JOC The Journal of Organic Chemistry

Note

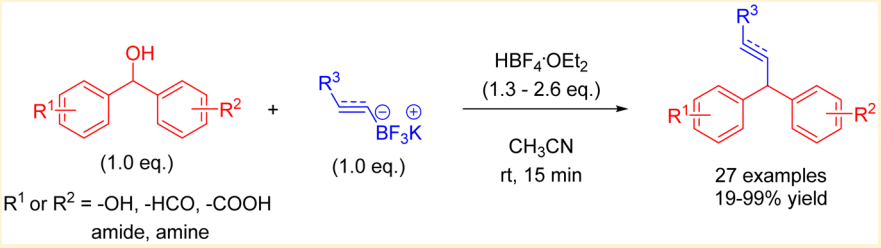
pubs.acs.org/joc

Brønsted Acid-Catalyzed Reactions of Trifluoroborate Salts with Benzhydryl Alcohols

Kayla M. Fisher and Yuri Bolshan*

University of Ontario Institute of Technology (UOIT), 2000 Simcoe Street North, Oshawa, Ontario L1H 7K4, Canada

Supporting Information



ABSTRACT: Brønsted acid-catalyzed carbon−carbon bond forming methodology using potassium alkynyl- and alkenyltrifluoroborate salts has been developed. Organotrifluoroborates react with benzhydryl alcohols to afford a broad range of alkynes and alkenes in good to excellent yields. This protocol features good atom economy because organotrifluoroborate salts and alcohols react in a 1:1 ratio. Furthermore, a variety of unprotected functional groups were tolerated under the developed conditions, including amide, aldehyde, free hydroxyl, and carboxylic acid.

Internal alkynes are important building blocks in organic chemistry and are a common structural unit in a vast array of pharmaceuticals, bioactive compounds, and natural products.[1] They are traditionally synthesized via harsh reaction conditions through substitution[2] or elimination[3] reactions. Metal catalysis emerged as an alternative to the classic approaches.[4] Additionally, reactions of trichloroacetimidates in the presence of AuCl/AgOTf[5] as well as secondary halides[6] and *N*-tosylhydrazones[7] using Pd catalysts have been reported. Furthermore, a direct C−H functionalization of benzylic position using DDQ and either CuOTf[8] or $Fe(OTf)_2$[9] is also known. Moreover, $FeCl_3$-catalyzed direct nucleophilic substitutions of ethers using carbon nucleophiles[10] and the cross-coupling of *N*-benzylic sulfonamides with terminal alkynes in the presence of catalytic amounts of $Bi(OTf)_3$ and $(Tf)_2NH$[11] have been reported. More recently, a direct metal-catalyzed dehydrative coupling of diarylmethanols to synthesize bis-benzylic secondary alkylacetylenes has gained attention due to its atom economy.[12] Numerous diarylmethanol derivatives are commercially available and can be easily prepared. Metal-catalyzed alkenylation of benzhydryl alcohols is also known.[13] Recently, Gandon and co-workers reported that $Ca(NTf_2)_2$ catalyzed the alkenylation of alcohols using two equivalents of vinylboronic acids.[14] Common disadvantages of the metal-catalyzed approach include the employment of frequently expensive and sensitive metal catalysts, which results in low functional group tolerance. Kabalka and co-workers described a metal-free methodology for the substitution of hydroxyl groups of benzylic alcohols with preformed alkenyl- and alkynylboron dihalides.[15] The same group reported dialkynylation of aldehydes using preformed dialkynylboron chlorides.[16] Other metal-free alkenylation reactions of benzhydryl alcohols have also been described in the literature.[17] Furthermore, Schaus and co-workers illustrated that the enantioselective alkenylation of benzhydryl alcohols and ethers proceeded in the presence of alkenylboronates and chiral biphenols.[18] More recently, acid-catalyzed propargylation of phenols has been developed.[19] The limitations of these protocols include the exposure of both starting materials to *n*-BuLi, the necessity to preform unstable haloborane intermediates, and narrow substrate scope.

Our research is focused on metal-free reactions of trifluoroborate salts. In general, organotrifluoroborates are attractive reagents due to their shelf-stability, straightforward preparation, and relatively nontoxic nature.[20] They have been shown to act as boronic acid equivalents in the palladium-catalyzed Suzuki−Miyaura couplings.[21] Recently, our group[23g,h] and others reported metal-free transformations of organotrifluoroborates.[22,23] Generally, these reactions rely on in situ generation of boron dihalide species using strong Lewis acids. These approaches, however, suffer from low functional group tolerance due to the instability of boron dihalide intermediates.

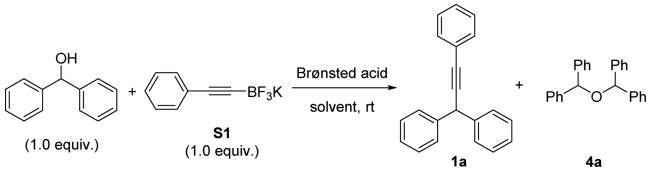
Recently, we developed a Brønsted acid-catalyzed methodology for the preparation of propargylic ethers from acetals and alkynyltrifluoroborates.[24] Here, we report a Brønsted acid-catalyzed reaction between trifluoroborate salts and benzhydryl alcohols. At the outset, we envisaged that the employment of the appropriate acid would address the deficiencies associated with previously reported Lewis acid- and metal-catalyzed protocols. Nucleophilic boron-ate complexes are known to react with preformed stabilized carbocations.[25] However,

Received: September 29, 2015
Published: November 20, 2015

DOI: 10.1021/acs.joc.5b02273
J. Org. Chem. 2015, 80, 12676−12685

examples of their generation in situ using a Brønsted acid in the presence of trifluoroborates under metal-free conditions are scarce. In addition to the recently published manuscript from this laboratory,[24] a literature survey indicated that organotrifluoroborates have been shown to participate in reactions whereby Brønsted acids are present.[26] In these cases, however, either HF or KHF_2 have been used as additives. Both reagents are known to serve as sources of fluoride for the conversion of boronic acids or boronate esters to trifluoroborates.[27] Allylation-like addition of trifluoroborates to aldehydes has been reported in the presence of trifluoromethanesulfonic acid.[28] This protocol, however, was mechanistically similar to Lewis acid-catalyzed transformations due to the formation of a boron dihalide intermediate. After careful consideration, we decided to utilize tetrafluoroboric acid (HBF_4) as a catalyst. It has a $pK_a = 0.5$ in water,[29] which is strong enough to promote the formation of benzhydrylium carbocations from diarylmethanols.[30] Therefore, our initial efforts were focused on the preparation of internal alkyne **1a** from diphenylmethanol and potassium phenylacetylenetrifluoroborate salt **S1** (Table 1).

Table 1. Optimization of Conditions for the Preparation of Secondary Alkylacetylene 1a



entry	acid	acid (equiv)	solvent	yield 1a (%)	ratio **1a**:**4a**
1	$HBF_4{\cdot}OEt_2$	1.0	DCM	trace	
2	$HBF_4{\cdot}OEt_2$	1.6	DMSO	trace	
3[a]	$HBF_4{\cdot}OEt_2$	0.5	CH_3CN		1:1
4[a]	$HBF_4{\cdot}OEt_2$	1.0	CH_3CN	35	1:0
5[a]	$HBF_4{\cdot}OEt_2$	1.2	CH_3CN	37	25:1
6	$HBF_4{\cdot}OEt_2$	1.6	CH_3CN	41	1:0
7	4.0 M HCl	1.6	CH_3CN	trace	
8	$HSbF_6{\cdot}6H_2O$	1.5	CH_3CN	trace	
9[b]	$HBF_4{\cdot}OEt_2$	1.6	CH_3CN	34	1:0

[a]The ratio has been determined by NMR analysis of crude reaction mixtures. [b]Anhydrous conditions.

A screen of solvents revealed that acetonitrile (CH_3CN) was well suited for the reaction (Table 1, entries 1−4). Conducting a reaction in the presence of a substoichiometric amount of HBF_4 resulted in the formation of the inseparable mixture of product **1a** and undesired dibenzhydryl ether byproduct **4a** (Table 1, entry 3). By gradually increasing the amount of HBF_4, we discovered that the optimal acid loading was 1.6 equiv (Table 1, entry 6). These results were consistent with the findings that increasing the amount of HBF_4 suppressed the formation of undesired dimer **4a**.[30] Efforts to use alternative acids, such as HCl and $HSbF_6{\cdot}6H_2O$, only resulted in trace amounts of product formation (Table 1, entries 7, 8). Interestingly, the yield decreased from 41 to 34% when the reaction was conducted under anhydrous conditions (Table 1, entry 9). Further attempts to optimize the reaction temperature and relative equivalents of alcohol or trifluoroborate salts were fruitless.

The investigation on the substituent effects revealed that electron-donating substituents result in higher yields (Figure 1). For instance, the presence of a 4-methyl substituent increased the yield of **1b** to 67% compared to 41% for unsubstituted product **1a**. The reaction exhibited mild sensitivity to the steric hindrance. The yield of the 2-methyl-substituted substrate **1c** was 51%. Electron-rich substrates afforded desired products **1d** and **1e** in excellent yields. Notably, a scale-up reaction afforded 0.20 g of **1d** with 10% yield erosion. Starting material bearing a 4-chloro substituent resulted in the formation of corresponding product **1f** only in 19%. Electron-withdrawing substituents destabilize the carbocation intermediate, thus resulting in the formation of unidentified byproducts. Efforts to decrease the reaction temperature to −40 °C led to the competing formation of dibenzyhydryl ether byproduct. This issue, however, can be alleviated by the introduction of an electron-donating functionality to offset the destabilizing effect. Product **1g** with 4-chloro-4′-methoxy substituents was isolated in 84% yield. Next, we decided to expand the scope to unprotected protic functional groups. Free phenol- and amide-containing substrates afforded products **1h** and **1i** in 66 and 61% yields, respectively. Modest 42% yield of **1j** was observed when a carboxylic acid functional group was present. The yield increased to 62% when the amount of HBF_4 was decreased to 1.3 equiv.

Next, we investigated the scope of potassium alkynyltrifluoroborate salts. Their reactivity was examined under the optimized conditions (Figure 2). Good to excellent yields were observed with a wide range of salts, such as trifluoromethyl-, chloro-, and fluorophenylacetylenetrifluoroborates. Unsubstituted biphenyl- and naphthylacetylenetrifluoroborates afforded the products in good yields (**2g**−**2i**). We further examined the effect of substituents on diarylmethanol starting material. The substrate scope was expanded to benzhydryl alcohols that contained an amine functional group. Modest 53% yield of **2f** was observed when dimethylamine functionality was present. The ability of basic amine functionality to undergo protonation in the presence of acid prompted us to increase the acid-to-substrate ratio. We observed that the yield of **2f** improved to 61% when the amount of HBF_4 was increased from 1.6 to 2.6 equiv. Applying these conditions to a Boc-protected amine bearing substrate resulted in 51% yield of deprotected product **2j.** In addition to phenylacetylenetrifluoroborates, hexynyltrifluoroborate salt was a good coupling partner. Desired product **2k** was formed in 73% yield.

Lastly, the scope of styryltrifluoroborate salts was explored (Figure 3). To our delight, alkenyl trifluoroborates, such as potassium styryl- and 2-(3-fluorophenyl)vinyltrifluoroborate salts, provided the desired products in good to excellent yields (**3a**−**3e**). Once again, increasing the amount of added acid for the amine-bearing substrate improved the yield of **3d** to 84%. Only a modest yield increase of **3e** was noted when 1.3 equiv of HBF_4 was used. Expanding the scope to alkenyltrifluoroborate salts further increases the utility of the developed methodology.

A plausible reaction mechanism includes the formation of benzhydrylium ion as a reaction intermediate. Subsequently, nucleophilic trifluoroborate salts react with the electrophilic center to afford the final product.

