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钯催化的碳(sp^3)–硅键转化实现碳(sp^3)–碳(sp^2)偶联制备三氟丙基(杂)芳烃

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摘要 使用商业可得的三烷氧基三氟丙基硅试剂, 通过钯催化的碳(sp^3)–硅键转化实现了 C(sp^3)—C(sp^2)偶联反应. 该偶联反应方法具有良好的官能团兼容性, 可以有效制备一系列含多种官能团的三氟丙基(杂)芳烃. 氟离子添加剂和双膦配体的脂肪链的调节对于提高反应效率有重要的作用.
关键词 钯催化; 桧山偶联反应; 氟烷基化; 有机硅试剂

Palladium-Catalyzed C(sp^3)—Si Bonds Transformation for Constructing Trifluoropropyl (Hetero)arenes through C(sp^3)—C(sp^2) Cross-Coupling Reactions

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Abstract Palladium-catalyzed C(sp^3)—Si bonds transformation of commercially available polyalkoxy trifluorosilane reagents has been developed through C(sp^3)—C(sp^2) cross-coupling reactions. This Hiyama cross-coupling reaction shows good functional group tolerance and provides a series of trifluoropropyl (hetero)arenes. The fluoride source and alkyl tether of bisphosphine ligand play important roles in improving yields.
Keywords palladium catalysis; Hiyama cross-coupling reaction; fluoroalkylation; organosilicon

1 Introduction

The palladium-catalyzed cross-coupling reaction between organometallic reagents and organic electrophiles is one of the most reliable and comparable methods for constructing C—C bonds, and has widespread applications in the pharmaceuticals, agrochemicals, natural products, and materials.[1] Among them, organosilicon reagents feature many advantages compared with other organometallic reagents, such as the ease of preparation and purification of silanes, high availability, low toxicity and high stability.[2] As a result, the palladium-catalyzed cross-coupling reaction with organosilicon reagents has provided a practical alternative to strategies using other organometallic reagents since Hiyama's pioneering and ground-breaking work.[3] By sharp contrast with the well-developed cleavage and transformation of C(sp^2)—Si bonds of aryl- and alkenylsilicon reagents, the C(sp^3)—C(sp^2) cross-coupling reaction[4] of alkylsilicon reagents remains less developed due to some problems[5] (Scheme 1, a): (1) the formation of key reactive intermediates, pentavalent silicon species, is more difficult for alkylsilicon than corresponding aryl- and alkenyl substrates; (2) the alkyl palladium intermediates possessing *β*-hydrogen(s) always tend to proceed *β*-hydride elimination during the transmetallation; and (3) sequential migratory reinsertion and reductive elimination result in the isomeric products. As far as we know, several alkyl silicon reagents have been developed to enhance the rate of formation and transformation of this intermediate by employing silanes bearing electrophilic heteroatom (polyhalosilanes and polyalkoxysilane) or silanol precursor,[6] such as alkyl trifluorosilanes,[7] benzyl 2-pyridylsilanes, alkyl 2-(2-hydro-

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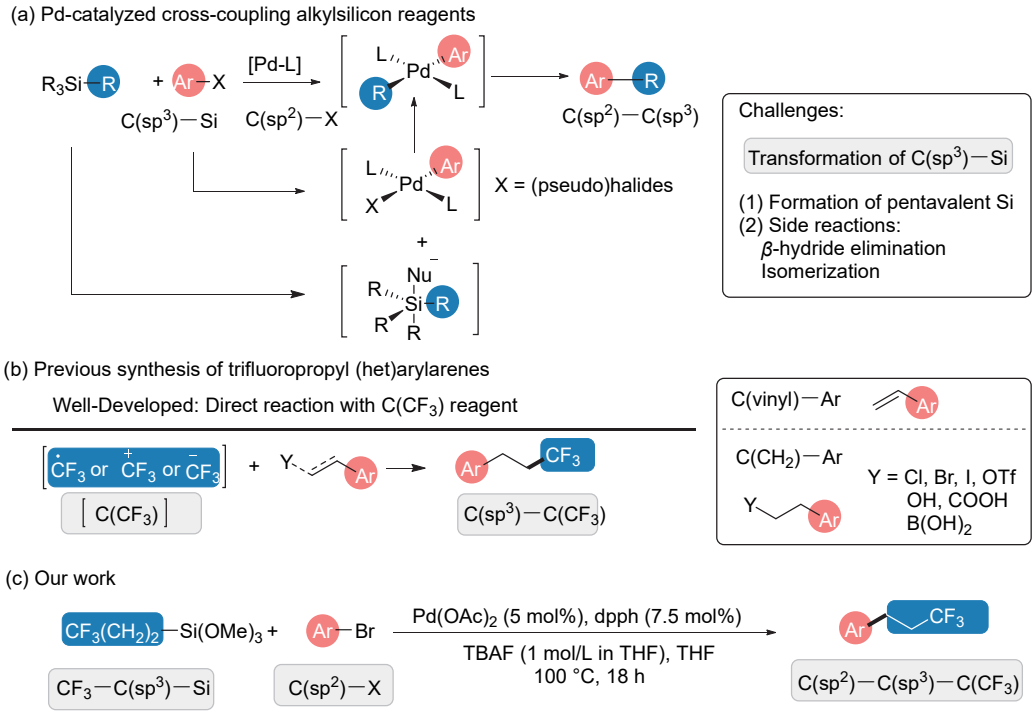
xyprop-2-yl)phenylsilanes,[8] and alkyl silacyclobutanes.[9] However, more effective and robust catalytic systems remain desired for the synthesis of functional molecules by taking advantage of various alkylsilicon reagents.

