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Ligand-Free Copper(I)-Mediated Cross-Coupling Reactions of Organostannanes with Sulfur Electrophiles

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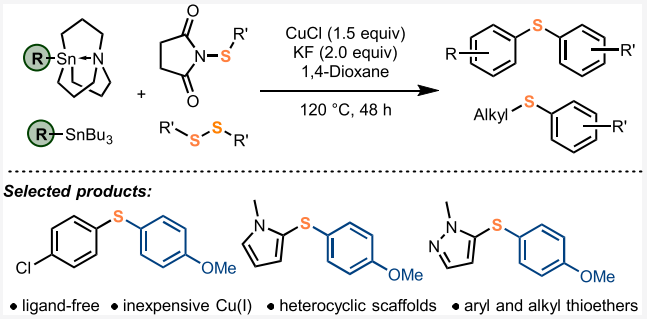
ABSTRACT: The synthesis of aryl thioether through the cross-coupling of C−S bond is a highly attractive area of research due to the prevalence of aryl thioether in bioactive natural products, functional materials, agrochemicals, and pharmaceutically active compounds. Herein, we report a ligand-free Cu(I) mediated electrophilic thiolation of organostannanes with sulfur electrophiles. A selective transfer of alkyl groups was achieved in reactions with alkyl carbastannatranes affording congested thioethers. This study offers a unified method to access diaryl and aryl alkyl thioethers and was demonstrated in the context of late-stage modifications..



Thioethers are a common structural motif found in bioactive natural products, functional materials, agrochemicals, and pharmaceutically active compounds.[1] S-Aryl fragments are becoming privileged architectures in commercial pharmaceuticals exemplified by montelukast,[2a] nelfinavir,[2b] retapamulin,[2c] amoxicillin,[2d] axitinib,[2e] nolatrexed,[2f] and ticagrelor[2g] (Figure 1). Therefore, the search for methods to construct a C−S bond beyond direct nucleophilic substitution is an active research area catering small-molecule and materials synthesis.[3] Among various synthetic approaches described to date, transition metal catalyzed cross-coupling reactions are a useful strategy for C−S bond construction because of the availability of a diverse pool of thiols and aryl halides or pseudohalides (Scheme 1A).[4] Nevertheless, most of the reported methods require a strong base additive, high catalyst loadings, and air-sensitive ligands designed for specific applications. Elevated temperatures are also needed to promote the reaction owing to strong chelation of the sulfur atom to transition metal catalysts, which can poison the active catalytic species and lead to deactivation.[5]

The C−S cross-coupling of organometallic reagents with sulfur electrophiles is a promising alternative to transition metal catalyzed reactions (Scheme 1B). Functionalized reagents such as organolithium,[6] Grignard,[7] organoboron,[8] organosilicon,[9] and organoznic[10] were employed in reactions with electrophilic sulfur sources of general formula RS−X (X = SR, halogen, *N*-succimidyl, and arylsulfonyl). Complementary to uncatalyzed processes, the leading catalytic methods require highly reactive nucleophiles such R−Li and R−MgX and unstable electrophilic sulfur sources (RS−Cl or RS−Br) to obtain synthetically useful yields. The nature of these reagents severely limits the scope and functional group tolerance. More recently, significant progress has been achieved in photoredox C−S bond formations involving thiols reacting with (hetero)-aryl halides (Scheme 1C).[11] The scope of thiol nucleophiles is mainly limited to aryl mercaptans, and only selected alkyl thiols can participate in this process.

Expensive photosensitizers required to promote these reactions are an inherent limitation of these protocols and introduce challenges in terms of scalability and sustainability. Collectively, these concerns motivate efforts to search for brand new methods for C−S formation or to improve existing catalytic strategies. Compared to the above-mentioned metal reagents, a direct coupling of electrophilic sulfur sources with organotin reagents is relatively scarce and limited to unique substrates such as allyl stannanes activated under radical conditions.[12] A direct coupling of organotin compounds is potentially appealing because of the following: (a) organotin compounds are known to be air- and moisture-stable, have excellent functional group tolerance, and can be introduced in complex molecules; (b) functionalized (hetero)aryl and alkyl tin reagents are easily accessible and commercially available; (c) stannatranes, a class of activated pentavalent tin reagents with reduced toxicity, can selectively transfer alkyl groups in the Stille couplings; (d) the byproduct of this coupling, $RSSnBu_3$, can reduce the concentration of sulfur and suppress potential catalyst poisoning. We recently reported the synthesis and reactions of carbohydrate C1-stannanes, a class of