Finally, the developed methodology was applied to the synthesis of benzofuran **7** (Scheme 1). Benzhydryl alcohol **5** reacted with alkynyltrifluoroborate in the presence of HBF_4 to afford alkyne **6**. Demethylation[31] and cyclization[19] proceeded under the reported conditions.

DOI: 10.1021/acs.joc.5b02273
J. Org. Chem. 2015, 80, 12676−12685

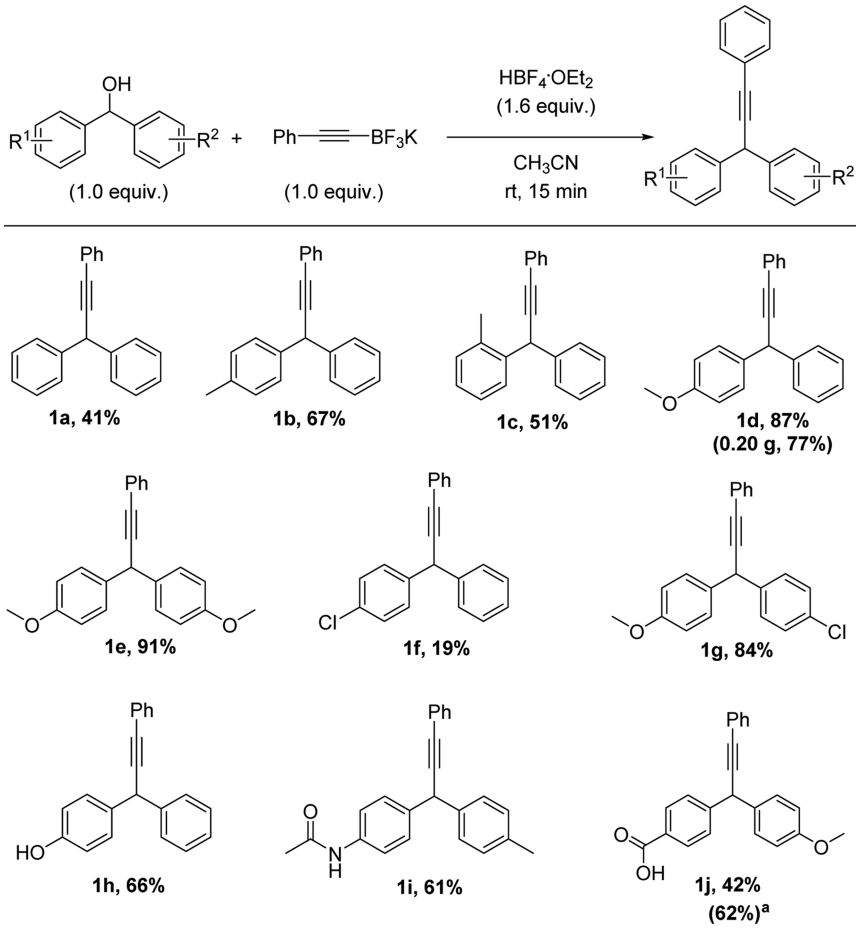


Figure 1. Reactions of phenylacetylenetrifluoroborate salt with benzhydryl alcohols. [a]Using 1.3 equiv of HBF_4.

In conclusion, we have developed a novel method for the preparation of internal alkynes and alkenes from benzhydryl alcohols and potassium trifluoroborate salts. This transformation proceeds rapidly in the presence of a Brønsted acid without exclusion of air or moisture. The developed protocol features good atom economy because organotrifluoroborate salts and alcohols reacted in a 1:1 ratio. Furthermore, this methodology demonstrates functional group tolerance superior to that of Lewis acid- and metal-catalyzed approaches.

EXPERIMENTAL SECTION

General. All reactions were set up in 2 mL glass vials at room temperature under atmosphere. Unless otherwise noted, all other reagents and materials were obtained from commercial suppliers and used without further purification. Potassium trifluoroborate salts were synthesized according to published procedures.[23g,i] Reaction progress was monitored via thin layer chromatography (TLC) on silica gel (60 Å) with visualization using ultraviolet light (254 nm) and by staining with potassium permanganate ($KMnO_4$). NMR characterization data was collected at 25 °C as solutions in deuterated solvents ($CDCl_3$, acetone-d_6 and DMSO-d_6). ^{1}H- and ^{19}F-NMR spectra were collected at 400 and 376 MHz, respectively, while ^{13}C {^{1}H} and ^{11}B NMR spectra were collected at 100 and 128 MHz, respectively. Chemical shifts are expressed in ppm values. IR spectra were recorded on an FTIR spectrometer using a platinum ATR with a diamond ATR crystal. Spectra are reported in terms of frequency of absorption (cm^{-1}), and only partial data is provided. Melting points were measured with a melting point apparatus and are uncorrected. High resolution mass spectra (HRMS) were recorded using electrospray ionization (ESI), electron impact ionization (EI), direct analysis in real time (DART) ion source, and time-of-flight (TOF) mass analysis. Column chromatography was carried out on silica gel (60 Å, low acidity) with reagent grade solvents.

Preparation of Alkynyl Potassium Organotrifluoroborate Salts. *General Procedure 1 (GP1).* To a solution of the indicated terminal alkyne (1.0 equiv) in dry THF at −70 °C under argon atmosphere was added *n*-BuLi (1.0 equiv) dropwise, and the solution was stirred for 1 h at this temperature. Trimethylborate (1.5 equiv) was added dropwise at −60 °C. The solution was stirred at this temperature for 2 h. A saturated aqueous solution of potassium hydrogen difluoride (6.0 equiv) was added at −20 °C. The mixture was allowed to stir for 1 h at −20 °C and for 1 h at room temperature. The solvent was removed under reduced pressure, and the resulting solid was placed under vacuum overnight to remove any remaining water. The solid was washed several times with hot acetone (4 × 10 mL), which was collected and concentrated to a volume of ∼5 mL. The product was precipitated with diethyl ether (30 mL) and cooled to 4 °C to complete precipitation. The crystalline trifluoroborate salt was collected by gravity filtration.

General Procedure 2 (GP2). To a solution of the indicated terminal alkyne (1.0 equiv) in dry THF at −78 °C under argon atmosphere was added *t*-BuLi (1.0 equiv) dropwise, and the solution was stirred for 2 h at this temperature. Trimethylborate (1.5 equiv) was added dropwise at −65 °C. The solution was stirred at this temperature for 1 h and 40 min. A saturated aqueous solution of potassium hydrogen difluoride (6.0 equiv) was added at −30 °C. The mixture was allowed to stir for 1 h at −30 °C and for 1 h at room temperature. The solvent was removed under reduced pressure, and the resulting solid was placed under vacuum overnight to remove any remaining water. The solid was washed several times with hot acetone (4 × 10 mL), which was collected and concentrated to a volume of ∼5 mL. The product was precipitated with diethyl ether (30 mL) and cooled to 4 °C to

DOI: 10.1021/acs.joc.5b02273
J. Org. Chem. 2015, 80, 12676−12685

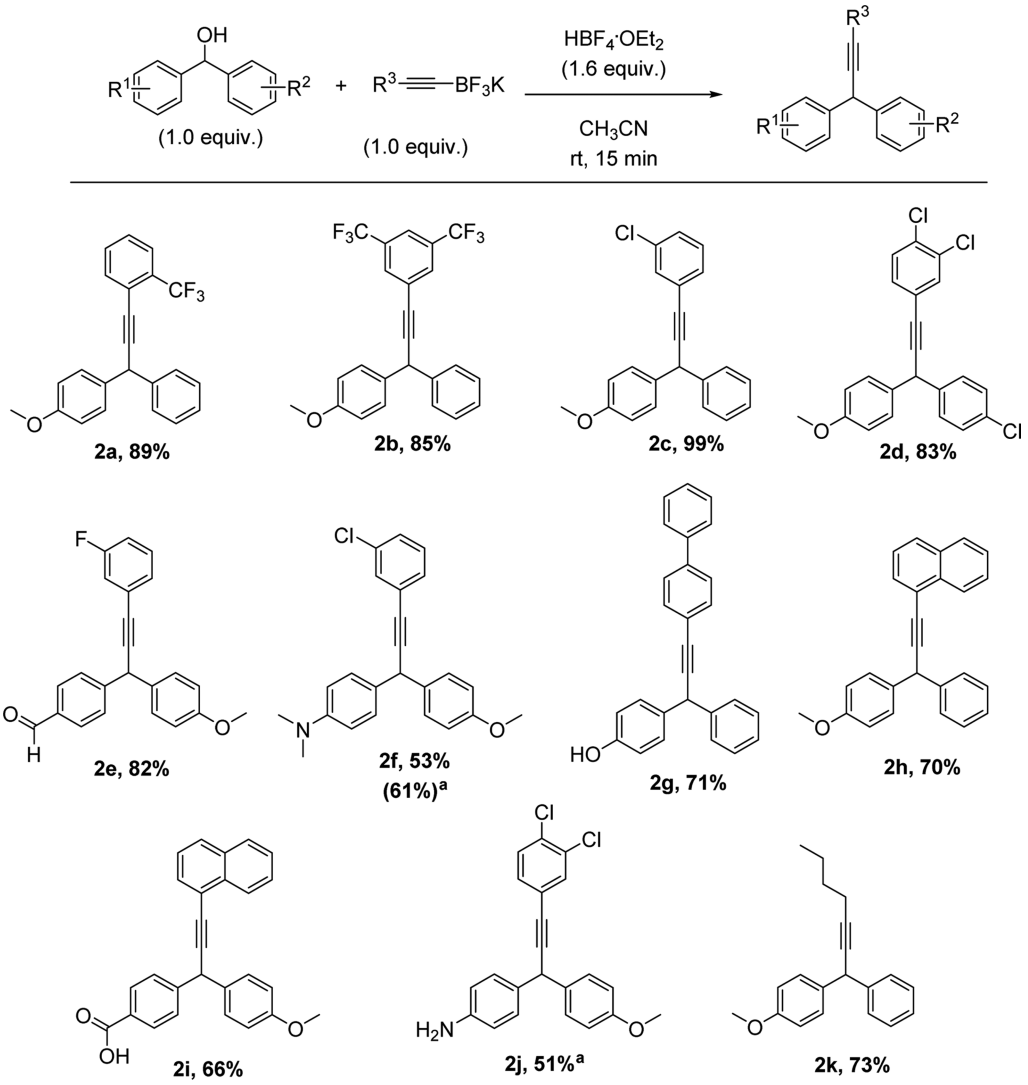


Figure 2. Reactions of various alkynyltrifluoroborates with benzhydryl alcohols. [a]Using 2.6 equiv of HBF_4 (for **2j**, Boc-protected amine was used as the starting material).

complete precipitation. The crystalline trifluoroborate salt was collected by gravity filtration.

*Potassium Trifluoro(phenylethynyl)borate (**S1**).*[24] Phenylacetylene (2.45 g, 24.0 mmol, 1.0 equiv), *n*-BuLi (1.54 g, 24.0 mmol, 1.0 equiv), $B(OMe)_3$ (3.75 g, 36.1 mmol, 1.5 equiv), and aqueous KHF_2 (11.26 g, 144.2 mmol, 6.0 equiv) in 50 mL of THF, following GP1, afforded **S1** (1.190 g, 24% yield) as a white crystalline solid. ^{1}H NMR (DMSO) δ 7.28−7.30 (m, 4H), 7.21−7.26 (m, 1H); ^{13}C {^{1}H} NMR (DMSO) δ 130.9, 128.2, 126.7, 125.5; ^{19}F NMR (DMSO) δ −131.71 (s, 3F).

*Potassium Trifluoro((2-(tluoromethyl)phenyl)ethynyl)borate (**S2**).*[24] 1-Ethynyl-2-trifluoromethylbenzene (1.00 g, 5.70 mmol, 1.0 equiv), *n*-BuLi (0.365 g, 5.70 mmol, 1.0 equiv), $B(OMe)_3$ (0.89 g, 8.55 mmol, 1.5 equiv), and aqueous KHF_2 (2.67 g, 34.2 mmol, 6.0 equiv) in 17.0 mL of THF, following GP1, afforded **S2** (0.879 g, 56% yield) as a white crystalline solid. ^{1}H NMR (DMSO) δ 7.65 (d, J = 7.4 Hz, 1H), 7.51−7.58 (m, 2H), 7.39−7.44 (m, 1H).