On the other hand, drug candidates and agrochemicals bearing the trifluoromethyl group display improved lipophilicity, membrane permeability, metabolic stability, and pharmacokinetics.[10] Various trifluoromethyl reagents have been rapidly developed in the past decades [11] while the formation of aliphatic trifluoromethyl group remains challenging. Up to date, there have been several strategies[12] for trifluoropropyl (hetero)arenes through trifluoromethylation in the presence of oxidants, bases and/or additives, including the addition to olefins,[13] the coupling of alkyl radicals,[14] the nucleophilic substitution of alkyl (pseudo)halides,[15] as well as the oxidative coupling of alkyl boronic acids.[16] The utilization of trifluoropropyl silicons with (hetero)arene (pseudo)halides could provide a direct and rapid access to trifluoropropyl (hetero)arenes, whereas it has rarely been reported.[17] Consequently, it is valuable to develop palladium-catalyzed direct C(sp^3)—Si bond transformations of commercially significant trifluoropropyl silicons for trifluoropropylation of (het)aryl halides as complementary.

Our group has focused on the Pd-catalyzed cross-coupling reactions of organometallic reagents and organic halides or pseudohalides in the presence of phosphine ligands for years.[18] Based on previous reports of Pd-catalyzed Hiyama coupling reactions,[19] we reasoned that suitable fluoride source, phosphine ligands and polyalkoxysilanes would achieve palladium-catalyzed trifluoropropylation of (hetero)arene halides or pseudohalides through activating silicon reagents and forming organopalladium species, accelerating the desired coupling (such as transmetalation and reductive elimination) and suppressing side reactions (such as β-hydride elimination and isomerization). In this context, we herein reported the palladium-catalyzed C(sp^3)—C(sp^2) cross-coupling reaction of (het)aryl halides for constructing trifluoropropyl (hetero)arenes through C(sp^3)—Si bonds transformation of trifluoropropyl polyalkoxysilane reagents (Scheme 1, c).

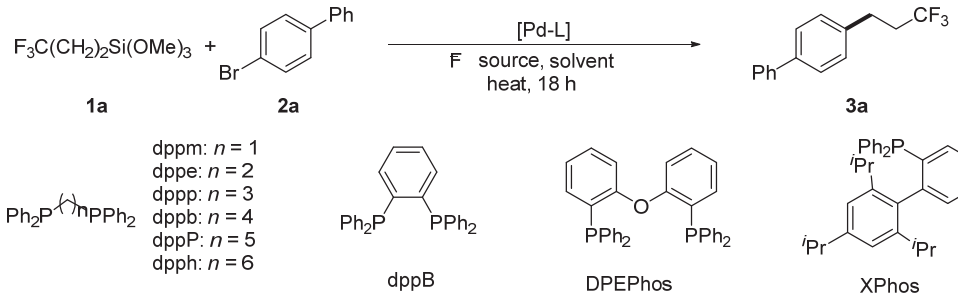
2 Results and discussion

Initially, commercially available (3,3,3-trifluoropropyl)-trimethoxysilane (**1a**) and 4-phenyl bromobenzene (**2a**) were used as model substrates at 100 ℃ oil bath for 18 h in the presence of tetrabutylammonium fluoride (TBAF) [1 mol/L in tetrahydrofuran (THF)], a well-proven fluoride source in Hiyama cross-coupling reaction. Desired β-CF_3 substituted product **3a** was obtained by using PPh_3 and PCy_3 in 36% and 42% yields, respectively (Table 1, Entries 1 and 2). By contrast, bulky monophosphine such as XPhos gave a 15% yield. To our delight, bis(diphenylphosphino)methane (dppm) gave a better yield of 49%. Thus, a series of bisphosphines were tested (Table 1, Entries 4～12). As shown in the Table 1, the length difference of alkyl tethers resulted in different yields from 24% to 52% (Table 1, Entries 4～9). Among them, 1,6-bis(diphenylphosphino)hexane (dpph) gave the best yield (Table 1, Entry 9). Compared with that, bisphosphines with arenes as tethers gave a lower yield (Table 1, Entries 10～12). Although the detailed mechanism is unclear, these results indicated that the flexibility and length of tethers should act as a critical role in improving the yield, probably influencing the formation and



Scheme 1 C(sp^3)—C(sp^2) Hiyama cross-coupling for trifluoropropyl (hetero)arene

Table 1 Optimization of the cross-coupling[a]



