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Cobalt-Catalyzed Biaryl Couplings via C−F Bond Activation in the Absence of Phosphine or NHC Ligands

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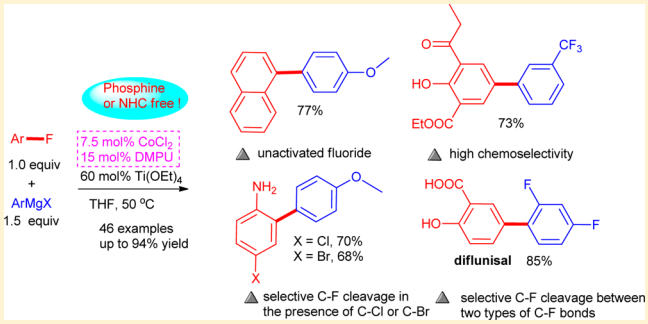
Supporting Information

ABSTRACT: A highly general and selective Co-catalyzed biaryl coupling through C−F cleavage under phosphine or NHC-free conditions was described. A broad range of aryl fluorides including unactivated fluorides as well as those with sensitive functionalities could couple with various $Ti(OEt)_4$-mediated aryl Grignard reagents with high selectivity under the catalysis of $CoCl_2$/DMPU. Importantly, selective C−F bond activation couplings between two types of fluorines (difluorinated aromatics and on two different coupling partners) and in the presence of C−Cl or C−Br bonds could also be achieved.



1. INTRODUCTION

Fluorine-containing organic compounds have become increasingly important in a wide range of areas such as medicine, agrochemistry, catalysis, materials science, and biochemistry.[1] The development of undocumented reactions for functionalization of carbon−fluorine bonds are of high significance[2] because (a) the reactions will help in understanding of the activation of highly stable bonds and in searching for highly reactive catalyst systems; (b) selective carbon−carbon formation couplings via C−F cleavage of polyfluorinated molecules also provide an attractive way to make new fluorine-containing compounds;[2] and (c) the conversions of fluorides via C−F cleavage to versatile building blocks such as organoborons are a stimulating way to derivatize the organoflorides.[3] In this context, numerous transition-metal-catalyzed cross-couplings of fluorinated compounds with Grignard reagents,[4] organozinc reagents,[5] and organoboron reagents[6] have been developed recently. Similar to the coupling reactions of aryl iodides, bromides, chlorides, and triflates, the catalysts in known couplings of C−F cleavage are mainly dominated by palladium and nickel complexes.[2] Great effort has been devoted to developing or identifying highly effective phosphine[4c,e,5a,6c] or NHC[4a,6b] ligands for Pd or Ni catalyst to activate the highly stable C−F bonds of aryl fluorides (Scheme 1A). On the other hand, a series of functional groups such as 2(4)-NO_2,[6a] 2-pyridyl,[6c] 2-C═NR,[5b] 2-C(R)═O,[6d] 2-oxazoline,[6e] etc. can usually function as an activating group to help to split the C−F bonds in the related Pd- or Ni-catalyzed coupling reactions (Scheme 1A). Until now, reports on Pd- or Ni-catalyzed biaryl couplings between aryl fluorides and arylmetal reagents without using the above-mentioned means (activating groups and phosphine/NHC ligands) were rare.

Recently, various Co-catalyzed cross-coupling reactions have been intensely and extensively investigated.[7] Although Co-mediated C−F bond activation in a stoichiometric manner has been reported,[8] there is only one report concerning the Co-catalyzed cross-couplings of aryl fluorides with aryl metal reagents where an *ortho* carbonyl group in the fluorides functioned as a key activating group.[9] To the best of our knowledge, there has been no report on Co-catalyzed biaryl couplings between aryl fluorides and aryl metal reagents in the absence of both activating groups and phosphine/NHC ligands to date. Herein, we report a general and facile Co-catalyzed cross-coupling of aryl fluorides with aryl Grignard reagents in the presence of substoichiometric $Ti(OEt)_4$ (40 mol % to ArMgX) (Scheme 1B). Salient features of this C−F bond activation reaction lie in the elimination of the need for phosphine/NHC ligands or activating groups. Importantly, selective C−F bond cleavage couplings in the presence of C−Cl or C−Br bonds and between two types of fluorines (difluorinated aromatics and on two different coupling partners) could also be achieved.

2. RESULTS AND DISCUSSION

We began our study with the optimization of reaction conditions using the model cross-coupling reaction of ethyl 2-fluorobenzoate (**1a**) with PhMgBr (**2a**). The results are outlined in Table 1. It can be seen from Table 1 that the Pd-catalyzed reactions hardly gave the desired product, while the Ni-catalyzed reaction could occur in 32% yield (entries 1−3). The reactions catalyzed by $CoCl_2/PR_3$ (R = Me, *n*-Bu, and Cy) proceeded well to afford the product in over 80% yields (entries 10−12).[10a] With no or other selected ligands, the Co-catalyzed reactions gave unsatisfactory results (entries 4−9). To our delight, 7.5 mol % $CoCl_2$ with 15 mol % of DMPU (1,3-

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Scheme 1. Two Means To Activate C−F Bonds in the Reported Pd/Ni-Catalyzed Couplings and Co-Catalyzed C−F Activation Biaryl Couplings in This Work

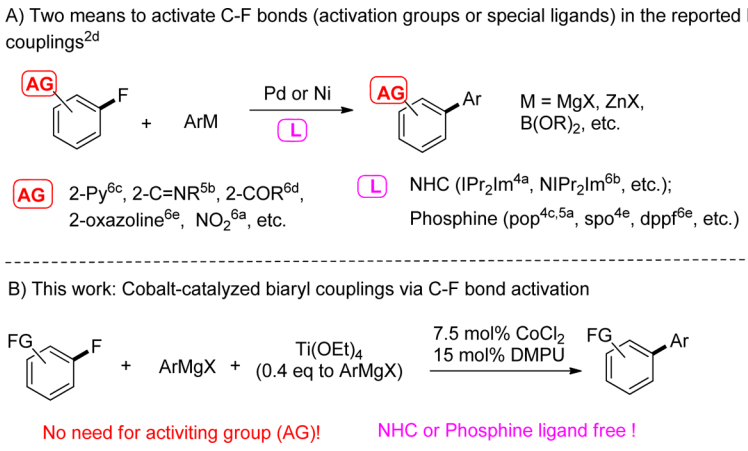
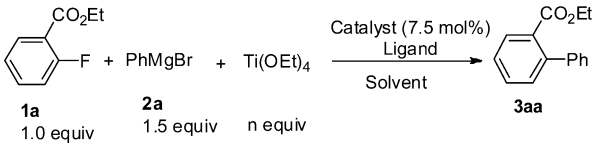


Table 1. Optimization Studies[a]



entry	catalyst/ligand[b]	*n* (equiv)	solvent	*T* (°C)	yield (%)
1	$NiCl_2/PBu_3$	0.6	THF	50	32
2	$Pd(PPh_3)_4$	0.6	THF	50	trace
3	$PdCl_2/PBu_3$	0.6	THF	50	trace
4	$CoCl_2$	0.6	THF	50	12
5	$CoCl_2$/isoquinoline	0.6	THF	50	7
6	$CoCl_2$ /bipyridine	0.6	THF	50	19
7	$CoCl_2$/tmeda	0.6	THF	50	25
8	$CoCl_2/PPh_3$	0.6	THF	50	32
9	$CoCl_2$ /dppp	0.6	THF	50	58
10	$CoCl_2/PBu_3$	0.6	THF	50	84
11	$CoCl_2/PMe_3$	0.6	THF	50	80
12	$CoCl_2/PCy_3$	0.6	THF	50	82
13[c]	$CoCl_2$	0.6	DMPU/THF	50	83
14[c]	$CoCl_2$	0.6	NMP/THF	50	21
15	$CoCl_2$	0.6	DMPU/ether	50	35
16	$CoCl_2$	0.6	DMPU/PhMe	50	29
17	$CoCl_2$	0.6	DMPU/THF	25	48
18	$CoCl_2$	0.6	DMPU/THF	reflux	78
19[d]	$CoCl_2$	0	DMPU/THF	50	11
20[d]	$CoCl_2$	0.3	DMPU/THF	50	30
21	$CoCl_2$	0.9	DMPU/THF	50	82
22	$CoCl_2$	1.5	DMPU/THF	50	67
23[e]	$CoCl_2$	0.6	DMPU/THF	50	85

