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Palladium-Catalyzed Desulfitative Direct C–H Arylation of Electron-Deficient Polyfluoroarenes with Sodium Arenesulfinates

Tao Miao[a] and Lei Wang[a,b,*]

[a] Department of Chemistry, Huaibei Normal University, Huaibei, Anhui 235000, People's Republic of China
Fax: (+86)-561-309-0518; phone: (+86)-561-380-2069; e-mail: leiwang@chnu.edu.cn
[b] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Shanghai 200032, People's Republic of China

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Abstract: The palladium-catalyzed direct arylation of electron-deficient polyfluorobenzenes was developed in the presence of silver carbonate and trisodium phosphate. This protocol allowed use of both electron-deficient and electron-rich aromatic sulfinic acid sodium salts as arylating reagents for the direct arylation of a variety of polyfluoroarenes to produce fluorobiaryls in good to excellent yields, providing a complement to the existing methods for the direct arylation of polyfluoroarenes.

Keywords: desulfitative reaction; direct C–H arylation; palladium; polyfluoroarenes; sodium arenesulfinates

Introduction

Biaryls containing polyfluoroarene structural moieties have demonstrated importance in medicinal chemistry and numerous functional materials such as electron transport devices and organic light emitting diodes.[1] Generally, the preparation of these structural units often requires the use of pentafluorophenyl organometallics (copper species, stannanes, boronic acids and benzoates) to react with electrophiles like aryl halides through traditional cross-coupling methodology.[2] While these methods have been generally versatile and used extensively, this "prefunctionalization" process is non-trivial and suffers from the tedious synthetic steps for the preparation of the organometallic reagents, the incompatibility of important functional groups and the use of toxic substrates (stannanes). In the past few years, significant progress has been made in the transition metal-catalyzed direct C–H arylation of polyfluoroarenes, which not only represents a more efficient synthetic route to the polyfluoroaryl-aryls, but also in some cases offers a solution to the problem arising from the use of oxygen- and moisture-sensitive or precious organometallic reagents.[3–6] In this regard, the elegant work by Fagnou displayed that C–H bonds of polyfluorobenzenes could be arylated with aryl halides or phenyl triflates under palladium catalysis.[4] After that, Su and co-works disclosed a Pd-catalyzed direct arylation of electron-deficient polyfluoroarenes with organoboron reagents and aromatic benzoic acids.[5] Subsequently, Su and Shi et al. have independently reported the noteworthy new development of polyfluoroarenes coupled with non-activated 'simple' arenes in the presence of $Pd(OAc)_2$ to form fluorinated biaryls.[6] Although remarkable advances in these types of transformations have been achieved, to develop new and reliable alternative direct arylation of polyfluoroarenes remains highly desirable from both scientific and practical points of view.

Palladium-catalyzed desulfitative C–C bond forming reactions *via* release of SO_2 provide another promising access to complex molecules, in which aromatic sulfinic acids (or salts) are used as complementary arylating reagents to aryl halides or expensive organometallics in traditional cross-coupling reactions. Since aromatic sulfinic acids (or salts) are comparatively stable, easy to handle, and accessible preparatively from their corresponding sulfonyl chlorides, the desulfitative cross-coupling reactions have attracted considerable interest in recent years. As a result, successes in desulfitative cross-coupling of aromatic sulfinic acids (or salts) with olefins, nitriles or aldehydes have been accomplished by using Pd/Cu, Pd/O_2, Pd and Rh catalysts,[7] and the desulfitative coupling reactions between sodium arenesulfinates and different electrophiles have been also established.[8] Very recently, such catalytic methods have been extended to the direct C–H arylation of heteroaromatics, which has further highlighted the great potential of sodium

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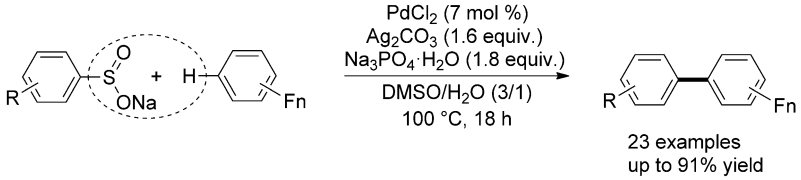


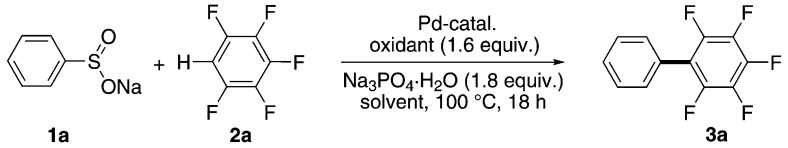
Scheme 1.

arenesulfinates to serve as versatile starting materials for the construction of aryl-substituted compounds.[9] Yet, general methodologies for the direct coupling of sodium arenesulfinates with fluorinated aromatics are scarce. Herein, we wish to report a palladium-catalyzed direct arylation of electron-deficient polyfluoroarenes with sodium arylsulfinates *via* C–H activation under mild conditions (Scheme 1).