*Potassium Trifluoro((3,5-bis(trifluoromethyl)phenyl)ethynyl)-borate (**S3**).*[24] 1-Ethynyl-3,5-bis(trifluoromethyl)benzene (1.00 g, 4.07 mmol, 1.0 equiv), *n*-BuLi (0.261 g, 4.07 mmol, 1.0 equiv), $B(OMe)_3$ (0.63 g, 6.11 mmol, 1.5 equiv), and aqueous KHF_2 (1.90 g, 24.4 mmol, 6.0 equiv) in 12.2 mL of THF, following GP1, afforded **S3** (0.444 g, 32% yield) as a white crystalline solid. ^{1}H NMR (DMSO) δ 7.92−7.93 (m, 3H).

*Potassium Trifluoro((3-chlorophenyl)ethynyl)borate (**S4**).*[24] 3-Chloro-1-ethynylbenzene (0.44 g, 3.25 mmol, 1.0 equiv), *t*-BuLi (0.21 g, 3.25 mmol, 1.0 equiv), $B(OMe)_3$ (0.51 g, 4.87 mmol, 1.5 equiv), and aqueous KHF_2 (1.52 g, 19.5 mmol, 6.0 equiv) in 10.0 mL of THF, following GP2, afforded **S4** (0.460 g, 59% yield) as a white crystalline solid. ^{1}H NMR (DMSO) δ 7.30−7.32 (m, 3H), 7.24−7.28 (m, 1H).

*Potassium Trifluoro((3-fluorophenyl)ethynyl)borate (**S5**).*[24] 1-Ethynyl-3-fluorobenzene (0.67 g, 5.44 mmol, 1.0 equiv), *n*-BuLi (0.349 g, 5.44 mmol, 1.0 equiv), $B(OMe)_3$ (0.85 g, 8.16 mmol, 1.5 equiv), and aqueous KHF_2 (2.55 g, 32.7 mmol, 6.0 equiv) in 17.0 mL of THF, following GP1, afforded **S5** (1.038 g, 84% yield) as a white crystalline solid. ^{1}H NMR (DMSO) δ 7.30−7.35 (m, 1H), 7.07−7.14 (m, 3H).

*Potassium Trifluoro((3,4-dichlorophenyl)ethynyl)borate (**S6**).*[24] 3,4-Dichloro-1-ethynylbenzene (0.894 g, 5.22 mmol, 1.0 equiv), *n*-BuLi (0.335 g, 5.22 mmol, 1.0 equiv), $B(OMe)_3$ (0.81 g, 7.84 mmol, 1.5 equiv), and aqueous KHF_2 (2.45 g, 31.3 mmol, 6.0 equiv) in 17.5 mL of THF, following GP1, afforded **S6** (0.618 g, 43% yield) as an off-white crystalline solid. ^{1}H NMR (DMSO) δ 7.51−7.54 (m, 2H), 7.26 (dd, J = 2.0, 8.2 Hz, 1H).

*Potassium Trifluoro([1,1′-biphenyl]-4-ylethynyl)borate (**S7**).*[24] 4-Ethynylbiphenyl (1.00 g, 5.44 mmol, 1.0 equiv), *n*-BuLi (0.349 g, 5.44 mmol, 1.0 equiv), $B(OMe)_3$ (0.85 g, 8.16 mmol, 1.5 equiv), and aqueous KHF_2 (2.55 g, 32.7 mmol, 6.0 equiv) in 17.0 mL of THF, following GP1, afforded **S7** (0.201 g, 13% yield) as an off-white crystalline solid. ^{1}H NMR (DMSO) δ 7.65−7.67 (d, J = 7.03 Hz, 2H),

DOI: 10.1021/acs.joc.5b02273
J. Org. Chem. 2015, 80, 12676−12685

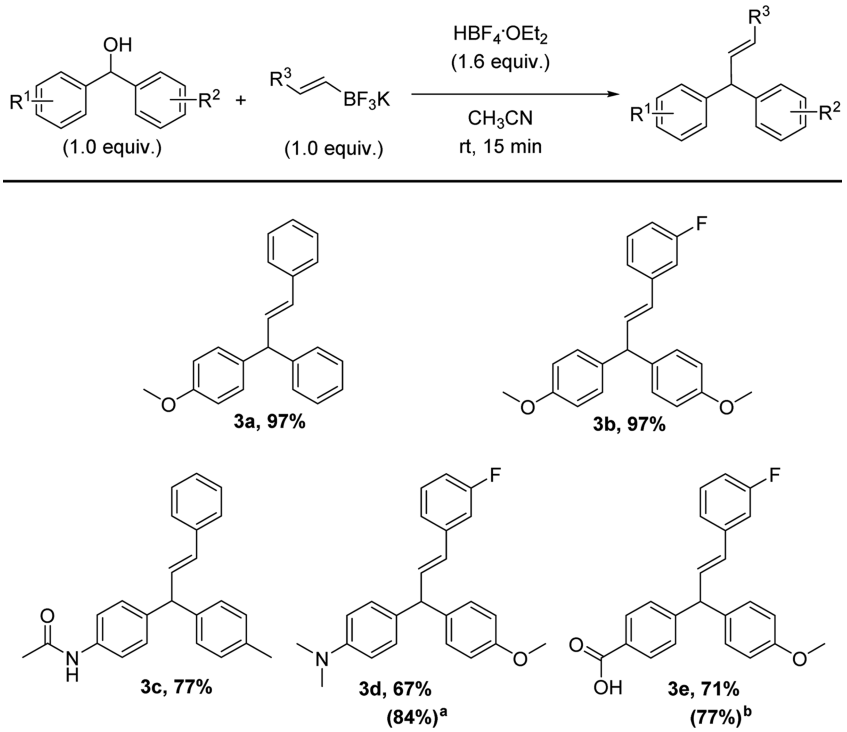
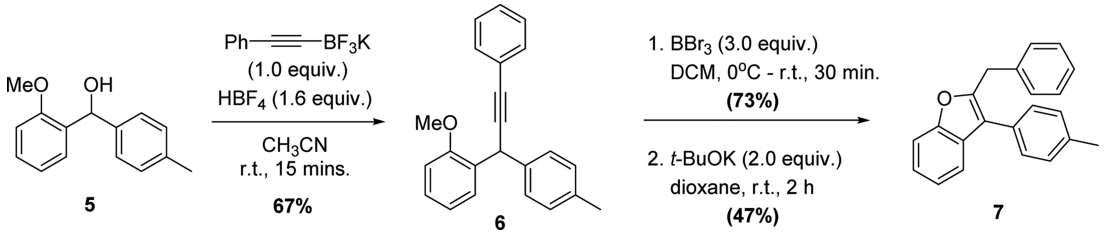


Figure 3. Reactions of styryltrifluoroborates with benzhydryl alcohols. Using [a]2.6 or [b]1.3 equiv of HBF_4.

Scheme 1. Application of the Developed Methodology to the Synthesis of Benzofuran



7.58−7.61 (d, J = 8.6 Hz, 2H), 7.44−7.47 (m, 2H), 7.33−7.39 (m, 3H).

*Potassium Trifluoro(naphthalen-1-ylethynyl)borate (**S8**).*[24] 1-Ethynylnaphthalene (0.854 g, 5.44 mmol, 1.0 equiv), *n*-BuLi (0.349 g, 5.44 mmol, 1.0 equiv), $B(OMe)_3$ (0.85 g, 8.16 mmol, 1.5 equiv), and aqueous KHF_2 (2.55 g, 32.7 mmol, 6.0 equiv) in 17.0 mL of THF, following GP1, afforded **S8** (0.876 g, 62% yield) as a slightly pink crystalline solid. ^{1}H NMR (DMSO) δ 8.33 (d, J = 8.2 Hz, 1H), 7.91 (d, J = 8.6 Hz, 1H), 7.82 (d, J = 8.2 Hz, 1H), 7.51−7.61 (m, 3H), 7.42−7.45 (m, 1H).

*Potassium Trifluoro(hex-1-yn-1-yl)borate (**S9**).*[23g] 1-Hexyne (2.0 g, 23.6 mmol, 1.0 equiv), *n*-BuLi (1.51 g, 23.6 mmol, 1.0 equiv), $B(OMe)_3$ (3.68 g, 35.4 mmol, 1.5 equiv), and aqueous KHF_2 (11.06 g, 142 mmol, 6.0 equiv) in 25 mL of THF, following GP1, afforded **S9** (1.659 g, 36% yield) as a white crystalline solid. ^{1}H NMR (DMSO) δ 1.98 (m, 2H) 1.33 (m, 4H), 0.85 (m, 3H); ^{13}C {^{1}H} NMR (DMSO) δ 31.1, 21.4, 18.5, 13.5; ^{19}F NMR (DMSO) δ −131.01 (s, 3F).

Preparation of Benzhydryl Alcohols (General Procedure 3, GP3). A solution of the indicated *para*-substituted benzaldehyde (1.0 equiv) in dry THF was treated with the indicated phenylmagnesium bromide solution (1.1−4.0 equiv) at 0 °C. After addition was complete, the mixture was allowed to stir at room temperature for 30−120 min. The reaction was quenched with aqueous 1 M HCl solution and extracted with 50 mL of EtOAc. The organic layer was washed with water (3 × 30 mL) followed by brine (1 × 25 mL). The organic layer was dried with $MgSO_4$ and concentrated. The product was purified by flash chromatography with hexanes/ethyl acetate.

*4-(Hydroxy(phenyl)methyl)phenol (**S10**).*[32] The title compound was derived from 4-hydroxybenzaldehyde (0.153 g, 1.25 mmol, 1.0 equiv) and phenylmagnesium bromide (0.453 g, 2.50 mmol, 2.0 equiv) in 5.0 mL of anhydrous THF following GP3. Purification by automated flash column chromatography on silica gel using hexanes/EtOAc (3:1) afforded product **S10** (0.196 g, 79% yield) as a white solid. ^{1}H NMR (DMSO) δ 9.22 (s, 1H), 7.26−7.34 (m, 4H), 7.12−7.19 (m, 3H), 6.67 (d, J = 8.6 Hz, 2H), 5.67 (d, J = 3.9 Hz, 1H), 5.59 (d, J = 3.9 Hz, 1H).

*Bis(4-methoxyphenyl)methanol (**S11**).*[33] The title compound was derived from 4-methoxybenzaldehyde (0.139 g, 1.02 mmol, 1.0 equiv) and 4-methoxyphenylmagnesium bromide (0.649 g, 3.07 mmol, 3.0 equiv) in 3.0 mL of anhydrous THF following GP3. Purification by silica gel column chromatography using hexanes/EtOAc (5:1) afforded product **S11** (0.248 g, 99% yield) as a yellow solid. ^{1}H NMR ($CDCl_3$) δ 7.26 (d, J = 8.2 Hz, 4H), 6.86 (d, J = 9.0 Hz, 4H), 5.75 (s, 1H), 3.78 (s, 6H), 2.18 (s, 1H).

*(4-Chlorophenyl)(4-methoxyphenyl)methanol (**S12**).*[34] The title compound was derived from 4-chlorobenzaldehyde (0.1413 g, 1.01 mmol, 1.0 equiv) and 4-methoxyphenylmagnesium bromide (0.850 g, 4.02 mmol, 4.0 equiv) in 3.0 mL of anhydrous THF following GP3. Purification by silica gel chromatography using hexanes/EtOAc (5:1) afforded product **S12** (0.203 g, 81% yield) as an off-white solid. ^{1}H NMR ($CDCl_3$) δ 7.30 (s, 4H), 7.24 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 5.77 (d, J = 3.1 Hz, 1H), 3.79 (s, 3H), 2.20 (d, J = 3.5 Hz, 1H).

