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Suzuki–Miyaura Coupling Reactions of Conjunctive Reagents: 2-Borylated Allylic Sulfones

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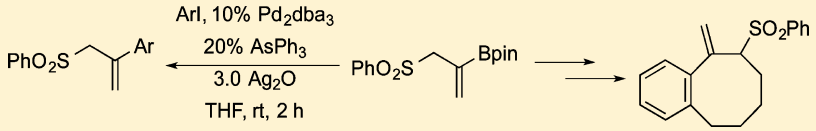
Supporting Information



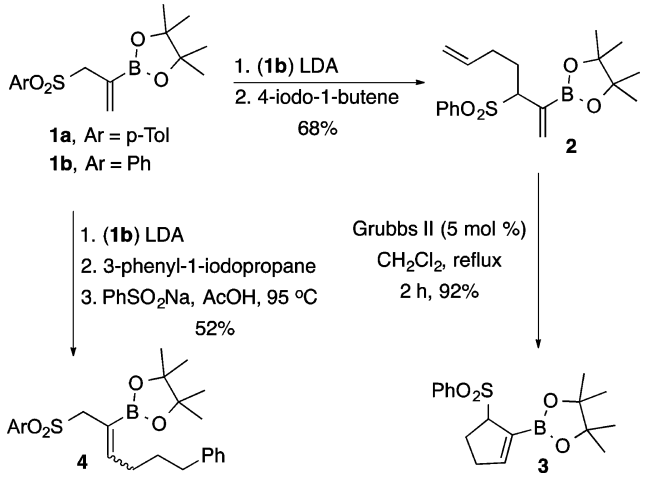
ABSTRACT: In support of various efforts in our group, we developed methods for the convenient Suzuki–Miyaura coupling of borylated allylic sulfones with various electrophiles in both inter- and the less common intramolecular modes. The procedure facilitates the preparation of a wide variety of sulfones in a straightforward fashion, including six- through eight-membered rings.

INTRODUCTION

We recently became interested in the chemistry of the known borylated allylic sulfone **1a**[1] as well as its congener **1b**. For example, we reported that **1b** could be readily deprotonated and alkylated with electrophiles, with the electrophilic boron atom surviving the process (e.g., **2**).[2] Further, we showed that certain alkylation products could be subjected to intramolecular ring-closing metathesis to produce cyclic boronates (e.g., **3**).[3] Intermolecular cross-metathesis was also possible, though limited in scope. A procedure involving the alkylation of **1b** followed by a radical isomerization more generally gave products (e.g., **4**) that were equivalent to those derived from cross-metathesis (Scheme 1).[4]

In the course of these preliminary studies, we also reported a small number of reactions that involved the inter- and intramolecular Suzuki–Miyaura (SM) coupling reactions.[2−4] This paper reports all of our studies in this area to date.

Scheme 1. Chemistry of Borylated Allylic Sulfones



Our interest in the SM reaction was initially stimulated by a desire to pursue an asymmetric phase-transfer-catalyzed 6π electrocyclization reaction on substrates such as **5** (Scheme 2).[5] Computational studies have suggested that with appropriate substitution on the hexatriene, such cyclizations might take place with facility at moderate temperatures.[5a]

Scheme 2. Motivation for Cross-Coupling Studies

RESULTS AND DISCUSSION

Using the procedure reported in the literature,[1] 2-boryl allylic sulfone **1a** was prepared from commercially available 2-isopropenyl boronate ester **7**. In addition, (*Z*)-iodobutadienes **8a** and **8b** could be quickly prepared from the corresponding aldehydes via *Z*-selective Wittig olefination.[6] Preliminary attempts to couple **1a** and either **8a**[6b] or **8b** proceeded in moderate yields, resulting in isolation of cyclohexadiene products **9a** and **9b** (Scheme 3). Diene **9a** remained impure and was not characterized, but **9b** was amenable to purification and characterization. It was clear from ^{1}H NMR spectra that **9b** was cyclic due to the presence of methylene protons, which appeared as triplets at 2.62 and 2.40 ppm and shared the same coupling constant (J = 8 Hz). Presumably, the high temperatures necessary to promote coupling also facilitated the in situ thermal 6π electrocyclization. This is an interesting and synthetically useful result. However, for our purposes, we needed uncyclized trienes. This marked the beginning of our work in the exploration of this coupling methodology.

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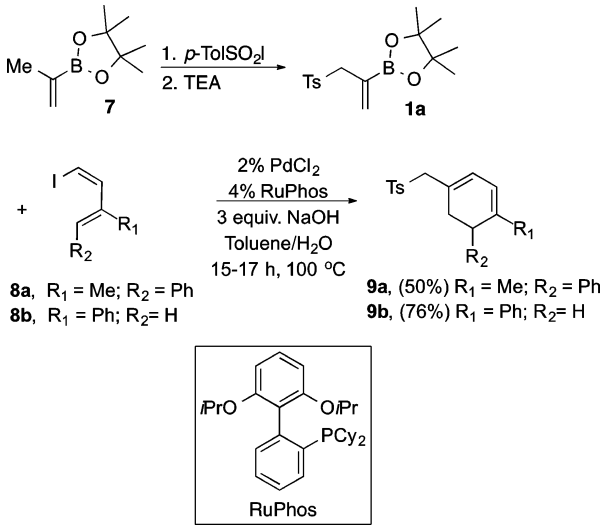
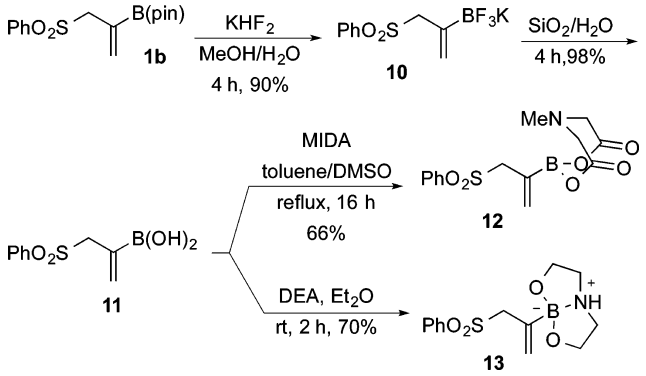
Scheme 3. Preliminary SM Coupling Studies



We thus set out to find mild conditions for the SM reaction of **1a,b** and various congeners. Efforts to achieve coupling without cyclization were focused on tuning the reactivity of boronate coupling partner and choosing the appropriate catalyst system for this reaction. Although the reactivity of the free boronic acids has proven to be effective for SM cross-coupling, the pinacol ester derivatives are typically preferred for their increased stability toward moisture/air, making them easier to handle.[7]