Entry	L	[Pd]	F^- source	Solvent	Temp./℃	Yield[b]/%
1[c]	PPh_3	$Pd(OAc)_2$	TBAF	THF	100	36
2[c]	PCy_3	$Pd(OAc)_2$	TBAF	THF	100	42
3[c]	XPhos	$Pd(OAc)_2$	TBAF	THF	100	15
4	dppm	$Pd(OAc)_2$	TBAF	THF	100	49
5	dppe	$Pd(OAc)_2$	TBAF	THF	100	24
6	dppp	$Pd(OAc)_2$	TBAF	THF	100	42
7	dppb	$Pd(OAc)_2$	TBAF	THF	100	48
8	dppP	$Pd(OAc)_2$	TBAF	THF	100	48
9	dpph	$Pd(OAc)_2$	TBAF	THF	100	52
10	dppB	$Pd(OAc)_2$	TBAF	THF	100	17
11	DPEPhos	$Pd(OAc)_2$	TBAF	THF	100	35
12	dppf	$Pd(OAc)_2$	TBAF	THF	100	23
13	dpph	$PdCl_2$	TBAF	THF	100	45
14	dpph	$Pd_2(dba)_3$	TBAF	THF	100	＜5
15	dpph	$[Pd(cinnamyl)Cl]_2$	TBAF	THF	100	＜5
16	dpph	$Pd(OTF)_2$	TBAF	THF	100	50
17	dpph	$Pd(OAc)_2$	TBAF	Tol	100	49
18	dpph	$Pd(OAc)_2$	TBAF	Dioxane	100	41
19	dpph	$Pd(OAc)_2$	TBAF	MeCN	100	18
20	dpph	$Pd(OAc)_2$	TBAF	DMF	100	35
21	dpph	$Pd(OAc)_2$	CsF	THF	100	＜5
22	dpph	$Pd(OAc)_2$	RbF	THF	100	ND
23	dpph	$Pd(OAc)_2$	KF	THF	100	ND
24[d]	dpph	$Pd(OAc)_2$	TBAF	THF	100	62 (57)
25[e]	dpph	$Pd(OAc)_2$	TBAF	THF	100	46
26[d]	dpph	$Pd(OAc)_2$	TBAF	THF	90	57
27[d]	dpph	$Pd(OAc)_2$	TBAF	THF	110	62
28[d]	dpph	$Pd(OAc)_2$	TBAF	THF	120	53

[a] Reaction conditions: **1a** (0.40 mmol), **2a** (0.20 mmol), [Pd] (5.0 mol%), ligand (7.5 mol%) and F^- source (2.0 equiv.) in 1.0 mL of solvent (including the solution of F^- source) in a sealed tube at 100 ℃ oil bath for 18 h. [b] Determined by GC/MS with tetradecane as internal standard, isolated yield in the parentheses. [c] 15 mol% of monophosphines. [d] 3.0 equiv. of TBAF. [e] **1a**∶**2a**=1∶1. TBAF (1 mol/L in THF). dppf═1,1'-bis(diphenylphosphino)ferrocene. ND: No detected.

transformation of organopalladium species due to different steric and electronic effects.

A brief screening of palladium precursors revealed that $Pd(OAc)_2$ gave a relatively better performance than examined Pd(0) and other Pd(II) precursors, although $Pd(OTF)_2$ gave a seemingly competitive result (Table 1, Entries 13～16). Solvents were also examined while replacing THF with other solvents always led to lower yields (Table 1, Entries 17～20). Considering the importance of the fluoride ion in activating the C—Si bond, other potential fluoride salts were examined, such as RbF, CsF, and KF. A dramatic decrease was observed in reactivity (Table 1, Entries 21～23). Furthermore, the amount of TBAF was examined carefully. A significant improvement was observed along with the increase of TBAF and 0.6 equiv. of TBAF gave a 62% yield (Table 1, Entry 24). Only 46% yield was obtained when reducing the amount of **1a** from 2 equiv. to 1.0 equiv. (Table 1, Entry 25). Besides, the screening of temperatures was also performed (Table 1, Entries 26～28). Both higher and lower temperatures resulted in the same result (Table 1, Entry 27 vs Entry 24) or a slight decrease in the yield.

With the optimized conditions, the substrate scope of **2** was investigated. Firstly, the influence of substituents on the phenyl rings was examined. The *para*-substituted substrate afforded desired products in moderate yields con-

taining whether a small methyl group or a bulky *tert*-butyl group (**3b** and **3c**). The substrate with electron-donating *para*-methyloxyl group gave a 50% yield (**3d**) while the substrate with the *para*-chloro group was well-compatible with a lower yield (**3e**). The substrate with electron-withdrawing acetyl group provided a 52% yield (**3f**) and the one with benzoyl group provided a 65% yield (**3g**). Notably, the carbonyl compound is sensitive to acids and bases, and also an excellent acceptor for nucleophiles or radicals, which might proceed side reactions in other methods.[20] Besides, the strong electron-withdrawing ester group resulted in a dramatic decrease in the yield (**3h**). The substrate with *meta*-phenyl group gave up to 56% yield (**3j**) while those with *meta*-methyl group and the *meta*-ester group gave lower yields (**3i** and **3k**). In addition, the substrates bearing 2-bromo naphthyl and 2-bromo-6-methoxyl naphthyl were tested, providing corresponding products with 53% (**3l**) and 44% (**3m**) yields, respectively. Afterward, a series of complex substrates were investigated. Oxygen-containing 5-bromobenzo[*d*][1,3]dioxole gave **3n** in 49% yield. Nitrogen-containing heterocycle 6-bromoquinoline was also well-compatible with 41% yield. 2-Bromo-9,9-dimethyl-9*H*-fluorene (**2p**) gave a 57% yield while 2-bromo-9,9'-spirobifluorene (**2q**) gave a 26% yield. However, there was no desired product when 3-bromopyridine was used as a substrate.

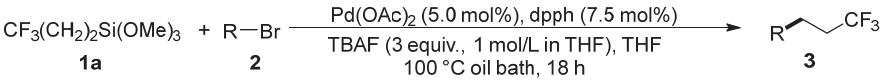
For the synthetic application of this method, the scale-up reactions of bromobenzenes bearing different substituents were performed (Scheme 2, a). It was noted that competitive results were obtained in a 1 mmol scale. Besides, the dibromo substituted substrates were also used for difunctionalization (Scheme 2, b). To our delight, the biphenyl-based product **3r** was obtained in 30% yield and fluorene-based product **3s** was obtained in 49% yield.

