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# Sonication and Microwave-Assisted Primary Amination of Potassium Aryltrifluoroborates and Phenylboronic Acids under Metal-Free Conditions

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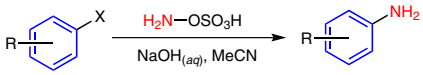


**Method A**: rt, sonication, 1–3 h
**Method B**: 100 °C, MW, 15 min

***X* = $BF_3K$**, *10 examples, up to 78%*
***X* = $B(OH)_2$**, *12 examples, up to 96%*
***R* =** *electron-donating & electron-withdrawing*

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**Abstract** The transition-metal-free generation of a series of primary arylamines from potassium aryltrifluoroborates and phenylboronic acids is reported. The method uses a mild, inexpensive source of nitrogen (hydroxylamine-*O*-sulfonic acid) in cooperation with aqueous sodium hydroxide in acetonitrile. Both a sonication and a microwave-assisted method were developed, which are capable of converting $ArBF_3K$ functionalities into primary arylamines ($ArNH_2$) in isolated yields of up to 78% (10 examples for each method). This report represents the first general method for the conversion of aryltrifluoroborates into primary arylamines under mild, transition-metal-free conditions in moderate to very good yields. The method is applicable to a wide array of substrates containing electron-donating, electron-neutral, or electron-withdrawing substituents. Both the sonication and microwave methods were also applied to the generation of anilines from phenylboronic acids in isolated yields of up to 96% (12 examples for each method) that were superior to existing room temperature methods in terms of yield, while also offering much shorter reaction times (15 min vs 16 h). In particular, the microwave method is the first to allow for the conversion of arylboronic acids containing strongly electron-withdrawing substituents into the corresponding anilines in good yields, along with electron-donating substituents in very good to excellent yields.

**Key words** trifluoroborates, boronic acids, amination, sonication, microwave synthesis

Organotrifluoroborate salts are readily available and serve as convenient alternative substrates to boronic acids and their esters.[1–4] This is primarily due to the ease with which they are handled and their relatively high chemical stability. Indeed, trifluoroborates are inert to many sets of reaction conditions that would be expected to adversely affect conventional tricoordinate boron species. For example, trifluoroborate containing substrates can undergo various oxidation,[5–7] reduction,[8] and strong base-mediated reactions[9,10] without transformation of the boron functionality. While the stability of these organoboron substrates is attractive in many cases, this behavior can pose problems when transformation of the boron group is desired. These properties can often manifest themselves in decreased reactivities when compared to other organoboron compounds.[11] On the one hand, the stability of trifluoroborates makes them inert to conditions that would normally modify boronic acids. On the other hand, their altered reactivity often requires forcing reaction conditions (e.g., high temperatures, longer reaction times) in order to allow the transformation of a trifluoroborate functionality to proceed towards completion, and can often lead to side-reactions or decomposition of the desired product.

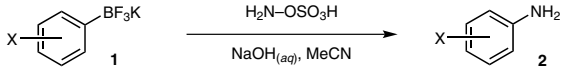
To date, the ability to use trifluoroborates as boronic acid surrogates has found numerous applications in organic synthesis and many aryltrifluoroborates are now commercially available. New methods, however, are required that will allow for the conversion of trifluoroborates into desirable functional groups, such as the generation of primary $C–NH_2$ bonds from $C–BF_3K$ functionalities. The synthesis of primary aromatic amines from arylboronic acids under copper-catalyzed conditions has been established, including Cu-catalyzed azidonation reactions,[12] however, the amination reactions generally require 12–24 hours to reach completion.[12–14] Indeed, only a single publication exists that details the copper-catalyzed amination of aryltrifluoroborates. The method described requires reaction times of 24 hours and has limited scope.[14] To the best of our knowledge, only four other publications have described an analogous transformation where an aryltrifluoroborate is converted into a primary arylamine. In each of these publications, only a single example is reported for this type of conversion, albeit with reaction times of 16 hours[15] or 30 hours,[16] in 13% yield as a by-product of the desired reaction,[17] or through the use of a toxic and potentially explosive azide as a reagent ($HN_3$).[18] As a result, the literature is distinctly lacking suitable methods that are capable of providing ac-

