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Nickel-Catalyzed Cross-Coupling of Aryl Fluorides and Organozinc Reagents

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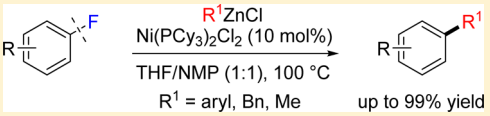
Supporting Information

ABSTRACT: $Ni(PCy_3)_2Cl_2$ was demonstrated to effectively catalyze cross-coupling of aryl fluorides and organozinc reagents. Both electron-poor and -rich aryl fluorides can react effectively with nucleophiles including aryl-, methyl-, and benzylzinc chlorides. A wide range of substituents and functional groups are tolerated. In the presence of a directing group, PhC(O), the reaction is selective for cleavage of the C−F bond *ortho* to the carbonyl substituent in a difluoroarene.



INTRODUCTION

Transition-metal-catalyzed activation and transformation of C−F bonds have received considerable attention over the years.[1] On one hand, fluorine forms the strongest known single bond to carbon. The conversion of organic fluorides is important for the fundamental understanding of the reactivity of very stable chemical bonds. On the other hand, activation of the carbon−fluorine bond is of importance for selective transformation of polyfluorinated compounds to partially fluorinated compounds which offer potential use in drug discovery and materials science.[1,2] The catalytic transformation of C−F bonds such as hydrodefluorination,[1e] C−C coupling,[1,3−7] C−N coupling,[8] and C−S coupling[9] of fluoride substrates has been reported. The reported C−C cross coupling includes Kumada coupling,[3] Negishi coupling,[1d,4] Suzuki coupling,[5] Stille coupling,[6] and Sonogashira coupling.[7] Among them, Kumada coupling of aryl fluorides appeared at very early stages of cross-coupling investigations, and subsequent studies also occurred more often than studies of other types of cross-coupling reactions. Negishi cross-coupling of aryl fluorides appeared relatively late, and only electron-poor fluoride substrates were successfully coupled. In addition, several Negishi cross-coupling reactions containing selective C−F bond activation of polyfluoroarenes for synthesis of partially fluorinated aromatics have been performed.[1d,4c−i] For example, Love et al. carried out platinum-catalyzed cross-coupling of polyfluoroarylimines with dimethylzinc in which the C−F bonds *ortho* to an imine substituent are selectively cleaved.[4d−f] Nakamura et al. performed nickel-catalyzed monosubstitution of polyfluoroarenes with organozinc reagents using alkoxydiphosphine ligand.[4c] Ogoshi et al. reported similar work using palladium(0)/PCy_3 catalyst.[4g] In our exploration of C−F bond activation we found that commercially available $Ni(PCy_3)_2Cl_2$ is an effective catalyst that can catalyze cross-coupling of activated and deactivated aryl fluorides with arylzinc reagents or β-hydrogen-free alkylzinc reagents and selective activation of C−F bonds in (2,5-difluorophenyl)(phenyl)methanone. Herein we report the results.

RESULTS AND DISCUSSION

We first screened the catalysts, solvents, and other reaction conditions using a model reaction between *p*-FC_6H_4OMe and 2.5 equiv of *p*-MeC_6H_4ZnCl prepared from *p*-MeC_6H_4Li and $ZnCl_2$ (Table 1). It has been reported that a 1:1 mixture of THF and NMP is a suitable solvent for cross-coupling of arylzinc reagents and aryl chlorides. We also employed 1:1 THF−NMP as the solvent to screen catalysts. $Pd(PPh_3)_2Cl_2$ and $Pd(OAc)_2$/dppp cannot give the desired products. $Pd(OAc)_2/PCy_3$ led to the corresponding cross-coupling product in low yield (Table 1, entries 1−3). Nickel complexes such as $Ni(dppe)Cl_2$ and $Ni(dppf)Cl_2$ gave better results compared with those mentioned above (Table 1, entries 4 and 5). This led us to explore nickel catalyts systematically. $Ni(acac)_2$ alone or a combination of $Ni(acac)_2$ and dppp or IPr·HCl was found to lead to the coupling product in 51%−72% yields (Table 1, entries 6−8). $Ni(PCy_3)_2Cl_2$ displayed a better catalytic activity, resulting in 74% yield of coupling product. By contrast, $Ni(PPh_3)_2Cl_2$ was inactive, and $Ni(PMe_3)_2Cl_2$ led to relatively low product yield (Table 1, entries 9−11). From the screened results it seems that an electron-rich ligand such as PCy_3 and IPr is better for the activation of C−F bonds. This may be because an electron-rich metal center is beneficial to the oxidative addition of the aryl fluoride. When 1.5 equiv of *p*-MeC_6H_4ZnCl were employed, the product yield decreased to 68% (Table 1, entry 12). However, if an additional 1 equiv of *p*-MeC_6H_4ZnCl was added after the reaction of *p*-FC_6H_4OMe and 1.5 equiv of *p*-MeC_6H_4ZnCl for 10 h, a marked increase of the yield was observed (Table 1, entry 13). Further improvement of the yield was carried out by changing the reaction temperature from 120 to 100 °C (both are bath temperature) (Table 1, entry 14). It was noted that decreasing the catalyst loading led to yield decrease (Table 1, entry 15). In the reaction, the presence of lithium ion seems to be important. If the zinc reagent used in the reaction was prepared from *p*-

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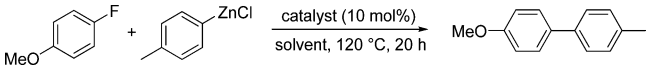
Table 1. Screening of Catalysts and Solvents in the Reaction of *p*-MeOC$_6$H$_4$F with *p*-MeC$_6$H$_4$ZnCl[a]



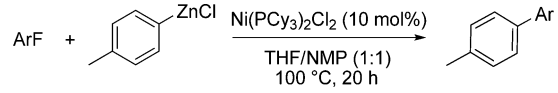
entry	catalyst	solvent	yield (%)
1	$Pd(PPh_3)_2Cl_2$	THF−NMP (1:1)	
2	$Pd(OAc)_2$ + 20 mol % dppp	THF−NMP (1:1)	
3	$Pd(OAc)_2$ + 20 mol % PCy_3	THF−NMP (1:1)	18
4	$Ni(dppe)Cl_2$	THF−NMP (1:1)	30
5	$Ni(dppf)Cl_2$	THF−NMP (1:1)	36
6	$Ni(acac)_2$	THF−NMP (1:1)	51
7	$Ni(acac)_2$ + 10 mol % dppp	THF−NMP (1:1)	66
8	$Ni(acac)_2$ + 20 mol % IPr·HCl	THF−NMP (1:1)	72
9	$Ni(PCy_3)_2Cl_2$	THF−NMP (1:1)	74
10	$Ni(PPh_3)_2Cl_2$	THF−NMP (1:1)	trace
11	$Ni(PMe_3)_2Cl_2$	THF−NMP (1:1)	44
12[b]	$Ni(PCy_3)_2Cl_2$	THF−NMP (1:1)	68
13[c]	$Ni(PCy_3)_2Cl_2$	THF−NMP (1:1)	90
14[c,d]	$Ni(PCy_3)_2Cl_2$	THF−NMP (1:1)	92
15[c,d,e]	$Ni(PCy_3)_2Cl_2$	THF−NMP (1:1)	80
16[g]	$Ni(PCy_3)_2Cl_2$	THF−NMP (1:1)	44
17[c,d,f]	$Ni(PCy_3)_2Cl_2$	THF−NMP (1:1)	56
18[c,d,f,g]	$Ni(PCy_3)_2Cl_2$	THF−NMP (1:1)	92
19	$Ni(PCy_3)_2Cl_2$	THF−NMP (1:2)	70
20	$Ni(PCy_3)_2Cl_2$	dioxane	26
21	$Ni(PCy_3)_2Cl_2$	toluene	
22	$Ni(PCy_3)_2Cl_2$	THF (reflux)	trace
23	$Ni(PCy_3)_2Cl_2$	THF−toluene (1:1)	trace
24	$Ni(PCy_3)_2Cl_2$	THF−dioxane (1:1)	39