[a]The reaction was carried out on a 2 mmol scale. [b]Unless indicated otherwise, the catalyst metals were charged in 7.5 mol % with 15 mol % (monodentate), 7.5 mol % (bidentate) ligand, or 15 mol % TMEDA, DMPU, and NMP. [c]Increasing the amount of DMPU and NMP from 15 to 100 mol % gave similar results. [d]In these reactions, the products of the addition of PhMgBr to the ester group were found. [e]The mixture of 1.5 equiv of PhMgBr with 0.6 equiv of $Ti(OEt)_4$ was added in two portions; 1.0 equiv was added at first, and after 2 h of reaction at 50 °C the remaining 0.5 equiv was added.

dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone)[10b,c] could catalyze the reaction equally well with those using PR_3, whereas NMP as a cosolvent gave a very low yield (entries 13 and 14).

A transition-metal-catalyzed C−F activation reaction in the absence of NHC or phosphine ligands is noteworthy; therefore, we focused on further optimization of the reaction conditions using $CoCl_2$/DMPU. Other solvents such as ether or toluene gave disappointing yields (entries 15 and 16). The reaction at room temperature could not proceed to completion and afforded the product only in 48% yield, while the reaction at a higher temperature did not give an improved yield (entries 17 and 18). The amount of $Ti(OEt)_4$ had a remarkable influence on the reaction: when $Ti(OEt)_4$ was loaded below 0.6 equiv (40 mol % based on the amount of PhMgBr), the products resulting from the addition of PhMgBr to the ester group were formed and the yield of cross-coupling product was rather low; on the other hand, increasing the amount of $Ti(OEt)_4$ over 0.9 equiv (60 mol % to PhMgBr) also resulted in a lowered yield (entries 19−22). It is worth mentioning that titanate complexes $[RTi(OR)_4{\cdot}M$, M = Li or MgX] have been used as a simple means to modify the reactivity of Grignard or lithium reagents for a long time; however, their structures have not been ascertained.[10a,11] The species of (hetero)aryl Grignard reagents tuned by substoichiometric titanates (40 mol % to ArMgBr) also exhibit reactivity and selectivity distinct from Grignard reagents,[10a] while their structures await further elucidation. Besides, it was found that adding the mixture of PhMgBr and $Ti(OEt)_4$ in two portions facilitated stirring and resulted in an increase in yield (to 85%, entry 23). This improvement became even more obvious in the reactions when active hydrogen containing substrates (for example **1f,g,t−x** in Table 2) were used.

With the optimized reaction conditions in hand, we then investigated the generality of this cobalt-catalyzed C−F activation coupling. The results are outlined in Table 2. This phosphine or NHC-free Co-catalyzed biaryl coupling via C−F bond cleavage proved to be quite general and could go to completion in 6−8 h. Without an activating group, unactivated aryl fluorides such as PhF, 4-$MeOC_6H_4F$, 1-$C_{10}H_7F$, and *m*-$C_6H_4F_2$ could all couple with various aryl Grignard reagents smoothly (Table 2, entries 1−9). Fluoroanilines are a class of deactivated fluorides, and the presence of a free amino group may also lead to a C−N formation side reaction;[12] remarkably, 2-fluoroaniline and 3-fluoroaniline underwent smooth couplings based on our present procedure with no C−N forming reaction observed (Table 2, entries 10 and 12). The corresponding couplings of the protected fluoroanilines (3-

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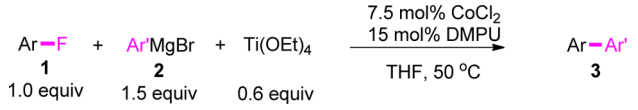
Table 2. Co-Catalyzed C−F Activation Biaryl Couplings under Phosphine or NHC-Free Conditions[a]



Entry	ArF	Ar′	Product
1	**1b**	4-$MeOC_6H_4$ **2b**	**3bb** 65%
2	**1b**	4-$EtOOCC_6H_4$ **2c**[b]	**3bc** 55%
3	**1b**	2-NCC_6H_4 **2d**[b]	**3bd** 55%
4	**1b**	2-Py **2e**[b]	**3be** 65%
5	**1c**	Ph **2a**	**3bb** 50% (78%)[c]
6	**1d**	**2b**	**3db** 77%
7	**1d**	4-$Me_2NC_6H_4$ **2f**	**3df** 70%
8	**1e**	3-$MeOC_6H_4$ **2g**	**3eg** 65%
9	**1e**	**2b**[d]	**4eb** 79%
10	**1f**	**2b**[e]	**3fb** 79%
11	**1f′**	**2b**	**3fb** 72%
12	**1g**	**2h**[e]	**3gh** 91%
13	**1g′**	**2h**	**3gh** 89%
14	**1h**	**2a**[d]	
29	**1w**	**2b**[d]	**3wb** 86%
30	**1x**	**2b**[d]	**3xb** 78%
31	**1x**	**2i**[d]	**3xi** 73%
15	**1i**	**2a**[d]	**3ia** 75%
16	**1j**	**2d**[b,d]	**3je** 72%
17	**1k**	**2a**	**3ka** 90%
18	**1l**	**2a**	**3la** 65%
19	**1m**	4-MeC_6H_4 **2g**	**3mg** 85%
20	**1n**	**2b**	**3nb** 82%
21	**1o**	3-$F_3CC_6H_4$ **2i**	**3oi** 63%
22	**1p**	2-thiophenyl **2j**	**3pj** 67%
23	**1q**	**2b**	**3qb** 75%
24	**1r**	**2i**	**3ri** 76%
25	**1s**	3-Py **2k**	**3sk** 76%
26	**1t**	**2d**[d]	**3td** 92%
27	**1u**	**2a**[d]	**3ua** 86%
28	**1v**	1-Naphthyl **2l**[d]	**3vl** 78%
32	**1y**	**2a**	**3ya** 84%
33	**1y′**	**2c**	**3je** 82%
34	**1z**	**2a**	**3za** 94%

[a]All reactions were carried out on a 2 mmol scale. [b]Pyridyl and aryl Grignard reagents with FG (CN, COOEt, etc.) were prepared via bromine or iodine−magnesium exchange using *i*-PrMgCl or *i*-PrMgCl·LiCl. [c]0.3 equiv of $Ti(OEt)_4$ was used. [d]2.5 equiv of Ar′MgBr and 0.6 equiv of $Ti(OEt)_4$ were used. [e]3.5 equiv of Ar′MgBr and 0.6 equiv of $Ti(OEt)_4$ were used.

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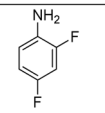
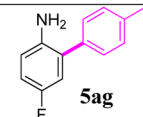
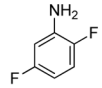
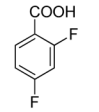
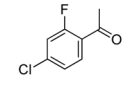
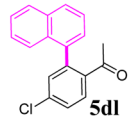
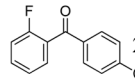
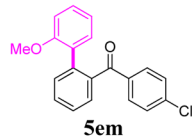
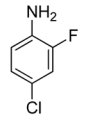
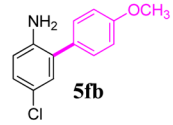
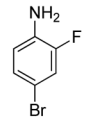
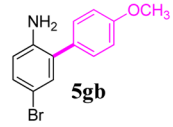
$FC_6H_4N{=}CHPh$ and 2-$FC_6H_4N{=}CHPh$) also proceeded equally well (Table 2, entries 11 and 13). Similarly, 2-fluorophenol and 4-fluorophenol also participated in the coupling to afford the desired products in 88% and 75% yields, respectively (Table 2, entries 14 and 15). In addition, the present C−F bond activation reaction exhibited high functional group compatibility, and the fluorides bearing sensitive functional groups such as ketone, ester, amide, imine, sulfonamide, sulfonate, free carboxylic acid, etc. could couple facilely (Table 2, entries 16−28). Although the similar functional group compatibility has been demonstrated in our previously reported Fe- or Co-catalyzed cross couplings of aryl Grignard reagents in the presence of substoichiometric titanates,[10,13] those couplings were conducted at −10 °C or room temperature. Such high functional group tolerance was observed for the first time under the heated conditions.

