JOC Article

Polymer-Assisted Solution-Phase (PASP) Suzuki Couplings Employing an Anthracene-Tagged Palladium Catalyst

Ping Lan,[†] Daniela Berta,[§] John A. Porco, Jr,[‡] Michael S. South,[†] and John J. Parlow*,[†]

Department of Medicinal and Combinatorial Chemistry, Pharmacia Corporation, 800 North Lindbergh Boulevard, St. Louis, Missouri 63167, Department of Medicinal Chemistry, Pharmacia Corporation, Viale Pasteur, 10, 20014 Nerviano, Italy, and Department of Chemistry and Center for Chemical Methodology and Library Development, Boston University, 590 Commonwealth Avenue, Boston, Massachusetts 02215

john.j.parlow@pfizer.com

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A general method for polymer-assisted solution-phase (PASP) Suzuki reactions employing a combination of anthracene-tagged palladium catalyst and anthracene-tagged boronic acid with a polymer-supported carbonate base is reported. The anthracene-tagged catalyst allows for the easy removal of the Pd catalyst along with the dissociated phosphine ligand and phosphine oxide byproducts by sequestration through a chemoselective Diels−Alder reaction with a maleimide resin. The polymer-supported carbonate base facilitates the removal of excess boronic acid and the borane-containing byproducts present at the end of the coupling reaction. The Suzuki coupling reaction can be efficiently conducted by using combinations of the anthracene-tagged Pd catalyst, polymer-supported carbonate base, and anthracene-tagged boronic acid to yield the desired product in high purity and yield without the use of chromatography.

Introduction

One of the chemical transformations that has received little attention in polymer-assisted solution-phase (PASP) based approaches is the Suzuki reaction. The Suzuki reaction, a palladium-catalyzed cross-coupling of organoboranes such as boronic acids, boronates, and trialkylboranes with organic halides and triflates in the presence of a base, has become a powerful tool in organic synthesis.[1] The Suzuki reaction has proved extremely versatile and has found extensive use in the formation of carbon−carbon bonds, especially the formation of aryl−aryl bonds. In particular, the biaryl unit is represented in many biologically active compounds and novel organic materials.[2]

The Suzuki reaction has gained popularity due to the mild reaction conditions, commercial availability of diverse boronic acids/esters, reaction efficiency, and compatibility with many functional groups present in the starting materials. Suzuki coupling reactions generally employ organic solvents such as DMF and THF in the presence of soluble Pd(II) or Pd(0) catalysts. Commonly used Pd catalysts are $Pd(PPh_3)_4$ and $Pd(PPh_3)_2Cl_2$. Frequently used bases are inorganic carbonates such as Na_2CO_3, K_2CO_3, and Cs_2CO_3. Substituted aryl halides (bromides or iodides) and triflates along with boronic acids or esters are suitable substrates. The major problems associated with the broad application of this reaction in parallel synthesis are the removal of the homogeneous Pd catalyst, disassociated ligand byproducts, unreacted starting materials (aryl halide and boronic acid), and the inorganic base. An additional problem is the formation of byproducts from two competing side reactions: the coupling of arylboronic acid with the phenyl group from the triphenylphosphine-stabilizing ligand and the self-coupling products generated from the starting aryl substrates when the desired cross-coupling is very slow.[3]

Over the past decade, several new methodologies have been developed to address some aspects of these problems associated with the Pd-catalyzed Suzuki reaction. One approach that allows for easy removal of the Pd catalyst employs the use of a supported catalyst that can be readily removed by filtration. The kind of supports studied thus far include polystyrene resin,[4] amphiphilic

* Corresponding author. Phone: 314-274-3494.
[†] Department of Medicinal and Combinatorial Chemistry, Pharmacia Corporation.
[§] Department of Chemistry, Pharmacia Corporation.
[‡] Boston University.

(1) (a) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633−9695. (b) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147−168. (c) Stanforth, S. P. *Tetrahedron* **1998**, *54*, 263−303. (d) Miraura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483.

(2) (a) Schiedel, M.-S.; Briehn, C. A.; Bäuerle, P. *J. Organomet. Chem.* **2002**, *653*, 200−208. (b) Chang, L. L.; Ashton, W. T.; Flanagan, K. L.; Strelitz, R. A.; MacCoss, M.; Greenlee, W. J.; Chang, R. S. L.; Lotti, V. J.; Faust, K. A.; Chen, T.-B.; Bunting, P.; Zingaro, G. J.; Kivlighn, S. D.; Siegl, P. K. S. *J. Med. Chem.* **1993**, *36*, 2558−2568. (c) Bovy, P. R.; Collins, J. T.; Olins, G. M.; MacMahon, E. G.; Hutton, W. C. *J. Med. Chem.* **1991**, *34*, 2410−2414.

(3) Moreno-Mañas, M.; Pérez, M.; Pleixats, R. *J. Org. Chem.* **1996**, *61*, 2346−2351.

(4) (a) Atrash, B.; Reader, J.; Bradley, M. *Tetrahedron Lett.* **2003**, *44*, 4779−4782. (b) Parrish, C. A.; Buchwald, S. L. *J. Org. Chem.* **2001**, *66*, 3820−3827. (c) Fenger, I.; Drian, C. L. *Tetrahedron Lett.* **1998**, *39*, 4287−4290. (d) Jang, S.-B. *Tetrahedron Lett.* **1997**, *38*, 1793−1796.

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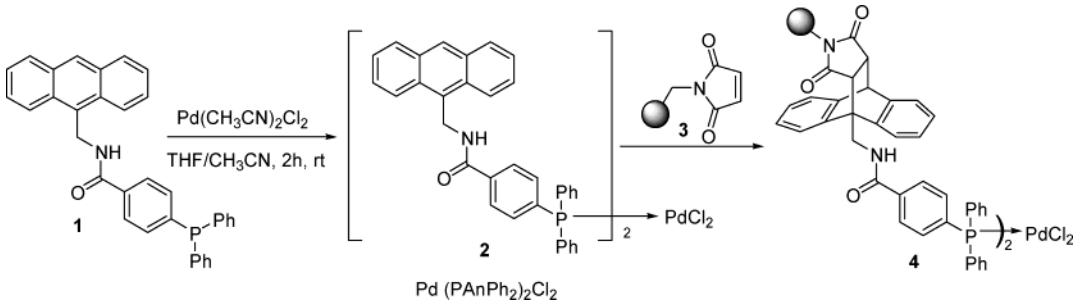
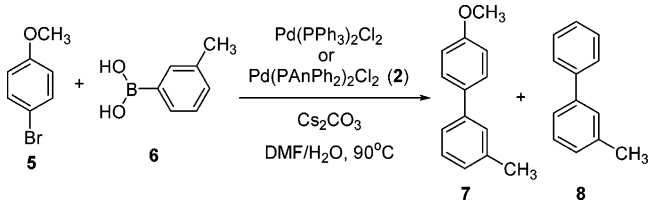
SCHEME 1. Synthesis and Sequestration of Anthracene-Tagged Pd Catalyst 2



polymers,[5] and glass beads,[6] which take advantage of the reaction's tolerance for aqueous phase, and application of ligandless charcoal.[7] A strategy that employs a fluorous biphase system, in which the perfluoro-tagged Pd catalyst is located in the fluorous phase, has also been reported.[8] These methods allow for the removal of the Pd catalyst but still rely on further purification for removal of the remaining unwanted species. Solid-phase Suzuki couplings, which involve reacting a resin-bound aryl halide with a solution-phase boronic acid, are an excellent approach to solve all the problems in terms of removing the catalyst, the base, and unreacted boronic acid along with the byproducts in one filtration step.[9] However, this approach is not always practical for a single step in a solution-phase synthesis. Recently, there have been reports of a similar approach involving immobilization of the boronic acid instead of the aryl halide on the solid phase.[10] However, products after Pd-catalyzed cleavage may still require purification.