cess to aromatic primary amines from a wide variety of aryltrifluoroborates. Ideally, a convenient method is required for this transformation, which features short reaction times, and mild, metal-free conditions. As part of a collaborative effort, we set out to develop an efficient method that is capable of converting potassium aryltrifluoroborates into anilines, a key building block of biologically active agents.[19] We expect the subsequent application of this general method to provide access to alternate primary arylamines, in addition to anilines, as a broader synthetic transformation. The methods described herein will serve as general examples of a key functional group interconversion, the generation of aromatic C–$NH_2$ moieties from trifluoroborates under transition-metal-free conditions that can be applied to the generation of alternate molecular frameworks, in addition to anilines.

Previously, the McCubbin group had reported a single example of the transformation of potassium 4-methoxyphenyltrifluoroborate into 4-methoxyaniline in 10% yield, with a 16 hour reaction time.[15] Following the addition of excess silica gel, an enhancement of the yield was observed (74%), presumably through the action of the silica gel in facilitating trifluoroborate hydrolysis.[20] Unfortunately, this publication provided only one example of this reaction, required long reaction times (16 hours), and necessitated the use of 1.0 gram of silica gel per mmol of trifluoroborate, limiting scale-up, and resulting in poor atom economy.[21] As a result, we set out to develop a robust reaction method that would enable the conversion of aryltrifluoroborates to primary arylamines with the benefit of microwave-assisted organic synthesis (MAOS),[22–24] and sonochemistry.[25,26]

Guided by the use of a common $^{+}NH_2$ equivalent under basic aqueous conditions,[15] we began our preliminary reaction studies by treating potassium phenyltrifluoroborate (**1a**) with hydroxylamine-*O*-sulfonic acid (HSA) and aqueous NaOH, in combination with acetonitrile at room temperature, overnight. The corresponding reaction was monitored via HPLC using aniline as a reference standard, and very little conversion of the trifluoroborate was observed. In a subsequent reaction, these reagents were combined with potassium *p*-tolyltrifluoroborate (**1b**) and an excess of silica gel, with some additional conversion to the aniline derivative being observed, albeit in poor yield, with the major product identified as *p*-tolylboronic acid by HPLC. At this point, the use of a microwave synthesizer was employed to assist in this reaction and aid in the generation of aryl primary amines. Concurrently, the use of an ultrasonic cleaner (35 kHz, 90 W) was employed to investigate the potential of an ultrasound-promoted rate enhancement of the desired reaction. Initial studies for the microwave and ultrasound promoted reactions focused on method optimization by varying reagent equivalence, solvent, and base. It was quickly realized, however, that acetonitrile served as the optimal solvent of choice, at concentrations of 0.2 M for sonication reactions and 0.25 M for microwave processing. The reactions were typically performed at a 0.5 mmol scale. However, increasing the scale to 1.0 mmol had little effect on the yields. The use of 1.5 equivalents of HSA gave good isolated yields in combination with 5 equivalents of a 1 M solution of aqueous sodium hydroxide. The ultrasound-promoted reactions could be readily monitored by HPLC. The microwave reactions, however, were normally too rapid to be monitored in this way. In most cases, commercially available anilines were used as reference standards for HPLC monitoring of reaction progress, and verification of the desired products. Using the sonication method outlined in Table 1, the sonication reactions were placed in the ultrasound bath for 30-minute intervals, at which time a small aliquot was sampled for reaction monitoring via HPLC. This process was repeated until the crude reaction HPLC trace indicated the absence of any starting material, or that the reaction had failed to progress any further, at which time the crude reaction was prepared for column chromatography purification. In general, the substrates with electron-donating substituents reacted much faster than those with electron-withdrawing substituents using the sonication method. For example, 2,6-dimethoxyphenyltrifluoroborate required only 1 hour of reaction time, while 4-chloro- and 4-iodophenyltrifluoroborate required 3 hours. Included in the Supporting Information (SI) section are the HPLC chromatograms of both the crude reactions and the pure isolated products for the substrates listed in Table 1. As can be seen through inspection of the HPLC chromatograms, the majority of the reactions proceeded relatively cleanly, with near complete consumption of starting material for the mi-