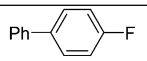
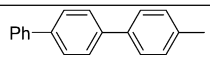
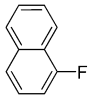
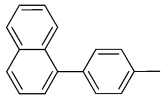
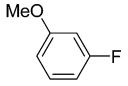
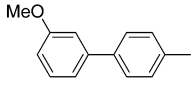
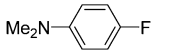
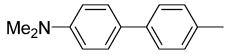
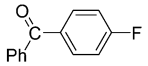
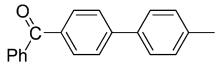
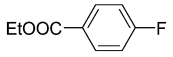
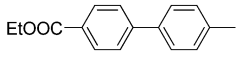
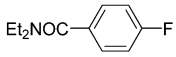
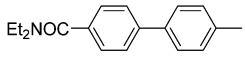
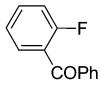
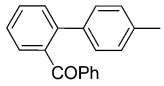
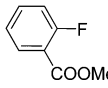
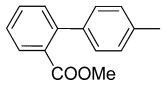
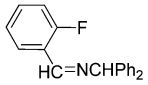
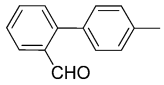
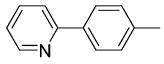
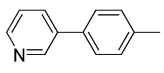
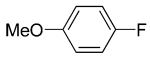
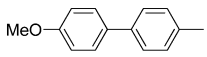
[a]Unless otherwise specified, the reactions were carried out on a 0.5 mmol scale according to the conditions indicated by the above equation; *p*-MeC$_6$H$_4$ZnCl was prepared from *p*-MeC$_6$H$_4$Li and $ZnCl_2$; 2.5 equiv of *p*-MeC$_6$H$_4$ZnCl was employed. [b]1.5 equiv of *p*-MeC$_6$H$_4$ZnCl was employed. [c]2.5 equiv of *p*-MeC$_6$H$_4$ZnCl was added in two portions. 1.5 equiv of *p*-MeC$_6$H$_4$ZnCl was added at first, after stirring for 10 h an additional 1 equiv of *p*-MeC$_6$H$_4$ZnCl was added. [d]The reaction was carried out at 100 °C. [e]5 mol % of $Ni(PCy_3)_2Cl_2$ was employed. [f]The *p*-MeC$_6$H$_4$ZnCl was prepared from *p*-MeC$_6$H$_4$MgBr and $ZnCl_2$. [g]2 equiv of LiCl was added.

MeC$_6$H$_4$MgBr and $ZnCl_2$, the product yield fell remarkably whether or not the zinc reagent was add in one or two portions (Table 1, entries 16 and 17). However, 2 equiv of LiCl additive evidently improved the reaction result (Table 1, entry 18). A similar phenomenon was observed by other groups.[4g,10a] The low reactivity of the zinc reagent prepared from a Grignard reagent and $ZnCl_2$ might be due to aggregation of the arylzinc reagent with the coproduct $MgCl_2$. The role of LiCl additive might include (i) to break the aggregation mentioned above and (ii) to enhance the elimination ability of fluorine through acting as a Lewis acid and forming a strong Li−F bond.[4a,g,10] In addition, $Ni(PCy_3)_2Cl_2$ was reported to be an effective catalyst for aryl−O bond activation.[11] However, no aryl-OMe activation product was obtained under the screening conditions. We also examined the solvent effect by employing different solvents in the reaction, including a 1:2 mixture of THF and NMP, dioxane, toluene, and THF and an equivalent mixture of THF and toluene or dioxane. However, the results showed that each of these solvents was less effective than a 1:1 mixture of THF and NMP (Table 1, entries 19−24).

Next, the scope of aryl fluorides was tested using *p*-MeC$_6$H$_4$ZnCl as the nucleophilic reagent under the optimized conditions (Table 2). Reaction of both 4-fluoro-1,1′-biphenyl and 1-fluoronaphthalene with *p*-MeC$_6$H$_4$ZnCl gave excellent

Table 2. Nickel-Catalyzed Coupling of Aryl or Heteroaryl Fluorides with *p*-MeC$_6$H$_4$ZnCl[a]



Entry	ArF	Product	Yield (%)
1			95
2			99
3			90
4[b]			75
5			88
6			81
7			98
8			89
9			86
10[c]			93
11[d]			99
12[d]			99
13[e]			90

[a]The reactions were carried out on a 0.5 mmol scale according to the conditions indicated by the above equation unless otherwise specified; *p*-MeC$_6$H$_4$ZnCl was prepared from *p*-MeC$_6$H$_4$Li and $ZnCl_2$. 1.5 equiv of *p*-MeC$_6$H$_4$ZnCl was added into the reaction system and reacted for 10 h; an additional 1 equiv of *p*-MeC$_6$H$_4$ZnCl was added. [b]Reaction was carried out at 120 °C. [c]3.0 equiv of *p*-MeC$_6$H$_4$ZnCl was added in one portion, and reaction was run at 80 °C. [d]2.5 equiv of *p*-MeC$_6$H$_4$ZnCl was added, and the reaction was run for 12 h. [e]The reaction was carried out on a 5 mmol scale.

yields (Table 2, entries 1 and 2). Deactivated aryl fluorides such as *p*-FC$_6$H$_4$OMe and *m*-FC$_6$H$_4$OMe also gave excellent results (Table 1, entries 13 and 14, and Table 2, entry 3). However, *p*-FC$_6$H$_4$NMe$_2$ resulted in relatively low yield (Table 2, entry 4). This is ascribed to strongly deactivated action of the amino group. A series of electron-withdrawing group substituted fluorobenzenes showed good reactivity (Table 2, entries 5−10), each giving high product yield. The high reactivity of the electron-poor aryl fluorides is because electron-withdrawing

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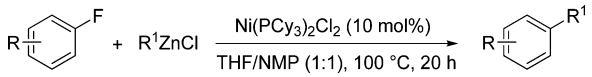
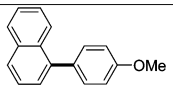
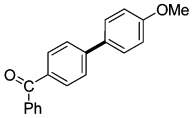
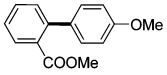
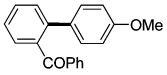
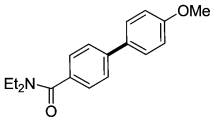
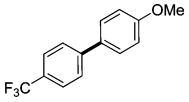
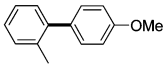
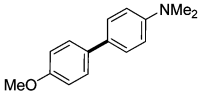
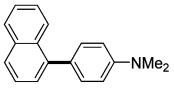
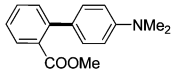
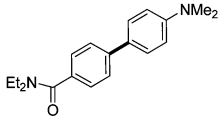
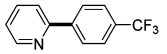
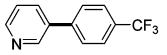
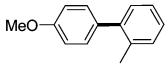
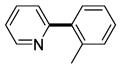
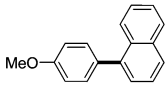
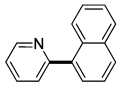
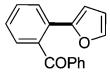
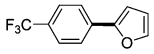
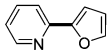
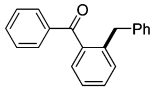
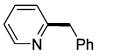
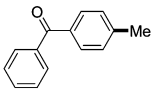
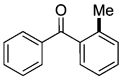
Table 3. Nickel-Catalyzed Coupling of Aryl Fluorides with Arylzinc/Alkylzinc Reagents[a]