As previously mentioned, ketone,[6d,9] imine (C═NR),[5b] and ester[9] functionalities usually act as an *ortho* position activating group in C−F bond activation; therefore, the C−F bond cleavage couplings beyond the *ortho*-positions of these groups have been investigated rarely. Our experiments clearly showed that the couplings at the *meta* or *para* position to these groups could also take place smoothly (Table 2, entries 16−22). Furthermore, the couplings of two series of 2-, 3-, or 4-substituted aryl fluorides further demonstrated that the present reactions could proceed well beyond the *ortho* position of an activation group (Table 2, entries 23−28). Besides, highly functionalized fluorides without an *ortho* group such as ethyl 5-fluoro-2-hydroxybenzoate and ethyl 5-fluoro-2-hydroxy-3-propionylbenzoate could also couple with aryl Grignard reagents to give the cross-coupling products in good yields (Table 2, entries 29−31). On the other hand, aryl Grignard reagents bearing various sensitive groups such as COOEt (Table 2, entry 2), CN (Table 2, entries 3 and 26) and CF_3 (Table 2, entries 21, 24, and 31) could also undergo this Co-catalyzed coupling. Moreover, heteroaryl Grignard reagents such as 2-thiophenylmagnesium (Table 2, entry 22) and pyridylmagnesium (Table 2, entries 4, 16, and 25) reagents were also good coupling substrates. It is noteworthy that pyridyl fluorides could also undergo C−F bond activation couplings, leading to the desired pyridine compounds in high yields (Table 2, entries 32−34).

Selective functionalization of C−F bonds of polyfluorinated molecules is a research area of high interest because it helps identify the intrinsic factors for cleaving C−F bonds and it also provides an alternative approach to new fluoro compounds. As illustrated in Table 2 (entry 8), a selective monoarylation through C−F bond activation of *m*-difluorobenzene was achieved based on our present procedure, leading to 3-phenylfluorobenzene product in 65% yield. While *ortho*-selective functionalization of C−F bonds of a range of polyfluorinated compounds has been well achieved in the literature utilizing a directing group such as C═NR,[5b] COR,[6d,9] 2-oxazoline,[6e] OH,[4d] etc., herein we have achieved highly *ortho*-selective arylations of difluoroaromatics bearing a free amino or carboxylic group using this Co-catalyzed C−F activation reaction (Table 3, entries 1−3). To the best of our knowledge, these were the first examples that a free amino or carboxylic group functioned as an *ortho*-directing group in the Co-catalyzed selective C−F bond activation. Based on these findings, we then investigated the *ortho*-selective C−F bond activation in the presence of C−Cl or C−Br bonds. To selectively cleave a highly strong bond (C−F) over a relatively weak bond (C−Cl or C−Br) is a remarkably challenging task.

Table 3. Selective C−F Activation Couplings in the Presence of C−F, C−Cl, and C−Br Bonds

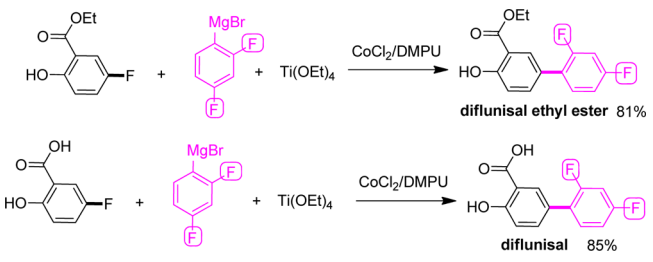
Entry	ArF	Ar′MgX (Ar′)	Product	Yield (%)
1[a]		4-MeC_6H_4	 **5ag**	90
2[a]		4-$MeOC_6H_4$	 **5bb**	67
3[b]		2-$F_3CC_6H_4$	 **5cm**	81
4[c,d]		1-Naphthyl	 **5dl**	85
5[c,d]		2-$MeOC_6H_4$	 **5em**	88
6[a,d]		4-$MeOC_6H_4$	 **5fb**	70
7[a,d]		4-$MeOC_6H_4$	 **5gb**	68

[a]3.0 equiv of Ar′MgBr and 0.4 equiv of $Ti(OEt)_4$ were used. [b]2.0 equiv of Ar′MgBr and 0.4 equiv of $Ti(OEt)_4$ were used. [c]1.0 equiv of Ar′MgBr and 0.4 equiv of $Ti(OEt)_4$ were used. [d]The diarylated products and those resulting from C−Cl or C−Br vs C−F cleavage were not observed.

Another challenge is that our previous investigation has showed that aryl bromides or aryl chlorides could undergo the cross-couplings with titanate-mediated aryl Grignard reagents under cobalt catalysis.[10a] Despite these challenges, *ortho*-selective C−F bond activation in the presence of C−Cl or C−Br bonds was achieved successfully under the catalysis of $CoCl_2$/DMPU (Table 3, entries 4−7).

Remarkably, a selective C−F bond activation between two types of C−F bonds on two coupling substrates was also achieved based on this Co-catalyzed reaction as outlined in Scheme 2. In the couplings, the C−F bonds of 5-fluoro-2-

Scheme 2. Synthesis of Diflunisal and Its Ethyl Ester via Selective C−F Bond Activation



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hydroxybenzoic acid and its ethyl ester were highly selectively replaced by the aryl group without any activating groups at *ortho* positions, whereas the two fluorine atoms in (2,4-difluorophenyl)magnesium bromide were left untouched.[14] It is worth mentioning that the reported methods to yield new fluorinated compound via C−F bond cleavage are mainly based on the selective C−F functionalization of polyfluorinated substrates.[2d] Our selective C−F bond activation illustrated in Scheme 2 provides a new approach to make new fluorine-containing molecules. It can be seen that our couplings facilely afforded an anti-inflammatory agent, diflunisal,[15] and its ethyl ester in high yields.

Mechanistically, we assume that the cobalt/titanium bimetallic cooperativity plays an important role in the present reaction. As in a tentative transition state (Figure 1), the bimetallic complex promoted the C−F bond cleavage in a synergetic manner.[4c,e,16] Further studies for the cobalt/titanium bimetallic complexes are underway in our laboratories.

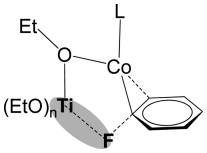

Figure 1. Proposed transition state for the Co/Ti cooperative oxidative addition step.

3. CONCLUSION

In conclusion, we have developed an unexpectedly facile Co-catalyzed biaryl cross-coupling reaction via C−F bond cleavage. In sharp contrast to the related reported reactions that are dominantly catalyzed by Pd or Ni complexes with NHC or phosphine ligand, and often in the presence of an activating group on the aryl fluorides, the present coupling reaction of C−F bond activation was catalyzed simply by $CoCl_2$/DMPU and proved to be quite general. Remarkably, highly selective C−F activation couplings in the presence of C−F, C−Cl, and C−Br bonds could be achieved. We believe that these findings will be helpful to the further development of C−F bond activation reactions and highly effective cobalt catalysts.

4. EXPERIMENTAL SECTION

General Information. IR spectra were recorded using an FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer (100 MHz for ^{13}C spectroscopy) using TMS as an internal standard. High-resolution mass spectra (HRMS) were obtained with a microTOF (ESI). Melting points recorded on a microscopic instrument and are uncorrected.