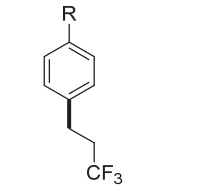
Then, we tried to extend the substrate scope to other halides or pseudohalides (Table 3). Consistent with the conventional reactivity order of halides in Pd-catalyzed coupling, iodide **2a'** gave **3a** with up to 70% yield. Only trace **3c** was detected when using more challenging aryl chloride **2c'** under these conditions, while an 11% yield was obtained in the presence of a 10 mol% catalyst (Table 3, Entries 2, 3). Unfortunately, desired products were not detected yet when aryl and alkenyl tosylates were used (**2c''**, **2t**～**2v**). The Pd-indolylphosphine catalytic system[21] also failed, which has achieved the Hiyama cross-coupling of (hetero)aryl trialkoxysilanes with (hetero)aryl chlorides[19a] and sulfonylates.[19b] Besides, it was found that there was no desired product when using propyl trimethoxysilane as a propylation reagent, suggesting the importance of CF_3 in this transformation of C(sp^3)—Si bond.

3 Conclusions

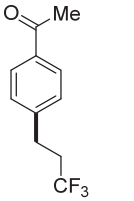
In summary, a palladium-catalyzed C(sp^3) — C(sp^2) cross-coupling reaction of commercially available trifluoropropyl polyalkoxysilicon with (hetero)aryl bromides was developed. This method provided a series of trifluoropropyl (hetero)arenes bearing various function groups with up to 65% isolated yields, including highly active acetyl group and quinoline heterocycle. The fluoride source and alkyl tether of bisphosphine ligands played important roles in the cleavage and transformation of the C(sp^3)—Si bond of alkyl silicon.

Table 2 Investigation of substrate scope: (hetero)aryl bromides[a]

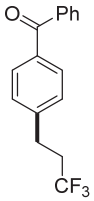




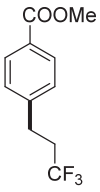
3a, R = Ph, 57% yield
3b, R = Me, 54% yield
3c, R = ^{t}Bu, 53% yield
3d, R = OMe, 50% yield
3e, R = Cl, 43% yield



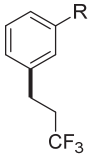
3f, 52% yield



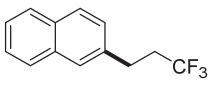
3g, 65% yield



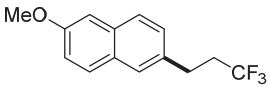
3h, 15% yield



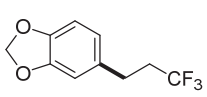
3i, R = Me, 37% yield
3j, R = Ph, 56% yield
3k, R = COOMe, 34% yield



