Large-Scale Preparation of Aromatic Fluorides via Electrophilic Fluorination with Functionalized Aryl- or Heteroarylmagnesium Reagents

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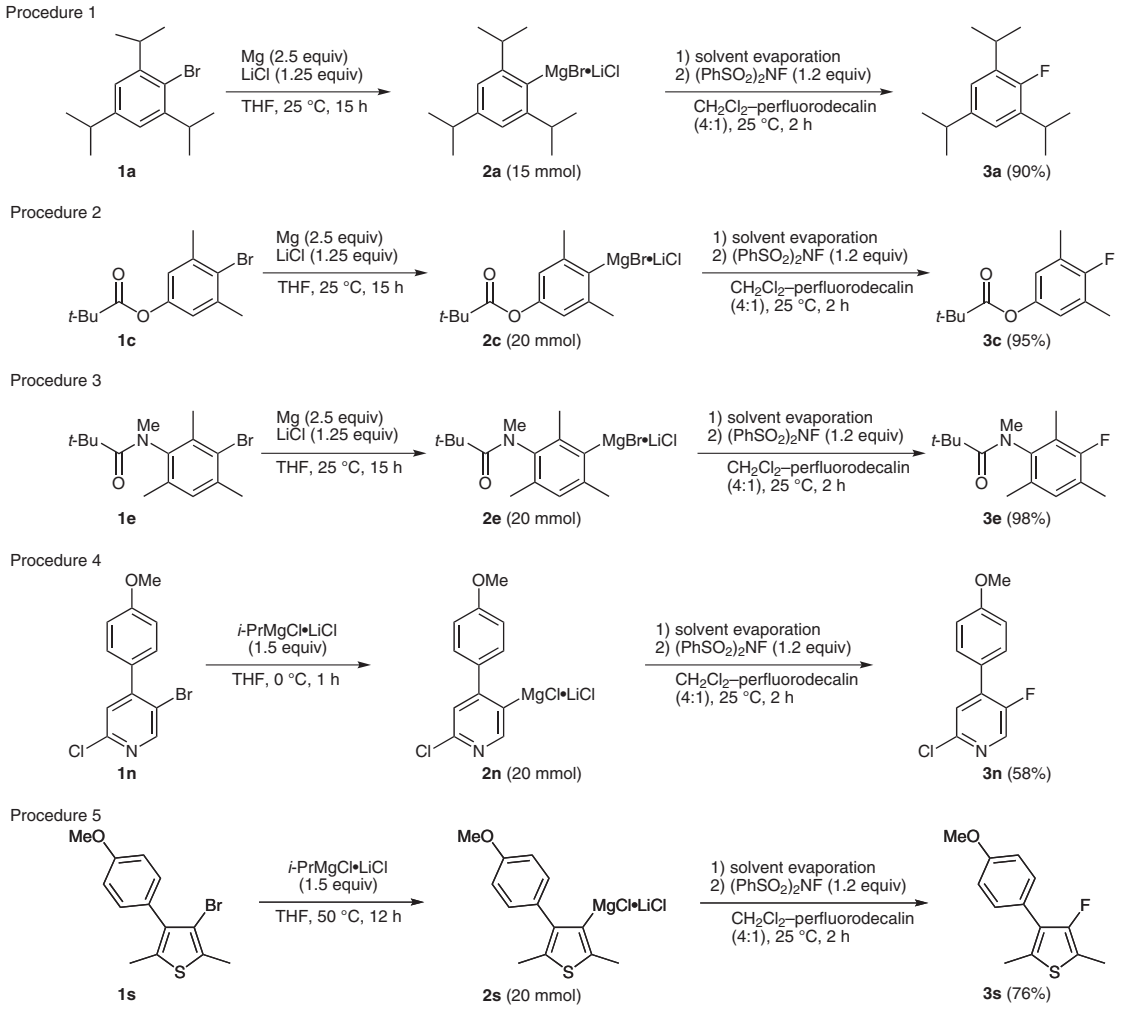
Abstract: Functionalized aryl- or heteroarylmagnesium reagents, prepared from the corresponding bromides or iodides using halogen–magnesium exchange or direct magnesium insertion in the presence of lithium chloride, reacted smoothly with *N*-fluorobenzenesulfonimide, $(PhSO_2)_2NF$, in the mixed solvent (4:1 CH_2Cl_2–perfluorodecalin) to give the corresponding aromatic fluorides in moderate to good yields.