Entry	ArF	R^1ZnCl	Product	Yield (%)
1	1-fluoronaphthalene	*p*-$MeOC_6H_4ZnCl$		84
2	*p*-$PhC(O)C_6H_4F$	*p*-$MeOC_6H_4ZnCl$		58
3	*o*-$MeOC(O)C_6H_4F$	*p*-$MeOC_6H_4ZnCl$		70
4	*o*-$PhC(O)C_6H_4F$	*p*-$MeOC_6H_4ZnCl$		72
5	*p*-$Et_2NC(O)C_6H_4F$	*p*-$MeOC_6H_4ZnCl$		97
6[b]	*p*-$CF_3C_6H_4F$	*p*-$MeOC_6H_4ZnCl$		90
7	*o*-MeC_6H_4F	*p*-$MeOC_6H_4ZnCl$		30
8[b]	*p*-$MeOC_6H_4F$	*p*-$Me_2NC_6H_4ZnCl$		96
9[b]	1-fluoronaphthalene	*p*-$Me_2NC_6H_4ZnCl$		93
10[b,c]	*o*-$MeOC(O)C_6H_4F$	*p*-$Me_2NC_6H_4ZnCl$		80
11[b,c]	*p*-$Et_2NC(O)C_6H_4F$	*p*-$Me_2NC_6H_4ZnCl$		97
12[b]	2-fluoropyridine	*p*-$CF_3C_6H_4ZnCl$		93
13[b]	3-fluoropyridine	*p*-$CF_3C_6H_4ZnCl$		76
14	*p*-$MeOC_6H_4F$	*o*-MeC_6H_4ZnCl		75
15	2-fluoropyridine	*o*-MeC_6H_4ZnCl		94
16	*p*-$MeOC_6H_4F$	(1-naphthyl)ZnCl		13
17[b]	2-fluoropyridine	(1-naphthyl)ZnCl		92
18	*o*-$PhC(O)C_6H_4F$	(2-furyl)ZnCl		91
19	*p*-$CF_3C_6H_4F$	(2-furyl)ZnCl		53
20	2-fluoropyridine	(2-furyl)ZnCl		86
21	*o*-$PhC(O)C_6H_4F$	$PhCH_2ZnCl$		88
22	2-fluoropyridine	$PhCH_2ZnCl$		92
23[d]	*p*-$PhC(O)C_6H_4F$	CH_3ZnCl		81
24[d]	*o*-$PhC(O)C_6H_4F$	CH_3ZnCl		99

[a]Unless otherwise specified, the reactions were carried out on a 0.5 mmol scale according to the conditions indicated by the above equation; R^1ZnCl was prepared from RLi and $ZnCl_2$ and was added into the reaction system in two portions; 1.5 equiv was added at first and an additional 1 equiv was added after 10 h. [b]2.5 equiv of ArZnCl was added in one portion. [c]Reaction was run at 80 °C. [d]3 equiv of CH_3ZnCl was added in one portion.

substituents on the aromatic rings are beneficial to the oxidative addition. *Ortho*-position substituted fluorobenzenes gave comparable results to their *para*-position partners. Functional groups including C(O)Ph, COOR, $CONEt_2$, and CH=$NCHPh_2$ can be tolerated. However, the CH=$NCHPh_2$ group was converted into a CHO group due to hydrolysis during workup. 2- and 3-fluoropyridines exhibited excellent reactivity when treated with *p*-MeC_6H_4ZnCl in the presence of $Ni(PCy_3)_2Cl_2$. The arylzinc reagent (2.5 equiv) was added in one portion, and the reaction can be completed in 12 h in almost quantitative yields (Table 2, entries 11 and 12). In addition, we examined reaction of *p*-FC_6H_4OMe with *p*-MeC_6H_4ZnCl on a 5 mmol scale. A yield was obtained similar to that of the 0.5 mmol scale under the same conditions (Table 2, entry 13).

Various zinc reagents were also tested for the couplings. *p*-$MeOC_6H_4ZnCl$ is a stronger nucleophilic reagent than *p*-MeC_6H_4ZnCl. However, it led to lower yields than *p*-MeC_6H_4ZnCl when reacted with aryl fluorides including 1-fluoronaphthalene, *p*-$PhC(O)C_6H_4F$, *o*-$MeOC(O)C_6H_4F$, and *o*-$PhC(O)C_6H_4F$ with unestablished reasons (Table 3, entries 1−4). Reaction of *p*-$MeOC_6H_4ZnCl$ with *p*-$Et_2NC(O)C_6H_4F$ or *p*-$CF_3C_6H_4F$ gave excellent results (Table 3, entries 5 and 6). *o*-MeC_6H_4F exhibited low reactivity upon reaction with *p*-$MeOC_6H_4ZnCl$ (Table 3, entry 7). This might be due to steric hindrance of he methyl group in *o*-MeC_6H_4F. *p*-$Me_2NC_6H_4ZnCl$ showed excellent reactivity toward either electron-rich or electron-poor fluoroarenes (Table 3, entries 8−11). *p*-$CF_3C_6H_4ZnCl$ showed relatively weak nucleophilicity. It did not react with *p*-$MeOC_6H_4Cl$. However, it can couple with 2- or 3-fluoropyridine, forming the desired coupling products in 93% and 76% yields, respectively. Both *o*-MeC_6H_4ZnCl and (1-naphthyl)ZnCl are hindral nucleophiles. Reaction of *o*-MeC_6H_4ZnCl with *p*-$MeOC_6H_4Cl$ gave 75% yield of the

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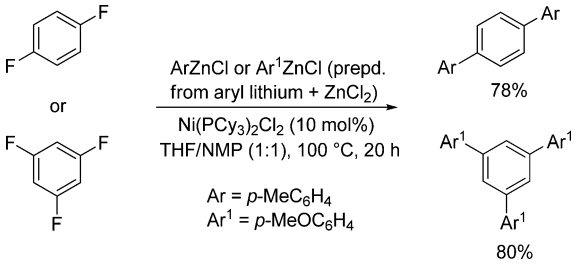
cross-coupling product, while reaction of (1-naphthyl)ZnCl with *p*-$MeOC_6H_4Cl$ afforded the corresponding product in only 13% yield. However, both zinc reagents resulted in high product yields when reacted with 2-fluoropyridine (Table 3, entries 15 and 17). The reactivity of (2-furyl)ZnCl was also tested. It reacted smoothly with activated fluoroarenes such as *o*-$PhC(O)C_6H_4F$ and 2-fluoropyridine and gave high product yields, but its reaction with *p*-$CF_3C_6H_4F$ led to relatively low yield. No reaction took place between (2-furyl)ZnCl and *p*-$MeOC_6H_4Cl$. *β*-Hydrogen-free alkylzinc reagents such as $PhCH_2ZnCl$ and MeZnCl can be used as the nucleophiles in the cross-coupling reactions (Table 3, entries 21−24). *p*-$PhC(O)C_6H_4F$, *o*-$PhC(O)C_6H_4F$, and 2-fluoropyridine were proven to couple with $PhCH_2ZnCl$ or MeZnCl effectively, affording the desired products in excellent yields. Reaction of *β*-hydrogen-containing alkylzinc reagents with an aryl fluoride resulted in a mixture of cross-coupling product and reductive product of the aryl fluoride. This showed that partial *β*-hydrogen elimination occurred during the reaction process. Recently, Love and co-workers carried out $Ni(PEt_3)_2Cl_2$-catalyzed cross-couplings of aryl fluorides with imino directing group and *β*-hydrogen-containing alkylzinc reagents.[4i] In the reactions, it seems that the PEt_3 ligand and the imino group together provide a proper coordination environment for the central nickel atom which effectively suppresses *β*-hydrogen elimination from the reaction intermediates. The preparative method of the organozinc reagents and reaction conditions such as reaction temperature and solvents may also be responsible for the outcomes in comparison with our reaction system.