The search for optimal cross-coupling conditions began with a survey of various organoboron derivatives of **1b**. To further explore potential options for the optimal organoboron derivative, the MIDA,[8] DABO,[9] and potassium trifluoroborate[10] derivatives of **1b**, **12**, **13**, and **10**, respectively, were prepared (Scheme 4). In the event, ester **1b** was converted to

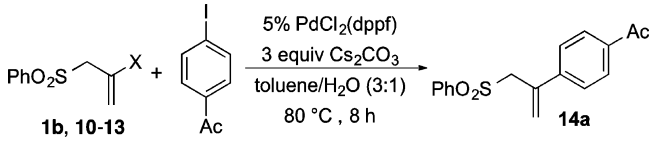
Scheme 4. Synthesis of Derivatives of 1b

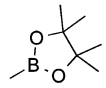
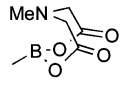


the potassium trifluoroborate **10** by treatment with potassium bifluoride in methanol (Scheme 4).[11] The potassium trifluoroborate could be hydrolyzed to the parent acid **11** in nearly quantitative yield in under 4 h by stirring with silica in the presence of water.[12] Esters **12** and **13** were prepared from **11** under normal esterification procedures using a Dean–Stark apparatus.

With each derivative in hand, we examined their relative reactivities through a simple cross-coupling reaction with *p*-iodoacetophenone (Table 1). Under the relatively mild conditions originally developed by Molander and co-workers,[10]

Table 1. Suzuki–Miyaura Couplings of 1b and 10–13 with *p*-Iodoacetophenone



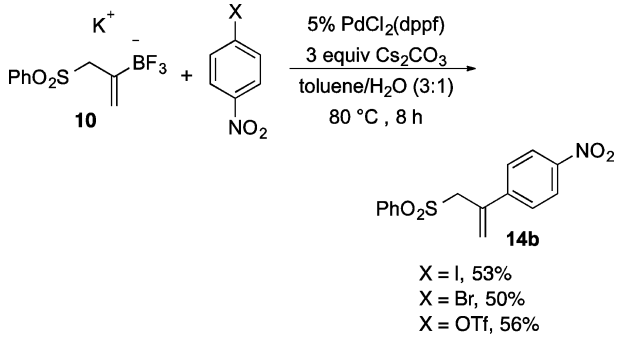
entry	#, -X	yield (%)
1	**10**, -BF_3K	59
2	**11**, -$B(OH)_2$	53
3	**1b**, 	21
4	**12**, 	34
5	**13**, 	32

the trifluoroborate derivative provided the cross-coupled product in the highest yield (Table 1, entry 1). Although each derivative would most likely require individual optimization with respect to each of the reaction variables, this study provided a benchmark that gave a rough approximation of the relative reactivities of the boron derivatives. The mass balance for several coupling reactions was low, and while it would have been nice to identify side products, they tended to be very polar and difficult to isolate from silica columns (reverse phase was not helpful here).

We anticipated that the boronate esters **1b**, **12**, and **13** would afford a yield lower than that of the boronic acid **11** because they need to hydrolyze to engage in transmetalation.[13] We made no special effort to optimize the yields of their SM reactions. For our purposes, given the popularity of potassium organotrifluoroborates, their facile synthesis, and the results of Table 1, this derivative seemed to be the best choice for further exploration.[10,14]

We therefore examined the reaction of **10** with a small number of *para*-substituted nitrobenzenes in order to determine the best "leaving group" in the coupling process. The results are summarized in Scheme 5. They show that for this class of substrates, bromide, iodide, and triflate all function

Scheme 5. Leaving Group Effects on SM Coupling of 10



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with essentially the same efficiency, with the triflate group performing only slightly better than the two halogens.

With the results in hand, we decided to explore the reaction of **10** with a variety of aryl iodides in order to determine the scope of the reaction. The results are summarized in Table 2. Cross-coupling was effective with aryl substituents in the *ortho*, *meta*, or *para* position, though the yield of coupling product obtained from 2-bromoiodobenzene was rather low (Table 2, entry 9). This particular reaction afforded a complex reaction mixture from which only a small amount of product could be isolated. We were unable to isolate anything else of sufficient purity to characterize by proton NMR. Yields were otherwise fair to good across the range of substrates examined. Interestingly, the adduct **14h** was obtained in reasonable yields, and the aliphatic iodide did not interfere with the coupling reaction.

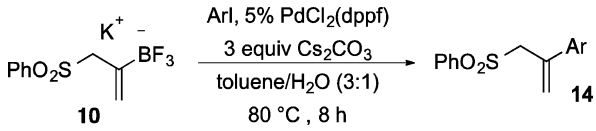
While these results were important, we still wanted to find a procedure that would allow for cross-coupling at or below room temperature. We searched the literature carefully in order to avoid intensive and expensive screening studies and fortunately found a methodology that worked very well without having to resort to any optimization. A protocol developed by Weeber and Gillmann that utilized silver oxide and triphenylarsine allowed for room temperature SM cross-coupling between aryl boronic acids and 2-halo-2,3-butadieneoates.[15] In addition, this procedure was also utilized in a SM cross-coupling reaction between a boronic ester and a bromobutadiene in the total synthesis of (+)-fostriecin.[16] We therefore adopted these conditions in anticipation of their being a likely solution to the problem of high temperatures associated with our other coupling reactions and in the hope that **1b** could be used directly in coupling. The results of our studies are shown in Table 3. Gratifyingly, under these new reaction conditions, various aryl iodides coupled with boronate ester **1b** to afford essentially quantitative yields of coupling products in under 2 h at room temperature, though the reaction slowed significantly when a methoxy group was *ortho* to the iodide functionality (Table 3, entry 7).

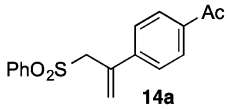
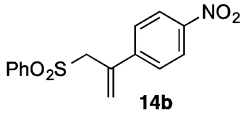
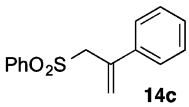
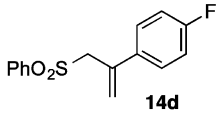
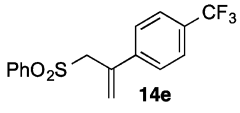
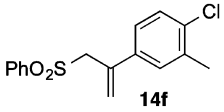
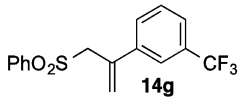
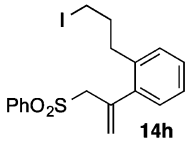
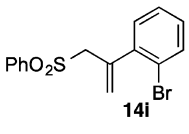
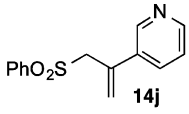
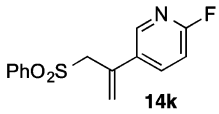
Extension of this procedure to alkenyl electrophiles such as **8b** resulted in a messy reaction mixture (Scheme 6, eq 1). The intended coupled product, **15**, was never observed. Although there was evidence for the formation of the corresponding cyclized product, attempts to isolate and purify the material were unsuccessful. The isolation of allylic alcohol **17** under identical conditions may be a result of the greater stability of compound **16** versus **8b**. Under the reaction conditions, decomposition of **8b** might occur at a faster rate than coupling.

