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Ligand-Promoted Rh(III)-Catalyzed Coupling of Aryl C−H Bonds with Arylboron Reagents

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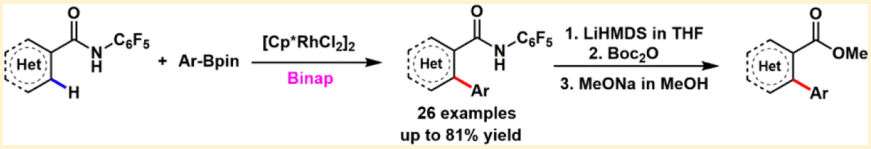
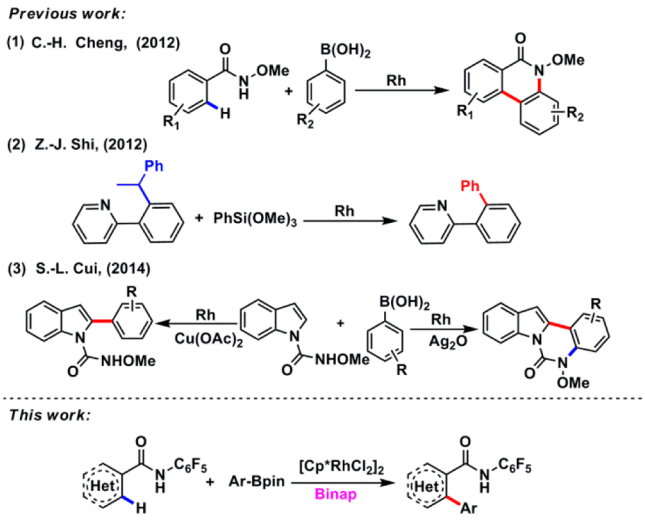
Supporting Information



ABSTRACT: Rhodium(III)-catalyzed C−H arylation of arenes with phenylboronic acid pinacol esters has been achieved using a readily removable *N*-pentafluorophenylbenzamide directing group for the first time. The use of a bidentate phosphine ligand (Binap) significantly increased the yield of the cross-coupling of C−H bonds with organoboron reagents.

As an essential structural motif, biaryls widely existed in many natural products[1] and antagonist drug molecules.[2] Traditional synthesis of biaryls is limited to the reactions between aryl halides and arylmetal compounds, releasing equivalent byproducts or more.[3] In the past decade, transition-metal-catalyzed functionalization of unactivated C−H bonds has emerged as a powerful approach to forging C−C bonds, especially for palladium,[4] ruthenium,[5] iridium[6] and copper.[7] Recently, Rh(III) complexes have presented their advantages in the step-economical synthesis of complex molecular scaffolds, which have increasingly attracted chemists' attention.[8] Although a large amount of rhodium(III)-catalyzed functionalization of C−H bonds with alkynes,[9] alkenes[10] and aldehydes,[11] have been reported, Rh(III)-catalyzed C−H activation/arylation reactions between arenes and organoboron or arylsilanes reagents remain relatively rare.[12] In 2008, Vogler and Studer reported a Rh-catalyzed *ortho*-arylation of 2-arylpridines and *N*-phenylbenzaldimines with arylboronic acids.[12a] In 2012, Cheng and co-workers reported a rhodium-(III)-catalyzed oxidative coupling of arylboronic acids with *N*-methoxybenzamides to give a formal [4 + 2] cyclization product.[12c] In the same year, Shi reported an unprecedented example of Rh(III)-catalyzed C−C cleavage of secondary alcohols and subsequent oxidative coupling with arylsilanes to construct biaryls.[12d] In 2014, Cui and co-workers reported a Rh(III)-catalyzed selective coupling of *N*-methoxy-1*H*-indole-1-carboxamides and arylboronic acids for arylation, [4 + 2] cyclization and [4 + 1] cyclization, respectively.[12f] On the other hand, phenylboronic acid pinacol esters are well-known as effective coupling partners in palladium(II)-, rhodium(I)- and copper(II)-catalyzed arylation reactions.[7d,13] However, rhodium(III)-catalyzed C−H activation/arylation reaction using arylboronic acid pinacol esters as reagents has not been reported before (Scheme 1).

Scheme 1. Rh(III)-Catalyzed C−H Coupling with Organometallic Reagent



We initiated our study on the cross-coupling of C−H with 4-methoxycarbonylphenylboronic acid pinacol ester using the *N*-pentafluoroarylbenzamide directing group.[14] Directed by this directing group, we have reported a Rh(III)-catalyzed C−H activation/olefination reaction of aryl and heteroarylbenzamides under air at atmospheric pressure without the addition of an external oxidant.[15] On the basis of this transformation, we reckoned that it was possible to devise reaction conditions that enable the cross-coupling of organoboron reagents with the *ortho*-C(sp^2)-H bonds of the synthetically and pharmaceutically

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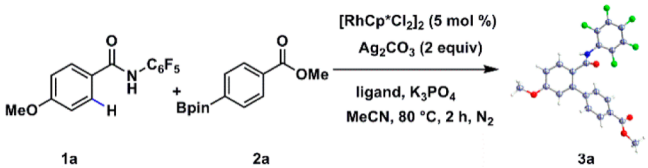
valuable benzoic acid derivatives. Herein, we disclose a Rh(III)-catalyzed C−H activation/arylation reaction using arylboronic acid pinacol esters as the coupling partner.

Systematic screening of the reaction conditions has been carried out using *N*-arylamide substrate (**1a**) and 4-methoxycarbonylphenylboronic acid pinacol ester (4-CO_2Me-Ph-BPin) (**2a**) as the coupling partner (Table S1). We found that the combination of $[RhCp^*Cl_2]_2$/AgOAc/DMF and arylboronic ester facilitated the arylation of (**1a**) to give (**3a**) in 16% yield (Table S1, entry 1). The coupling product (**3a**) has been structurally characterized by X-ray crystallography (Table 1). Then we examined various oxidants and bases as well as solvents and found that the reaction of (**1a**) with 2 equiv of (**2a**) in the presence of 5 mol % $[RhCp^*Cl_2]_2$, 2 equiv of K_3PO_4 and 2 equiv of Ag_2CO_3 increased the yield to 40% (Table S1, entry 6). Analysis of the reaction mixture revealed that a substantial amount of boronic acid pinacol esters were homocoupled to afford the biaryl side product. Encouraged by the previous discovery that MPAA (mono-*N*-protected amino acid) ligands promoted C−H coupling with organoboron reagents,[13g,16] we therefore began to screen a variety of MPAA ligands that would alter the steric and electronic properties of the active catalyst and could potentially accelerate C(sp^2)−H activation and subsequent coupling reactions further to outcompete the homocoupling process (Table 1). When we introduced Boc-L-asparagine into the reaction mixture, we obtained the desired arylation product in 70% yield within 70 min (Table 1, entry 11 and Table S2), which provides evidence that the introduction of MPAA ligand could drastically accelerate C−H activation and subsequent coupling reactions.