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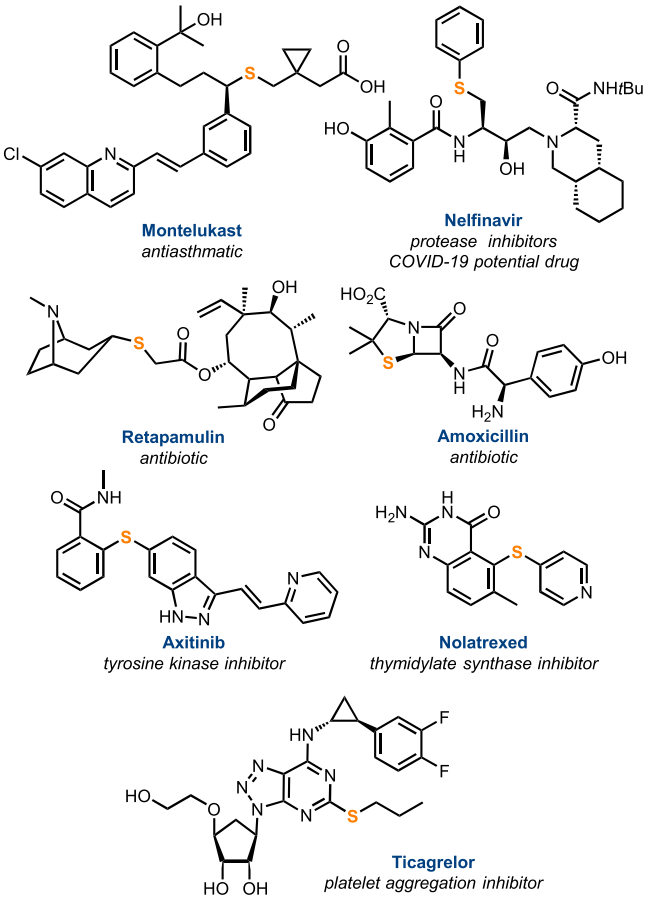
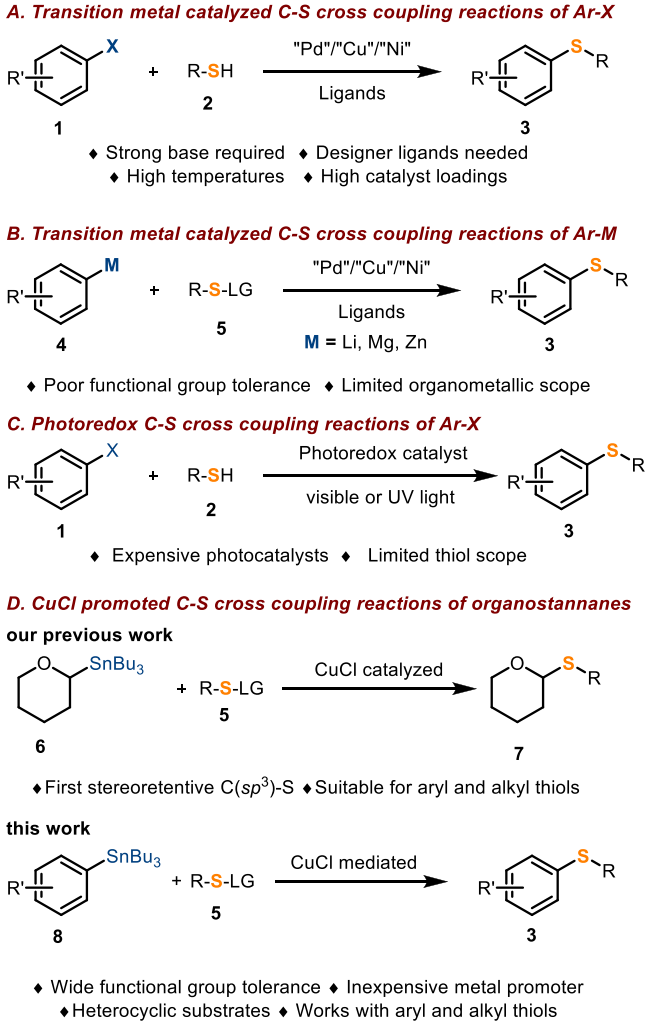


Figure 1. Selected pharmaceutical drugs featuring thioethers.

anomeric nucleophiles, as competent partners in the glycosyl cross-coupling.[13] These reactions proceed with high levels of anomeric stereoselectivity across a broad substrate scope. Inspired by the prior work on the stereoretentive cross-coupling reaction of configurationally stable C(sp^3) stannanes to construct a C(sp^3)−S bond,[13c] we wondered if unactivated C(sp^2) or C(sp^3) stannanes can also react with sulfur electrophiles to realize aromatic thioethers synthesis (Scheme 1D). Herein, we report a simple and ligand-free protocol for the synthesis of aromatic thioethers which can be achieved by coupling of aryl and alkyl stannanes with disulfides and *N*-sulfenylsuccinimide donors promoted by Cu(I).

For the initial optimizations of the reaction conditions, we selected tributyl(phenyl)stannane **9** and bis(4-methoxyphenyl) disulfide **10** as the model substrates (Table 1). Cu(I) additives were first examined on the basis of our recent reports.[13b,c] We were pleased to find that the reaction reached completion furnishing the desired product in 82% isolated yield when 1.5 equiv of CuCl and 2.0 equiv of KF were employed at 120 °C for 48 h (Table 1, entry 1). We next attempted to reduce the copper loading to 1.0 equiv and 0.5 equiv, and a marked decrease in yield was observed (Table 1, entries 2 and 3). However, the yields did not increase with higher loadings of CuCl to 3.0 equiv (Table 1, entry 4). Control experiments showed that CuCl was essential, but KF and a phosphine ligand (JackiePhos)[13c] are not necessary for the cross-coupling reaction (Table 1, entries 5−7). The role of KF is to facilitate the Sn/Cu transmetalation when the tin group is converted into insoluble Bu_3SnF and improve the efficiency of the reaction.[13b] Disulfide **10** was replaced with more active *N*-(4-

Scheme 1. Selected Methods for the Synthesis of Aromatic Thioethers



methoxyphenyl)thiosuccinimide resulting in a slightly improved yield, 86% (Table 1, entry 8). It showed that both disulfides and *N*-thiosuccinimides are good electrophilic sulfur reagents. When the ratio of **9** and **10** was changed from 1.5:1 to 1:1.5, the reaction yield reduced from 82% to 68% (Table 1, entry 9). The efficiency of this process was also reduced when a lower temperature (80 °C) was screened (Table 1, entry 10). Other common metals such as palladium and nickel salts were found to give a low yield (<30%) (Table 1, entry 11). Under the same conditions, a 1 mmol scale of tributyl(phenyl)-stannane could be completely transformed to afford 76% yield of the desired product.