Results and Discussion

In our initial study, we chose benzenesulfinic acid sodium (**1a**) and pentafluorobenzene (**2a**) as model substrates to optimize the reaction conditions with different catalysts, oxidants and solvents (Table 1). When $Pd(OAc)_2$ was used as the catalyst with Ag_2CO_3 as oxidant, $Na_3PO_4{\cdot}12\,H_2O$ as additive and mixture of DMSO and H_2O (3:1) as the solvent, the reaction of **1a** with **2a** gave the desulfitative arylated product (**3a**) in 66% yield (Table 1, entry 1). Meanwhile, arylation also proceeded in comparable yield

Table 1. Palladium-catalyzed desulfitative direct arylation of pentafluorobenzene with sodium benzenesulfinate under various conditions.[a]



1a **2a** **3a**

Entry	Pd source	Oxidant	Solvent	Yield [%][b]
1	$Pd(OAc)_2$	Ag_2CO_3	DMSO/H_2O (3:1)	66
2	$Pd(OCOCF_3)_2$	Ag_2CO_3	DMSO/H_2O (3:1)	61
3	**$PdCl_2$**	**Ag_2CO_3**	**DMSO/H_2O (3:1)**	**86**
4	$Pd(CH_3CN)_2Cl_2$	Ag_2CO_3	DMSO/H_2O (3:1)	80
5	$Pd(PPh_3)_2Cl_2$	Ag_2CO_3	DMSO/H_2O (3:1)	72
6	$Pd(PPh_3)_4$	Ag_2CO_3	DMSO/H_2O (3:1)	27
7	$PdCl_2$	AgOAc	DMSO/H_2O (3:1)	46
8	$PdCl_2$	Ag_2O	DMSO/H_2O (3:1)	35
9	$PdCl_2$	$AgSbF_6$	DMSO/H_2O (3:1)	10
10	$PdCl_2$	$Cu(OAc)_2$	DMSO/H_2O (3:1)	16
11	$PdCl_2$	$K_2S_2O_8$	DMSO/H_2O (3:1)	0
12	$PdCl_2$	BQ	DMSO/H_2O (3:1)	0
13	$PdCl_2$	TBHP	DMSO/H_2O (3:1)	0
14	$PdCl_2$	Ag_2CO_3	DMA/H_2O (3:1)	37
15	$PdCl_2$	Ag_2CO_3	DMF/H_2O (3:1)	8
16	$PdCl_2$	Ag_2CO_3	NMP/H_2O (3:1)	0
17	$PdCl_2$	Ag_2CO_3	DMSO/H_2O (1:1)	51
18	$PdCl_2$	Ag_2CO_3	DMSO/H_2O (6:1)	58
19[c]	$PdCl_2$	Ag_2CO_3	DMSO/H_2O (3:1)	64
20[d]	$PdCl_2$	Ag_2CO_3	DMSO/H_2O (3:1)	60
21[e]	$PdCl_2$	Ag_2CO_3	DMSO/H_2O (3:1)	31

[a] *Reaction conditions*: **1a** (0.40 mmol), **2a** (0.25 mmol) and Pd catalyst (7 mol%), oxidants (0.40 mmol), $Na_3PO_4{\cdot}12\,H_2O$ (0.45 mmol), in DMSO/H_2O (3:1, 2.0 mL), 100 °C for 18 h.
[b] Isolated yield.
[c] 5 mol% $PdCl_2$ was used.
[d] Reaction for 10 h.
[e] In the absence of $Na_3PO_4{\cdot}12\,H_2O$.

