalyzed trifluoromethylation of aryl boronic acids or pinacolboronate with the electrophilic trifluoromethylating reagent (Togni's reagent and Umemoto's reagent, respectively);[7] Yu et al. reported Pd(II)-catalyzed *ortho*-trifluoromethylation of arenes with Umemoto's reagent;[8] Bräse et al. recently reported a $AgCF_3$ mediated highly *ortho*-selective trifluoromethylation of aromatic triazenes.[9] Qing et al. reported copper-catalyzed oxidative trifluoromethylation of aryl boronic acids using the Ruppert-Prakash reagent (Me_3SiCF_3).[10]

However, most of these reactions typically require elevated temperatures and an excess of either inorganic and organic base or oxidants. Accordingly, these existing protocols can be incompatible with the presence of some functional groups. Therefore, there is still a strong need for procedures that would allow for a room temperature, base-free preparation of trifluoromethylarenes.

In our continuing research efforts directed toward the development of metal-catalyzed trifluoromethylation, we have recently demonstrated the silver-assisted copper-catalyzed trifluoromethylation of aryl iodides using Me_3SiCF_3.[11] Moreover, we have developed a mild copper-catalyzed trifluoromethylation of terminal alkynes using an electrophilic trifluoromethylating reagent.[12] Initially inspired by these results and recent advances in the field of copper-catalyzed cross-coupling reactions,[13] we hypothesized that efficient and attractive alternatives for the preparation of trifluoromethylarenes would rely on the use of organotrifluoroborates as reactive substrates.

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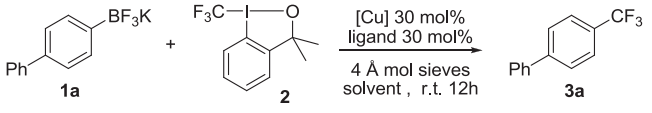
Although many boronic acids and boronate esters have been successfully applied in various cross-coupling reactions, they are suspected to undergo protodeboronation and to react with bases, nucleophiles, and oxidants, which make them prone to undesirable side reactions. Compared with the corresponding boronic acids, organotrifluoroborates have many advantages,[14] such as their ease of handling, storability, and robustness under harsh reaction conditions. This superior characteristic allows extensive elaboration of a simple substructure, while leaving the carbon–boron bond intact. To the best of our knowledge, only one example of trifluoromethylation of organotrifluoroborates has been reported recently;[15] Accordingly, we were prompted to conduct an experiment to develop a mild and convenient method for the preparation of trifluoromethylarenes using aryltrifluoroborates as substrate. Herein, we report a copper-catalyzed trifluoromethylation of organotrifluoroborates to synthesize trifluoromethylarenes under very mild conditions, using an electrophilic trifluoromethylating reagent in the absence of either added base or oxidant.

2. Results and discussion

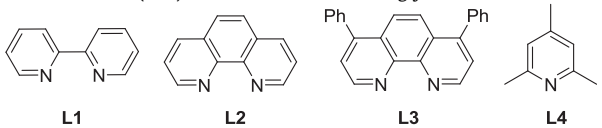
Trifluoromethylation of potassium 4-biphenylborate with Togni's reagent was investigated. We began our studies by examining $Cu(TFA)_2$ and 2,2′-bipyridine (L1) as a potential catalyst. Indeed, it was found that the reaction produces the desired product in 96% yield as determined by GC with an internal standard (Table 1, entry 3). It is noted that the reaction occurs smoothly in the absence of either added base or oxidant. This result is in sharp contrast to those of the reactions involving its boronic acids analogs,[7a] in which the reaction efficacy is sensitive to the base and 2 equiv of base is required.

The reaction was ineffective when using only $Cu(TFA)_2$ in the absence of ligands (entry 2). It should be noted that the presence of molecular sieves was found to be essential for the efficient trifluoromethylation to proceed (entry 4). Other diamine ligands (L2, L3) and 2,4,6-trimethylpyridine (L4) have also been examined and showed lower reactivity (entries 5–7). Various copper precursors, such as CuI, CuCl, Cu, CuF_2, and CuO have been investigated, and the trifluoromethylation was mostly suppressed in these cases (entries 8–12). With the use of $Cu(OTf)_2$, the product was generated in 25% yield (entry 13). Employing $Cu(TFA)_2$ (30 mol %) and L1 (30 mol %), changing the solvent systems (e.g., acetone, DCE, and diglyme) did not lead to more favorable outcomes (entries 14–16).

