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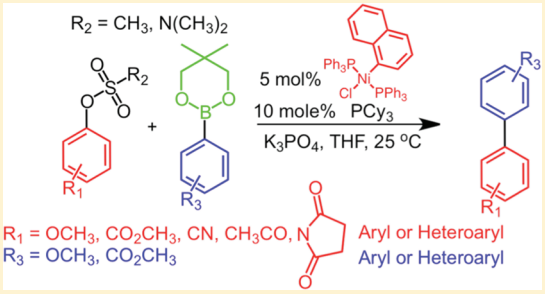
trans-Chloro(1-Naphthyl)bis(triphenylphosphine)nickel(II)/PCy_3 Catalyzed Cross-Coupling of Aryl and Heteroaryl Neopentylglycolboronates with Aryl and Heteroaryl Mesylates and Sulfamates at Room Temperature

Pawaret Leowanawat, Na Zhang, Mehtap Safi, David J. Hoffman, Miriam C. Fryberger, Aiswaria George, and Virgil Percec*

Roy & Diana Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104-6323, United States

Supporting Information

ABSTRACT: *trans*-Chloro(1-naphthyl)bis(triphenylphosphine)nickel-(II) complex/PCy_3 system has been successfully applied as catalyst for the Suzuki–Miyaura cross-coupling of aryl and heteroaryl neopentylglycolboronates with aryl and heteroaryl mesylates and sulfamates in THF at room temperature. This cross-coupling reaction tolerates various functional groups, including keto, imino, ester, ether, and cyano. Together with the nickel-catalyzed, one-pot, two-step neopentylglycolborylation, this bench stable and inexpensive Ni(II)-based catalyst can be utilized as an alternative to $Ni(COD)_2/PCy_3$ to provide an inexpensive, robust, and convenient synthesis of biaryl and heterobiaryl compounds.



INTRODUCTION

Transition-metal-catalyzed Suzuki–Miyaura cross-coupling reaction is one of the most powerful transformations used for the construction of biaryl compounds. Traditionally, this reaction involves the use of aryl halides as electrophiles, aryl boronic acids as nucleophiles, and a Pd catalyst.[1] Phenol derivatives were recently developed as alternative electrophiles for the Suzuki–Miyaura cross-coupling reaction since these electrophiles are inexpensive and widely available, even though they are less reactive than aryl halides due to the stronger C–O bond.[2] In 1995, our laboratory reported the $NiCl_2(dppf)$/Zn-catalyzed Suzuki–Miyaura cross-coupling of aryl sulfonates with boronic acids at elevated temperatures.[3] Since then, Ni-based catalysts have received substantial research interest.[2a] The Monteiro laboratory reported that $NiCl_2(PCy_3)_2$ is an active catalyst for the cross-coupling of aryl tosylates with aryl boronic acids.[4] Subsequently, $NiCl_2(PCy_3)_2$ proved to be a very versatile and successful catalyst for the cross-coupling of various C–O-based electrophiles, including aryl carboxylates,[5] aryl carbonates,[6] aryl carbamates,[6–8] aryl sulfamates,[6,7c,8] and aryl phosphates.[9]

The most common nucleophiles used in the nickel-catalyzed Suzuki–Miyaura cross-coupling reaction of C–O electrophiles are aryl boronic acids,[3,4,5a,6,7c,8,9] aryl boronates,[10,11] and aryl potassium trifluoroborates.[12] Our laboratory is interested in the synthesis and application of aryl neopentylglycolboronates as coupling partners in the Suzuki–Miyaura cross-coupling reactions. Unlike aryl boronic acids, which are a mixture of monomer, dimer, and trimer due to anhydride formation, aryl neopentylglycolboronates are present only in monomeric form.[1i] Hence, the stoichiometry of these aryl neopentylglycolboronates can be precisely controlled, and their cross-coupling is suitable for the perfectly stoichiometric requirement of reactions such as step polymerization.[13] Moreover, aryl neopentylglycolboronates are less reactive but more selective than aryl boronic acids.[10c,14] Therefore, aryl neopentylglycolboronates can be used in orthogonal cross-coupling reactions with different C–O electrophiles.[14]

Aryl and heteroaryl neopentylglycolboronates are easily prepared by a two-step, one-pot reaction starting from aryl iodides and bromides,[10a,b,15] aryl chlorides,[15,16] and aryl sulfonates.[17] Recently, Ni(II)-catalyzed borylation of aryl carbamates was reported by the Shi laboratory.[18]

$Ni(II)Cl_2PCy_3$ is the most widely used catalyst for the cross-coupling reactions of aryl boronic acids and boroxines with C–O electrophiles.[4–9] However, this catalyst does not cross-couple aryl neopentylglycolboronates.[14] Hu and co-workers reported that $Ni(COD)_2/PCy_3$ is active for the room-temperature Suzuki–Miyaura cross-coupling of aryl sulfonates with aryl boronic acids.[19] Our laboratory utilized this catalyst to successfully cross-couple aryl neopentylglycolboronates with electron-rich and electron-deficient aryl and heteroaryl mesylates and sulfamates.[10c] Although $Ni(COD)_2/PCy_3$ is an excellent catalyst that tolerates a variety of functional groups, it is air sensitive, toxic, and expensive. The inexpensive and air-stable $Ni(II)Cl_2(PR_3)_2$ catalysts seem to provide a superior option. However, they have to be activated to convert Ni(II)