All reagents and solvents used for arylmagnesium reagents or lithium reagents and reactions were freshly dehydrated and distilled before use. $Ti(OEt)_4$ was distilled under vacuum before use. The corresponding glassware was oven dried (120 °C) and cooled under a stream of argon gas. Aryl Grignard reagents such as phenylmagnesium or (4-methoxyphenyl)-magnesium were prepared according to the standard procedure. Pyridyl Grignard reagents were prepared via bromine−magnesium exchange using *i*-PrMgCl while functionalized aryl Grignard reagents such as 2-cyanophenylmagnesium chloride or 4-(ethoxycarbonyl)phenyl magnesium chloride were prepared via iodine−magnesium exchange using *i*-PrMgCl·LiCl according to Knochel's method.[17] All of the Grignard reagents were titrated before use.[18]

Typical Procedure for Co-Catalyzed Biaryl Couplings via C−F Cleavage (3aa). Under Ar atmosphere, a solution of PhMgBr in THF (3.0 mmol, 1.0 M in THF) was added dropwise to a solution of $Ti(OEt)_4$ (273.6 mg, 1.2 mmol) in 10 mL of THF under magnetic stirring at room temperature. After addition, stirring was continued for 0.5 h.

Under Ar atmosphere, to another three-necked round-bottom flask were added $CoCl_2$ (19.5 mg, 0.015 mmol), DMPU (38 mg, 0.03 mmol), 2-fluorobenzoic acid ethyl ester (308 mg, 2 mmol), and 10 mL of THF. The resulting mixture was heated to 50 °C under magnetic stirring, and about 2/3 volume of the above-prepared mixture of PhMgBr and $Ti(OEt)_4$ was added dropwise. After addition, the mixture was stirred at 50 °C for about 3 h. The remaining mixture of PhMgBr and $Ti(OEt)_4$ was added dropwise, and the resulting mixture was stirred at 50 °C until the completion of the reaction. The reaction was quenched with 30 mL distilled water and the product was taken up with CH_2Cl_2 (50 mL × 4). The organic layer was dried over Na_2SO_4 and concentrated to yield the crude compound, which was purified by column chromatography to yield the desired product **3aa** (180 mg, 85% yield).

Note: For the reactions where the fluorinated substrates contain active hydrogen(s) (for example, **3fb**, **3gh**, **3ha**, **3ia**, **3td**, etc.), after $CoCl_2$, DMPU, the fluorinated substrate, and THF were added in the flask, 1 or 2 equiv of Ar′MgX was added dropwise to the mixture to neutralize the active hydrogen(s). After that, the mixture was heated slowly to 50 °C. The other operations were conducted as described in typical procedure.

*Ethyl Biphenyl-2-carboxylate (**3aa**).* The product was prepared as described in the typical procedure and isolated as a colorless oil in 85% yield (384 mg); R_f = 0.50 (petroleum ether/ethyl acetate = 20:1, v/v); IR (cm^{-1}, KBr) 1710, 1601, 1258, 698; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.82 (dd, J = 7.6 Hz, J = 0.9 Hz, 1H), 7.55−7.50 (m, 1H), 7.43−7.31 (m, 7H), 4.08 (q, J = 7.1 Hz, 2H), 0.99 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ 168.8, 142.4, 141.6, 134.3, 131.4, 131.1, 130.6, 129.7, 128.4, 128.0, 127.1, 60.9, 13.6. Data were consistent with those reported in the literature.[19]

*4-Methoxybiphenyl (**3bb**).* The product was prepared as described in the typical procedure and isolated as a white solid in 78% yield (287 mg): mp 85−86 °C (lit. mp 85−87 °C); R_f = 0.55 (petroleum ether); IR (cm^{-1}, KBr) 3025, 2918,1605, 1487, 834, 760, 683; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.59−7.55 (m, 4H), 7.44 (t, J = 6.0 Hz, 2H), 7.34−7.28 (m, 1H), 7.01 (d, J = 6.8 Hz, 2H), 3.88 (s, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ 159.2, 140.8, 133.8, 128.7, 128.2, 126.8, 126.7, 114.2, 55.4. Data were consistent with those reported in the literature.[20]

*Ethyl Biphenyl-4-yl carboxylate (**3bc**).* The product was prepared as described in the typical procedure and isolated as a colorless oil in 55% yield (249 mg): R_f = 0.51 (petroleum ether/ethyl acetate = 20:1, v/v); IR (cm^{-1}, KBr) 3027, 2975, 1705, 1600, 1257, 701; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.12 (d, J = 8.3 Hz, 2H), 7.67−7.62 (m, 4H), 7.49−7.45 (m, 2H), 7.39 (t, J = 7.2 Hz, 1H), 4.40 (q, J = 7.2 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ 166.5, 145.5, 140.1, 130.1, 129.3, 128.9, 128.1, 127.3, 127.0, 61.0, 14.4. Data were consistent with those reported in the literature.[21]

*Biphenyl-2-carbonitrile (**3bd**).* The product was prepared as described in the typical procedure and isolated as a colorless oil

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J. Org. Chem. 2017, 82, 1291−1300

in 55% yield (197 mg): R_f = 0.48 (petroleum ether); IR (cm^{-1}, KBr) 3046, 2225, 1599, 1480, 760; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.80 (d, J = 6.2 Hz, 1H), 7.69−7.66 (m, 1H), 7.60 (d, J = 5.8 Hz, 2H), 7.56−7.51 (m, 3H), 7.48 (t, J = 5.6 Hz, 2H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 145.5, 138.2, 133.8, 132.9, 130.1, 128.79, 128.77, 127.6, 127.2, 118.8, 111.3. Data were consistent with those reported in the literature.[22]

*2-Phenylpyridine (**3be**).* The product was prepared as described in the typical procedure and isolated as a yellow oil in 65% yield (202 mg): R_f = 0.58 (petroleum ether/ethyl acetate = 20:1, v/v); IR (cm^{-1}, KBr) 3056, 1592, 1565, 693; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.67 (d, J = 4.8 Hz, 1H), 7.99−7.97 (m, 2H), 7.67−7.66 (m, 2H), 7.46−7.40 (m, 2H), 7.38−7.36 (m, 1H), 7.17−7.14 (m, 1H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 157.4, 149.7, 139.4, 136.7, 129.0, 128.8, 126.9, 122.1, 120.5. Data were consistent with those reported in the literature.[23]

*1-(4-Methoxyphenyl)naphthalene (**3db**).* The product was prepared as described in the typical procedure and isolated as a white solid in 77% yield (360 mg): mp = 116.5−118 °C (lit. 116−117 °C); R_f = 0.45 (petroleum ether/ethyl acetate = 10:1, v/v); IR (cm^{-1}, KBr) 3028, 2987, 1601, 1514, 1104, 756; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.93−7.81 (m, 3H), 7.52−7.39 (m, 6H), 7.04−7.01 (m, 2H), 3.88 (s, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ (ppm) 159.0, 140.0, 133.9, 133.2, 131.9, 131.1, 128.3, 127.3, 127.0, 126.1, 125.9, 125.7, 125.4, 113.8, 55.4. Data were consistent with those reported in the literature.[24]

*N,N-Dimethyl-4-(naphthalen-1-yl)aniline (**3df**).* The product was prepared as described in the typical procedure and isolated as a white solid in 70% yield (346 mg): mp = 108−110 °C (lit. 109−112 °C); R_f = 0.40 (petroleum ether/ethyl acetate = 10:1, v/v); IR (cm^{-1}, KBr) 3045, 2851, 1394, 1352, 1198, 799, 775; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.01 (d, J = 8.3 Hz, 1H), 7.88 (d, J = 7.7 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.51−7.39 (m, 6H), 6.87 (d, J = 7.9 Hz, 2H), 3.02 (s, 6H,); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 149.8, 140.6, 134.1, 131.0, 129.0, 128.4, 128.1, 127.0, 126.9, 126.5, 125.9, 125.7, 125.6, 112.5, 40.8. Data were consistent with those reported in the literature.[25]