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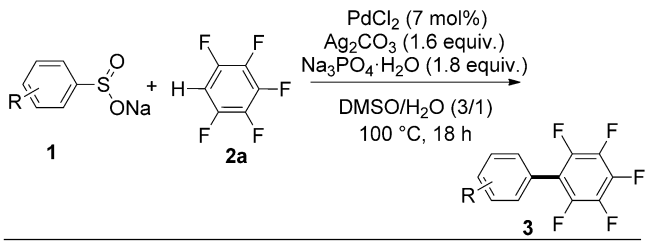
and efficiency in the presence of $Pd(OCOCF_3)_2$ (Table 1, entry 2 *vs.* 1). To our delight, $PdCl_2$ showed excellent activity and the desired product (**3a**) was isolated in 86% yield (Table 1, entry 3). $Pd(CH_3CN)_2Cl_2$ and $Pd(PPh_3)_2Cl_2$ were also effective catalysts and generated **3a** in good yields (Table 1, entries 4 and 5). However, $Pd(PPh_3)_4$ was not beneficial for the catalytic reaction and lower a yield was obtained (Table 1, entry 6). Further exploration of oxidants in the model reaction indicated that Ag_2CO_3 was superior to the others, the inorganic oxidants including AgOAc, Ag_2O, $AgSbF_6$ and $Cu(OAc)_2$ gave the inferior results and led to the formation of product (**3a**) in 10–46% yields (Table 1, entries 7–10). However, $K_2S_2O_8$ did not work in the model reaction (Table 1, entry 11). Under the present reaction conditions, the organic oxidants, BQ and TBHP were also examined and were harmful to this transformation (Table 1, entries 12 and 13). The influence of solvents was also investigated. A mixture of DMSO and H_2O (3:1) was optimal, it is supposed that DMSO might serve as a ligand to activate the Pd catalyst and prevent the formation of palladium black.[3a,6b,10] The yield decreased sharply when the reaction was carried out in a mixture of DMA and H_2O (3:1) (Table 1, entry 14). The other solvents such as mixtures of DMF or NMP and H_2O showed very poor performance and this reaction almost completely suppressed (Table 1, entries 15 and 16). The amount of water has an obvious effect on this reaction, lower yields were obtained when the DMSO/H_2O ratio was changed from 3:1 to 1:1 and 6:1 (Table 1, entries 17 and 18). Subsequently, when the catalyst was reduced to 5 mol%, the reaction only afforded the desired product in 64% yield (Table 1, entry 19). On shortening the reaction time to 10 h, the cross-coupling reaction of **1a** with **2a** produced a 60% yield under otherwise identical conditions (Table 1, entry 20). Furthermore, removal of the $Na_3PO_4{\cdot}12H_2O$ additive afforded a poor result of 31%, suggesting that this additive was an essential component for this arylated reaction (Table 1, entry 21).

Based on the optimized reaction conditions (7 mol% of $PdCl_2$, 1.6 equiv. of Ag_2CO_3, 1.8 equiv. of $Na_3PO_4{\cdot}12H_2O$, 2.0 mL of a 3:1 mixture of DMSO and H_2O, 100 °C, 18 h), the scope and limitation of the Pd-catalyzed desulfitative direct arylation of polyfluorobenzene reaction was examined. As can be seen from Table 2, the reactions of a wide range of sodium arenesulfinates with pentafluorobenzene could proceed well and generate the desired arylated products in good to excellent yields. The substituted benzenesulfinic acid sodium salts with electron-donating groups, such as methyl, *tert*-butyl and methoxy reacted with pentafluorobenzene efficiently and afforded the corresponding arylated products **3a–3e** in 71%–91% yields (Table 2, entries 1–5). Meanwhile, this re-

Table 2. Palladium-catalyzed desulfitative direct arylation of pentafluorobenzene with various arylsulfinic acid sodiums.[a]



Entry	Sodium sulfinate	Product	Yield [%][b]
1	**1a**	**3a**	86
2	**1b**	**3b**	84
3	**1c**	**3c**	91
4[c]	**1d**	**3d**	80
5[c]	**1e**	**3e**	71
6	**1f**	**3f**	90
7	**1g**	**3g**	82
8[c]	**1h**	**3h**	75
9	**1i**	**3i**	83
10	**1j**	**3j**	77
11	**1k**	**3k**	0

[a] *Reaction conditions*: **1** (0.40 mmol), **2a** (0.25 mmol) and $PdCl_2$ (7 mol%), Ag_2CO_3 (0.40 mmol), $Na_3PO_4{\cdot}12H_2O$ (0.45 mmol), in DMSO/H_2O (3:1, 2.0 mL), 100 °C for 18 h.

[b] Isolated yields.

[c] Solvent (4.0 mL) was used.