As part of our interest to develop new methodology for PASP synthesis and purification of final products, we have studied the application of Diels–Alder cycloaddition-removable tags, specifically anthracene-tagged reagents or substrates.[11] The anthracenyl moiety has been shown by us and other researchers to be a useful chemical "tag" aiding in the purification process.[11,12] A major advantage of the cycloaddition-removable anthracene tag is the highly orthogonal and chemoselective reactivity of the Diels–Alder reaction for the immobilization and removal of the tagged molecule, thus allowing the presence of numerous functional groups. Additionally,

SCHEME 2. Suzuki Reaction Evaluating Pd Catalyst 2



the intense fluorescence of the anthracene permits easy monitoring of reaction progress. We have demonstrated the use of anthracene-tagged reagents for the Mitsunobu reaction permitting the simple removal of excess reagent and reagent byproducts.[11a] Another application employs anthracene-tagged substrates in the Stille coupling allowing for chemistry to be conducted in the solution phase followed by "phase switching" immobilization onto a solid support via Diels–Alder cycloaddition to aid compound purification, and cleavage of the desired purified products.[11b] Others have demonstrated the use of anthracene-tagged substrates by immobilizing an anthracene-tagged carboxylic acid followed by solid-phase Suzuki couplings, activation, and then cleavage with nucleophiles to afford ester and amide products.[12] Herein, we report the use of an anthracene-tagged catalyst and substrates in conjunction with a polymer-bound base for parallel PASP Suzuki coupling reactions.

Results and Discussion

Previously, anthracene-tagged triphenylphosphine **1** was synthesized and applied in PASP Mitsunobu reactions.[11a] We reasoned that an anthracene-tagged catalyst prepared by complexation of phosphine **1** with palladium would allow for the sequestration of both the Pd catalyst and any dissociated ligand byproducts from the Suzuki reaction. Thus, the tagged phosphine **1** was reacted with palladium dichloride to afford the anthracene-tagged Pd catalyst **2** (Scheme 1).

Catalyst **2** was evaluated and compared to the corresponding untagged catalyst, $Pd(PPh_3)_2Cl_2$, in a Suzuki coupling (Scheme 2). Both catalysts gave very similar yields of the coupled product **7** (81% vs 80%). However, with the tagged catalyst **2**, the amount of side-product **8** from the reaction between the boronic acid **6** and the phenyl of triarylphosphine ligand was reduced (4% vs 9%), presumably due to the increased crowdedness around the phosphine.[13]

(5) (a) Yamada, Y. A.; Takeda, K.; Takahashi, H.; Ikegami, S. *Org. Lett.* **2002**, *4*, 3371–3374. (b) Uozumi, Y.; Nakai, Y. *Org. Lett.* **2002**, *4*, 2997–3000. (c) Uozumi, Y.; Danjo, H.; Hayashi, T. *J. Org. Chem.* **1999**, *64*, 3384–3388.

(6) Lawson Daku, K. M.; Newton, R. F.; Pearce, S. P.; Vile, J.; Williams, J. M. J. *Tetrahedron Lett.* **2003**, *44*, 5095–5098.

(7) (a) Organ, M. G.; Mayer, S. *J. Comb. Chem.* **2003**, *5*, 118–124. (b) Sakurai, H.; Tsukuda, T.; Hirao, T. *J. Org. Chem.* **2002**, *67*, 2721–2722. (c) LeBlond, C. R.; Andrews, A. T.; Sun, Y.; Sowa, J. R., Jr. *Org. Lett.* **2001**, *3*, 1555–1557. (d) Ennis, D. S.; McManus, J.; Wood-Kaczmar, W.; Richardson, J.; Smith, G. E.; Carstairs, A. *Org. Proc. Res. Dev.* **1999**, *3*, 248–252. (e) Gala, D.; Stamford, A.; Jenkins, J.; Kugelman, M. *Org. Proc. Res. Dev.* **1997**, *1*, 163–164. (f) Marck, G.; Villiger, A.; Buchecker, R. *Tetrahedron Lett.* **1994**, *35*, 3277–3280.

(8) Schneider, S.; Bannwarth, W. *Helv. Chim. Acta* **2001**, *84*, 735–742.

(9) For review see: Bräse, S.; Kirchhoff, J. H.; Köbberling, J. *Tetrahedron* **2003**, *59*, 885–939 and references therein.

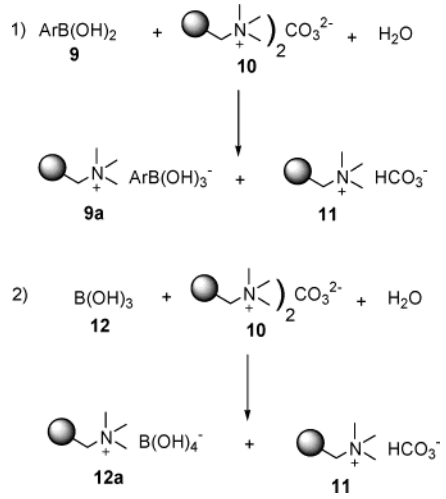
(10) (a) Pourbaix, C.; Carreaux, F.; Carboni, B. *Org. Lett.* **2001**, *3*, 803–805. (b) Li, W.; Burgess, K. *Tetrahedron Lett.* **1999**, *40*, 6527–6530.

(11) (a) Lan, P.; Porco, J. A., Jr.; South, M. S.; Parlow, J. J. *J. Comb. Chem.* **2003**, *5*, 660–669. (b) Wang, X.; Parlow, J. J.; Porco, J. A., Jr. *Org. Lett.* **2000**, *2*, 2999–3001.

(12) Li, X.; Abell, C.; Ladlow, M. *J. Org. Chem.* **2003**, *68*, 4189–4194.

(13) It is known that a bulky phosphine ligand such as MOP can help retard the phenyl shifting side reaction. See ref 1a.

SCHEME 3. Multiple Roles of Polymer-Supported Carbonate Base 10



A model sequestration study was performed by incubating polymer-bound maleimide **3** with catalyst **2** in deuterated DMF at 90 °C for 10 h. Catalyst **2** was completely sequestered, affording polymer-bound palladium catalyst **4**[14] as indicated by phosphorus NMR (Scheme 1). Filtration and evaporation left a residue-free vial.

With a sequesterable Pd catalyst in hand, attention was focused evaluation of bases. A polymer-supported carbonate, such as tetraalkylammonium carbonate resin **10**,[15] should act in the same way as an inorganic carbonate base to activate the boronic acid **9** for coupling and to neutralize the boric acid byproduct **12** (Scheme 3). In addition, any unreacted boronic acid should be sequestered by the polymer-supported base. The mechanistic study from Smith and his colleagues[16] suggested that the $ArB(OH)_3^-$ anion, resulting from the reaction between Lewis acid boronic acid and carbonate base is likely the reactive species rather than boronic acid itself. Therefore, additional water and carbonate base are necessary to neutralize the coupling byproduct boric acid to afford the boric anion $B(OH)_4^-$. Thus, replacement of the inorganic base with polymer-supported carbonate **10** can serve multiple roles: as the base to activate the boronic acid for coupling and as the scavenger to sequester the unreacted boronic acid and boric acid byproduct.