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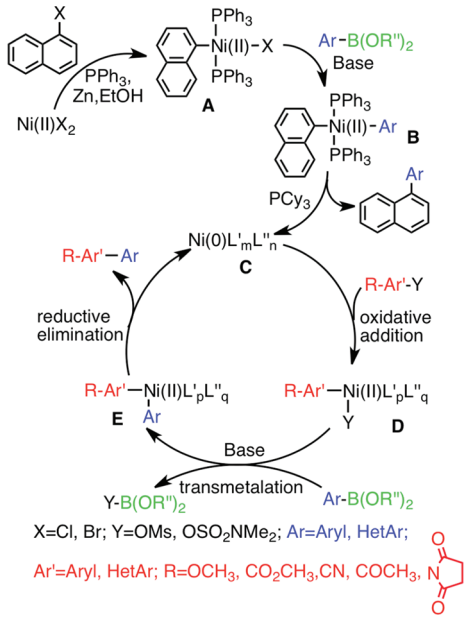
into Ni(0) for oxidative addition of the C−O bond to take place. This process can be accomplished by reducing agents such as Zn,[3] *n*-BuLi,[20] or boronic acid mostly at elevated temperatures.[4] Although the application of *n*-BuLi as a reductant allows the cross-coupling to occur also at room temperature, the catalyst is not compatible with base-sensitive functional groups. Therefore, mild and room-temperature Suzuki−Miyaura cross-coupling reaction is not accessible using the $Ni(II)Cl_2(PR_3)_2$ catalysts.[21] Recently, an alternative easily prepared and air-stable *trans*-chloro(aryl)bis(triphenylphosphine)Ni(II) complex and related compounds from the same class of Ni(II)−*σ*-aryl complexes have received research interest. Ni(II)−*σ*-aryl complexes were discovered in 1960.[22] *trans*-Chloro(aryl)bis(triphenylphosphine)Ni(II) complex was found to be active for the cyanation[23] of aryl halides and recently for the amination[24] and Suzuki−Miyaura cross-coupling of aryl halides and sulfonates with aryl boronic acids.[19,25] The room-temperature Suzuki−Miyaura cross-coupling reaction of aryl halides[25c] and aryl sulfonates[25c,d] with aryl boronic acids has been reported with this Ni(II)−*σ*-aryl complex. However, the activity of this complex in cross-coupling with aryl boronates is not known. In this paper, we report that the air- and moisture-stable as well as the readily accessible *trans*-chloro(aryl)bis(triphenylphosphine)Ni(II) complex catalyzes the Suzuki−Miyaura cross-coupling of aryl neopentylglycolboronates with both aryl and heteroaryl mesylates and sulfamates at room temperature.

RESULTS AND DISCUSSION

A Brief Discussion of the Preparation and Activation of Ni(II)−*σ*-Aryl Complexes. In general, Ni(II)(*σ*-aryl) complexes can be synthesized by two general methodologies. The first method involves the transmetalation of NiL_2X_2 with aryl Grignard or organolithium reagents.[22] The second method involves the oxidative addition of aryl halides[23,26,27] or aryl sulfonates[25d] to Ni(0) complexes such as $Ni(COD)_2$ or $Ni(PPh_3)_4$ and/or by in situ formation and reduction of $Ni(II)Cl_2(PPh_3)_2$ with Zn[23c] or other reducing reagents such as manganese/iron alloy.[23b] It was decided to employ the in situ reduction method for the preparation of the complex in order to avoid the need of using the air sensitive and/or expensive reagents. The synthesis and the proposed mechanism of cross-coupling mediated by the Ni(II)−*σ*-aryl complexes is shown in Scheme 1. By stirring $NiCl_2{\cdot}6H_2O$ and PPh_3 in refluxing ethanol, $NiCl_2(PPh_3)_2$ was formed without isolation. After its in situ reduction with Zn to Ni(0) followed by oxidative addition to 1-chloronaphthalene, Ni(II)Cl(1-naphthyl)$(PPh_3)_2$ (Scheme 1, compound A) was obtained.[25b] The same approach can be applied to the synthesis of Ni(II)Br(1-naphthyl)$(PPh_3)_2$. This precatalyst can be prepared on a multigram scale from inexpensive starting materials and kept on the bench for several months with no decrease in its catalytic activity. In the presence of a base, solvent, and aryl boronic ester, the Ni(II)Cl(1-naphthyl)$(PPh_3)_2$ (Scheme 1, compound A) catalyst precursor was activated before entering the catalytic cycle in a similar way as in the case of aryl boronic acids.[25a,c] Transmetalation facilitated by base produced naphthyl−Ni(II)-$(PPh_3)_2$−Ar (Scheme 1, compound B) complex followed by reductive elimination to yield the naphthyl−aryl product and $Ni(0)L'_mL''_n$. The naphthyl−aryl product generated in small amounts can be detected by its fluorescence in TLC and removed from the desired product by column chromatography. Then the $Ni(0)L'_mL''_n$ (Scheme 1, compound C) generated will

Scheme 1. Synthesis of *trans*-Chloro(aryl)bis(triphenylphosphine)Ni(II) Complex and the Proposed Mechanism for the Cross-Coupling Reaction



enter the general catalytic cycle of the Ni(0)/Ni(II) mechanism by following the sequence of oxidative addition and transmetalation with aryl neopentylglycolboronates, followed by reductive elimination to give the desired biaryl product. This process is facile enough to occur at room temperature.

Optimization of Cross-Coupling Reaction Conditions of Aryl Neopentylglycolboronates with Aryl Mesylates. Various bases, solvents, and catalyst loadings were investigated in order to provide the optimum reaction conditions for the cross-coupling of aryl mesylates with aryl neopentylglycolboronates. The amount of boronic ester used in the reaction was also examined in order to reduce the amount of aryl boronate used in these cross-coupling experiments.

K_3PO_4 proved to be the base of choice (Table 1, entries 3, 4 and entries 1, 2). Using dry THF and K_2CO_3 as base gave the lowest yields for all combinations (Table 1, entries 1 and 9). Both PCy_3 and PPh_3 were efficient ligands in the cross-coupling of methyl 4-methanesulfonyloxybenzoate with *p*-methoxyphenyl neopentylglycol boronate in the presence of K_3PO_4. Decreasing the amount of boronate to 1 equiv with respect to mesylate maintained excellent reaction yield (Table 1, entry 7). Although dried THF worked as well as wet as received THF, in this reaction we used dry THF as solvent throughout the rest of the study.

In order to compare PCy_3 and PPh_3 ligands, we further decreased the catalyst and ligand loading for both ligands and screened several more challenging substrates using PPh_3 as ligand. Decreasing the complex loading to as low as 2% did not reduce the yield. However, further decrease of the complex loading to 1% significantly decreased the reaction yield. PCy_3 was shown to be more efficient than PPh_3 at low complex loading (Table 2, entries 5 and 10). With PCy_3 as the ligand and 5% complex loading, the reaction was complete in 3 h. Although PCy_3 was more efficient, the less expensive and oxidatively more stable PPh_3 is preferable. Hence, several substrates utilizing PPh_3 as ligand were also investigated.