Table 1
Optimization of copper-mediated trifluoromethylation of potassium organotrifluoroborates with trifluoromethylating reagent[a]

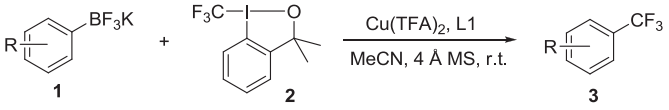


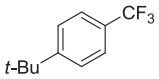
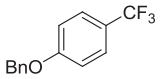
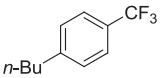
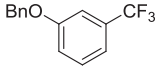
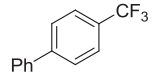
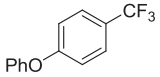
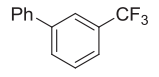
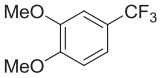
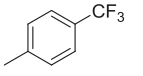
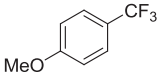
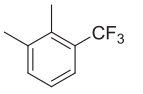
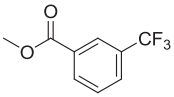
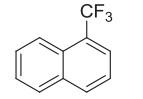
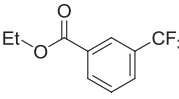
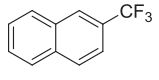
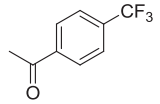
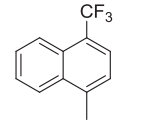
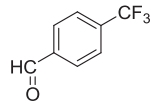
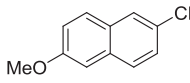
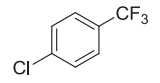
Entry	[Cu]	Ligand	Solvent	Yield (%)[b]
1	—	—	MeCN	1.3
2	$Cu(TFA)_2$	—	MeCN	48
3	$Cu(TFA)_2$	L1	MeCN	96
4	$Cu(TFA)_2$	L1	MeCN	42[c]
5	$Cu(TFA)_2$	L2	MeCN	80
6	$Cu(TFA)_2$	L3	MeCN	65
7	$Cu(TFA)_2$	L4	MeCN	77
8	CuI	L1	MeCN	2
9	CuCl	L1	MeCN	2
10	Cu	L1	MeCN	3
11	CuF_2	L1	MeCN	3
12	CuO	L1	MeCN	Trace
13	$Cu(OTf)_2$	L1	MeCN	25
14	$Cu(TFA)_2$	L1	Acetone	7
15	$Cu(TFA)_2$	L1	DCE	9
16	$Cu(TFA)_2$	L1	Diglyme	28



[a] Reaction conditions: **1a** (0.10 mmol), **2** (0.12 mmol), solvent (1.0 mL), 4 Å mol sieves (200 mg/mmol) ArBF3K rt, 12 h under Ar atmosphere.
[b] Yield were determined by GC analysis of the crude reaction mixture with an internal standard.
[c] Without addition of mol sieves.

Table 2
Copper-catalyzed trifluoromethylation of potassium aryltrifluoroborates with an electrophilic trifluoromethylating reagent[a]

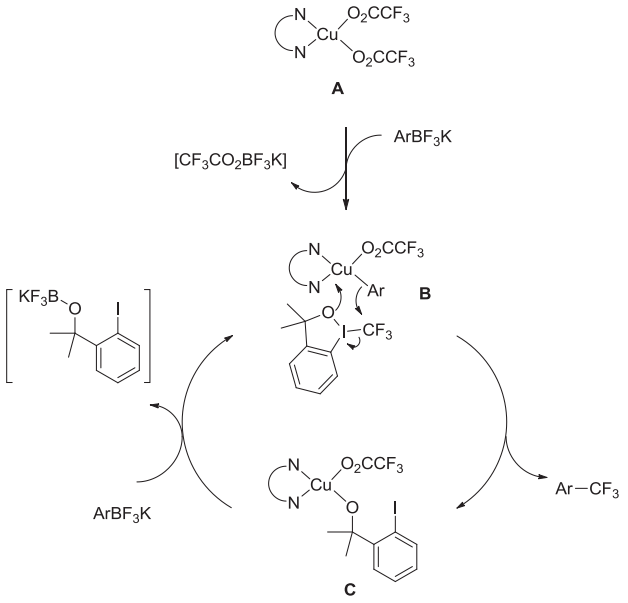


Entry	Product	Yield (%)[b]	Entry	Product	Yield (%)[b]
1		91	11		92
2		89	12		90
3		95	13		94
4		82	14		65
5		69[c]	15		60
6		65	16		61
7		50[c]	17		72
8		51[d]	18		42
9		70[d]	19		39[e]
10		65[d]	20		50

[a] Reaction conditions: $ArBF_3K$ (0.10 mmol), **2** (0.12 mmol), $Cu(TFA)_2$ (0.030 mmol), bipy (0.030 mmol), 4 Å mol sieves (200 mg/mmol), MeCN (1.0 mL), rt, 12 h under Ar atmosphere.
[b] Isolated yield.
[c] Yield were determined by GC analysis of the crude reaction mixture with an internal standard.
[d] Addition of Ag_2O (0.030 mmol).
[e] ^{19}F NMR yield.