Key words: arenes, electrophilic substitution, fluorination, Grignard reagents, heteroaromatic compounds



Scheme 1 General procedures for the preparation of various types of functionalized aromatic and heteroaromatic fluorides

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Introduction

Fluorine-substituted aromatic and heteroaromatic compounds are valuable compounds as pharmaceuticals[1] and agrochemicals[2] due to the special nature of the fluorine atom, such as very high electronegativity and small atomic radius. Although electrophilic[3] and nucleophilic[4] fluorination, as well as the pyrolysis of diazonium tetrafluoroborates,[5] are well-known methods for the preparation of fluorinated molecules, conventional fluorination reactions require harsh reaction conditions and they are mostly limited to electron-poor substrates. Therefore, the development of effective and convenient fluorination methods is highly desirable.[6] We have developed effective methods for preparing functionalized unsaturated Grignard reagents either by using halogen–magnesium exchange[7] or by direct Mg insertion in the presence of lithium chloride.[8] The electrophilic fluorination of arylmagnesium compounds has been reported for unfunctionalized Grignard reagents, however, it proceeds with moderate to poor yields.[9] Very recently, we have found a convenient and highly versatile one-pot method for the conversion of aromatic and heteroaromatic bromides into the corresponding fluorides using an optimized fluorinating agent (*N*-fluorobenzenesulfonimide; NFSI) and solvent system (CH_2Cl_2–perfluorodecalin, 4:1).[10] Herein, we wish to describe five practical synthetic procedures for the preparation of functionalized aromatic and heteroaromatic fluorides to illustrate this method (Scheme 1); all were performed on a 15–20-mmol scale.

Scope and Limitations

Electron-rich bromoarenes **1a–f** (Table 1, entries 1–6) and electron-poor bromoarenes **1h**,**i**,**k** (entries 8, 9, and 11) can be readily converted into the corresponding fluorides of type **3** using this procedure. Highly sterically hindered substrates such as 2,4,6-triisopropylphenylmagnesium bromide (**2a**) or even 2,4,6-trimethylphenylmagnesium bromide (**2b**) react especially smoothly and afford the fluorinated products in high yields (Procedure 1; entries 1 and 2). Functional groups like an ester (Procedure 2; entry 3) or an amide (entry 4) are well tolerated. Noticeably, aniline-derived Grignard reagents **2e**,**f** were also suitable nucleophiles for electrophilic fluorination, leading to the corresponding fluorides **3e** and **3f** in 98% and 64% yields, respectively (Procedure 3; entries 5 and 6). Halogenated aryl bromides **1g–k** were converted into the corresponding Grignard reagents using isopropylmagnesium chloride–lithium chloride in tetrahydrofuran and led to the fluorinated products **3g–k** in 34–55% isolated yield (entries 7–11).

Our practical fluorination procedure allows the preparation of various fluorinated heterocyclic compounds. Halogenated pyridines **1l–o**, an isoquinoline **1p**, a pyrrole **1q**, a benzo[*b*]thiophene **1r**, thiophenes **1s–u**, and a furan **1v** afford the corresponding fluorinated derivatives using our procedure in satisfactory yields (entries 12–22).

Thus, the substituted pyridines **1l–o** are readily converted into the corresponding magnesium reagents of type **2** by Br–Mg exchange. After replacing tetrahydrofuran by dichloromethane–perfluorodecalin (4:1) and treatment with *N*-fluorobenzenesulfonimide (1.2 equiv), the expected fluorinated pyridines **3l–o** were obtained in 58–75% yields (Procedure 4; entries 12–15). The magnesiated isoquinoline **2p**, obtained by I–Mg exchange, is smoothly fluorinated to give 1-fluoroisoquinoline (**3p**) in 63% yield (entry 16). Sensitive electron-rich heterocycles such as pyrrole, thiophenes, and furan are readily magnesiated by either direct Mg insertion (leading to **2q**, **2r**) or Br–Mg exchange (leading to **2s–v**). Using the same fluorination procedure, these heterocyclic Grignard reagents are converted into the fluorinated five-membered heterocycles **3q–v** in 43–76% yields (Procedure 5; entries 17–22).

