JOC The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.8b00412 • Publication Date (Web): 14 Mar 2018

Just Accepted

ACS Publications

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Reactivity of 1,2,3- and 1,2,4-trifluorobenzenes in Palladium-catalyzed direct arylation

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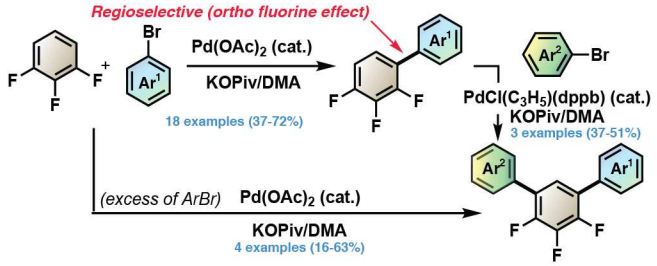
Graphical abstract

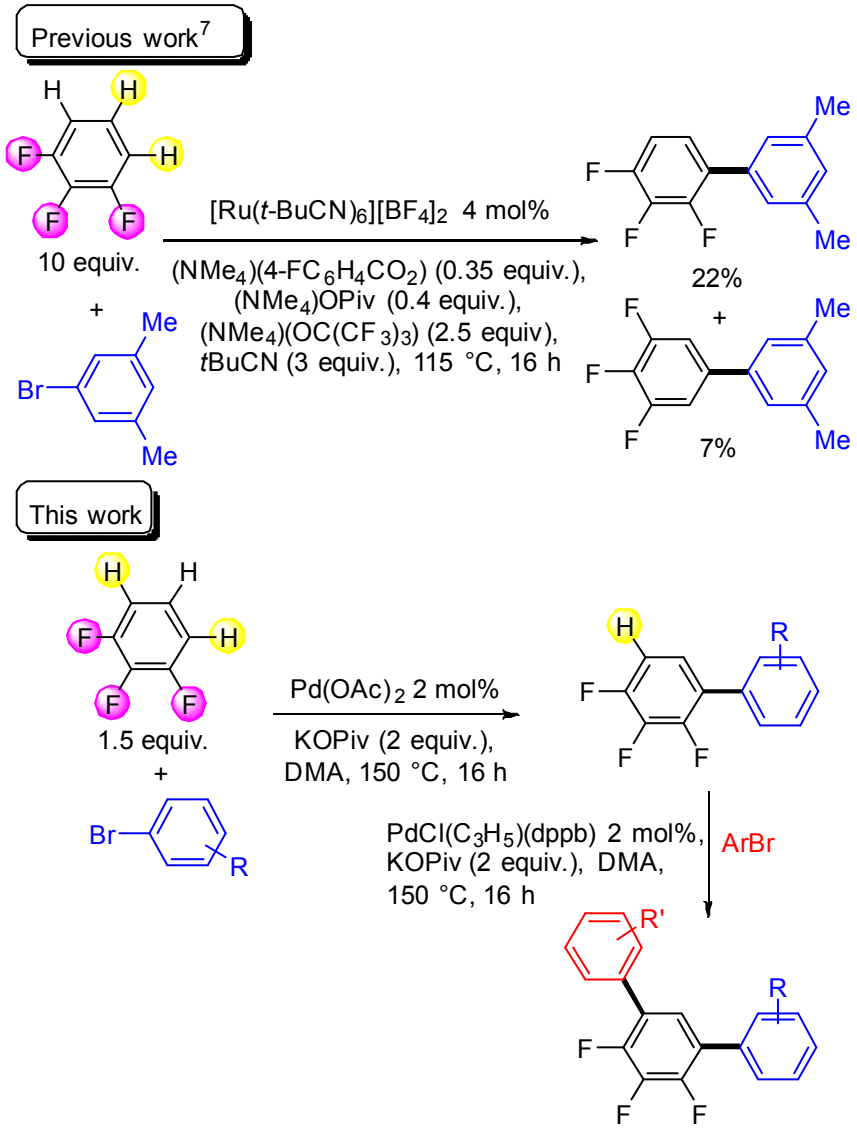


Abstract: The higher reactivity of C4-H bond as compared to C5-H bond of 1,2,3-trifluorobenzene in palladium-catalyzed direct arylation allows the selective synthesis of 4-aryl-1,2,3-trifluorobenzenes in moderate to high yields. In most cases, phosphine-free $Pd(OAc)_2$ catalyst and inexpensive KOAc base were employed. Then, from these 4-aryl-1,2,3-trifluorobenzenes, the palladium-catalyzed C-H bond functionalization of the C6-position allows the synthesis of the corresponding 4,6-diarylated 1,2,3-trifluorobenzenes. We also applied these reaction conditions to the regioselective direct C3-arylation of 1,2,4-trifluorobenzene.

Introduction

Several bioactive compounds contain a (poly)fluorobiphenyl motif, such as Diflunisal which exhibits analgesic and anti-inflamatory activity. Therefore, the discovery of simple, but general routes to (poly)fluorobiphenyls has potential for medicinal chemistry. The Pd-catalyzed direct arylation of a wide variety of (hetero)aromatics, *via* a C–H bond activation step, has brought a synthesis revolution in the preparation of bi(hetero)aryls in recent years. Such couplings are very

attractive, compared to the more classical Pd-catalysed reactions such as Stille, Suzuki or Negishi couplings as they do not require the preliminary synthesis of organometallic derivatives.[1] Several examples of metal-catalyzed arylations *via* a C-H bond activation[2] of polyfluorobenzenes with aryl halides have been reported.[3] Fagnou et al. and a few other groups have already reported examples of Pd-catalyzed direct arylations of tetra-and penta-fluorobenzenes.[4-6] They observed that the C-H bonds flanked by two fluoro substituents such as in pentafluorobenzene, 1,2,4,5-tetrafluorobenzene or even 1,3,5-trifluorobenzene, could be easily arylated with aryl halides.[4a-g] In contrast, to our knowledge, a single example of metal-catalyzed direct arylation of 1,2,3-trifluorobenzene has been reported (Scheme 1, top).[7] For this reaction, Larrosa et al. employed $[Ru(t\text{-BuCN})_6][BF_4]_2$ as the catalyst and $(NMe_4)(4\text{-}FC_6H_4CO_2)$ (0.35 equiv.), $(NMe_4)OPiv$ (0.4 equiv.), $(NMe_4)(OC(CF_3)_3)$ (2.5 equiv) as additives. The coupling product was obtained as a mixture of two regioisomers (C4:C5 77:23) in 29 % yield. To our knowledge, the regioselective metal-catalyzed direct arylation of 1,2,3-trifluorobromobenzene has not yet been described (Scheme 1, bottom).



Scheme 1. Metal-catalyzed arylations of 1,2,3-trifluorobenzene

As the discovery of an effective method, for the arylation of such trifluorobenzene derivatives, especially using easily available catalyst and base is highly desirable, the reactivity and regioselectivity for direct arylation using 1,2,3-trifluorobromobenzene in the presence of palladium catalysts needed to be investigated. Here, we report (i) on the regioselectivity of the palladium-catalyzed direct arylation of 1,2,3-trifluorobenzene using a low loading of a phosphine-free palladium catalyst; (ii) on the scope of the reaction; (iii) on the subsequent reactivity of these 4-aryl-1,2,3-trifluorobenzenes in Pd-catalysed C-H bond functionalization; and (iv) on the reactivity in direct arylation of 1,2,4-trifluorobenzene using a phosphine-free catalyst.

The free energy of activation for direct arylation in the presence of palladium-catalysts *via* Concerted Metalation Deprotonation (CMD)[8,9] pathway for several poly(fluoro)benzenes has been calculated by Gorelsky (Figure 1). C-H bonds flanked by two fluoro-substituents such as in pentafluorobenzene, 1,3,5-trifluorobenzene or even 1,3-difluorobenzene are generally very reactive, as their energy of activation is quite low (<26 kcal mol^{-1}). Conversely, for 1,2,3-trifluorobenzene, the energy of activation of the C-H bonds adjacent to one fluorine atom is higher (28.8 kcal mol^{-1}), and the other C-H bond has an energy of activation of 31.7 kcal mol^{-1}. Therefore, due to the lower energy of activation of the C-H bonds adjacent to one fluorine atoms of 1,2,3-trifluorobenzene, for reactions which proceed *via* a Pd-catalyzed CMD mechanism, we expected to be able to control the regioselectivity of their functionalization using Pd-catalysis instead of Ru-catalysis.