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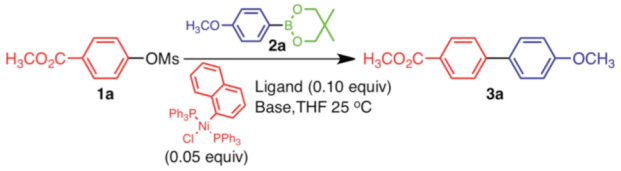
Table 1. Cross-Coupling of Methyl 4-(Methanesulfonyloxy)benzoate with *p*-Methoxyphenyl Neopentylglycolboronate Catalyzed by Ni(II)Cl(1-naphthyl)(PPh_3)$_2$/Phosphine Ligand at 25 °C



entry	2a	ligand	base	THF	time (h)	convn[a]/yield[b] (%)
1	1.5	PPh_3	K_2CO_3	dry	37	89/57
2	1.5	PPh_3	K_2CO_3	wet	36	97/85
3	1.5	PPh_3	K_3PO_4	dry	12	100/94
4	1.5	PPh_3	K_3PO_4	wet	18	99/93
5	1.5	PCy_3	K_3PO_4	dry	12	100/90
6	1.2	PCy_3	K_3PO_4	dry	5	100/99
7	1.0	PCy_3	K_3PO_4	dry	4	100/99
8	1.5	PCy_3	K_3PO_4	wet	12	100/96
9	1.5	PCy_3	K_2CO_3	dry	37	75/49

[a]Conversion determined by GC. The GC yield always has the same value as conversion. [b]Isolated yield.

Electron-rich aryl mesylates and sulfamates gave low yields when PPh_3 was used as ligand even at longer reaction times (Table 2, entries 12 and 14). Under the same conditions, electron-deficient aryl mesylates were cross-coupled in good yields (Table 2, entries 1−4 and 11) while aryl sulfamates were cross-coupled in moderate yields (Table 2, entry 13). The combination of 5% Ni catalyst/10% PCy_3/K_3PO_4, in dry THF was selected for experiments to be reported in the following subchapters.

Cross-Coupling Reaction of Aryl Neopentylglycolborates with Aryl Mesylates. The cross-coupling reaction of aryl mesylates with aryl neopentylglycolboronates bearing both electron-withdrawing and electron-donating functional groups was studied in order to survey the scope and limitations of this catalytic system. Both the electronic and steric properties of the aryl mesylates and aryl boronic esters were investigated. In general, cross-coupling reactions were complete within 14 h and produced good to excellent yields despite steric hindrance or the presence of a deactivating electron-donating substituent. *Ortho*−*ortho* coupling was shown to be more challenging due to steric hindrance. Nevertheless, with longer reaction time and higher complex loading (Table 3, **3u**, **3w**, **3x**), *ortho*−*ortho* coupling was accomplished in good to excellent yields with the exception of *o*-methyl benzoate with *o*-methyl benzoate (Table 3, **3t**).

Cross-Coupling Reaction of Aryl Neopentylglycolborates with Aryl Sulfamates. In recent studies,[10c,14] it has been shown that aryl mesylates and sulfamates behave similarly in their Suzuki−Miyaura cross-coupling reactions with aryl neopentylglycolboronates. With the Ni(COD)$_2$/PCy_3/K_3PO_4 catalytic system at room temperature, both mesylates and sulfamates were cross-coupled efficiently. Although mesylates are important C−O electrophiles, the cross-coupling reaction of sulfamates is also important due to their reactivity in *ortho*-metalation reactions.[28] It was expected that the Ni(II)Cl(1-naphthyl)(PPh_3)$_2$ precatalyst would provide reaction results similar to those obtained with Ni(COD)$_2$, and therefore, the cross-coupling of aryl neopentylglycolboronates with aryl sulfamates was also investigated. To our surprise, aryl sulfamates were less reactive than aryl mesylates when Ni(II)Cl(1-naphthyl)(PPh_3)$_2$/PCy_3 was used as a precatalyst. However, good yields were still obtained with longer reaction time. 4-Methoxyphenyl sulfamate was found to be challenging for this catalytic system. The reason is still under investigation. A certain degree of steric hindrance was tolerated as well (Table 4, **3i**, **3g**). *Ortho*−*ortho* coupling was again more challenging as in the case of aryl mesylates. Cross-coupling reaction of substrates with *ortho*-electron-withdrawing groups and aryl boronates with *ortho*-withdrawing groups (Table 4, **3t**, and Table 3, **3t**) did not give good yields even with higher catalyst loading and reaction time as long as 64 h. An increased reaction time did not result in an increased reaction yield. Instead, methyl benzoate was detected by GC in the reaction mixture after 90 h.

Scope of Cross-Coupling Reaction of Aryl and Heteroaryl Neopentylglycolboronates with Aryl and Heteroaryl Mesylates and Sulfamates. Various functional groups including keto, cyano, and imido were tested for these reaction conditions (Table 5). It was found that these reaction conditions tolerated these functional groups with good isolated yields when cross-coupling electron-rich aryl neopentylglycolboronates with aryl mesylates bearing a keto group (81%, Table 5, **3y**), cyano group (93%, Table 5, **3z**; X = OMs), and imido group (94%, Table 5, **3af**). However, the isolated yields were lower with longer reaction time when these aryl mesylates were coupled with electron-deficient aryl neopentylglycolboronates (keto group (57%, Table 5, **3ab**), cyano group (85%, Table 5, **3ac**), and imido group (49%, Table 5, **3ai**)). The functionalized aryl sulfamates also gave the coupled product but in diminished yield (45%, Table 5, **3z**).

The cross-coupling reaction of heteroaryl mesylates and heteroaryl sulfamates with aryl or heteroaryl neopentylglycolboronates was also investigated. Generally, the isolated yields for both heteroaryl mesylates and sulfamates were excellent (81−99%) regardless of the electronic properties of aryl neopentylglycolboronates (**3ae**, **3ah**, **3aa**, **3ad**, **3ag**). Only the cross-coupling of 3-pyridinyl mesylate with 2-thienyl neopentylglycolboronates showed diminished isolated yield (67%, Table 5, **3aj**). This diminished efficiency might come from *ortho* hindrance introduced by the lone pair of electrons of sulfur.