In summary, a practical preparation method for various types of aromatic fluorides using functionalized aryl- or heteroarylmagnesium reagents has been demonstrated. We have extended our previous work, it has been scaled-up under optimized conditions and five reactions of Grignard reagents with *N*-fluorobenzenesulfonimide have been performed on a larger scale (15–20 mmol scale); see Procedures 1–5. These reactions could be performed with standard laboratory glassware and usual laboratory techniques. Also, these procedures are compatible with a wide variety of functionalities. Further studies are underway in our laboratory to extend this method.

Table 1 Electrophilic Fluorination of Various Types of Aromatic Grignard Reagents with NFSI (CH_2Cl_2–perfluorodecalin, 4:1)

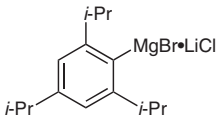
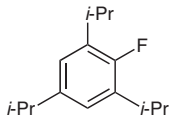
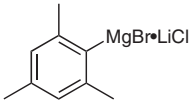
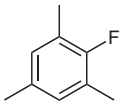
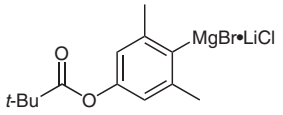
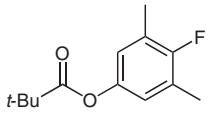
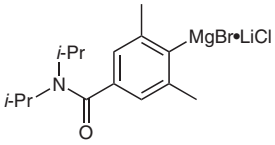
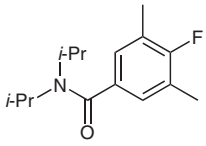
Entry	Grignard reagent (Method of magnesiation[a])	Product, Yield[b]
1	 **2a** (**B**, 25 °C, 15 h)	 **3a**, 90%
2	 **2b** (**B**, 25 °C, 15 h)	 **3b**, 74% (91%)
3	 **2c** (**B**, 25 °C, 15 h)	 **3c**, 95%[c,d]
4	 **2d** (**B**, 25 °C, 2 h)	 **3d**, 94%[c]

Table 1 Electrophilic Fluorination of Various Types of Aromatic Grignard Reagents with NFSI (CH_2Cl_2–perfluorodecalin, 4:1) (continued)