With the optimized conditions in hand, we next evaluated the scope of the C−S cross-coupling protocol of C(sp^2) stannanes. Aryl and heteroaryl stannanes **12** were found to be suitable reaction partners in reactions with S(sp^2) and S(sp^3) electrophilic sulfur reagents to provide the corresponding aromatic thioethers shown in Scheme 2. *para*-Substituted aryl stannanes bearing benzyloxy and chloro groups engaged in the cross-couplings to forge C−S bonds in good yields (**14a** and **14b**). It is worth noting that the 2.5 mmol of (4-benzyloxyphenyl)tributylstannane could be coupled to afford the desired product without significant reduction of yield. We were delighted to find that aryl stannanes containing functional

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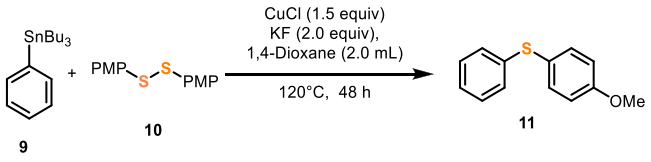
Table 1. Optimization of Electrophilic Thiolations with 9[a]

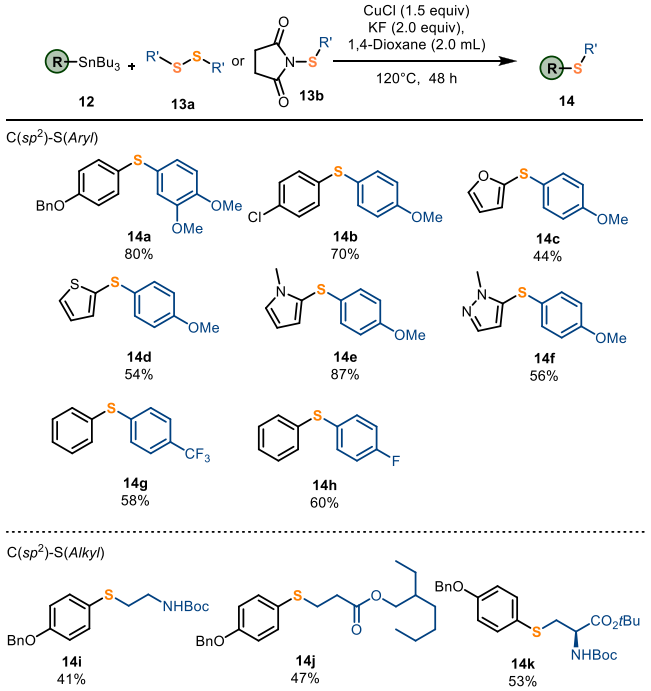


9 10 11

Entry	Variation from the standard conditions	Yield (%)[b]
1	none	82
2	1.0 equiv of CuCl instead of 1.5 equiv	52
3	0.5 equiv of CuCl instead of 1.5 equiv	28
4	3.0 equiv of CuCl instead of 1.5 equiv	82
5	no KF	45
6	no CuCl	ND
7	JackiePhos (100 mmoll%) added	38[c]
8	*N*-(4-methoxyphenyl)thiosuccinimide instead of disulfide	86
9	The ratio of **9**:**10** 1:1.5	68[d]
10	80 °C instead of 120 °C	
11	(50 mmol %) $PdCl_2$ or $NiCl_2$(DME) instead of CuCl	<30[c]

[a]General conditions: **9** (0.15 mmol), $(PMPS)_2$ (0.10 mmol), CuCl (1.5 equiv), KF (2.0 equiv), 1,4-dioxane (2.0 mL), 120 °C, 48 h, N_2. [b]Isolated yield. [c]CuCl (50 mmol %) and JackiePhos (100 mmol %) were used. [d]**9** (0.10 mmol), $(PMPS)_2$ (0.15 mmol). ND = not detected.

Scheme 2. Scope of C−S Cross-Coupling with Aryl Stannanes 12[a,b]

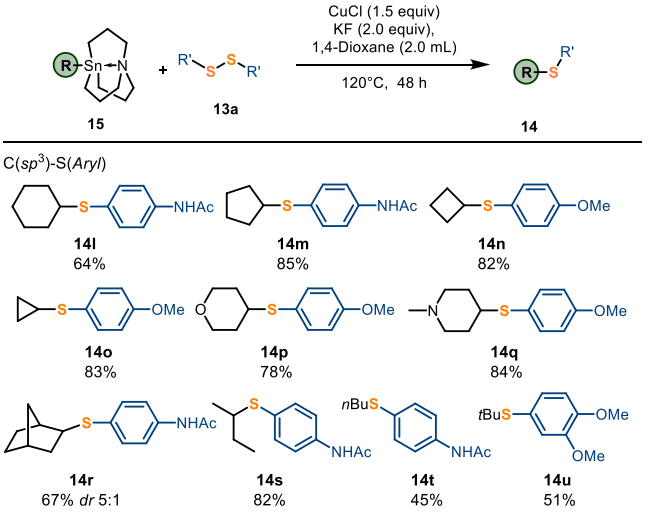


[a]General conditions: **12** (0.15 mmol), **13a** or **13b** (0.10 mmol), CuCl (1.5 equiv), KF (2.0 equiv), 1,4-dixoane (2.0 mL), 120 °C, 48 h, N_2. [b]Isolated yield.