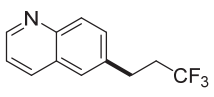
3l, 53% yield



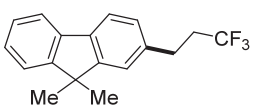
3m,44% yield



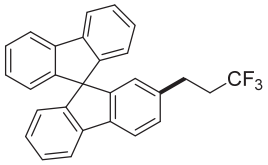
3n, 49% yield



3o, 41% yield

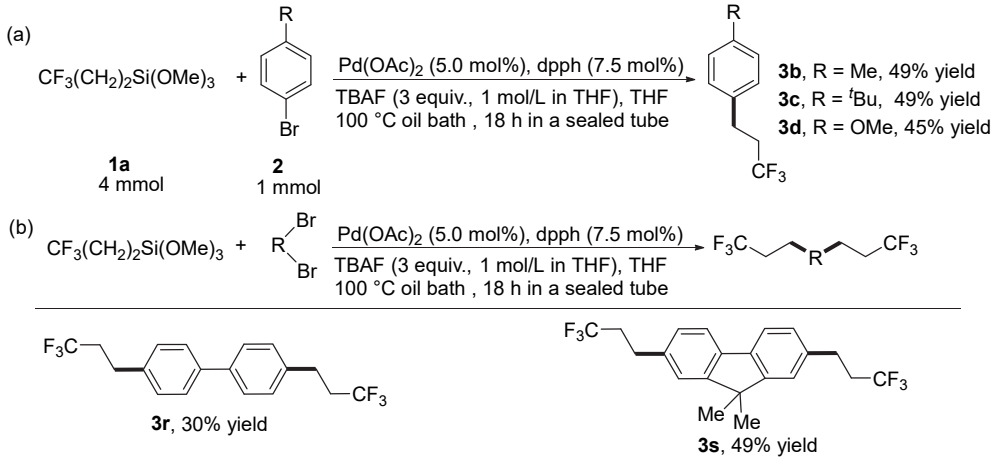


3p, 57% yield



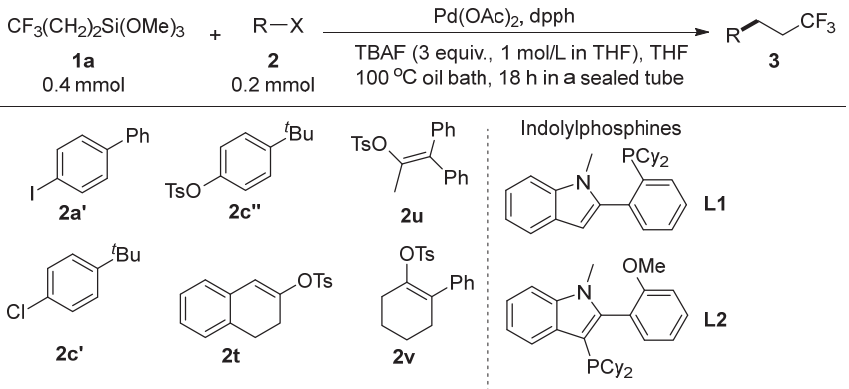
3q, 26% yield

[a] Reaction conditions: **1a** (0.40 mmol), **2a** (0.20 mmol), $Pd(OAc)_2$ (5.0 mol%), dpph (7.5 mol%) and TBAF (0.6 mL, 1 mol/L in THF) in THF (0.4 mL) in a sealed tube at 100 ℃ oil bath for 18 h; Isolated yields. **1a** (0.40 mmol) with 6 equiv. TBAF was used for **3r** and **3s**.



Scheme 2 C(sp^3)—C(sp^2) Hiyama cross-coupling for trifluoropropyl (hetero)arene

Table 3 Investigation of other halides or pseudohalides



Entry	R—X	[Pd-L]/mol%	Yield[b]/%
1	**2a'**	5	70%
2	**2c'**	5	<5%
3	**2c'**	10	11

4 Experimental section

4.1 General considerations

All the catalytic reactions were performed using a crew-capped Schlenk tube with a Teflon-coated magnetic stirrer bar under N_2. Unless otherwise noted, commercially available reagents were purchased and used as received.

All solvents including extra dry solvents were purchased. $Pd(OAc)_2$ was purchased from Strem. Trimethoxy(3,3,3-trifluoropropyl)silane was purchased from J&K Scientific. Phosphine ligands were purchased from Strem or J&K Scientific. Other solvents were distilled from sodium benzophenone under nitrogen. Silica gel (column chromatography) and thin layer chromatography plate (GF254) were purchased from Merck.

Melting points were recorded on an uncorrected Büchi Melting Point B-545 instrument. NMR spectra were recorded on Bruker spectrometers (400 MHz & 500 MHz) with tetramethylsilane (TMS, δ 0.00) as the internal standard (for ^{1}H NMR) or referenced to $CDCl_3$ (for ^{13}C NMR). High-resolution mass spectra (HRMS) were obtained on a ThermoFinnigan MAT95XL. The GC yields and NMR yields were accorded to the standard authentic samples/tetradecane calibration from Agilent 7890B GC-FID system.

4.2 General procedures for conditions screening

Pd sources and ligand were loaded to a Schlenk tube equipped with a Teflon-coated stir bar and screw cap. The tube was carefully evacuated and backfilled with nitrogen for three cycles. Then, F^- sources, bromo(hetero)arylarene, trimethoxy(3,3,3-trifluoropropyl)silane and solvents were added by syringe. The tube was placed into a preheated oil bath and stirred. After completion of the reaction, the reaction tube was allowed to reach room temperature. Ethyl acetate (*ca.* 8 mL), tetradecane (52 μL, internal standard) and water (*ca.* 3 mL) were added. The organic layer was separated and the aqueous layer was washed with ethyl acetate. The filtrate was concentrated under reduced pres-

sure. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by an authentic sample/tetradecane calibration curve.

4.3 General procedures for different substrates and products characterization

$Pd(OAc)_2$ (0.010 mmol) and 1,6-bis(diphenylphosphino)hexane (dpph) (0.015 mmol) were loaded to a Schlenk tube equipped with a Teflon-coated stir bar and screw cap. The tube was carefully evacuated and backfilled with nitrogen for three cycles. Then, bromo(hetero)arylarene (0.2 mmol), trimethoxy(3,3,3-trifluoropropyl)silane (0.4 mmol), TBAF (0.6 mL, 1 mol/L in THF) and THF (0.4 mL) were added. The tube was placed into a preheated oil bath (100 ℃) and stirred for 18 h. After completion of the reaction, the reaction tube was allowed to reach room temperature. Ethyl acetate (*ca.* 5 mL) and water (*ca.* 2 mL) were added. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (15 mL×3). The combined organic layers were washed with brine, dried over Na_2SO_4 and then concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel [eluent: from hexane to *V*(hexane)/ *V*(ethyl acetate)=100/1] to afford the desired product.

4.3 Characterization of compounds **3a**～**3s**

4-(3,3,3-Trifluoropropyl)-1,1'-biphenyl (**3a**): White solid, yield 57%. m.p. 83～84 ℃; ^{1}H NMR (500 MHz, Chloroform-*d*) *δ*: 7.62～7.53 (m, 2H), 7.49～7.30 (m, 6H), 7.18 (d, *J*=7.5 Hz, 1H), 2.97～2.90 (m, 2H), 2.50～2.36 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) *δ*: 141.9, 141.1, 139.6, 129.3, 128.9, 127.6, 127.3, 127.3, 127.2, 126.8 (q, *J*=276.8 Hz), 125.7, 35.8 (q, *J*=28.5 Hz), 28.4 (q, *J*=3.3 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) *δ*: −66.60 (t, *J*=10.5 Hz); HRMS (ESI) calcd for $C_{15}H_{14}F_3$ $[M+H]^+$ 251.1042, found 251.1046.