With the optimized reaction conditions in hand, different substrates were investigated (Table 2). Both electron-donating and electron-withdrawing substituents at the *para*, *meta*, or *ortho* position of the aryltrifluoroborates afforded a useful range of products in good to excellent isolated yields. Various functionality and substitution patterns can be tolerated. The butyl- and phenyl-substituted phenyltrifluoroborates proceeded smoothly in the trifluoromethylation with Togni's reagent to give trifluoromethylated products in 82–95% yield (entries 1–4). The use of methyl-substituted phenyltrifluoroborates afforded products in moderate yields (entries 5 and 6). The scope of naphthyltrifluoroborate substrates was also briefly surveyed. The 1- and 2- naphthyltrifluoroborate gave yields of 50 and 51%, respectively (entries 7 and 8), while the 4-methyl 1-naphthyltrifluoroborate was more reactive and afforded a good yield of 70% (entry 9). We were pleased to find that electron-donating groups on the phenyl or naphthyl rings did not reduce the reactivity. The reactions with benzyloxy and phenyloxy-substituted phenyltrifluoroborates generated the products in good yields of 90–94% (entries 11–13). Meanwhile, substrates with methoxy substituents afforded 60–65% yield of products (entries 10, 14, and 15). Moreover, a variety of electron-withdrawing groups (ester, ketone, and aldehyde groups) were tolerated in this reaction although some of them suffered from the relatively poorer reactivities. The ester-substituted phenyltrifluoroborates gave the corresponding products in moderate to good yields (entries 16 and 17), meanwhile a *para*-ketone-substituted phenyltrifluoroborate afforded the product in 42% yield (entry 18). The phenyltrifluoroborate having an aldehyde group provided the desired products in 39% yield (entry 19). It should be noted that the reaction was also effective with halide-containing organotrifluoroborates (entry 20).

A plausible mechanism for the trifluoromethylation of potassium arylborate with the Togni's reagent is proposed in Scheme 1. The bipyridine ligated (N,N)Cu(CF_3CO_2)$_2$ complex (**A**) could be initially generated in situ. A then undergoes the transmetallation reaction with potassium arylborate to give a copper(II) intermediate **B**. Subsequent nucleophilic attack of the aryl group of **B** to the CF_3^+ moiety in the Togni's reagent might proceed to form the product and a Cu-alkoxide complex (**C**), which can further react with potassium arylborate to regenerate **B** to complete the catalytic cycle.



Scheme 1. Plausible Mechanism.

3. Conclusions

In summary, we have reported an effective copper catalyst system for the trifluoromethylation of organotrifluoroborates using an electrophilic trifluoromethylating reagent. Our catalytic reactions proceed smoothly at room temperature, in the absence of either added base or oxidant to afford trifluoromethylarenes in good to excellent yields and can tolerate a variety of functionalities. Research efforts seeking to expand the process to other distinctive substrates and substituents are currently ongoing in our laboratories.

4. Experimental

4.1. General experimental

All solvents were purified by stand method. ^{1}H NMR, ^{19}F NMR and ^{13}C NMR spectra were recorded using BrukerAVIII 400 or AVIII 500 spectrometer. ^{1}H NMR and ^{13}C NMR chemical shifts were reported in parts per million (ppm) downfield from tetramethylsilane and ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as outside standard and low field is positive. Coupling constants (*J*) are reported in Hertz (Hz). The residual solvent peak was used as an internal reference: ^{1}H NMR (chloroform δ 7.26) and ^{13}C NMR (chloroform δ 77.0). The following abbreviations were used to explain the multiplicities: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad. The potassium organotrifluoroborates were prepared according to literature procedures.[16] Other reagents were received from commercial sources. Solvents were freshly dried and degassed according to the purification handbook Purification of Laboratory Chemicals before using. Column chromatography purifications were performed by flash chromatography using Merck silica gel 60.