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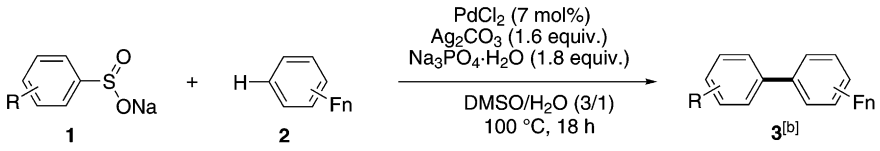
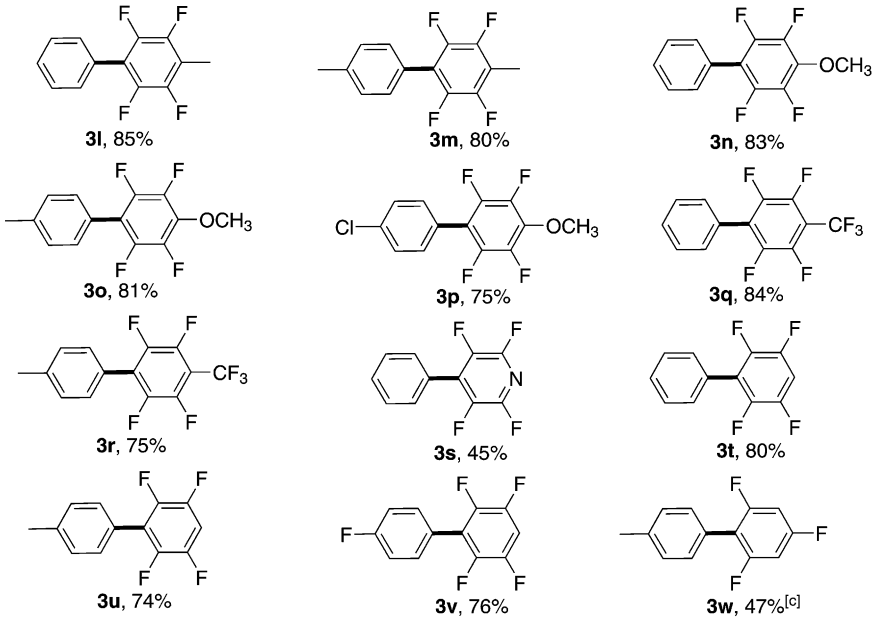
Table 3. Palladium-catalyzed desulfitative direct arylation of polyfluorobenzenes with arylsulfinic acid sodiums.[a]





[a] *Reaction conditions*: **1** (0.40 mmol), **2** (0.25 mmol) and $PdCl_2$ (7 mol%), Ag_2CO_3 (0.40 mmol), $Na_3PO_4{\cdot}12H_2O$ (0.45 mmol), in DMSO/H_2O (3:1, 2.0 mL), 100 °C for 18 h.
[b] Isolated yields.
[c] 1,3,5-Trifluorobenzene (3 equiv.) was used.

action is also tolerant of electron-withdrawing fluoro, chloro, bromo and nitro substituents in the aromatic ring of sodium arenesulfinates and arylated products **3f**, **3g**, **3h** and **3i** were observed in 90%, 82%, 75%, 83% yields, respectively (Table 2, entries 6–9). It is important to note that chloro- and bromo-substituted sodium arenesulfinates selectively underwent the desulfitative arylation, which may allow for further synthetic transformations by transition metal-catalyzed coupling and other reactions. Moreover, the more bulky 2-naphthalenesulfinic acid sodium salt (**1j**) was a good substrate for this arylation reaction as shown for the the successful formation of **3j** in 77% yield under the present reaction conditions (Table 2, entry 10). However, this reaction was extremely sensitive to steric hindrance. For example, when sodium arenesulfinate bearing an *ortho*-substitutent (sodium 2-methylbenzenesulfinate, **1k**) was treated with pentafluorobenzene, no desired product **3k** was obtained, in agreement with the observations by Su[5a,6a] and Shi[6b] (Table 2, entry 11).

The substrate scope with respect to polyfluorobenzenes was also investigated and is presented in Table 3. Under the standard conditions, tetrafluoro- and trifluorobenzenes can be selectively cross-arylated with sodium arenesulfinates. For example, 2,3,5,6-tetrafluorotoluene, 2,3,5,6-tetrafluoroanisole and 2,3,5,6-tetrafluorobenzotrifluoride effectively underwent direct arylation with good yields obtained (**3l–w**). However, these reaction conditions are not suitable for 2,3,5,6-tetrafluoropyridine, which participated in the reaction with benzenesulfinic acid sodium to furnish the corresponding products **3s**, displaying 45% yield. Maybe the substrate coordinated with the palladium catalyst and so reduced the catalyst efficiency. Gratifyingly, although 1,2,4,5-tetrafluorobenzene and 1,3,5-trifluorobenzene have more than one potential site for reaction, the reactions of these polyfluorobenzenes mainly generated the monoarylated product. 1,2,4,5-Tetrafluorobenzene underwent the reactions smoothly and monoarylated products (**3t–3w**) were achieved in 74%–80% yields.

However, 1,3,5-trifluorobenzene exhibits low reactivity, probably due to the low acidity of the C–H bond, and requires 3 equiv. of the fluorobenzene to produce **3w** in moderate yield.