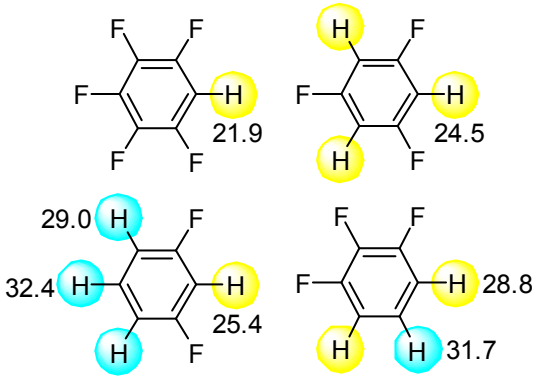


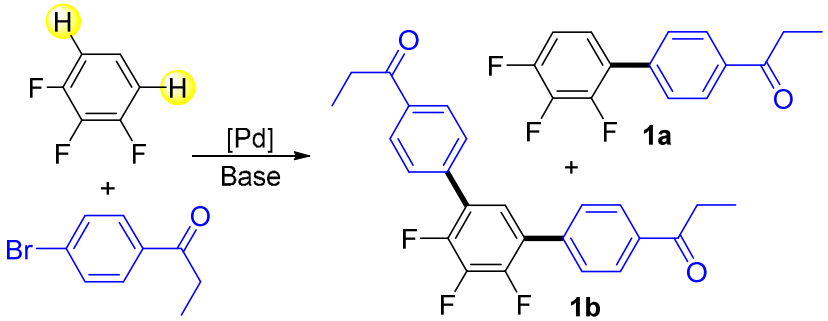
Figure 1. Free energy of activation ($\Delta G^{\ddagger}_{298K}$, kcal mol^{-1}) for direct arylation via the CMD pathway involving an acetate ligand with the [Pd(C_6H_5)(PMe_3)(OAc)] catalyst.[8]

Results and discussion

4-Bromopropiophenone (1 equiv.) and 1,2,3-trifluorobenzene (1.5 equiv.) were employed as model substrates for our study (Table 1). We initially examined the influence of the nature of the base on the aryl bromide conversion and on the regioselectivity of the reaction using 2 mol% $Pd(OAc)_2$ catalyst and DMA as the solvent. We had previously observed that

this catalyst precursor associated to this solvent promoted the coupling of several polyfluorobenzenes with aryl bromides in high yields.[10] Cs_2CO_3, K_2CO_3 or NaOAc bases, led to high conversions of 4-bromopropiophenone, but the desired product **1a** was only obtained in trace amount (Table 1, entries 1-3). The use of the acetate salts, KOAc or CsOAc, afforded **1a** in higher yields; however, the yields remained moderate, even when an higher catalyst loading (5 mol%) or a palladium-diphosphine catalyst were used (Table 1, entries 4-7). PivOK was found to be the most effective base for this reaction, as **1a** was obtained in 41% yield (Table 1, entry 8). The good performance of pivalate as base/ligand is consistent with a CMD pathway.[8,9] Finally, the use of 3 equiv. of 1,2,3-trifluorobenzene in the presence of 2 mol% $Pd(OAc)_2$ catalyst and PivOK as base in DMA afforded **1a** in 54% yield (Table 1, entry 11). In all cases, the 4,6-diarylated 1,2,3-trifluorobenzene **1b** was produced in very low yields (<10%) and C5-arylated 1,2,3-trifluorobenzene was not detected.

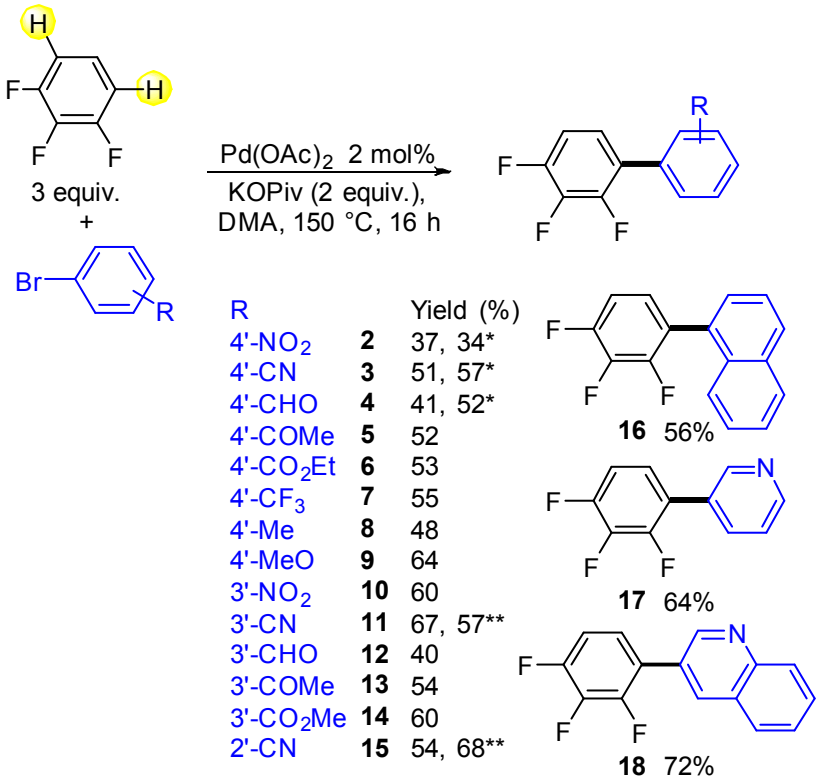
Table 1: Influence of the reaction conditions on the Pd-catalyzed C4-arylation of 1,2,3-trifluorobenzene with 4-bromopropiophenone



Entry	Catalyst (mol%)	Solvent	Base	Conv. (%)	Ratio **1a**:**1b**	Yield in **1a** (%)
1	$Pd(OAc)_2$ (2)	DMA	Cs_2CO_3	100	0:0	0
2	$Pd(OAc)_2$ (2)	DMA	K_2CO_3	100	100:0	<5
3	$Pd(OAc)_2$ (2)	DMA	NaOAc	100	100:0	<5
4	$Pd(OAc)_2$ (2)	DMA	KOAc	100	93:7	31
5	$Pd(OAc)_2$ (5)	DMA	KOAc	88	100:0	21
6	$Pd(OAc)_2$ (2)	DMA	CsOAc	50	98:2	14
7	$PdCl(C_3H_5)(dppb)$ (2)	DMA	KOAc	100	100:0	24
8	$Pd(OAc)_2$ (2)	DMA	KOPiv	100	91:9	41
9	$Pd(OAc)_2$ (2)	DMF	KOAc	100	100:0	8
10	$Pd(OAc)_2$ (2)	DMA	KOAc	100	93:7	37[a]
11	$Pd(OAc)_2$ (2)	DMA	KOPiv	100	95:5	54[a]

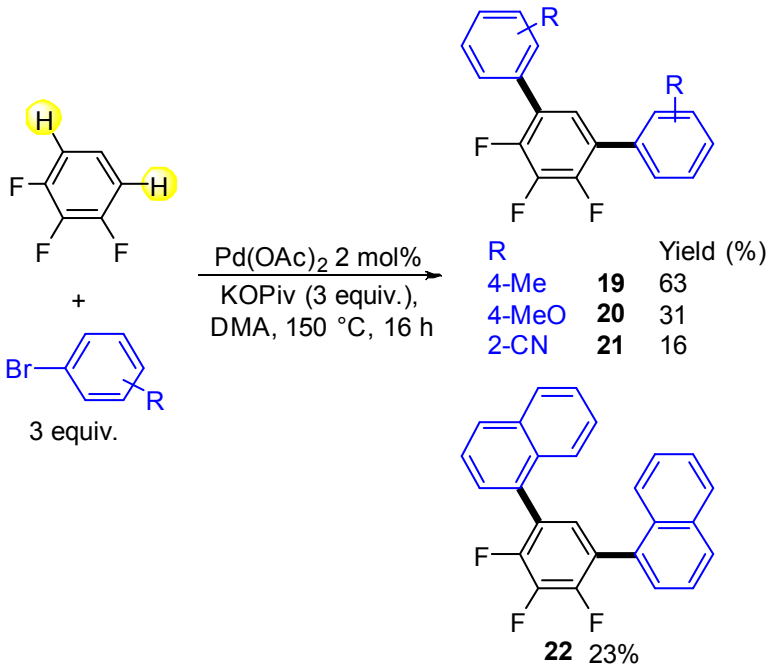
Conditions: 4-Bromopropiophenone (1 equiv.), 1,2,3-trifluorobenzene (1.5 equiv.), base (2 equiv.), 16 h, 150 °C, conversion of 4-bromopropiophenone, isolated yields. [a] 3 equiv. of 1,2,3-trifluorobenzene.