*(4-(Dimethylamino)phenyl)(4-methoxyphenyl)methanol (**S13**).*[35] The title compound was derived from 4-(dimethylamino)-

DOI: 10.1021/acs.joc.5b02273
J. Org. Chem. 2015, 80, 12676−12685

benzaldehyde (0.174 g, 1.17 mmol, 1.0 equiv) and 4-methoxyphenylmagnesium bromide (0.271 g, 1.28 mmol, 1.1 equiv) in 3.0 mL of anhydrous THF following GP3. Purification by automated flash column chromatography on silica gel using hexanes/EtOAc (5:1) afforded product **S13** (0.174, 58% yield) as an off-white solid. ^{1}H NMR ($CDCl_3$) δ 7.29 (d, J = 8.6 Hz, 2H), 7.20 (d, J = 8.2 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 6.69 (d, J = 9.0 Hz, 2H), 5.73 (d, J = 3.5 Hz, 1H), 3.78 (s, 3H), 2.92 (s, 6H), 2.07 (d, J = 3.9 Hz, 1H).

*N-(4-(Hydroxy(p-tolyl)methyl)phenyl)acetamide (**S14**).* The title compound was derived from 4-acetamidobenzaldehyde (0.192 g, 1.18 mmol, 1.0 equiv) and 4-methylphenylmagnesium bromide (0.459 g, 2.35 mmol, 2.0 equiv) in 3.0 mL of anhydrous THF following GP3. Purification by automated flash column chromatography on silica gel using hexanes/EtOAc (1:1) afforded product **S14** (0.199 g, 66% yield) as a yellow solid. Mp 139−142 °C; IR (Diamond-ATR) ν 3309, 1657, 1601, 1535, 1412, 1318, 1268, 1012, 819, 758, 552, 477 cm^{-1}; ^{1}H NMR (DMSO) δ 9.85 (s, 1H), 7.48 (d, J = 8.6 Hz, 2H), 7.21−7.25 (m, 4H), 7.09 (d, J = 7.8 Hz, 2H), 5.72 (d, J = 4.3 Hz, 1H), 5.60 (d, J = 3.9 Hz, 1H), 2.25 (s, 3H), 2.01 (s, 1H); ^{13}C {^{1}H} NMR (DMSO) δ 168.0, 142.8, 140.5, 137.8, 135.5, 128.5, 126.5, 126.1, 118.7, 73.7, 23.9, 20.6; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{16}H_{18}NO_2$ 256.1332, found 256.1329.

*tert-Butyl (4-(Hydroxy(p-tolyl)methyl)phenyl)carbamate (**S15**).* The title compound was derived from 4-(Boc-amino)benzaldehyde (0.100 g, 0.45 mmol, 1.0 equiv) and 4-methoxyphenylmagnesium bromide (0.239 g, 1.13 mmol, 2.5 equiv) in 3.0 mL of anhydrous THF following GP3. Purification by silica gel chromatography using hexanes/EtOAc (3:1) afforded product **S15** (0.111 g, 74% yield) as a yellow solid. Mp 106−109 °C; IR (Diamond-ATR) ν 3367, 1696, 1507, 1235, 1157, 1035, 824, 574 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.24−7.32 (m, 6H), 6.85 (d, J = 8.6 Hz, 2H), 6.47 (s, 1H), 5.75 (s, 1H), 3.78 (s, 3H), 2.16 (s, 1H), 1.50 (s, 9H); ^{13}C {^{1}H} NMR ($CDCl_3$) δ 159.0, 152.7, 138.7, 137.6, 136.2, 127.8, 127.1, 118.5, 113.8, 80.5, 75.4, 55.3, 28.3; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{19}H_{23}NO_4Na$ 352.1519, found 352.1520.

*4-(Hydroxy(4-methoxyphenyl)methyl)benzoic Acid (**S16**).* The title compound was derived from 4-formylbenzoic acid (0.174 g, 1.16 mmol, 1.0 equiv) and 4-methoxyphenylmagnesium bromide (0.737 g, 3.48 mmol, 3.0 equiv) in 5.0 mL of anhydrous THF following GP3. Purification by silica gel chromatography using hexanes/EtOAc/AcOH (1.5:1:0.01% v/v) afforded product **S16** (0.208 g, 69% yield) as a white solid. Mp 158−160 °C; IR (Diamond-ATR) ν 3468, 2920, 1675, 1607, 1508, 1423, 1293, 1228, 1169, 1025, 742, 551 cm^{-1}; ^{1}H NMR (DMSO) δ 12.80 (s, 1H), 7.87 (d, J = 8.6 Hz, 2H), 7.47 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 5.92 (s, 1H), 5.71 (s, 1H), 3.71 (s, 3H); ^{13}C {^{1}H} NMR (DMSO) δ 167.2, 158.2, 150.9, 137.2, 129.2, 129.1, 127.5, 126.1, 113.5, 73.4, 55.0; HRMS (ESI-TOF) m/z [M − H]$^-$ calcd for $C_{15}H_{13}O_4$ 257.0819, found 257.0817.

*4-(Hydroxy(4-methoxyphenyl)methyl)benzaldehyde (**S17**).* The title compound was derived from 4-(diethoxymethyl) benzaldehyde (0.258 g, 1.24 mmol, 1.0 equiv) and 4-methoxyphenylmagnesium bromide (0.419 g, 1.98 mmol, 1.6 equiv) in 3.0 mL of anhydrous THF following GP3. Purification by silica gel chromatography using hexanes/EtOAc (3:1) afforded product **S17** (66.0 mg, 22% yield) as a yellow oil. IR (Diamond-ATR) ν 3421, 1690, 1605, 1509, 1244, 1169, 1027, 818, 785, 554 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.98 (s, 1H), 7.84 (d, J = 8.6 Hz, 2H), 7.56 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 5.86 (s, 1H), 3.79 (s, 3H), 2.34 (s, 1H); ^{13}C {^{1}H} NMR ($CDCl_3$) δ 191.9, 159.4, 150.6, 135.5, 135.4, 129.9, 128.1, 126.8, 114.2, 75.5, 55.3; HRMS (EI) m/z [M$^+$] calcd for $C_{15}H_{14}O_3$ 242.0943, found 242.0944.

*(2-Methoxyphenyl)(p-tolyl)methanol (**5**).*[36] The title compound was derived from 2-methoxybenzaldehyde (0.298 g, 2.19 mmol, 1.0 equiv) and *p*-tolylmagnesium bromide (0.642 g, 3.29 mmol, 1.5 equiv) in 5.0 mL of anhydrous THF following GP3. Purification by automated flash column chromatography on silica gel using hexanes/EtOAc (gradient: 49:1 → 12:1) afforded product **5** (0.396 g, 79% yield) as a white solid. ^{1}H NMR ($CDCl_3$) δ 7.26−7.20 (m, 4H), 7.10 (d, J = 7.8 Hz, 2H), 6.92 (t of d, J = 0.8, 7.4 Hz, 1H), 6.85 (d of d, J = 0.8, 8.6 Hz, 1H), 6.00 (s, 1H), 3.76 (s, 3H), 3.05 (s, 1H), 2.31 (s, 3H).

Synthesis of Internal Alkenes and Alkynes (General Procedure 4, GP4). In a 2 mL vial containing a stir bar, the indicated benzhydrol alcohol (1.0 equiv) and potassium trifluoroborate salt (1.0 equiv) were added followed by addition of anhydrous acetonitrile (0.3 mL). HBF_4·OEt_2 (1.3−2.6 equiv) was added dropwise, and the reaction was allowed to stir at room temperature for 15 min. The reaction was quenched with water and extracted in 20 mL of ethyl acetate. The organic layer was washed with water (3 × 15 mL) followed by brine (1 × 10 mL). The organic layer was dried with $MgSO_4$ and concentrated. Purification procedures varied based on the product synthesized. For specific details, see below. In the cases where a CH_3CN/hexanes extraction was required, the product was solubilized in 5 mL of anhydrous acetonitrile in a 20 mL vial. Then, 1 mL of hexanes was added, forming a bilayer. The two layers were thoroughly mixed and then allowed to settle. The bottom acetonitrile layer was then removed and concentrated. In the cases where a pentane wash was required, in a minimum of chloroform, the product was washed with 5 mL of pentane on a pipet column and eluted with diethyl ether to afford the product.

*Prop-2-yne-1,1,3-triyltribenzene (**1a**).*[15b] The title compound was derived from diphenylmethanol (13.3 mg, 0.072 mmol, 1.0 equiv), potassium trifluoro(phenylethynyl)borate (**S1**) (15.0 mg, 0.072 mmol, 1.0 equiv), and HBF_4·OEt_2 (18.7 mg, 0.12 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by automated flash column chromatography on silica gel using hexanes and subsequent CH_3CN/hexanes extraction afforded product **1a** (7.8 mg, 41% yield) as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.43−7.49 (m, 6H), 7.29−7.34 (m, 7H), 7.21−7.25 (m, 2H), 5.21 (s, 1H).

*(3-(p-Tolyl)prop-1-yne-1,3-diyl)dibenzene (**1b**).*[7] The title compound was derived from phenyl(*p*-tolyl)methanol (21.1 mg, 0.11 mmol, 1.0 equiv), potassium trifluoro(phenylethynyl)borate (**S1**) (22.1 mg, 0.11 mmol, 1.0 equiv), and HBF_4·OEt_2 (27.5 mg, 0.17 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by silica gel column chromatography using hexanes afforded product **1b** (20.2 mg, 67% yield) as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.42−7.48 (m, 4H), 7.28−7.33 (m, 7H), 7.20−7.24 (m, 1H), 7.13 (d, J = 7.8 Hz, 2H), 5.17 (s, 1H), 2.31 (s, 3H).

*(3-(o-Tolyl)prop-1-yne-1,3-diyl)dibenzene (**1c**).*[37] The title compound was derived from phenyl(*o*-tolyl)methanol (21.1 mg, 0.11 mmol, 1.0 equiv), potassium trifluoro(phenylethynyl)borate (**S1**) (22.1 mg, 0.11 mmol, 1.0 equiv), and HBF_4·OEt_2 (27.5 mg, 0.17 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by silica gel column chromatography using hexanes afforded product **1c** (15.2 mg, 51% yield) as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.50 (dd, J = 1.6, 7.03 Hz, 1H), 7.44−7.46 (m, 2H), 7.37−7.39 (m, 2H), 7.27−7.32 (m, 5H), 7.14−7.25 (m, 4H), 5.38 (s, 1H), 2.33 (s, 3H).

*(3-(4-Methoxyphenyl)prop-1-yne-1,3-diyl)dibenzene (**1d**).*[38] The title compound was derived from (4-methoxyphenyl) (phenyl)-methanol (21.5 mg, 0.10 mmol, 1.0 equiv), potassium trifluoro-(phenylethynyl)borate (**S1**) (20.9 mg, 0.10 mmol, 1.0 equiv), and HBF_4·OEt_2 (26.0 mg, 0.16 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by silica gel column chromatography using hexanes/diethyl ether (40:1) afforded product **1d** (26.2 mg, 87% yield) as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.41−7.48 (m, 4H), 7.28−7.36 (m, 7H), 7.20−7.24 (m, 1H), 6.85 (d, J = 9.0 Hz, 2H), 5.16 (s, 1H), 3.77 (s, 3H).

*4,4′-(3-Phenylprop-2-yne-1,1-diyl)bis(methoxybenzene) (**1e**).*[15b] The title compound was derived from bis(4-methoxyphenyl)methanol (**S11**) (22.3 mg, 0.091 mmol, 1.0 equiv), potassium trifluoro-(phenylethynyl)borate (**S1**) (19.0 mg, 0.091 mmol, 1.0 equiv), and HBF_4·OEt_2 (23.7 mg, 0.14 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Aqueous workup afforded product **1e** (27.2 mg, 91% yield) as a yellow/orange oil. ^{1}H NMR ($CDCl_3$) δ 7.48−7.51 (m, 2H), 7.36 (d, J = 8.2 Hz, 4H), 7.31−7.33 (m, 3H), 6.88 (d, J = 8.6 Hz, 4H), 5.15 (s, 1H), 3.81 (s, 6H).