*3-Fluoro-3′-methoxybiphenyl (**3eg**).* The product was prepared as described in the typical procedure and isolated as a pale yellow oil in 65% yield (263 mg): R_f = 0.58 (petroleum ether/ethyl acetate = 10:1, v/v); IR (cm^{-1}, KBr) 3073, 2998, 2965, 2938, 2839, 1608, 1587, 700; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.37−7.32 (m, 3H), 7.28−7.25 (m, 1H), 7.15−7.12 (m, 1H), 7.09−7.08 (m, 1H), 7.04−6.99 (m, 1H), 6.91−6.88 (m, 1H), 3.83 (s, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 163.4 (d, J = 243.9 Hz), 160.3, 143.6 (d, J = 7.5 Hz), 141.5 (d, J = 2.1 Hz), 130.4 (d, J = 8.3 Hz), 130.1, 123.0 (d, J = 2.4 Hz), 119.7, 114.3 (d, J = 21.0 Hz), 114.1 (d, J = 21.9 Hz), 113.4, 113.1, 55.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −113.1. Data were consistent with those reported in the literature.[26]

*1,3-Bis(4-methoxyphenyl)benzene (**4eb**).* The product was prepared as described in the typical procedure and isolated as a white solid in 79% yield (458 mg): mp = 203−205 °C (lit. 203−204 °C); R_f = 0.47 (petroleum ether/ethyl acetate = 10:1, v/v); IR (cm^{-1}, KBr) 1685, 1571, 1498, 1321, 759; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.72 (t, J = 1.8 Hz, 1H), 7.58 (d, J = 8.9 Hz, 4H), 7.51−7.46 (m, 3H), 7.00 (d, J = 8.8 Hz, 4H), 3.86 (s, 6H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 159.2, 141.3, 133.8, 129.1, 128.3, 125.3, 125.2, 114.2, 55.4. Data were consistent with those reported in the literature.[27]

*4′-Methoxybiphenyl-3-amine (**3fb**).* The product was prepared as described in the typical procedure and isolated as a pale yellow solid in 79% yield (314 mg): mp = 89−91 °C (lit. 91 °C); R_f = 0.48 (petroleum ether/ethyl acetate = 5/1, v/v); IR (cm^{-1}, KBr) 3367, 3022, 1612, 1523, 1296,1243, 1032, 836, 758, 698; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.49 (d, J = 8.8 Hz, 2H), 7.20 (t, J = 7.8 Hz, 1H), 6.96−6.94 (m, 3H), 6.88−6.87 (m, 1H), 6.65−6.63 (m, 1H), 3.84 (s, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 159.1, 146.7, 142.1, 134.0, 129.6, 128.1, 117.4, 114.1, 113.57, 113.55, 55.3. Data were consistent with those reported in the literature.[28]

*4′-Methylbiphenyl-2-amine (**3gh**).* The product was prepared as described in the typical procedure and isolated as a pale yellow oil in 91% yield (333 mg): R_f = 0.62 (petroleum ether/ethyl acetate = 10/1, v/v); IR (cm^{-1}, KBr) 3381, 1614, 1492, 1295, 820, 748, 733; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.34 (d, J = 7.9 Hz, 2H), 7.24 (d, J = 7.8 Hz, 2H), 7.15−7.10 (m, 2H), 6.81 (t, J = 7.4 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 3.71 (br, 2H), 2.39 (s, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 143.9, 137.1, 136.9, 130.8, 129.8, 129.3, 128.7, 128.0, 119.0, 116.0, 21.5. Data were consistent with those reported in the literature.[29]

*2-Phenylphenol (**3ha**).* The reaction was quenched with 2 M HCl aqueous solution, and the product was isolated as a white solid in an 88% yield (299 mg): mp = 58−59 °C (lit. 56−58 °C); R_f = 0.49 (petroleum ether/ethyl acetate = 10/1, v/v); IR (cm^{-1}, KBr) 3513, 1608, 1511, 825, 740, 688; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.54−7.50 (m, 4H), 7.44 (t, J = 5.4 Hz, 1H), 7.32−7.28 (m, 2H), 7.05−7.02 (m, 2H), 5.24 (br, 1H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 152.5, 137.2, 130.3, 129.3, 129.23, 129.18, 128.2, 127.9, 120.9, 115.9. Data were consistent with those reported in the literature.[30]

*4-Phenylphenol (**3ia**).* The reaction was quenched with 2 M HCl aqueous solution, and the product was isolated as a white solid in 75% yield (255 mg): mp =164 °C (lit. 163−165 °C); R_f = 0.55 (petroleum ether/ethyl acetate = 10/1, v/v); IR (cm^{-1}, KBr) 3422, 1613, 1523, 836, 758, 698; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.56 (d, J = 6.1 Hz, 2H), 7.51 (d, J = 6.6 Hz, 2H), 7.45−7.42 (m, 2H), 7.34−7.31 (m, 1H), 6.93 (d, J = 6.7 Hz, 2H), 4.81 (br, 1H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 155.1, 140.8, 134.1, 128.7, 128.4, 126.7, 115.6. Data were consistent with those reported in the literature.[31]

*Ethyl 4-(Pyridin-2-yl)benzoate (**3je**).* The product was prepared as described in the typical procedure and isolated as a white solid in 72% yield (327 mg): mp = 50.5−51.5 °C (lit. 50.5−52.0 °C); R_f = 0.45 (petroleum ether/ethyl acetate = 5/1, v/v); IR (cm^{-1}, KBr) 3056, 2983, 1708, 1607,1585, 1468, 1363, 1281, 1018, 870; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.73 (d, J = 4.6 Hz, 1H), 8.16−8.06 (m, 4H), 7.79 (d, J = 3.8 Hz, 2H), 7.31−7.27 (m, 1H), 4.41 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 166.4, 156.2, 149.8, 143.4, 136.9, 130.7, 130.0, 126.8, 122.8, 121.0, 61.0, 14.3. Data were consistent with those reported in the literature.[32]

*Biphenyl-2-yl Propanone (**3ka**).* The product was prepared as described in the typical procedure and isolated as a yellow oil in 90% yield (378 mg): R_f = 0.35 (petroleum ether); IR (cm^{-1}, KBr) 3060, 2975, 2937, 2877, 1681, 1605, 1423, 778, 755, 690; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.45−7.39 (m, 2H), 7.38−7.29 (m, 5H), 7.27−7.25 (m, 2H), 2.18 (q, J = 7.3 Hz, 2H), 0.83 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 207.7, 140.1, 139.7, 138.9, 129.3, 129.1, 127.8, 127.6, 126.8, 126.6, 126.4, 35.1, 7.5. Data were consistent with those reported in the literature.[33]

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J. Org. Chem. 2017, 82, 1291−1300

*Biphenyl-4-yl Ethanone (**3la**).* The product was prepared as described in the typical procedure and isolated as a white solid in 65% yield (255 mg): mp = 121−122 °C (lit. 121−123 °C); R_f = 0.50 (petroleum ether/ethyl acetate = 20:1, v/v); IR (cm^{-1}, KBr) 1682, 1601, 1263, 961, 764; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.04 (d, J = 8.4 Hz, 2H), 7.69 (d, J = 8.4 Hz, 2H), 7.64−7.62 (m, 2H), 7.48 (t, J = 7.4 Hz, 2H), 7.40 (t, J = 7.3 Hz, 1H), 2.64 (s, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ 197.7, 145.8, 139.9, 135.9, 129.0, 128.9, 128.2, 127.3, 127.2, 26.7. Data were consistent with those reported in the literature.[34]

*Ethyl 4′-Methylbiphenyl-4-yl Sulfonate (**3 mg**).* The product was prepared as described in the typical procedure and isolated as a white solid in 85% yield (469 mg): mp = 132−133 °C (lit. 131−133 °C); R_f = 0.52 (petroleum ether/ethyl acetate = 10:1, v/v); IR (cm^{-1}, KBr) 1595, 1483, 1358, 808, 794, 636; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.96 (d, J = 8.4 Hz, 2H), 7.74 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 7.9 Hz, 2H), 4.17 (q, J = 7.1 Hz, 2H), 2.42 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ 146.6, 138.8, 136.1, 134.5, 129.8, 128.3, 127.5, 127.2, 67.0, 21.2, 14.8. Data were consistent with those reported in the literature.[10a]

*4-(4′-Methoxybiphenyl-4-ylsulfonyl)morpholine (**3nb**).*[35] The product was prepared as described in the typical procedure and isolated as a white solid in 82% yield (572 mg): mp = 198−199 °C; R_f = 0.48 (petroleum ether/ethyl acetate = 3:1, v/v); IR (cm^{-1}, KBr) 1597, 1485, 1108, 945, 766; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.78 (d, J = 8.4 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H), 7.56 (d, J = 8.7 Hz, 2H), 7.02 (d, J = 8.7 Hz, 2H), 3.87 (s, 3H), 3.76 (t, J = 4.7 Hz, 4H), 3.04 (t, J = 4.6 Hz, 4H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ 160.2, 145.6, 132.9, 131.5, 128.5, 128.4, 127.1, 114.6, 66.1, 55.4, 46.0.