In a recent publication, we demonstrated the generation of bicyclic molecules through an alkylation/metathesis sequence.[3] We thought that similar, but unique, bicyclic structures could be prepared through an intramolecular SM cross-coupling variant. We have, in fact, reported one example of this approach to a polycyclic compound, as shown in eq 3.[4] Thus, the intramolecular SM coupling of **18** proceeded at room temperature under the reaction conditions shown in Table 3 to give **19** in excellent yield.

That reaction served as part of our investigation of intramolecular SM cross-coupling chemistry, which was initiated with the preparation of alkylated compounds bearing aryl iodide functionality that would allow for future intramolecular cross-coupling. The results are shown in Table 4. Using primary iodides and triflates with varying chain lengths, substrates **21a–d** were prepared in a straightforward fashion.

Table 2. Coupling Reactions of 10



entry	product	yield (%)
1	 **14a**	59
2	 **14b**	53
3	 **14c**	56
4	 **14d**	74
5	 **14e**	72
6	 **14f**	81
7	 **14g**	60[a]
8	 **14h**	63
9	 **14i**	35
10	 **14j**	72
11	 **14k**	72

[a]Product was contaminated with allyl phenyl sulfone, from which it could not be separated.

We then applied the silver-oxide-promoted SM cross-coupling conditions (Table 3) to prepare benzo-fused bicyclic products (Table 5). With the exception of substrate **21a**, the

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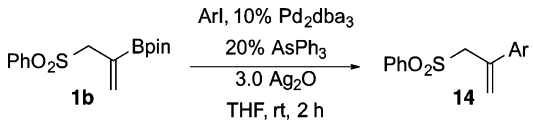
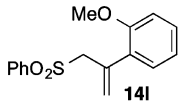
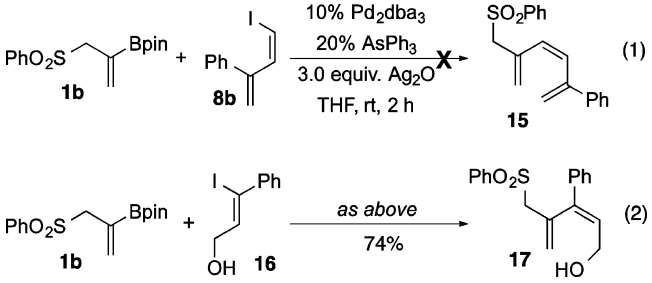
Table 3. Room Temperature SM Couplings of 1b with Aryl Iodides



entry	product	yield (%)
1	**14b**	99
2	**14c**	99
3	**14f**	63
4	**14g**	71
5	**14j**	99
6	**14k**	99
7	 **14l**	83[a]

[a]Reaction required 5 days to complete.

Scheme 6. Coupling of 1b to Alkenyl Iodides



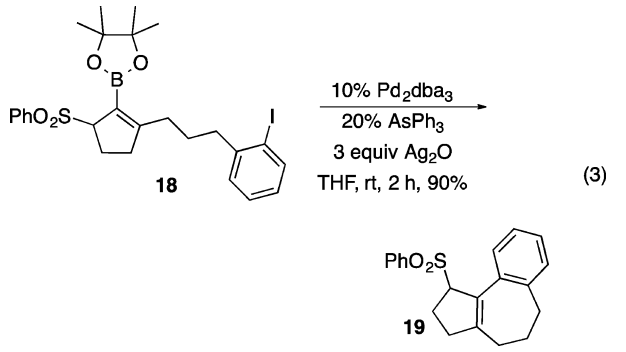
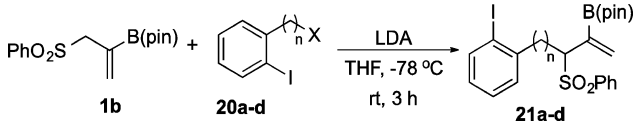


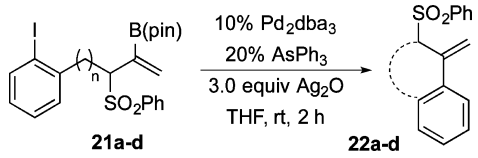
Table 4. Synthesis of Substrates for Intramolecular SM Coupling

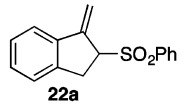
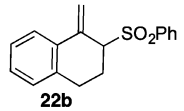
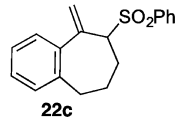
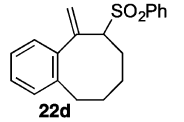


entry	starting material	product	yield (%)
1	**20a**, X = I, n = 1	**21a**	67
2	**20b**, X = I, n = 2	**21b**	71
3	**20c**, X = OTf, n = 3[a]	**21c**	65
4	**20d**, X = OTf, n = 4[a]	**21d**	70

[a]Triflates were prepared from their corresponding alcohols.

Table 5. Intramolecular SM Coupling of 21a–d

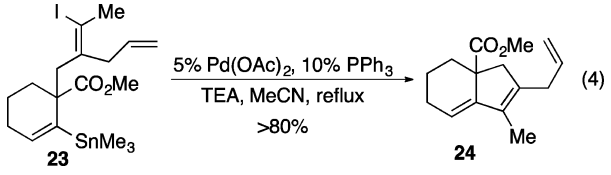


entry	starting material	product	yield (%)
1	**21a**	 **22a**	0[a]
2	**21b**	 **22b**	96
3	**21c**	 **22c**	99
4	**21d**	 **22d**	93

[a]Reaction was incomplete at 2 h and was allowed to stir for an additional 20 h.

formation of six-, seven-, and even eight-membered benzo-fused bicyclics occurred within 2 h in high yields. The formation of **22d** is noteworthy because earlier attempts to access eight-membered rings via cross-metathesis were unsuccessful.[3] These results are interesting and apparently unique; intramolecular SM cyclizations of this type are rather rare.[17] The reaction of **21a** led to the decomposition of starting material.