Then, 1,2,3-trifluorobenzene was coupled with a set of (hetero)aryl bromides in the presence of 2 mol% $Pd(OAc)_2$, KOPiv as the base in DMA (Scheme 2). Very regioselective C4-arylations and quite good yields in **2**-**7** were obtained using aryl bromides bearing nitro, cyano, formyl, acetyl, ester or trifluoromethyl *para*-substitutents. In all cases, a regioselective arylation at the C-H adjacent to a C-F bond was observed, and low amounts of diarylated 1,2,3-trifluorobenzene were observed by GC/MS and ^{1}H NMR analysis of the crude mixtures. Similar yields were obtained for the coupling of the electron-rich aryl bromides, 4-bromotoluene and 4-bromoanisole with 1,2,3-trifluorobenzene to give **8** and **9** in 48% and 64% yield, respectively. Nitro-, nitrile-, formyl-, acetyl- and ester-substituents at *meta*-position on the aryl bromides were also tolerated giving access to **10**-**14** in 40-67% yield. Reactions with the more hindered substrates, 2-bromobenzonitrile and 1-bromonaphthalene were also successful. The use of the *N*-containing heterocycles, 3-bromopyridine and 3-bromoquinoline afforded the desired C4-arylated trifluorobenzene derivatives **17** and **18** in 64% and 72% yields, respectively. In all cases, no formation of the C5-arylated 1,2,3-trifluorobenzenes was detected by GC/MS analysis of the crude mixture. It should be noted that in a few cases such as for the preparation of **3**, **4** and **15**, the use of KOAc as base led to higher yields than with PivOK, due to cleaner reactions.



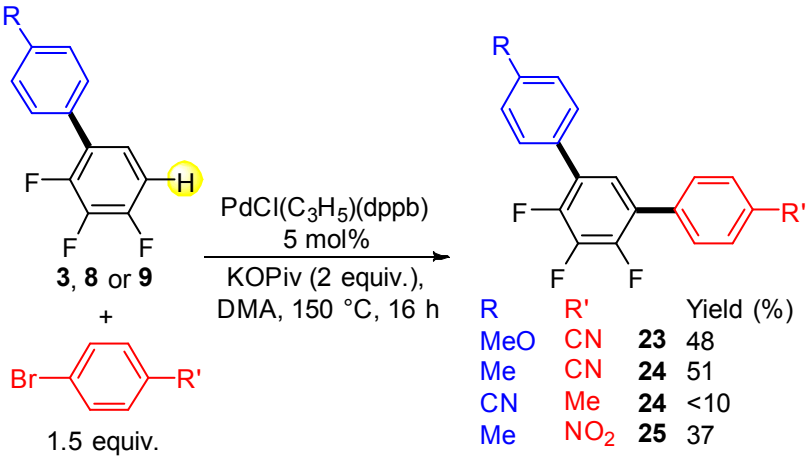
Scheme 2. Scope of the C4-arylation of 1,2,3-trifluorobenzene

The one pot synthesis of 4,6-diarylated 1,2,3-trifluorobenzene from 1,2,3-trifluorobenzene was then examined (Scheme 3). As seen in the table 1 and in the scheme 2, the 4,6-diarylation of this trifluorobenzene derivative using only one equiv. of aryl bromide is generally observed in trace amount, revealing that the second arylation is much slower than the first one. The use of an excess of the electron-rich aryl bromides, 4-bromotoluene and 4-bromoanisole (3 equiv.) in the presence of 2 mol% $Pd(OAc)_2$ catalyst afforded the desired product **19** and **20** in 63% and 31% yields, respectively. Lower yields in **21** and **22** were obtained from 2-bromobenzonitrile and 1-bromonaphthalene. In all cases, no arylation at the C5-position of 1,2,3-trifluorobenzene was detected.



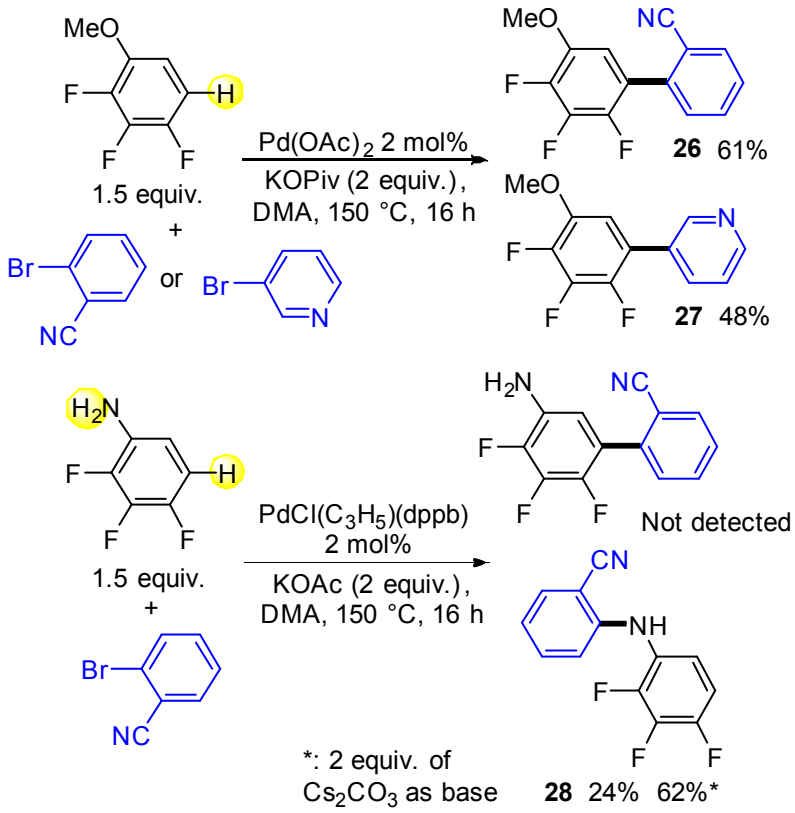
Scheme 3. Scope of the one pot 4,6-diarylation of 1,2,3-trifluorobenzene

Then, the reactivity for C6-arylation, *via* a C-H bond activation of the trifluorobenzene moiety of some of the previously obtained C4-arylated trifluorobenzene derivatives was evaluated (Scheme 4). The reaction of **9** with 4-bromobenzonitrile using 5 mol% $PdCl(C_3H_5)(dppb)$ catalyst and KOPiv as base afforded **23** in 48% yield; whereas the use of $Pd(OAc)_2$ catalyst led to a low yield. From **8** and 4-bromobenzonitrile, under the same conditions, the desired product **24** was obtained in 51% yield. Conversely, the reaction of **3** and 4-bromotoluene was quite sluggish affording **24** in <10% yield revealing that 1,2,3-trifluorobenzene derivatives bearing an electron-deficient benzene unit at C4-position are poorly reactive for C6-arylation. Therfore, for the preparation of non-symmetrically substituted 4,6-diaryl-1,2,3-trifluorobenzenes, the most electron-rich arene should be introduced in the first step.



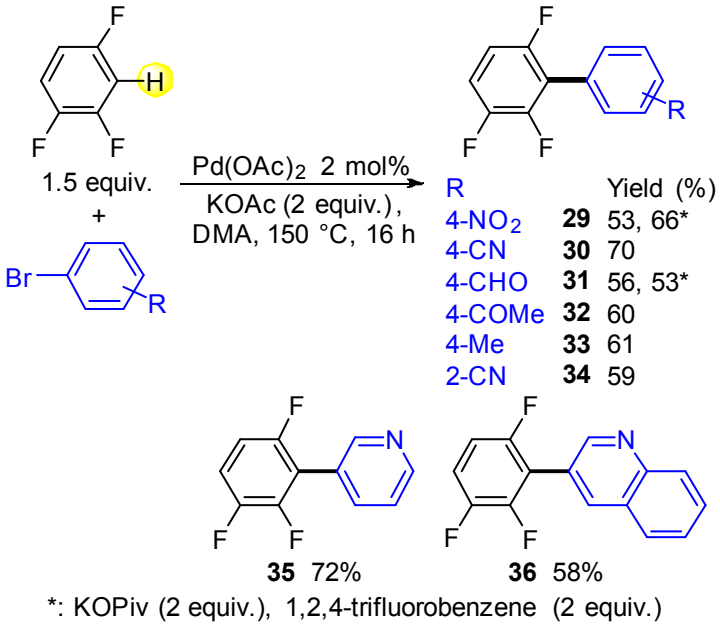
Scheme 4. Scope of the C6-arylation of 1,2,3-trifluoro-4-aryl-benzenes

The reactivity of two 1,2,3-trifluorobenzene derivatives bearing a functional group at C4-position was also studied (Scheme 5). For the coupling reactions with 1-methoxy-2,3,4-trifluorobenzene, both C5 and C6 positions might have been arylated (Scheme 5, top). However, with both 2-bromobenzonitrile and 3-bromopyridine, only the C-H bond adjacent to one fluorine atom was arylated to give **26** and **27** in 61% and 48% yields, respectively. This is certainly due to the higher acidity of this position. Conversely, the reaction of 2,3,4-trifluoroaniline, under the same reaction conditions, gave no coupling product; whereas, the use of the thermally more stable catalyst $PdCl(C_3H_5)(dppb)$[12] associated to KOAc as base led exclusively to the amination product **28** in low yield (Scheme 5, bottom). This amination product **28** could be obtained in a higher yield of 62% using Cs_2CO_3 as base.