*3′-(Trifluoromethyl)biphenyl-3-carbaldehyde (**3oi**).* The reaction was post-treated as described in the literature,[10b] and the product was isolated as a yellow solid in 63% yield (315 mg): mp = 142.5−144 °C (lit. 143−144 °C); R_f = 0.39 (petroleum ether/ethyl acetate = 10:1, v/v); IR (cm^{-1}, KBr) 3025, 2998, 1692, 1598, 1580, 1336, 1165, 825, 790, 761, 700; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.11 (s, 1H), 8.15 (t, J = 1.5 Hz, 1H), 7.93−7.90 (m, 2H), 7.69−7.65 (m, 2H), 7.57−7.45 (m, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ 192.1, 143.9, 140.6, 137.1, 133.0, 131.1 (q, J = 34.8 Hz, 1C), 129.9, 129.8, 129.5, 129.2, 128.0, 124.8, 123.3, 120.9. Data were consistent with those reported in the literature.[36]

*4-(Thiophene-2-yl)benzaldehyde (**3pj**).* The reaction was post-treated as described in the literature,[10b] and the product was isolated as a yellow solid in 67% yield (252 mg): mp = 68−69 °C (lit. 69.0−69.5 °C); R_f = 0.52 (petroleum ether/ethyl acetate = 10:1, v/v); IR (cm^{-1}, KBr) 3011, 1701, 1604, 1276, 792; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.0 (s, 1H), 7.90 (d, J = 1.8 Hz, 2H), 7.89−7.78 (m, 2H), 7.77 (d, J = 5.0 Hz, 2H), 7.48−7.46 (m, 1H), 7.41−7.39 (m, 1H), 7.15−7.13 (m, 1H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ 191.5, 142.8, 140.1, 135.1, 130.5, 128.5, 126.9, 126.1, 125.1. Data were consistent with those reported in the literature.[37]

*N,N-Dimethyl 4′-Methoxybiphenyl-2-carboxamide (**3qb**).* The product was prepared as described in the typical procedure and isolated as a yellow oil in 75% yield (383 mg): R_f = 0.45 (petroleum ether/ethyl acetate = 1:1, v/v); IR (cm^{-1}, KBr) 3051, 2970, 1624, 1427, 1286, 768, 759; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45−7.34 (m, 6H), 6.93 (d, J = 8.5 Hz, 2H), 3.84 (s, 3H), 2.88 (s, 3H), 2.41 (s, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ 171.6, 159.2, 132.39, 132.35, 131.2, 131.1, 130.9, 129.6, 127.4, 127.2, 113.8, 55.2, 38.29, 38.27; HRMS calcd for $C_{16}H_{18}NO_2^+$ $[M + H]^+$ 256.1332, found 256.1327.

***N,N*-Dimethyl 3′-(Trifluoromethyl)biphenyl-3-carboxamide (3ri).** The product was prepared as described in the typical procedure and isolated as a pale yellow solid in 76% yield (445 mg): mp = 108−109 °C; R_f = 0.48 (petroleum ether/ethyl acetate = 3:1, v/v); IR (cm^{-1}, KBr) 1597, 1485, 1108, 945, 766; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.84 (s, 1 H), 7.77 (d, J = 7.6 Hz, 1H), 7.66−7.61 (m, 3H), 7.56 (t, J = 7.7 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.43 (d, J = 7.6 Hz, 1H), 3.14 (s, 3H), 3.03 (s, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ 171.1, 141.1, 139.9, 137.2, 131.1 (q, J = 32.0 Hz, 1C), 130.4, 129.4, 129.0, 128.1, 126.4, 125.8, 124.2 (q, J = 3.7 Hz, 1C), 123.8 (q, J = 3.8 Hz, 1C), 122.7, 39.4, 35.2; HRMS calcd for $C_{16}H_{15}F_3NO^+$ $[M + H]^+$ 294.1100, found 294.1101.

*N,N-Dimethyl 4-Pyridin-3-ylbenzamide (**3sk**).* The product was prepared as described in the typical procedure and isolated as a white solid in 76% yield (344 mg): mp = 95 °C (lit. 94−96 °C); R_f = 0.32 (petroleum ether/ethyl acetate = 1/1, v/v); IR (cm^{-1}, KBr) 1638, 1562, 1395, 1084; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.87 (s, 1H), 8.64 (s, 1H), 7.90 (d, J = 6.2 Hz, 1H), 7.63 (d, J = 6.6 Hz, 2H), 7.55 (d, J = 6.8 Hz, 2H), 7.41 (s, 1H), 3.15 (s, 3H), 3.05 (s, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ 171.1, 148.7, 148.1, 138.9, 136.1, 136.0, 134.6, 128.0, 127.1, 123.7, 39.6, 35.4. Data were consistent with those reported in the literature.[10a]

*2′-Cyanobiphenyl-2-carboxylic Acid (**3td**).* The reaction was quenched with 2 M HCl aqueous solution, and the product was isolated as a white solid in 92% yield (410 mg): mp = 170.4−172.3 °C (lit. 170−172 °C); R_f = 0.48 (petroleum ether/ethyl acetate/acetic acid = 5:1:0.01, v/v/v); IR (cm^{-1}, KBr) 3433, 3267, 3051, 2229, 1701, 1602, 1433, 1384, 1095, 692, 521; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.12 (d, J = 7.4 Hz, 1H), 7.48 (t, J = 7.8 Hz, 1H), 7.35−7.31 (m, 2H), 7.28−7.24 (m, 4H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ (ppm) 171.0, 135.0, 134.9, 133.7, 132.2, 132.1, 130.2, 130.0, 128.6, 128.54, 128.49, 127.9, 119.2, 117.6. Data were consistent with those reported in the literature.[38]

*Biphenyl-3-carboxylic Acid (**3ua**).* The reaction was quenched with 2 M HCl aqueous solution, and the product was isolated as a white solid in 86% yield (341 mg): mp = 163−165 °C (lit. 160−161 °C); R_f = 0.32 (petroleum ether/ethyl acetate/acetic acid = 5:1:0.01, v/v/v); IR (cm^{-1}, KBr) 1708, 1693, 1584, 1277, 745, 701; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.37 (s, 1H), 8.11 (d, J = 7.8 Hz, 1H), 7.85 (d, J = 7.8 Hz, 1H), 7.65 (d, J = 7.4 Hz, 2H), 7.57 (t, J = 7.7 Hz, 1H), 7.48 (t, J = 7.5 Hz, 2H), 7.40 (t, J = 7.3 Hz, 1H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ 171.8, 141.7, 140.0, 132.5, 129.8, 129.02, 128.98, 128.96, 128.9, 127.9, 127.2. Data were consistent with those reported in the literature.[39]

*4-Naphthalen-1-ylbenzoic Acid (**3vl**).* The reaction was quenched with 2 M HCl aqueous solution, and the product was isolated as a white solid in 78% yield (387 mg): mp = 234−236 °C (lit. 235.2−236.1 °C); R_f = 0.47 (petroleum ether/ethyl acetate/acetic acid = 5:1:0.01, v/v/v); IR (cm^{-1}, KBr) 1685, 1571, 1498, 1321, 759; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.29−7.89 (m, 5H), 7.66−7.50 (m, 6H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz) δ 171.8, 146.6, 139.0, 133.8, 131.9, 131.7, 131.2, 130.29, 130.27, 128.4, 127.0, 126.4, 126.0, 125.6, 125.3. Data were consistent with those reported in the literature.[40]