While the reasons behind the failure of substrate **21a** to cyclize can only be speculated upon, it is interesting to note that Piers reported the intramolecular Stille cyclization shown in eq 4.[18] It is conceivable that different mechanisms associated



with transmetalation in Stille and SM couplings give rise to an endocyclic restriction[19] that prevents cyclization in the case of **21a**. Further studies are needed to support this hypothesis.[20]

CONCLUSION

In summary, we have discovered a mild method for both the inter- and intramolecular Suzuki–Miyaura coupling of 2-borylated allylic sulfones. These reactions, particularly those that are intramolecular, afford opportunities for the simple and rapid construction of polycyclic structures. Such studies, as well as further studies in the synthesis of hexatrienes using this methodology, are of interest to us for the construction of molecules that could be used to test concepts in electrocyclization reactions. Further results will be reported in due course.

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EXPERIMENTAL SECTION

General Information. All glassware and needles were oven-dried and allowed to cool in a desiccator prior to use. All glass vessels used in metal-catalyzed coupling reactions were cleaned with aqua regia. Toluene and THF were distilled from sodium benzophenone prior to use. Solvents used in coupling reactions were degassed prior to use via three freeze−pump−thaw cycles. Reactions were monitored by TLC using a UV lamp or cerium molybdate stain. All products were purified by flash chromatography using 230−400 mesh silica and, if crystalline, were recrystallized from ethyl acetate or hexane/diethyl ether until a constant melting point was observed. All compounds were characterized by ^{1}H and ^{13}C NMR spectroscopy using a 500 MHz spectrometer. Proton spectra were reported in δ units (ppm) relative to a trimethylsilane internal standard (0.00 ppm). Carbon spectra are reported in parts per million relative to deuterated chloroform peak (77.0 or 39.52 ppm) where DMSO was used. Infrared spectra were recorded on a FT-IR spectrometer. High-resolution mass spectra were acquired on a FTICR-MS with an ion cyclotron resonance analyzer (ICR) by an electrospray ionization.

*(Z)-(4-Iodobuta-1,3-dien-2-yl)benzene (**8b**).* To a slurry of iodomethyltriphenylphosphonium iodide (5.36 g, 10.1 mmol) in 20 mL of dry THF were added NaHMDS (0.8 M in THF, 13.6 mL, 10.9 mmol) and HMPA (2.1 mL). The dark red solution was stirred for 5 min at room temperature and cooled to −78 °C. To the ylide was added atropaldehyde (1.11 g, 8.42 mmol) as a solution in THF (1.0 mL) dropwise. After addition, the reaction was allowed to reach room temperature and stirred for 30 min before being quenched with aqueous NH_4Cl. The organic layer was separated and concentrated under a rotary evaporator, and the crude oil was purified by flash chromatography (100% hexanes), resulting in a yellow oil (600 mg, 28%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39−7.29 (m, 5H), 6.96 (d, J = 8.5 Hz, 1H), 6.66 (d, J = 8 Hz, 1H), 5.72 (s, 1H), 5.51 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.1, 139.5, 138.5, 128.5, 128.0, 126.6, 116.8, 86.6; IR (film) ν_{max} 3062, 3027, 2978, 2931, 1447, 1423, 1330, 1305, 1214, 1143, 1084 cm^{-1}; no molecular ion in HRMS.

Suzuki−Miyaura Cross-Coupling Procedure A. *4-((Phenylsulfonyl)methyl)-2,3-dihydro-1,1′-biphenyl (**9b**).* In a sealed tube containing 1.0 mL of toluene and 0.1 mL of water vinyl iodide **8b** (50 mg, 0.196 mmol), boronic ester **1a** (94 mg, 0.292 mmol), palladium(II) chloride (0.70 mg, 3.9 μmol), RuPhos (3.64 mg, 7.8 μmol), and sodium hydroxide (25 mg, 0.62 mmol) were added. The reaction was sealed and heated to 100 °C for 17 h. The reaction was cooled to room temperature and extracted with dichloromethane. The organic extracts were washed with brine, dried over magnesium sulfate, and concentrated under reduced pressure. The crude was purified via column chromatography (20% ethyl acetate/hexanes), yielding a white solid (48 mg, 76%): mp = 168 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 7.33 (t, J = 8.0 Hz, 4H), 7.23 (d, J = 8.0 Hz, 1H), 6.21 (d, J = 5.5 Hz, 1H), 5.76 (d, J = 5.5 Hz, 1H), 3.87 (s, 2H), 2.62 (t, J = 10.0 Hz, 2H), 2.45 (s, 3H), 2.40 (t, J = 10.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.8, 140.4, 137.7, 135.7, 129.8, 129.3, 128.8, 128.6, 127.6, 125.2, 125.1, 120.3, 64.5, 27.1, 26.0, 21.8; IR (film) ν_{max} 3062, 3027, 2978, 2931, 1447, 1423, 1330, 1305, 1214, 1143, 1084 cm^{-1}; HRMS calcd for $(C_{20}H_{20}O_2S)Na^+$ 347.1076, found 347.1079.

*(3-(Phenylsulfonyl)prop-1-en-2-yl)potassium Trifluoroborate (**10**).* The pinacol ester **1b** (3.0 g, 9.7 mmol) was dissolved in methanol (80 mL) and treated with an aqueous solution of potassium hydrogen fluoride (5.3 g, 67.9 mmol). The slurry was stirred for 2 h at 25 °C, and the solvent was removed under reduced pressure. The crude product was dissolved in boiling acetonitrile and hot-filtered to remove excess potassium hydrogen fluoride. The acetonitrile was removed under reduced pressure, and the resulting white solid could be purified by being rinsed with ethyl acetate, leaving behind a fluffy white solid (2.37 g, 85%): mp = 214−215 °C; ^{1}H NMR (500 MHz, acetone-d_6) δ 7.89 (d, J = 7.0 Hz, 2H), 7.65 (t, J = 7.0 Hz, 1H), 7.56 (t, J = 7.0 Hz, 2H), 5.26 (s, 1H), 4.96 (s, 1H), 3.89 (s, 2H); ^{13}C NMR (500 MHz, CD_3CN) 141.1, 134.1, 129.8, 129.4, 124.3, 118.3 (CN + buried peak?), 62.8; HRMS calcd for $(C_9H_9BF_3KO_2S)Na^+$ 310.9897, found 310.9895.