4.2. General procedure for the copper-catalyzed trifluoromethylation of potassium aryltrifluoroborates using an electrophilic trifluoromethylating reagent

In a glovebox, Cu(TFA)$_2$ (34.8 mg, 0.120 mmol), bipy (18.4 mg, 0.120 mmol), and electrophilic trifluoromethylating reagent (160 mg, 0.480 mmol), Potassium organotrifluoroborates (0.4 mmol)were added to a Schlenk tube that was equipped with a stirring bar. Freshly distilled solvent MeCN (2 mL) was added into this tube. Both the tube and the vial were capped with a septum, the reaction mixture was kept for another 12 h at room temperature. Distilled water (20 mL) and Et_2O (10 mL) were added and the organic phase was separated. The aqueous phase was extracted with Et_2O (3×10 mL) and the combined organic extracts were dried over anhydrous Na_2SO_4, and concentrated in vacuo. The product was purified by flash chromatography on silica gel with pentane.

4.2.1. 1-tert-Butyl-4-(trifluoromethyl)benzene (Table 2, entry 1).[3a] Obtained as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.58 (d, *J*=8.4 Hz, 2H), 7.52 (d, *J*=8.4 Hz, 2H), 1.37 (s, 9H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −62.29 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 155.2, 127.8 (q, *J*=32.5 Hz), 125.6, 125.0 (q, *J*=3.7 Hz), 124.4 (q, *J*=271.8 Hz), 35.0, 31.2. GC–MS *m*/*z* 202 (M^+).

4.2.2. 1-Butyl-4-(trifluoromethyl)benzene (Table 2, entry 2).[3b] Obtained as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.55 (d, *J*=8.0 Hz, 2H), 7.31 (d, *J*=8.0 Hz, 2H), 2.69 (t, *J*=7.7 Hz, 2H), 1.63 (dd, *J*=14.4, 6.8 Hz, 2H), 1.41–1.36 (m, 2H), 0.96 (t, *J*=7.4 Hz, 3H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −62.24 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 147.0, 128.7, 128.0 (q, *J*=32.2 Hz), 125.2

(q, J=3.8 Hz), 124.4 (q, J=271.6 Hz), 35.5, 33.3, 22.3, 13.9. GC–MS m/z 202 (M^+).

4.2.3. 4-(Trifluoromethyl)-1,1′-biphenyl (Table 2, entry 3).[3a] Obtained as white solid, mp 67–69 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.72 (s, 4H), 7.63 (d, J=7.1 Hz, 2H), 7.51 (t, J=7.1 Hz, 2H), 7.46–7.42 (m, 1H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −62.37 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 144.8, 139.8, 129.4 (q, J=32.5 Hz), 128.4, 128.2, 127.5, 127.3, 125.8 (q, J=3.7 Hz), 124.4 (q, J=271.8 Hz). GC–MS m/z 222 (M^+).

4.2.4. 3-(Trifluoromethyl)biphenyl (Table 2, entry 4).[17] Obtained as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.87 (s, 1H), 7.80 (d, J=7.6 Hz, 1H), 7.67–7.56 (m, 4H), 7.51 (t, J=7.6 Hz, 2H), 7.44 (t, J=7.6 Hz, 1H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −62.57 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 142.0, 139.8, 131.1 (q, J=32.3 Hz), 130.5, 129.3, 129.0, 128.1, 127.2, 125.3, 124.2 (q, J=272.3 Hz), 124.0 (q, J=3.7 Hz). GC–MS m/z 222 (M^+).

4.2.5. 4-Trifluoromethyltoluene (Table 2, entry 5).[5] Obtained as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.53 (d, J=8.1 Hz, 2H), 7.30 (d, J=8.1 Hz, 2H), 2.44 (s, 3H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −62.27 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 142.0, 129.3, 127.9 (q, J=32.4 Hz), 125.1 (q, J=3.8 Hz), 124.4 (q, J=271.6 Hz), 21.4. GC–MS m/z 160 (M^+).

4.2.6. 2,3-Dimethylbenzotrifluoride (Table 2, entry 6).[18] Obtained as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.50 (d, J=7.5 Hz, 1H), 7.34 (d, J=7.5 Hz, 1H), 7.19 (t, J=7.5 Hz, 1H), 2.39 (s, 3H), 2.35 (s, 3H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −60.39 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 138.6, 135.3 (d, J=1.5 Hz), 133.2, 129.0 (q, J=28.9 Hz), 125.3, 124.8 (q, J=273.8 Hz), 123.5 (q, J=5.9 Hz), 20.4, 15.4. GC–MS m/z 174 (M^+).