*Ethyl 4-Hydroxy-4′-methoxybiphenyl-3-carboxylate (**3wb**).* The reaction was quenched with 2 M HCl aqueous solution, and the product was isolated as a white solid in 86%

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J. Org. Chem. 2017, 82, 1291−1300

yield (468 mg): mp = 120−122 °C; R_f = 0.62 (petroleum ether/ethyl acetate = 10/1, v/v); IR (cm^{-1}, KBr) 3138, 1712, 1485, 1439, 1210, 766, 590; ^1H NMR ($CDCl_3$, 400 MHz) δ 10.81 (s, 1H), 8.01 (d, J = 2.4 Hz, 1H), 7.65 (dd, J = 8.6 Hz, J = 2.4 Hz, 1H), 7.47 (d, J = 8.8 Hz, 2H), 7.03 (d, J = 8.6 Hz, 1H), 6.97 (d, J = 8.8 Hz, 2H), 4.44 (q, J = 7.2 Hz, 2H), 3.85 (s, 3H), 1.43 (t, J = 7.2 Hz, 3H) ; $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 170.2, 160.7, 159.0, 134.0, 132.6, 132.1, 127.7, 127.6, 117.9, 114.3, 112.7, 61.5, 55.3, 14.2; HRMS calcd for $C_{16}H_{17}O_4^+$ $[M + H]^+$ 273.1121, found 273.1120.

*Ethyl 4-Hydroxy-4′-methoxy-5-propionylbiphenyl-3-carboxylate (**3xb**).* The reaction was quenched with 2 M HCl aqueous solution, and the product was isolated as a white solid in 78% yield (512 mg): mp = 110−112 °C; R_f = 0.45 (petroleum ether/ethyl acetate = 5:1, v/v); IR (cm^{-1}, KBr) 3369, 1685, 1658, 1439, 1251, 766, 699; ^1H NMR ($CDCl_3$, 400 MHz) δ 12.22 (s, 1H), 8.21 (d, J = 2.5 Hz, 1H), 8.15 (d, J = 2.5 Hz, 1H), 7.51−7.48 (m, 2H), 7.00−6,96 (m, 2H), 4.46 (q, J = 7.2 Hz, 2H), 3.86 (s, 3H), 3.15 (q, J = 7.2 Hz, 2H); 1.44 (t, J = 7.2 Hz, 3H), 1.23(t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 203.4, 169.1, 160.4, 159.3, 134.1, 133.1, 131.68, 131.64, 127.8, 125.8, 115.7, 114.4, 61.9, 55.4, 35.8, 14.2, 8.3; HRMS calcd for $C_{19}H_{21}O_5^+$ $[M + H]^+$ 329.1384, Found 329.1383.

*Ethyl 4-Hydroxy-5-propionyl-3′-(trifluoromethyl)biphenyl-3-carboxylate (**3xi**).* The reaction was quenched with 2 M HCl aqueous solution, and the product was isolated as a white solid in 73% yield (534 mg): mp = 102−104 °C; R_f = 0.45 (petroleum ether/ethyl acetate = 5:1, v/v); IR (cm^{-1}, KBr) 3398, 1683, 1667, 1447, 1249, 763, 700; ^1H NMR ($CDCl_3$, 400 MHz) δ 12.3 (s, 1H), 8.26−8.25 (m, 1H), 8.21−8.20 (m, 1H), 7.79−7.74 (m, 2H), 7.63−7.56 (m, 2H), 4.49 (q, J = 7.1 Hz, 2H), 3.17 (q, J = 7.2 Hz, 2H), 1.46 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 202.7, 169.0, 161.3, 139.9, 134.6, 133.2, 131.3 (q, J = 32.1 Hz, 1C), 130.4, 130.0, 129.4, 126.3, 124.1 (q, J = 3.6 Hz, 1C), 123.4 (q, J = 3.7 Hz, 1C), 122.7, 115.7, 62.1, 36.1, 14.2, 8.2; HRMS calcd for $C_{19}H_{18}F_3O_4^+$ $[M + H]^+$ 367.1152, found 367.1150.

*3-Phenylpyridine (**3ya**).* The product was prepared as described in the typical procedure and isolated as a colorless oil in 81% yield (260 mg): R_f = 0.54 (petroleum ether/ethyl acetate = 5:1, v/v); IR (cm^{-1}, KBr) 3038, 1603, 1521, 699; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.87 (d, J = 1.6 Hz, 1H), 8.61−8.60 (m, 1H), 7.90−7.87 (m, 1H), 7.60−7.58 (m, 2H), 7.49 (t, J = 7.2 Hz, 2H), 7.44−7.36 (m, 2H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 148.4, 148.3, 137.8, 136.7, 134.4, 129.1, 128.1, 127.2, 123.6. Data were consistent with those reported in the literature.[41]

*Methyl 6-Phenylnicotinate (**3za**).* The product was prepared as described in the typical procedure and isolated as a white solid in 92% yield (400 mg): mp = 117−118 °C (lit. 118 °C); R_f = 0.53 (petroleum ether/ethyl acetate = 20:1, v/v); IR (cm^{-1}, KBr) 1716, 1596, 1288, 1117, 752, 698; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.71 (s, 2H), 7.64 (d, J = 5.0 Hz, 1H), 7.47−7.39 (m, 3H), 7.35−7.32 (m, 2H), 3.70 (s, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 167.3, 151.4, 148.9, 137.7, 137.1, 136.0, 128.5, 128.4, 128.1, 122.5, 52.4. Data were consistent with those reported in the literature.[42]

*5-Fluoro-4′-methylbiphenyl-2-amine (**5ag**).* The product was prepared as described in the typical procedure and isolated as a colorless oil in 90% yield (362 mg): R_f = 0.49 (petroleum ether/ethyl acetate =10:1, v/v); IR (cm^{-1}, KBr) 3422, 3375, 1712, 1599, 1487, 1241, 1168, 1034, 829, 814, 755, 697; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.33 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 7.6 Hz, 2H), 6.88−6.83 (m, 2H), 6.70−6.67 (m, 1H), 3.59 (s, 2H), 2.40 (s, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 156.4 (d, J = 234.7 Hz), 139.6 (d, J = 1.2 Hz), 137.4, 135.6 (d, J = 1.2 Hz), 129.6, 128.8, 116.7 (d, J = 22.2 Hz), 116.4 (d, J = 7.9 Hz), 114.6 (d, J = 22.2 Hz), 21.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −127.0. Data were consistent with those reported in the literature.[43]

*4-Fluoro-4′-methoxybiphenyl-2-amine (**5bb**).* The product was prepared as described in the typical procedure and isolated as a yellow oil in 67% yield (291 mg): R_f = 0.31 (petroleum ether/ethyl acetate = 5:1, v/v); IR (cm^{-1}, KBr) 3425, 3380, 1598 1480, 1167, 698; ^1H NMR(400 MHz, $CDCl_3$) δ 7.32 (d, J = 8.7 Hz, 2H), 7.25−7.00 (m, 1H), 6.97 (d, J = 8.7 Hz, 2H), 6.51−6.42 (m, 2H), 3.84 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 163.0 (d, J = 241.6 Hz), 158.9, 145.2 (d, J = 10.8 Hz), 131.6 (d, J = 9.7 Hz), 130.9, 130.3, 123.3 (d, J = 2.7 Hz), 114.3, 105.0 (d, J = 21.2 Hz), 101.9 (d, J = 24.6 Hz), 55.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ −135.1. Data were consistent with those reported in the literature.[44]