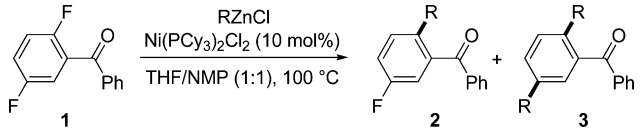
Di- or trifluorobenzenes were also effectively coupled with arylzinc reagents under the conditions mentioned above (Scheme 1). Reaction of 1,4-difluorobenzene with 5.0 equiv

Scheme 1. Nickel-Catalyzed Cross-Coupling of Multibenzenes with Arylzinc Chlorides



of *p*-MeC_6H_4ZnCl afforded 1,4-bis(*p*-tolyl)benzene in 78% yield. Treatment of 1,3,5-trifluorobenzene with 7.5 equiv of *p*-$MeOC_6H_4ZnCl$ (4.5 equiv of ArZnCl was added at first and then an additional 3 equiv of ArZnCl was added after 10 h) gave 1,3,5-tris(4-methoxyphenyl)benzene in 80% yield. Attempts to selectively prepare a monoarylated product using a smaller amount of arylzinc reagents under the same catalyst and conditions were unsuccessful. This may result from "ring walking" in the product/catalyst complex caused by strong back-donation as indicated by Nakamura et al.[4c] Two strategies have been used to achieve selective C−F monofunctionalization from polyfluoroarenes. One is ligand design and metal ligand cooperation. The proper ligands can provide the most appropriate coordination environment for the metal center, which makes the catalyst complex suppress multisubstitution of polyfluoroarenes caused by ring walking. The other strategy is to introduce a suitable directing group onto the fluoride substrate. Indeed, in the presence of a directing group PhC(O) in the fluoride substrate partial C−F bond activation can be carried out by $Ni(PCy_3)_2Cl_2$ (Table 4). Reaction of (2,5-

Table 4. Selective Substitution of (2,5-Difluorophenyl)(phenyl)methanone[a]



			yield (%)	
entry	RZnCl	time (h)	**2**	**3**
1	*p*-MeC_6H_4ZnCl (1.5 equiv)	12	85	0
2	(2-furyl)ZnCl (1.5 equiv)	12	79	0
3[b]	$PhCH_2ZnCl$ (1.5 equiv)	16	52	0
4[c]	$PhCH_2ZnCl$ (2.5 equiv)	16	61	0
5[d]	CH_3ZnCl (2.5 equiv)	16	91	9

[a]The reactions were carried out on a 0.5 mmol scale according to the conditions indicated by the above equation; R^1ZnCl was prepared from R^1Li and $ZnCl_2$ and was added into the reaction system in one portion. [b]A mixture of **2** and starting material was obtained, and their ratio was calculated by ^1H NMR integrals. [c]Products isolated by preparative TLC. [d]GC yield.

difluorophenyl)(phenyl)methanone with 1.5 equiv of *p*-MeC_6H_4ZnCl under the same catalyst, solvents, and temperature as above for 12 h afforded an *o*-arylated product (4-fluoro-4′-methylbiphenyl-2-yl)(phenyl)methanone in 85% yield. No 5-position arylated product or biarylated product was obtained. A similar *ortho*-arylated product was obtained when (2-furyl)ZnCl was employed as the nucleophile (Table 4, entry 2). A small amount of starting material was determined by TLC in the reactions with either *p*-MeC_6H_4ZnCl or (2-furyl)ZnCl. $PhCH_2ZnCl$ showed relatively low reactivity. Reaction of 1.5 equiv of $PhCH_2ZnCl$ with (2,5-difluorophenyl)(phenyl)-methanone under the same conditions for 16 h gave a mixture of *o*-benzylated product (52%) and starting material (41%). Excess $PhCH_2ZnCl$ (2.5 equiv) can lead to an increase of the yield of *o*-benzylated product (61% yield), but 21% of the starting material still remained (Table 4, entries 3 and 4). MeZnCl exhibited higher reactivity than $PhCH_2ZnCl$ in the reaction with (2,5-difluorophenyl)(phenyl)methanone. The reaction resulted in 91% yield of *o*-methylated product (5-fluoro-2-methylphenyl)(phenyl)methanone, accompanied by 9% yield of bimethylated product (2,5-dimethylphenyl)-(phenyl)methanone (Table 4, entry 5). We also tested other potential directing groups including COOMe and imine group in a difluoride system, but both led to mixtures when they reacted with *p*-MeC_6H_4ZnCl under the same conditions as above.

Our previous work showed that the C−CN bond of *p*-FC_6H_4CN can be catalytically cut off and coupled with a manganese reagent.[12] In the present study, we noticed that the C−CN bond and C−F bond can be sequentially activated and coupled in one pot, giving an unsymmetrical terphenyl (Scheme 2). In this reaction, two very inert chemical bonds were respectively activated. The $Ni(PMe_3)_2Cl_2$ catalyst and excess manganese reagent added in the first step did not affect the following Negishi-type coupling.

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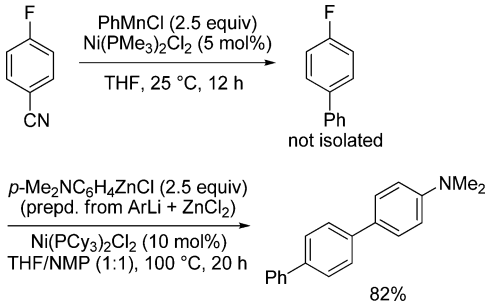
Scheme 2. Sequential Cross-Coupling To Construct Unsymmetrical Terphenyl

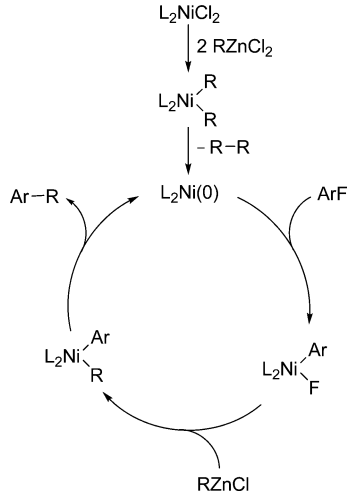


A preliminary study of the mechanism for the nickel-catalyzed reaction of aryl fluorides with organozinc reagents was also carried out. The reaction of *p*-FC_6H_4OMe with *p*-MeC_6H_4ZnCl was first tested in the absence of $Ni(PCy_3)_2Cl_2$ in a mixed solvent of THF and NMP (1:1) at 120 °C for 20 h. No cross-coupling product was obtained. Next we tested the reaction of (2-fluorophenyl)(phenyl)methanone with *p*-$MeOC_6H_4ZnCl$ in the absence of $Ni(PCy_3)_2Cl_2$ in THF–NMP (1:1) at 100 °C for 12 h. No cross-coupling product can be isolated either. These experimental facts ruled out the possibility of a direct nucleophilic substitution and a coordination-assisted nucleophilic substitution. 1,1-Diphenylethylene additive (an equimolar amount with *p*-FC_6H_4OMe) did not affect the reaction of *p*-FC_6H_4OMe with *p*-MeC_6H_4ZnCl catalyzed by $Ni(PCy_3)_2Cl_2$ (10 mol %). It seems that the reaction did not proceed via a free-radical process. Further experiment showed that a mixture of $Ni(COD)_2$ (10 mol %) and PCy_3 (20 mol %) effectively catalyzed the cross-coupling of *p*-FC_6H_4OMe with *p*-MeC_6H_4ZnCl, giving the desired product in 76% yield. Hence, the active catalyst may be a Ni(0) species. Attempts to isolate the oxidative addition product of Ni(0) and aryl fluoride via reaction of $Ni(COD)_2/2PCy_3$ and (2-fluorophenyl)(phenyl)methanone failed. Reaction of $Ni(COD)_2/2PCy_3$ and 1 equiv of (2-fluorophenyl)(phenyl)methanone was run at 80 °C for 12 h. The $^{19}F\{1H\}$ NMR spectrum of the reaction mixture showed that about 30% of (2-fluorophenyl)(phenyl)methanone was transformed to a new species, supposing oxidative addition product. Most (2-fluorophenyl)(phenyl)methanone remained. However, after *p*-MeC_6H_4ZnCl (2.5 equiv) was added into the reaction system and the mixture was stirred at 100 °C for 12 h, the cross-coupling product was obtained in 94% yield. Hence, arylzinc reagent may promote the oxidative addition process. Based on the above experimental facts and the mechanism studies of transition-metal-catalyzed cross-coupling reactions reported in the literature,[13] a possible mechanism is proposed as shown in Scheme 3. Thus, a Ni(0) species is first generated by reaction of $Ni(PCy_3)_2Cl_2$ with the zinc reagent. The Ni(0) species $L_2Ni(0)$ reacts with ArF results in a oxidative addition product $L_2Ni(F)Ar$. Reaction of $L_2Ni(F)Ar$ with a organozinc reagent, RZnCl, affords $L_2Ni(R)Ar$ which undergoes reductive elemination to give cross-coupling product and regenerates $L_2Ni(0)$.