Table 1. Screening of Ligands[a]



1a 2a 3a

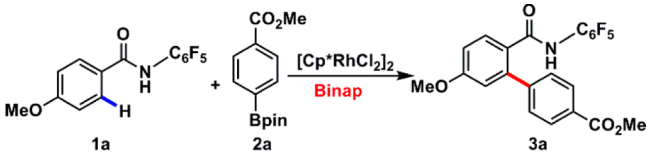
entry	ligand	yield[b] (%)	entry	ligand	yield[b] (%)
1	–	40	12	Fmoc-L-asparagine	24
2	Ac-leucine	60	13	carbethoxy-L-asparagine	48
3	Fmoc-leucine	58	14	Cbz-L-asparagine	54
4	Boc-leucine	48	15	Ac-L-asparagine	61
5	Boc-D-valine	42	16	L-tyrosine	57
6	Ac-glycine	56	17	PPh_3	56
7	Boc-L-phenylalanine	38	**18**	**Binap**	**68** (74[e])
8	Ac-L-glutamic acid	58	19	Xantphos	56
9	Boc-tyrosine	48	20	Dppbz	62
10	Bz-leucine	40	21	Dppf	50
11	**Boc-L-asparagine**	**70**[c] (**68**[d])			

[a]Conditions: 1a (0.1 mmol), 2a (0.2 mmol), $[RhCp^*Cl_2]_2$ (5 mol %), Ag_2CO_3 (0.2 mmol), ligand (10 mol %), K_3PO_4 (0.2 mmol) and MeCN (2 mL) under N_2, 2 h, 80 °C. [b]The yield was determined by ^{1}H NMR analysis of crude reaction mixture using CH_2Br_2 as an internal standard. [c]70 min. [d]KF (0.2 mmol), 2 h. [e]KF (0.2 mmol), 3 h. Binap = 2,2′-Bis(diphenylphosphino)-1,1′-binaphthalene; Xantphos = Dimethylbis-diphenylphosphinoxanthene; Dppf = 1,1′-bis(diphenylphosphino)ferrocene; Dppbz = 1,2-bis(diphenylphosphino)benzene.

Considering that phosphine ligands play a decisive role in some cross-coupling reactions,[17] we then screened phosphine ligands and found that Binap afforded the highest yield of 74% using KF as the base in 3 h (Table 1, entry 18).

With preliminary conditions in hand, we proceeded to re-examine oxidants, bases and solvents using Binap as the ligand in an effort to develop a high-yield protocol (Table 2). We found that a combination of Ag_2CO_3/K_2CO_3/Binap/MeCN afforded the highest yield of 80% (Table 2, entry 5). The desired product was obtained in only 46% yield in the absence of Binap, which testified that the introduction of Binap significantly increased the yield of arylation product (Table S6, entry 10). The use of 2 mol % Rh catalyst dropped the yield to 60% (Table 2, entry 13). The control experiment carried out in the absence of a Rh(III) catalyst gave no product (Table 2, entry 14). Further comprehensive screening data are presented in the Supporting Information.

Table 2. Optimization of Reaction Conditions[a]



1a 2a 3a

entry	oxidant	base	solvent	yield[b] (%)
1	Ag_2CO_3	K_3PO_4	MeCN	68
2	Ag_2CO_3	KF	MeCN	74
3	Ag_2CO_3	Na_2CO_3	MeCN	65
4	Ag_2CO_3	KH_2PO_4	MeCN	60
5	**Ag_2CO_3**	**K_2CO_3**	**MeCN**	**80**
6	AgF	K_2CO_3	MeCN	40
7	$Cu(OAc)_2$	K_2CO_3	MeCN	24
8	Ag_2O	K_2CO_3	MeCN	42
9	AgOAc	K_2CO_3	MeCN	48
10	Ag_2CO_3	K_2CO_3	*tert*-Amyl-OH	24
11	Ag_2CO_3	K_2CO_3	DCE	n.r.
12	Ag_2CO_3	K_2CO_3	toluene	30
13[c]	Ag_2CO_3	K_2CO_3	MeCN	60
14[d]	Ag_2CO_3	K_2CO_3	MeCN	n.r.
15[e]	Ag_2CO_3	K_2CO_3	MeCN	66

[a]Conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), $[RhCp^*Cl_2]_2$ (5 mol %), oxidant (0.2 mmol), ligand (10 mol %), base (0.2 mmol) and solvent (2 mL) under N_2, 3 h, 80 °C. [b]Yield determined by ^{1}H NMR analysis of crude reaction mixture using CH_2Br_2 as an internal standard. [c]$[RhCp^*Cl_2]_2$ (2 mol %). [d]No catalyst. [e]70 °C.

With the optimized conditions for the cross-coupling in hand, we then examined the reaction of various substituted *N*-pentafluoroarylbenzamides (**1b−1r**) with 4-methoxycarbonylphenylboronic acid pinacol ester. As shown in Scheme 2, both electron-rich substrates (**1a−1g**), electron-deficient substrates (**1j−1r**) and nonsubstituted substrate (**1h**) afforded the desired products in good yields (59−80% yields). Notably, selective C−H functionalization was observed at the less-hindered site for substrate bearing a *meta* methyl group (**1d**). However, for *meta*-methoxy and *meta*-fluorinate substrates (**1b** and **1k**), the *ortho* position to the substituted and functional groups had been functionalized as well. The *ortho* position coupling product for 2-Naphthamide (**1i**) reached 27% due to the least steric hindrance of the substituted group. In addition, the heterocyclic amides (thiophene **1s**) can also be arylated in 54% yield.

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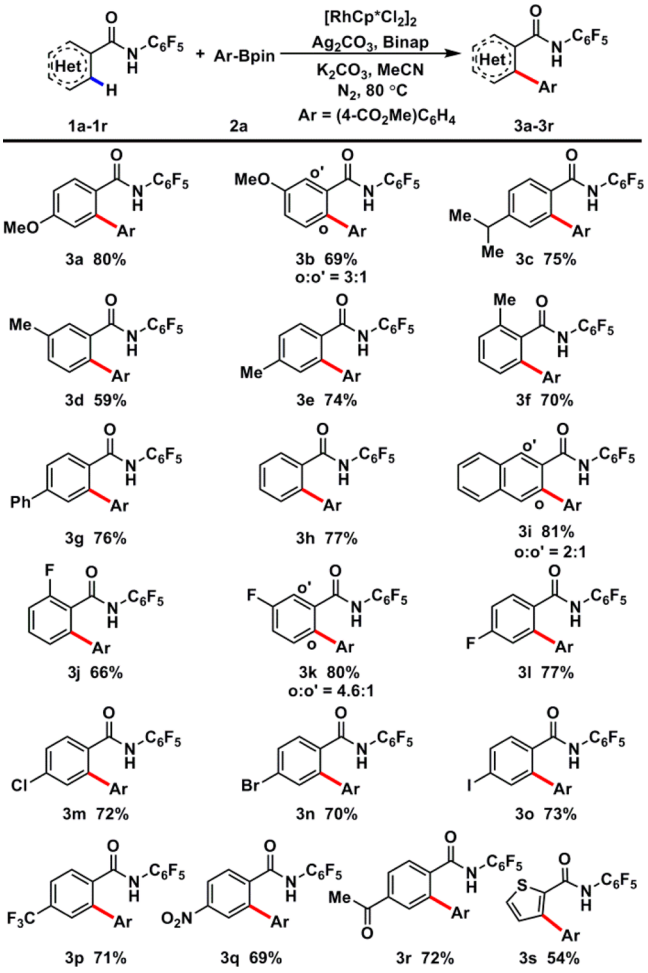
Scheme 2. Scope of Benzamide Substrates[a,b]