groups suitable for downstream orthogonal transformations such as chlorine were coupled with complete chemoselectivity and good efficiencies to generate the thioether in 70% isolated yield (**14b**). A series of heterocyclic substrates such as furan-2-yl (**14c**), thiophen-2-yl (**14d**), 1-methyl-1*H*-pyrrol-2-yl (**14e**), and 1-methyl-1*H*-pyrazol-5-yl (**14f**) all proceeded well to give products in moderate to good yields (44%−87%). Disulfane reagents bearing trifluoromethyl and fluoro groups engaged in the cross-couplings to obtain the desired product in 58% and 60% yield, respectively (**14g** and **14h**). We also tested other reactions with (4-(benzyloxy)phenyl)tri-*n*-butylstannane and alkyl *N*-sulfenylsuccinimide as alkyl electrophilic sulfur reagents (**14i**−**14j**), because dialkyl disulfide are significantly less active. It is clear that the cross-coupling yields of alkyl electrophilic sulfur reagents (41% to 53%) are lower than in the case of the above-mentioned aryl electrophilic sulfur reagents. Meanwhile, functional groups such as esters and carbamates were well tolerated as demonstrated in the synthesis of S-aryl cysteine **14k**.

Next, we tested the scope of the C−S cross-coupling reaction using various alkyl stannanes (Scheme 3). Alkyl

Scheme 3. Scope of C−S Cross-Coupling with Alkyl Carbastannatranes



[a]General conditions: **15** (0.15 mmol), **13a** (0.10 mmol), CuCl (1.5 equiv), KF (2.0 equiv), 1,4-dioxane (2.0 mL), 120 °C, 48 h, N_2. [b]Isolated yield.

stannanes are considered as poor nucleophiles in the alkyl−aryl Stille couplings. In addition to a difficult reductive elimination, the key challenge in the Stille coupling is the selective transfer of an alkyl group when tetraalkylstannanes are used. A promising strategy reported in the literatures uses alkyl tin nucleophiles that bear an activated tin center such as heteroatoms and/or strongly coordinating substituents,[13,14] that have been shown to facilitate transmetalation of the intrinsically hindered, secondary alkyl centers. Carbastannatrane, reported in 1984, are attractive substrates due to their increased reactivity.[15] Compared with their tetraalkylorganostannane counterparts, alkyl carbastannatranes proceed via a selective alkyl transfer and are known to be air- and moisture-stable, as well as generally less toxic.[16] Inspired by these findings, we tested selected alkyl carbastannatranes under the previously optimized conditions (Scheme 3), we found that primary, secondary, and tertiary stannanes resulted in moderate to good yields of alkyl thioethers. Cyclic alkyl thioethers are a challenge to synthesize by traditional substitution methods,[17] and we found that cyclic carbastannatranes of three- to six-membered carbocycles smoothly underwent coupling to form thioether products **14l**−**14o**. Other heterocyclic compounds such as tetrahydro-2*H*-pyran-4-

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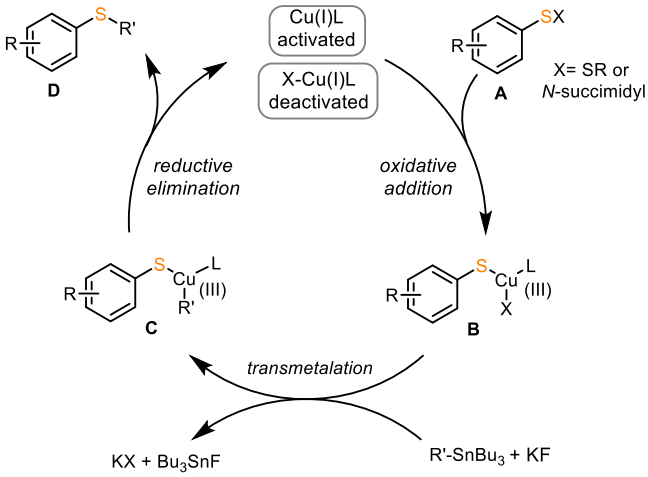
yl (**14p**) and 1-methylpiperidin-4-yl (**14q**) were well compatible under the standard conditions. Endocyclic carbastannatrane such as exo-2-norbornyl carbastannatranes gave **14r** in a moderate yield of 67% and *exo*/*endo dr* 5:1. Acyclic carbastannatranes were also employed to test the generality of this method—6-(*sec*-butyl)-1-aza-6-stannabicyclo-[4.3.3]dodecane afforded thioether **14s** in good yield, but 6-butyl-1-aza-6-stannabicyclo[4.3.3]dodecane gave a reduced yield of **14t** due to the lower nucleophilicity of the carbastannatrane substrate. It is noteworthy that sterically hindered 6-(*tert*-butyl)-1-aza-6-stannabicyclo[4.3.3]dodecane also delivered the C−S cross-coupling product **14u** in 51% yield. Taken together, these results indicate the potential application of the new method in the synthesis of sterically hindered aromatic thioethers.