A model Suzuki reaction with use of the anthracene-tagged palladium catalyst **2** and polymer-supported carbonate base **10** was examined (Scheme 4). The coupling of 4′-bromoacetophenone **13b** with 1.2 equiv of 4-ethoxyphenylboronic acid **9E** occurred smoothly in the presence of 10 mol % of palladium complex **2** and 3.6 equiv of polymer-supported carbonate **10** in a mixed solvent DMF/H_2O (2 mL/0.1 mL) at 80 °C to give biphenyl product **14bE**, which was 97% pure as determined by GC analysis. Subsequent addition of PS-maleimide **3** and continued heating at 90 °C for 10 h followed by filtration and evaporation afforded the desired product **14bE** in 90% yield. ^1H and ^{13}C NMR showed high purity of the product without detectable boronic acid **9E** or other byproducts. Analysis of the filtered reaction mixture by ^{31}P NMR indicated the complete removal of phosphine ligand, and ICP-AES analysis showed that palladium was completely removed.[17]

To demonstrate the application of this methodology, a parallel array of reactions was designed involving a variety of aryl bromides **13** and aryl boronic acids **9**, each containing electron-withdrawing or electron-donating substituents (Figure 1). Thus, all combinations of each of the four substituted aryl bromides **13** with each of the five substituted aryl boronic acids **9** were subjected to the established coupling conditions with the tagged catalyst **2** and polymer-supported carbonate **10** (Scheme 4). After heating overnight, PS-maleimide resin **3** was added and heating continued at 90 °C for 10 h. Filtration removed the polymer-sequestered catalyst and dissociated phosphine or phosphine oxide, the polymer-supported base, and any species attached to the base. Subsequent evaporation afforded a product mixture containing the desired product **14** and varying amounts of minor products **15**−**17**. The purities of the coupling products were determined by GC analysis after filtration and by NMR analysis after concentration and drying. The yields were determined based on the weights. The results are shown in Table 1.

It is known that there are several side reactions competing with the major reaction pathway of the Suzuki coupling. The ratio of the products depends on the reaction rate of each step in the cycle. Scheme 4 shows the common products resulting from the Suzuki reaction: the desired product **14** and the major byproducts **15**, **16**, and **17**. For aryl bromides, the oxidative addition is believed to be rate determining,[16] and the results from Table 1 support this observation. For aryl bromides with electron-withdrawing substituents (**13a** and **13b**), the coupling reactions generally gave higher than 92% (GC purity, Table 1) of the desired product **14**. Self-coupling (**15**) from the boronic acid **9** was the only significant byproduct. This reflected a much faster reaction rate of the major pathway. When the aryl bromide was substituted with a slightly electron-donating group (**13c**), the GC purity ratio of the product was slightly lower with an average of 89% desired product **14**. The major byproducts **15** and **17** resulted from self-coupling of boronic acid **9** and from debromination of the aryl bromide **13c**, respectively. The debromination was presumably due to the ortho-substitution of the starting material. Aryl bromide **13d**, with a strong electron-donating substituent, afforded the desired product **14** with an average GC purity of 73%. The major byproducts, **15** and **16**, resulted from self-coupling of boronic acid **9** and cross-coupling between the boronic acid **9** and the phenyl group of the phosphine ligand, respectively. The substituents on the aryl boronic acids did not have much influence on the outcome of the reactions, as the product ratio for each

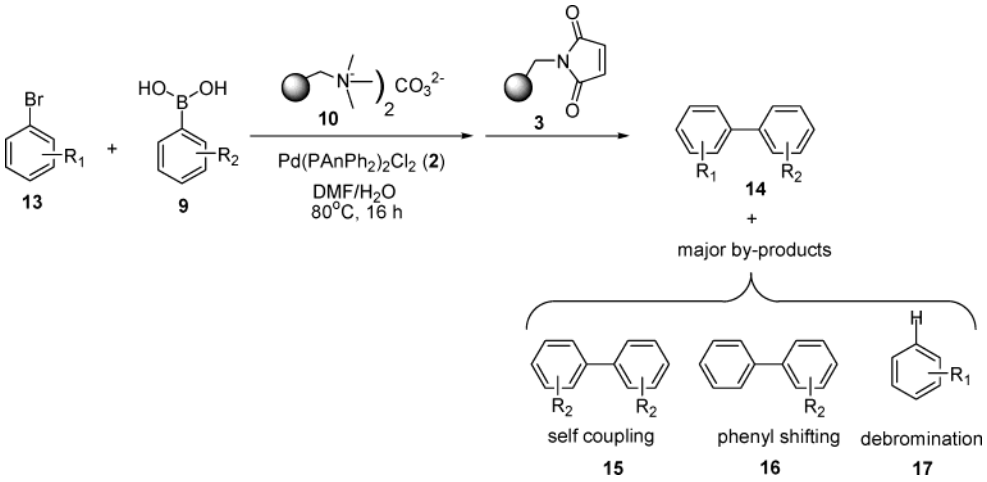
(14) Polymer-supported palladium catalyst **4** may also serve as a polystyrene-based palladium catalyst such as those cited in ref 4.

(15) The polymer-supported tetraalkylammonium carbonate was purchased from Aldrich (50−90 mesh, 2.5 mmol/g−3.5 mmol N/g.)

(16) Smith, G. B.; Dezeny, G. C.; Hughes, D. L.; King, A. O.; Verhoeven, T. R. *J. Org. Chem.* **1994**, *59*, 8151−8156.

(17) An ICP-AES analysis for palladium was conducted on the product mixture of **14bE** after sequestration with PS-maleimide **3**. ICP-AES analysis showed less than 1 ppm of Pd present with an expected theoretical value without sequestration of 91 000 ppm. A second analysis on the same sample prior to sequestration had an actual value of 5 430 ppm. The difference between the theoretical and actual value was due to lack of solubility of the sample. Thus, >99.98% of palladium had been removed from the product mixture.

SCHEME 4. PASP Suzuki Coupling



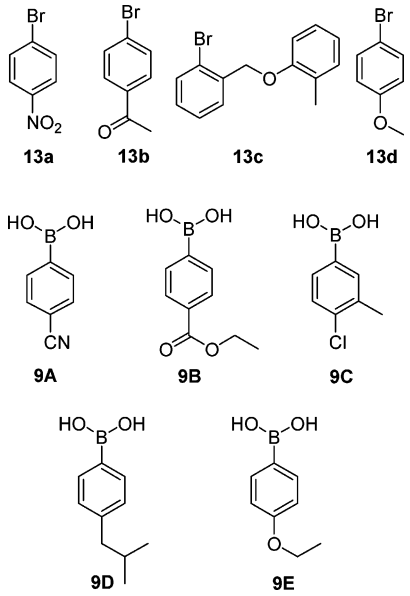


FIGURE 1. Aryl bromides **13** and aryl boronic acids **9** for Suzuki couplings.

specific aryl bromide was essentially the same for boronic acids having an electron-withdrawing or -donating group. The formation of self-coupling byproduct from the aryl bromide **13** and competitive hydrolytic deboronation of the arylboronic acid **9** was negligible in all cases.

An improved protocol for the Suzuki reaction involving electron-rich aryl bromides was investigated. Variations of the stoichiometric amounts of the Suzuki substrates were considered in an attempt to increase the percent of desired product relative to the byproducts. At the end of the reaction, the excess substrate could be removed by reacting it with the corresponding anthracene-tagged Suzuki partner followed by sequestration with the maleimide resin.