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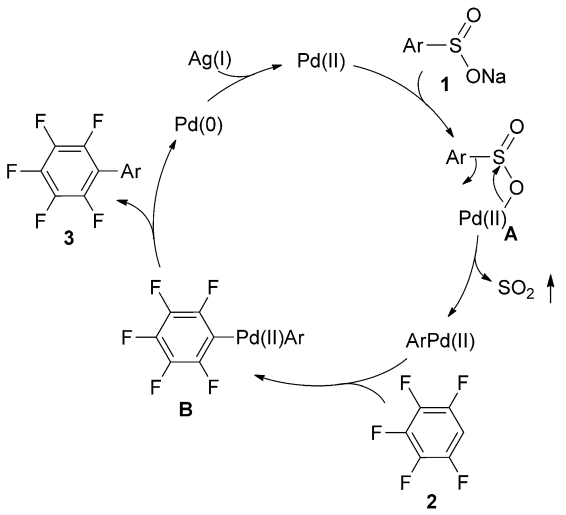


Scheme 2. The proposed reaction mechanism.

Although the exact mechanism of the reaction is still not clear, on the basis of the above observations and the results reported by others,[4a,5,7c,f] a possible reaction pathway is proposed and shown in Scheme 2. The first step is reaction of Pd(II) with arenesulfinic acid sodium salt provides palladium salt **A**. Then release of SO_2 from complex **A** is envisioned to take place leading to ArPd(II), which activates the fluorinated arene probably assisted by CO_3^{2-} or PO_4^{3-} to form intermediate **B**. Reductive elimination from intermediate **B** produces the polyfluoaryl-aryls **3** and Pd(0) species. Finally, oxidation of Pd(0) species by Ag(I) regenerates the catalytically active Pd(II) to finish the catalytic cycle.

Conclusions

In conclusion, we have demonstrated an efficient palladium-catalyzed method for the direct arylation of electron-deficient polyfluorobenzenes with sodium arenesulfinates. By using $PdCl_2$ as a catalyst, a broad range of sodium arenesulfinates efficiently underwent desulfitative coupling with an array of polyfluoroarenes in the presence of a stoichiometric amount of silver salts to generate fluorobiaryls. This new arylation reaction provides an alternative to the use of organometallic reagents in the synthesis of perfluoroaryl molecules and broadens the scope of Pd-catalyzed desulfitative coupling reactions. The investigation of sodium arenesulfinates as the aryl source in other coupling reactions is underway.

Experimental Section

General Considerations

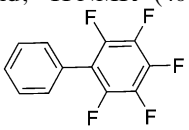
All ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a 400 MHz Bruker FT-NMR spectrometer (400 MHz, 100 MHz or 377 MHz, respectively). All chemical shifts are given as δ values (ppm) with reference to tetramethylsilane (TMS) as an internal standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; q, quartet. The coupling constants, *J*, are reported in Hertz (Hz). The chemicals and solvents were purchased from commercial suppliers either from Aldrich, USA or Shanghai Chemical Company, China. Products were purified by flash chromatography on 100–200 mesh silica gels, SiO_2.

Typical Procedure for Direct C–H Arylation of Electron-Deficient Polyfluoroarenes with Arenesulfinic Acid Sodium Salts

The Schlenk tube equipped with a stir bar was charged with $PdCl_2$ (0.0175 mmol), Ag_2CO_3 (0.40 mmol), $Na_3PO_4{\cdot}12H_2O$ (0.45 mmol), sodium arenesulfinate (0.40 mmol), and a mixture of DMSO and H_2O (3:1, 2.0 mL), then polyfluoroarene (0.25 mmol) was added by syringe. The reaction mixture was stirred at 100 °C for 18 h. Then it was cooled to room temperature, the reaction mixture was diluted with 5.0 mL of ethyl ether, filtered through a pad of silica gel, followed by washing the pad of the silica gel with the same solvent (10.0 mL). The filtrate was washed with water (3×5.0 mL). The organic phase was dried over $MgSO_4$, filtered, concentrated under reduced pressure to yield the crude product, which was further purified by flash chromatography on silica gel with petroleum ether to provide the corresponding product.

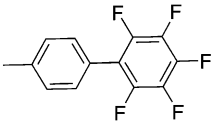
Characterization Data for all Products

2,3,4,5,6-Pentafluoro-1,1′-biphenyl (3a):[2d] Yield: 52.5 mg (86%); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=$



7.51–4.46 (m, 3H), 7.43–7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=145.5$–145.3 (m), 143.0–142.8 (m), 141.8–141.5 (m), 139.1–139.0 (m), 136.8–136.4 (m), 130.2–130.1 (m), 129.3, 128.7, 126.4, 116.2–115.8 (m).