*(3-(4-Chlorophenyl)prop-1-yne-1,3-diyl)dibenzene (**1f**).*[15b] The title compound was derived from (4-chlorophenyl) (phenyl)methanol (21.7 mg, 0.10 mmol, 1.0 equiv), potassium trifluoro(phenylethynyl)-

DOI: 10.1021/acs.joc.5b02273
J. Org. Chem. 2015, 80, 12676−12685

borate (**S1**) (20.6 mg, 0.10 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (25.7 mg, 0.16 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by automated flash column chromatography on silica gel using hexanes and subsequent CH_3CN/hexanes extraction afforded product **1f** (5.7 mg, 19% yield) as a yellow oil. ^1H NMR ($CDCl_3$) δ 7.46−7.48 (m, 2H), 7.35−7.42 (m, 5H), 7.29−7.33 (m, 6H), 7.24−7.27 (m, 1H), 5.18 (s, 1H).

*1-Chloro-4-(1-(4-methoxyphenyl)-3-phenylprop-2-yn-1-yl)-benzene (**1g**).*[39] The title compound was derived from (4-chlorophenyl)(4-methoxyphenyl)methanol (**S12**) (22.4 mg, 0.090 mmol, 1.0 equiv), potassium trifluoro(phenylethynyl)borate (**S1**) (18.7 mg, 0.090 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (23.4 mg, 0.14 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by silica gel column chromatography using hexanes/EtOAc (10:1) afforded product **1g** (25.3 mg, 84% yield) as a yellow oil. ^1H NMR ($CDCl_3$) δ 7.45−7.47 (m, 2H), 7.27−7.36 (m, 9H), 6.86 (d, J = 8.6 Hz, 2H), 5.13 (s, 1H), 3.78 (s, 3H).

*4-(1,3-Diphenylprop-2-yn-1-yl)phenol (**1h**).*[38] The title compound was derived from 4-(hydroxy(phenyl)methyl)phenol (**S10**) (21.1 mg, 0.11 mmol, 1.0 equiv), potassium trifluoro(phenylethynyl)borate (**S1**) (21.9 mg, 0.11 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (27.3 mg, 0.17 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification was conducted by automated flash column chromatography on silica gel using hexanes/EtOAc (5:1) and subsequent CH_3CN/hexanes extraction afforded product **1h** (19.9 mg, 66% yield) as a burgundy/brown oil. ^1H NMR ($CDCl_3$) 7.41−7.48 (m, 4H), 7.28−7.33 (m, 7H), 7.22−7.24 (m, 1H), 6.77−6.79 (m, 2H), 5.14 (s, 1H).

*N-(4-(3-Phenyl-1-(p-tolyl)prop-2-yn-1-yl)phenyl)acetamide (**1i**).* The title compound was derived from *N*-(4-hydroxy(*p*-tolyl)methyl)-phenyl)acetamide (**S14**) (22.6 mg, 0.088 mmol, 1.0 equiv), potassium trifluoro(phenylethynyl)borate (**S1**) (18.4 mg, 0.088 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (22.9 mg, 0.141 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification was conducted by silica gel column chromatography using hexanes/EtOAc (1:2) and subsequent CH_3CN/hexanes extraction afforded product **1i** (18.3 mg, 61% yield) as a yellow oil. IR (Diamond-ATR) ν 3301, 2922, 1662, 1599, 1508, 1407, 1314, 754, 689 cm^{-1}; ^1H NMR ($CDCl_3$) 7.45−7.49 (m, 4H), 7.38−7.40 (m, 3H), 7.30−7.33 (m, 4H), 7.14 (d, J = 7.8 Hz, 2H), 5.15 (s, 1H), 2.34 (s, 3H), 2.15 (s, 3H); ^{13}C {^1H} NMR ($CDCl_3$) δ 168.3, 138.7, 137.9, 136.6, 136.5, 131.6, 129.3, 128.4, 128.2, 127.9, 127.7, 123.5, 120.1, 90.3, 84.7, 42.8, 24.5, 21.0; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{24}H_{22}NO$ 340.1696, found 340.1693.

*4-(1-(4-Methoxyphenyl)-3-phenylprop-2-yn-1-yl)benzoic acid (**1j**).* The title compound was derived from 4-(hydroxy(4-methoxyphenyl)methyl)benzoic acid (**S16**) (13.8 mg, 0.053 mmol, 1.0 equiv), potassium trifluoro(phenylethynyl)borate (**S1**) (11.1 mg, 0.053 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (11.2 mg, 0.069 mmol, 1.3 equiv) in 0.2 mL of CH_3CN following GP4. Purification was conducted by silica gel column chromatography using hexanes/EtOAc/AcOH (2:1:0.01% v/v) and subsequent CH_3CN/hexanes extraction afforded product **1j** (11.3 mg, 62% yield) as a yellow oil. IR (Diamond-ATR) ν 2919, 1691, 1607, 1508, 1297, 1246, 1173, 758, 740, 691, 554 cm^{-1}; ^1H NMR (acetone-d_6) 8.02 (d, J = 8.2 Hz, 2H), 7.63 (d, J = 8.2 Hz, 2H), 7.50−7.53 (m, 2H), 7.44 (d, J = 8.6 Hz, 2H), 7.37−7.38 (m, 3H), 6.92 (d, J = 8.6 Hz, 2H), 5.41 (s, 1H), 3.77 (s, 3H); ^{13}C {^1H} NMR (acetone-d_6) δ 159.9, 148.3, 134.5, 132.5, 131.0, 129.8, 129.4, 129.2, 128.7, 124.3, 115.0, 91.0, 85.8, 55.6, 43.3 (the carbonyl carbon and one aromatic carbon were not resolved in this spectrum); HRMS (ESI-TOF) m/z [M − H]$^-$ calcd for $C_{23}H_{17}O_3$ 341.1183, found 341.1186.

*1-(3-(4-Methoxyphenyl)-3-phenylprop-1-yn-1-yl)-2-(trifluoromethyl)benzene (**2a**).* The title compound was derived from (4-methoxyphenyl) (phenyl)methanol (17.6 mg, 0.082 mmol, 1.0 equiv), potassium trifluoro((2-(trifluoromethyl)phenyl)ethynyl)borate (**S2**) (22.6 mg, 0.082 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (21.2 mg, 0.13 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by silica gel column chromatography using hexanes/EtOAc (15:1) afforded product **2a** (26.8 mg, 89% yield) as a yellow/orange oil. IR (Diamond-ATR) ν 2929, 1601, 1508, 1314, 1249, 1167, 1127, 1031, 764, 697 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.64 (d, J = 7.4 Hz, 1H), 7.58 (d, J = 7.4 Hz, 1H), 7.42−7.47 (m, 3H), 7.30−7.38 (m, 5H), 7.21−7.24 (m, 1H), 6.85 (d, J = 8.6 Hz, 2H), 5.20 (s, 1H), 3.77 (s, 3H); ^{13}C {^1H} NMR ($CDCl_3$) δ 158.5, 141.6, 134.1, 133.5, 131.6, 131.3, 128.9, 128.6, 127.8, 127.6, 126.9, 125.7 (q, J = 5.4 Hz), 123.6 (q, J = 273.7 Hz), 121.8, 114.0, 96.4, 80.7, 55.2, 43.2; ^{19}F NMR ($CDCl_3$) δ −62.17 (s, 3F); HRMS (EI) m/z [M$^+$] calcd for $C_{23}H_{17}F_3O$ 366.1232, found 366.1231.

*1-(3-(4-Methoxyphenyl)-3-phenylprop-1-yn-1-yl)-3,5-bis-(trifluoromethyl)benzene (**2b**).* The title compound was derived from (4-methoxyphenyl) (phenyl)methanol (14.8 mg, 0.069 mmol, 1.0 equiv), potassium trifluoro((3,5-bis(trifluoromethyl)phenyl)ethynyl)-borate (**S3**) (23.8 mg, 0.069 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (17.9 mg, 0.11 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by silica gel column chromatography using hexanes/EtOAc (14:1) afforded product **2b** (25.6 mg, 85% yield) as a yellow/orange oil. IR (Diamond-ATR) ν 2928, 1600, 1509, 1381, 1275, 1171, 1129, 697, 681 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.88 (s, 2H), 7.78 (s, 1H), 7.25−7.41 (m, 7H), 6.88 (d, J = 9.0, 2H), 5.20 (s, 1H), 3.79 (s, 3H); ^{13}C {^1H} NMR ($CDCl_3$) δ 158.8, 141.1, 132.9, 131.8 (q, J = 33.7 Hz), 131.6 (q, J = 4.6 Hz), 128.9, 128.8, 127.8, 127.2, 125.8, 123.0 (q, J = 273.0 Hz), 121.3 (q, J = 3.8 Hz), 114.2, 94.5, 81.8, 55.3, 42.9; ^{19}F NMR ($CDCl_3$) δ −63.13 (s, 6F); HRMS (EI) m/z [M$^+$] calcd for $C_{24}H_{16}F_6O$ 434.1105, found 434.1100.

*1-Chloro-3-(3-(4-methoxyphenyl)-3-phenylprop-1-yn-1-yl)-benzene (**2c**).* The title compound was derived from (4-methoxyphenyl) (phenyl)methanol (19.3 mg, 0.090 mmol, 1.0 equiv), potassium trifluoro((3-chlorophenyl)ethynyl)borate (**S4**) (21.9 mg, 0.090 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (23.4 mg, 0.14 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by silica gel column chromatography using hexanes/EtOAc (14:1) afforded product **2c** (29.7 mg, 99% yield) as a yellow/orange oil. IR (Diamond-ATR) ν 2930, 1592, 1507, 1247, 1173, 1030, 780, 696, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.45−7.46 (m, 1H), 7.39−7.41 (m, 2H), 7.30−7.35 (m, 5H), 7.19−7.28 (m, 3H), 6.86 (d, J = 9.0 Hz, 2H), 5.16 (s, 1H), 3.77 (s, 3H); ^{13}C {^1H} NMR ($CDCl_3$) δ 158.6, 141.7, 134.0, 133.5, 131.6, 129.8, 129.4, 128.9, 128.6, 128.2, 127.8, 126.9, 125.2, 114.0, 91.9, 83.3, 55.3, 42.9; HRMS (EI) m/z [M$^+$] calcd for $C_{22}H_{17}ClO$ 332.0968, found 332.0962.

*1,2-Dichloro-4-(3-(4-chlorophenyl)-3-(4-methoxyphenyl)prop-1-yn-1-yl)benzene (**2d**).* The title compound was derived from (4-chlorophenyl)(4-methoxyphenyl)methanol (**S12**) (18.6 mg, 0.075 mmol, 1.0 equiv), potassium trifluoro((3,4-dichlorophenyl)ethynyl)-borate (**S6**) (20.7 mg, 0.075 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (19.3 mg, 0.12 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by silica gel column chromatography using hexanes/EtOAc (20:1) afforded product **2d** (25.0 mg, 83% yield) as a yellow oil. IR (Diamond-ATR) ν 2926, 1508, 1487, 1461, 1173, 1089, 1031, 817 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.54 (d, J = 2.0 Hz, 1H), 7.35−7.37 (m, 1H), 7.25−7.33 (m, 7H), 6.87 (d, J = 9.0 Hz, 2H), 5.12 (s, 1H), 3.79 (s, 3H); ^{13}C {^1H} NMR ($CDCl_3$) δ 158.8, 140.0, 133.3, 132.9, 132.8, 132.48, 132.45, 130.8, 130.3, 129.1, 128.80, 128.79, 123.2, 114.2, 92.1, 82.8, 55.3, 42.3; HRMS (EI) m/z [M$^+$] calcd for $C_{22}H_{15}Cl_3O$ 400.0188, found 400.0186.