**Table 1** Scope of Amination Reaction Using Microwave and Ultrasound Processing for Potassium Aryltrifluoroborates




**Method A**: ))), 1–3 h
**Method B**: MW, 100 °C, 15 min

| Entry | 2 | Sonication Yield (%)[a] | Microwave Yield (%)[b] |
|---|---|---|---|
| 1 | **2a** (X = H) | 58 | 77 |
| 2 | **2b** (X = 4-Me) | 69 | 78 |
| 3 | **2c** (X = 4-MeO) | 64 | 74 |
| 4 | **2d** (X = 4-Cl) | 40 | 53 |
| 5 | **2e** (X = 3-thiophenyl) | 55 | 68[c] |
| 6 | **2f** (X = 2-naphthyl) | 48 | 55 |
| 7 | **2g** (X = 3-MeO) | 46 | 76 |
| 8 | **2h** (X = 3,4-methylenedioxy) | 59 | 73 |
| 9 | **2i** (X = 4-I) | 49 | 45 |
| 10 | **2j** [X = 2,6-$(MeO)_2$] | 77 | 74 |

[a] Isolated yields, 1–3 h, as monitored by HPLC.
[b] Isolated yields, 100 °C for 15 min.
[c] Reaction conducted using 3.0 equiv of HSA for 20 min.

crowave reactions. For the sonication reactions, in most cases some starting material remained (<3 h), while the use of microwave irradiation usually resulted in complete conversion following 15 minutes of reaction time. Table 1 summarizes the final results of the optimized reactions using both microwave and ultrasound reaction processing.

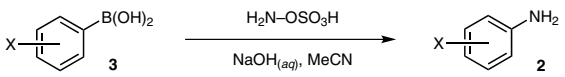
The isolated yields for the sonication reactions were found to be between 40% and 77%, and in general, the higher yielding reactions required less time in the ultrasound bath to approach completion. In comparison to phenyltrifluoroborate (58%), the substrates possessing electron-withdrawing groups (Cl, I) afforded products in lower yields (40%, 49%, respectively), while those with electron-donating substituents gave higher yields; 4-methyl- (69%), 4-methoxy- (64%), or 2,6-dimethoxy- (77%). 3,4-Methylenedioxyphenyltrifluoroborate was found to react with similar isolated yield (59%) to that of the unsubstituted phenyl (X = H) substrate, while the 2-naphthyl substrate afforded the desired product in 48% yield, and the electron-rich heteroaromatic 3-thiophenetrifluoroborate substrate afforded product in 55% yield. The majority of the reactions proceeded relatively clean and gave products in good isolated yields. However, reaction of the 3-methoxyphenyl substrate was found to produce an unidentified by-product with a diminished isolated yield of 46% for the desired product, in comparison to the other methoxy-bearing substrates. The use of additional HSA (~3.0 equiv) provided for increased conversion of starting material and shorter sonication times. However, we found that the use of 1.5 equivalents provided a good balance between yield, reaction time, and reagent economy.