2,3,4,5,6-Pentafluoro-4′-methyl-1,1′-biphenyl (3b):[2d] Yield: 54.2 mg (84%); colorless solid; ^{1}H NMR (400 MHz,



$CDCl_3$): $\delta=7.30$ (s, 4H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=145.5$–145.3 (m), 143.0–142.9 (m), 141.5–141.4 (m), 139.4, 139.1–138.9 (m), 136.8–136.5 (m), 130.0, 129.4, 123.4, 116.2–115.8 (m), 21.3.

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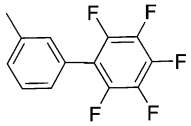
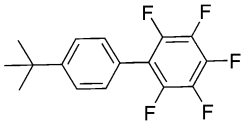
2,3,4,5,6-Pentafluoro-3′-methyl-1,1′-biphenyl (3c):[2d] Yield: 58.7 mg (91%); colorless solid; ^{1}H NMR (400 MHz,



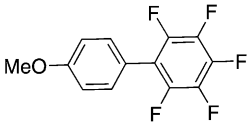
$CDCl_3$): $\delta = 7.38$ (t, $J = 7.6$ Hz, 1H), 7.27 (d, $J = 7.6$ Hz, 1H), 7.25–7.20 (m, 2H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 145.5$–145.3 (m), 143.1–142.8 (m), 141.7–141.4 (m), 139.2–138.9 (m), 138.5, 136.8–136.4 (m), 130.7, 130.1, 128.6, 127.2, 126.2, 116.3–115.9 (m), 21.4.

4′-(*tert*-Butyl)-2,3,4,5,6-pentafluoro-1,1′-biphenyl (3d):[11] Yield: 60.1 mg (80%); colorless solid; ^{1}H NMR (400 MHz,



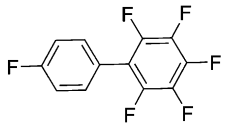
$CDCl_3$): $\delta = 7.51$ (d, $J = 8.0$ Hz, 2H), 7.36 (t, $J = 8.0$ Hz, 2H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 152.5$, 145.5–145.4 (m), 143.1–142.9 (m), 141.6–141.3 (m), 139.3–138.9 (m), 136.8–136.4 (m), 129.8, 125.7, 123.4, 116.1–115.7 (m), 34.8, 31.2; ^{19}F NMR (377 MHz, $CDCl_3$): $\delta = -143.4$ (dd, $J =$ 22.1, 8.0 Hz, 2F), −156.2 (t, $J = 22.1$ Hz, 1F), −162.5 (td, $J =$ 22.1, 8.0 Hz, 2F); anal calcd. for $C_{16}H_{13}F_5$: C 64.00, H 4.36; found: C 64.05, H 4.38.

2,3,4,5,6-Pentafluoro-4′-methoxy-1,1′-biphenyl (3e):[2d] Yield: 48.7 mg (71%); colorless solid; ^{1}H NMR (400 MHz,



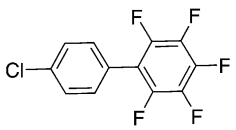
$CDCl_3$): $\delta = 7.36$ (d, $J = 8.4$ Hz, 2H), 7.01 (d, $J = 8.4$ Hz, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 160.3$, 145.5–145.3 (m), 143.0–142.9 (m), 141.4–141.1 (m), 139.3–138.6 (m), 136.8–136.4 (m), 131.4, 118.4, 115.9–115.5 (m), 114.2, 55.3.

2,3,4,4′,5,6-Hexafluoro-1,1′-biphenyl (3f):[2d] Yield: 59.0 mg (90%); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$):



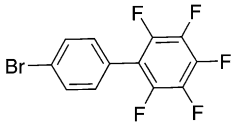
$\delta = 7.43$–7.40 (m, 2H), 7.19 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 163.2$ (d, $J = 248.4$ Hz), 145.4–145.3 (m), 143.0–142.9 (m), 141.9–141.7 (m), 139.3–138.9 (m), 136.8–136.5 (m), 132.1–132.0 (m), 122.3, 116.0 (d, $J =$ 21.8 Hz), 115.2–114.8 (m).

4′-Chloro-2,3,4,5,6-pentafluoro-1,1′-biphenyl (3g):[3d] Yield: 57.1 mg (82%); colorless solid; ^{1}H NMR (400 MHz,



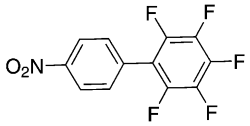
$CDCl_3$): $\delta = 7.48$ (d, $J = 8.2$ Hz, 2H), 7.37 (d, $J = 8.2$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 145.4$–145.2 (m), 142.9–141.7 (m), 139.3–139.0 (m), 136.8–136.6 (m), 135.6, 131.5–131.4 (m), 129.1, 124.8, 115.0–114.6 (m).