Initially, 9-bromoanthracene and 9,10-dibromoanthracene were evaluated as potential Suzuki aryl bromide coupling partners for reaction with excess boronic acid. Each was evaluated in a sequestration study with maleimide resin **3**. Despite prolonged reaction times and the use of excess maleimide resin **3**, starting material remained. Thus, a more reactive anthracene-tagged aryl bromide was required. Aminomethylanthracene **18** was coupled with 4-bromobenzoic acid **19** to afford the tagged aryl bromide **20** (Scheme 5). Anthracene-tagged aryl bromide **20** proved to be an excellent partner in the Suzuki coupling and both the coupled product and starting anthracene-tagged bromide **20** were quantitatively sequestered by the maleimide resin **3**.

A second option was to design an anthracene-tagged boronic acid to react with and sequester excess aryl bromide. The anthracene-tagged boronic acid **25** was synthesized employing the elegant protocol developed by Hall and co-workers (Scheme 6).[18] Boronic acid **22** was loaded onto the *N*,*N*-diethanolaminomethyl polystyrene **21** (PS-DEAM) followed by coupling with aminomethylanthracene **18** to afford polymer-bound amide **24**. Cleavage of the boronic acid from the solid phase afforded the tagged boronic acid **25** in good yield and high purity.

To prove the anthracene-tagged boronic acid **25** could react with excess aryl bromide and subsequently be sequestered, **25** was subjected to a Suzuki coupling with a fluoro-labeled aryl bromide **26** under typical conditions (Scheme 7). GC/MS and ^{19}F NMR confirmed the disappearance of the aryl bromide **26** and formation of the tagged derivative **27**. After addition of the maleimide resin **3**, complete sequestration of the coupling product **27** was evident by a ^{19}F NMR of the PS-maleimide resin **28**, revealing a signal at −134.54 ppm (Scheme 7), and a ^{19}F NMR of the resulting solution, with no observable fluorine signal.

Thus, with both anthracene-tagged Suzuki substrates prepared, optimization of the Suzuki reaction with the electron- rich aryl bromide **13d** was evaluated by varying the stoichiometric amounts of each substrate. Not surprisingly, using an excess of boronic acid resulted in an increase in the self-coupling product **15** from the boronic substrate **9** (Scheme 4). To eliminate formation of the self-coupled byproduct, an excess of the aryl bromide rather than an excess of the boronic acid was used. By using an excess of the aryl bromide, an increased amount of the oxidative addition intermediate should be available for transmetalation with the boronic acid, effectively

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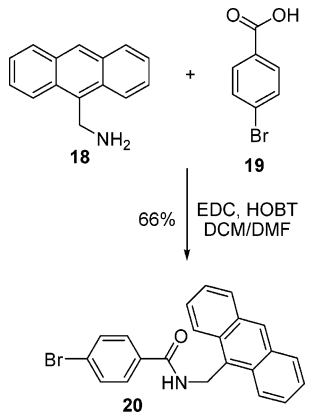
TABLE 1. PASP Suzuki Coupling Results: Percentage Ratio of Products (14:15:16:17)[a] and Yields[b] of 14

aryl boronic acids	aryl bromides				
	13a	**13b**	**13c**	**13d**[c]	**13d**[d]
9A	**14aA** 95:5:0:0 (89)	**14bA** 94:6:0:0 (89)	**14cA** 89:6:0:5 (72)	**14dA** 70:22:8:0 (83)	**14dA** 84:9:6:0 (84)
9B	**14aB** 94:6:0:0 (100)	**14bB** 92:8:0:0 (99)	**14cB** 86:9:0:5 (86)	**14dB** 73:19:8:0 (92)	**14dB** 90:4:6:0 (80)
9C	**14aC** 94:5:1:0 (80)	**14bC** 94:5:1:0 (82)	**14cC** 91:7:0:5 (86)	**14dC** 73:18:9:0 (96)	**14dC** 87:7:6:0 (78)
9D	**14aD** 95:3:2:0 (69)	**14bD** 95:3:2:0 (66)	**14cD** 89:9:0:2 (84)	**14dD** 75:17:8:0 (88)	**14dD** 87:7:6:0 (80)
9E	**14aE** 97:2:1:0 (97)	**14bE** 96:3:1:0 (99)	**14cE** 90:7:0:3 (70)	**14dE** 76:17:7:0 (94)	**14dE** 81:8:11:0 (82)

[a] The GC purities are reported as the percentage ratio of the desired coupling product **14**, the self-coupling byproduct **15** from the boronic acid **9**, byproduct **16** formed between the boronic acid **9** and phenyl group from the phosphine ligand, and desbromo product **17** from debromination of the aryl halide **13**. [b] Yield is based on mass recovery. [c] Products generated form Suzuki protocol in Scheme 4. [d] Products generated from modified Suzuki protocol in Scheme 8.

SCHEME 5. Synthesis of Anthracene-Tagged Aryl Bromide 20



minimizing the amount of self-coupling product from the boronic acid substrate.

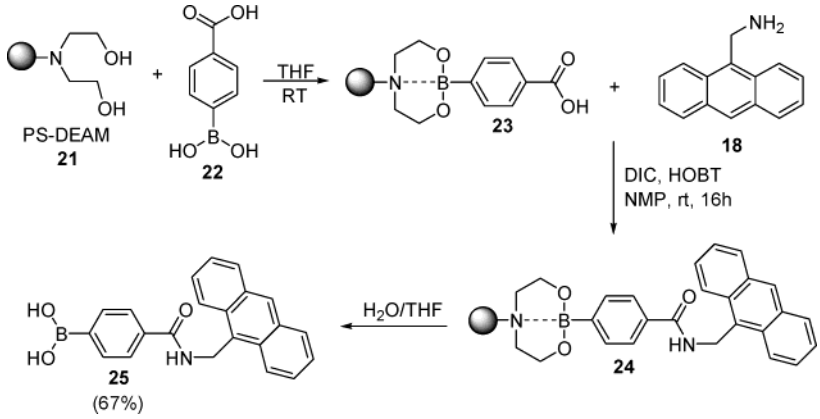
The improved Suzuki reaction involving electron-rich aryl bromides is shown in Scheme 8. The reaction was conducted with 1.8 equiv of aryl bromide **13d** relative to the boronic acid **9**. Upon complete consumption of the boronic substrate **9**, a second Suzuki coupling was initiated by the addition of the tagged boronic acid **25**. This transformed starting aryl bromide **13d** into sequesterable anthracene-tagged species **29**. Incubation of the product mixture with the PS-maleimide **3** resulted in sequestration of the unreacted tagged boronic acid **25**, anthracene derivative **29**, and Pd catalyst **2**. Filtration and evaporation afforded the purified products **14**. Comparisons of the product ratio with use of this modified protocol vs the standard protocol are impressive (Table 1). The average desired product ratio increased from 73% to 86% with the modified protocol, and a significant decrease in both byproducts **15** and **16** was observed.