Scheme 5. Reactivity of 1-methoxy-2,3,4-trifluorobenzene and 2,3,4-trifluoroaniline

Very few results concerning the Pd-catalyzed direct C3-arylation of 1,2,4-trifluorobenzene,[9] especially using aryl halides as aryl source,[9c] have been reported so far. A single example was reported by Cazin et al. in 2014.[9c] They described that from this trifluorobenzene derivative and 4-bromotoluene, using a dual metal system involving Cu(Cl)(NHC) and Pd(Cl)(cinnamyl)(NHC) as catalyst, the C3-arylated trifluorobenzene could be obtained in good yield. As our "ligand-free" catalytic system was quite efficient for the regioselective C4-arylation of 1,2,3-trifluorobenzene, we also investigated its efficiency for the arylation of 1,2,4-trifluorobenzene (Scheme 6). In all cases, we observed a highly regioselective arylation at C3-position of 1,2,4-trifluorobenzene, as no other regioisomers could be detected by GC/MS analysis of the crude mixtures. Both electron-donating and electron-withdrawing sustituents on the aryl bromide were tolerated affording the desired products **29-34** in 53-70% yields. From 3-bromopyridine and 3-bromoquinoline, the expected products **35** and **36** were also regioselectively obtained in good yields. For most of these reactions, the formation of side-products in low yields arising from the aryl-bromides homo-coupling and from the diarylation of 1,2,4-trifluorobenzene was also observed by GC/MS analysis of the crude mixtures.



Scheme 6. Scope of the C3-arylation of 1,2,4-trifluorobenzene

In summary, the use of a Pd-catalyst instead of a Ru-catalyst for the direct arylation of 1,2,3-trifluorobenzene allowed its regioselective functionalization at C4-position. We demonstrated that, using only 2 mol% of easily available $Pd(OAc)_2$ catalyst precursor and KOAc or KOPiv as inexpensive bases, a wide variety of 4-(hetero)arylated 1,2,3-trifluorobenzenes can be obtained with high regioselectivities and good yields. This strategy allowed the straightforward synthesis of C4-arylated 1,2,3-trifluorobenzenes in only one step from commercially available compounds. The access to a few symmetrical and non-symmetrical 4,6-diaryl-1,2,3-trifluorobenzenes in moderate yields *via* successive C-H bond functionalizations is also described. This "phosphine-free" catalyst procedure was also successfully employed for the regioselective C3-arylation of 1,2,4-trifluorobenzene.

Experimental section

General procedure for palladium-catalyzed direct (di)arylations of trifluorobenzenes

The reaction of the aryl bromide, trifluorobenzene derivative and KOPiv or KOAc in the presence of $Pd(OAc)_2$ or $PdCl(C_3H_5)(dppb)$[12] (see schemes) at 150 °C during 16 h in DMA (4 mL) under argon affords the coupling products **1**-**36** after evaporation of the solvent and purification on silica gel. Eluent heptane:ethyl acetate 9:1 for compounds **1**-**6**, **10**-**15**, **20**, **21**, **23**-**26**, **28**, **30**-**32**, **34**; heptane:ethyl acetate 4:1 for compounds **17**, **18**, **35**, **36**; heptane:ethyl acetate 1:1 for compound **27**; heptane for compounds **7**-**9**, **16**, **19**, **22**, **29**, **33**.

1-(2',3',4'-Trifluoro-[1,1'-biphenyl]-4-yl)propan-1-one (1a)

From 4-bromopropiophenone (0.213 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **1a** was obtained in 54% yield (0.142 g) as a white solid: mp 89-92 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.3 Hz, 2H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.23-7.02 (m, 2H), 3.03 (q, *J* = 7.6 Hz, 2H), 1.25 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.2, 150.9 (ddd, *J* = 251.8, 10.0, 3.0 Hz), 148.8 (ddd, *J* = 252.6, 10.7, 3.3 Hz), 140.2 (dt, *J* = 251.7, 15.5 Hz), 138.4, 136.4, 129.0 (d, *J* = 3.0 Hz), 128.3, 125.6 (dd, *J* = 10.5, 3.7 Hz), 123.8 (m), 112.5 (dd, *J* = 17.5, 4.0 Hz), 31.9, 8.23. Anal. Calcd for $C_{15}H_{11}F_3O$ (264.25): C, 68.18; H, 4.20. Found: C, 67.98; H, 4.00.

4,4''-Di(propionyl)-4',5',6'-trifluoro-1,1':3',1''-terphenyl (1b) was also isolated in low yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, *J* = 8.5 Hz, 4H), 7.64 (d, *J* = 8.5 Hz, 4H), 7.30 (td, *J* = 7.7, 2.3 Hz, 1H), 3.05 (q, *J* = 7.5 Hz, 4H), 1.26 (t, *J* = 7.5 Hz, 6H).

2,3,4-Trifluoro-4'-nitro-1,1'-biphenyl (2)

From 4-bromonitrobenzene (0.202 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **2** was obtained in 37% yield (0.093 g) as a yellow solid: mp 145-148 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, *J* = 8.7 Hz, 2H), 7.68 (d, *J* = 8.7 Hz, 2H), 7.25-7.04 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.4 (ddd, *J* = 253.1, 10.0, 3.1 Hz), 148.9 (ddd, *J* = 253.0, 10.0, 3.4 Hz), 147.6 (m), 140.5 (dt, *J* = 252.6, 15.5 Hz), 140.4, 129.7 (d, *J* = 3.1 Hz), 124.5 (dd, *J* = 10.5, 3.9 Hz), 123.9, 123.8 (m), 112.8 (dd, *J* = 17.6, 4.0 Hz). Anal. Calcd for $C_{12}H_6F_3NO_2$ (253.18): C, 56.93; H, 2.39; N, 5.53. Found: C, 56.98; H, 2.21; N, 5.78.

2',3',4'-Trifluoro-[1,1'-biphenyl]-4-carbonitrile (3)

From 4-bromobenzonitrile (0.182 g, 1 mmol), 1,2,3-trifluorobenzene (0.198 g, 1.5 mmol), KOAc (0.196 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **3** was obtained in 57% yield (0.133 g) as a white solid: mp 132-135 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.22-7.03 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.1 (ddd, *J* = 251.3, 10.1, 3.0 Hz), 148.8 (ddd, *J* = 252.6, 10.7, 3.3 Hz), 140.4 (dt, *J* = 252.4, 15.5 Hz), 138.6, 132.5, 129.5 (d, *J* = 3.1 Hz), 124.8 (dd, *J* = 10.4, 3.7 Hz), 123.8 (m), 118.4, 112.7 (dd, *J* = 17.5, 4.1 Hz), 112.1. Anal. Calcd for $C_{13}H_6F_3N$ (233.19): C, 66.96; H, 2.59; N, 6.01. Found: C, 66.70; H, 2.41; N, 6.12.

2',3',4'-Trifluoro-[1,1'-biphenyl]-4-carbaldehyde (4)

From 4-bromobenzaldehyde (0.185 g, 1 mmol), 1,2,3-trifluorobenzene (0.198 g, 1.5 mmol), KOAc (0.196 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **4** was obtained in 52% yield (0.123 g) as a white solid: mp 153-156 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.08 (s, 1H), 7.97 (d, *J* = 8.3 Hz, 2H), 7.66 (d, *J* = 8.3 Hz, 2H), 7.23-7.04 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.7, 151.0 (ddd, *J* = 252.2, 10.3, 3.0 Hz), 148.9 (ddd, *J* = 252.9, 10.7, 3.3 Hz), 140.3 (dt, *J* = 252.1, 15.5 Hz), 140.0, 135.9, 130.0, 129.5 (d, *J* = 3.0 Hz), 125.5 (dd, *J* = 10.5, 3.7 Hz), 123.9 (m), 112.5 (dd, *J* = 17.4, 4.1 Hz). Anal. Calcd for $C_{13}H_7F_3O$ (236.19): C, 66.11; H, 2.99 66.30; H, 3.21.

4,4''-Di(formyl)-4',5',6'-trifluoro-1,1':3',1''-terphenyl was also isolated in low yield in an impure form: ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.07 (s, 2H), 7.98 (d, *J* = 8.2 Hz, 4H), 7.71 (d, *J* = 8.2 Hz, 4H), 7.32 (td, *J* = 7.7, 2.3 Hz, 1H).