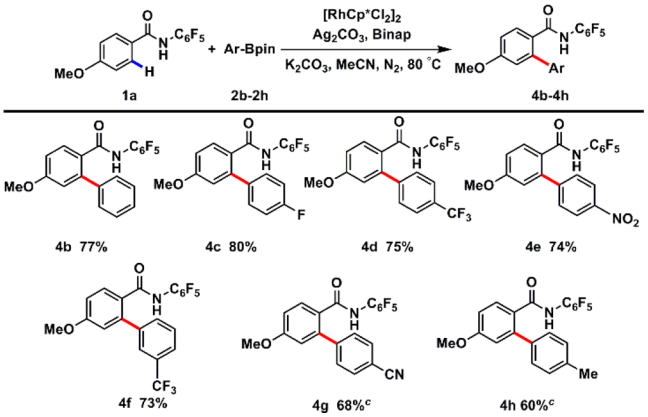


[a]Conditions: **1a**−**1r** (0.1 mmol), **2a** (0.2 mmol), $[RhCp^*Cl_2]_2$ (5 mol %), Ag_2CO_3 (0.2 mmol), Binap (10 mol %), K_2CO_3 (0.2 mmol) and MeCN (2 mL) under N_2, 3 h, 80 °C. [b]Isolated yield.

To explore the scope of the reaction further, we investigated the reaction of various arylboronic acid pinacol esters (**4b**−**4h**) with (**1a**) as the substrate under the optimized conditions (Scheme 3). Nonsubstituted arylboronic acid pinacol ester (**2b**) gave the desired product in good yield (**4b**, 77% yield). The coupling of (**1a**) with electron-withdrawing groups such as fluoro trifluoromethyl and nitro gave the arylated products in 73−80% yields (**4c**−**f**). The presence of a nitrile group slightly reduced the yield to 68% (**4g**). Coupling partner containing an electron-rich group (**2h**) afforded moderate yield (**4h**, 60% yield) owing to the faster homocoupling. Investigation on other organoboron reagents had been carried out under the optimized conditions, and no desired product had been obtained [See Supporting Information (SI) for more details, Table S7] since a substantial amount of organoboron reagents were homocoupled to afford the biaryl side-products.

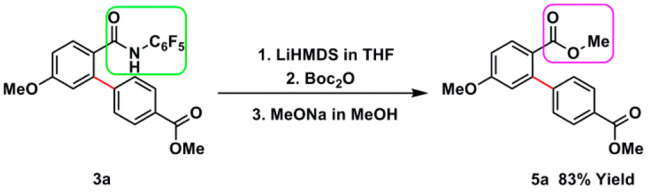
As shown in Scheme 4, the cross-coupling products formed in this transformation are readily converted to methyl esters. Treatment of **3a** with LiHMDS (lithium hexamethyldisilazide), Boc_2O, and MeONa step by step in one pot provides methyl ester **5a** in good yield. We also prepared **3a** on gram scale in order to demonstrate the further application of this transformation (Scheme 5).

Scheme 3. Scope of Arylation Reagents[a,b]

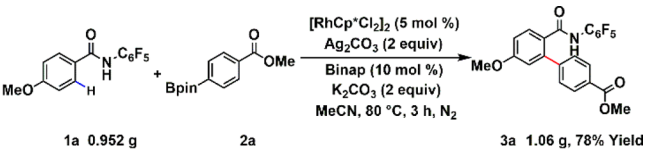


[a]Conditions: **1a** (0.1 mmol), **2b**−**2h** (0.2 mmol), $[RhCp^*Cl_2]_2$ (5 mol %), Ag_2CO_3 (0.2 mmol), Binap (10 mol %), K_2CO_3 (0.2 mmol) and MeCN (2 mL) under N_2, 3 h, 80 °C. [b]Isolated yield. [c]6 h.

Scheme 4. Removal of the Auxiliary

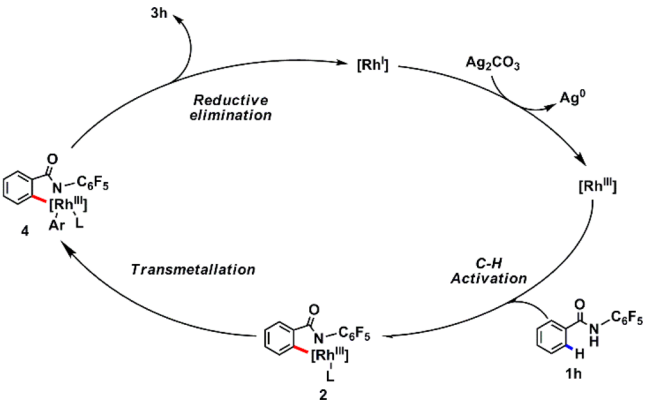


Scheme 5. Gram-Scale Synthesis



A plausible reaction mechanism for this transformation is proposed in Scheme 6. The coordination of the amide to the

Scheme 6. Proposed Reaction Mechanism



[Rh(III)] catalyst is followed by *ortho*-C−H bond activation to give a corresponding five-membered rhodacycle intermediate **2**. Subsequent transmetalation with Ar-Bpin leads to intermediate **4**, which undergoes reductive elimination to give the *ortho*-arylated product **3h** and Rh^I species, which is oxidized by Ag_2CO_3 to regenerate the active Rh^{III} species for the next cycle.

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In summary, we have developed a ligand-promoted Rh(III)-catalyzed cross-coupling reaction of aryl C−H bonds using a readily removable *N*-pentafluorophenyl amide auxiliary. Both the benzamide substrates and the coupling partners tolerate a large array of functional groups.

EXPERIMENTAL SECTION

General Information. Anhydrous solvents were prepared according to standard methods.[18] Commercial available chemicals were used as received without further purification. NMR spectra were recorded on 300, 400 and 500 MHz spectrometers. Chemical shifts are quoted in ppm relative to TMS and $CDCl_3$. High-resolution mass spectra (HR-MS) were obtained with a Q-TOF (ESI).

General Procedure for the Preparation of Benzamides. An acid chloride (20 mmol), prepared from the corresponding carboxylic acid and oxalyl chloride, was added to a vigorously stirring solution of 2,3,4,5,6-pentafluoroaniline (22 mmol) in toluene (50 mL). The reaction mixture was stirred for 24 h under reflux. After cooling to room temperature, the white precipitate was filtered off and washed with water, and recrystallized from toluene or ethyl acetate/hexane to give the products.

Characterization of New Synthesized Compounds. *4-Isopropyl-N-(perfluorophenyl)benzamide (**1c**).* White solid (5.9 g, 90%); mp 172−173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.4 Hz, 2 H), 7.72 (s, 1 H), 7.33 (d, J = 8.0 Hz, 2 H), 2.99 (m, 1 H), 1.29 (s, 3 H), 1.27 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 165.7, 154.4, 143.1 (d, J_{CF} = 251.3 Hz), 143.0 (d, J_{CF} = 245.0 Hz), 137.9 (d, J_{CF} = 252.5 Hz), 137.8, 129.8, 127.8, 127.0, 34.2, 23.7. HRMS (EI-TOF) m/z Calcd for $C_{16}H_{13}F_5NO$ [M + H]$^+$ 330.0917, found 330.0912.