4.2.7. 1-(Trifluoromethyl)naphthalene (Table 2, entry 7).[6] Obtained as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.24 (d, J=9.4 Hz, 1H), 8.06 (d, J=8.3 Hz, 1H), 7.97–7.89 (m, 2H), 7.69–7.59 (m, 2H), 7.54 (t, J=7.8 Hz, 1H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −59.74 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 133.9, 132.8, 129.0, 128.8, 127.7, 126.6, 126.1 (q, J=30.1 Hz), 124.8 (q, J=273.5 Hz), 124.7 (q, J=6.0 Hz), 124.3 (q, J=2.5 Hz), 124.2. GC–MS m/z 196 (M^+).

4.2.8. 2-(Trifluoromethyl)naphthalene (Table 2, entry 8).[3a] Obtained as white solid, mp 53–55 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.19 (s, 1H), 8.02–7.91 (m, 3H), 7.72–7.57 (m, 3H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −62.25 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 134.6, 132.2, 129.0, 128.8, 128.1, 127.9, 127.2, 125.7 (q, J=4.5 Hz), 124.4 (q, J=272.1 Hz), 121.5 (q, J=3.1 Hz). GC–MS m/z 196 (M^+).

4.2.9. 1-Methyl-4-(trifluoromethyl)naphthalene (Table 2, entry 9).[19] Obtained as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.26–8.20 (m, 1H), 8.13–8.10 (m, 1H), 7.79 (d, J=7.4 Hz, 1H), 7.69–7.62 (m, 2H), 7.38 (d, J=7.4 Hz, 1H), 2.78 (s, 3H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −59.31 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 139.6, 133.0, 129.0, 127.2, 126.4, 125.0, 124.9 (q, J=273.1 Hz), 124.8, 124.7, 124.5 (q, J=6.0 Hz), 20.0. GC–MS m/z 210 (M^+).

4.2.10. Methoxy-6-(trifluoromethyl)naphthalene (Table 2, entry 10).[3a] Obtained as white solid, mp 68–69 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 8.09 (s, 1H), 7.90–7.80 (m, 2H), 7.63 (d, J=8.6 Hz, 1H), 7.26 (dd, J=9.0, 2.5 Hz, 1H), 7.20 (d, J=2.4 Hz, 1H), 3.98 (s, 3H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −61.88 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 159.3, 136.1, 130.3, 127.7, 127.6, 125.5 (q, J=32.2 Hz), 125.4 (q, J=4.4 Hz), 124.6 (q, J=271.9 Hz), 122.0 (q, J=3.2 Hz), 120.2, 105.7, 55.4. GC–MS m/z 226 (M^+).

4.2.11. 1-(Benzyloxy)-4-(trifluoromethyl)benzene (Table 2, entry 11).[20] Obtained as white solid, mp 82–84 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.58 (d, J=8.6 Hz, 2H), 7.50–7.32 (m, 5H), 7.06 (d, J=8.6 Hz, 2H), 5.14 (s, 2H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −61.48 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 161.2, 136.3, 128.8, 128.3, 127.5, 127.0 (q, J=3.7 Hz), 124.5 (q, J=271.1 Hz). 123.1 (q, J=32.7 Hz), 114.9, 70.2. GC–MS m/z 252 (M^+).

4.2.12. 1-(Benzyloxy)-3-(trifluoromethyl)benzene (Table 2, entry 12).[6] Obtained as white solid, mp 60–62 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.50–7.33 (m, 6H), 7.27–7.22 (m, 2H), 7.16 (dd, J=8.3, 2.1 Hz, 1H), 5.12 (s, 2H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −62.69 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 158.9, 136.3, 131.9 (q, J=32.3 Hz), 130.0, 128.7, 128.3, 127.6, 124.0 (q, J=272.3 Hz), 118.3, 117.7 (q, J=3.9 Hz), 111.8 (q, J=3.7 Hz), 70.3. GC–MS m/z 252 (M^+).

4.2.13. Phenoxy-4-(trifluoromethyl)benzene (Table 2, entry 13).[7a] Obtained as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.60 (d, J=8.7 Hz, 2H), 7.45–7.39 (m, 2H), 7.22 (t, J=7.4 Hz, 1H), 7.08 (t, J=8.0 Hz, 4H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −61.74 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 160.5, 155.7, 130.1, 127.1 (q, J=3.7 Hz), 124.9 (q, J=32.6 Hz), 124.5, 124.2 (q, J=271.4 Hz), 119.9, 117.9. GC–MS m/z 238 (M^+).