1-(2',3',4'-Trifluoro-[1,1'-biphenyl]-4-yl)ethan-1-one (5)

From 4-bromoacetophenone (0.199 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **5** was obtained in 52% yield (0.130 g) as a white solid: mp 69-72 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.3 Hz, 2H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.23-7.04 (m, 2H), 2.65 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5, 150.9 (ddd, *J* = 251.8, 10.0, 3.0 Hz), 148.8 (ddd, *J* = 252.6, 10.7, 3.3 Hz), 140.4 (dt, *J* = 251.8, 15.5 Hz), 138.7, 136.6, 129.0 (d, *J* = 3.0 Hz), 128.7, 125.6 (dd, *J* = 11.0, 3.7 Hz), 123.8 (m), 112.5 (dd, *J* = 17.4, 4.0 Hz), 26.7. Anal. Calcd for $C_{14}H_9F_3O$ (250.22): C, 67.20; H, 3.63; found: C, 67.34; H, 3.80.

Ethyl 2',3',4'-trifluoro-[1,1'-biphenyl]-4-carboxylate (6)

From ethyl 4-bromobenzoate (0.229 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **6** was obtained in 53% yield (0.148 g) as a white solid: mp 81-84 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.21-7.02 (m, 2H), 4.41 (q, *J* = 7.6 Hz, 2H), 1.42 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.2, 150.9 (ddd, *J* = 251.5, 10.2, 2.9 Hz), 148.9 (ddd, *J* = 252.5, 10.6, 3.4 Hz), 140.3 (dt, *J* = 251.7, 15.5 Hz), 130.2, 129.9, 128.8 (d, *J* = 3.0 Hz), 125.7 (dd, *J* = 10.5, 3.8 Hz), 123.9 (m), 112.4 (dd, *J* = 17.4, 4.0 Hz), 61.2, 14.3. Anal. Calcd for $C_{15}H_{11}F_3O_2$ (280.25): C, 64.29; H, 3.96; found: C, 64.07; H, 4.11.

2,3,4-Trifluoro-4'-(trifluoromethyl)-1,1'-biphenyl (7)[13]

From 4-bromobenzotrifluoride (0.225 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **7** was obtained in 55% yield (0.152 g) as a white solid: mp 64-67 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.61 (d, *J* = 8.2 Hz, 2H), 7.20-7.03 (m, 2H).

4,4''-Di(trifluoromethyl)-4',5',6'-trifluoro-1,1':3',1''-terphenyl was also isolated in low yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.3 Hz, 4H), 7.74 (d, *J* = 8.3 Hz, 4H), 7.37 (td, *J* = 7.7, 2.3 Hz, 1H).

2,3,4-Trifluoro-4'-methyl-1,1'-biphenyl (8)[13]

From 4-bromotoluene (0.171 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **8** was obtained in 48% yield (0.106 g) as a white oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 7.8 Hz, 2H), 7.18-6.97 (m, 2H), 2.44 (s, 3H).

2,3,4-Trifluoro-4'-methoxy-1,1'-biphenyl (9)[14]

From 4-bromoanisole (0.187 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **9** was obtained in 64% yield (0.152 g) as a white solid: mp 73-76 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 8.0 Hz, 2H), 7.15-7.07 (m, 1H), 7.05-6.97 (m, 1H), 6.99 (d, *J* = 8.0 Hz, 2H), 3.86 (s, 3H).

2,3,4-Trifluoro-3'-nitro-1,1'-biphenyl (10)

From 3-bromonitrobenzene (0.202 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **10** was obtained in 60% yield (0.152 g) as a yellow solid: mp 102-105 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (s, 1H), 8.25 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.24-7.05 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.1 (ddd, *J* = 252.5, 10.1, 3.0 Hz), 148.7 (ddd, *J* = 252.5, 10.7, 3.4 Hz), 148.5, 140.2 (dt, *J* = 252.5, 15.5 Hz), 135.6, 134.8 (d, *J* = 3.3 Hz), 129.7, 124.3 (dd, *J* = 10.5, 3.8 Hz), 123.9 (m), 123.7 (d, *J* = 2.7 Hz), 123.1, 112.7 (dd, *J* = 17.5, 4.1 Hz).Anal. Calcd for $C_{12}H_6F_3NO_2$ (253.18): C, 56.93; H, 2.39; N, 5.53. Found: C, 56.74; H, 2.24; N, 5.47.

2',3',4'-Trifluoro-[1,1'-biphenyl]-3-carbonitrile (11)

From 3-bromobenzonitrile (0.182 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **11** was obtained in 67% yield (0.156 g) as a white solid: mp 92-95 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (s, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.58 (t, *J* = 7.8 Hz, 1H), 7.20-7.04 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.0 (ddd, *J* = 252.3, 10.1, 3.0 Hz), 148.8 (ddd, *J* = 252.5, 10.7, 3.4 Hz), 140.1 (dt, *J* = 252.5, 15.5 Hz), 135.3, 133.1 (d, *J* = 3.0 Hz), 132.3 (d, *J* = 2.8 Hz), 131.7, 129.6, 124.4 (dd, *J* = 10.6, 3.7 Hz), 123.7 (m), 118.3, 113.1, 112.8 (dd, *J* = 17.5, 4.1 Hz). Anal. Calcd for $C_{13}H_6F_3N$ (233.19): C, 66.96; H, 2.59; N, 6.01. Found: C, 66.78; H, 2.69; N, 5.92.

3,3''-Dicyano-4',5',6'-trifluoro-1,1':3',1''-terphenyl was also isolated in low yield: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (s, 2H), 7.85 (d, *J* = 8.0 Hz, 2H), 7.79 (d, *J* = 8.0 Hz, 2H), 7.67 (t, *J* = 7.8 Hz, 2H), 7.32 (td, *J* = 7.7, 2.3 Hz, 1H).

2',3',4'-Trifluoro-[1,1'-biphenyl]-3-carbaldehyde (12)

From 3-bromobenzaldehyde (0.185 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **12** was obtained in 40% yield (0.094 g) as a white solid: mp 69-72 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.08 (s, 1H), 8.00 (s, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 7.25-7.14 (m, 1H), 7.13-7.04 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.8, 151.0 (ddd, *J* = 252.3, 10.1, 3.0 Hz), 148.8 (ddd, *J* = 252.5, 10.6, 3.3 Hz), 140.4 (dt, *J* = 252.0, 15.5 Hz), 136.8, 135.1, 134.6 (d, *J* = 3.1 Hz), 129.8 (d, *J* = 2.5 Hz), 129.5, 129.4, 125.3 (dd, *J* = 10.7, 3.7 Hz), 123.8 (m), 112.5 (dd, *J* = 17.4, 4.1 Hz). Anal. Calcd for $C_{13}H_7F_3O$ (236.19): C, 66.11; H, 2.99. Found: C, 66.00; H, 2.87.

1-(2',3',4'-Trifluoro-[1,1'-biphenyl]-3-yl)ethan-1-one (13)

From 3-bromoacetophenone (0.199 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **13** was obtained in 54% yield (0.135 g) as a white solid: mp 92-95 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.24-7.13 (m, 1H), 7.13-7.01 (m, 1H), 2.65 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.6, 150.7 (ddd, *J* = 251.3, 10.1, 3.0 Hz), 148.8 (ddd, *J* = 251.8, 10.5, 3.3 Hz), 140.1 (dt, *J* = 252.0, 15.5 Hz), 137.5, 134.6, 133.3 (d, *J* = 3.1 Hz), 129.0, 128.6 (d, *J* = 2.5 Hz), 128.1, 125.7 (dd, *J* = 10.7, 3.9 Hz), 123.9 (m), 112.4 (dd, *J* = 17.3, 4.0 Hz), 26.7. Anal. Calcd for $C_{14}H_9F_3O$ (250.22): C, 67.20; H, 3.63. Found: C, 67.40; H, 3.69.

Methyl 2',3',4'-trifluoro-[1,1'-biphenyl]-3-carboxylate (14)

From methyl 3-bromobenzoate (0.215 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **14** was obtained in 60% yield (0.160 g) as a yellow solid: mp 64-67 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (s, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.23-7.14 (m, 1H), 7.12-7.03 (m, 1H), 3.95 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 150.7 (ddd, *J* = 251.0, 10.1, 3.0 Hz), 148.7 (ddd, *J* = 251.9, 10.5, 3.3 Hz), 140.1 (dt, *J* = 251.7, 15.5 Hz), 134.4, 133.2 (d, *J* = 3.1 Hz), 130.8, 129.9 (d, *J* = 2.3 Hz), 129.3, 128.8, 125.7 (dd, *J* = 10.7, 3.9 Hz), 123.9 (m), 112.4 (dd, *J* = 17.3, 4.0 Hz), 52.3. Anal. Calcd for $C_{14}H_9F_3O_2$ (266.22): C, 63.16; H, 3.41. Found: C, 63.08; H, 3.34.