To gain preliminary mechanistic information about the electrophilic thiolations of organostannanes, radical trapping experiments were carried out under the standard conditions. When coupling of **9** and **10** was attempted with 3 equiv of a free-radical inhibitor, 1,1-diphenylethylene, the product yield, was slightly reduced from 82% to 71%. This experiment indicates that the radical pathway is not operational under the optimized conditions. Based on the above experimental observations and the previous work from our group,[13c] a possible Cu(I)/Cu(III) mechanism for the C−S cross-coupling reaction is outlined in Scheme 4. First, the Cu(I)

Scheme 4. Proposed Mechanism for the C−S Cross-Coupling



species reacts with electrophilic sulfur reagents RS−X (X = SR, *N*-succimidyl) **A** to generate oxidative addition product LCu(SR)X **B**. Base-assisted transmetalation of organostannanes with product LCu(SR)X **B** occurs to form Cu(III) intermediate **C**, which then undergoes reductive elimination to give the final product **D** along with regeneration of the deactivated X−Cu(I)L such as RS−Cu species.[13c,18] Because of the potential coordination of sulfur atoms resulting in catalyst poisoning, a stoichiometric amount of copper is required. An alternative nucleophilic substitution mechanism of organostannanes and electrophilic sulfur reagents cannot be excluded at this point.[13d]

In summary, we have developed a simple and ligand-free method for the cross-coupling of aryl and alkyl stannanes with electrophilic sulfur reagents mediated by inexpensive Cu(I) salt. To the best of our knowledge, this study represents the first method that allows for direct coupling of aryl and unactivated alkyl stannanes with electrophilic sulfur reagents. The ability of the system to operate with high efficiency in the presence of alkyl carbastannatranes further enhances the practical utility of this method. We believe our method is a significant alternative to the current systems and will find widespread application in organic synthesis and drug discovery.

EXPERIMENTAL SECTION

General Information. All chemicals were purchased as reagent grade and used without further purification unless otherwise noted. Solvents were filtered through a column of activated alumina prior to use. All reactions were carried out under anhydrous N_2 in oven-dried glassware. Anhydrous 1,4-dioxane, CuCl, tributylphenylstannane, (4-(benzyloxy)phenyl)tributylstannane, tributyl(4-chlorophenyl)-stannane, tributyl(furan-2-yl)stannane, tributyl(thiophen-2-yl)-stannane, 1-methyl-2-(tributylstannyl)-1*H*-pyrrole, and 1-methyl-4-(tributylstannyl)-1*H*-pyrazole were purchased from Sigma-Aldrich. Alkyl lithium reagents, Grignard reagents, and zinc reagents were purchased from Sigma-Aldrich. Anhydrous KF was purchased from Strem Chemicals, Inc. Disulfane reagents were synthesized following the reported method.[13c] Visualizations were performed with UV light and/or Hanessian stain and/or sulfuric acid stain (5% H_2SO_4 in MeOH). Column chromatography was performed on silica gel (230−400 mesh). ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded on Bruker/Varian 300/400/500 MHz instruments and are reported as follows: chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. The residual solvent reference peaks were used from published literature. 2D NMR experiments were performed using standard parameters (*200 and More NMR Experiments*, S. Berger, S. Braun, Wiley-VCH, 2004). IR measurements were performed on an Agilent Cary 630 FT/IR instrument, and optical rotations were measured on a JASCO P-1030 and are reported as the average of five data points. High-resolution mass spectra (HR-MS) were recorded on a Waters Synapt G2 HDMS q-TOF hybrid mass spectrometer.

General Procedure A for Cross-Coupling Reactions. Stannane reagents (1.50 equiv), sulfide reagents (1.00 equiv), KF (2.00 equiv), and CuCl (1.50 equiv) were added to a one-dram vial with a screw-top septum, and the vial was then evacuated and refilled with N_2 (3×). Anhydrous 1,4-dioxane (2.00 mL) were added and the reaction mixture was heated in an oil bath (120 °C) for the indicated period of time, cooled to rt, filtered through a pad of Celite, and concentrated. The crude material was purified by column chromatography on SiO_2.

General Procedure B for the Preparation of Alkyl Azastannatranes. To a solution of 5-chloro-1-aza-5-stannabicyclo[3.3.3]-undecane (1.00 equiv) in anhydrous THF (5.00 mL) alkyl lithium/Grignard reagent solution (2.00−5.00 equiv) was added under N_2 at 0 °C. The mixture was allowed to stir for 15 min and then warmed up to rt. After stirring for 12 h, the reaction was quenched by H_2O (10.0 mL). The resulted mixture was then extracted with EtOAc (3 × 50.0 mL). The combined organic layer was dried over Na_2SO_4, concentrated, and vacuumed to afford the crude product. The crude alkyl tin reagents were used without further purification.

*1,2-Bis(4-methoxyphenyl)disulfane (**10**).* According to the reported literature,[13c] $NaBO_3{\cdot}H_2O$ (3.00 g, 30.0 mmol) was added to a stirring solution of 4-methoxybenzenethiol (1.90 mL, 15.0 mmol) in AcOH (40.0 mL) and H_2O (15.0 mL). The reaction mixture was stirred for 4 h and concentrated in vacuo. The crude mixture was purified via flash chromatography on SiO_2 (Hexanes/EtOAc, 50:1) to afford **10** (1.90 g, 87%) as a pale yellow solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50−7.33 (m, 4H), 6.94−6.68 (m, 4H), 3.80 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, CDCl3) δ 160.0, 132.8, 128.6, 114.7, 55.5. Characterization data matched the literature report.[13c]

*(4-Methoxyphenyl)(phenyl)sulfane (**11**).* According to the general protocol A, tributylphenylstannane (55.1 mg, 0.150 mmol), 1,2-bis(4-methoxyphenyl)disulfane (27.8 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for

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48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 25:1) **11** (17.7 mg, 82%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50−7.38 (m, 2H), 7.28−7.09 (m, 5H), 6.94−6.86 (m, 2H), 3.83 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 160.0, 138.8, 135.5, 129.1, 128.4, 125.9, 124.5, 115.1, 55.5. Characterization data matched the literature report.[19]