*(3-(Phenylsulfonyl)prop-1-en-2-yl)boronic Acid (**11**).* Potassium trifluoroborate **10** (100 mg, 0.347 mmol) was dissolved in 5 mL of water (0.07 M) and stirred with excess silica for 4 h at 25 °C. Once the reaction was complete, the silica was filtered and the filter cake was washed several times with ethyl acetate. The filtrate was added to a separatory funnel, and the aqueous phase was extracted with ethyl acetate (3 × 10 mL). The organic layers were collected and dried over magnesium sulfate. The solvent was removed, leaving behind a white solid that became an oil (90 mg, 98%): ^{1}H NMR (500 MHz, acetone-d_6) δ 7.86 (d, J = 7.0 Hz, 2H), 7.72 (d, J = 7.5 Hz, 1H), 7.62 (t, J = 7.0 Hz, 2H), 6.94 (s, 2H), 5.99 (d, J = 3.0 Hz, 1H), 5.57 (s, 1H), 4.07 (s, 2H); ^{13}C NMR (125 MHz, acetone-d_6) δ 140.1, 136.1, 134.4, 129.8, 129.5, 62.1; IR (film) ν_{max} 3062, 3027, 2978, 2931, 1447, 1423, 1372, 1305, 1214, 1143, 1084 cm^{-1}; HRMS calcd for $(C_9H_{11}BO_4S)Na^+$ 249.0363, found 249.0363.

*6-Methyl-2-(3-(phenylsulfonyl)prop-1-en-2-yl)-1,3,6,2-dioxazaborocane-4,8-dione (**12**).* Boronic acid **11** (134 mg, 0.592 mmol) and *N*-methyliminodiacetic acid (96 mg, 0.651 mmol) were dissolved in 5 mL of toluene/DMSO (1:1). The solution was heated to 120 °C for 17 h and diluted with dichloromethane. The organic layer was separated and washed with water and brine and dried over magnesium sulfate. The solvent was removed under reduced pressure, resulting in a solid that was purified by washing with boiling hexanes and decanting (159 mg, 80%): mp = 184 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.86 (d, J = 7.5 Hz, 2H), 7.74 (t, J = 7.5 Hz, 1H), 7.65 (t, J = 7.5 Hz, 2H), 5.73 (t, J = 7.5 Hz, 2H), 5.70 (s, 1H), 4.25 (d, J = 17.0 Hz, 2H), 4.01 (d, J = 17.0 Hz, 2H), 4.02 (s, 2H), 2.82 (s, 3H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 169.1, 139.3, 133.7, 133.6, 129.3, 127,8, 62.4, 59.2, 47.2; HRMS calcd for $(C_{14}H_{16}BNO_6S)Na^+$ 360.0683, found 360.0684.

*8-(3-(Phenylsulfonyl)prop-1-en-2-yl)hexahydro-[1,3,2]-oxazaborolo[2,3-b][1,3,2]oxazaborol-4-ium-8-uide (**13**).* Pinacol boronate **1b** (614 mg, 1.99 mmol) was dissolved in 16 mL of dry diethyl ether and treated with diethanolamine (202 μL, 2.19 mmol) dropwise. Stirring was continued for 2 h, and the white precipitate was filtered and washed with diethyl ether. The crude solid was recrystallized from ethyl acetate (469 mg, 80%): mp = 154−155 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 7.7 Hz, 2H), 7.66 (t, J = 7.7 Hz, 1H), 7.56 (t, J = 7.7 Hz, 2H), 6.15 (br s, 1H), 5.83 (d, J = 3.5 Hz, 1H), 5.22 (d, J = 2.0 Hz) 1H), 4.07 (ddd, J = 5.5 Hz, J = 9.5 Hz, J = 9.5 Hz, 2 H), 4.01−3.97 (m, 4H), 3.43−3.36 (m, 2H), 2.91−2.86 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.8, 133.9, 131.9, 129.2, 128.3, 63.7, 62.5, 51.3; IR (film) ν_{max} 3062, 3027, 2978, 2931, 1447, 1423, 1372, 1305, 1214, 1143, 1084 cm^{-1}; HRMS calcd for $(C_{13}H_{18}BNO_4S)Na^+$ 318.0942, found 318.0940.

*1-(4-(3-(Phenylsulfonyl)prop-1-en-2-yl)phenyl)ethanone (**14a**).* A 25 mL sealed tube was oven-dried and allowed to cool under an argon atmosphere. The vessel was charged with 4.8 mL of toluene, aryl iodide (153 mg, 0.693 mmol), 1,1′-bis(diphenylphosphinoferrocene)-dichloropalladium(II) (28.0 mg, 34 μmol), potassium trifluoroborate **10** (219 mg, 0.762 mmol), and cesium carbonate (677 mg, 2.07 mmol). The mixture was stirred vigorously, and 2.0 mL of water was added. The tube was purged with argon before being sealed and placed in an oil bath at 80 °C for 8 h. Once consumption of the iodide was determined via TLC, the reaction was transferred to a separatory funnel and diluted with 10 mL of ethyl acetate. The organic layer was separated and dried over magnesium sulfate. After removal of solvent, the crude product was dry loaded onto a silica column and eluted with 20% EtOAc/hexanes to give the product as a solid (122 mg, 59%): mp = 134 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 8.5 Hz, 2H), 7.80 (d, J = 8.0 Hz, 2H), 7.58 (t, J = 8.0 Hz, 1H), 7.46 (t, J = 8.0 Hz, 2H), 0.39 (d, J = 8.5 Hz, 2H), 5.70 (s, 1H), 5.32 (s, 1H), 4.28 (s, 2H), 2.58 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.5, 143.4, 138.2, 136.6, 135.9, 134.0, 129.2, 128.8, 128.6, 126.6, 124.0, 61.9, 26.8; IR (film) ν_{max} 3061, 2977, 2934, 1643, 1447, 1423,1372, 1305, 1145 cm^{-1}; HRMS calcd for $(C_{17}H_{16}O_3S)Na^+$ 323.0712, found 323.0714.

*1-Nitro-4-(3-(phenylsulfonyl)prop-1-en-2-yl)benzene (**14b**).* Cross-coupling procedure A: mp = 134−135 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, J = 9.0 Hz, 2H), 7.81 (d, J = 8.0 Hz, 2H), 7.61 (t, J = 7.5 Hz, 1H), 7.51−7.47 (m, 4H), 5.75 (s, 1H), 5.40 (s,

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1H), 4.28 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.5, 145.3, 138.3, 135.2, 134.2, 129.3, 128.7, 127.3, 125.5, 123.9, 61.9; IR (film) ν_{max} 2978, 2931, 1492, 1447, 1423, 1305 cm^{-1}; HRMS calcd for $(C_{15}H_{13}NO_4S)Na^+$ 326.0457, found 326.0454.