1-Methyl-4-(3,3,3-trifluoropropyl)benzene (**3b**):[13e] Colorless oil, yield 54%. ^{1}H NMR (500 MHz, Chloroform-*d*) *δ*: 7.12 (d, *J*=7.9 Hz, 2H), 7.08 (d, *J*=7.9 Hz, 2H), 2.85～2.79 (m, 2H), 2.41～2.33 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) *δ*: 135.4, 135.1, 128.5, 127.2, 125.9 (q, *J*=276.8 Hz), 34.9 (q, *J*=28.2 Hz), 26.9 (q, *J*=3.2 Hz), 20.1; ^{19}F NMR (471 MHz, Chloroform-*d*) *δ*: −66.67 (t, *J*=10.7 Hz).

1-(*tert*-Butyl)-4-(3,3,3-trifluoropropyl)benzene (**3c**): Colorless oil, yield 53%. ^{1}H NMR (500 MHz, Chloroform-*d*) *δ*: 7.34 (d, *J*=8.1 Hz, 2H), 7.13 (d, *J*=8.1 Hz, 2H), 2.89～2.77 (m, 2H), 2.47～2.27 (m, 2H), 1.31 (s, 9H); ^{13}C NMR (126 MHz, Chloroform-*d*) *δ*: 149.7, 136.1, 128.0, 126.5 (d, *J*=276.3 Hz), 125.8, 35.8 (q, *J*=28.3 Hz), 34.6, 31.5 (q, *J*=17.8 Hz), 27.8 (q, *J*=3.3 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) *δ*: −66.72 (t, *J*=10.6 Hz); HRMS (ESI) calcd for $C_{13}H_{17}F_3$ 230.1277, found 230.1276.

1-Methoxy-4-(3,3,3-trifluoropropyl)benzene (**3d**): Colorless oil, yield 50%. ^{1}H NMR (500 MHz, Chloroform-*d*) *δ*: 7.10 (d, *J*=8.5 Hz, 2H), 6.84 (d, *J*=8.5 Hz, 2H), 3.78 (s, 3H), 2.87～2.75 (m, 2H), 2.41～2.26 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) *δ*: 158.5, 131.2, 129.3, 126.9 (q, *J*=276.7 Hz), 114.2, 55.4 (d, *J*=28.4 Hz), 36.0 (q, *J*=28.1 Hz), 27.5 (q, *J*=3.3 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) *δ*: −66.64 (t, *J*=10.8 Hz); HRMS (ESI) calcd for $C_{10}H_{11}F_3O$ 204.0757, found 204.0755.

1-Chloro-4-(3,3,3-trifluoropropyl)benzene (**3e**): Colorless oil, yield 43%. ^{1}H NMR (500 MHz, Chloroform-*d*) *δ*: 7.28 (d, *J*=7.3 Hz, 2H), 7.13 (d, *J*=7.4 Hz, 2H), 2.90～2.77 (m, 2H), 2.46～2.27 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) *δ*: 137.5, 132.7, 129.7, 129.0, 126.7 (q, *J*=276.8 Hz), 35.6 (q, *J*=28.4 Hz), 27.8 (q, *J*=2.8 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) *δ*: −66.59 (t, *J*=10.5 Hz); HRMS (ESI) calcd for $C_9H_8ClF_3$ 208.0261, found 208.0260.

1-(4-(3,3,3-Trifluoropropyl)phenyl)ethan-1-one (**3f**): Colorless oil, yield 52%. ^{1}H NMR (500 MHz, Chloroform-*d*) *δ*: 7.92 (d, *J*=8.2 Hz, 2H), 7.30 (d, *J*=8.2 Hz, 2H), 2.99～2.88 (m, 2H), 2.59 (s, 3H), 2.49～2.35 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) *δ*: 197.8, 144.6, 135. 9, 129.0, 128.6, 126.6 (q, *J*=276.8 Hz), 35.2 (q, *J*=28.7 Hz), 28.3 (q, *J*=3.3 Hz), 26.7; ^{19}F NMR (471 MHz, Chloroform-*d*) *δ*: −66.57; HRMS (ESI) calcd for $C_{11}H_{12}F_3O$ $[M+H]^+$ 217.0835, found 217.0835.

Phenyl(4-(3,3,3-trifluoropropyl)phenyl)methanone (**3g**): White solid, yield 65%. m.p. 70～71 ℃; ^{1}H NMR (500 MHz, Chloroform-*d*) *δ*: 7.78 (t, *J*=7.4 Hz, 4H), 7.59 (t, *J*=7.4 Hz, 1H), 7.48 (t, *J*=7.7 Hz, 2H), 7.32 (d, *J*=8.1 Hz, 2H), 2.99～2.94 (m, 2H), 2.53～2.38 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) *δ*: 196.4, 143.9, 137.7, 136.2, 132.5, 130.7, 130.1, 128.4, 128.3, 126.7 (q, *J*=276.7 Hz), 35.3 (q, *J*=28.7 Hz), 28.4 (q, *J*=3.3 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) *δ*: −66.54 (t, *J*=10.7 Hz); HRMS (ESI) calcd for $C_{16}H_{14}F_3O$ $[M+H]^+$ 279.0991, found 279.0994.