In general, higher isolated yields were obtained when microwave irradiation was used to incubate the reactions, as compared to sonication. In particular, for entries 1–8 in Table 1, the yields were found to be 8% to 30% higher, while the reactions shown in entries 9 and 10 occurred with similar isolated yields. The increase in yields are presumably due to an increase in the conversion of starting material to product for the reactions as demonstrated by the crude reactions HPLC chromatograms (see SI). For instance, comparing the HPLC chromatograms of the crude reactions for phenyltrifluoroborate (microwave vs sonication methods), the ratio of product to starting material (Product/SM) for the sonication method is ~1.8:1, while for the microwave method it is ~6:1 (SM retention time 6.18 min, product retention time 6.35 min). Additionally, the trends in the yields were similar between the microwave and ultrasound methods in terms of substituent effects. For electron-donating groups, the isolated yields were found to be 73–78% (Table 1, entries 2, 3, 7, 8, 10), while substrates bearing electron-withdrawing substituents afforded products in much lower yields, (entry 4, X = Cl, 53% and entry 9, X = I, 45%). Additionally, the 2-naphthyl substrate also afforded product in moderate yield (55%, entry 6). It was also noted that for the 3-thiophene substrate (entry 5) only moderate conversion was observed when 1.5 equivalents of HSA was used. The use of 3.0 equivalents of HSA, however, was found to afford the desired product in a much higher yield of 68%. For the majority of the microwave reactions, high conversions were observed and the less than quantitative yields obtained are likely a function of the slight water solubility of anilines and their moderate volatility (aniline, bp 184 °C), resulting in product loss during aqueous workup and purification.

Once the sonication and microwave methods had been developed for the conversion of aryltrifluoroborates to primary arylamines, the methods were applied to provide for similar transformations involving the conversion of arylboronic acids into analogous primary arylamines. Previously, the McCubbin group had published a method that provided for transition-metal-free access to primary anilines. However, this method required 16 hours of reaction time and did not provide access to anilines possessing strongly deactivating groups, such as nitro substituents.[15] Thus, we proposed to develop both sonication and microwave methods that would allow for shortened reaction times for this transformation, while also allowing access to anilines bearing strong electron-withdrawing substituents. Using the methods previously developed for the aryltrifluoroborates, Table 2 represents the scope of these reactions, which directly compares the yields of the 16-hour room temperature reaction with sonication and microwave batch processing techniques using the same concentrations and reagent equivalents. For each of the entries, the reactions were performed at room temperature overnight (16 h) to establish a baseline isolated yield in our hands,[15] from which the sonication and microwave methods can be compared. In almost all cases, the sonication and microwave methods offered an increase in isolated yield, with a corresponding reduction in reaction times from 16 hours to 15 minutes for microwave processing. Additionally, boronic acids refluxed for 5 hours under these conditions tended to generate multiple by-product peaks via HPLC analysis, demonstrating the advantage of microwave irradiation over the use of conventional heating.

The results shown in Table 2 demonstrate the relative improvement in yields, and reduction in reaction times, that can be obtained through the use of sonication and microwave processing. Under otherwise identical reaction conditions, a room temperature reaction required a minimum of 16 hours to give acceptable yields for the desired reaction. However, the use of ultrasound reduced the reaction times to between one and three hours. Over time, the temperature of the sonication bath was found to slowly increase when active. This increase was negligible at 1 hour, and the bath temperature rose to 35 °C at 3 hours. However, reactions refluxed for 5 hours were found to afford lower yields than the sonication reactions performed between room temperature and 35 °C. These results suggest a sub-

**Table 2** Comparison of Amination Reactions Using Room Temperature, Sonication, and Microwave Processing for Arylboronic Acids




**Method A**: rt, 16 h
**Method B**: ))), 1–3 h
**Method C**: MW, 100 °C, 15 min

| Entry | **2** | Room temp, 16 h Yield (%)[a] | Sonication Yield (%)[b] | Microwave Yield (%)[c] |
|---|---|---|---|---|
| 1 | **2a** (X = H) | 78 | 86 | 88 |
| 2 | **2b** (X = 4-Me) | 61 | 75 | 76 |
| 3 | **2c** (X = 4-MeO) | 75 | 79 | 72 |
| 4 | **2d** (X = 4-Cl) | 69 | 70 | 74 |
| 5 | **2f** (X = 2-naphthyl) | 61 | 75 | 87 |
| 6 | **2g** (X = 3-MeO) | 70 | 77 | 87 |
| 7 | **2j** [X = 2,6-$(MeO)_2$] | 68 | 96 | 80 |
| 8 | **2k** (X = 2-Br) | 43 | 39 | 60 |
| 9 | **2l** (X = 4-Br) | 71 | 70 | 63 |
| 10 | **2m** (X = 2-I) | 38 | 59 | 53[d] |
| 11 | **2n** (X = 8-quinolinyl) | 62 | 95 | 92 |
| 12 | **2o** (X = 3-$NO_2$) | 31 | 26[d] | 68[d] |