*1-(3-(Phenylsulfonyl)prop-1-en-2-yl)-4-(trifluoromethyl)benzene (**14e**).* Cross-coupling procedure A: mp = 64 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, J = 7.0 Hz, 2H), 7.57 (t, J = 7.5 Hz, 1H), 7.49 (d, J = 9.0 Hz, 2H), 7.44 (t, J = 7.5 Hz, 2H), 7.38 (d, J = 8.5 Hz, 2H), 5.67 (s, 1H), 5.33 (s, 1H), 4.27 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.4, 138.4, 135.7, 134.0, 130.0 (q, J_{C-F} = 32.5 Hz), 129.2, 128.7, 126.8, 125.5 (q, J = 3.8 Hz), 124.0, 123.9 (q, J_{C-F} = 271.1 Hz), 62.1; IR (film) ν_{max} 3062, 3027, 2978, 2931, 1447, 1372, 1305, 1214, 1143, 1084 cm^{-1}; HRMS calcd for $(C_{16}H_{13}F_3O_2S)Na^+$ 349.0480, found 349.0477.

*1-Chloro-2-methyl-4-(3-(phenylsulfonyl)prop-1-en-2-yl)benzene (**14f**).* Cross-coupling procedure A: mp = 61 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, J = 7.5 Hz, 2H), 7.57 (t, J = 7.0 Hz, 1H), 7.45 (t, J = 7.5 Hz, 2H), 7.19 (d, J = 8 Hz, 1H), 7.06 (s, 1H), 7.03 (dd, J = 1.5 Hz, J = 8 Hz, 1H), 5.57 (s, 1H), 5.21 (s, 1H), 4.23 (s, 2H), 2.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 137.4, 136.1, 135.8, 134.4, 133.8, 129.2, 129.0, 128.9, 128.8, 125.1, 122.3, 62.2, 20.2; IR (film) ν_{max} 2978, 2931, 1492, 1447, 1423, 1380, 1372, 1305, 1214, 1143, 1084 cm^{-1}; HRMS calcd for $(C_{16}H_{15}ClO_2S)Na^+$ 329.0373, found 329.0372.

*1-(3-Iodopropyl)-2-(3-(phenylsulfonyl)prop-1-en-2-yl)benzene (**14h**).* Cross-coupling procedure A: oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (dd, J = 7.5, 1.5 Hz, 2H), 7.60 (t, J = 7.0 Hz, 1H), 7.49 (t, J = 7.5 Hz, 2H), 7.18 (dt, J = 1.5, 7.0 Hz, 1H), 7.12 (d, J = 8.0 Hz, 1H), 7.07 (dt, J = 1.5, 7.0 Hz, 1H), 6.97 (dd, J = 1.0. 7.5 Hz, 1H), 5.55 (s, 1H), 5.31 (d, J = 1.0 Hz, 1H), 4.16 (s, 2H), 3.16 (t, J = 7.0 Hz, 2H), 2.65−2.62 (m, 2H), 2.04 (p, J = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.3, 139.2, 137.4, 136.4, 133.8, 129.4, 129.2, 129.2, 128.4, 128.1, 126.2, 124.8, 63.7, 34.9, 33.8, 6.6; IR (film) ν_{max} 3072, 2977, 2931, 1640, 1447, 1423, 1380, 1372, 1306, 1213, 1143, 1085, 1024 cm^{-1}; HRMS calcd for $(C_{18}H_{19}IO_2S)Na^+$ 449.0042, found 449.0037.

*1-Bromo-2-(3-(phenylsulfonyl)prop-1-en-2-yl)benzene (**14i**).* Cross-coupling procedure A: mp = 67 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 7.5 Hz, 2H), 7.58 (t, J = 7.0 Hz, 1H), 7.47 (t, J = 8.0 Hz, 2H), 7.43 (d, J = 8.0 Hz, 1H), 7.19 (t, J = 7.0 Hz, 1H), 7.11−7.08 (m, 2H), 5.49 (s, 1H), 5.39 (s, 1H), 4.32 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.0, 139.0, 137.4, 133.7, 132.7, 131.6, 129.5, 129.2, 128.5, 127.51, 125.8, 121.5, 62.3; IR (film) ν_{max} 2978, 2954, 1493, 1442, 1425, 1305, 1002 cm^{-1}; HRMS calcd for $(C_{15}H_{13}BrO_2S)Na^+$ 358.9711, found 358.9708.

*3-(3-(Phenylsulfonyl)prop-1-en-2-yl)pyridine (**14j**).* Cross-coupling procedure A: mp = 88 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, J = 2.5 Hz, 1H), 8.46 (d, J = 5.0 Hz, 1H), 7.80 (d, J = 7.8 Hz, 2H), 7.62 (d, J = 7.5 Hz, 1H), 7.58 (t, J = 7.5 Hz, 1H), 7.47 (t, J = 7.5 Hz, 2H), 7.18 (dd, J = 4.5, 7.5 Hz, 1H), 5.66 (s, 1H), 5.32 (s, 1H), 4.26 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.2, 147.6, 138.2, 134.9, 134.0, 133.8, 133.6, 129.3, 129.2, 128.6, 128.5, 123.7, 123.2, 61.8; IR (film) ν_{max} 2978, 2931, 1492, 1447, 1623, 1455, 1385, 1356, 1454, 1143, 1085 cm^{-1}; HRMS calcd for $(C_{14}H_{13}NO_2S)Na^+$ 282.0559, found 282.0556.

*2-Fluoro-5-(3-(phenylsulfonyl)prop-1-en-2-yl)pyridine (**14k**).* Cross-coupling procedure A: mp = 96 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, J = 2.0 Hz, 1H), 7.81 (d, J = 7.5 Hz, 2H), 7.76 (dt, J = 2.5, 8.0 Hz, 1H), 7.62 (d, J = 7.0 1H), 7.51 (t, J = 7.5 Hz, 2H), 6.84 (dd, J = 3.0, 8.5 Hz, 1H), 5.62 (s, 1H), 5.30 (s, 1H), 4.22 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2 (d, J_{C-F} = 238.8 Hz), 143.6 (d, J_{C-F} = 15 Hz), 139.1 (d, J_{C-F} = 8.7 Hz), 138.3, 134.2, 132.7 (d, J_{C-F} = 5.0 Hz), 132.6 129.3, 128.7, 123.9, 109.1 (d, J_{C-F} = 37.5 Hz), 62.1; IR (film) ν_{max} 3060, 1591, 1490, 1447, 1371, 1309, 1295, 1256, 1140, 1084 cm^{-1}; HRMS calcd for $(C_{14}H_{12}FNO_2S)Na^+$ 300.0464, found 300.0463.