2',3',4'-Trifluoro-[1,1'-biphenyl]-2-carbonitrile (15)

From 2-bromobenzonitrile (0.182 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOAc (0.196 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **15** was obtained in 68% yield (0.158 g) as a yellow solid: mp 121-124 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.6 Hz, 1H), 7.69 (t, *J* = 7.8 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.22-7.06 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.5 (ddd, *J* = 252.6, 10.1, 3.0 Hz), 148.7 (ddd, *J* = 252.3, 10.7, 3.5 Hz), 140.2 (dt, *J* = 252.9, 15.5 Hz), 137.5, 133.4, 132.8, 130.9 (d, *J* = 1.2 Hz), 128.9, 124.8 (m), 123.4 (dd, *J* = 12.3, 3.7 Hz), 117.6, 112.8, 112.5 (dd, *J* = 17.6, 4.0 Hz). Anal. Calcd for $C_{13}H_6F_3N$ (233.19): C, 66.96; H, 2.59; N, 6.01. Found: C, 67.05; H, 2.75; N, 5.80.

1-(2,3,4-Trifluorophenyl)naphthalene (16)

From 1-bromonaphthalene (0.207 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **16** was obtained in 56% yield (0.144 g) as a white solid: mp 63-66 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.60-7.46 (m, 3H), 7.44 (d, *J* = 7.8 Hz, 1H), 7.18-7.06 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.8 (ddd, *J* = 250.1, 10.1, 2.9 Hz), 149.1 (ddd, *J* = 250.1, 10.0, 3.4 Hz), 140.1 (dt, *J* = 251.9, 15.5 Hz), 133.6, 131.9 (d, *J* = 1.8 Hz), 131.6, 129.1, 128.5, 127.9, 126.6, 125.7, 125.6 (m), 125.3, 125.2, 112.0 (dd, *J* = 17.3, 4.0 Hz). Anal. Calcd for $C_{16}H_9F_3$ (258.24): C, 74.42; H, 3.51. Found: C, 74.61; H, 3.34.

3-(2,3,4-Trifluorophenyl)pyridine (17)

From 3-bromopyridine (0.158 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **17** was obtained in 64% yield (0.134 g) as a yellow solid: mp 94-97 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.77 (s, 1H), 8.68 (s, 1H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.43 (bs, 1H), 7.21-7.04 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.0 (ddd, *J* = 251.8, 10.1, 2.9 Hz), 149.4 (bs), 148.8 (ddd, *J* = 251.5, 10.0, 3.6 Hz), 140.5 (dt, *J* = 252.2, 15.5 Hz), 136.1, 130.1, 123.8 (m), 123.4 (bs), 112.6 (dd, *J* = 17.5, 4.0 Hz). Anal. Calcd for $C_{11}H_6F_3N$ (209.17): C, 63.16; H, 2.89; N, 6.70. Found: C, 63.27; H, 2.74; N, 6.57.

3-(2,3,4-Trifluorophenyl)quinoline (18)

From 3-bromoquinoline (0.208 g, 1 mmol), 1,2,3-trifluorobenzene (0.396 g, 3 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **18** was obtained in 72% yield (0.186 g) as a yellow solid: mp 158-161 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.04 (s, 1H), 8.28 (s, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.77 (t, *J* = 7.8 Hz, 1H), 7.60 (t, *J* = 7.8 Hz, 1H), 7.32-7.22 (m, 1H), 7.16-7.06 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.0 (ddd, *J* = 250.8, 10.1, 2.9 Hz), 150.8 (m), 148.9 (ddd, *J* = 252.2, 10.5, 3.6 Hz), 140.3 (dt, *J* = 252.2, 15.5 Hz), 147.5, 135.6 (d, *J* = 3.2 Hz), 130.2, 129.3, 128.1, 127.5, 127.3, 127.0, 124.0 (m), 123.5 (dd, *J* = 11.0, 3.7 Hz), 112.7 (dd, *J* = 17.5, 4.0 Hz). Anal. Calcd for $C_{15}H_8F_3N$ (259.23): C, 69.50; H, 3.11; N, 5.40. Found: C, 69.42; H, 3.04; N, 5.24.

4',5',6'-Trifluoro-4,4''-dimethyl-1,1':3',1''-terphenyl (19)

From 4-bromotoluene (0.513 g, 3 mmol), 1,2,3-trifluorobenzene (0.132 g, 1 mmol), KOPiv (0.420 g, 3 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **19** was obtained in 63% yield (0.196 g) as a white solid: mp 90-93 °C.

^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.43 (d, *J* = 8.0 Hz, 4H), 7.28 (d, *J* = 8.0 Hz, 4H), 7.23 (td, *J* = 7.7, 2.3 Hz, 1H), 2.40 (s, 6H). ^{13}C NMR (100 MHz, CD_2Cl_2): δ 147.5 (ddd, *J* = 250.2, 10.6, 2.9 Hz), 140.4 (dt, *J* = 249.0, 16.3 Hz), 138.4, 131.1, 129.4, 128.7 (m), 126.3 (dd, *J* = 9.6, 5.5 Hz), 124.4 (m), 20.9. Anal. Calcd for $C_{20}H_{15}F_3$ (312.34): C, 76.91; H, 4.84. Found: C, 76.74; H, 5.04.

4',5',6'-Trifluoro-4,4''-dimethoxy-1,1':3',1''-terphenyl (20)

From 4-bromoanisole (0.561 g, 3 mmol), 1,2,3-trifluorobenzene (0.132 g, 1 mmol), KOPiv (0.420 g, 3 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **20** was obtained in 31% yield (0.106 g) as a white solid: mp 131-134 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, *J* = 8.5 Hz, 4H), 7.19 (td, *J* = 8.0, 2.2 Hz, 1H), 6.99 (d, *J* = 8.5 Hz, 4H), 3.86 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 147.2 (ddd, *J* = 250.4, 10.6, 2.9 Hz), 140.6 (dm, *J* = 250.0 Hz), 130.0 (m), 126.5, 125.8 (dd, *J* = 9.2, 5.8 Hz), 123.9 (m), 114.2, 55.4. Anal. Calcd for $C_{20}H_{15}F_3O_2$ (344.33): C, 69.76; H, 4.39. Found: C, 69.58; H, 4.31.

2,2''-Dicyano-4',5',6'-trifluoro-1,1':3',1''-terphenyl (21)

From 2-bromobenzonitrile (0.546 g, 3 mmol), 1,2,3-trifluorobenzene (0.132 g, 1 mmol), KOPiv (0.420 g, 3 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **21** was obtained in 16% yield (0.053 g) as a yellow solid: mp 192-195 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.72 (t, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.56 (t, *J* = 7.8 Hz, 2H), 7.29 (td, *J* = 7.7, 2.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.9 (ddd, *J* = 255.6, 10.8, 3.6 Hz), 140.5 (dt, *J* = 254.6, 15.7 Hz), 137.0, 133.4, 133.1, 131.1, 129.2, 126.3 (m), 123.2 (dd, *J* = 10.4, 6.4 Hz), 117.7, 112.8. Anal. Calcd for $C_{20}H_9F_3N_2$ (334.30): C, 71.86; H, 2.71; N, 8.38. Found: C, 71.99; H, 2.59; N, 8.40.

1,1'-(4,5,6-Trifluoro-1,3-phenylene)dinaphthalene (22)

From 1-bromonaphthalene (0.621 g, 3 mmol), 1,2,3-trifluorobenzene (0.132 g, 1 mmol), KOPiv (0.420 g, 3 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **22** was obtained in 23% yield (0.088 g) as a yellow solid: mp 182-185 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.0 Hz, 4H), 7.82-7.78 (m, 2H), 7.60-7.48 (m, 8H), 7.26 (td, *J* = 7.7, 2.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.5 (ddd, *J* = 250.9, 10.1, 2.9 Hz), 140.1 (dt, *J* = 253.9, 17.0 Hz), 133.6, 131.7 (m), 131.6, 129.1, 128.5, 128.1, 127.9, 126.7, 126.2, 125.3, 125.2. Anal. Calcd for $C_{26}H_{15}F_3$ (384.40): C, 81.24; H, 3.93. Found: C, 81.40; H, 3.98.