[a] Isolated yields, 16 h at r.t.
[b] Isolated yields, 1–2.5 h, as monitored by HPLC.
[c] Isolated yields, 100 °C for 15 min.
[d] With an additional 1.0 equiv of HSA.

stantial rate enhancement for the sonication reactions beyond any temperature effects. The use of microwave processing reduced this time even further to just 15 minutes. Using the sonication method, 9 of the 12 entries in Table 2 allowed for isolation of products in yields between 70 and 96%, while the use of microwave processing provided products in yields between 60 and 92% for 11 of the 12 entries. For the sonication method, only substrates that possessed an electron-withdrawing substituent gave desired products in yields less than 70%, entries 8 (X = Br, 39%), 10 (X = I, 59%) and 12 (X = $NO_2$, 26%). Using the microwave method, only entry 10 (X = I, 53%) afforded the desired product in an isolated yield less than 60%. For this reaction an additional 1.0 equivalent of HSA was added to provide for more complete conversion. Of special note is the success of this method in transforming an arylboronic acid possessing a strongly electron-withdrawing substituent (X = $NO_2$, 68%) into an aniline, a reaction that has not appeared in the literature to date under metal-free conditions. This particular reaction required the addition of an extra 0.5 equivalent of HSA after the initial 15 minutes of reaction time, followed by an extra 7 minutes of microwave irradiation, (repeated twice), to afford the nitroaniline product in this yield. A microwave reaction temperature of 100°C was found to be optimal, since higher temperatures produced additional peaks in the crude reactions (confirmed by HPLC analysis) while 15 minutes provided acceptable conversion of starting material. Under room temperature conditions, the reduced yields, in comparison to the microwave method, were largely attributed to unreacted starting material. Overall, both the sonication and microwave methods afford products in very good yields.

In conclusion, we have developed a simple, mild, transition-metal-free method for the transformation of aryltrifluoroborates and arylboronic acids into primary anilines using sonication and microwave irradiation. The reaction methods require only inexpensive, commercially-available reagents (HSA, aq NaOH) that typically afford products in good to excellent yields. For both the aryltrifluoroborates and arylboronic acids, the methods are highly effective for both electron-rich and electron-neutral substrates, while also providing efficient access to primary anilines with electron-withdrawing substituents. Additionally, microwave irradiation allows for the conversion of phenylboronic acids with strongly electron-withdrawing substituents (X = $NO_2$) to anilines, a first under metal-free conditions. The primary advantage of this method over those previously reported is the ability to provide rapid access (1–3 hours under sonication, or 15 minutes for microwave) to this important functional group interconversion (C–$BX_n$ to C–$NH_2$). This reduction in reaction times provides for a real-world improvement in the synthetic methods that are available to the typical organic chemist. The majority of synthetic labs possess an ultrasonic cleaner, which is the only equipment required to conduct the sonication method. Most industrial synthetic labs do possess a microwave reactor, however, some academic labs and chemists in developing nations do not have access to this costly piece of equipment. Using the methods developed herein, either the sonication and/or the microwave methods can be utilized by scientists and provide useful acceleration of rates for this reaction, depending upon laboratory resources. We are currently exploring the nature of the observed rate enhancement for the sonication reactions and believe that heterogeneous sonochemical effects may be in operation.[27] For more information on the relevance of the reaction medium and homo- versus heterogeneous sonochemistry, the corresponding reviews are recommended.[25,26] We are also extending our efforts in the development of this transformation to include additional heteroaromatic trifluoroborates and multicyclic scaffolds, as well as efforts to avoid aqueous workup procedures. We are also developing methods that would employ modern flow chemistry techniques[28–30] that would provide for the generation of primary arylamines from arylboronic esters.