*N-(Perfluorophenyl)biphenyl-4-carboxamide (**1g**).* White solid (6.2 g, 86%); mp 215−216 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.4 Hz, 2 H), 7.74 (s, J = 8.4 Hz, 2 H), 7.64 (d, J = 6.8 Hz, 2 H), 7.51−7.47 (m, 3 H), 7.42 (t, J_1 = 16.8 Hz, J_2 = 8.4 Hz, 1 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 165.2, 145.8, 145.0, 143.0 (d, J_{CF} = 248.8 Hz), 141.0 (d, J_{CF} = 246.3 Hz), 139.6, 138.9, 131.0, 129.0, 128.4, 128.2, 127.6, 127.3. HRMS (EI-TOF) m/z Calcd for $C_{19}H_{11}F_5NO$ [M + H]$^+$ 364.0761, found 364.0755.

*N-(Perfluorophenyl)-2-naphthamide (**1i**).* White solid (5.1 g, 78%); mp 187−188 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1 H), 7.98−7.91 (m, 4 H), 7.66−7.57 (m, 3 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 165.8, 143.1 (d, J_{CF} = 260.0 Hz), 143.0 (d, J_{CF} = 250.0 Hz), 137.9 (d, J_{CF} = 246.3 Hz), 137.0, 135.3, 132.5, 129.6, 129.1, 128.9, 128.7, 128.5, 127.9, 127.2, 123.6. HRMS (EI-TOF) m/z Calcd for $C_{17}H_9F_5NO$ [M + H]$^+$ 338.0604, found 338.0600.

General Procedure for Rh(III)-Catalyzed C−H Arylation. To a 50 mL Schlenk-type sealed tube equipped with a magnetic stirring bar, was added the substrate (0.1 mmol), $[RhCp^*Cl_2]_2$ (3.1 mg, 0.005 mmol), arylboronic acid pinacol esters (0.2 mmol), Ag_2CO_3 (55.2 mg, 0.2 mmol), Binap (6.2 mg, 0.01 mmol), K_2CO_3 (27.6 mg, 0.2 mmol) and MeCN (2.0 mL) under N_2 atmosphere. The tube was capped, and heated to 80 °C for 3 h. After cooled to room temperature, the reaction mixture was filtered through a pad of Celite. The filtrate was concentrated in vacuo to afford crude products, which was purified by flash column chromatography on silica gel using hexanes/EtOAc (8/1−2/1) as the eluent to give the pure product.

*Methyl 5′-methoxy-2′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3a**).* White solid (36.1 mg, 80%); mp 157−158 °C; ^{1}H NMR (400 MHz, CDCl3) δ 8.08 (d, J = 8.4 Hz, 2 H), 7.79 (d, J = 8.8 Hz, 1 H), 7.52 (d, J = 8.0 Hz, 2 H), 6.99 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1 H), 6.89 (d, J = 2.8 Hz, 1 H), 6.71 (s, 1 H), 3.93 (s, 3 H), 3.89 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, CDCl3) δ 166.6, 161.7, 144.2, 142.84 (d, J_{CF} = 255.0 Hz), 142.78 (d, J_{CF} = 247.5 Hz), 141.5, 140.1, 137.7 (d, J_{CF} = 250.0 Hz), 136.7, 131.6, 130.0, 128.8, 125.5, 116.1, 113.5, 111.6, 55.6, 52.3. HRMS (EI-TOF) m/z Calcd for $C_{22}H_{15}F_5NO_4$ [M + H]$^+$ 452.0921, found 452.0919.

*Methyl 4′-methoxy-2′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3b**).* White solid (23.4 mg, 52%); mp 169−170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.4 Hz, 2 H), 7.52 (d, J = 8.4 Hz, 2 H), 7.37 (d, J = 8.4 Hz, 1 H), 7.32 (d, J = 2.8 Hz, 1 H), 7.12 (d, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 1 H), 6.64 (s, 1H), 3.93 (s, 3 H), 3.90 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 167.0, 166.7, 159.6, 142.9 (d, J_{CF} = 255.0 Hz), 142.8 (d, J_{CF} = 246.3 Hz), 137.8 (d, J_{CF} = 246.3 Hz), 137.6, 134.5, 132.0, 131.4, 130.1, 129.5, 128.9, 117.6, 114.2, 111.3, 55.7, 52.2. HRMS (EI-TOF) m/z Calcd for $C_{22}H_{15}F_5NO_4$ [M + H]$^+$ 452.0921, found 452.0916.

*Methyl 2′-methoxy-6′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3b′**).* White solid (7.8 mg, 17%); mp 163−164 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.4 Hz, 2 H), 7.50−7.46 (m, 3 H), 7.41 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1 H), 7.15 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1 H), 6.56 (s, 1 H), 3.93 (s, 3 H), 3.78 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 166.8, 166.7, 156.8, 142.85 (d, J_{CF} = 256.3 Hz), 142.77 (d, J_{CF} = 255.0 Hz), 140.1, 138.6, 137.7 (d, J_{CF} = 258.8 Hz), 135.5, 130.1, 129.7, 128.9, 128.1, 121.0, 113.8, 111.3, 56.1, 52.1. HRMS (EI-TOF) m/z Calcd for $C_{22}H_{15}F_5NO_4$ [M + H]$^+$ 452.0921, found 452.0916.

*Methyl 5′-isopropyl-2′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3c**).* White solid (34.8 mg, 75%); mp 184−185 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.4 Hz, 2 H), 7.76 (d, J = 8.0 Hz, 1 H),7.53 (d, J = 8.4 Hz, 2 H), 7.38 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 1 H), 7.28 (d, J = 1.6 Hz, 1 H), 6.67 (s, 1 H), 3.94 (s, 3 H), 3.03 (m, 1 H), 1.33 (s, 3 H), 1.31 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 167.2, 166.7, 152.9, 144.5, 142.9 (d, J_{CF} = 251.3 Hz), 142.8 (d, J_{CF} = 248.9 Hz), 139.5, 137.7 (d, J_{CF} = 241.3 Hz), 130.9, 130.0, 129.8, 129.6, 128.9, 128.8, 126.5, 111.5, 52.2, 34.2, 23.7. HRMS (EI-TOF) m/z Calcd for $C_{24}H_{18}F_5NO_3Na$ [M + Na]$^+$ 486.1105, found 486.1100.