In conclusion, we have developed a practical and efficient protocol for PASP parallel Suzuki couplings by employing the combination of anthracene-tagged catalyst, anthracene-tagged boronic acid, and polymer-supported tetramethylammonium carbonate as base. Polymer-supported carbonate base, the inorganic base necessary for the reaction, greatly facilitates the removal of excess boronic acid and the borane-containing byproducts present at the end of the coupling via a simple filtration, therefore eliminating the need for aqueous workup. Similarly, the development of an anthracene-tagged catalyst allows for the easy removal of the Pd catalyst along with the dissociated phosphine ligand and phosphine oxide byproducts by a Diels−Alder cycloaddition with polymer-bound maleimide followed by removal of the polymer-bound adducts via filtration. It was demonstrated that the Diels−Alder reaction of the anthracene-tagged Pd catalyst with PS-maleimide is highly efficient, as no observable phosphorus or palladium was detected in solution after the sequestration process. Thus, the Suzuki coupling can be efficiently conducted by using both the tagged catalyst and polymer-supported carbonate to yield the desired product in high purity and yield without the use of chromatography. For the sluggish aryl bromide substrates with strong electron-donating groups, a slightly modified protocol can be applied by increasing the stoichiometric amount of aryl bromide, which upon completion of the reaction can be consumed by addition of anthracene-tagged boronic acid followed by sequestration with PS-maleimide. Using this modified procedure afforded an increase in the desired Suzuki coupled product and minimized the byproduct formation. The anthracene-tagged catalyst and substrates are easily prepared in large quantities and stable under storage at low temperature for several months. The removal of anthracene-tagged species by PS-maleimide via Diels−Alder reaction is highly chemoselective and allows for the tolerance of many functional groups. One can envision applying this basic methodology to other Pd-catalyzed reactions, allowing for their use in a parallel format.

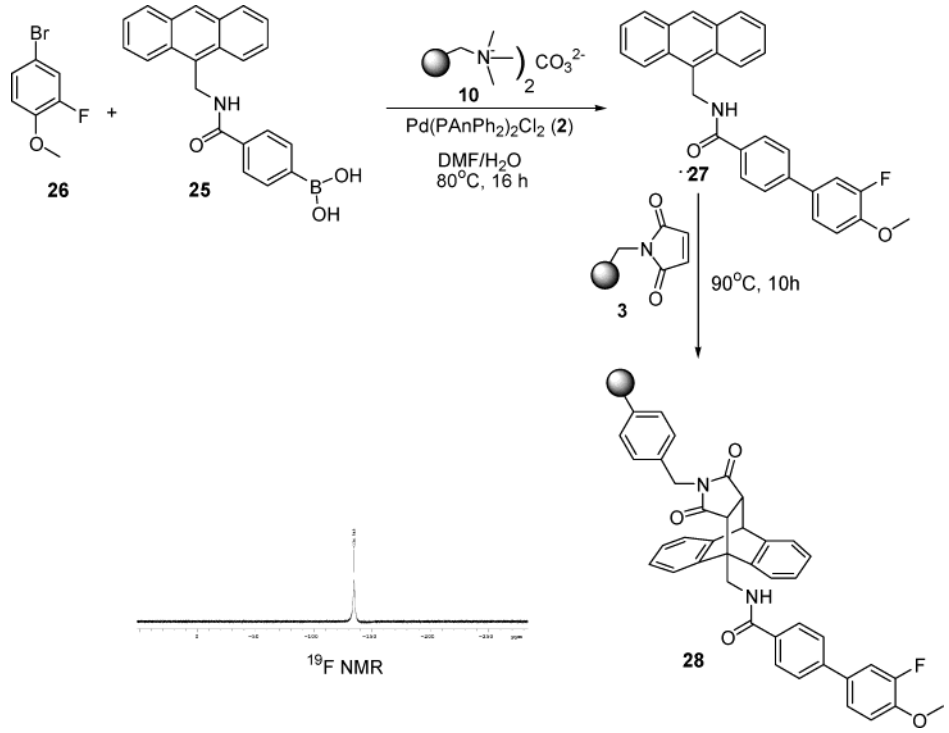
Experimental Section

General Information. ^{1}H NMR spectra were recorded on a 300-MHz spectrometer at ambient temperature unless otherwise stated. ^{13}C NMR spectra were recorded on a 75.4-MHz spectrometer at ambient temperature. ^{31}P NMR spectra were recorded on a 121.1-MHz spectrometer at ambient temperature. ^{19}F NMR spectra were recorded on a 282.2-MHz spectrometer at ambient temperature. Chemical shifts are reported in parts per million relative to TMS. Data for ^{1}H NMR are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constants. All ^{13}C and ^{31}P NMR spectra were recorded with complete proton decoupling. GC-MS was performed on Agilent Technologies 6890N Network GC System. Column: 5% phenyl methyl siloxane; capillary 30.0 m × 0.25 mm; film thickness 0.25 μm; the flow rate of He, 1.0 mL/min. GC oven temperature: initial at 100 °C for 1 min,

SCHEME 6. Synthesis of Anthracene-Tagged Aryl Boronic Acid 25



SCHEME 7. Application of Anthracene-Tagged Boronic Acid 25

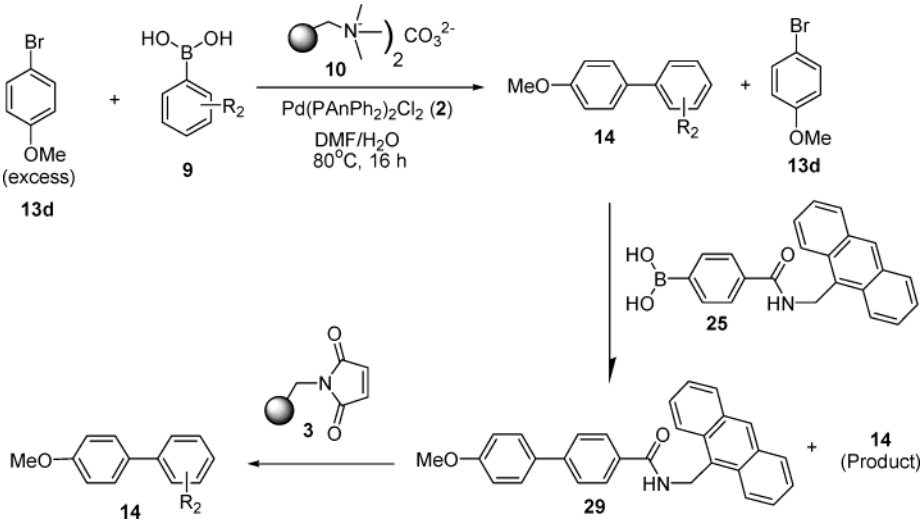


increase to 300 °C at 20 °C/min, hold for 5 min. The detector was an Agilent 5973 Network Mass Selective Detector. LC-MS was performed on a Hewlett-Packard (series 1100), using 5 to 95% of B (4.5 min, 50 °C), then 95% of B (0.5 min, 50 °C), with water (0.5% TFA) as A and CH_3CN as B, and a flow rate of 1 mL/min. The column was an Eclipse XDB-C18 Rapid Resolution cartridge 2.1 × 30 mm × 3.5 μm from P. J. Cobert Associates. Retention times are in minutes. Thin-layer chromatography was performed on 0.25 mm silica gel 1B−F plates (J. D. Baker). The XPERTEK filtration cartridge (15 mL and 70 mL) was obtained from P. J. Cobert Associates. All reagents, including polymer-bound tetraalkylammonium carbonate (PS-TAA carbonate) (macroporous, 50−90 mesh, typical loading: 2.5−3.5 mmol N/g), and solvents were purchased from commercial vendors.

Preparation of Pd Complex $Pd(PAnPh_2)_2Cl_2$ (2). A suspension of $PdCl_2$ (0.6 g, 3.4 mmol) was mixed with CH_3CN (125 mL) in a flask with stirring under N_2. After being stirred overnight, the afforded orange solution was degassed under N_2 with ultrasonic cleaner for 30 min and then cannulated into another flask containing a pre-degassed THF solution of the phosphine ligand **1** (3.4 g, 6.8 mmol, in 85 mL of THF). The mixed solution was degassed again under N_2 with ultrasonic cleaner, which acted as a stirrer also. The mixed solution was initially clear, but the formation of solid was observed shortly after mixing. The mixture was left to stand still to allow the continuing formation of the solid until the ^{31}P NMR of the upper solution showed no presence of phosphine ligand. The mixture was filtered under N_2, and the solid was collected and dried to afford the Pd complex **2** as a light yellow powder (3.2 g, 80% yield). ^{31}P NMR of the complex showed one sharp signal at 24.3 ppm in THF.