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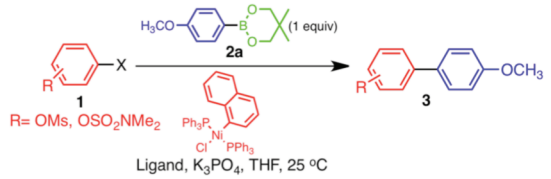
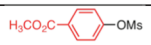
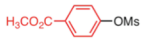
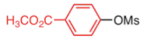
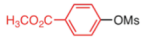
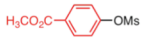
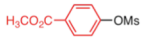
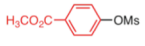
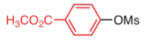
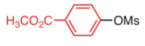
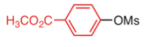
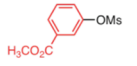
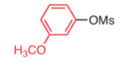
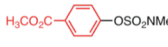
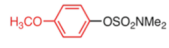
Table 2. Cross-Coupling of Aryl Mesylates and Sulfamates with *p*-Methoxyphenyl Neopentylglycolboronates. Screening for Optimum Combinations of Catalyst and Ligand Loadings



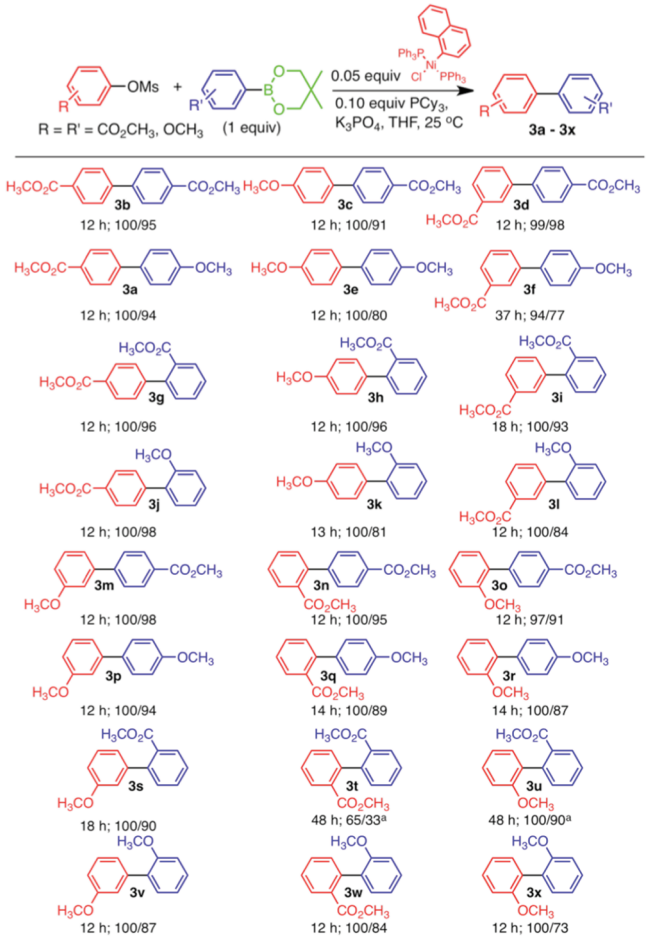
entry	1	Catalyst (%)	ligand (%)	time (h)	convn[a]/ yield[b] (%)
1		5	PPh_3(10)	12	100/94
2		5	PPh_3(10)	6	100/86
3		2.5	PPh_3(5)	12	100/85
4		2	PPh_3(4)	12	100/86
5		1	PPh_3(2)	28	79/42
6		5	PCy_3(10)	12	100/90[c]
7		5	PCy_3(10)	3	100/84[c]
8		2.5	PCy_3(5)	12	100/89[c]
9		2	PCy_3(4)	12	100/89[c]
10		1	PCy_3(2)	23	84/78[c]
11		5	PPh_3(10)	37	94/77
12		5	PPh_3(10)	48	60/53
13		5	PPh_3(10)	48	81/68
14		5	PPh_3(10)	48	28/23

[a]Conversion determined by GC. The GC yield always has the same value as conversion. [b]Isolated yield. [c]Aryl boronate 1.5 equiv.

CONCLUSIONS

The bench-stable, inexpensive, and readily available *trans*-chloro(1-naphthyl)bis(triphenylphosphine) Ni(II) complex was demonstrated to be an efficient precatalyst for the cross-coupling of electron-rich and electron-deficient aryl and heteroaryl mesylates and sulfamates with aryl and heteroaryl neopentylglycolboronates. The reaction is carried out in THF at room temperature without external reducing reagent and tolerates a variety of functional groups. The ability of *trans*-chloro(1-naphthyl)bis(triphenylphosphine)Ni(II) complex to catalyze the Suzuki–Miyaura cross-coupling of aryl and heteroaryl neopentylglycolboronates provides support for the Ni(0)/Ni(II) catalytic cycle mechanism for this nickel catalyzed cross-coupling reaction. Now, room-temperature Suzuki–Miyaura cross-coupling reaction can be achieved without the use of an air-sensitive and expensive $Ni(COD)_2/PCy_3$ catalytic system. With this development, large-scale synthesis of complex building blocks and macromolecules can be achieved at lower cost and in fewer steps.

Table 3. Cross-Coupling of Aryl Mesylates with Aryl Neopentylglycolboronates Catalyzed by Ni(II)Cl(1-Naphthyl)$(PPh_3)_2/PCy_3$ in THF at 25 °C[a]



[a]10% Catalyst and 20% PCy_3 for **3t** and **3u**. Reaction conditions: ArOMs (0.3 mmol), aryl neopentylglycolboronate (0.3 mmol), Ni(II)Cl(1-naphthyl)$(PPh_3)_2$ (0.015 mmol), PCy_3 (0.03 mmol), K_3PO_4 (0.9 mmol), THF (1.0 mL). Conversion/isolated yield. The GC yield has the same value as conversion.

EXPERIMENTAL SECTION

General Experimental Methods. Ni(II)Cl(1-naphthyl)$(PPh_3)_2$ was prepared according to a literature method.[25b,c] 2-(4-Methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**2a**) was synthesized by the esterification of the boronic acid with neopenthyl glycol. K_3PO_4 from a commercial source was dried at 40 °C under vacuum overnight prior to use. PPh_3 was recrystallized from hexane. THF was distilled over sodium/benzophenone. Aryl mesylates and aryl sulfamates were synthesized according to literature procedures.[6,10c,17] All other reagents were used as received from commercial sources. ^1H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded using TMS as internal standard. High-resolution mass spectra of new compounds were obtained on a high-resolution double-focusing chemical ionization mass spectrometer. A GC coupled with an FID detector and column HP 19091J-413 (5% phenyl)methylpolysiloxane 30 m length 0.32 mm internal diameter was used to follow the reaction conversions and to assess the purity of the final compounds. This method is complementary to the NMR technique. The crude reaction