*Methyl 4′-methyl-2′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3d**).* White solid (25.7 mg, 59%); mp 168−169 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.0 Hz, 2 H), 7.61 (s, 1 H), 7.52 (d, J = 8.4 Hz, 2 H), 7.41 (d, J = 7.6 Hz, 1 H), 7.33 (d, J = 8.0 Hz, 1 H), 6.66 (s, 1 H), 3.93 (s, 3 H), 2.46 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 167.4, 166.7, 144.0, 142.9 (d, J_{CF} = 252.5 Hz), 142.8 (d, J_{CF} = 246.3 Hz), 141.2, 137.6 (d, J_{CF} = 252.5 Hz), 136.4, 133.3, 132.2, 130.5, 130.0, 129.9, 129.7, 128.8, 111.3, 52.2, 21.0. HRMS (EI-TOF) m/z Calcd for $C_{22}H_{15}F_5NO_3$ [M + H]$^+$ 436.0972, found 436.0970.

*Methyl 5′-methyl-2′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3e**).* White solid (32.2 mg, 74%); mp 153−154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.4 Hz, 2 H), 7.70 (d, J = 8.0 Hz, 1 H), 7.51 (d, J = 8.0 Hz, 2 H), 7.30 (d, J = 8.0 Hz, 1 H), 7.24 (s, 1 H), 6.75 (s, 1 H), 3.93 (s, 3 H), 2.46 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.2, 166.7, 144.3, 143.1 (d, J_{CF} = 241.0 Hz), 142.8 (d, J_{CF} = 251.0 Hz), 139.4, 137.7 (d, J_{CF} = 254.0 Hz), 137.6, 131.3, 130.6, 130.0, 129.7, 129.5, 129.0, 128.8, 111.5, 52.2, 21.4. HRMS (EI-TOF) m/z Calcd For $C_{22}H_{15}F_5NO_3$ [M + H]$^+$ 436.0972, found 436.0970.

*Methyl 3′-methyl-2′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3f**).* White solid (30.5 mg, 70%); mp 162−163 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, J = 8.4 Hz, 2 H), 7.52 (d, J = 8.4 Hz, 2 H), 7.44 (t, J_1 = 15.3 Hz, J_2 = 7.5 Hz, 1 H), 7.32 (d, J = 7.2 Hz, 1 H), 7.27 (d, J = 8.0 Hz, 1 H), 6.82 (s, 1 H), 3.93 (s, 3 H), 2.49 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 167.7, 166.8, 144.3, 143.0 (d, J_{CF} = 255.0 Hz), 142.9 (d, J_{CF} = 252.5 Hz), 137.7 (d, J_{CF} = 246.3 Hz), 136.7, 136.2, 134.6, 130.2, 130.0, 129.9, 129.6, 128.7, 127.4, 110.9, 52.2, 19.4. HRMS (EI-TOF) m/z Calcd for $C_{22}H_{14}F_5NO_3Na$ [M + Na]$^+$ 458.0792, found 458.0788.

*Methyl (2′-(perfluorophenylcarbamoyl)-5′-phenyl)biphenyl-4-carboxylate (**3g**).* White solid (37.8 mg, 76%); mp 229−230 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.4 Hz, 2 H), 7.88 (d, J = 8.0 Hz, 1 H), 7.71 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1 H), 7.64−7.62 (m, 3 H), 7.58 (d, J = 8.0 Hz, 2 H), 7.48 (t, J_1 = 14.8 Hz, J_2 = 7.2 Hz, 2 H), 7.42 (dd, J_1 = 14.8 Hz, J_2 = 7.2 Hz, 1 H), 6.81 (s, 1 H), 3.93 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.0, 166.6, 144.4, 142.9 (d, J_{CF} = 250.0 Hz), 141.6, 140.2 (d, J_{CF} = 244.0 Hz), 139.9, 137.7 (d, J_{CF} = 251.0 Hz), 136.4, 132.0, 130.09, 130.05, 130.0, 129.3, 129.1, 128.9, 128.4, 127.2, 126.9, 111.3, 52.3. HRMS (EI-TOF) m/z Calcd for $C_{27}H_{16}F_5NO_3Na$ [M + Na]$^+$ 520.0948, found 520.0945.

*Methyl 2′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3h**).* White solid (32.4 mg, 77%); mp 128−129 °C; ^{1}H NMR (400

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MHz, $CDCl_3$) δ 8.08 (d, J = 8.4 Hz, 2 H), 7.77 (d, J = 7.2 Hz, 1 H), 7.60 (td, J_1= 15.2 Hz, J_2 = 7.6 Hz, J_3= 1.2 Hz, 1 H), 7.58−7.43 (m, 3 H) 7.44 (d, J = 7.6 Hz, 1 H), 3.92 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.3, 166.7, 144.0, 143.0 (d, J_{CF} = 250.0 Hz), 142.8 (d, J_{CF} = 252.0 Hz), 139.3, 137.7 (d, J_{CF} = 248.0 Hz), 136.4, 133.5, 131.4, 130.6, 130.0, 129.8, 129.2, 128.8, 128.4, 52.2. HRMS (EI-TOF) m/z Calcd for $C_{21}H_{13}F_5NO_3$ $[M + H]^+$ 422.0816, found 422.0812.

*Methyl 4-(3-(perfluorophenylcarbamoyl)naphthalen-2-yl)-benzoate (**3i**).* White solid (25.5 mg, 54%); mp 181−182 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1 H), 8.11 (d, J = 8.0 Hz, 2 H), 7.95−7.89 (m, 3 H), 7.66−7.58 (m, 4 H), 6.91 (s, 1 H), 3.94 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 167.1, 166.7, 144.3, 142.9 (d, J_{CF} = 251.3 Hz), 141.9, 137.8 (d, J_{CF} = 263.8 Hz), 137.7 (d, J_{CF} = 250.0 Hz), 135.9, 134.2, 131.9, 131.3, 130.2, 130.0, 129.7, 128.5, 129.0, 128.6, 128.0, 127.6, 111.4, 52.2. HRMS (EI-TOF) m/z Calcd for $C_{25}H_{15}F_5NO_3$ $[M + H]^+$ 472.0972, found 472.0966.

*Methyl 4-(2-(perfluorophenylcarbamoyl)naphthalen-1-yl)-benzoate (**3i′**).* White solid (12.7 mg, 27%); mp 190−191 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.0 Hz, 2 H), 8.00 (d, J = 8.4 Hz, 1 H), 7.95 (d, J = 8.0 Hz, 1 H), 7.88 (d, J = 8.4 Hz, 1 H), 7.60 (td, J_1 = 14.8 Hz, J_2 = 8.0 Hz, J_3= 1.2 Hz, 1 H), 7.56−7.53 (m, 3 H), 7.48 (td, J_1 = 15.2 Hz, J_2 = 8.0 Hz, J_3= 1.2 Hz, 1 H), 6.65 (s, 1 H), 3.98 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 167.1, 166.6, 142.7 (d, J_{CF} = 246.3 Hz), 142.3, 141.9, 139.8, 137.4, 136.8, 135.5 (d, J_{CF} = 261.3 Hz), 131.7, 130.9, 130.2, 129.0, 128.2, 128.7, 127.8, 127.4, 127.0, 124.8, 111.31, 52.3. HRMS (EI-TOF) m/z Calcd for $C_{25}H_{15}F_5NO_3$ $[M + H]^+$ 472.0972, found 472.0966.