Preparation of Anthracene-Tagged Aryl Bromide (20). To a solution of 4-bromobenzoic acid **19** (2.13 g, 10.6 mmol) in DCM (120 mL) and DMF (10 mL) was added 1-hydroxybenzotriazole (HOBt) (1.4 g, 10.6 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) (2 g, 10.6 mmol), and 9-methylaminoanthracene **18** (2 g, 9.6 mmol) in the above order. The mixture was stirred overnight at room temperature, followed by addition of polyamine resin (20.2 g, 53 mmol, 2.63 mmol/g), and the resulting slurry was stirred at room temperature for 2 h. The slurry was filtered and rinsed with a mixture of DCM/DMF 10:1 and the yellow filtrate was evaporated to dryness. The crude solid was crystallized from

SCHEME 8. PASP Suzuki Coupling Employing Anthracene-Tagged Boronic Acid 25



a mixture of hexane, ethyl acetate, and DCM (500 mL) to yield pure **20** (2.5 g, 66%) as a yellow solid. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 8.97 (1H, br t), 8.59 (1H, s), 8.44 (2H, d, J = 6.3 Hz), 8.09 (2H, d, J = 6.0 Hz), 7.76 (2H, d, J = 6.6 Hz), 7.57 (2H, d, J = 6.3 Hz), 7.58−7.48 (4H, m), 5.46 (2H, d, J = 3.9 Hz); ^{13}C NMR (DMSO-d_6, 75.4 MHz) δ 165.9, 133.9, 131.8, 131.7, 130.9, 130.3, 130.3, 129.5, 128.1, 126.8, 125.8, 125.5, 125.3, 36.6; HPLC purity (retention time) 98% (3.42 min); LRMS (ESI) for $C_{22}H_{16}BrNO$ (M + H) 390.

Immobilization of 4-Carboxyphenylboronic Acid to PS-DEAM Resin (23). PS-DEAM resin **21** (loading 2.1 mmol/g, 8.9 g, 18.8 mmol) was weighed into a polypropylene bottle (120 mL), followed by the addition of 4-carboxyphenylboronic acid **22** (4.34 g, 26.2 mmol) and dry THF (115 mL). The bottle was shaken at room temperature for 3 h and then the resin was transferred to a polypropylene filtration cartridge for draining and washing with dry THF (3 × 115 mL). The resin was dried in vacuo overnight, affording the boronic acid immobilized resin **23** (11.7 g). The loading of the resin was calculated to be 1.79 mmol/g based on the weights.

Preparation of Anthracene-Tagged Boronic Acid (25). Into a polypropylene bottle (125 mL) was added the PS-DEAM resin immobilized boronic acid **23** (5.3 g, 9.5 mmol), followed by HOBT as a solid in one portion (3.9 g, 28.6 mmol). Then 9-aminomethylanthracene **18** (5.92 g, 28.6 mmol) was transferred in as a NMP solution followed by addition of diisopropylcarbodiimide (DIC) (4.5 mL, 3.6 g, 28.6 mmol). The bottle was shaken on an orbit shaker overnight, after which the resin was drained through a polypropylene filtration cartridge and washed with dry NMP (3 × 60 mL), dry THF (5 × 60 mL) and dry CH_2Cl_2 (5 × 60 mL) followed by a final washing with dry THF (3 × 60 mL) to give pale yellow resin **24**. The resin-bound boronic acid was cleaved by vortexing the resin **24** with 10% H_2O/THF (5 × 60 mL) for 10 min at room temperature. The filtrate from each cleavage was combined and concentrated to afford the anthracene-tagged boronic acid **25** asa pale yellow solid (2.52 g, 67% yield). The product was used without purification. ^{1}H NMR (acetone-d_6, 300 MHz) δ 8.63 (1H, s), 8.56 (2H, d, J = 9.0 Hz), 8.15 (2H, d, J = 7.8 Hz), 7.94−7.88 (4H, m), 7.65−7.54 (4H, m), 7.32 (1H, s), 5.69 (2H, d, J = 5.1 Hz); ^{13}C NMR (acetone-d_6, 75.4 MHz) δ 166.7, 136.5, 134.1, 132.0, 131.0, 130.0, 129.2, 127.9, 126.6, 126.5, 125.4, 125.3, 124.9, 36.2; LC-MS t_R = 2.6 min, m/z 191 (fragmentation), 356 (M + 1), 733 (2M + 23); HRMS m/z calcd for $C_{22}H_{19}BNO_3$ (M + H) 356.1457, found 356.1469.

General Procedure of Suzuki Coupling of Aryl Bromide Substrates 13a, 13b, and 13c with Boronic Acids 9. Each vial (8 mL) was charged with aryl bromide **13** (0.15 mmol, 1 equiv), boronic acid **9** (0.18 mmol, 1.2 equiv), polymer-supported tetraalkylammonium carbonate **10** (loading 2.86 mmol/g, 0.2 g, 0.6 mmol, 4 equiv), Pd complex **2** (17.5 mg, 0.015 mmol, 0.1 equiv), water (0.1 mL), and DMF (2 mL). The vial was tightly capped and the mixture was set onto a heating block, which was preheated and remained at 80 °C, for 16 h with stirring. During the reaction, the color of the carbonate-bound resin **10** changed from light brown to deep dark, and the solution of the reaction became yellow. At the end of the reaction, GC-MS analysis of the crude solution was taken to determine the identity and the percentage ratio of each product. Then, PS-maleimide resin **3** was added to the reaction mixture (loading 1.56 mmol/g, 0.1 g, 0.16 mmol, 10 equiv to catalyst **2**) and the mixture was heated at 90 °C for 10 h. The resin was filtered with use of a filtration cartridge and washed with CH_2Cl_2 (2 × 5 mL). The collected filtrate was concentrated in a dry-down box with constant N_2 blowing to give the product. In some cases, a second filtration was needed by adding CH_2Cl_2 (2 mL) to the solid and filtering through a cartridge to remove an insoluble residue (believed to be tiny particles from resin degradation), which was not soluble in either CH_2Cl_2 or water. The filtrate was dried in vacuo to afford the product **14**, which was weighed and fully characterized.

4′-Nitro-1,1′-biphenyl-4-carbonitrile (14aA). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.38 (2H, d, J = 9.0 Hz), 7.85−7.75 (6H, m); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 145.6, 143.4, 133.2, 128.4, 128.3, 128.2, 124.6, 124.5, 118.6; GC-MS t_R = 9.98 min, m/z 224; HRMS m/z calcd for $C_{13}H_8N_2O_2$ (M^+) 224.0586, found 224.0603.

Ethyl 4′-Nitro-1,1′-biphenyl-4-carboxylate (14aB). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.34 (2H, d, J = 8.7 Hz), 8.19 (2H, d, J = 8.7 Hz), 7.80 (2H, d, J = 8.7 Hz), 7.72 (2H, d, J = 8.7 Hz), 4.45 (2H, q, J = 7.2 Hz), 1.46 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 166.3, 146.6, 143.1, 130.6, 130.4, 128.3, 127.6, 127.4, 124.4, 61.5, 14.6; GC-MS t_R = 10.64 min, m/z 271; HRMS m/z calcd for $C_{15}H_{13}NO_4$ (M^+) 271.0845, found 271.0861.