Suzuki−Miyaura Cross-Coupling Procedure B. *1-Methoxy-2-(3-(phenylsulfonyl)prop-1-en-2-yl)benzene (**14l**).* Boronate **1b** (100 mg, 0.324 mmol), *o*-iodoanisole (46 μL, 0.340 mmol), tris(dibenzylideneacetone)dipalladium(0) (15 mg, 47 μmol), triphenylarsine (20 mg, 65 μmol), and silver oxide (225 mg, 0.972 mmol) were added to a flask and placed under vacuum. The reaction vessel was backfilled with argon and charged with degassed THF (3.24 mL). The black mixture was stirred for 2 h at room temperature, and the solvent was removed under reduced pressure. The crude mixture was dry loaded onto a flash column and eluted using 20% EtOAc/hexanes (oil, 77 mg, 83%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, J = 8.0 Hz, 2H), 7.49 (t, J = 8.0 Hz, 1H), 7.36 (t, J = 8.0 Hz, 2H), 7.17 (t, J = 8.0 Hz, 1H), 7.02 (d, J = 8.0 Hz, 1H), 6.83 (t, J = 8.0 Hz, 1H), 6.63 (d, J = 8.0 Hz, 1H), 5.35 (s, 1H), 5.30 (s, 1H), 4.44 (s, 2H), 3.71 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.9, 138.8, 136.7, 133.1, 130.6, 129.4, 128.5, 128.3, 123.9, 120.7, 110.2, 62.1, 55.2; IR (film) ν_{max} 2978, 2954, 1493, 1442, 1425, 1305, 1002 cm^{-1}; HRMS calcd for $(C_{16}H_{16}O_3S)Na^+$ 311.0712, found 311.0712.

*(Z)-3-Phenyl-4-((phenylsulfonyl)methyl)penta-2,4-dien-1-ol (**17**).* Cross-coupling procedure B, oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 7.5 Hz, 2H), 7.65 (t, J = 7.5 Hz, 1H), 7.54 (t, J = 7.5 Hz, 2H), 7.31−7.28 (m, 3H), 7.23−7.21 (m, 2H), 6.11 (t, J = 7.5 Hz, 1H), 5.46 (s, 1H), 5.36 (s, 1H), 4.37 (d, J = 7.5 Hz, 2H), 3.79 (s, 2H), 3.24 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.8, 139.2, 138.5, 133.8, 132.9, 130.0, 129.3, 128.7, 128.3, 128.1, 127.3, 126.8, 61.6, 59.7; IR (film) ν_{max} 3509, 3060, 3024, 2925, 1491, 1447, 1307, 1246, 1153, 1128, 1085 cm^{-1}; HRMS calcd for $(C_{18}H_{18}O_3S)Na^+$ 337.0868, found 337.0868.

General Preparation of Triflates. *3-(2-Iodophenyl)propyl Trifluoromethanesulfonate (**20c**).* To a solution of 3-(2-iodophenyl)-propan-1-ol (440 mg, 1.7 mmol) in dichloromethane (17 mL) at −78 °C was added 2,6-lutidine (312 μL, 3.4 mmol) followed by dropwise addition of trifluoromethanesulfonic anhydride (386 μL, 1.9 mmol). The solution was stirred for 1 h at −78 °C before being quenched with water slowly. The reaction was diluted with dichloromethane and washed with brine. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure. The crude oil was purified on a flash column (100% hexanes), affording a yellow oil (283 mg, 43%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 8.0 Hz, 1H), 7.30 (t, J = 7.5 Hz, 1H), 7.20 (d, J = 8.0 Hz, 1H), 6.93 (t, J = 7.5 Hz, 1H), 4.58 (t, J = 6.0 Hz, 2H), 2.88 (t, J = 7.5 Hz, 2H), 2.17−2.12 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.4, 140.0, 129.7, 128.8, 128.6, 118.8 (q, J_{C-F} = 317.5 Hz), 100.3, 76.6, 36.4, 29.7; IR (film) ν_{max} 2978, 2931, 1492, 1447, 1423, 1372, 1305, 1214, 1143, 1084 cm^{-1}; no molecular ion in HRMS.

*4-(2-Iodophenyl)butyl Trifluoromethanesulfonate (**20d**).* Triflate procedure, oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 8 Hz, 1H), 7.28 (t, J = 8.0 Hz, 1H), 7.19 (dd, J = 1.5, 7.5 Hz, 1H), 6.90 (t, J = 1.5, 8.0 Hz, 1H), 4.57 (t, J = 6.5 Hz, 2H), 2.78 (t, J = 7.5 Hz, 2H), 1.95−1.89 (m, 2H), 1.78−1.72 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.7, 139.6, 129.3, 128.5, 128.1, 118,6 (q, J_{C-F} = 319.7 Hz) 100.4, 39.8, 28.7, 25.7; IR (film) ν_{max} 2978, 2931, 1492, 1447, 1423, 1372, 1305, 1214, 1143, 1084 cm^{-1}; no molecular ion in HRMS.

General Alkylation Procedure. *2-(4-(2-Iodophenyl)-3-(phenylsulfonyl)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**21a**).* To a solution of diisopropylamine (60 μL, 0.42 mmol) in THF (2.2 mL) was added *n*-butyllithium (2.04 M in THF, 174 μL, 0.35 mmol) at −78 °C and stirred for 1 h. The solution of lithium diisopropylamide was then treated with a solution of **1b** (100 mg, 0.324 mmol) in 1.0 mL of THF and stirred for an additional hour before addition of electrophile (0.356 mmol). After dropwise addition of electrophile, the reaction was removed from the cold bath and allowed to warm to room temperature over 3 h. The reaction was quenched with a saturated solution of aqueous NH_4Cl, and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was absorbed onto silica and purified via flash chromatography (20% EtOAc in hexanes), affording the corresponding monoalkylated product as an oil (113 mg, 67%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 8.2 Hz, 2H), 7.75 (d, J = 8.0 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.51 (t, J = 8.0 Hz, 2H), 7.20−7.16 (m, 2H), 6.86−6.83 (m, 1H), 6.06 (d, J = 2.0 Hz, 1H), 5.94 (s, 1H), 4.39 (dd, J = 4.0, 10.5 Hz, 1H), 3.61 (dd, J = 3.5, 14.0 Hz, 1H), 3.43 (dd, J = 12.0, 14.0 Hz, 1H), 1.12 (s, 6H), 1.09 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.7, 139.6, 138.4, 137.4, 133.3, 131.2, 129.57, 128.7,

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128.3, 127.9, 100.7, 83.9, 67.0, 38.1, 24.79, 24.4; IR (film) ν_{max} 2973, 2930, 1447, 1423, 1305, 1216, 1145, 1085 cm^{-1}; HRMS calcd for $(C_{22}H_{26}BIO_4S)Na^+$ 547.0582, found 547.0577.