Automated flash chromatography was performed using a normal phase disposable silica gel columns, (40–60 µm). For sonication reactions, an ultrasonic cleaner 2.8 L was employed, operating frequency 35 kHz, power consumption 90 W. HPLC was performed using a 5 µm, 150 mm × 4.6 mm column, and a diode array detector. HPLC method

($H_2O$/MeCN): 0–1.0 min, 95% $H_2O$; 9.0–10.0 min, 95% MeCN, 11.0–12.0 min 95% $H_2O$. All solvents were purchased as ACS reagents and used without further purification. All other chemicals and starting materials, aryltrifluoroborates and arylboronic acids, were purchased commercially and used as received.

HPLC chromatograms of all the reaction products with indicated numbers (DKA or DKB) are provided in the Supporting Information.

### Amination of Aryltrifluoroborates; General Procedures (Table 1)

#### Sonication; Method A

Reactions were performed under sonication on a 0.5 mmol scale. Aryltrifluoroborate **1** (1.0 equiv) and MeCN (2.5 mL) were added to a 25 mL microwave vial equipped with stir bar, followed by HSA (1.5 equiv) and aq 1 M NaOH (5 equiv). The vial was capped and set to stir for 5 min, then placed in a VWR ultrasonic cleaner for 30 min (35 kHz, 90 W), at which time the vial was removed and a small aliquot was taken for reaction monitoring via HPLC analysis. The mixture was then placed back in the VWR sonication bath for 30 min. This process was repeated until the reaction had either reacted completion, or the reaction failed to progress any further, as monitored by HPLC. The reaction mixture was then diluted with $H_2O$ (30 mL) and extracted with EtOAc (2 × 30 mL). The combined organic extracts were dried ($Na_2SO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (EtOAc/hexanes) to afford the desired amine product **2**.

Compounds **2a** (2.5 h sonication time, 27.3 mg, 58%, purified product chromatogram DKB6-Purified),[12] **2b** (2.5 h sonication time, 37.1 mg, 69%, purified product chromatogram DKA86-Purified),[31] **2c** (2.5 h sonication time, 39.4 mg, 64%, purified product chromatogram DKA75-Purified),[31] **2d** (3 h sonication time, 25.6 mg, 40%, purified product chromatogram DKB02-Purified),[31] **2e** (1.5 h sonication time, 27.4 mg, 55%, purified product chromatogram DKB07-Purified),[32] **2f** (2.5 h sonication time, 34.2 mg, 48%, purified product chromatogram DKB08-Purified),[12] **2g** (2.5 h sonication time and performed on a 1.0 mmol scale, 56.3 mg, 46%, purified product chromatogram DKB11-Purified),[12] **2h** (1.5 h sonication time, 40.4 mg, 59%, purified product chromatogram DKB12-Purified),[33] **2i** (3 h sonication time, 43.4 mg, 49%, purified product chromatogram DKB14-Purified),[34] **2j** (1 h sonication time, 39.3 mg, 77%, purified product chromatogram DKB17-Purified),[35] were prepared by this method and afforded NMR data that matched those reported in the literature.

#### Microwave; Method B

Reactions facilitated by microwave irradiation were performed on a 0.5 mmol scale. Aryltrifluoroborate **1** (1.0 equiv) and MeCN (2.0 mL) were added to a 10 mL microwave vial equipped with stir bar, followed by HSA (1.5 equiv) and aq 1 M NaOH (5 equiv). The mixture was capped and set to stir for 5 min at r.t., then placed in a microwave reactor and heated to 100 °C for 15 min, and then cooled. The vial was removed from the microwave and a small aliquot was taken for reaction monitoring via HPLC analysis. The reaction mixture was diluted with $H_2O$ (30 mL) and extracted with EtOAc (2 × 30 mL). The combined organic extracts were dried ($Na_2SO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (EtOAc/hexanes) to afford the desired amine product **2**.