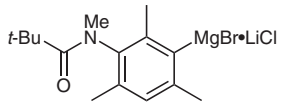
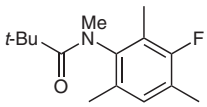
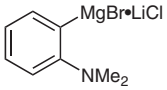
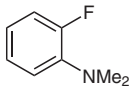
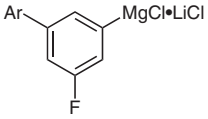
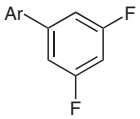
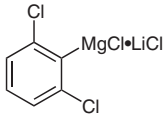
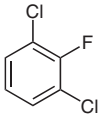
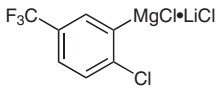
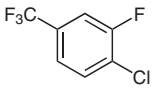
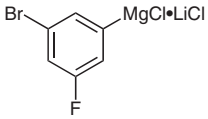
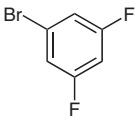
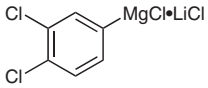
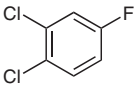
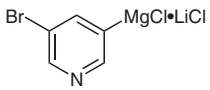
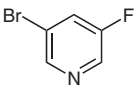
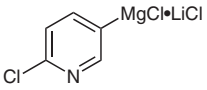
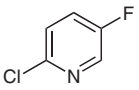
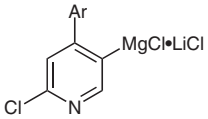
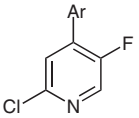
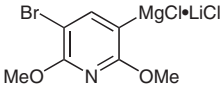
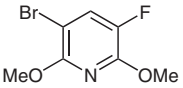
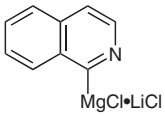
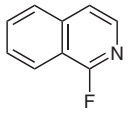
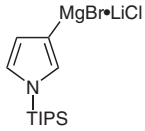
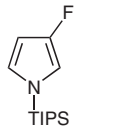
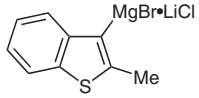
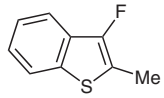
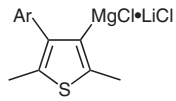
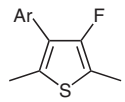
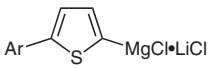
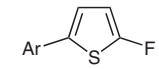
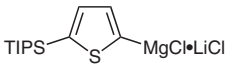
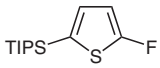
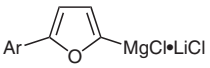
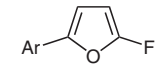
Entry	Grignard reagent (Method of magnesiation[a])	Product, Yield[b]
5		
	2e (**B**, 25 °C, 15 h)	**3e**, 98%[d]
6		
	2f (**B**, 25 °C, 15 h)	**3f**, 64%
7		
	Ar = 4-MeOC$_6$H$_4$	Ar = 4-MeOC$_6$H$_4$
	2g (**A**, 25 °C, 1 h)	**3g**, 55%
8		
	2h (**A**, 0 °C, 1 h)	**3h**, 53%
9		
	2i (**A**, 0 °C, 0.5 h)	**3i**, 52% (88%)
10		
	2j (**A**, 25 °C, 1 h)	**3j**, 66%
11		
	2k (**A**, 25 °C, 1 h)	**3k**, 34% (62%)
12		
	2l (**A**, 0 °C, 1 h)	**3l**, 58% (92%)
13		
	2m (**A**, 0 °C, 1 h)	**3m**, 75% (97%)[e]
14		
	Ar = 4-MeOC$_6$H$_4$	Ar = 4-MeOC$_6$H$_4$
	2n (**A**, 0 °C, 1 h)	**3n**, 58%[d]
15		
	2o (**A**, 25 °C, 1 h)	**3o**, 65%

Table 1 Electrophilic Fluorination of Various Types of Aromatic Grignard Reagents with NFSI (CH_2Cl_2–perfluorodecalin, 4:1) (continued)

Entry	Grignard reagent (Method of magnesiation[a])	Product, Yield[b]
16		
	2p (**A**, 0 °C, 1 h)	**3p**, 63%
17		
	2q (**B**, 25 °C, 24 h)	**3q**, 43%[c]
18		
	2r (**B**, 25 °C, 15 h)	**3r**, 60%[c]
19		
	Ar = 4-MeOC$_6$H$_4$	Ar = 4-MeOC$_6$H$_4$
	2s (**A**, 50 °C, 1 h)	**3s**, 76%[d]
20		
	Ar = 4-MeOC$_6$H$_4$	Ar = 4-MeOC$_6$H$_4$
	2t (**A**, 25 °C, 1 h)	**3t**, 57%[f]
21		
	2u (**A**, 25 °C, 1 h)	**3u**, 56%
22		
	Ar = 4-MeOC$_6$H$_4$	Ar = 4-MeOC$_6$H$_4$
	2v (**A**, 25 °C, 1 h)	**3v**, 49%

[a] Method A: Br–Mg exchange using *i*-PrMgCl·LiCl. Method B: Mg insertion in the presence of LiCl.
[b] Yields of isolated products >95% pure as determined by NMR spectroscopy. Yields in parentheses are determined by GC analysis (comparison with an authentic sample).
[c] The remaining starting material **1** was removed by performing a Negishi cross-coupling with 4-methoxyphenylzinc chloride on the reaction mixture.
[d] Performed at 15–20-mmol scale.
[e] NFSI (2.4 equiv) was used.
[f] $PhOCF_3$ was used as a co-solvent instead of perfluorodecalin.