4.2.14. 1,2-Dimethoxy-4-(trifluoromethyl)benzene (Table 2, entry 14).[7c] Obtained as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.24 (dd, J=8.4, 1.0 Hz, 1H), 7.10 (d, J=1.9 Hz, 1H), 6.94 (d, J=8.4 Hz, 1H), 3.95 (d, J=1.4 Hz, 6H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −61.54 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 151.6, 149.1, 124.3 (q, J=271.3 Hz), 122.9 (q, J=32.7 Hz), 118.4 (q, J=4.2 Hz), 110.6, 108.0 (q, J=3.4 Hz), 56.1, 56.0. GC–MS m/z 206 (M^+).

4.2.15. 4-Trifluoromethylanisole (Table 2, entry 15).[5] Obtained as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.58 (d, J=8.5 Hz, 2H), 6.99 (d, J=8.5 Hz, 2H), 3.88 (s, 3H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −61.50 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 162.0, 126.9 (q, J=3.8 Hz), 124.5 (q, J=270.9 Hz), 122.9 (q, J=32.7 Hz), 114.0, 55.5. GC–MS m/z 176 (M^+).

4.2.16. Methyl 3-(trifluoromethyl)benzoate (Table 2, entry 16).[7c] Obtained as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.33 (s, 1H), 8.25 (d, J=7.8 Hz, 1H), 7.84 (d, J=7.8 Hz, 1H), 7.61 (t, J=7.8 Hz, 1H), 3.98 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ ppm −62.86 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 165.8, 132.8 (q, J=1.1 Hz), 131.1 (q, J=33.0 Hz), 131.0, 129.4 (q, J=3.7 Hz), 129.0, 126.5 (q, J=3.9 Hz), 123.7 (q, J=272.3 Hz), 52.5. GC–MS m/z 204 (M^+).

4.2.17. Ethyl 3-(trifluoromethyl)benzoate (Table 2, entry 17).[4b] Obtained as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.33 (s, 1H), 8.25 (d, J=7.8 Hz, 1H), 7.83 (d, J=7.8 Hz, 1H), 7.61 (t, J=7.8 Hz, 1H), 4.44 (q, J=7.1 Hz, 2H), 1.44 (t, J=7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ ppm −62.83 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 165.3, 132.8 (q, J=1.2 Hz), 131.4, 131.0 (q, J=32.9 Hz), 129.3 (q, J=3.7 Hz), 129.0, 126.5 (q, J=3.9 Hz), 123.7 (q, J=272.4 Hz), 61.5, 14.2. GC–MS m/z 218 (M^+).

4.2.18. 1-(4-(Trifluoromethyl)phenyl)ethanone (Table 2, entry 18).[3a] Obtained as pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.08 (d, J=8.0 Hz, 2H), 7.75 (d, J=8.0 Hz, 2H), 2.67 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ ppm −63.15 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 197.0, 139.7 (q, J=1.1 Hz), 134.4

(q, J=32.7 Hz), 128.6, 125.7 (q, J=3.8 Hz), 123.6 (q, J=272.6 Hz), 26.8. GC–MS m/z 188 (M^+).

4.2.19. 4-(Trifluoromethyl)benzaldehyde (Table 2, entry 19).[3e] Obtained as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.13 (s, 1H), 8.03 (d, J=7.8 Hz, 2H), 7.83 (d, J=7.8 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ ppm −63.20 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 191.1, 138.7 (q, J=1.2 Hz), 135.6 (q, J=32.7 Hz), 129.9, 126.1 (q, J=3.8 Hz), 123.4 (q, J=272.9 Hz). GC–MS m/z 174 (M^+).

4.2.20. 1-Chloro-4-(trifluoromethyl)benzene (Table 2, entry 20).[7c] Obtained as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.59 (d, J=8.3 Hz, 2H), 7.49 (d, J=8.3 Hz, 2H). ^{19}F NMR (470 MHz, $CDCl_3$) δ ppm −62.63 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 138.1, 129.1, 129.0 (q, J=33.3 Hz), 126.8 (q, J=3.7 Hz), 123.8 (q, J=272.1 Hz). GC–MS m/z 180 (M^+).

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Supplementary data

Copies of NMR spectra for all products. Supplementary data related to this article. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2012.09.083.

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