*5-Fluoro-2′-(trifluoromethyl)biphenyl-2-carboxylic Acid (**5cm**).* The reaction was quenched with 2 M HCl aqueous solution, and the product was isolated as a yellow solid in 81% yield (460 mg): mp = 164.5−165.4 °C; 81%; R_f = 0.49 (petroleum ether/ethyl acetate/acetic acid = 5:1:0.01); IR (cm^{-1}, KBr) 3421, 3066, 1692, 1600, 1435, 766; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.33 (s, 1H), 7.57−7.53 (m, 3H), 7.46−7.42 (m, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 167.7, 167.1, 136.5, 134.4, 131.1, 129.7, 129.5, 127.2, 126.4, 125.4, 124.7, 124.1, 115.2, 110.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −98.7, −104.6. Data were consistent with those reported in the literature.[10c]

*1-(4-Chloro-2-(naphthalen-1-yl)phenyl)ethanone (**5dl**).* The product was prepared as described in the typical procedure and isolated as a white solid in 85% yield (476 mg): mp = 118−120 °C; R_f = 0.52 (petroleum ether/ethyl acetate = 20:1, v/v); IR (cm^{-1}, KBr) 3061, 2998, 2937, 1682, 1608, 1421, 751, 698; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.92 (d, J = 8.2 Hz, 2H), 7.72 (d, J = 8.4 Hz, 1H), 7.58 (d, J = 8.4 Hz, 1H), 7.54−7.45 (m, 4H), 7.423−7.418 (m, 1H), 7.34−7.32 (m, 1H), 1.75 (s, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 201.6, 141.0, 139.4, 137.4, 137.1, 133.6, 131.7, 131.5, 130.1, 128.9, 128.5, 128.1, 127.3, 126.9, 126.3, 125.33, 125.31, 29.7; HRMS calcd for $C_{18}H_{14}ClO^+$ $[M + H]^+$ 281.0728, found 281.0726.

*(2′-Methoxy-biphenyl-2-yl)(4-chlorophenyl)methanone (**5em**).* The product was prepared as described in the typical procedure and isolated as a white solid in 92% yield (592 mg): mp = 97−98 °C; R_f = 0.38 (petroleum ether/ethyl acetate = 10:1, v/v); IR (cm^{-1}, KBr) 1659, 1572, 1497, 1319, 758; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.68 (d, J = 8.5 Hz, 2H), 7.59−7.54 (m, 1H), 7.48−7.38 (m, 3H), 7.30−7.18 (m, 4H), 6.97−6.93 (m, 1H), 6.67 (d, J = 8.2 Hz, 1H), 3.38 (s, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 195.7, 155.2, 138.7, 138.5, 137.9, 135.7, 131.5, 131.3, 131.0, 130.8, 129.3, 129.1, 128.5, 128.2, 126.8, 121.0, 110.2, 54.4. HRMS calcd for $C_{20}H_{16}ClO_2^+$ $[M + H]^+$ 323.0833, found 323.0831.

*5-Chloro-4′-methoxybiphenyl-2-amine (**5fb**).* The product was prepared as described in the typical procedure and isolated as a white solid in 78% yield (326 mg): mp = 83.5−85.5 °C (lit. 84.5−85.5 °C); R_f = 0.43 (petroleum ether/ethyl acetate = 10:1, v/v); IR (cm-1, KBr) 3463, 3372, 1608, 1487, 1241, 1168, 1034, 829, 814, 697; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.34 (d, J

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J. Org. Chem. 2017, 82, 1291−1300

= 8.6 Hz, 2H), 7.09−7.07 (m, 2H), 6.97 (d, J = 8.7 Hz, 2H), 6.71−6.68 (m, 1H), 3.84 (s, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 159.1, 142.3, 130.5, 130.1, 130.0, 128.7, 127.9, 123.1, 116.6, 114.4, 55.4. Data were consistent with those reported in the literature.[45]

*5-Bromo-4′-methoxybiphenyl-2-amine (**5gb**).* The product was prepared as described in the typical procedure and isolated as a white solid in 68% yield (377 mg): mp = 89−91 °C (lit. 89.1−90.6 °C); R_f = 0.42 (petroleum ether/ethyl acetate = 10:1, v/v); IR (cm^{-1}, KBr) 3458, 3369, 1598, 1477, 1290, 1168, 1034, 814, 697; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.33 (d, J = 8.8 Hz, 2H), 7.21−7.19 (m, 2H), 6.97 (d, J = 8.8 Hz, 2H), 6.63−6.61 (m, 1H), 3.84, (s, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 159.1, 142.9, 132.8, 130.7, 130.4, 130.1, 129.2, 117.0, 114.4, 110.1, 55.4. Data were consistent with those reported in the literature.[46]

Ethyl 2′,4′-Difluoro-4-hydroxybiphenyl-3-carboxylate (Diflunisal Ethyl Ester). The reaction was quenched with 2 M HCl aqueous solution, and the product was isolated as a pale yellow oil in 92% yield (450 mg); R_f = 0.55 (petroleum ether/ethyl acetate = 10:1, v/v); IR (cm^{-1}, KBr) 3137, 1679, 1485, 1439, 1210,766; ^1H NMR ($CDCl_3$, 400 MHz) δ 10.9 (s, 1H), 7.98−7.97 (m, 1H), 7.59 (d, J = 8.7 Hz, 1H), 7.40−7.34 (m, 1H), 7.05 (d, J = 8.6 Hz, 1H), 6.97−6.88 (m, 2H), 4.44 (q, J = 7.2 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$NMR ($CDCl_3$, 100 MHz) δ 170.0, 162.2 (dd, J = 247.2 Hz, J = 11.7 Hz, 1C), 161.3, 159.7 (dd, J = 248.0 Hz, J = 11.7 Hz, 1C), 136.1 (d, J = 2.9 Hz, 1C), 131.1(dd, J = 9.4 Hz, J = 4.9 Hz, 1C), 130.1 (d, J = 2.7 Hz, 1C), 126.0, 124.2 (dd, J = 13.4 Hz, J = 3.7 Hz, 1C), 117.8, 112.7, 111.6 (dd, J = 21.0 Hz, J = 3.7 Hz, 1C), 104.4 (dd, J = 26.5 Hz, J = 25.1 Hz, 1C), 61.7, 14.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −111.5 (d, J = 7.8 Hz, 1F), −113.7 (d, J = 7.4 Hz, 1F). Data were consistent with those reported in the literature.[47]

2′,4′-Difluoro-4-hydroxybiphenyl-3-carboxylic Acid (Diflunisal). The reaction was quenched with 2 M HCl aqueous solution, and the product was isolated as a white solid in 87% yield (425 mg): mp = 210−212 °C (lit., 210−211 °C); R_f = 0.33 (petroleum ether/ethyl acetate/acetic acid = 10:1:0.01, v/v/v); IR (cm^{-1}, KBr) 3098, 1682, 1600, 1496, 1467, 1326, 1162, 701; ^1H NMR (CD_3SOCD_3, 400 MHz) δ 7.92 (s, 1H), 7.70−7.67 (m, 1H), 7.61−7.55 (m, 1H), 7.39- 7.33 (m, 1H), 7.21−7.16 (m, 1H), 7.08 (d, J = 8.6 Hz, 1H); $^{13}C\{^1H\}$NMR (CD_3SOCD_3, 100 MHz) δ (ppm) 171.5, 160.7, 160.4 (dd, J = 245.1 Hz, J = 12.2 Hz, 1C), 158.9 (dd, J = 246.5 Hz, J = 12.3 Hz, 1C), 135.8 (d, J = 2.2 Hz, 1C), 131.5 (dd, J = 9.5 Hz, J = 4.6 Hz, 1C), 130.2 (d, J = 3.1 Hz, 1C), 125.1, 123.7 (dd, J = 13.2 Hz, J = 3.7 Hz, 1C), 117.5, 113.1, 112.0 (dd, J = 20.9 Hz, J = 3.6 Hz, 1C), 104.1 (t, J = 26.4 Hz, 1C); ^{19}F NMR (376 MHz, $CDCl_3$) δ −111.4 (d, J = 7.4 Hz, 1F), −114.2 (d, J = 7.4 Hz, 1F). Data were consistent with those reported in the literature.[48]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02354.

^1H NMR and ^{13}C NMR spectra for all products; ^{19}F NMR spectra for the fluorine-containing products; HRMS spectra for the new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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J. Org. Chem. 2017, 82, 1291−1300