All reactions were carried out under an N_2 atmosphere in dried glassware. THF was continuously refluxed and freshly distilled from Na benzophenone ketyl under N_2. CH_2Cl_2 was predried over CaH_2 and distilled from CaH_2 under N_2. Column chromatography was performed using silica gel (0.040–0.063 mm, 230–400 mesh ASTM) from Merck. NFSI and perfluorodecalin were purchased from Apollo Scientific Limited. GC yields were determined by using an internal standard and comparison with an authentic commercial compound. Yields refer to isolated compounds estimated to be >95% pure as determined by ^{1}H NMR and capillary GC analysis.

Preparation of Grignard Reagents by Br–Mg Exchange Reaction; General Procedure (Method A)

A dry and N_2-flushed 50-mL Schlenk flask, equipped with a magnetic stirrer bar and a septum, was charged with a soln of aryl bromide (20 mmol) in THF. To the stirred soln was added dropwise 1.18 M *i*-PrMgCl·LiCl in THF (25.4 mL, 30 mmol) and anhyd dioxane (2.0 mL) at 0 °C. The mixture was stirred at the temperature and for the time given in Table 1. When the Br–Mg exchange was complete (GC analysis), THF was carefully removed using high vacuum (40 °C/1.0 mbar). Et_2O (20 mL) was added to the flask and volatiles were removed again using high vacuum (40 °C). CH_2Cl_2 (20 mL) was added and removed again (40 °C). Finally, CH_2Cl_2 (20 mL) was added to the flask and the mixture was stirred until the residue dissolved.

Preparation of Grignard Reagents by Direct Mg Insertion; General Procedure (Method B)

Anhyd LiCl (1.590 g, 37.5 mmol) and Mg turnings (1.823 g, 75 mmol) were placed in an N_2-flushed 250-mL Schlenk flask and dried using a heat gun under high vacuum. THF (60 mL) was added and the Mg was activated with 0.5 M DIBAL-H in THF (0.6 mL, 0.3 mmol). The mixture was stirred for 5 min and then the aryl bromide (30 mmol) was added in one portion at 0 °C. The mixture was stirred at r.t. for the indicated time (Table 1). The concentration of the resulting arylmagnesium bromide was determined by iodiometric titration and the clear soln (for 20 mmol) was cannulated into a new Schlenk flask for the reaction. THF was removed under high vacuum (oil pump, 40 °C/~1.0 mbar). Et_2O (20 mL) was added to the flask and volatiles were removed again (40 °C). CH_2Cl_2 (20 mL) was added and also removed in vacuo (40 °C). Finally, CH_2Cl_2 (20 mL) was added to the resulting Grignard reagent and stirred until dissolved.

1-Fluoro-2,4,6-triisopropylbenzene (3a); Typical Procedure 1

The Grignard reagent was prepared using Method B. To a suspended soln of Mg turnings (1.22 g, 50 mmol) and LiCl (1.06 g, 25 mmol) in THF (40 mL) was added 1-bromo-2,4,6-triisopropylbenzene (**1a**, 5.67 g, 20 mmol) via syringe at 0 °C and the mixture was stirred at 25 °C for 15 h. The resulting soln of Grignard reagent in THF (0.42 M, 36 mL, 15 mmol) was transferred to a new Schlenk flask. Then, the solvent was removed in vacuo (40 °C/1.0 mbar, 1 h). CH_2Cl_2 (20 mL) was added and then NFSI (5.68 g, 18 mmol) in CH_2Cl_2 (20 mL) and perfluorodecalin (10 mL) were slowly added at –78 °C. The mixture was stirred at 0 °C for 30 min and at r.t. for 2 h; it was poured into ice-cooled sat. aq NH_4Cl (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (anhyd Na_2SO_4), filtered, and concentrated in vacuo and the product **3a** was purified by column chromatography (pentane) to give a colorless oil; yield: 3.01 g (90%).