4',5',6'-Trifluoro-4''-methoxy-[1,1':3',1''-terphenyl]-4-carbonitrile (23)

From 4-bromobenzonitrile (0.273 g, 1.5 mmol), 2,3,4-trifluoro-4'-methoxy-1,1'-biphenyl **9** (0.238 g, 1 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $PdCl(C_3H_5)$(dppb) (30.5 mg, 0.05 mmol) in DMA (4 mL) at 150 °C during 16 h, product **23** was obtained in 48% yield (0.163 g) as a white solid: mp 151-154 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.5 Hz, 2H), 7.66 (d, *J* = 8.5 Hz, 2H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.23 (td, *J* = 7.8, 2.3 Hz, 1H), 7.00 (d, *J* = 8.5 Hz, 2H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 148.3 (ddd, *J* = 253.1, 10.6, 2.8 Hz), 147.4 (ddd, *J* = 252.7, 11.2, 2.7 Hz), 140.7 (dt, *J* = 251.7, 16.1 Hz), 138.7, 132.5, 130.0 (d, *J* = 2.8 Hz), 129.5 (d, *J* = 2.9 Hz), 126.7 (dd, *J* = 11.0, 4.1 Hz), 125.8, 124.2 (dd, *J* = 11.3, 4.2 Hz), 124.1 (m), 118.5, 114.3, 112.1, 55.4. Anal. Calcd for $C_{20}H_{12}F_3NO$ (339.32): C, 70.80; H, 3.56; N, 4.13. Found: C, 71.07; H, 3.39; N, 4.40.

4',5',6'-Trifluoro-4''-methyl-[1,1':3',1''-terphenyl]-4-carbonitrile (24)

From 4-bromobenzonitrile (0.273 g, 1.5 mmol), 2,3,4-trifluoro-4'-methyl-1,1'-biphenyl **8** (0.222 g, 1 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $PdCl(C_3H_5)$(dppb) (30.5 mg, 0.05 mmol) in DMA (4 mL) at 150 °C during 16 h, product **24** was obtained in 51% yield (0.164 g) as a white solid: mp 167-170 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.5 Hz, 2H), 7.66 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 8.5 Hz, 2H), 7.24 (td, *J* = 7.8, 2.3 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.5 (ddd, *J* = 253.4, 10.6, 2.9 Hz), 147.6 (ddd, *J* = 253.0, 10.2, 2.9 Hz), 140.7 (dt, *J* = 251.9, 16.0 Hz), 138.7 (m), 132.5, 130.6, 129.5 (m), 128.6 (d, *J* = 2.7 Hz), 127.0 (dd, *J* = 11.0, 4.1 Hz), 124.3 (m), 118.5, 112.2, 21.2. Anal. Calcd for $C_{20}H_{12}F_3N$ (323.32): C, 74.30; H, 3.74; N, 4.33. Found: C, 74.41; H, 3.78; N, 4.60.

4',5',6'-Trifluoro-4-methyl-4''-nitro-1,1':3',1''-terphenyl (25)

From 4-bromonitrobenzene (0.303 g, 1.5 mmol), 2,3,4-trifluoro-4'-methyl-1,1'-biphenyl **8** (0.222 g, 1 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $PdCl(C_3H_5)$(dppb) (30.5 mg, 0.05 mmol) in DMA (4 mL) at 150 °C during 16 h, product **25** was obtained in 37% yield (0.127 g) as a yellow solid: mp 150-153 °C.

^{1}H NMR (400 MHz, CD_2Cl_2): δ 8.30 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 8.5 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.35-7.27 (m, 3H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, CD_2Cl_2): δ 148.6 (ddd, *J* = 253.9, 10.6, 2.9 Hz), 147.6, 147.5 (ddd, *J* = 252.3, 11.0, 2.9 Hz), 140.6 (dt, *J* = 250.9, 16.0 Hz), 140.5, 138.8, 130.6, 129.8 (d, *J* = 3.0 Hz), 129.5, 128.6 (d, *J* = 2.2 Hz), 127.0 (dd, *J* = 11.0, 4.2 Hz), 124.6 (m), 124.0 (dd, *J* = 10.4, 4.4 Hz), 123.8, 20.9. Anal. Calcd for $C_{19}H_{12}F_3NO_2$ (343.31): C, 66.47; H, 3.52; N, 4.08. Found: C, 66.57; H, 3.41; N, 3.79.

2',3',4'-Trifluoro-5'-methoxy-[1,1'-biphenyl]-2-carbonitrile (26)

From 2-bromobenzonitrile (0.182 g, 1 mmol), 1,2,3-trifluoro-4-methoxybenzene (0.243 g, 1.5 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **26** was obtained in 61% yield (0.160 g) as a white solid: mp 128-131 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.6 Hz, 1H), 7.67 (t, *J* = 7.8 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 8.2 Hz, 1H), 6.78 (td, *J* = 6.3, 2.4 Hz, 1H), 3.93 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.8 (m), 142.8 (ddd, *J* = 245.5, 11.2, 1.7 Hz), 142.3 (ddd, *J* = 253.1, 11.7, 1.9 Hz), 141.2 (ddd, *J* = 251.3, 16.7, 13.0 Hz), 137.5, 133.5, 132.8, 131.0 (m), 128.9, 121.1 (dd, *J* = 12.7, 4.5 Hz), 117.7, 112.8, 108.5 (m), 57.1. Anal. Calcd for $C_{14}H_8F_3NO$ (263.22): C, 63.88; H, 3.06; N, 5.32. Found: C, 64.11; H, 3.00; N, 5.07.

3-(2,3,4-Trifluoro-5-methoxyphenyl)pyridine (27)

From 3-bromopyridine (0.158 g, 1 mmol), 1,2,3-trifluoro-4-methoxybenzene (0.243 g, 1.5 mmol), KOPiv (0.280 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **27** was obtained in 48% yield (0.115 g) as a yellow solid: mp 142-145 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.77 (bs, 1H), 8.67 (bs, 1H), 7.84 (d, *J* = 7.3 Hz, 1H), 7.42 (bs, 1H), 6.75 (t, *J* = 6.3 Hz, 1H), 3.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.3, 145.1 (dt, *J* = 8.2, 2.8 Hz), 143.1 (ddd, *J* = 245.5, 11.6 Hz), 141.7 (ddd, *J* = 252.5, 11.7, 2.7 Hz), 141.2 (ddd, *J* = 251.3, 17.0, 13.0 Hz), 136.3, 130.4, 123.5, 121.1 (d, *J* = 10.5, 2.9 Hz), 107.6, 57.1. Anal. Calcd for $C_{12}H_8F_3NO$ (239.20): C, 60.26; H, 3.37; N, 5.86. Found: C, 60.07; H, 3.24; N, 5.68.

2-((2,3,4-Trifluorophenyl)amino)benzonitrile (28)

From 2-bromobenzonitrile (0.182 g, 1 mmol), 2,3,4-trifluoroaniline (0.220 g, 1.5 mmol), KOAc (0.196 g, 2 mmol) in the presence of $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol), in DMA (4 mL) at 150 °C during 16 h, product **28** was obtained in 24% yield (0.059 g) as a yellow solid: mp 123-126 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.10-6.96 (m, 3H), 6.93 (d, *J* = 7.1 Hz, 1H), 6.13 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.0 (ddd, *J* = 248.0, 10.2, 2.5 Hz), 146.2, 145.2 (ddd, *J* = 250.1, 11.1, 3.2 Hz), 140.6 (ddd, *J* = 252.6, 16.0, 13.9 Hz), 134.1, 133.2, 125.5 (dd, *J* = 9.4, 3.6), 120.5, 117.4 (ddd, *J* = 7.5, 3.7, 0.8 Hz), 117.0, 114.4, 111.8 (dd, *J* = 18.2, 4.1 Hz), 99.6. Anal. Calcd for $C_{13}H_7F_3N_2$ (248.21): C, 62.91; H, 2.84; N, 11.29. Found: C, 62.99; H, 2.90; N, 11.47.

2,3,6-Trifluoro-4'-nitro-1,1'-biphenyl (29)[15]

From 4-bromonitrobenzene (0.202 g, 1 mmol), 1,2,4-trifluorobenzene (0.198 g, 1.5 mmol), KOAc (0.196 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **29** was obtained in 53% yield (0.134 g) as a white solid: mp 127-130 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (d, *J* = 8.7 Hz, 2H), 7.67 (d, *J* = 8.7 Hz, 2H), 7.30-7.17 (m, 1H), 7.06-6.94 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.8 (ddd, *J* = 247.0, 4.5, 3.0 Hz), 147.9, 147.6 (dm, *J* = 252.2 Hz), 147.5 (dm, *J* = 246.1 Hz), 135.0 (d, *J* = 1.9 Hz), 131.3 (t, *J* = 2.1 Hz), 123.6, 118.1 (dd, *J* = 20.2, 14.0 Hz), 117.3 (ddd, *J* = 19.5, 10.0, 1.6 Hz), 111.4 (ddd, *J* = 25.0, 6.6, 4.2 Hz).