Compounds **2a** (36.0 mg, 77%, purified product chromatogram DKB01-Purified),[12] **2b** (42.0 mg, 78%, purified product chromatogram DKA85-Purified),[31] **2c** (45.6 mg, 74%, purified product chromatogram DKA76-Purified),[31] **2d** (33.6 mg, 53%, purified product chromatogram DKB03-Purified),[31] **2e** (reaction performed using 3.0 equiv of HSA and heated for 20 min, 33.7 mg, 68%, purified product chromatogram DKB05-Purified),[32] **2f** (39.6 mg, 55%, purified product chromatogram DKB09-Purified),[12] **2g** (performed on a 1.0 mmol scale, 94.3 mg, 76%, purified product chromatogram DKB10-Purified),[12] **2h** (50.0 mg, 73%, purified product chromatogram DKB13-Purified),[33] **2i** (39.0 mg, 45%, purified product chromatogram DKB15-Purified),[34] **2j** (56.9 mg, 74%, purified product chromatogram DKB16-Purified),[35] were prepared by this method and afforded NMR data that matched those reported in the literature.

### Amination of Arylboronic Acids; General Procedures (Table 2)

#### Room Temperature; Method A

Room-temperature reactions were performed on a 1.0 mmol scale. Arylboronic acid **3** (1.0 equiv) and MeCN (5.0 mL) were added to a 25 mL round-bottomed flask equipped with stir bar, followed by HSA (1.5 equiv) and aq 1 M NaOH (5 equiv). The mixture was capped and set to stir for 16 h overnight, after which a small aliquot was taken for reaction monitoring via HPLC analysis. The reaction mixture was diluted with $H_2O$ (30 mL) and extracted with EtOAc (2 × 30 mL). The combined organic extracts were dried ($Na_2SO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (EtOAc/hexanes) to afford the desired amine product **2**.

Compounds **2a** (72.6 mg, 78%, purified product chromatogram DKA29-Purified),[12] **2b** (65.3 mg, 61%, purified product chromatogram DKA20-Purified),[31] **2c** (92.8 mg, 75%, purified product chromatogram DKA60-Purified),[31] **2d** (87.9 mg, 69%, purified product chromatogram DKA54-Purified),[31] **2f** (87.0 mg, 61%, purified product chromatogram DKA33-Purified),[12] **2g** (69.0 mg, 70%, purified product chromatogram DKA30-Purified),[12] **2j** (102.3 mg, 68%, purified product chromatogram DKA34-Purified),[35] **2k** (74.0 mg, 43%, purified product chromatogram DKA39-Purified shows two peaks with a yield taken as ratio of 37:63 for impurity/product, respectively),[36] **2l** (122.1 mg, 71%, purified product chromatogram DKA40-Purified),[37] **2m** (83.8 mg, 38%, purified product chromatogram DKA45-Purified),[35] **2n** (90.0 mg, 62%, purified product chromatogram DKA59-Purified),[38] **2o** (42.6 mg, 31%, purified product chromatogram DKA53-Purified),[39] were prepared by this method and afforded NMR data that matched those reported in the literature.

#### Sonication; Method B

Reactions facilitated by sonication were performed on a 1.0 mmol scale. Arylboronic acid **3** (1.0 equiv) and MeCN (5.0 mL) were added to a 25 mL microwave vial equipped with a stir bar, followed by HSA (1.5 equiv) and aq 1 M NaOH (5 equiv). The mixture was capped and set to stir for 5 min, then placed in an ultrasonic cleaner for 30 min (35 kHz, 90 W), at which time the vial was removed and a small aliquot was taken for reaction monitoring via HPLC analysis. The mixture was then placed back in the sonication bath for 30 min. This process was repeated until the reaction had gone to completion, or the reaction failed to progress, as monitored by HPLC. The reaction mixture was diluted with $H_2O$ (30 mL) and extracted with EtOAc (2 × 30 mL). The combined organic extracts were dried ($Na_2SO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (EtOAc/hexanes) to afford the desired amine product **2**.