*4-(3-(3-Fluorophenyl)-1-(4-methoxyphenyl)prop-2-yn-1-yl)-benzaldehyde (**2e**).* The title compound was derived from 4-(hydroxy(4-methoxyphenyl)methyl)benzaldehyde (**S17**) (21.1 mg, 0.087 mmol, 1.0 equiv), potassium trifluoro((3-fluorophenyl)ethynyl)-borate (**S5**) (19.7 mg, 0.087 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (22.6 mg, 0.14 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by silica gel column chromatography using hexanes/EtOAc (6:1) afforded product **2g** (24.6 mg, 82% yield) as a yellow oil. IR (Diamond-ATR) ν 2926, 1697, 1603, 1578, 1508, 1246, 1148, 1032, 783, 681 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.99 (s, 1H), 7.84 (d, J = 8.2 Hz, 2H), 7.58 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.6 Hz, 2H), 7.25−7.28 (m, 2H), 7.15−7.18 (m, 1H), 7.00−7.05 (m, 1H), 6.88 (d, J = 9.0 Hz, 2H), 5.23 (s, 1H), 3.79 (s, 3H); ^{13}C {^1H} NMR ($CDCl_3$) δ 191.7, 162.3 (d, J = 246.14 Hz), 158.9, 148.5, 135.2, 132.4, 130.1, 129.8 (d, J = 6.2 Hz), 128.9, 128.4, 127.5 (d, J = 3.1 Hz), 124.9, 118.5 (d, J = 23.0 Hz), 115.6 (d, J = 21.5 Hz), 114.3, 90.3, 84.3, 55.3, 43.0; ^{19}F NMR

DOI: 10.1021/acs.joc.5b02273
J. Org. Chem. 2015, 80, 12676−12685

($CDCl_3$) δ −112.97 (s, 1F); HRMS (EI) m/z [M^+] calcd for $C_{23}H_{17}FO_2$ 344.1213, found 344.1217.

*4-(3-(3-Chlorophenyl)-1-(4-methoxyphenyl)prop-2-yn-1-yl)-N,N-dimethylaniline (**2f**).* The title compound was derived from (4-(dimethylamino)phenyl)(4-methoxyphenyl)methanol (**S13**) (20.5 mg, 0.080 mmol, 1.0 equiv), potassium trifluoro((3-chlorophenyl)-ethynyl)borate (**S4**) (19.4 mg, 0.080 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (33.6 mg, 0.21 mmol, 2.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by automated flash column chromatography on silica gel using hexanes/EtOAc (3:1) afforded product **2h** (18.4 mg, 61% yield) as a brown oil. IR (Diamond-ATR) ν 2926, 1607, 1507, 1246, 1172, 1033, 782, 680, 555 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.44−7.45 (m, 1H), 7.31−7.33 (m, 3H), 7.18−7.26 (m, 4H), 6.85 (d, J = 8.6 Hz, 2h), 6.69 (d, J = 9.0 Hz, 2H), 5.08 (s, 1H), 3.78 (s, 3H), 2.91 (s, 6H); ^{13}C {^1H} NMR ($CDCl_3$) δ 158.4, 149.6, 134.3, 134.0, 131.5, 129.8, 129.6, 129.4, 128.8, 128.4, 128.0, 125.5, 113.9, 112.7, 92.7, 82.8, 55.3, 41.9, 40.6; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{24}H_{23}ClNO$ 376.1463, found 376.1458.

*4-(3-([1,1′-Biphenyl]-4-yl)-1-phenylprop-2-yn-1-yl)phenol (**2g**).* The title compound was derived from 4-(hydroxy(phenyl)methyl)-phenol (**S10**) (16.7 mg, 0.083 mmol, 1.0 equiv), potassium trifluoro([1,1′-biphenyl]-4-ylethynyl)borate (**S7**) (23.6 mg, 0.083 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (21.6 mg, 0.13 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by automated flash column chromatography on silica gel using hexanes/EtOAc (5:1) afforded product **2i** (21.3 mg, 71% yield) as an orange/pink oil. IR (Diamond-ATR) ν 3331, 2922, 1597, 1508, 1485, 1447, 1170, 840, 761, 692, 560 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.57−7.59 (m, 2H), 7.53 (s, 4H), 7.41−7.45 (m, 4H), 7.29−7.36 (m, 5H), 7.21−7.25 (m, 1H), 6.78 (d, J = 8.6 Hz, 2H), 5.17 (s, 1H), 4.84 (s, 1H); ^{13}C {^1H} NMR ($CDCl_3$) δ 154.4, 142.0, 140.7, 140.4, 134.1, 132.1, 129.1, 128.8, 128.6, 127.8, 127.5, 127.0, 126.9, 126.8, 122.4, 115.4, 91.1, 84.6, 43.0; HRMS (EI) m/z [M^+] calcd for $C_{27}H_{20}O$ 360.1514, found 360.1509.

*1-(3-(4-Methoxyphenyl)-3-phenylprop-1-yn-1-yl)naphthalene (**2h**).* The title compound was derived from (4-methoxyphenyl) (phenyl)methanol (18.5 mg, 0.086 mmol, 1.0 equiv), potassium trifluoro(naphthalen-1-ylethynyl)borate (**S8**) (22.2 mg, 0.086 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (22.3 mg, 0.14 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by automated flash column chromatography on silica gel using hexanes/EtOAc (20:1) afforded product **2j** (21.0 mg, 70% yield) as a yellow oil. IR (Diamond-ATR) ν 2926, 1603, 1507, 1246, 1174, 1030, 797, 772, 696, 564 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.33 (d, J = 7.42, Hz, 1H), 7.78−7.84 (m, 2H), 7.70 (d, J = 7.4 Hz, 1H), 7.47−7.54 (m, 4H), 7.33−7.44 (m, 5H), 7.23−7.27 (m, 1H), 6.88 (d, J = 8.6 Hz, 2H), 5.33 (s, 1H), 3.78 (s, 3H); ^{13}C {^1H} NMR ($CDCl_3$) δ 158.6, 142.1, 134.0, 133.5, 133.2, 130.4, 129.0, 128.7, 128.4, 128.2, 127.9, 126.9, 126.7, 126.3, 125.2, 121.2, 114.1, 95.5, 82.9, 55.3, 43.3 (one aromatic carbon was not resolved in this spectrum); HRMS (EI) m/z [M^+] calcd for $C_{26}H_{20}O$ 348.1514, found 348.1508.

*4-(1-(4-Methoxyphenyl)-3-(naphthalen-1-yl)prop-2-yn-1-yl)-benzoic Acid (**2i**).* The title compound was derived from 4-(hydroxy(4-methoxyphenyl)methyl)benzoic acid (**S16**) (19.7 mg, 0.076 mmol, 1.0 equiv), potassium trifluoro(naphthalen-1-ylethynyl)-borate (**S8**) (19.7 mg, 0.076 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (19.8 mg, 0.12 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by silica gel column chromatography using hexanes/EtOAc/AcOH (1.5:1:0.01% v/v) afforded product **2k** (19.8 mg, 66% yield) as a yellow oil. IR (Diamond-ATR) ν 2922, 1689, 1606, 1507, 1245, 1174, 1032, 771 cm^{-1}; ^1H NMR (acetone-d_6) δ 8.33−8.36 (m, 1H), 8.06 (d, J = 8.2 Hz, 2H), 7.93−7.97 (m, 2H), 7.72−7.78 (m, 3H), 7.49−7.62 (m, 5H), 6.96 (d, J = 8.6 Hz, 2H), 5.61 (s, 1H), 3.79 (s, 3H); ^{13}C {^1H} NMR (acetone-d_6) δ 159.9, 148.3, 134.5, 134.4, 134.3, 131.4, 131.1, 129.9, 129.6, 129.4, 128.8, 127.9, 127.5, 126.8, 126.4, 121.8, 115.1, 96.2, 83.8, 55.6, 43.7 (the carbonyl carbon and one aromatic carbon were not resolved in this spectrum); HRMS (EI) m/z [M^+] for $C_{27}H_{20}O_3$ 392.1412, found 392.1417.

*4-(1-(4-Methoxyphenyl)-3-phenylprop-2-yn-1-yl)aniline (**2j**).* The title compound was derived from *tert*-butyl (4-(hydroxy(*p*-tolyl)-methyl)phenyl)carbamate (**S15**) (20.5 mg, 0.062 mmol, 1.0 equiv), potassium trifluoro((3,4-dichlorophenyl)ethynyl)borate (**S6**) (17.3 mg, 0.062 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (26.2 mg, 0.16 mmol, 2.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification was conducted by silica gel column chromatography using hexanes/EtOAc (1.3:1) followed by a pentane wash and subsequent CH_3CN/hexanes extraction to afford product **2l** (15.3 mg, 51% yield) as a burgundy oil. IR (Diamond-ATR) ν 3372, 2928, 1607, 1506, 1461, 1244, 1173, 1127, 1030, 817, 729, 569 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53 (m, 1H), 7.34−7.36 (m, 1H), 7.24−7.30 (m, 3H), 7.15 (d, J = 8.2 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 6.64 (d, J = 8.2 Hz, 2H), 5.05 (s, 1H), 3.78 (s, 3H); ^{13}C {^1H} NMR ($CDCl_3$) δ 158.5, 145.3, 133.9, 133.3, 132.3, 132.1, 131.5, 130.8, 130.2, 128.7, 128.6, 123.7, 115.3, 114.0, 93.3, 82.0, 55.3, 42.0; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{22}H_{18}Cl_2NO$ 382.0760, found 382.0758.

*1-Methoxy-4-(1-phenylhept-2-yn-1-yl)benzene (**2k**).*[40] The title compound was derived from (4-methoxyphenyl) (phenyl)methanol (23.1 mg, 0.11 mmol, 1.0 equiv), potassium trifluoro(hex-1-yn-1-yl)borate (**S9**) (20.3 mg, 0.11 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (27.9 mg, 0.17 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by silica gel column chromatography using hexanes/EtOAc (15:1) afforded product **2m** (21.9 mg, 73% yield) as a yellow oil. ^1H NMR ($CDCl_3$) δ 7.34−7.36 (m, 2H), 7.26−7.30 (m, 4H), 7.17−7.21 (m, 1H), 6.82 (d, J = 9.0 Hz, 2H), 4.92 (s, 1H), 3.76 (s, 3H), 2.28 (td, J = 2.4, 7.0 Hz, 2H), 1.51−1.56 (m, 2H), 1.41−1.46 (m, 2H), 0.92 (t, J = 7.0 Hz, 3H).

*(E)-(3-(4-Methoxyphenyl)prop-1-ene-1,3-diyl)dibenzene (**3a**).*[41] The title compound was derived from (4-methoxyphenyl) (phenyl)-methanol (21.4 mg, 0.100 mmol, 1.0 equiv), potassium trifluoro(*E*)-2-phenylethenylborate (21.0 mg, 0.100 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (25.9 mg, 0.16 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by silica gel column chromatography using hexanes/EtOAc (15:1) afforded product **3a** (29.0 mg, 97% yield) as a pale yellow oil. ^1H NMR ($CDCl_3$) δ 7.35−7.37 (m, 2H), 7.19−7.32 (m, 8H), 7.14 (d, J = 8.6 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 6.65 (dd, J = 7.4, 15.6 Hz, 1H), 6.32 (d, J = 15.6 Hz, 1H), 4.84 (d, J = 7.4 Hz, 1H), 3.77 (s, 3H).