CONCLUSION

We have demonstrated that the cross-coupling of aryl fluorides with organozinc reagents can be carried out using $Ni(PCy_3)_2Cl_2$ as the catalyst. Both activated and deactivated aryl fluorides can be efficiently coupled. Electron-rich and electron-poor arylzinc reagents including substituted phenylzinc chlorides, 1-naphthylzinc chloride, and 2-furylzinc chloride and *β*-hydrogen free alkylzinc reagents such as benzylzinc chloride and methylzinc chloride were proven to be suitable nucleophiles. Pyridyl ring and a range of functional groups involving NMe_2, OMe, CF_3, COOEt, $C(O)NEt_2$, PhC(O), and imino groups were tolerated. We also confirmed that the PhC(O) group is an effective directing group for the selective activation of C–F bonds in (2,5-difluorophenyl)(phenyl)-methanone molecule, with *o*-arylated or *o*-alkylated products being formed.

Scheme 3. Proposed Mechanism for the Coupling of Aryl Fluorides and Organozinc Reagents



EXPERIMENTAL SECTION

The reactions were performed under nitrogen atmosphere. Toluene and 1,4-dioxane were distilled under nitrogen over sodium and degassed prior to use. THF was distilled under nitrogen over sodium/benzophenone and degassed prior to use. NMP was dried over 4 Å molecular sieves, fractionally distilled under reduced pressure, and stored under nitrogen atmosphere. *N*-(2-Fluorobenzylidene)-1,1-diphenylmethanamine[14] and aryllithium reagents[15] were prepared according to literature methods. Other chemicals and solvents were purchased from commercial venders and used as received. NMR spectra were determined on a 300 or 400 MHz NMR spectrometer at room temperature using $CDCl_3$ as solvent. The chemical shifts of the ^1H and ^{13}C NMR spectra were referenced to TMS or internal solvent resonances. High-resolution mass spectra (HR-MS) were acquired in the electron impact mode (EI) using a TOF mass analyzer.

General Procedure for Reaction of Aryl Fluorides with RZnCl. A Schlenk tube was charged with aryl fluoride (0.5 mmol), $Ni(PCy_3)_2Cl_2$ (34.6 mg, 0.05 mmol), and NMP (1.5 mL). To the solution was added a solution of RZnCl (1.5 mL, 0.5 M in THF, 1.5 mmol) at 25 °C with stirring. After the mixture was stirred at 100 °C (bath temperature) for 10 h, NMP (1 mL) and RZnCl (1 mL, 0.5 M in THF, 1 mmol) were successively added. The resulting mixture was stirred at 100 °C (bath temperature) for an additional 10 h. Water (10 mL) and several drops of acetic acid were successively added into the Schlenk tube. The mixture was extracted with Et_2O (3 × 10 mL). The combined organic phases were dried over Na_2SO_4, concentrated by rotary evaporation, and purified by column chromatography on silica gel.

Spectral Data for the Cross-Coupling Products. *4-Methoxy-4′-methylbiphenyl.*[16] Eluent: petroleum ether; yield 92 mg (92%). ^1H NMR: δ 2.36 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 6.94 (d, J = 8.7 Hz, 2H, C_6H_4), 7.20 (d, J = 8.2 Hz, 2H, C_6H_4), 7.43 (d, J = 8.1 Hz, 2H, C_6H_4), 7.49 (d, J = 8.6 Hz, 2H, C_6H_4). $^{13}C\{^1H\}$ NMR: δ 21.2, 55.4, 114.3, 126.7, 128.1, 129.6, 133.9, 136.4, 138.1, 159.1.

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4-(4-Methylphenyl)biphenyl.[5a] Eluent: petroleum ether; yield 116 mg (95%). ^{1}H NMR: δ 2.40 (s, 3H), 7.25 (d, J = 8.1 Hz, 2H), 7.31−7.37 (m, 1H), 7.44 (t, J = 7.5 Hz, 2H), 7.53 (d, J = 8.1 Hz, 2H), 7.63 (d, J = 7.2 Hz, 2H), 7.65 (s, 4H). ^{13}C{^{1}H} NMR: δ 21.3, 127.0, 127.2, 127.4, 127.6, 128.9, 129.7, 137.3, 138.0, 140.0, 140.2, 140.9.

1-p-Tolylnaphthalene.[16] Eluent: petroleum ether; yield 108 mg (99%). ^{1}H NMR: δ 2.45 (s, 3H, CH_3), 7.29 (d, J = 8.1 Hz, 2H, Ar), 7.38−7.53 (m, 6H, Ar), 7.83 (d, J = 8.1 Hz, 1H, Ar), 7.90 (t, J = 8.1 Hz, 2H, Ar). ^{13}C{^{1}H} NMR: δ 21.4, 125.5, 125.9, 126.1, 126.3, 127.0, 127.6, 128.4, 129.1, 130.1, 131.9, 134.0, 137.1, 138.0, 140.4.

3-Methoxy-4′-methylbiphenyl.[17] Eluent: petroleum ether; yield 90 mg (90%). ^{1}H NMR: δ 2.39 (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 6.87 (dd, J = 2.4, 8.1 Hz, 1H, C_6H_4), 7.11 (s, 1H, C_6H_4), 7.16 (d, J = 7.8 Hz, 1H, C_6H_4), 7.24 (d, J = 7.8 Hz, 2H, C_6H_4), 7.33 (t, J = 7.9 Hz, 1H, C_6H_4), 7.48 (d, J = 8.1 Hz, 2H, C_6H_4). ^{13}C{^{1}H} NMR: δ 21.2, 55.4, 112.5, 112.9, 119.6, 127.2, 129.6, 129.8, 137.3, 138.4, 142.9, 160.1.

4′-Methyl-N,N-dimethylbiphenyl-4-amine.[16] Eluent: petroleum ether/ethyl acetate = 100:1; yield 79 mg (75%). ^{1}H NMR: δ 2.28 (s, 3H, CH_3), 2.88 (s, 6H, NCH_3), 6.70 (d, J = 8.7 Hz, 2H, C_6H_4), 7.11 (d, J = 7.8 Hz, 2H, C_6H_4), 7.35−7.41 (m, 4H, C_6H_4). ^{13}C{^{1}H} NMR: δ 21.2, 40.8, 113.0, 126.3, 127.7, 129.5, 135.7, 138.5, 149.9.

(4′-Methylbiphenyl-4-yl)(phenyl)methanone.[18] Eluent: petroleum ether/ethyl acetate = 100:1; yield 120 mg (88%). ^{1}H NMR: δ 2.31 (s, 3H), 7.18 (d, J = 7.8 Hz, 2H), 7.36−7.51 (m, 5H, C_6H_4), 7.58 (d, J = 8.4 Hz, 2H), 7.71−7.79 (m, 4H). ^{13}C{^{1}H} NMR: δ 21.3, 126.8, 127.2, 128.4, 129.8, 130.1, 130.8, 132.4, 136.1, 137.2, 138.0, 138.3, 145.3, 196.4.

Ethyl 4′-Methylbiphenyl-4-carboxylate.[18] Eluent: petroleum ether/ethyl acetate = 120:1; yield 97 mg (81%). ^{1}H NMR: δ 1.32 (t, J = 7.2 Hz, 3H), 2.32 (s, 3H), 4.31 (q, J = 7.2 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H), 7.44 (d, J = 8.1 Hz, 2H), 7.55 (d, J = 8.4 Hz, 2H), 8.01 (d, J = 8.4 Hz, 2H). ^{13}C{^{1}H} NMR: δ 14.5, 21.3, 61.0, 126.9, 127.2, 129.1, 129.8, 130.2, 137.3, 138.2, 145.6, 166.7.