*Methyl 3′-fluoro-2′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3j**).* White solid (29.0 mg, 66%); mp 145−146 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.4 Hz, 2 H), 7.56−7.50 (m, 3 H), 7.24−7.18 (m, 3 H), 3.92 (s, 3 H); ^{13} $C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.7, 162.8, 159.6 (J_{CF} = 250.0 Hz), 143.04 (d, J_{CF} = 243.8 Hz), 142.9 (d, J_{CF} = 247.5 Hz), 141.7, 137.7 (d, J_{CF} = 255.0 Hz), 137.6 (d, J_{CF} = 248.8 Hz), 132.0 (d, J_{CF} = 8.8 Hz), 130.0, 129.9, 128.5, 126.0, 122.5 (d, J_{CF} = 17.5 Hz), 115.5 (d, J_{CF} = 22.5 Hz), 110.8, 52.2. HRMS (EI-TOF) m/z Calcd for $C_{21}H_{11}F_6NO_3Na$ $[M + Na]^+$ 462.0541, found 462.0539.

*Methyl 4′-fluoro-2′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3k**).* White solid (28.9 mg, 66%); mp 174−175 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.4 Hz, 2 H), 7.60 (d, J = 7.6 Hz, 1 H), 7.52−7.48 (m, 3 H), 7.35 (td, J_1 = 16.4 Hz, J_2 = 8.0 Hz, J_3 = 2.8 Hz, 1 H), 6.78 (s, 1 H), 3.93 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.6, 165.8, 159.4 (d, J_{CF} = 248.0 Hz), 142.9 (d, J_{CF} = 246.0 Hz), 142.8 (d, J_{CF} = 251.0 Hz), 137.8 (d, J_{CF} = 255.0 Hz), 137.7 (d, J_{CF} = 251.0 Hz), 135.9, 130.4, 130.1 (d, J_{CF} = 9.0 Hz), 129.9, 129.8, 127.0 (d, J_{CF} = 17.0 Hz), 124.8 (d, J_{CF} = 4.0 Hz), 118.9 (d, J_{CF} = 23.0 Hz), 111.0, 52.3. HRMS (EI-TOF) m/z Calcd for $C_{21}H_{12}F_6NO_3$ $[M + H]^+$ 440.0721, found 440.0716.

*Methyl 2′-fluoro-6′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3k′**).* White solid (6.3 mg, 14%); mp 180−181 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 8.4 Hz, 2 H), 7.57−7.52 (m, 3 H), 7.52−7.48 (dd, J_1 = 8.4 Hz, J_2 = 6.0 Hz, 1H), 7.31 (td, J_1 = 17.6 Hz, J_2 = 8.8 Hz, J_3 = 1.2 Hz, 1 H), 6.57 (s, 1 H), 3.95 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.6, 164.5 (d, J_{CF} = 246.5 Hz), 143.0, 142.0, 140.6, 139.8 (d, J_{CF} = 256.3 Hz), 137.7 (d, J_{CF} = 256.3 Hz), 137.6 (d, J_{CF} = 257.5 Hz), 135.3, 135.2, 132.6, 130.2, 128.9, 118.6 (d, J_{CF} = 21.2 Hz), 116.6 (d, J_{CF} = 23.8 Hz), 110.0, 52.3. HRMS (EI-TOF) m/z Calcd for $C_{21}H_{12}F_6NO_3$ $[M + H]^+$ 440.0721, found 440.0715.

*Methyl 5′-fluoro-2′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3l**).* White solid (33.8 mg, 77%); mp 152−153 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.0 Hz, 2 H), 7.83 (dd, J_1= 8.4 Hz, J_2 = 5.6 Hz, 1 H), 7.54 (d, J = 8.4 Hz, 2 H), 7.21 (td, J_1= 16.4 Hz, J_2 = 8.0 Hz, J_3 = 2.4 Hz, 1 H), 7.15 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1 H), 6.64 (s, 1 H), 3.94 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.5, 166.2, 163.9 (d, J_{CF} = 252.5 Hz), 143.0, 142.8 (d, J_{CF} = 247.5 Hz), 142.77, 137.7 (d, J_{CF} = 251.3 Hz), 137.6 (d, J_{CF} = 250.0 Hz), 132.0 (d, J_{CF} = 8.8 Hz), 130.4, 130.2, 129.6, 128.7, 117.6 (d, J_{CF} = 21.3 Hz), 115.5 (d, J_{CF} = 21.3 Hz), 111.1, 52.3. HRMS (EI-TOF) m/z Calcd for $C_{21}H_{11}F_6NO_3Na$ $[M + Na]^+$ 462.0541, found 462.0537.

*Methyl 5′-chloro-2′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3m**).* White solid (32.8 mg, 72%); mp 168−169 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.4 Hz, 2 H), 7.71 (d, J = 8.0 Hz, 1 H), 7.50 (d, J = 8.4 Hz, 2 H), 7.46 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1 H), 7.43 (s, 1 H), 6.90 (s, 1H), 3.93 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.5, 166.4, 142.8 (d, J_{CF} = 243.8 Hz), 142.6, 140.9, 137.7 (d, J_{CF} = 248.8 Hz), 137.6 (d, J_{CF} = 252.5 Hz), 137.5, 131.8, 130.7, 130.5, 130.3, 130.1, 128.7, 128.4, 111.1, 52.3. HRMS (EI-TOF) m/z Calcd for $C_{21}H_{11}ClF_5NO_3Na$ $[M + Na]^+$ 478.0245, found 478.0243.

*Methyl 5′-bromo-2′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3n**).* White solid (35.0 mg, 70%); mp 173−174 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.4 Hz, 2 H), 7.67−7.61 (m, 3 H), 7.51 (d, J = 8.0 Hz, 2 H), 6.80 (s, 1 H), 3.93 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.5, 142.9 (d, J_{CF} = 257.5 Hz), 142.5, 141.8, 141.0, 137.7 (d, J_{CF} = 251.3 Hz), 136.7 (d, J_{CF} = 252.5 Hz), 133.4, 132.3, 131.5, 130.8, 130.4, 130.2, 128.7, 125.8, 111.1, 52.3. HRMS (EI-TOF) m/z Calcd for $C_{21}H_{11}BrF_5NO_3Na$ $[M + Na]^+$ 521.9740, found 521.9737.

*Methyl 5′-iodo-2′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3o**).* White solid (39.9 mg, 73%); mp 182−183 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.4 Hz, 2 H), 7.85 (d, J_1= 8.0 Hz, J_2 = 1.6 Hz, 1 H), 7.82 (s, 1 H), 7.50 (d, J = 8.0 Hz, 2 H), 6.77 (s, 1 H), 3.93 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.5, 142.9 (d, J_{CF} = 246.3 Hz), 142.8 (d, J_{CF} = 250.0 Hz), 141.8, 140.9, 139.3, 137.73 (d, J_{CF} = 256.3 Hz), 137.68 (d, J_{CF} = 253.8 Hz), 137.5, 132.8, 130.7, 130.4, 130.2, 128.7, 111.3, 98.0, 52.3. HRMS (EI-TOF) m/z Calcd for $C_{21}H_{12}F_5INO_3$ $[M + H]^+$ 547.9782, found 547.9776.