4′-Bromo-2,3,4,5,6-pentafluoro-1,1′-biphenyl (3h):[3b] Yield: 60.6 mg (75%); colorless solid; ^{1}H NMR (400 MHz,



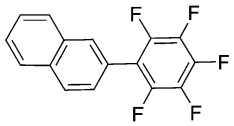
$CDCl_3$): $\delta = 7.63$ (d, $J = 8.2$ Hz, 2H), 7.29 (d, $J = 8.2$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 145.4$–145.2 (m), 142.9–142.7 (m), 141.9–141.8 (m), 139.5–139.0 (m), 136.8–136.5 (m), 132.1, 131.7 (m), 125.3, 123.8, 115.0–114.7 (m).

2,3,4,5,6-Pentafluoro-4′-nitro-1,1′-biphenyl (3i):[2d] Yield: 60.0 mg (83%); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$):



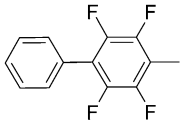
$\delta = 8.37$ (d, $J = 8.4$ Hz, 2H), 6.65 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 148.3$, 145.4–145.2 (m), 142.9–142.5 (m), 140.2–139.9 (m), 139.4–139.1 (m), 136.9–136.6 (m), 132.9, 131.3, 123.9, 114.0–113.6 (m).

2-(Perfluorophenyl)naphthalene (3j):[2d] Yield: 56.6 mg (77%); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$



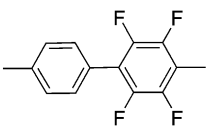
7.96–7.89 (m, 4H), 7.57–7.48 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 145.6$–145.5 (m), 143.1–143.0 (m), 141.7 (m), 139.3–139.0 (m), 136.6 (m), 133.7, 133.0, 130.1, 128.4, 128.3, 127.8, 127.2, 127.0, 126.7, 123.7, 116.0–115.8 (m).

2,3,5,6-Tetrafluoro-4-methyl-1,1′-biphenyl (3l):[3d] Yield: 51.0 mg (85%); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$):



$\delta = 7.50$–7.41 (m, 5H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 146.6$–146.4 (m), 144.9–144.7 (m), 144.2–144.0 (m), 142.5–142.2 (m), 130.2, 128.9, 128.5, 127.8, 118.0, 115.1, 7.5.

2,3,5,6-Tetrafluoro-4,4′-dimethyl-1,1′-biphenyl (3m):[4a] Yield: 50.8 mg (80%); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.34$ (d, $J = 7.8$ Hz, 2H), 7.31 (d, $J = 7.8$ Hz, 2H), 2.41(s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$



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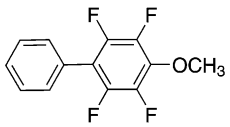
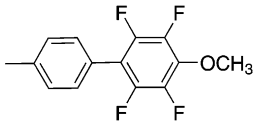
146.6–146.4 (m), 144.9–144.7 (m), 144.2–144.0 (m), 142.5–142.2 (m), 138.9, 130.0, 129.3, 124.7, 117.9, 114.7, 21.3, 7.5.

2,3,5,6-Tetrafluoro-4-methoxy-1,1′-biphenyl (3n):[3d] Yield: 53.2 mg (83%); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$):



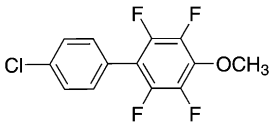
δ = 7.49–7.45 (m, 5H), 4.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.6–145.4 (m), 143.2–142.9 (m), 142.5–142.3 (m), 140.1–139.8 (m), 137.6–137.3 (m), 130.2, 128.8, 128.6, 127.3, 114.4–114.0 (m), 62.1 (t, J = 3.7 Hz).

2,3,5,6-Tetrafluoro-4-methoxy-4′-methyl-1,1′-biphenyl (3o):[4a] Yield: 54.7 mg (81%); colorless solid; ^{1}H NMR



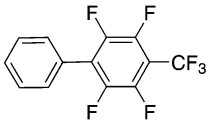
(400 MHz, $CDCl_3$): δ = 7.32 (d, J = 7.8 Hz, 2H), 7.28 (t, J = 7.8 Hz, 2H), 4.11 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.6–145.4 (m), 143.2–142.9 (m), 142.5–142.3 (m), 140.1–139.8 (m), 138.9, 137.3–137.1 (m), 130.0, 129.3, 124.2, 114.4–114.1 (m), 62.2 (t, J = 3.7 Hz), 21.3; ^{19}F NMR (377 MHz, $CDCl_3$): δ = −145.26 (dd, J = 22.0, 8.7 Hz, 2F), −158.4 (dd, J = 22.0, 8.7 Hz, 2F); anal calcd. for $C_{14}H_{10}F_4O$: C 62.23, H 3.73; found: C 62.30, H 3.77.