Compounds **2a** (1 hour sonication time, 80.2 mg, 86%, purified product chromatogram DKA25-Purified),[12] **2b** (1.25 h sonication time, 79.9 mg, 75%, purified product chromatogram DKA21-Purified),[31] **2c** (1.5 h sonication time, 96.9 mg, 79%, purified product chromatogram DKA55-Purified),[31] **2d** (1.5 h sonication time, 89.2 mg, 70%, purified product chromatogram DKA49-Purified),[31] **2f** (1 h sonication time, 107.6 mg, 75%, purified product chromatogram DKA31-Purified),[12] **2g**

(1 h sonication time, 95.3 mg, 77%, purified product chromatogram DKA27-Purified),[12] **2j** (1 h sonication time, 146.8 mg, 96%, purified product chromatogram DKA35-Purified),[35] **2k** (2.5 h sonication time, 67.8 mg, 39%, purified product chromatogram DKA37-Purified),[36] **2l** (1.5 h sonication time, 121.5 mg, 70%, purified product chromatogram DKA41-Purified),[37] **2m** (2.5 h sonication time, 128.5 mg, 59%, purified product chromatogram DKA43-Purified),[35] **2n** (1.5 h sonication time, 137.2 mg, 95%, purified product chromatogram DKA47-Purified),[38] **2o** (2.5 total h sonication time with additional 0.5 equiv of HSA added after 1 h and 0.5 equiv of HSA added after 1.5 h, 36.3 mg, 26%, purified product chromatogram DKA57-Purified),[39] were prepared by this method and furnished NMR data that matched those reported in the literature.

#### Microwave; Method C

Reactions facilitated by microwave irradiation were performed on a 1.0 mmol scale. Arylboronic acid **3** (1.0 equiv) and MeCN (5.0 mL) were added to a 10 mL microwave vial equipped with stir bar, followed by HSA (1.5 equiv) and aq 1 M NaOH (5 equiv). The mixture was capped and set to stir for 5 min, then placed in a microwave reactor, and heated to 100 °C for 15 min, and then cooled to r.t. The vial was removed from the microwave and a small aliquot was taken for reaction monitoring via HPLC analysis. The reaction mixture was diluted with $H_2O$ (30 mL) and extracted with EtOAc (2 × 30 mL). The combined organic extracts were dried ($Na_2SO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (EtOAc/hexanes) to afford the desired amine product **2**.

Compounds **2a** (81.7 mg, 88%, purified product chromatogram DKA4-Purified),[12] **2b** (81.1 mg, 76%, purified product chromatogram DKA8-Purified),[31] **2c** (89.0 mg, 72%, purified product chromatogram DKA56-Purified),[31] **2d** (94.3 mg, 74%, purified product chromatogram DKA50-Purified),[31] **2f** (126.8 mg, 87%, purified product chromatogram DKA32-Purified),[12] **2g** (108.1 mg, 87%, purified product chromatogram DKA11-Purified),[12] **2j** (122.6 mg, 80%, purified product chromatogram DKA36-Purified),[35] **2k** (104.8 mg, 60%, purified product chromatogram DKA38-Purified),[36] **2l** (109.2 mg, 63%, purified product chromatogram DKA42-Purified),[38] **2m** (an additional 1.0 equiv of HSA was added after 15 min, and heated for an additional 14 min, 117.0 mg, 53%, purified product chromatogram DKA61-Purified),[35] **2n** (132.2 mg, 92%, purified product chromatogram DKA48-Purified),[38] **2o** (an additional 1.0 equiv of HSA was added after 15 min, and heated for an additional 14 min, 94.6 mg, 68%, purified product chromatogram DKA58-Purified),[39] were prepared by this method and furnished NMR data that matched those reported in the literature.

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## Supporting Information

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