N,N-Diethyl-4′-methylbiphenyl-4-carboxamide.[18] Eluent: petroleum ether/ethyl acetate = 8:1; yield 131 mg (98%). ^{1}H NMR: δ 1.18 (b, 6H), 2.38 (s, 3H), 3.32 (b, 2H), 3.52 (b, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 8.1 Hz, 2H), 7.48 (d, J = 8.0 Hz, 2H), 7.58 (d, J = 8.1 Hz, 2H). ^{13}C{^{1}H} NMR: δ 12.8, 14.2, 21.0, 39.2, 43.2, 126.7, 126.8, 129.5, 135.6, 137.4, 141.8, 171.0.

(4′-Methylbiphenyl-2-yl)(phenyl)methanone.[19] Eluent: petroleum ether/ethyl acetate = 100:1; yield 121 mg (89%). ^{1}H NMR: δ 2.12 (s, 3H), 6.89 (d, J = 7.8 Hz, 2H), 7.05 (d, J = 8.1 Hz, 2H), 7.15 (t, J = 7.8 Hz, 2H), 7.26−7.46 (m, 5H), 7.56 (d, J = 7.2 Hz, 2H). ^{13}C{^{1}H} NMR: δ 21.1, 126.8, 128.2, 128.7, 128.9, 129.1, 130.0, 130.2, 130.3, 132.9, 137.1, 137.4, 137.5, 139.0, 141.2, 198.8.

Methyl 2-(p-tolyl)benzoate.[20] Eluent: petroleum ether/ethyl acetate = 120:1; yield 113 mg (86%). ^{1}H NMR: δ 2.28 (s, 3H), 3.55 (s, 3H), 7.10 (s, 4H), 7.26 (t, J = 6.9 Hz, 2H), 7.36−7.41 (m, 1H), 7.69 (d, J = 6.9 Hz, 1H). ^{13}C{^{1}H} NMR: δ 21.2, 51.9, 127.0, 128.3, 128.9, 129.8, 130.8, 131.0, 131.2, 136.9, 138.4, 142.5, 169.3.

2-(p-Tolyl)benzaldehyde.[19] Eluent: petroleum ether/ethyl acetate = 100:1; yield 91 mg (93%). ^{1}H NMR: δ 2.34 (s, 3H), 7.19 (s, 4H), 7.33−7.40 (m, 2H), 7.53 (dt, J = 1.5, 7.5 Hz, 1H), 7.94 (dd, J = 1.2, 7.8 Hz, 1H), 9.90 (s, 1H). ^{13}C{^{1}H} NMR: δ 21.3, 127.7, 127.7, 129.3, 130.1, 130.9, 133.6, 133.9, 134.9, 138.2, 146.1, 192.7.

2-p-Tolylpyridine.[16] Eluent: petroleum ether/ethyl acetate = 30:1; yield 84 mg (99%). ^{1}H NMR: δ 2.38 (s, 3H), 7.11−7.19 (m, 1H), 7.26 (d, J = 8.1 Hz, 2H), 7.67 (d, J = 3.6 Hz, 2H), 7.88 (d, J = 8.1 Hz, 2H), 8.66 (d, J = 4.8 Hz, 1H). ^{13}C{^{1}H} NMR: δ 21.2, 120.3, 121.8, 126.8, 129.5, 136.7, 139.0, 149.7, 157.5.

3-p-Tolylpyridine.[21] Eluent: petroleum ether/ethyl acetate = 30:1; yield 84 mg (99%). ^{1}H NMR: δ 2.39 (s, 3H), 7.26 (d, J = 7.8 Hz, 2H), 7.28−7.33 (m, 1H), 7.46 (d, J = 8.1 Hz, 2H), 7.80−7.84 (m, 1H), 8.55 (dd, J = 1.5, 4.8 Hz, 1H), 8.83 (dd, J = 0.9, 2.4 Hz, 1H). ^{13}C{^{1}H} NMR: δ 20.8, 123.5, 127.0, 129.8, 134.1, 135.0, 136.6, 138.0, 148.2.

1-(4-Methoxyphenyl)naphthalene.[5a] Eluent: petroleum ether; yield 98 mg (84%). ^{1}H NMR: δ 3.73 (s, 3H), 6.89 (d, J = 8.6 Hz, 2H), 7.26−7.39 (m, 6H), 7.68−7.83 (m, 3H). ^{13}C{^{1}H} NMR: δ 55.4, 113.8, 125.5, 125.8, 126.0, 126.2, 127.0, 127.5, 128.4, 131.2, 131.9, 133.2, 134.0, 140.0, 159.1.

(4′-Methoxybiphenyl-4-yl)(phenyl)methanone.[22] Eluent: petroleum ether/ethyl acetate = 8:1; yield 84 mg (58%). ^{1}H NMR: δ 3.87 (s, 3H), 7.01 (d, J = 8.8 Hz, 2H), 7.50 (d, J = 8 Hz, 2H), 7.58−7.61 (m, 3H), 7.66 (d, J = 8.4 Hz, 2H), 7.83 (d, J = 7.2 Hz, 2H), 7.88 (d, J = 8.4 Hz, 2H). ^{13}C{^{1}H} NMR: δ 55.5, 114.6, 126.5, 128.4, 128.5, 130.1, 130.9, 132.4, 132.5, 135.7, 138.0, 145.0, 160.0, 196.4.

Methyl 4′-Methoxybiphenyl-2-carboxylate.[19] Eluent: petroleum ether/ethyl acetate = 100:1; yield 85 mg (70%). ^{1}H NMR: δ 3.65 (s, 3H), 3.81 (s, 3H), 6.92 (d, J = 8.7 Hz, 2H), 7.23 (d, J = 8.7 Hz, 2H), 7.32−7.37 (m, 2H), 7.45−7.50 (m, 1H), 7.76−7.79 (m, 1H). ^{13}C{^{1}H} NMR: δ 52.0, 55.3, 113.6, 126.8, 129.5, 129.8, 130.8, 131.0, 131.2, 133.7, 142.1, 159.1, 169.4.

(4′-Methoxylbiphenyl-2-yl)(phenyl)methanone.[23] Eluent: petroleum ether/ethyl acetate = 100:1; yield 104 mg (72%). ^{1}H NMR: δ 3.59 (s, 3H), 6.63 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H), 7.16 (t, J = 7.7 Hz, 2H), 7.27−7.46 (m, 5H), 7.55 (d, J = 7.5 Hz, 2H). ^{13}C{^{1}H} NMR: δ 55.2, 113.9, 126.7, 128.2, 128.7, 129.97, 130.04, 130.2, 130.4, 132.7, 132.9, 137.5, 139.0, 140.8, 159.1, 199.0.

N,N-Diethyl-4′-methoxybiphenyl-4-carboxamide.[16] Eluent: petroleum ether/ethyl acetate = 8:1; yield 137 mg (97%). ^{1}H NMR: δ 1.17 (b, 6H), 3.31 (b, 2H), 3.50 (b, 2H,), 3.79 (s, 3H), 6.94 (d, J = 8.7 Hz, 2H), 7.40 (d, J = 8.1 Hz, 2H), 7.50 (d, J = 8.7 Hz, 2H), 7.54 (d, J = 8.1 Hz, 2H). ^{13}C{^{1}H} NMR: δ 13.0, 14.2, 39.1, 43.0, 55.0, 114.2, 126.4, 126.8, 128.0, 132.7, 135.4, 141.5, 159.4, 171.1.

4-Trifluoromethyl-4′-methoxybiphenyl.[3h] Eluent: petroleum ether; yield 114 mg (90%). ^{1}H NMR: δ 3.88 (s, 3H), 7.02 (d, J = 8.7 Hz, 2H), 7.56 (d, J = 8.7 Hz, 2H), 7.67 (s, 4H). ^{13}C{^{1}H} NMR: δ 55.5, 114.6, 124.6 (q, J = 271.9 Hz), 125.8 (q, J = 3.9 Hz), 127.0, 128.5, 128.8 (q, J = 32.4 Hz), 132.3, 144.3, 160.0.