*(4-(Benzyloxy)phenyl)(3,4-dimethoxyphenyl)sulfane (**14a**).* According to the general protocol A, (4-(benzyloxy)phenyl)tributylstannane (71.0 mg, 0.150 mmol), 1,2-bis(3,4-dimethoxyphenyl)-disulfane (33.8 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 10:1) **14a** (28.2 mg, 80%) as a light yellow oil: IR (ATR) ν = 3067, 3033, 3003, 2933, 2840, 1592, 1495, 1465, 1443, 1398, 1253, 1235, 1179, 1141, 1030, 881, 829, 810, 743, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45−7.26 (m, 7H), 6.96−6.86 (m, 4H), 6.80 (d, J = 8.3 Hz, 1H), 5.07−5.03 (m, 2H), 3.86 (s, 3H), 3.81 (d, J = 0.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 158.3, 149.5, 148.7, 136.8, 132.7, 128.8, 128.2, 127.7 (2), 127.6, 124.2, 115.9, 114.6, 111.9, 70.3, 56.1, 56.1; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{21}H_{20}O_3SNa$ 375.1025; found 375.1027.

According to the general protocol A, (4-(benzyloxy)phenyl)-tributylstannane (1.20 g, 2.50 mmol), 1,2-bis(3,4-dimethoxyphenyl)-disulfane (0.57 g, 1.67 mmol), KF (192 mg, 3.34 mmol), and CuCl (248 mg, 2.50 mmol) were added to anhydrous 1,4-dioxane (33.0 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 10:1) **14a** (845 mg, 72%).

*(4-Chlorophenyl)(4-methoxyphenyl)sulfane (**14b**).* According to the general protocol A, tributyl(4-chlorophenyl)stannane (60.2 mg, 0.150 mmol), 1,2-bis(4-methoxyphenyl)disulfane (27.8 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 10:1) **14b** (17.6 mg, 70%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.37 (m, 2H), 7.22−7.16 (m, 2H), 7.11−7.04 (m, 2H), 6.95−6.87 (m, 2H), 3.83 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 160.2, 137.5, 135.6, 133.1, 131.8, 129.5, 129.2, 115.3, 55.5. Characterization data matched the literature report.[20]

*2-((4-Methoxyphenyl)thio)furan (**14c**).* According to the general protocol A, tributyl(furan-2-yl)stannane (55.6 mg, 0.150 mmol), 1,2-bis(4-methoxyphenyl)disulfane (27.8 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 20:1) **14c** (9.00 mg, 44%) as a colorless oil: IR (ATR) ν = 2959, 2933, 2840, 1595, 1499, 1465, 1290, 1249, 1179, 1156, 1037, 1011, 911, 829, 750 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (dd, J = 2.0, 0.9 Hz, 1H), 7.28−7.21 (m, 2H), 6.86−6.80 (m, 2H), 6.64 (dd, J = 3.2, 0.9 Hz, 1H), 6.41 (dd, J = 3.3, 2.0 Hz, 1H), 3.77 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 159.2, 146.1, 133.1, 131.4, 126.1, 117.9, 114.9, 111.8, 55.5; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{11}H_{11}O_2SH$ 207.0474; found 207.0470.

*2-((4-Methoxyphenyl)thio)thiophene (**14d**).* According to the general protocol A, tributyl(thiophen-2-yl)stannane (56.0 mg, 0.150 mmol), 1,2-bis(4-methoxyphenyl)disulfane (27.8 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 20:1) **14d** (12.0 mg, 54%) as a light yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (dd, J = 5.4, 1.2 Hz, 1H), 7.30−7.27 (m, 2H), 7.21 (dd, J = 3.6, 1.3 Hz, 1H), 7.00 (dd, J = 5.3, 3.5 Hz, 1H), 6.87−6.78 (m, 2H), 3.78 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 159.1, 134.0, 133.1, 131.3, 130.2, 128.5, 127.8, 114.8, 55.5. Characterization data matched the literature report.[21]

*2-((4-Methoxyphenyl)thio)-1-methyl-1H-pyrrole (**14e**).* According to the general protocol A, 1-methyl-2-(tributylstannyl)-1*H*-pyrrole (55.5 mg, 0.150 mmol), 1,2-bis(4-methoxyphenyl)disulfane (27.8 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 10:1) **14e** (19.1 mg, 87%) as a light yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.04−6.96 (m, 2H), 6.87−6.83 (m, 1H), 6.82−6.74 (m, 2H), 6.55 (dd, J = 3.7, 1.8 Hz, 1H), 6.24−6.16 (m, 1H), 3.76 (s, 3H), 3.57 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 158.1, 133.0, 129.3, 128.2, 125.8, 119.1, 114.8, 108.3, 55.5, 34.2. Characterization data matched the literature report.[22]

*4-((4-Methoxyphenyl)thio)-1-methyl-1H-pyrazole (**14f**).* According to the general protocol A, 1-methyl-4-(tributylstannyl)-1*H*-pyrazole (55.7 mg, 0.150 mmol), 1,2-bis(4-methoxyphenyl)disulfane (27.8 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 3:1) **14f** (12.3 mg, 56%) as a light yellow oil: IR (ATR) ν = 3123, 2936, 2840, 1596, 1577, 1521, 1496, 1465, 1443, 1290, 1246, 1179, 1123, 1033, 981, 829, 709, 661 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58−7.43 (m, 2H), 7.19−7.12 (m, 2H), 6.84−6.74 (m, 2H), 3.90 (s, 3H), 3.76 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 158.4, 144.1, 134.5, 129.7, 129.2, 114.7, 55.5, 39.4; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{11}H_{13}OSN_2$ 221.0743; found 221.0739.