*(E)-4,4′-(3-(3-Fluorophenyl)prop-2-ene-1,1-diyl)bis-(methoxybenzene) (**3b**).* The title compound was derived from bis(4-methoxyphenyl)methanol (**S11**) (21.0 mg, 0.086 mmol, 1.0 equiv), potassium trifluoro(2-(3-fluorophenyl)vinyl) borate (19.6 mg, 0.086 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (22.3 mg, 0.14 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by silica gel column chromatography using hexanes/EtOAc (9:1) afforded product **3b** (29.1 mg, 97% yield) as a pink oil. IR (Diamond-ATR) ν 2929, 1608, 1581, 1506, 1242, 1173, 1033, 964, 825, 553 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.20−7.25 (m, 1H), 7.05−7.13 (m, 6H), 6.84−6.91 (m, 5H), 6.61−6.66 (m, 1H), 6.26 (d, J = 15.6 Hz, 1H), 4.79 (d, J = 7.4 Hz, 1H), 3.78 (s, 6H); ^{13}C {^1H} NMR ($CDCl_3$) δ 163.1 (d, J = 245.4 Hz), 158.2, 139.7 (d, J = 7.7 Hz), 135.6, 134.7, 129.9 (d, J = 3.1 Hz), 129.8 (d, J = 2.3 Hz), 129.5, 122.1 (d, J = 2.3 Hz), 113.94 (d, J = 21.5 Hz), 113.87, 112.7 (d, J = 22.2 Hz), 55.2, 52.4; ^{19}F NMR ($CDCl_3$) δ −113.71 (s, 1F); HRMS (EI) m/z [M^+] calcd for $C_{23}H_{21}FO_2$ 348.1526, found 348.1523.

*(E)-N-(4-(3-Phenyl-1-(p-tolyl)allyl)phenyl)acetamide (**3c**).* The title compound was derived from *N*-(4-hydroxy(*p*-tolyl)methyl)-phenyl)acetamide (**S14**) (22.4 mg, 0.088 mmol, 1.0 equiv), potassium trifluoro(*E*)-2-phenylethenylborate (18.5 mg, 0.088 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (22.8 mg, 0.14 mmol, 1.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification was conducted by silica gel column chromatography using hexanes/EtOAc (1:2) and subsequent CH_3CN/hexanes extraction afforded product **3c** (23.2 mg, 77% yield) as a pale white/yellow oil. IR (Diamond-ATR) ν 3294, 2922, 1662, 1599, 1509, 1407, 1369, 1315, 1262, 966, 816, 741, 691, 522 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.41−7.43 (m, 2H), 7.34−7.37 (m, 2H), 7.15−7.29 (m, 5H), 7.10 (s, 4H), 6.61 (dd, J = 7.4, 16.0 Hz, 1H), 6.31 (d, J = 15.6 Hz, 1H), 4.81 (d, J = 7.4 Hz, 1H), 2.32 (s, 3H), 2.13 (s, 3H); ^{13}C {^1H} NMR ($CDCl_3$) δ 168.3, 140.4, 139.7, 137.2, 136.2, 136.0, 132.6, 131.2, 129.2, 129.1, 128.5, 128.4, 127.2, 126.3, 120.0, 53.2, 24.5, 21.0; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{24}H_{24}NO$ 342.1852, found 342.1849.

DOI: 10.1021/acs.joc.5b02273
J. Org. Chem. 2015, 80, 12676−12685

*(E)-4-(3-(3-Fluorophenyl)-1-(4-methoxyphenyl)allyl)-N,N-dimethylaniline (**3d**).* The title compound was derived from (4-(dimethylamino)phenyl)(4-methoxyphenyl)methanol (**S13**) (21.4 mg, 0.083 mmol, 1.0 equiv), potassium trifluoro(2-(3-fluorophenyl)-vinyl) borate (18.9 mg, 0.083 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (34.9 mg, 0.2 mmol, 2.6 equiv) in 0.3 mL of CH_3CN following GP4. Purification by silica gel column chromatography using hexanes/EtOAc (6:1) afforded product **3d** (25.1 mg, 84% yield) as a pale white/yellow oil. IR (Diamond-ATR) ν 2926, 1609, 1507, 1244, 1174, 1140, 1034, 813, 774, 552 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.19−7.25 (m, 1H), 7.04−7.15 (m, 6H), 6.83−6.90 (m, 3H), 6.62−6.71 (m, 3H), 6.27 (d, J = 16.0 Hz, 1H), 4.75 (d, J = 7.4 Hz, 1H), 3.78 (s, 3H), 2.91 (s, 6H); ^{13}C {^1H} NMR ($CDCl_3$) δ 163.1 (d, J = 244.6 Hz), 158.1, 149.3, 140.0 (d, J = 7.7 Hz), 136.0, 135.1, 131.4, 129.9, 129.8, 129.5, 129.1, 122.1 (d, J = 3.1 Hz), 113.79, 113.78 (d, J = 21.5 Hz), 112.74 112.65 (d, J = 22.2 Hz), 55.2, 52.3, 40.7; ^{19}F NMR ($CDCl_3$) δ −113.82 (s, 1F); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{24}H_{25}FNO$ 362.1915, found 362.1912.

*(E)-4-(3-(3-Fluorophenyl)-1-(4-methoxyphenyl)allyl)benzoic Acid (**3e**).* The title compound was derived from 4-(hydroxy(4-methoxyphenyl)methyl)benzoic acid (**S16**) (21.4 mg, 0.083 mmol, 1.0 equiv), potassium trifluoro(2-(3-fluorophenyl)vinyl) borate (18.9 mg, 0.083 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (17.4 mg, 0.12 mmol, 1.3 equiv) in 0.3 mL of CH_3CN following GP4. Purification was conducted by silica gel column chromatography using hexanes/EtOAc/AcOH (2:1:0.01% v/v) and subsequent CH_3CN/hexanes extraction afforded product **3e** (23.0 mg, 77% yield) as a pale yellow oil. IR (Diamond-ATR) ν 2922, 1685, 1607, 1508, 1245, 1176, 1033, 963, 778, 683, 548 cm^{-1}; ^1H NMR (acetone-d_6) δ 8.01 (d, J = 8.2 Hz, 2H), 7.44 (d, J = 8.2 Hz, 2H), 7.22−7.37 (m, 5H), 6.89−7.01 (m, 4H), 6.49 (d, J = 16.0 Hz, 1H), 5.01 (d, J = 8.2 Hz, 1H), 3.77 (s, 3H); ^{13}C {^1H} NMR (acetone-d_6) δ 164.1 (d, J = 243.1 Hz), 159.5, 150.4, 141.0 (d, J = 7.7 Hz), 136.0, 134.9, 131.3, 131.2, 131.1 (d, J = 3.1 Hz), 130.8, 130.4, 129.4, 123.52, 123.50, 114.8 (d, J = 20.7 Hz), 113.4 (d, J = 22.2 Hz), 55.6, 54.2; ^{19}F NMR (acetone-d_6) δ −115.09 (s, 1F); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{23}H_{20}FO_3$ 363.1391, found 363.1388.

*1-Methoxy-2-(3-phenyl-1-(p-tolyl)prop-2-yn-1-yl)benzene (**6**).* The title compound was derived from (2-methoxyphenyl)(*p*-tolyl)-methanol (**S**) (65.8 mg, 0.288 mmol, 1.0 equiv), potassium trifluoro(phenylethynyl)borate (**S1**) (60.0 mg, 0.288 mmol, 1.0 equiv), and $HBF_4{\cdot}OEt_2$ (74.6 mg, 0.461 mmol, 1.6 equiv) in 1.0 mL of CH_3CN following GP4. Purification by automated flash column chromatography on silica gel using hexanes/diethyl ether (99:1) afforded product **6** (60.1 mg, 67% yield) as a yellow oil. IR (Diamond-ATR) ν 1597, 1488, 1460, 1243, 1103, 1026, 803, 749, 690, 560, 524 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.60−7.62 (m, 1H), 7.44−7.47 (m, 2H), 7.35 (d, J = 8.2 Hz, 2H), 7.25−7.29 (m, 3H), 7.19−7.23 (m, 1H), 7.09 (d, J = 7.8 Hz, 2H), 6.95 (t of d, J = 1.1, 7.4 Hz, 1H), 6.84−6.86 (m, 1H), 5.65 (s, 1H), 3.82 (s, 3H), 2.29 (s, 3H); ^{13}C {^1H} NMR ($CDCl_3$) δ 156.1, 138.8, 136.0, 131.7, 130.5, 129.0, 128.9, 128.13, 128.05, 127.71, 127.68, 123.8, 120.9, 110.7, 91.2, 83.3, 55.5, 36.2, 21.0; HRMS (DART-TOF+) m/z [M + H] calcd for $C_{23}H_{21}O$ 313.1592, found 313.1600.

Demethylation Procedure (General Procedure 5, GP5). A solution of the indicated *ortho*-methoxy-substituted product (1.0 equiv) in dry DCM (0.1 M) was treated with boron tribromide solution (3.0 equiv) at 0 °C. After addition was complete, the mixture was allowed to stir at room temperature for 30 min. The reaction was quenched with water and extracted with 20 mL of EtOAc. The organic layer was washed with water (3 × 15 mL) followed by brine (1 × 10 mL). The organic layer was dried with $MgSO_4$ and concentrated. The product was purified by flash chromatography with hexanes/ethyl acetate and concentrated. Extraction from hexanes with acetonitrile afforded the desired demethylated product.

*2-(3-Phenyl-1-(p-tolyl)prop-2-yn-1-yl)phenol (**S18**).* The title compound was derived from 1-methoxy-2-(3-phenyl-1-(*p*-tolyl)prop-2-yn-1-yl)benzene (**6**) (60.1 mg, 0.192 mmol, 1.0 equiv) and boron tribromide solution [1.0 M in methylene chloride] (0.145 g, 0.577 mmol, 3.0 equiv) in 2.0 mL of anhydrous DCM following GP5. Purification by automated flash column chromatography on silica gel using hexanes/EtOAc (gradient: 24:1 → 9:1) and subsequent CH_3CN/hexanes extraction afforded product **S18** (42.0 mg, 73% yield) as a yellow oil. IR (Diamond-ATR) ν 3527, 1595, 1488, 1454, 1185, 1087, 822, 749, 689 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.48−7.52 (m, 2H), 7.41−7.44 (m, 1H), 7.39 (d, J = 8.2 Hz, 2H), 7.31−7.35 (m, 3H), 7.19−7.22 (m, 1H), 7.17 (m, 2H), 6.96 (t of d, J = 1.2, 7.4 Hz, 1H), 6.85 (d of d, J = 1.2, 8.2 Hz, 1H), 5.50 (s, 1H), 5.44 (s, 1H), 2.35 (s, 3H); ^{13}C {^1H} NMR ($CDCl_3$) δ 153.3, 137.2, 136.7, 131.7, 129.5, 129.4, 128.5, 128.23, 128.19, 127.6, 127.5, 123.0, 121.0, 116.6, 89.1, 85.3, 38.2, 21.0; HRMS (DART-TOF+) m/z [M + H] calcd for $C_{22}H_{19}O$ 299.1436, found 299.1437.

Cyclization Procedure (General Procedure 6, GP6). The indicated *ortho*-hydroxy-substituted product (1.0 equiv) was dissolved in anhydrous dioxane. Then, potassium *tert*-butoxide (2.0 equiv) was added, and the reaction mixture was stirred at ambient temperature for 105 min. The reaction solution was then diluted with DCM (10 mL) and washed with brine (10 mL). The aqueous phase was extracted with DCM (2 × 10 mL). The combined organic phase was washed with deionized water (3 × 15 mL) and brine (1 × 10 mL). The organic layer was dried with $MgSO_4$ and concentrated. The product was purified by flash chromatography with hexanes/diethyl ether and concentrated. Extraction from hexanes with acetonitrile afforded the desired demethylated product.

*2-Benzyl-3-(p-tolyl)benzofuran (**7**).* The title compound was derived from 2-(3-phenyl-1-(*p*-tolyl)prop-2-yn-1-yl)phenol (**S18**) (42.0 mg, 0.141 mmol, 1.0 equiv) and *t*-BuOK (31.6 mg, 0.282 mmol, 2.0 equiv) in 1.13 mL of anhydrous dioxane following GP6. Purification by automated flash column chromatography on silica gel using hexanes/diethyl ether (gradient: 99:1 → 49:1) and subsequent CH_3CN/hexanes extraction afforded product **7** (19.7 mg, 47% yield) as a yellow solid. Mp 65−68 °C; IR (Diamond-ATR) ν 1512, 1492, 1453, 1159, 977, 820, 740, 719, 694, 492, 454 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.57−7.59 (m, 1H), 7.40−7.45 (m, 3H), 7.20−7.31 (m, 9H), 4.20 (s, 2H), 2.42 (s, 3H); ^{13}C {^1H} NMR ($CDCl_3$) δ 154.3, 152.3, 138.0, 137.0, 129.5, 129.4, 128.9, 128.8, 128.6, 128.5, 126.5, 123.9, 122.6, 119.8, 118.1, 111.1, 32.9, 21.3; HRMS (DART-TOF+) m/z [M + H] calcd for $C_{22}H_{19}O$ 299.1436, found 299.1440.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02273.