4-Methoxy-2′-methylbiphenyl.[16] Eluent: petroleum ether; yield 74 mg (75%). ^{1}H NMR: δ 2.27 (s, 3H), 3.84 (s, 3H), 6.94 (d, J = 8.7 Hz, 2H), 7.21−7.26 (m, 6H). ^{13}C{^{1}H} NMR: δ 20.7, 55.4, 113.6, 125.9, 127.1, 130.0, 130.4, 130.4, 134.5, 135.6, 141.7, 158.7.

4′-Methoxy-N,N-dimethylbiphenyl-4-amine.[16] Eluent: petroleum ether/ethyl acetate = 100:1; yield 109 mg (96%). ^{1}H NMR: δ 2.99 (s, 6H), 3.85 (s, 3H), 6.83 (d, J = 8.7 Hz, 2H), 6.96 (d, J = 8.7 Hz, 2H), 7.45−7.51 (m, 4H). ^{13}C{^{1}H} NMR: δ 40.9, 55.5, 113.2, 114.3, 127.5, 134.1, 149.7, 158.4.

N,N-Dimethyl-4-(naphthalen-1-yl)aniline.[3h] Eluent: petroleum ether/ethyl acetate = 100:1; yield 115 mg (93%). ^{1}H NMR: δ 2.85 (s, 6H), 6.71 (d, J = 8.7 Hz, 2H), 7.25−7.38 (m, 6H), 7.65 (d, J = 7.9 Hz, 1H), 7.73 (d, J = 8.7 Hz, 1H), 7.91 (d, J = 7.5 Hz, 1H). ^{13}C{^{1}H} NMR: δ 40.7, 112.5, 125.6, 125.7, 125.8, 126.5, 126.9, 127.0, 128.4, 129.0, 131.0, 132.1, 134.1, 140.6, 149.9.

Methyl 4′-(Dimethylamino)biphenyl-2-carboxylate.[20] Eluent: petroleum ether/ethyl acetate = 60:1; yield 102 mg (80%). ^{1}H NMR: δ 2.97 (s, 6H), 3.68 (s, 3H), 6.75 (d, J = 8.5 Hz, 2H), 7.21 (d, J = 8.7 Hz, 2H), 7.31 (t, J = 7.4 Hz, 1H), 7.37 (d, J = 7.5 Hz, 1H), 7.46 (t, J = 7.2 Hz, 1H), 7.73 (d, J = 7.5 Hz, 1H). ^{13}C{^{1}H} NMR: δ 40.9, 52.0, 112.2, 126.2, 129.1, 129.2, 129.6, 130.6, 130.9, 131.1, 142.4, 149.9, 170.0.

4′-(Dimethylamino)-N,N-diethylbiphenyl-4-carboxamide.[20] Eluent: petroleum ether/ethyl acetate = 4:1; yield 144 mg (97%). ^{1}H NMR: δ 1.19 (b, 6H), 3.00 (s, 6H), 3.37 (b, 2H), 3.48 (b, 2H), 6.80 (d, J = 8.8 Hz, 2H), 7.40 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.8 Hz, 2H), 7.57 (d, J = 8.2 Hz, 2H). ^{13}C{^{1}H} NMR: δ 13.0, 14.0, 39.4, 40.5, 43.1, 112.8, 126.0, 126.9, 127.7, 128.2, 134.7, 142.1, 150.3, 171.5.

2-(4-(Trifluoromethyl)phenyl)pyridine.[24] Eluent: petroleum ether/ethyl acetate = 30:1; yield 104 mg (93%). ^{1}H NMR: δ 7.28−7.32 (m, 1H), 7.72−7.83 (m, 4H), 8.11 (d, J = 8.1 Hz, 2H), 8.73 (d, J = 4.8 Hz, 1H). ^{13}C{^{1}H} NMR: δ 120.9, 123.1, 124.4 (q, J = 272.2 Hz), 125.8 (q, J = 3.9 Hz), 127.3, 130.9 (q, J = 32.4 Hz), 137.1, 142.8, 150.1, 156.0.

3-(4-(Trifluoromethyl)phenyl)pyridine.[25] Eluent: petroleum ether/ethyl acetate = 8:1; yield 84 mg (76%). ^{1}H NMR: δ 7.41−7.47 (m, 1H), 7.70 (d, J = 8.1 Hz, 2H), 7.75 (d, J = 8.1 Hz, 2H), 7.91 (d, J = 6 Hz, 1H), 8.67 (s, 1H), 8.88 (s, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 115.8, 123.9, 124.2 (q, J = 272.2 Hz), 126.2 (q, J = 3.8 Hz), 127.6, 130.4 (q, J = 32.6 Hz), 134.7, 135.5, 141.4, 148.3, 149.3.

2-o-Tolylpyridine.[26] Eluent: petroleum ether/ethyl acetate = 30:1; yield 80 mg (94%). ^{1}H NMR: δ 2.40 (s, 3H), 7.26−7.34 (m, 3H), 7.47

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(d, J = 8.1 Hz, 2H), 7.83 (d, J = 8.1 Hz, 1H), 8.55 (d, J = 3.3 Hz, 1H), 8.83 (d, J = 1.5 Hz, 1H). $^{13}C\{^1H\}$ NMR: δ 20.3, 121.6, 124.2, 125.9, 128.3, 129.7, 130.8, 135.8, 136.2, 140.5, 149.2, 160.1.

2-(Naphthalen-1-yl)pyridine.[27] Eluent: petroleum ether/ethyl acetate = 30:1; yield 94 mg (92%). ^1H NMR: δ 7.24−7.29 (m, 1H), 7.41−7.47 (m, 2H), 7.49−7.59 (m, 3H), 7.75 (dt, J = 1.8, 7.8 Hz, 1H), 7.87 (d, J = 9 Hz, 2H), 8.04−8.09 (m, 1H), 8.76−8.78 (m, 1H). $^{13}C\{^1H\}$ NMR: δ 122.0, 125.1, 125.3, 125.6, 125.9, 126.5, 127.5, 128.4, 128.9, 131.2, 134.0, 136.4, 138.5, 149.5, 159.3.

(2-(Furan-2-yl)phenyl)(phenyl)methanone. Eluent: petroleum ether/ethyl acetate = 100:1; pale yellow liquid, yield 113 mg (91%). ^1H NMR: δ 6.26 (s, 1H), 6.42 (d, J = 3.2 Hz, 1H), 7.23 (s, 1H), 7.34−7.40 (m, 4H), 7.48−7.55 (m, 2H), 7.72−7.77 (m, 3H) . $^{13}C\{^1H\}$ NMR: δ 108.8, 111.7, 126.7, 127.5, 128.3, 128.5, 129.1, 129.8, 130.1, 133.2, 137.0, 137.2, 142.8, 151.9, 198.5. HR-MS: m/z 249.0916 $[M + H]^+$, calcd for $C_{17}H_{13}O_2$ 249.0903.

2-(4-(Trifluoromethyl)phenyl)furan.[28] Eluent: petroleum ether; yield 56 mg (53%). ^1H NMR: δ 6.48−6.50 (m, 1H), 6.74 (d, J = 3.3 Hz, 1H), 7.50 (s, 1H), 7.61 (d, J = 8.4 Hz, 2H), 7.74 (d, J = 8.2 Hz, 2H). $^{13}C\{^1H\}$ NMR: δ 107.1, 112.1, 123.9, 124.4 (q, J = 272 Hz), 125.8 (q, J = 3.9 Hz), 129.1 (q, J = 33.1 Hz), 134.0, 143.2, 152.7.

2-(Furan-2-yl)pyridine.[29] Eluent: petroleum ether/ethyl acetate = 30:1; yield 125 mg (86%). ^1H NMR: δ 6.50−6.51 (m, 1H), 7.04 (d, J = 3.3 Hz, 1H), 7.09−7.13 (m, 1H), 7.50 (d, J = 0.9 Hz, 1H), 7.65−7.68 (m, 2H), 8.57 (d, J = 4.8 Hz, 1H). $^{13}C\{^1H\}$ NMR: δ 108.7, 112.2, 118.7, 122.0, 136.7, 143.4, 149.5, 149.7, 153.7.