*(4-Trifluoromethyl)phenyl)(phenyl)sulfane (**14g**).* According to the general protocol A, tributylphenylstannane (55.1 mg, 0.150 mmol), 1,2-bis(4-(trifluoromethyl)phenyl)disulfane (35.4 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO2 (Hexanes/EtOAc, 30:1) **14g** (14.8 mg, 58%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48−7.38 (m, 4H), 7.38−7.27 (m, 3H), 7.25−7.19 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 143.0 (J(C−F) = 1.5), 133.7, 132.6, 129.8, 128.8, 128.4, 128.0, 143.0 (J(C−F) = 3.9), 122.4. Characterization data matched the literature report.[23]

*(4-Fluorophenyl)(phenyl)sulfane (**14h**).* According to the general protocol A, tributylphenylstannane (55.1 mg, 0.150 mmol), 1,2-bis(4-fluorophenyl)disulfane (25.4 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 30:1) **14h** (12.1 mg, 60%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.28 (m, 2H), 7.27−7.12 (m, 5H), 7.05−6.90 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 164.2 and 160.9 (J(C−F) = 247.7 Hz), 136.8, 134.3, and 134.2 (J(C−F) = 8.2 Hz), 130.4 and 130.3 (J(C−F) = 3.5 Hz), 130.1, 129.3, 126.9, 116.7, and 116.4 (J(C−F) = 22.1 Hz). Characterization data matched the literature report.[24]

*tert-Butyl (2-((4-(Benzyloxy)phenyl)thio)ethyl)carbamate (**14i**).* According to the general protocol A, (4-(benzyloxy)phenyl)tributylstannane (71.0 mg, 0.150 mmol), *tert*-butyl (2-((2,5-dioxopyrrolidin-1-yl)thio)ethyl)carbamate (27.4 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 10:1) **14i** (14.7 mg, 41%) as a colorless oil: IR (ATR) ν = 3424, 3362, 2977, 2929, 1704, 1596, 1495, 1458, 1395, 1369, 1246, 1171, 1026, 952, 829, 739, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44−7.31 (m, 7H), 6.97−6.87 (m, 2H), 5.05 (s, 2H), 1.43 (s, 9H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 158.6, 155.9, 136.8, 133.8, 128.8, 128.2, 127.6, 125.6, 115.8, 79.6, 70.3, 39.6, 36.3, 28.5; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{20}H_{25}O_3SNNa$ 382.1447; found 382.1450.

*2-Ethylhexyl 3-((4-(Benzyloxy)phenyl)thio)propanoate (**14j**).* According to the general protocol A, (4-(benzyloxy)phenyl)tributylstannane (71.0 mg, 0.150 mmol), 2-ethylhexyl 3-((2,5-dioxopyrrolidin-1-yl)thio)propanoate (31.5 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to

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anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 25:1) **14j** (18.8 mg, 47%) as a colorless oil: IR (ATR) ν = 3342, 2987, 2945, 1710, 1596, 1490, 1458, 1403, 1365, 1243, 1168, 1020, 957, 819, 734, 690 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46−7.30 (m, 7H), 6.96−6.88 (m, 2H), 5.05 (s, 2H), 3.99 (dd, J = 5.8, 1.2 Hz, 2H), 3.05 (t, J = 7.4 Hz, 2H), 2.57 (t, J = 7.4 Hz, 2H), 1.32−1.22 (m, 8H), 0.95−0.82 (m, 7H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 172.2, 158.6, 136.8, 134.2, 128.8, 128.2, 127.6, 125.8, 115.7, 70.3, 67.3, 38.9, 34.8, 31.2, 30.5, 29.1, 23.9, 23.1, 14.2, 11.1; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{24}H_{32}O_3SNa$ 423.1964; found 423.1971.

*tert-Butyl S-(4-(Benzyloxy)phenyl)-N-(tert-butoxycarbonyl)-L-cysteinate (**14k**).* According to the general protocol A, (4-(benzyloxy)-phenyl)tributylstannane (71.0 mg, 0.150 mmol), *tert*-butyl *N*-(*tert*-butoxycarbonyl)-*S*-(2,5-dioxopyrrolidin-1-yl)-L-cysteinate (37.4 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 8:1) **14k** (24.4 mg, 53%) as a colorless oil: IR (ATR) ν = 3442, 3350, 2982, 2955, 1710, 1594, 1496, 1458, 1400, 1368, 1247, 1165, 1024, 957, 823, 736, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44−7.29 (m, 7H), 6.93−6.84 (m, 2H), 5.29−5.16 (m, 1H), 5.04 (s, 2H), 4.39 (d, J = 6.6 Hz, 1H), 3.39−3.02 (m, 2H), 1.46−1.39 (m, 18H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 169.9, 158.6, 155.1, 136.8, 135.0, 132.8, 128.8, 128.2, 127.6, 115.8, 82.6, 70.3, 54.3, 39.0, 28.4, 28.1; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{25}H_{33}O_5SNNa$ 482.1972; found 482.1978.