IR (film): 2960 (vs), 2871 (m), 1472 (vs), 1459 (s), 1320 (m), 1172 (s), 1120 (m), 875 (s), 749 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.92 (s, 1 H, Ar*H*), 6.90 (s, 1 H, Ar*H*), 3.22 (qq, *J* = 9.0, 9.0 Hz, 2 H, CH), 2.88 (qq, *J* = 9.0, 9.0 Hz, 1 H, CH), 1.25 (d, *J* = 9.0 Hz, 12 H, CH_3), 1.23 (d, *J* = 9.0 Hz, 6 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 156.6 (d, *J* = 242.2 Hz), 143.85, 134.5 (d, *J* = 15.8 Hz), 122.1 (d, *J* = 5.3 Hz), 33.9, 27.4 (d, *J* = 3.0 Hz), 24.3, 22.79.

^{19}F NMR (282 MHz, $CDCl_3$, 25 °C): δ = –130.35 (dd, *J* = 8.5, 8.5 Hz, 1 F).

MS (EI, 70 eV): *m*/*z* (%) = 222 (19) [M^+], 208 (15), 207 (100), 179 (18), 43 (21).

HRMS: *m*/*z* [M^+] calcd for $C_{15}H_{23}F$: 222.1784; found 222.1776.

1-Fluoro-2,6-dimethyl-4-(pivaloyloxy)benzene (3c); Typical Procedure 2

The Grignard reagent was prepared using Method B. To a suspended soln of Mg turnings (3.038 g, 125 mmol) and LiCl (2.650 g, 62.5 mmol) in THF (100 mL) was added 1-bromo-2,6-dimethyl-4-(pivaloyloxy)benzene (**1c**, 14.26 g, 50 mmol) at 0 °C and the mixture was stirred at 25 °C for 15 h. The resulting Grignard reagent in THF (0.34 M, 58.8 mL, 20 mmol) was transferred to a new Schlenk flask. Then, the solvent was removed in vacuo (40 °C/1.0 mbar, 1 h). CH_2Cl_2 (20 mL) was added and then NFSI (7.568 g, 24 mmol) in CH_2Cl_2 (20 mL) and perfluorodecalin (10 mL) were slowly added at –78 °C. The mixture was stirred at 0 °C for 30 min and at r.t. for 2 h; it was then poured into ice-cooled sat. aq NH_4Cl (200 mL) and extracted with CH_2Cl_2 (3 × 200 mL). The combined organic layers were dried (anhyd Na_2SO_4), filtered, and concentrated in vacuo. In order to remove the remaining starting bromide, the crude mixture was passed through a plug of silica and the filtrate was treated with 4-methoxyphenylzinc chloride (10 mmol) in the presence of bis{di-*tert*-butyl[4-(dimethylamino)phenyl]phosphine}dichloropalladium(II)[11] (1 mol%, 142 mg), and the mixture was stirred at 50 °C for 15 h. The mixture was extracted with Et_2O (3 × 100 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude residue was purified by column chromatography (silica gel, pentane–Et_2O, 20:1) to give a white solid; yield: 4.48 g (95%); mp 59–60 °C.

IR (KBr): 2976 (w), 1746 (vs), 1478 (s), 1274 (m), 1141 (vs), 1108 (vs), 1030 (m), 910 (m), 756 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.69 (s, 1 H, Ar*H*), 6.67 (s, 1 H, Ar*H*), 2.24 (s, 3 H, CH_3), 2.23 (s, 3 H, CH_3), 1.33 (s, 9 H, *t*-Bu).

^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 177.3, 157.2 (d, *J* = 241.0 Hz), 151.0, 125.3 (d, *J* = 20.1 Hz), 121.3 (d, *J* = 5.1 Hz), 39.0, 27.1, 14.68, 14.63.

^{19}F NMR (282 MHz, $CDCl_3$, 25 °C): δ = –125.65 to –125.8 (m, 1 F).

MS (EI, 70 eV): *m*/*z* (%) = 224 (14) [M^+], 220 (11), 140 (100), 125 (12), 122 (12), 57 (39).

HRMS: *m*/*z* [M^+] calcd for $C_{13}H_{17}FO_2$: 224.1213; found 224.1212.