4′-Chloro-2,3,5,6-tetrafluoro-4-methoxy-1,1′-biphenyl (3p):[6a] Yield: 54.5 mg (75%); colorless solid; ^{1}H NMR



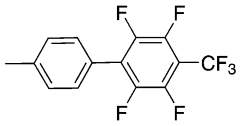
(400 MHz, $CDCl_3$): δ = 7.46 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 4.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.6–145.3 (m), 143.1–142.9 (m), 142.5–142.3 (m), 140.0–139.8 (m), 137.9–137.6 (m), 135.1, 131.5, 128.9, 125.7, 113.1–112.8 (m), 62.2 (t, J = 3.7 Hz); ^{19}F NMR (377 MHz, $CDCl_3$): δ = −145.1 (dd, J = 21.2, 8.9 Hz, 2F), −157.9 (dd, J = 21.2, 8.9 Hz, 2F); anal calcd. for $C_{13}H_7ClF_4O$: C 53.72, H 2.43; found: C 53.75, H 2.44.

2,3,5,6-Tetrafluoro-4-(trifluoromethyl)-1,1′-biphenyl (3q):[6a] Yield: 61.8 mg (84%); colorless solid; ^{1}H NMR



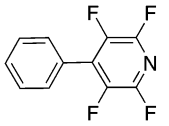
(400 MHz, $CDCl_3$): δ = 7.53–7.25 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.8–145.3 (m), 143.2–142.8 (m), 130.0–129.9 (m), 128.8, 126.1, 125.1–124.7 (m), 122.3, 119.5, 108.7–108.4 (m), 29.7.

2,3,5,6-Tetrafluoro-4′-methyl-4-(trifluoromethyl)-1,1′-biphenyl (3r):[3b] Yield: 57.8 mg (75%); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, J = 8.0 Hz, 2H),



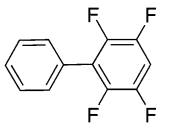
7.33 (d, J = 8.0 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.8–145.3 (m), 143.2–142.8 (m), 140.3, 129.8, 129.6, 125.1–124.8 (m), 123.1, 122.3, 119.5, 108.4–108.0 (m), 21.4.

2,3,5,6-Tetrafluoro-4-phenylpyridine (3s):[3d] Yield: 25.6 mg (45%); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$):



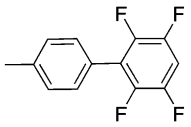
δ = 7.54 (s, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.4–145.0 (m), 143.0–142.6 (m), 140.7–140.3 (m), 138.1–137.8 (m), 133.6–133.3 (m), 130.5, 129.7, 128.9, 125.9.

2,3,5,6-Tetrafluoro-1,1′-biphenyl (3t):[3d] Yield: 45.2 mg (80%); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ =



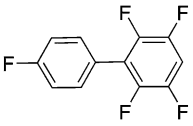
7.49–7.47 (m, 5H), 7.10–7.02 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.6–147.3 (m), 145.1–144.9 (m), 142.6–142.4 (m), 130.1, 129.2, 128.6, 127.5, 121.7–121.3 (m), 105.0–104.6 (m).

2,3,5,6-Tetrafluoro-4′-methyl-1,1′-biphenyl (3u):[4a] Yield: 45.4 mg (74%); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$):



δ = 7.35 (d, J = 7.6 Hz, 2H), 7.30 (d, J = 7.6 Hz, 2H), 7.08–6.99 (m, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.6–147.3 (m), 145.1–144.9 (m), 142.6–142.4 (m), 139.3, 129.9, 129.3, 124.4, 121.7–121.3 (m), 104.7–104.3 (m), 21.3.

2,3,4′,5,6-Pentafluoro-1,1′-biphenyl (3v):[12] Yield: 46.4 mg (76%); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ =



7.47–7.43 (m, 2H), 7.19 (t, J = 8.2 Hz, 2H), 7.12–7.03 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1 (d, J = 248.2 Hz), 147.6–147.3 (m), 145.2–144.9 (m), 142.6–142.4 (m), 132.1–132.0 (m), 123.3, 120.5, 115.8 (d, J = 21.7 Hz), 105.0.

2,4,6-Trifluoro-4′-methyl-1,1′-biphenyl (3w):[4a] Yield: 26.1 mg (47%); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 6.74 (t,

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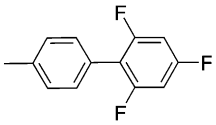

$J = 8.0$ Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 163.0$–162.6 (m), 161.7–161.4 (m), 160.5–160.2 (m), 159.2–158.9 (m), 138.3, 130.1, 129.1, 125.3, 115.2–114.8 (m), 100.7–100.1 (m), 21.3.

Acknowledgements

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