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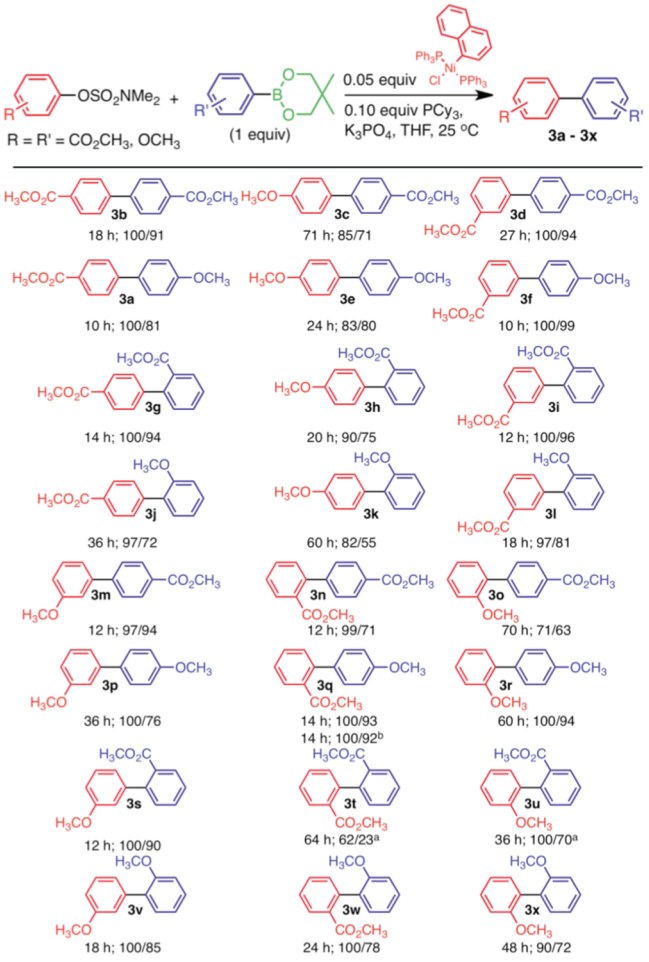
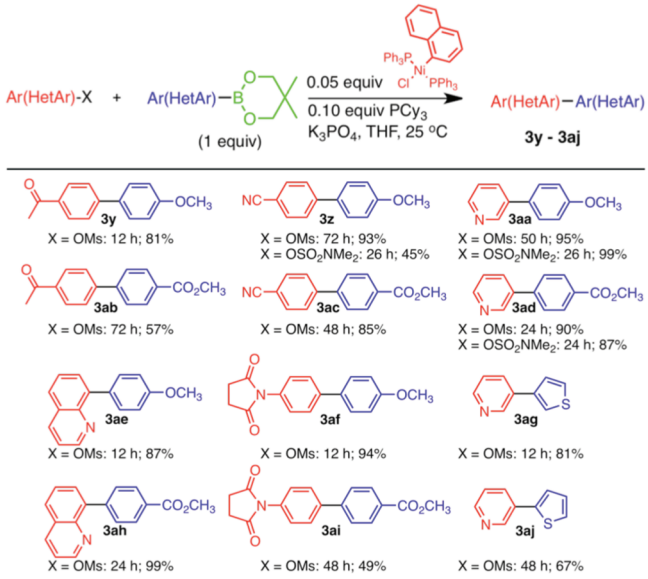
Table 4. Cross-Coupling of Aryl Sulfamates with Aryl Neopentylglycolboronates Catalyzed by Ni(II)Cl(1-naphthyl)$(PPh_3)_2/PCy_3$ in THF at 25 °C[a]



[a]10% catalyst and 20% PCy_3 for **3t** and **3u**. Reaction conditions: $ArOSO_2NMe_2$ (0.3 mmol), aryl neopentylglycolboronate (0.3 mmol), Ni(II)Cl(1-naphthyl)$(PPh_3)_2$ (0.015 mmol), PCy_3 (0.03 mmol), K_3PO_4 (0.9 mmol), THF (1.0 mL). Conversion/isolated yield. The GC yield has the same value as conversion except for **3t** (48%). [b]Aryl pinacolboronate as nucleophile.

Table 5. Cross-Coupling of Aryl and Heteroaryl Mesylates and Sulfamates with Aryl and Heteroaryl Neopentylglycolboronates Catalyzed by Ni(II)Cl(1-naphthyl)$(PPh_3)_2/PCy_3$ in THF at 25 °C[a]



[a]Reaction conditions: Ar(HetAr)-OMs or $Ar(HetAr)-OSO_2NMe_2$ (0.3 mmol), aryl neopentylglycolboronate (0.3 mmol), Ni(II)Cl(1-naphthyl)$(PPh_3)_2$ (0.015 mmol), PCy_3 (0.03 mmol), K_3PO_4 (0.9 mmol), THF (1.0 mL). All yields are isolated.

mixtures were diluted with THF and analyzed by GC as reported in the previous publications from our laboratory.[10,15−17]

General Method for the Preparation of Neopentylglycolborane. A procedure elaborated in our laboratory was used.[10a,b] To a cooled solution (0 °C) of neopentylglycol (6.0 mmol, 2.0 equiv) in toluene (3 mL) was slowly added $(CH_3)_2S{\cdot}BH_3$ (6 mmol, 2.0 equiv) under nitrogen. The reaction was allow to stir at 0 °C for 30 min and then at room temperature for 90 min. The neopentylglycolborane was used directly without further purification.

General Procedure for Neopentylglycolborylation. The aryl boronic esters (except 2-(4-methoxyphenyl)5,5-dimethyl-1,3,2-dioxaborinane (**2a**)) were prepared according to literature procedures.[10,15−17] To an oven-dried 25 mL Schlenk tube were added Zn powder (6.0 mmol), $NiCl_2$(dppp) (1.5 mmol), and PPh_3 (3.0 mmol) along with the appropriate aryl halide (if it is solid) (3.0 mmol). The aryl halide, catalyst, and PPh_3 were degassed by pumping and backfilling with nitrogen three times. Dry toluene (3 mL) was added to the reaction mixture along with the appropriate aryl halide (if it is liquid) and Et_3N (9.0 mmol). The neopentylglycolborane was added dropwise to the reaction mixture. The reaction was placed into an oil bath at 100 °C with stirring under nitrogen. After the starting material was consumed, the reaction was quenched by addition of saturated NH_4Cl solution and extracted with EtOAc three times. The organic fractions were combined and dried over $MgSO_4$, followed by filtration and evaporation of the solvent. The crude product was purified by column chromatography.