*2-(5-(2-Iodophenyl)-3-(phenylsulfonyl)pent-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**21b**).* Alkylation procedure, oil: ^1H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 8.0 Hz, 1H), 7.59 (t, J = 8.0 Hz, 1H), 7.49 (t, J = 8.0 Hz, 2H), 7.24 (d, J = 8.0 Hz, 1H), 7.18 (dd, J = 1.5, 8.0 Hz, 1H), 6.89 (dt, J = 1.5, 8.0 Hz, 1H), 6.23 (d, J = 2 Hz, 1H), 6.00 (s, 1H), 3.99 (dd, J = 3.5, 11.5 Hz, 1H), 2.78−2.72 (m, 1H), 2.66−2.60 (m, 1H), 2.45 (dddd, J = 3.5, 6.0, 10.0, 13.5 Hz, 1H), 2.30−2.22 (m, 1H), 1.183 (s, 6H), 1.177 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.4, 139.5, 138.0, 136.8, 133.2, 129.6, 129.5, 128.6, 128.3, 128.0, 100.3, 83.9, 67.3, 37.80, 27.3, 24.7, 24.6; IR (film) ν_{max} 2973, 2930, 1447, 1423, 1305, 1216, 1145, 1085 cm^{-1}; HRMS calcd for $(C_{23}H_{28}BIO_4S)Na^+$ 561.0744, found 561.0733.

*2-(7-(2-Iodophenyl)-3-(phenylsulfonyl)hept-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**21d**).* Alkylation procedure, oil: ^1H NMR (500 MHz, $CDCl_3$) δ 7.79 (t, J = 8.5 Hz, 3H), 7.58 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 8.0 Hz, 2H), 7.24 (t, J = 7.5 Hz, 1H), 7.15 (d, J = 7.5 Hz, 1H), 6.86 (t, J = 8.0 Hz, 1H), 6.14 (d, J = 2.0 Hz, 1H), 5.89 (s, 1H), 3.92 (dd, J = 3.5, 11.5, 1H), 2.71−2.61 (m, 2H), 2.23 (dddd, J = 3.5, 6.0, 10.0, 13.5 Hz, 1H), 2.11−2.03 (m, 1H), 1.60−1.52 (m, 2H), 1.47−1.40 (m, 1H), 1.37−1.31 (m, 1H), 1.14 (s, 6H), 1.13 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.8, 139.4, 138.2, 136.5, 133.2, 129.6, 129.2, 128.6, 128.2, 127.6, 100.5, 83.8, 68.0, 40.4, 29.7, 26.5, 26.4, 24.65, 24.57; IR (film) ν_{max} 2973, 2930, 1447, 1423, 1305, 1216, 1145, 1085 cm^{-1}; HRMS calcd for $(C_{25}H_{32}BIO_4S)Na^+$ 589.1051, found 589.1045.

*1-Methylene-2-(phenylsulfonyl)-1,2,3,4-tetrahydronaphthalene (**22b**).* Cross-coupling procedure B, oil: ^1H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 7.6 Hz, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.52−7.47 (m, 3H), 7.21−7.14 (m, 2H), 7.06 (d, J = 7.0 Hz, 1H), 5.72 (s, 1H), 4.92 (s, 1H), 4.12 (t, J = 5.0 Hz, 1H), 3.21 (ddd, J = 5.5, 10.0, 16.0 Hz, 1H), 2.73 (dt, J = 16.5, 5.5 Hz, 1H), 2.54 (dq, J = 15.0, 5.0 Hz, 1H), 2.27−2.19 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.7, 136.1, 135.2, 133.7, 133.5, 132.7, 129.3, 128.7, 128.3, 126.5, 124.5, 118.0, 67.0, 26.2, 23.0; IR (film) ν_{max} 2973, 2930, 1447, 1423, 1305, 1216, 1145, 1085 cm^{-1}; HRMS calcd for $(C_{17}H_{16}O_2S)Na^+$ 307.0763, found 307.0762.

*5-Methylene-6-(phenylsulfonyl)-6,7,8,9-tetrahydro-5H-benzo[7]annulene (**22c**).* Cross-coupling procedure B, oil: ^1H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 8.0 Hz, 2H), 7.62 (t, J = 8.0 Hz, 1H), 7.51 (t, J = 8.0 Hz, 2H), 7.18 (t, J = 8.0 Hz, 1H), 7.10 (t, J = 8.0 Hz, 1H), 7.03 (d, J = 7.0 Hz, 1H), 6.85 (d, J = 7.5 Hz, 1H), 5.57 (s, 1H), 5.30 (s, 1H), 3.95 (d, J = 8.0 Hz, 1H), 2.78−2.72 (m, 1H), 2.69−2.65 (m, 1H), 2.32−2.13 (m, 1H), 1.94−1.87 (m, 1H), 1.85−1.76 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.4, 140.1, 137.8, 133.5, 130.0, 129.4, 128.8, 128.3, 128.2, 128.1, 126.6, 122.8, 68.5, 32.2, 26.0, 23.4; IR (film) ν_{max} 2978, 2931, 1492, 1447, 1423, 1372, 1305, 1214, 1143, 1084 cm^{-1}; HRMS calcd for $(C_{18}H_{18}O_2S)Na^+$ 321.0919, found 321.0917.

*5-Methylene-6-(phenylsulfonyl)-5,6,7,8,9,10-hexahydrobenzo[8]annulene (**22d**).* Cross-coupling procedure B, oil: ^1H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 7.5 Hz, 2H), 7.65 (t, J = 7.5 Hz, 1H), 7.57 (t, J = 7.5 Hz, 2H), 7.25−7.16 (m, 3H), 7.10 (d, J = 7.5 Hz, 1H), 5.28 (s, 2H), 3.81 (dd, J = 2.5, 12.0 Hz, 1H), 2.72−2.63 (m, 2H), 2.23−2.18 (m, 1H), 2.07−1.94 (m, 2H), 1.59−1.52 (m, 1H), 1.51−1.43 (m, 1H), 1.31−1.24 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.1, 141.0, 138.2, 138.0, 133.7, 133.4, 130.0, 129.1, 128.9, 128.2, 125.6, 124.9, 74.9, 34.2, 30.4, 27.9, 24.3; IR (film) ν_{max} 2978, 2931, 1492, 1447, 1423, 1372, 1305, 1214, 1143, 1084 cm^{-1}; HRMS calcd for $(C_{19}H_{20}O_2S)Na^+$ 335.1076, found 335.1078.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01253.

Proton and carbon NMR data for new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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