3-Fluoro-*N*,2,4,6-tetramethyl-*N*-pivaloylaniline (3e); Typical Procedure 3

The Grignard reagent was prepared using Method B. To a suspended soln of Mg turnings (1.823 g, 75 mmol) and LiCl (1.590 g, 37.5 mmol) in THF (60 mL) was added 3-bromo-*N*,2,4,6-tetramethyl-*N*-pivaloylaniline (**1e**, 9.337 g, 30 mmol) via syringe at 0 °C and the mixture was stirred at 25 °C for 15 h. The resulting Grignard reagent in THF (0.29 M, 69.0 mL, 20 mmol) was transferred to a new Schlenk flask. Then, the solvent was removed in vacuo (40 °C/1.0 mbar, 1 h). CH_2Cl_2 (20 mL) was added and then NFSI (7.568 g, 24 mmol) in CH_2Cl_2 (20 mL) and perfluorodecalin (10 mL) were slowly added at –78 °C. The mixture was stirred at 0 °C for 30 min and at r.t. for 2 h; it was poured into ice-cooled sat. aq NH_4Cl (200 mL) and extracted with CH_2Cl_2 (3 × 200 mL). The combined organic layers were dried (anhyd Na_2SO_4), filtered, and concentrated in vacuo. The crude mixture was passed through a plug of silica, and the filtrate was purified by column chromatography (silica gel, pentane–Et_2O, 2:1) to give a yellow oil; yield: 5.01 g (98%).

IR (film): 2957 (m), 2627 (m), 1694 (w), 1633 (vs), 1481 (s), 1346 (s), 1210 (m), 1162 (s), 1086 (vs), 782 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.88 (d, *J* = 6.0 Hz, 1 H, Ar*H*), 3.06 (s, 3 H, NCH_3), 2.25–2.05 (m, 9 H, 3 CH_3), 1.00 (s, 9 H, *t*-Bu).

^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 176.39, 158.19 (d, *J* = 243.7 Hz), 141.41 (d, *J* = 5.3 Hz), 130.97 (d. *J* = 3.8 Hz), 129.96 (d, *J* = 6.0 Hz), 124.05 (d, *J* = 18.1 Hz), 123.02 (d, *J* = 16.6

Hz), 41.06, 38.44, 28.95, 17.54, 14.42 (d, J = 3.8 Hz), 10.81 (d, J = 4.5 Hz).

^{19}F NMR (282 MHz, $CDCl_3$, 25 °C): δ = –120.2 to –120.3 (m, 1 F).

MS (EI, 70 eV): m/z (%) = 251 (4) [M^+], 194 (16), 176 (11), 166 (12), 98 (100), 57 (14).

HRMS: m/z [M^+] calcd for $C_{15}H_{22}FNO$: 251.1685; found 251.1690.

2-Chloro-5-fluoro-4-(4-methoxyphenyl)pyridine (3n); Typical Procedure 4

The Grignard reagent was prepared using Method A. In a 100-mL Schlenk flask under N_2 was placed 5-bromo-2-chloro-4-(4-methoxyphenyl)pyridine (**1n**, 5.951 g, 20 mmol) in THF (10 mL). 1.18 M *i*-PrMgCl·LiCl in THF (25.4 mL, 30 mmol) was added at 0 °C and the mixture was stirred at this temperature for 1 h. Then the solvent was removed in vacuo (40 °C/1.0 mbar, 1 h). CH_2Cl_2 (20 mL) was added and then NFSI (7.568 g, 24 mmol) in CH_2Cl_2 (20 mL) and perfluorodecalin (10 mL) were slowly added at –78 °C. The mixture was stirred at 0 °C for 30 min and at 25 °C for 2 h; it was then poured into ice-cooled sat. aq NH_4Cl soln (200 mL) and extracted with CH_2Cl_2 (3 × 200 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude mixture was passed through a plug of silica and the filtrate was purified by column chromatography (silica gel, pentane–CH_2Cl_2, 1:2) to give a pale yellow solid; yield: 2.61 g (58%); mp 74.3–76.0 °C.