General Procedure for Cross-Coupling Reactions. To an oven-dried test tube (15 × 85 mm) were added aryl mesylate or aryl sulfamate (0.3 mmol), neopentylglycol boronic ester (0.30 mmol), Ni(II)Cl(1-naphthyl)$(PPh_3)_2$ (0.015 mmol), and K_3PO_4 (0.9 mmol). The tube was taken into a glovebox, and PCy_3 (0.030 mmol) was added. Dried THF (1.0 mL) was then added, and the tube was capped with a rubber septum. The reaction was stirred at room temperature under nitrogen in the glovebox for 10−72 h (see Tables 3−5). The crude mixture was filtered through a short column of silica gel. The solvent was evaporated and the product was purified by column chromatography with dichloromethane/hexane or EtOAc/hexane as eluent.

Methyl 4′-methoxy(1,1′-biphenyl)-4-carboxylate (3a): white solid (from mesylate: 68 mg, 94%; from sulfamate: 59 mg, 81%); mp 173−174 °C (lit.[10c] mp 172−173 °C); ^1H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, J = 8.3, 2H), 7.62 (d, J = 8.3, 2H), 7.57 (d, J = 8.7, 2H), 6.99 (d, J = 8.7, 2H), 3.93 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 160.0, 145.4, 132.6, 130.2, 128.5, 128.4, 126.6, 114.53, 55.5, 52.2.

Dimethyl (1,1′-biphenyl)-4,4′-dicarboxylate (3b): white solid (from mesylate: 77 mg, 95%; from sulfamate: 74 mg, 91%); mp 213-214 °C (lit.[10c] mp 212−214 °C); ^1H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, J = 8.4, 4H), 7.69 (d, J = 8.4, 4H), 3.95 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 144.5, 130.4, 129.9, 127.4, 52.4.

Dimethyl (1,1′-biphenyl)-3,4′-dicarboxylate (3d): white solid (from mesylate: 79 mg, 98%; from sulfamate: 76 mg, 94%); mp 95−96 °C (lit.[10c] mp 95 °C); ^1H NMR (500 MHz, $CDCl_3$) δ 8.29 (s, 1H), 8.11 (d, J = 7.7, 2H), 8.05 (d, J = 7.3, 1H), 7.78 (d, J = 7.2, 1H), 7.67 (d, J = 7.7, 2H), 7.52 (t, J = 7.5, 1H), 3.94 (s, 3H), 3.93 (s,3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 166.8, 144.5, 140.3, 131.6, 131.0, 130.3, 129.4, 129.2, 129.1, 128.4, 127.1, 52.3, 52.2.

4,4′-Dimethoxy-1,1′-biphenyl (3e): white solid (from mesylate: 51 mg, 80%; from sulfamate: 51 mg, 80%); mp 172−173 °C (lit.[10c] mp

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171−172 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, J = 8.8, 4H), 6.96 (d, J = 8.8, 4H), 3.84 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.9, 132.7, 126.9, 113.3, 54.5.

Methyl 4′-methoxy(1,1′-biphenyl)-3-carboxylate (3f): white solid (from mesylate: 56 mg, 77%; from sulfamate: 72 mg, 99%); mp 69−70 °C (lit.[10c] mp 68−70 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.96 (d, J = 7.7, 1H), 7.72 (d, J = 7.7, 1H), 7.55 (d, J = 8.7, 2H), 7.46 (t, J = 7.7, 1H), 6.98 (d, J = 8.7, 2H), 3.93 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 159.6, 141.2, 132.7, 131.2, 130.8, 128.9, 128.3, 127.9, 127.8, 114.4, 55.4, 52.2.

Dimethyl (1,1′-biphenyl)-2,4′-dicarboxylate (3g): white solid (from mesylate: 78 mg, 96%; from sulfamate: 76 mg, 94%); mp 58−59 °C (lit.[10c] mp 56−58 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, J = 8.2, 2H), 7.88 (d, J = 7.6, 1H), 7.54 (t, J = 7.1, 1H), 7.44 (t, J = 7.3, 1H), 7.41−7.31 (m, J = 8.8, 3H), 3.93 (s, 3H), 3.63 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.6, 167.0, 146.3, 141.7, 131.6, 130.7, 130.6, 130.2, 129.4, 129.0, 128.5, 127.9, 52.2, 52.1.

Methyl 4′-methoxy(1,1′-biphenyl)-2-carboxylate[10c] (3h): colorless oil (from mesylate: 68 mg, 94%; from sulfamate: 55 mg, 75%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, J = 7.8, 1H), 7.49 (td, J = 7.6, 1.4, 1H), 7.40−7.31 (m, J = 12.0, 4.5, 2H), 7.24 (d, J = 8.7, 2H), 6.93 (d, J = 8.7, 2H), 3.84 (s, 3H), 3.66 (s, 3H). 52.08; ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.5, 159.1, 142.1, 133.8, 131.3, 131.0, 130.8, 129.8, 129.6, 126.9, 113.7, 55.4, 52.1.

Dimethyl (1,1′-biphenyl)-2,3′-dicarboxylate[29] (3i): colorless oil (from mesylate: 75 mg, 93%; from sulfamate: 78 mg, 96%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (dt, J = 7.2, 1.7, 1H), 8.01 (s, 1H), 7.90 (d, J = 7.8, 1H), 7.56 (td, J = 7.5, 1.3, 1H), 7.52−7.42 (m, 3H), 7.37 (d, J = 7.6, 1H), 3.92 (s, 3H), 3.64 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.7, 167.1, 141.9, 133.1, 131.7, 131.0, 130.6, 130.3, 130.2, 129.6, 128.6, 128.2, 127.8, 52.3, 52.1.

Methyl 2′-methoxy(1,1′-biphenyl)-4-carboxylate (3j): white solid (from mesylate: 71 mg, 98%; from sulfamate: 52 mg, 72%); mp 78−80 °C (lit.[10c] mp 80 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, J = 8.3, 2H), 7.60 (d, J = 8.3, 2H), 7.38−7.28 (m, J = 15.1, 7.5, 2H), 7.03 (t, J = 7.5, 1H), 6.98 (d, J = 8.2, 1H), 3.92 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 156.6, 143.5, 130.9, 129.7, 129.7, 129.5, 129.4, 128.6, 121.0, 111.5, 55.6, 52.1.

2,4′-Dimethoxy-1,1′-biphenyl (3k): white solid (from mesylate: 52 mg, 81%; from sulfamate: 35 mg, 55%); mp 69−70 °C (lit.[10c] mp 64−66 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J = 8.5, 2H), 7.33−7.25 (m, 2H), 7.01 (t, J = 7.4, 1H), 6.98−6.91 (m, 3H), 3.84 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.8, 156.6, 131.1, 130.8, 130.7, 130.5, 128.3, 121.0, 113.6, 111.4, 55.7, 55.4.