4-Chloro-3-methyl-4′-nitro-1,1′-biphenyl (14aC). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.32 (2H, d, J = 9.0 Hz), 7.73 (2H, d, J = 8.7 Hz), 7.52−7.42 (3H, m); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 146.8, 137.5, 137.2, 135.7, 130.1, 127.9, 126.2, 124.4, 20.5; GC-MS t_R = 9.72 min, m/z 247; HRMS m/z calcd for $C_{13}H_{10}ClNO_2$ (M^+) 247.0400, found 247.0380.

4-Isobutyl-4′-nitro-1,1′-biphenyl (14aD). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.32 (2H, d, J = 9.0 Hz), 7.77 (2H, d, J = 9.0 Hz), 7.59 (2H, d, J = 8.1 Hz), 7.31 (2H, d, J = 8.1 Hz), 2.58 (2H, d, J = 7.2 Hz), 2.03−1.89 (1H, m), 0.98 (6H, d, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 147.9, 143.2, 136.3, 130.2, 127.8,

127.4, 124.4, 45.3, 30.5, 22.6; GC-MS t_R = 9.95 min, *m/z* 255; HRMS *m/z* calcd for $C_{16}H_{17}NO_2$ (M^+) 255.1259, found 255.1239.

4-Ethoxy-4′-nitro-1,1′-biphenyl (14aE). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.29 (2H, d, J = 9.0 Hz), 7.72 (2H, d, J = 9.0 Hz), 7.60 (2H, d, J = 9.0 Hz), 7.04 (2H, d, J = 9.0 Hz), 4.13 (2H, q, J = 6.9 Hz), 1.49 (3H, t, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 160.1, 147.5, 146.8, 131.1, 128.8, 127.3, 124.4, 115.4, 63.9, 15.0; GC-MS t_R = 9.89 min, *m/z* 243; HRMS *m/z* calcd for $C_{14}H_{13}NO_3$ (M^+) 243.0895, found 243.0871.

4′-Acetyl-1,1′-biphenyl-4-carbonitrile (14bA). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.10 (2H, d, J = 8.4 Hz), 7.78−7.70 (6H, m), 2.68 (3H, s); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 197.8, 144.6, 143.8, 137.2, 133.2, 133.0, 129.4, 128.2, 127.7, 118.9, 27.0; GC-MS t_R = 9.71 min, *m/z* 221; HRMS *m/z* calcd for $C_{15}H_{11}NO$ (M^+) 221.0841, found 221.0820.

Ethyl 4′-Acetyl-1,1′-biphenyl-4-carboxylate (14bB). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.16 (2H, d, J = 8.4 Hz), 8.08 (2H, d, J = 8.4 Hz), 7.74 (2H, d, J = 8.0 Hz), 7.71 (2H, d, J = 8.0 Hz), 4.44 (2H, q, J = 7.2 Hz), 2.67 (3H, s), 1.45 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 197.9, 166.5, 144.8, 144.3, 136.7, 130.4, 129.2, 127.7, 127.4, 61.4, 26.9, 14.6; GC-MS t_R = 10.50 min, *m/z* 268; HRMS *m/z* calcd for $C_{17}H_{16}O_3$ (M^+) 268.1099, found 268.1116.

1-(4′-Chloro-3′-methyl-1,1′-biphenyl-4-yl)ethanone (14bC). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.05 (2H, d, J = 8.4 Hz), 7.67 (2H, d, J = 8.4 Hz), 7.52−7.42 (3H, m), 2.67 (3H, s), 2.48 (3H, s); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 197.9, 145.0, 138.6, 136.9, 136.3, 134.9, 130.0, 129.8, 129.2, 127.3, 126.1, 26.9, 20.5; GC-MS t_R = 9.53 min, *m/z* 244; HRMS *m/z* calcd for $C_{15}H_{13}ClO$ (M^+) 244.0655, found 244.0654.

1-(4′-Isobutyl-1,1′-biphenyl-4-yl)ethanone (14bD). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.06 (2H, d, J = 8.1 Hz), 7.72 (2H, d, J = 8.1 Hz), 7.59 (2H, d, J = 8.1 Hz), 7.28 (2H, d, J = 8.1 Hz), 2.67 (3H, s), 2.57 (2H, d, J = 7.2 Hz), 2.02−1.88 (1H, m), 0.98 (6H, d, J = 6.3 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 198.0, 146.0, 142.3, 137.4, 135.9, 130.0, 129.2, 127.2, 45.4, 30.5, 26.9, 22.7; GC-MS t_R = 9.78 min, *m/z* 252; HRMS *m/z* calcd for $C_{18}H_{20}O$ (M^+) 252.1514, found 252.1510.

1-(4′-Ethoxy-1,1′-biphenyl-4-yl)ethanone (14bE). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.04 (2H, d, J = 8.4 Hz), 7.68 (2H, d, J = 8.4 Hz), 7.60 (2H, d, J = 8.8 Hz), 7.02 (2H, d, J = 8.8 Hz), 4.12 (2H, q, J = 7.2 Hz), 2.66 (3H, s), 1.48 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 198.0, 159.6, 145.7, 135.5, 132.3, 129.2, 128.6, 126.8, 115.2, 63.8, 26.9, 15.1; GC-MS t_R = 9.70 min, *m/z* 240; HRMS *m/z* calcd for $C_{16}H_{16}O_2$ (M^+) 240.1150, found 240.1133.

2′-[(2-Methylphenoxy)methyl]-1,1′-biphenyl-4-carbonitrile (14cA). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.75−7.70 (3H, m), 7.59−7.47 (4H, m), 7.37−7.34 (1H, m), 7.21−7.13 (2H, m), 6.95−6.90 (1H, m), 6.74 (1H, d, J = 8.1 Hz), 4.94 (2H, s), 2.26 (3H, s); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 156.8, 145.7, 140.2, 134.6, 133.2, 132.4, 131.1, 130.2, 130.1, 130.0, 128.9, 128.6, 127.2, 127.0, 121.2, 119.0, 111.6, 68.2, 16.6; GC-MS t_R = 11.26 min, *m/z* 299; HRMS *m/z* calcd for $C_{21}H_{18}NO$ (M + H) 300.1383, found 300.1388.

Ethyl 2′-[(2-Methylphenoxy)methyl]-1,1′-biphenyl-4-carboxylate (14cB). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.14 (2H, d, J = 8.1 Hz), 7.76−7.71 (1H, m), 7.54 (2H, d, J = 8.1 Hz), 7.51−7.37 (3H, m), 7.21−7.11 (2H, m), 6.91 (1H, dd, J = 6.6, 6.6 Hz), 6.74 (1H, d, J = 8.1 Hz), 4.98 (2H, s), 4.46 (2H, q, J = 6.9 Hz), 2.30 (3H, s), 1.47 (3H, t, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 166.7, 156.9, 145.5, 141.0, 134.7, 131.0, 130.1, 129.8, 129.6, 129.4, 128.3, 127.5, 127.3, 127.0, 121.0, 111.6, 68.2, 61.3, 16.7, 14.6; GC-MS t_R = 11.96 min, *m/z* 346; HRMS *m/z* calcd for $C_{23}H_{23}O_3$ (M + H) 347.1642, found 347.1621.

4′-Chloro-3′-methyl-2-[(2-methylphenoxy)methyl]-1,1′-biphenyl (14cC). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.73−7.70 (1H, m), 7.49−7.33 (6H, m), 7.24−7.13 (3H, m), 6.92 (1H, t, J = 7.5 Hz), 6.77 (1H, d, J = 8.1 Hz), 4.99 (2H, s), 2.43 (3H, s), 2.33 (3H, s); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 157.0, 141.0, 139.4, 136.2, 134.8, 133.9, 132.0, 131.0, 130.2, 129.5, 129.1, 128.3, 128.1, 128.0, 127.3, 127.0, 120.9, 111.7, 68.3, 20.3, 16.7; GC-MS t_R = 10.96 min, *m/z* 322; HRMS *m/z* calcd for $C_{21}H_{20}ClO$ (M + H) 323.1197, found 323.1215.