Copies of NMR spectra for **S1**−**18**, **1a**−**j**, **2a**−**k**, **3a**−**e**, and **5**−**7** (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: yuri.bolshan@uoit.ca.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the UOIT start-up fund and Natural Sciences and Engineering Research Council of Canada (NSERC) Discovery grant. K.F. thanks Cassandra Taylor (UOIT) and Matthew Baxter (UOIT) for assistance in the laboratory.

■ REFERENCES

(1) (a) Lopez, S.; Fernandez-Trillo, F.; Castedo, L.; Saa, C. *Org. Lett.* **2003**, *5*, 3725−3728. (b) Stutz, A.; Petranyi, G. *J. Med. Chem.* **1984**, *27*, 1539−1543. (c) Yates, S. G.; England, R. E. *J. Agric. Food Chem.* **1982**, *30*, 317−320. (d) Sugiura, Y.; Arakawa, T.; Uesugi, M.; Shiraki, T.; Ohkuma, H.; Konishi, M. *Biochemistry* **1991**, *30*, 2989−2992. (e) Pierce, M. E.; et al. *J. Org. Chem.* **1998**, *63*, 8536−8543.

DOI: 10.1021/acs.joc.5b02273
J. Org. Chem. 2015, 80, 12676−12685

(f) Saravanan, S.; Azath, I. A.; Muthusubramanian, S. *J. Org. Chem.* **2008**, *73*, 2323−2329.
(2) Negishi, E.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979−2017.
(3) (a) Orita, A.; Otera, J. *Chem. Rev.* **2006**, *106*, 5387−5412. (b) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, *13*, 3769−3772.
(4) Bandini, M.; Tragni, M. *Org. Biomol. Chem.* **2009**, *7*, 1501−1507.
(5) Li, C.; Li, W.; Wang, J. *Tetrahedron Lett.* **2009**, *50*, 2533−2535.
(6) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467. (b) Altenhoff, G.; Würtz, S.; Glorius, F. *Tetrahedron Lett.* **2006**, *47*, 2925−2928. (c) Chinchilla, R.; Najera, C. *Chem. Rev.* **2007**, *107*, 874−922.
(7) Zhou, L.; Ye, F.; Zhang, Y.; Wang, J. *J. Am. Chem. Soc.* **2010**, *132*, 13590−13591.
(8) Correia, C.; Li, C.-J. *Adv. Synth. Catal.* **2010**, *352*, 1446−1450.
(9) Xiang, S.-K.; Zhang, B.; Zhang, L.-H.; Cui, Y.; Jiao, N. *Sci. China: Chem.* **2012**, *55*, 50−54.
(10) Sawama, Y.; Goto, R.; Nagata, S.; Shishido, Y.; Monguchi, Y.; Sajiki, H. *Chem. - Eur. J.* **2014**, *20*, 2631−2636.
(11) Liu, C.; Yang, F.; Wang, T. *Chin. J. Chem.* **2014**, *32*, 387−390.
(12) Kumar, R.; Van der Eycken, E. V. *Chem. Soc. Rev.* **2013**, *42*, 1121−1146.
(13) For selected references, see: (a) Narahashi, H.; Shimizu, I.; Yamamoto, A. *J. Organomet. Chem.* **2008**, *693*, 283−296. (b) Nishimoto, Y.; Kajioka, M.; Saito, T.; Yasuda, M.; Baba, A. *Chem. Commun.* **2008**, 6396−6398. (c) Liu, Z.-Q.; Zhang, Y.; Zhao, L.; Wang, J.; Li, H.; Wu, L.-M. *Org. Lett.* **2011**, *13*, 2208−2211.
(14) Leboeuf, D.; Presset, M.; Michelet, B.; Bour, C.; Bezzenine-Lafollée, S.; Gandon, V. *Chem. - Eur. J.* **2015**, *21*, 11001−11005.
(15) (a) Kabalka, G. W.; Yao, M.-L.; Borella, S.; Wu, Z.-Z. *Org. Lett.* **2005**, *7*, 2865−2867. (b) Kabalka, G. W.; Yao, M.-L.; Borella, S. *Org. Lett.* **2006**, *8*, 879−881.
(16) Yao, M.-L.; Pippin, A. B.; Wu, Z.-Z.; Quinn, M. P.; Yong, L.; Reddy, M. S.; Kabalka, G. W. *J. Organomet. Chem.* **2012**, *721*−*722*, 164−166.
(17) For selected references, see: (a) Yue, H.-L.; Wei, W.; Li, M.-M.; Yang, Y.-R.; Ji, J.-X. *Adv. Synth. Catal.* **2011**, *353*, 3139−3145. (b) Aoyama, T.; Koda, S.; Takeyoshi, Y.; Ito, T.; Takido, T.; Kodomari, M. *Chem. Commun.* **2013**, *49*, 6605−6607. (c) Wagh, K. V.; Bhanage, B. M. *RSC Adv.* **2014**, *4*, 22763−22767. (d) Han, F.; Li, Z.; Zhao, Y.; Xia, C. *Adv. Synth. Catal.* **2014**, *356*, 2506−2516.
(18) Luan, Y.; Schaus, S. E. *J. Am. Chem. Soc.* **2012**, *134*, 19965−19968.
(19) Li, W.-T.; Nan, W.-N.; Luo, Q.-L. *RSC Adv.* **2014**, *4*, 34774−34779.
(20) (a) Darses, S.; Genêt, J.-P. *Chem. Rev.* **2008**, *108*, 288−355. (b) Stefani, H. A.; Cella, R.; Vieira, A. S. *Tetrahedron* **2007**, *63*, 3623−3658. (c) Molander, G. A.; Figueroa, R. *Aldrichimica Acta* **2005**, *38*, 49−56. (d) Darses, S.; Genêt, J. P. *Eur. J. Org. Chem.* **2003**, *2003*, 4313−4327.
(21) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007**, *40*, 275−286.
(22) For reviews on Petasis reaction and metal-free reactions of organoboranes, see: (a) Candeias, N. R.; Montalbano, F.; Cal, P. M. S. D.; Gois, P. M. P. *Chem. Rev.* **2010**, *110*, 6169−6193. (b) Roscales, S.; Csákÿ, A. *Chem. Soc. Rev.* **2014**, *43*, 8215−8225.
(23) For selected references, see: (a) Matteson, D.; Kim, G. *Org. Lett.* **2002**, *4*, 2153−2155. (b) Mitchell, T.; Bode, J. *J. Am. Chem. Soc.* **2009**, *131*, 18057−18059. (c) Dumas, A.; Bode, J. *Org. Lett.* **2012**, *14*, 2138−2141. (d) Vo, C.-V.; Mitchell, T.; Bode, J. *J. Am. Chem. Soc.* **2011**, *133*, 14082−14089. (e) Dumas, A.; Molander, G.; Bode, J. *Angew. Chem., Int. Ed.* **2012**, *51*, 5683−5686. (f) Zeng, J.; Vedachalam, S.; Xiang, S.; Liu, X.-W. *Org. Lett.* **2011**, *13*, 42−45. (g) Taylor, C.; Bolshan, Y. *Org. Lett.* **2014**, *16*, 488−491. (h) Taylor, C.; Bolshan, Y. *Tetrahedron Lett.* **2015**, *56*, 4392−4396. (i) Vieira, A. S.; Fiorante, P. F.; Hough, T. L. S.; Ferreira, F. P.; Lüdtke, D. S.; Stefani, H. A. *Org. Lett.* **2008**, *10*, 5215−5218.
(24) Baxter, M.; Bolshan, Y. *Chem. - Eur. J.* **2015**, *21*, 13535−13538.
(25) (a) Larouche-Gauthier, R.; Elford, T. G.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2011**, *133*, 16794−16797. (b) Berionni, G.; Maji, B.; Knochel, P.; Mayr, H. *Chem. Sci.* **2012**, *3*, 878−882. (c) Petruzziello, D.; Gualandi, A.; Giaffar, H.; Lopez-Carrillo, V.; Cozzi, P. G. *Eur. J. Org. Chem.* **2013**, *2013*, 4909−4917. (d) Berionni, G.; Leonov, A. I.; Mayer, P.; Ofial, A. R.; Mayr, H. *Angew. Chem., Int. Ed.* **2015**, *54*, 2780−2783.
(26) (a) Lee, S.; MacMillan, D. *J. Am. Chem. Soc.* **2007**, *129*, 15438−15439. (b) Hamilton, J.; Sarlah, D.; Carreira, E. *J. Am. Chem. Soc.* **2013**, *135*, 994−997. (c) Hamilton, J.; Sarlah, D.; Carreira, E. *Angew. Chem., Int. Ed.* **2013**, *52*, 7532−7535.
(27) (a) Darses, S.; Michaud, G.; Genêt, J.-P. *Eur. J. Org. Chem.* **1999**, *1999*, 1875−1883. (b) Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020−3027. (c) Vedejs, E.; Fields, S. C.; Hayashi, R.; Hitchcock, S. R.; Powell, D. R.; Schrimpf, M. R. *J. Am. Chem. Soc.* **1999**, *121*, 2460−2470. (d) Molander, G. A.; Biolatto, B. *Org. Lett.* **2002**, *4*, 1867−1870. (e) Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302−4314.
(28) Ros, A.; Bermejo, A.; Aggarwal, V. K. *Chem. - Eur. J.* **2010**, *16*, 9741−9745.
(29) Perrin, D. D. *Ionization Constants of Inorganic Acids and Bases in Aqueous Solution*, 2nd ed.; Pergamon: Oxford, 1982.
(30) Yan, X.; Zhang, Q.; Wei, W.; Ji, J. *Tetrahedron Lett.* **2014**, *55*, 3750−3752.
(31) Weiser, P. T.; Chang, C.-Y.; McDonnell, D. P.; Hanson, R. N. *Bioorg. Med. Chem.* **2014**, *22*, 917−926.
(32) Diao, L.; Wan, P. *Can. J. Chem.* **2008**, *86*, 105−118.
(33) Denegri, B.; Kronja, O. *J. Org. Chem.* **2007**, *72*, 8427−8433.
(34) He, P.; Lu, Y.; Dong, C.-G.; Hu, Q.-S. *Org. Lett.* **2007**, *9*, 343−346.
(35) Capdevila, M.; Emer, E.; Benfatti, F.; Gualandi, A.; Wilson, C.; Cozzi, P. *Asian J. Org. Chem.* **2012**, *1*, 38−42.
(36) Xing, C.-H.; Liu, T.-P.; Zheng, J. R.; Ng, J.; Esposito, M.; Hu, Q.-S. *Tetrahedron Lett.* **2009**, *50*, 4953−4957.
(37) Xiang, S.-K.; Zhang, L.-H.; Jiao, N. *Chem. Commun.* **2009**, 6487−6489.
(38) Kennedy-Smith, J.; Young, L.; Toste, F. *Org. Lett.* **2004**, *6*, 1325−1327.
(39) Masuyama, Y.; Hayashi, M.; Suzuki, N. *Eur. J. Org. Chem.* **2013**, *2013*, 2914−2921.
(40) Zhan, Z.-P.; Cui, Y.-Y.; Liu, H.-J. *Tetrahedron Lett.* **2006**, *47*, 9143−9146.
(41) Siedlecka, R. *Tetrahedron* **2009**, *65*, 2351−2355.

DOI: 10.1021/acs.joc.5b02273
J. Org. Chem. 2015, 80, 12676−12685