Methyl 2′-methoxy(1,1′-biphenyl)-3-carboxylate (3l): white solid (from mesylate: 61 mg, 84%; from sulfamate: 59 mg, 81%); mp 96−97 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (t, J = 1.5, 1H), 8.03−7.97 (m, 1H), 7.73 (ddd, J = 7.7, 1.7, 1.3, 1H), 7.47 (t, J = 7.7, 1H), 7.38−7.30 (m, 2H), 7.04 (td, J = 7.5, 1.0, 1H), 6.99 (d, J = 8.2, 1H), 3.92 (s, 3H), 3.81 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4, 156.6, 139.0, 134.3, 131.0, 130.9, 130.1, 129.8, 129.2, 128.2, 128.1, 121.1, 111.4, 100.1, 55.7, 52.2; HRMS (CI+) calcd for $C_{15}H_{14}O_3Na$ (M^+ + Na) 265.0841, found 265.0842.

Methyl 3′-methoxy(1,1′-biphenyl)-4-carboxylate (3m): white solid (from mesylate: 71 mg, 98%; from sulfamate: 68 mg, 94%); mp 54−55 °C (lit.[10c] mp 52−54 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, J = 8.4, 2H), 7.63 (d, J = 8.4, 2H), 7.35 (t, J = 7.9, 1H), 7.18 (d, J = 7.6, 1H), 7.15−7.10 (m, 1H), 6.92 (dd, J = 8.2, 1.9, 1H), 3.92 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 160.1, 145.6, 141.5, 130.1, 130.0, 129.1, 127.2, 119.8, 113.6, 113.1, 55.4, 52.2.

3,4′-Dimethoxy-1,1′-biphenyl (3p): white solid (from mesylate: 60 mg, 94%; from sulfamate: 49 mg, 76%); mp 53−54 °C (lit.[10c] mp 56−58 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J = 7.3, 2H), 7.33 (t, J = 7.9, 1H), 7.14 (d, J = 8.5, 1H), 7.09 (s, 1H), 6.97 (d, J = 7.3, 2H), 6.89−6.81 (m, 1H), 3.86 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 158.4, 141.5, 132.8, 128.8, 127.3, 118.4, 113.3, 111.7, 111.2, 54.5, 54.4.

Methyl 3′-methoxy(1,1′-biphenyl)-2-carboxylate (3s): colorless oil (from mesylate: 65 mg, 90%; from sulfamate: 65 mg, 90%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (dd, J = 7.7, 1.0, 1H), 7.52 (td, J = 7.5, 1.4, 1H), 7.44−7.37 (m, 2H), 7.30 (t, J = 7.9, 1H), 6.94−6.84 (m, 3H), 3.83 (s, 3H), 3.65 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.3, 158.5, 141.9, 141.4, 130.3, 130.2, 129.7, 128.8, 128.2, 126.4, 120.0, 113.0, 112.0, 54.4, 51.1; HRMS (CI+) calcd for $C_{15}H_{14}O_3Na$ (M^+ + Na) 265.0841, found 265.0834.

Dimethyl (1,1′-biphenyl)-2,2′-dicarboxylate (3t): white solid (from mesylate: 27 mg, 33%; from sulfamate: 19 mg, 23%); mp 72−73 °C (lit.[30] mp 74 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 7.7, 2H), 7.53 (t, J = 7.5, 2H), 7.43 (t, J = 7.6, 2H), 7.21 (d, J = 7.5, 2H), 3.61 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.6, 143.4, 131.6, 130.3, 130.0, 129.5, 127.3, 51.9.

Methyl 2′-methoxy(1,1′-biphenyl)-2-carboxylate[10c] (3u): colorless oil (from mesylate: 64 mg, 90%; from sulfamate: 51 mg, 70%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (dd, J = 7.7, 1.1, 1H), 7.52 (td, J = 7.6, 1.3, 1H), 7.37 (td, J = 7.6, 1.1, 1H), 7.34−7.28 (m, 2H), 7.23 (dt, J = 6.2, 3.1, 1H), 7.02 (t, J = 7.4, 1H), 6.88 (d, J = 8.2, 1H), 3.69 (s, 3H), 3.63 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.7, 156.1, 138.9, 131.7, 131.6, 131.4, 130.6, 130.0, 129.4, 128.9, 127.2, 120.8, 110.2, 55.3, 51.7.

2,3′-Dimethoxy-1,1′-biphenyl[29] (3v): colorless oil (from mesylate: 62 mg, 97%; from sulfamate: 55 mg, 85%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, J = 7.3, 3H), 7.12−7.06 (m, 2H), 7.01 (td, J = 7.5, 1.0, 1H), 6.97 (d, J = 7.8, 1H), 6.87 (ddd, J = 8.2, 2.6, 0.9, 1H), 3.83 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.4, 156.6, 140.1, 131.0, 130.7, 129.0, 128.8, 122.2, 120.9, 115.5, 112.6, 111.4, 55.7, 55.4.

2,2′-Dimethoxy-1,1′-biphenyl (3x): white solid (from mesylate: 47 mg, 73%; from sulfamate: 46 mg, 72%); mp 153−155 °C (lit.[10c] mp 152−154 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, J = 7.8, 2H), 7.24 (d, J = 7.4, 2H), 6.99 (t, J = 7.5, 2H), 6.96 (d, J = 8.3, 2H), 3.75 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.2, 131.6, 128.7, 128.0, 120.5, 111.2, 55.8.

1-(4′-Methoxy(1,1′-biphenyl)-4-yl)ethanone[10c] (3y): white solid (from mesylate: 55 mg, 81%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 8.4, 2H), 7.64 (d, J = 8.4, 2H), 7.58 (d, J = 8.8, 2H), 7.00 (d, J = 8.8, 2H), 3.86 (s, 3H), 2.63 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.9, 160.1, 145.5, 135.5, 132.4, 129.1, 128.5, 126.8, 114.6, 55.5, 26.8. ^{1}H NMR matches with literature data.

4′-Methoxy(1,1′-biphenyl)-4-carbonitrile (3z): white solid (from mesylate: 58 mg, 93%; from sulfamate: 28 mg, 45%); mp 102−103 °C (lit.[10c] mp 102−103 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 8.3, 2H), 7.64 (d, J = 8.1, 2H), 7.54 (d, J = 8.7, 2H), 7.01 (d, J = 8.7, 2H), 3.86 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.4, 145.4, 132.7, 131.7, 128.5, 127.3, 119.2, 114.7, 110.3, 55.6.