(2-Benzylphenyl)(phenyl)methanone.[30] Eluent: petroleum ether/ethyl acetate = 30:1; yield 120 mg (88%). ^1H NMR: δ 3.96 (s, 2H), 6.97−6.99 (m, 3H), 7.04−7.08 (m, 2H), 7.13−7.20 (m, 3H), 7.26−7.31 (m, 3H), 7.42 (t, J = 7.6 Hz, 1H), 7.62 (d, J = 7.2 Hz, 2H). $^{13}C\{^1H\}$ NMR: δ 38.9, 125.7, 126.1, 128.36, 128.39, 128.7, 129.3, 130.2, 130.4, 130.9, 133.2, 137.7, 138.9, 140.2, 140.5, 198.6.

2-Benzylpyridine.[31] Eluent: petroleum ether/ethyl acetate = 30:1; yield 78 mg (92%). ^1H NMR: δ 4.06 (s, 2H), 6.96−7.00 (m, 2H), 7.08−7.22 (m, 5H), 7.41−7.47 (m, 1H), 8.44 (d, J = 4.6 Hz, 1H). $^{13}C\{^1H\}$ NMR: δ 44.8, 121.3, 123.1, 126.4, 128.6, 129.2, 136.5, 139.5, 149.4, 161.0.

Phenyl(p-tolyl)methanone.[32] Eluent: petroleum ether/ethyl acetate = 100:1; yield 79 mg (81%). ^1H NMR: δ 2.34 (s, 3H), 7.18 (d, J = 8.1 Hz, 2H), 7.37 (t, J = 7.4 Hz, 2H), 7.48 (t, J = 7.4 Hz, 1H), 7.63 (d, J = 8.1 Hz, 2H), 7.67−7.70 (m, 2H). $^{13}C\{^1H\}$ NMR: δ 21.7, 128.3, 129.1, 130.0, 130.4, 132.2, 134.9, 138.0, 143.3, 196.6.

Phenyl(o-tolyl)methanone.[33] Eluent: petroleum ether/ethyl acetate = 100:1; yield 97 mg (99%). ^1H NMR: δ 2.24 (s, 3H), 7.12−7.23 (m, 3H), 7.27−7.32 (m,1H), 7.35 (t, J = 7.5 Hz, 2H), 7.48 (t, J = 7.4 Hz, 1H), 7.69−7.72 (m, 2H). $^{13}C\{^1H\}$ NMR: δ 20.1, 125.3, 128.5, 128.6, 130.2, 130.3, 131.1, 133.2, 136.8, 137.9, 138.8, 198.7.

1,4-Di(p-methylphenyl)benzene.[5a] Eluent: petroleum ether; yield 101 mg (78%). ^1H NMR: δ 2.40 (s, 6H), 7.26 (d, J = 7.8 Hz, 4H), 7.53 (d, J = 7.9 Hz, 4H), 7.64 (s, 4H). $^{13}C\{^1H\}$ NMR: δ 21.3, 127.0, 127.4, 129.7, 137.2, 138.1, 139.9.

1,3,5-Tris(4′-methoxyphenyl)benzene.[32] Eluent: petroleum ether/ethyl acetate = 20:1; yield 159 mg (80%). ^1H NMR: δ 3.83 (s, 9H), 6.99 (d, J = 8.7 Hz, 6H), 7.60 (d, J = 8.7 Hz, 6H), 7.64 (s, 3H). $^{13}C\{^1H\}$ NMR: δ 55.5, 114.4, 124.2, 128.5, 134.0, 142.0, 159.4.

(4-Fluoro-4′-methylbiphenyl-2-yl)(phenyl)methanone. Eluent: petroleum ether/ethyl acetate = 100:1; light yellow oil, yield 123 mg (85%). ^1H NMR: δ 2.15 (s, 3H), 6.91 (d, J = 8 Hz, 2H), 7.03 (d, J = 8 Hz, 2H), 7.09−7.18 (m, 2H), 7.21 (t, J = 7.8 Hz, 2H), 7.33−7.37 (m, 2H), 7.58 (d, J = 7.2 Hz, 2H). $^{13}C\{^1H\}$ NMR: δ 21.1, 115.6 (d, J = 22.9 Hz), 117.3 (d, J = 21.2 Hz), 128.3, 128.9, 129.2, 130.1, 132.0 (d, J = 7.7 Hz), 133.3, 136.3, 136.8, 137.26, 137.29, 140.5 (d, J = 6.3 Hz), 161.6 (d, J = 249.5 Hz), 197.4. $^{19}F\{^1H\}$ NMR: δ −115.12. HR-MS: m/z 290.1101 $[M]^+$, calcd for $C_{20}H_{15}FO$ 290.1107.

(5-Fluoro-2-(furan-2-yl)phenyl)(phenyl)methanone. Eluent: petroleum ether/ethyl acetate = 100:1; light yellow oil, yield 105 mg (79%). ^1H NMR: δ 6.24 (dd, J = 1.8, 3.4 Hz, 1H), 6.34−6.35 (m,1H), 7.10 (dd, J = 2.6, 8.4 Hz, 1H), 7.20−7.25 (m, 2H), 7.35−7.39 (m, 2H), 7.48−7.53 (m, 1H), 7.70 (dd, J = 5.2, 8.7 Hz, 1H), 7.73−7.76 (m, 2H). $^{13}C\{^1H\}$ NMR: δ 108.6, 111.7, 115.4 (d, J = 23.3 Hz), 117.3 (d, J = 21.8 Hz), 125.5 (d, J = 3.5 Hz), 128.6, 128.9 (d, J = 8 Hz), 129.8, 133.6, 136.6, 138.8 (d, J = 6.3 Hz), 142.7, 151.0, 163.8 (d, J = 251.3 Hz), 196.8. $^{19}F\{^1H\}$ NMR: δ −113.17. HR-MS: m/z 266.0737 $[M]^+$, calcd for $C_{17}H_{11}FO_2$ 266.0743.

(2-Benzyl-5-fluorophenyl)(phenyl)methanone. Eluent: petroleum ether/ethyl acetate = 100:1; light yellow oil, yield 89 mg (61%). ^1H NMR (400 MHz, $CDCl_3$): δ 3.99 (s, 2H), 6.99−7.06 (m, 3H), 7.08−7.13 (m, 2H), 7.14−7.19 (m, 2H), 7.21−7.25 (m, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.70−7.73 (m, 2H). $^{13}C\{^1H\}$ NMR: δ 38.2, 115.4 (d, J = 22.7 Hz), 117.3 (d, J = 20.9 Hz), 126.3, 128.5, 128.6, 129.2, 130.3, 132.6 (d, J = 7.6 Hz), 133.7, 135.9 (d, J = 3.5 Hz), 137.1, 140.3, 140.4 (d, J = 5.9 Hz), 160.6 (d, J = 248.1 Hz), 197.2. $^{19}F\{^1H\}$ NMR: δ −116.26. HR-MS: m/z 290.1057 $[M]^+$, calcd for $C_{20}H_{16}FO$ 290.1107.

N,N-Dimethyl-[1,1′:4′,1″-terphenyl]-4-amine.[34] Eluent: petroleum ether/ethyl acetate = 100:1; yield 112 mg (82%). ^1H NMR: δ 3.00 (s, 6H), 6.83 (d, J = 8.1 Hz, 2H), 7.33 (t, J = 7.3 Hz, 1H), 7.44 (t, J = 7.2 Hz, 2H), 7.55 (d, J = 8.4 Hz, 2H,), 7.63 (s, 6H). $^{13}C\{^1H\}$ NMR: δ 40.9, 113.2, 126.7, 127.1, 127.2, 127.5, 127.8, 128.9, 139.0, 140.3, 141.1.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^1H, ^{13}C, and ^{19}F NMR spectra of the cross-coupling products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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