IR (KBr): 2935 (w), 1597 (m), 1518 (m), 1461 (s), 1359 (m), 1254 (vs), 1178 (s), 1043 (s), 827 cm^{-1} (vs).

^{1}H NMR (300 MHz, $CDCl_3$, 27 °C): δ = 8.27 (d, J = 2.2 Hz, 1 H, Py*H*), 7.56 (ABq, J = 9.0, 9.0 Hz, 2 H, Ar*H*), 7.40 (d, J = 5.6 Hz, 1 H, Py*H*), 7.01 (ABq, J = 9.0, 9.0 Hz, 2 H, Ar*H*), 3.88 (s, 3 H, OCH_3).

^{13}C NMR (75 MHz, $CDCl_3$, 27 °C): δ = 160.90, 155.94 (d, J = 255.8 Hz), 146.52 (d, J = 3.0 Hz), 138.93 (d, J = 12.8 Hz), 138.09 (d, J = 28.7 Hz), 130.14, 130.09, 123.99 (d, J = 2.3 Hz), 123.88 (d, J = 1.5 Hz), 114.43, 55.37.

^{19}F NMR (282 MHz, $CDCl_3$, 27 °C): δ = –136.25 to –136.32 (m, 1 F).

MS (EI, 70 eV): m/z (%) = 239 (33), 237 (100) [M^+], 222 (11), 222 (10), 194 (22).

HRMS: m/z [M^+] calcd for $C_{12}H_9ClFNO$: 237.0357; found 237.0457.

3-Fluoro-2,5-dimethyl-4-(4-methoxyphenyl)thiophene (3s); Typical Procedure 5

The Grignard reagent was prepared using Method A. In a 100-mL Schlenk flask under N_2 was placed 3-bromo-2,5-dimethyl-4-(4-methoxyphenyl)thiophene (**1s**, 5.944 g, 20 mmol) in THF (10 mL). 1.18 M *i*-PrMgCl·LiCl in THF (25.4 mL, 30 mmol) and dioxane (2.0 mL) were added at 0 °C and the mixture was stirred at 50 °C for 12 h. Then, the solvent was removed in vacuo (40 °C/1.0 mbar, 1 h). CH_2Cl_2 (20 mL) was added and NFSI (7.568 g, 24 mmol) in CH_2Cl_2 (20 mL) and perfluorodecalin (10 mL) were slowly added at –78 °C. The mixture was stirred at 0 °C for 30 min and at 25 °C for 2 h; it was then poured into ice-cooled sat. aq NH_4Cl soln (200 mL) and extracted with CH_2Cl_2 (3 × 200 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude mixture was passed through a plug of silica and the filtrate was purified by column chromatography (silica gel, pentane–CH_2Cl_2, 4:1) to give a yellow oil; yield: 3.58 g (76%).

IR (film): 2920 (w), 1599 (m), 1529 (m), 1497 (m), 1244 (vs), 1177 (s), 1150 (m), 1035 (s), 833 cm^{-1} (vs).

^{1}H NMR (300 MHz, $CDCl_3$, 27 °C): δ = 7.32 (ABq, J = 9.0, 9.0 Hz, 2 H, Ar*H*), 7.01 (ABq, J = 9.0, 9.0 Hz, 2 H, Ar*H*), 3.90 (s, 3 H, OCH_3), 2.40 (s, 3 H, CH_3), 2.35–2.75 (m, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$, 27 °C): δ = 158.73, 151.31 (d, J = 256.5 Hz), 130.45 (d, J = 1.5 Hz), 129.03, 127.57 (d, J = 21.9 Hz), 125.62 (d, J = 3.0 Hz), 113.77, 111.65 (d, J = 19.6 Hz), 55.22, 14.64, 9.95.

^{19}F NMR (282 MHz, $CDCl_3$, 27 °C): δ = –133.49 (t, J = 2.8 Hz, 1 F).

MS (EI, 70 eV): m/z (%) = 236 (100) [M^+], 221 (48), 57 (45), 55 (40), 43 (42).

HRMS: m/z [M^+] calcd for $C_{13}H_{13}FO^{32}S$: 236.0671; found 236.0659.

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