*Methyl 2′-(perfluorophenylcarbamoyl)-5′-(trifluoromethyl)-biphenyl-4-carboxylate (**3p**).* White solid (34.7 mg, 71%); mp 149−150 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 11.2 Hz, 2 H), 7.93 (d, J = 10.8 Hz, 1 H), 7.78 (d, J = 10.8 Hz, 1 H), 7.73 (s, 1 H), 7.57 (d, J = 10.8 Hz, 2 H), 6.69 (s, 1 H), 3.95 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.5, 166.1, 142.9 (d, J_{CF} = 246.3 Hz), 142.4, 142.8 (d, J_{CF} = 253.8 Hz), 140.0, 137.8 (d, J_{CF} = 251.3 Hz), 137.6 (d, J_{CF} = 255.0 Hz), 133.4 (d, J_{CF} = 32.5 Hz), 133.2, 130.6, 130.3, 129.9, 128.8, 127.3 (d, J_{CF} = 277.5 Hz), 127.2, 110.8, 52.4. HRMS (EI-TOF) m/z Calcd for $C_{22}H_{11}F_8NO_3Na$ $[M + Na]^+$ 512.0509, found 512.0509.

*Methyl 5′-nitro-2′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3q**).* White solid (32.2 mg, 69%); mp 213-214 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.37−8.34 (m, 2 H), 8.16 (d, J = 8.4 Hz, 2 H), 7.99 (d, J = 8.0 Hz, 1 H), 7.60 (d, J = 8.0 Hz, 2 H), 6.73 (s, 1 H), 3.96 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.3, 165.4, 149.2, 147.6, 144.9 (d, J_{CF} = 245.0 Hz), 144.8 (d, J_{CF} = 241.3 Hz), 142.0, 141.4, 140.8, 139.0, 137.8 (d, J_{CF} = 252.5 Hz), 131.0, 130.7, 128.7, 125.4, 123.1, 52.4. HRMS (EI-TOF) m/z Calc. for $C_{21}H_{11}F_5N_2O_5Na$ $[M + Na]^+$ 489.0486, found 489.0483.

*Methyl 5′-acetyl-2′-(perfluorophenylcarbamoyl)biphenyl-4-carboxylate (**3r**).* Yellow solid (33.4 mg, 72%); mp 167−168 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.4 Hz, 2 H), 8.03 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 1 H), 7.99 (s, 1 H), 7.87 (d, J = 7.6 Hz, 1 H), 7.55 (d, J = 8.0 Hz, 2 H), 6.97 (s, 1 H), 3.94 (3 H), 2.67 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 197.0, 166.8, 166.5, 142.94, 142.9 (d, J_{CF} = 253.8 Hz), 141.4, 139.7, 138.7 (d, J_{CF} = 251.3 Hz), 137.72 (d, J_{CF} = 250.0 Hz), 137.68, 137.5, 137.0, 130.1, 129.6, 128.7, 127.9, 111.0, 52.3, 26.8. HRMS (EI-TOF) m/z Calcd for $C_{23}H_{14}F_5NO_4Na$ $[M + Na]^+$ 486.0741, found 486.0734.

*Methyl 4-(2-(perfluorophenylcarbamoyl)thiophen-3-yl)benzoate (**3s**).* White solid (23.1 mg, 54%); mp 124−125 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.4 Hz, 2 H), 7.64−7.62 (m, 3 H), 7.00 (d, J = 5.2 Hz, 1 H), 6.78 (s, 1 H), 3.95 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.3, 160.0, 143.1 (d, J_{CF} = 245.0 Hz), 143.0, 142.9 (d, J_{CF} = 254.0 Hz), 139.3, 137.8 (d, J_{CF} = 248.0 Hz), 137.7 (d, J_{CF} = 247.0 Hz), 132.6, 130.9, 130.7, 130.4, 129.2, 111.2, 52.4. HRMS (EI-TOF) m/z Calcd for $C_{19}H_{10}F_5NO_3S$ $[M + H]^+$ 428.0380, found 428.0378.

*5-Methoxy-N-(perfluorophenyl)biphenyl-2-carboxamide (**4b**).* White solid (30.3 mg, 77%); mp 128−129 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.4 Hz, 1 H), 7.48−7.42 (m, 5 H), 7.00

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(dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1 H), 6.89 (d, J = 2.4 Hz, 1 H), 6.46 (s, 1 H), 3.89 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 161.8, 142.7 (d, J_{CF} = 250.0 Hz), 142.4, 141.5, 139.6, 137.8 (d, J_{CF} = 256.3 Hz), 137.7 (d, J_{CF} = 243.8 Hz), 132.2, 129.1, 128.8, 128.6, 125.1, 116.0, 113.3, 111.8, 55.6. HRMS (EI-TOF) m/z Calcd for $C_{20}H_{13}F_5NO_2$ $[M + H]^+$ 394.0866, found 394.0863.

*4′-Fluoro-5-methoxy-N-(perfluorophenyl)biphenyl-2-carboxamide (**4c**).* White solid (32.9 mg, 80%); mp 163−164 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.8 Hz, 1 H), 7.45−7.41 (m, 2 H), 7.16−7.12 (m, 2 H), 6.98 (dd, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 1 H), 6.86 (d, J_1 = 2.8 Hz, 1 H), 6.57 (s, 1 H), 3.89 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.7, 162.9 (d, J_{CF} = 246.3 Hz), 161.7, 142.9 (d, J_{CF} = 245.0 Hz), 142.8 (d, J_{CF} = 251.3 Hz), 141.3, 137.7 (d, J_{CF} = 252.5 Hz), 137.7 (d, J_{CF} = 247.5 Hz), 135.5, 131.8, 130.5 (d, J_{CF} = 7.5 Hz), 125.4, 116.2, 116.0 (d, J_{CF} = 21.3 Hz), 113.2, 55.6. HRMS (EI-TOF) m/z Calcd for $C_{20}H_{11}F_6NO_2Na$ $[M + Na]^+$ 434.0592, found 434.0587.

*5-Methoxy-N-(perfluorophenyl)-4′-(trifluoromethyl)biphenyl-2-carboxamide (**4d**).* White solid (34.6 mg, 75%); mp 149−150 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J = 8.4 Hz, 1 H), 7.69 (d, J = 8.1 Hz, 2 H), 7.56 (d, J = 8.1 Hz, 2 H), 7.01 (dd, J_1 = 8.7 Hz, J_2 = 2.7 Hz, 1 H), 6.90 (d, J = 3.2 Hz, 1 H), 6.66 (s, 1 H), 3.90 (s, 3 H); ^{13}C NMR$\{^1H\}$ (125 MHz, $CDCl_3$) δ 166.7, 161.8, 142.9 (d, J_{CF} = 258.8 Hz), 142.8 (d, J_{CF} = 253.8 Hz), 142.2 (d, J_{CF} = 262.5 Hz), 137.8 (d, J_{CF} = 256.3 Hz), 137.7 (d, J_{CF} = 252.5 Hz), 131.5, 130.5 (d, J_{CF} = 31.3 Hz), 130.3, 129.1, 125.8, 125.6, 116.3, 113.5, 111.6, 55.6. HRMS (EI-TOF) m/z Calcd for $C_{21}H_{11}F_8NO_2Na$ $[M + Na]^+$ 484.0560, found 484.0557.