2',3',6'-Trifluoro-[1,1'-biphenyl]-4-carbonitrile (30)[14]

From 4-bromobenzonitrile (0.182 g, 1 mmol), 1,2,4-trifluorobenzene (0.198 g, 1.5 mmol), KOAc (0.196 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **30** was obtained in 70% yield (0.163 g) as a white solid: mp 143-146 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.27-7.16 (m, 1H), 7.04-6.94 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.8 (ddd, *J* = 246.8, 4.4, 2.9 Hz), 147.6 (dm, *J* = 252.2 Hz), 147.5 (dm, *J* = 246.1 Hz), 133.1 (d, *J* = 1.8 Hz), 132.2, 131.0 (t, *J* = 2.2 Hz), 118.4, 118.3 (dd, *J* = 20.1, 14.6 Hz), 117.1 (ddd, *J* = 19.5, 10.0, 1.5 Hz), 112.6, 111.4 (ddd, *J* = 25.1, 6.7, 4.3 Hz).

2',3',6'-Trifluoro-[1,1'-biphenyl]-4-carbaldehyde (31)

From 4-bromobenzaldehyde (0.185 g, 1 mmol), 1,2,4-trifluorobenzene (0.198 g, 1.5 mmol), KOAc (0.196 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **31** was obtained in 56% yield (0.132 g) as a white solid: mp 100-103 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.07 (s, 1H), 7.98 (d, *J* = 8.3 Hz, 2H), 7.64 (d, *J* = 8.3 Hz, 2H), 7.24-7.11 (m, 1H), 7.00-6.92 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.7, 155.0 (ddd, *J* = 247.5, 4.4, 2.9 Hz), 147.6 (ddd, *J* = 251.8, 14.5, 7.1 Hz), 147.5 (ddd, *J* = 245.6, 13.5, 3.7 Hz), 136.2, 134.5 (d, *J* = 1.6 Hz), 130.9 (t, *J* = 2.1 Hz), 129.6, 119.0 (dd, *J* = 20.2, 14.7 Hz), 116.8 (ddd, *J* = 19.4, 10.0, 1.3 Hz), 111.2 (ddd, *J* = 25.3, 6.7, 4.3 Hz). Anal. Calcd for $C_{13}H_7F_3O$ (236.19): C, 66.11; H, 2.99. Found: C, 66.00; H, 3.19.

1-(2',3',6'-Trifluoro-[1,1'-biphenyl]-4-yl)ethan-1-one (32)

From 4-bromoacetophenone (0.199 g, 1 mmol), 1,2,4-trifluorobenzene (0.198 g, 1.5 mmol), KOAc (0.196 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **32** was obtained in 60% yield (0.150 g) as a white solid: mp 127-130 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, *J* = 8.3 Hz, 2H), 7.58 (d, *J* = 8.3 Hz, 2H), 7.22-7.11 (m, 1H), 6.99-6.92 (m, 1H), 2.65 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5, 155.1 (ddd, *J* = 246.1, 4.4, 2.9 Hz), 147.7 (ddd, *J* = 251.8, 14.5, 7.1 Hz), 147.6 (ddd, *J* = 245.6, 13.5, 3.7 Hz), 137.0, 133.1 (d, *J* = 1.6 Hz), 130.5 (t, *J* = 2.1 Hz), 128.3, 119.2

(dd, *J* = 20.3, 14.8 Hz), 116.5 (ddd, *J* = 19.4, 10.0, 1.3 Hz), 111.1 (ddd, *J* = 25.3, 6.7, 4.2 Hz), 26.7. Anal. Calcd for $C_{14}H_9F_3O$ (250.72): C, 67.20; H, 3.63. Found: C, 66.97; H, 3.47.

2,3,6-Trifluoro-4'-methyl-1,1'-biphenyl (33)[16]

From 4-bromotoluene (0.171 g, 1 mmol), 1,2,4-trifluorobenzene (0.198 g, 1.5 mmol), KOAc (0.196 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **33** was obtained in 61% yield (0.135 g) as a white oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 2H), 7.15-7.05 (m, 1H), 6.95-6.85 (m, 1H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.3 (ddd, *J* = 245.0, 4.6, 2.8 Hz), 147.8 (ddd, *J* = 249.6, 14.3, 7.5 Hz), 147.6 (ddd, *J* = 244.5, 13.8, 3.7 Hz), 138.7, 130.0 (t, *J* = 2.0 Hz), 129.2, 125.3 (d, *J* = 2.0 Hz), 120.2 (dd, *J* = 20.7, 15.1 Hz), 115.3 (ddd, *J* = 19.4, 10.0, 1.4 Hz), 110.8 (ddd, *J* = 25.5, 6.6, 4.2 Hz), 21.3.

2',3',6'-Trifluoro-[1,1'-biphenyl]-2-carbonitrile (34)

From 2-bromobenzonitrile (0.182 g, 1 mmol), 1,2,4-trifluorobenzene (0.198 g, 1.5 mmol), KOAc (0.196 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **34** was obtained in 59% yield (0.137 g) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.3 Hz, 1H), 7.72 (t, *J* = 7.9 Hz, 1H), 7.57 (t, *J* = 7.9 Hz, 1H), 7.49 (d, *J* = 8.3 Hz, 1H), 7.33-7.19 (m, 1H), 7.06-6.95 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0 (ddd, *J* = 246.7, 4.0, 2.8 Hz), 147.6 (ddd, *J* = 252.0, 14.2, 6.8 Hz), 147.4 (ddd, *J* = 246.2, 13.0, 3.7 Hz), 133.2, 132.7, 132.2 (d, *J* = 1.9 Hz), 131.6, 129.4, 117.8 (ddd, *J* = 19.3, 9.9, 1.4 Hz), 117.3, 116.9 (dd, *J* = 21.9, 16.0 Hz), 113.9, 111.3 (ddd, *J* = 24.6, 6.6, 4.3 Hz). Anal. Calcd for $C_{13}H_6F_3N$ (233.19): C, 66.96; H, 2.59; N, 6.01. Found: C, 66.88; H, 2.40; N, 5.68.

3-(2,3,6-Trifluorophenyl)pyridine (35)[15]

From 3-bromopyridine (0.158 g, 1 mmol), 1,2,4-trifluorobenzene (0.198 g, 1.5 mmol), KOAc (0.196 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **35** was obtained in 72% yield (0.150 g) as a white solid: mp 53-56 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73 (bs, 1H), 8.66 (d, *J* = 3.7 Hz, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.42 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.25-7.12 (m, 1H), 7.02-6.93 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.3 (ddd, *J* = 246.3, 4.6, 2.8 Hz), 150.6 (m), 149.7, 147.7 (ddd, *J* = 251.5, 14.6, 7.2 Hz), 147.5 (ddd, *J* = 245.5, 13.4, 3.7 Hz), 137.5 (t, *J* = 2.0 Hz), 124.8, 123.3; 116.9 (dd, *J* = 20.7, 15.1 Hz), 116.8 (ddd, *J* = 19.4, 10.1, 1.4 Hz), 111.2 (ddd, *J* = 25.1, 6.6, 4.2 Hz).

3-(2,3,6-Trifluorophenyl)quinoline (36)[17]

From 3-bromoquinoline (0.208 g, 1 mmol), 1,2,4-trifluorobenzene (0.198 g, 1.5 mmol), KOAc (0.196 g, 2 mmol) in the presence of $Pd(OAc)_2$ (2.4 mg, 0.02 mmol) in DMA (4 mL) at 150 °C during 16 h, product **36** was obtained in 58% yield (0.150 g) as a white solid: mp 109-112 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.00 (s, 1H), 8.30 (s, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.77 (t, *J* = 7.8 Hz, 1H), 7.59 (t, *J* = 7.8 Hz, 1H), 7.25-7.17 (m, 1H), 7.05-6.97 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.4 (ddd, *J* = 246.1, 4.6, 3.8 Hz), 150.8 (m), 148.1 (ddd, *J* = 251.3, 14.6, 7.2 Hz), 147.7 (ddd, *J* = 245.5, 13.5, 3.7 Hz), 147.6, 137.5 (t, *J* = 2.0 Hz), 130.4, 129.4, 128.2, 127.5, 127.2, 121.9, 117.0 (dd, *J* = 20.5, 15.0 Hz), 116.7 (ddd, *J* = 19.4, 10.1, 1.4 Hz), 111.3 (ddd, *J* = 25.0, 6.6, 4.2 Hz).

Acknowledgment We are grateful to the ANR for a grant to X. S. We thank CNRS and "Rennes Metropole" for providing financial support.

Supporting Information Available ^{1}H and ^{13}C NMR spectra of new compounds and ^{1}H NMR spectra of known compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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