Methyl 4-(3,3,3-trifluoropropyl)benzoate (**3h**): Colorless oil, yield 15%. ^{1}H NMR (500 MHz, Chloroform-*d*) *δ*: 7.99 (d, *J*=8.2 Hz, 2H), 7.27 (d, *J*=8.2 Hz, 2H), 3.91 (s, 3H), 2.99～2.89 (m, 2H), 2.48～2.35 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) *δ*: 167.0, 144.4, 130.3, 128.9, 128.4, 126.7 (q, *J*=276.8 Hz), 52.2 (q, *J*=27.9 Hz), 35.3 (q, *J*=28.6 Hz), 28.4 (q, *J*=3.3 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) *δ*: −66.60 (t, *J*=10.4 Hz); HRMS (ESI) calcd for $C_{11}H_{12}F_3O_2$ $[M+H]^+$ 233.0784, found 233.0784.

1-Methyl-3-(3,3,3-trifluoropropyl)benzene (**3i**): Colorless oil, yield 37%. ^{1}H NMR (500 MHz, Chloroform-*d*) *δ*: 7.24～7.15 (m, 1H), 7.07～7.03 (m, 1H), 7.03～6.97 (m, 2H), 2.86～2.80 (m, 2H), 2.43～2.35 (m, 2H), 2.34 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) *δ*: 138.9, 138.4, 129.0, 128.6, 127.3, 126.7 (q, *J*=276.8 Hz), 125.2, 35.7 (q, *J*=28.5 Hz), 28.1 (q, *J*=3.3 Hz), 21.3; ^{19}F NMR (471 MHz, Chloroform-*d*) *δ*: −66.72 (t, *J*=10.8 Hz).; HRMS (ESI) calcd for $C_{10}H_{11}F_3$ 188.0807, found 188.0806.

3-(3,3,3-Trifluoropropyl)-1,1'-biphenyl (**3j**): Sticky oil, yield 56%. ^{1}H NMR (500 MHz, Chloroform-*d*) *δ*: 7.57 (d, *J*=7.4 Hz, 2H), 7.50～7.30 (m, 6H), 7.17 (d, *J*=7.5 Hz, 1H), 2.99～2.88 (m, 2H), 2.52～2.30 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) *δ*: 141.9, 141.1, 139.6, 129.3, 128.9, 127.57, 127.3, 127.3, 127.2, 126.8 (q, *J*=276.7 Hz),

125.7, 35.8 (q, J=28.5 Hz), 28.4 (q, J=3.3 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) δ: −66.60 (t, J=10.6 Hz); HRMS (ESI) calcd for $C_{15}H_{13}F_3$ 250.0964, found 250.0959.

Methyl 3-(3,3,3-trifluoropropyl)benzoate (**3k**): Sticky oil, yield 34%. ^{1}H NMR (500 MHz, Chloroform-*d*) δ: 7.99～7.84 (m, 2H), 7.43～7.35 (m, 2H), 3.92 (s, 3H), 2.98～2.87 (m, 2H), 2.50～2.33 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ: 166.1, 138.4, 132.0, 129.8, 128.4, 128.0, 127.1, 125.7 (q, J=276.6 Hz), 51.3, 34.6 (q, J=28.8 Hz), 27.2 (q, J=3.3 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) δ: −66.60; HRMS (ESI) calcd for $C_{11}H_{12}F_3O_2$ $[M+H]^+$ 233.0784, found 233.0784.

2-(3,3,3-Trifluoropropyl)naphthalene (**3l**): White solid, yield 53%. m.p. 78～79 ℃; ^{1}H NMR (500 MHz, Chloroform-*d*) δ: 7.88～7.74 (m, 3H), 7.64 (s, 1H), 7.50～7.42 (m, 2H), 7.35～7.29 (m, 1H), 3.08～3.00 (m, 2H), 2.56～2.43 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ: 136.6, 133.7, 132.4, 128.6, 127.8, 127.6, 126.9 (q, J=276.8 Hz), 126.8, 126.7, 126.4, 125.8, 35.7 (q, J=28.4 Hz), 28.5 (q, J=3.5 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) δ: −66.55 (t, J=10.5 Hz); HRMS (ESI) calcd for $C_{13}H_{12}F_3$ $[M+H]^+$ 225.0886, found 225.0883.

2-Methoxy-6-(3,3,3-trifluoropropyl)naphthalene (**3m**): White solid, yield 44%. m.p. 46～47 ℃; ^{1}H NMR (500 MHz, Chloroform-*d*) δ: 7.69 (t, J=8.7 Hz, 2H), 7.57 (s, 1H), 7.34～7.23 (m, 1H), 7.18～7.09 (m, 2H), 3.92 (s, 3H), 3.04～2.97 (m, 2H), 2.52～2.40 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ: 157.66, 134.21, 133.47, 129.17, 129.09, 127.39, 127.26, 126.90 (q, J=276.4 Hz), 126.52, 119.22, 105.78, 55.44, 35.83 (q, J=28.3 Hz), 28.30 (q, J=3.1 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) δ: −66.57 (t, J=10.7 Hz); HRMS (ESI) calcd for $C_{14}H_{14}F_3O$ $[M+H]^+$ 255.0991, found 255.0992.

5-(3,3,3-Trifluoropropyl)benzo[*d*][1,3]dioxole (**3n**): White solid, yield 49%. m.p. 78～79 ℃; ^{1}H NMR (500 MHz, Chloroform-*d*) δ: 6.77～6.72 (m, 1H), 6.70～6.62 (m, 2H), 5.93 (s, 2H), 2.83～2.75 (m, 2H), 2.43～2.25 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ: 148.0, 146.4, 132.9, 126.8 (q, J=276.9 Hz), 121.1, 108.9, 108.7, 101.1, 36.1 (q, J=28.1 Hz), 28.1 (q, J=2.9 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) δ: −66.61 (t, J=10.6 Hz); HRMS (ESI) calcd for $C_{10}H_9F_3O_2$ 218.0549, found 218.0549.