3-(4-Methoxyphenyl)pyridine[10c] (3aa): white solid (from mesylate: 53 mg, 95%; from sulfamate: 55 mg, 99%); mp 62−64 °C (lit.[10c] mp 60−61 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.55 (d, J = 4.4, 1H), 7.83 (d, J = 7.9, 1H), 7.53 (dd, J = 6.9, 4.8, 2H), 7.33 (dd, J = 7.8, 4.8, 1H), 7.01 (d, J = 8.7, 2H), 3.86 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.9, 148.1, 148.0, 136.4, 134.0, 130.4, 128.4, 123.7, 114.7, 55.5.

Methyl 4′-acetyl(1,1′-biphenyl)-4-carboxylate[31] (3ab): white solid (from mesylate: 43 mg, 57%); mp 164−165 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, J = 8.2, 2H), 8.05 (d, J = 8.2, 2H), 7.72 (d, J = 8.3, 2H), 7.69 (d, J = 8.3, 2H), 3.95 (s, 3H), 2.65 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.8, 166.9, 144.6, 144.4, 136.7, 130.4, 129.9, 129.1, 127.6, 127.4, 52.4, 26.8.

Methyl 4′-cyano(1,1′-biphenyl)-4-carboxylate (3ac): white solid (from mesylate: 61 mg, 85%); mp 141−142 °C (lit.[10c] mp 141−142 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.5, 2H), 7.76 (d, J = 8.5, 2H), 7.72 (d, J = 8.6, 2H), 7.66 (d, J = 8.5, 2H), 3.96 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7, 144.5, 143.5, 132.8, 130.5, 130.3, 128.1, 127.4, 118.8, 112.0, 52.4.

Methyl 4-(pyridin-3-yl)benzoate (3ad): white solid (from mesylate: 58 mg, 90%; from sulfamate: 56 mg, 87%); mp 103−104 °C (lit.[32] mp 105−107 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.64 (d, J = 4.7, 1H), 8.15 (d, J = 8.2, 2H), 7.91 (dd, J = 7.9, 1.5, 1H), 7.66 (d, J = 8.2, 2H), 7.40 (dd, J = 7.8, 4.8, 1H), 3.95 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 149.4, 148.5, 142.4, 135.7, 134.6, 130.5, 129.9, 127.2, 123.8, 52.4.

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8-(4-Methoxyphenyl)quinoline (3ae): white solid (from mesylate: 62 mg, 87%); mp 111−112 °C (lit.[10c] mp 113−114 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.95 (dd, J = 4.1, 1.8, 1H), 8.19 (dd, J = 8.3, 1.8, 1H), 7.79 (dd, J = 8.1, 1.3, 1H), 7.71 (dd, J = 7.1, 1.4, 1H), 7.66 (d, J = 8.7, 2H), 7.62−7.56 (m, 1H), 7.40 (dd, J = 8.2, 4.1, 1H), 7.04 (d, J = 8.7, 2H), 3.88 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2, 150.3, 146.3, 140.7, 136.4, 132.1, 131.9, 130.1, 129.0, 127.2, 126.4, 121.1, 113.7, 55.5.

1-(4′-Methoxy(1,1′-biphenyl)-4-yl)pyrrolidine-2,5-dione (3af): white solid (from mesylate: 79 mg, 94%); mp 212−213 °C (lit.[10c] mp 212−213 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, J = 8.5, 2H), 7.52 (d, J = 8.7, 2H), 7.33 (d, J = 8.5, 2H), 6.98 (d, J = 8.7, 2H), 3.85 (s, 3H), 2.92 (s, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.4, 159.6, 141.4, 132.8, 130.5, 128.4, 127.6, 126.8, 114.4, 55.5, 28.6.

3-(Thiophene-3-yl)pyridine (3ag): white solid (from mesylate: 39 mg, 81%); mp 75−76 °C (lit.[10c] 76−77 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.54 (s, 1H), 7.90−7.83 (m, 1H), 7.52 (dd, J = 2.9, 1.3, 1H), 7.45 (dd, J = 5.0, 3.0, 1H), 7.40 (dd, J = 5.0, 1.3, 1H), 7.33 (dd, J = 7.8, 4.8, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.4, 147.9, 139.0, 133.7, 131.7, 127.1, 126.1, 123.8, 121.6.

Methyl 4-(quinolin-8-yl)benzoate (3ah): white solid (from mesylate: 78 mg, 99%); mp 91−92 °C (lit.[10c] mp 92−93 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.95 (dd, J = 4.1, 1.6, 1H), 8.22 (dd, J = 8.3, 1.6, 1H), 8.17 (d, J = 8.2, 2H), 7.86 (d, J = 8.1, 1H), 7.78 (d, J = 8.1, 2H), 7.75 (d, J = 7.1, 1H), 7.62 (t, J = 7.6, 1H), 7.43 (dd, J = 8.3, 4.1, 1H), 3.95 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.3, 150.6, 146.0, 144.5, 140.0, 136.5, 130.8, 130.5, 129.4, 129.1, 128.9, 128.4, 126.4, 121.4, 52.2.

Methyl 4′-(2,5-dioxopyrrolidin-1-yl)(1,1′-biphenyl)-4-carboxylate (3ai): white solid (from mesylate: 46 mg, 49%); mp 217−219 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, J = 8.2, 2H), 7.72 (d, J = 8.4, 2H), 7.65 (d, J = 8.2, 2H), 7.41 (d, J = 8.3, 2H), 3.94 (s, 3H), 2.93 (s, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.2, 167.0, 144.7, 140.6, 131.9, 130.3, 129.5, 128.2, 127.3, 127.0, 52.3, 28.6; HRMS (CI^+) calcd for $C_{18}H_{16}NO_4$ (M^+ + H) 310.1079, found 310.1075.

3-(Thiophene-2-yl)pyridine[10c] (3aj): light brown oil (from mesylate: 32 mg, 67%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.51 (d, J = 4.2, 1H), 7.90−7.81 (m, 1H), 7.40−7.33 (m, 2H), 7.33−7.28 (m, 1H), 7.16−7.06 (m, 1H)l ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.6, 147.1, 140.5, 133.1, 130.5, 128.4, 126.2, 124.3, 123.7.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H NMR and ^{13}C NMR spectra of compounds **3a−aj**. This information is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: percec@sas.upenn.edu.

Notes

The authors declare no competing financial interest.

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