4′-Isobutyl-2-[(2-methylphenoxy)methyl]-1,1′-biphenyl (14cD). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.74−7.71 (1H, m), 7.48−7.36 (5H, m), 7.30−7.12 (4H, m), 6.91 (1H, t, J = 7.5 Hz), 6.76 (1H, d, J = 8.1 Hz), 5.05 (2H, s), 2.59 (2H, d, J = 7.2 Hz), 2.33 (3H, s), 2.02−1.93 (1H, m), 1.01 (6H, d, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 157.1, 141.9, 141.1, 138.2, 134.9, 130.9, 130.3, 129.3, 129.1, 129.0, 128.1, 127.7, 127.4, 127.0, 120.8, 111.8, 68.3, 45.4, 30.5, 22.7, 16.7; GC-MS t_R = 11.14 min, *m/z* 330; HRMS *m/z* calcd for $C_{24}H_{27}O$ (M + H) 331.2056, found 331.2083.

4′-Ethoxy-2-[(2-methylphenoxy)methyl]-1,1′-biphenyl (14cE). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.72−7.69 (1H, m), 7.46−7.35 (5H, m), 7.22−7.12 (2H, m), 7.02−6.98 (2H, m), 6.91 (1H, t, J = 7.5 Hz), 6.77 (1H, d, J = 8.1 Hz), 5.02 (2H, s), 4.12 (2H, q, J = 6.9 Hz), 2.33 (3H, s), 1.50 (3H, t, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 158.6, 157.1, 141.6, 134.9, 133.1, 130.9, 130.5, 130.3, 129.1, 128.1, 127.5, 127.3, 127.0, 120.8, 114.5, 111.7; GC-MS t_R = 11.10 min, *m/z* 318; HRMS *m/z* calcd for $C_{22}H_{23}O_2$ (M + H) 319.1693, found 319.1722.

General Procedure of Suzuki Coupling of 4-Bromoanisole 13d with Boronic Acids 9. Each vial (8 mL) was charged with 4-bromoanisole **13d** (0.27 mmol, 1.8 equiv), boronic acid **9** (0.15 mmol, 1 equiv), polymer-supported tetraalkylammonium carbonate **10** (loading 2.86 mmol/g, 0.2 g, 0.6 mmol, 4 equiv), Pd complex **2** (17.5 mg, 0.015 mmol, 0.1 equiv), water (0.1 mL), and DMF (2 mL). The vial was tightly capped and the mixture was set onto a heating block, which was preheated and remained at 80 °C, for 16 h with stirring. To consume the unreacted starting material **13d**, the anthracene-tagged boronic acid **25** was added (115 mg, 0.324 mmol) followed by another charge of Pd catalyst **2** (18.7 mg, 0.016 mmol) and polymer-supported carbonate **10** (0.34 g, 0.972 mmol). The reaction was resumed at 80 °C and left overnight. A GC-MS analysis was taken at this point to assess the completion of the reaction and the product ratio. Then, PS-maleimide resin **3** was added to the reaction mixture (loading 1.56 mmol/g, 1.13 g, 1.76 mmol, 5 equiv to all the anthracene-tagged species presented in the reaction including the anthracene-tagged catalyst) and the mixture was heated at 90 °C for 10 h. The resin was filtered through a filtration cartridge and washed with CH_2Cl_2 (2 × 5 mL). The collected filtrate was concentrated in a dry-down box with constant N_2 blowing to give a solid. In some cases, a second filtration was needed by adding CH_2Cl_2 (2 mL) to the solid and filtering through a cartridge to remove an insoluble residue (believed to be tiny particles from resin degradation), which was not soluble in either CH_2Cl_2 or water. The filtrate was dried in vacuo to afford the product **14**, which was weighed and fully characterized.

4′-Methoxy-1,1′-biphenyl-4-carbonitrile (14dA). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.84−7.66 (4H, m), 7.58 (2H, d, J = 8.7 Hz), 7.04 (2H, d, J = 8.7 Hz), 3.90 (3H, s); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 160.5, 145.5, 133.2, 132.8, 128.6, 128.2, 127.4, 119.4, 114.8, 55.7; GC-MS t_R = 8.90 min, *m/z* 209; HRMS *m/z* calcd for $C_{14}H_{11}NO$ (M^+) 209.0841, found 209.0834.

Ethyl 4′-Methoxy-1,1′-biphenyl-4-carboxylate (14dB). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.12 (2H, d, 8.7 Hz), 7.65 (2H, d, J = 8.7 Hz), 7.61 (2H, d, J = 9.0 Hz), 7.03 (2H, d, J = 9.0 Hz), 4.43 (2H, q, J = 6.9 Hz), 3.89 (3H, s), 1.45 (3H, t, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 166.9, 160.1, 145.4, 132.7, 130.4, 130.3, 128.6, 126.7, 114.6, 61.2, 55.6, 14.6; GC-MS t_R = 9.81 min, *m/z* 256; HRMS *m/z* calcd for $C_{16}H_{16}O_3$ (M^+) 256.1099, found 256.1078.

4′-Chloro-3′-methyl-1,1′-biphenyl-4-yl Methyl Ether (14dC). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.52 (2H, d, J = 9.0 Hz), 7.45−7.32 (3H, m), 7.01 (2H, d, J = 9.0 Hz), 3.89 (3H, s), 2.47 (3H, s); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 159.6, 139.6, 136.4, 133.2, 133.0, 129.6, 129.5, 128.3, 125.6, 114.5, 55.6, 20.5; GC-MS t_R = 8.69 min, *m/z* 232; HRMS *m/z* calcd for $C_{14}H_{13}ClO$ (M^+) 232.0655, found 232.0644.

4′-Isobutyl-1,1′-biphenyl-4-yl Methyl Ether (14dD). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.57 (2H, d, J = 9.0 Hz), 7.51 (2H, d, J = 8.1 Hz), 7.24 (2H, d, J = 8.1 Hz), 7.01 (2H, d, J = 9.0 Hz), 3.88 (3H, s), 2.55 (2H, d, J = 7.2 Hz), 2.02−1.88 (1H, m), 0.99 (6H, d, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 159.2, 140.5, 138.4, 134.0, 129.8, 128.2, 126.7, 114.4, 55.6, 45.3, 30.5, 22.7; GC-MS t_R = 8.93 min, m/z 240; HRMS m/z calcd for $C_{17}H_{20}O$ (M^+) 240.1514, found 240.1515.

4-Ethoxy-4′-methoxy-1,1′-biphenyl (14dE). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.52 (2H, d, J = 8.7 Hz), 7.51 (2H, d, J = 9.0 Hz), 7.00 (2H, d, J = 8.7 Hz), 6.99 (2H, d, J = 9.0 Hz), 4.11 (2H, q, J = 6.9 Hz), 3.88 (3H, s), 1.48 (3H, t, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 158.9, 158.3, 133.8, 133.6, 128.0, 115.0, 114.4, 63.8, 55.6, 15.2; GC-MS t_R = 8.82 min, m/z 228; HRMS m/z calcd for $C_{15}H_{16}O_2$ (M + H) 228.1150, found 228.1139.

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Supporting Information Available: Characterization and spectral data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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