*5-Methoxy-4′-nitro-N-(perfluorophenyl)biphenyl-2-carboxamide (**4e**).* White solid (32.4 mg, 74%); mp 213-214 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 8.8 Hz, 2 H), 7.77 (d, J = 8.4 Hz, 1 H), 7.60 (d, J = 8.8 Hz, 2 H), 7.04 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1 H), 6.92 (d, J = 2.4 Hz, 1 H), 6.78 (s, 1 H), 3.92 (s, 3 H); ^{13}C NMR$\{^1H\}$ (125 MHz, $CDCl_3$) δ 166.5, 161.9, 147.6, 146.4, 142.9 (d, J_{CF} = 253.8 Hz), 142.8 (d, J_{CF} = 256.3 Hz), 140.7, 137.8 (d, J_{CF} = 248.8 Hz), 137.7 (d, J_{CF} = 255.0 Hz), 131.1, 129.6, 125.6, 123.8, 116.5, 113.8, 55.7. HRMS (EI-TOF) m/z Calcd for $C_{20}H_{12}F_5N_2O_4$ $[M + H]^+$ 439.0717, found 439.0713.

*5-Methoxy-N-(perfluorophenyl)-3′-(trifluoromethyl)biphenyl-2-carboxamide (**4f**).* White solid (33.7 mg, 73%); mp 138−139 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.8 Hz, 1 H), 7.71 (s, 1 H), 7.66 (m, 2 H), 7.57 (m, 2 H), 7.01 (dd, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 1 H), 6.90 (d, J = 2.4 Hz, 1 H), 6.61 (s, 1 H), 3.91 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.6, 161.8, 142.9 (d, J_{CF} = 250.0 Hz), 142.8 (d, J_{CF} = 249.0 Hz), 141.0, 140.4, 137.8 (d, J_{CF} = 242.0 Hz), 137.6 (d, J_{CF} = 254.0 Hz), 132.1, 131.5, 131.3 (d, J_{CF} = 32.0 Hz), 129.3, 125.6, 125.3, 125.1 (q, J_{CF} = 5.5 Hz), 116.3, 113.5, 111.5, 55.6. HRMS (EI-TOF) m/z Calcd for $C_{21}H_{12}F_8NO_2$ $[M + H]^+$ 462.0740, found 462.0735.

*4′-Cyano-5-methoxy-N-(perfluorophenyl)biphenyl-2-carboxamide (**4g**).* White solid (28.4 mg, 68%); mp 180−181 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, J = 8.7 Hz, 1 H), 7.72 (d, J = 8.4 Hz, 2 H), 7.55 (d, J = 8.4 Hz, 2 H), 7.02 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1 H), 6.89 (d, J = 2.7 Hz, 1 H), 6.73 (s, 1 H), 3.91 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.5, 161.9, 144.4, 142.9 (d, J_{CF} = 246.3 Hz), 142.8 (d, J_{CF} = 245.0 Hz), 141.0, 137.8 (d, J_{CF} = 247.5 Hz), 137.6 (d, J_{CF} = 250.0 Hz), 132.4, 131.2, 129.4, 125.6, 118.5, 116.3, 113.7, 112.1, 55.7. HRMS (EI-TOF) m/z Calcd for $C_{21}H_{12}F_5N_2O_2$ $[M + H]^+$ 419.0819, found 419.0814.

*5-Methoxy-4′-methyl-N-(perfluorophenyl)biphenyl-2-carboxamide (**4h**).* White solid (24.4 mg, 60%); mp 175−176 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.8 Hz, 1 H), 7.36 (d, J = 8.0 Hz, 2 H), 7.26 (d, J = 7.6 Hz, 2 H), 6.97 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1 H), 6.86 (d, J = 2.4 Hz, 1 H), 6.55 (s, 1 H), 3.88 (s, 3 H), 2.40 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.6, 161.7, 142.8 (d, J_{CF} = 249.0 Hz), 142.7 (d, J_{CF} = 247.0 Hz), 142.5, 138.5, 137.7 (d, J_{CF} = 254.0 Hz), 137.5 (d, J_{CF} = 248.0 Hz), 136.6, 136.4, 132.2, 129.7, 128.67, 125.0, 116.0, 55.5, 21.2. HRMS (EI-TOF) m/z Calcd for $C_{21}H_{14}F_5NO_2Na$ $[M + Na]^+$ 430.0842, found 430.0840.

Procedure for Directing Group Removal. To an oven-dried 10 mL round bottle flask equipped with a magnetic stir bar was added **2a** (45.1 mg, 0.1 mmol) and 1 mL anhydrous THF under N_2 atmosphere. After cooling to −78 °C, LiHMDS (1.0 M in THF, 5 equiv) was added dropwise within 5 min. The mixture was warmed up to −20 °C naturally in 50 min. Then Boc_2O (6 equiv) was added in −78 °C followed by warming up to 0 °C naturally in 2 h. MeONa (1.0 M in MeOH, 10 equiv) was added. After stirred at room temperature for 30 min, the reaction was quenched with saturated NH_4Cl/HOAc (10/1, 2 mL). Extract with EtOAc (3 × 3 mL). The combined organic layer was washed with brine and dried over $MgSO_4$, filtrated and concentrated under vacuum, and purified by preparative TLC using hexanes/EtOAc (4/1) as the eluent to afford 24.9 mg of **5a** (83%) as white solid.

*Dimethyl 5-methoxybiphenyl-2,4′-dicarboxylate (**5a**).* White solid (24.9 mg, 83%); mp 203−204 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.8 Hz, 2 H), 7.94 (d, J = 8.8 Hz, 1 H), 7.36 (d, J = 8.4 Hz, 2 H), 6.95 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1 H), 6.81 (d, J = 2.8 Hz, 1 H), 3.94 (s, 3 H), 3.87 (s, 3 H), 3.61 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 167.6, 167.0, 161.9, 146.6, 144.5, 132.7, 129.2, 128.9, 128.3, 122.2, 116.2, 113.0, 55.5, 52.1, 51.7. HRMS (EI-TOF) m/z Calcd for $C_{17}H_{16}O_5Na$ $[M + Na]^+$ 323.0895, found 323.0891.

Procedure for Gram-Scale Synthesis. To a 350 mL Schlenk-type sealed tube equipped with a magnetic stirring bar, was added the substrate (0.952 g, 3 mmol), $[RhCp^*Cl_2]_2$ (93.0 mg, 0.15 mmol), arylboronic acid pinacol esters (1.57 g, 6 mmol), Ag_2CO_3 (1.65 g, 6 mmol), Binap (0.186 g, 0.01 mmol), K_2CO_3 (0.828 g, 6 mmol) and MeCN (60 mL) under N_2 atmosphere. The tube was capped, and heated to 80 °C for 12 h. After cooled to room temperature, the reaction mixture was filtered through a pad of Celite. The filtrate was concentrated in vacuo to afford crude products, which was purified by flash column chromatography on silica gel using hexanes/EtOAc (4/1) as the eluent to give the pure product (1.06 g, 78%).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00083.

Optimization studies and characterization data of all new compounds. (PDF)

Crystallographic data for compound **3a**. (CIF)

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Notes

The authors declare no competing financial interest.

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