6-(3,3,3-Trifluoropropyl)quinoline (**3o**): White solid, yield 41%. m.p. 43～44 ℃; ^{1}H NMR (500 MHz, Chloroform-*d*) δ: 8.89 (d, J=3.7 Hz, 1H), 8.09 (dd, J=14.9, 8.5 Hz, 2H), 7.62 (s, 1H), 7.56 (dd, J=8.6, 2.1 Hz, 1H), 7.39 (dd, J=8.3, 4.2 Hz, 1H), 3.16～2.96 (m, 2H), 2.60～2.35 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ: 150.3, 147.4, 137.4, 135.8, 130.3, 130.1, 128.4, 126.7 (q, J=276.7 Hz), 126.4, 121.5, 35.5 (q, J=28.7 Hz), 28.3 (q, J=3.2 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) δ: −66.49 (t, J=10.5 Hz); HRMS (ESI) calcd for $C_{12}H_{11}F_3N$ $[M+H]^+$: 226.0838, found 226.0837.

9,9-Dimethyl-2-(3,3,3-trifluoropropyl)-9*H*-fluorene (**3p**): Sticky oil, yield 57%. ^{1}H NMR (500 MHz, Chloroform-*d*) δ: 7.70～7.67 (m, 1H), 7.64 (d, J=7.8 Hz, 1H), 7.43～7.40 (m, 1H), 7.35～7.27 (m, 2H), 7.26～7.23 (m, 1H), 7.15 (dd, J=7.8, 1.7 Hz, 1H), 2.97～2.91 (m, 2H), 2.51～2.37 (m, 2H), 1.47 (s, 6H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ: 154.4, 153.7, 139.0, 138.3, 138.0, 127.3, 127.1, 126.9 (q, J=276.8 Hz), 122.7, 122.6, 120.3, 120.3, 120.0, 120.0, 46.9, 36.1 (q, J=28.2 Hz), 28.6 (q, J=3.2 Hz), 27.3 (q, J=6.5 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) δ: −66.58 (t, J=10.5 Hz); HRMS (ESI) calcd for $C_{18}H_{18}F_3$ $[M+H]^+$ 291.1355, found 291.1355.

2-(3,3,3-Trifluoropropyl)-9,9'-spirobi[fluorene] (**3q**): White solid, yield 26%. m.p. 177～178 ℃; ^{1}H NMR (500 MHz, Chloroform-*d*) δ: 7.85 (d, J=7.6 Hz, 2H), 7.82～7.75 (m, 2H), 7.40～7.31 (m, 3H), 7.20～7.16 (m, 1H), 7.13～7.04 (m, 3H), 6.76～6.67 (m, 3H), 6.55 (s, 1H), 2.75～2.68 (m, 2H), 2.29～2.17 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ: 149.6, 149.0, 148.9, 141.9, 141.5, 140.6, 138.9, 128.0, 128.0, 127.9, 127.9, 126.7 (q, J=276.9 Hz), 124.2, 124.1, 123.9, 123.9, 120.3, 120.2, 120.0, 66.0, 35.7 (q, J=28.3 Hz), 28.3 (dd, J=3.2 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) δ: −66.73 (t, J=10.8 Hz); HRMS (ESI) calcd for $C_{28}H_{20}F_3$ $[M+H]^+$ 413.1512, found 413.1509.

4,4'-Bis(3,3,3-trifluoropropyl)-1,1'-biphenyl (**3r**): White solid, yield 30%. m.p. 115～116 ℃; ^{1}H NMR (500 MHz, Chloroform-*d*) δ: 7.52 (d, J=8.1 Hz, 4H), 7.26 (d, J=8.1 Hz, 4H), 2.97～2.84 (m, 4H), 2.58～2.27 (m, 4H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ: 139.3, 138.2, 128.8, 127.4, 126.8 (q, J=276.8 Hz), 35.7 (q, J=28.3 Hz), 28.0 (q, J=3.3 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) δ: −66.61 (t, J=10.7 Hz; HRMS (ESI) calcd for $C_{18}H_{17}F_6$ $[M+H]^+$ 347.1229, found 347.1228.

9,9-Dimethyl-2,7-bis(3,3,3-trifluoropropyl)-9*H*-fluorene (**3s**): White solid, yield 49%. m.p. 36～37 ℃; ^{1}H NMR (500 MHz, Chloroform-*d*) δ: 7.62 (d, J=7.7 Hz, 2H), 7.24 (s, 2H), 7.15 (d, J=7.7 Hz, 2H), 3.01～2.89 (m, 4H), 2.53～2.37 (m, 4H), 1.46 (s, 6H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ: 154.4, 138.2, 137.7, 127.2, 126.9 (q, J=276.8 Hz), 122.7, 120.3, 120.1, 46.9, 36.1 (q, J=28.3 Hz), 28.6 (q, J=3.6 Hz), 27.3 (q, J=25.2 Hz); ^{19}F NMR (471 MHz, Chloroform-*d*) δ: −66.60 (t, J=10.7 Hz); HRMS (ESI) calcd for $C_{21}H_{21}F_6$ $[M+H]^+$ 387.1542, found 387.1537.

Supporting Information ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of all products. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

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