*Cyclohexyl(4-acetylaminophenyl)sulfane (**14l**).* According to the general protocol B, to a solution of 5-chloro-1-aza-5-stannabicyclo-[3.3.3]undecane (150 mg, 0.510 mmol) in anhydrous THF (5.00 mL) was added cyclohexylmagnesium chloride solution (1.53 mL, 1.53 mmol, 1.0 M in methyltetrahydrofuran) under N_2 at 0 °C. The mixture was allowed to stir for 15 min and then warmed up to rt. After stirring for 12 h, the reaction was quenched by H_2O (10.0 mL). The resulted mixture was then extracted with EtOAc (3 × 50.0 mL). The combined organic layer was dried over Na_2SO_4, concentrated, and vacuumed to afford the crude product (147 mg, 84%) as a light-yellow oil. The crude alkyl tin reagents were used without further purification. According to the general protocol A, 5-cyclohexyl-1-aza-5-stannabicyclo[3.3.3]undecane[25] (51.3 mg, 0.150 mmol), 1,2-bis(4-acetylaminophenyl)disulfane (33.2 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 100:1) **14l** (16.0 mg, 64%) as a white foam: ^1H NMR (300 MHz, $CDCl_3$) δ 7.51−7.29 (m, 5H), 2.99 (td, J = 10.3, 3.6 Hz, 1H), 2.16 (s, 3H), 2.02−1.84 (m, 2H), 1.81−1.75 (m, 2H), 1.44−1.13 (m, 6H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 168.5, 137.1, 133.8, 130.1, 120.3, 47.5, 33.5, 26.2, 25.9, 24.7. Characterization data matched the literature report.[26]

*N-(4-(Cyclopentylthio)phenyl)acetamide (**14m**).* According to the general protocol B, to a solution of 5-chloro-1-aza-5-stannabicyclo-[3.3.3]undecane (200 mg, 0.680 mmol) in anhydrous THF (5.00 mL) was added cyclopentylmagnesium bromidee solution (2.00 mL, 2.00 mmol, 1.0 M in tetrahydrofuran) under N_2 at 0 °C. The mixture was allowed to stir for 15 min and then warmed up to rt. After stirring for 12 h, the reaction was quenched by H_2O (10.0 mL). The resulted mixture was then extracted with EtOAc (3 × 50.0 mL). The combined organic layer was dried over Na_2SO_4, concentrated, and vacuumed to afford the crude product (159 mg, 74%) as light-yellow oil. The crude alkyl tin reagents were used without further purification. According to the general protocol A, the above crude 5-cyclopentyl-1-aza-5-stannabicyclo[3.3.3]undecane (49.2 mg, 0.150 mmol), *N*,*N*′-(disulfanediylbis(4,1-phenylene))diacetamide (33.2 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 2:1) **14m** (20.0 mg, 85%) as a light yellow oil: IR (ATR) ν = 3294, 3249, 3175, 3108, 3052, 2929, 2854, 1666, 1599, 1544, 1495, 1451, 1398, 1324, 1261, 1182, 1097, 1019, 836, 747 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.55−7.38 (m, 3H), 7.36−7.28 (m, 2H), 3.51 (dq, J = 13.3, 7.1, 6.3 Hz, 1H), 2.15 (s, 3H), 2.07−1.92 (m, 2H), 1.88−1.46 (m, 6H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 168.5, 136.5, 132.2, 131.8, 120.4, 46.9, 33.6, 24.8, 24.7; HRMS (ESI) m/z calcd for $C_{13}H_{17}OSNNa$ $[M + Na]^+$ 258.0929; found 258.0930. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{13}H_{17}OSNNa$ 258.0923; found 258.0926.

*Cyclobutyl(4-methoxyphenyl)sulfane (**14n**).* According to the general protocol B, to a solution of 5-chloro-1-aza-5-stannabicyclo-[3.3.3]undecane (150 mg, 0.510 mmol) in anhydrous THF (5.00 mL) was added cyclobutylmagnesium bromide solution (3.10 mL, 1.55 mmol, 0.5 M in methyltetrahydrofuran) under N_2 at 0 °C. The mixture was allowed to stir for 15 min and then warmed up to rt. After stirring for 12 h, the reaction was quenched by H_2O (10.0 mL). The resulted mixture was then extracted with EtOAc (3 × 50.0 mL). The combined organic layer was dried over Na_2SO_4, concentrated, and vacuumed to afford the crude product (151 mg, 91%) as a yellow oil. The crude alkyl tin reagents were used without further purification. According to the general protocol A, the above crude 5-cyclobutyl-1-aza-5-stannabicyclo[3.3.3]undecane (47.1 mg, 0.150 mmol), 1,2-bis(4-methoxyphenyl)disulfane (27.8 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 100:1) **14n** (15.7 mg, 82%) as a colorless oil: IR (ATR) ν = 2940, 2858, 2836, 1596, 1573, 1495, 1465, 1443, 1287, 1246, 1179, 1104, 1033, 829, 713 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34−7.26 (m, 2H), 6.90−6.79 (m, 2H), 3.79 (s, 3H), 3.78−3.66 (m, 1H), 2.39−2.25 (m, 2H), 2.10−1.81 (m, 4H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 159.0, 133.6, 126.3, 114.5, 55.4, 42.1, 30.6, 18.5; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{11}H_{15}OS$ 195.0838; found 195.0844.

*Cyclopropyl(4-methoxyphenyl)sulfane (**14o**).* According to the general protocol B, to a solution of 5-chloro-1-aza-5-stannabicyclo-[3.3.3]undecane (100 mg, 0.340 mmol) in anhydrous THF (5.00 mL) was added cyclobutylmagnesium bromide solution (2.80 mL, 1.68 mmol, 0.6 M in THF) under N_2 at 0 °C. The mixture was allowed to stir for 15 min and then warmed up to rt. After stirring for 12 h, the reaction was quenched by H_2O (10.0 mL). The resulted mixture was then extracted with EtOAc (3 × 50.0 mL). The combined organic layer was dried over Na_2SO_4, concentrated, and vacuumed to afford the crude product (81.6 mg, 80%) as a light-yellow oil. The crude alkyl tin reagents were used without further purification. According to the general protocol A, the above crude 5-cyclopropyl-1-aza-5-stannabicyclo[3.3.3]undecane (45.0 mg, 0.150 mmol), 1,2-bis(4-methoxyphenyl)disulfane (27.8 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 100:1) **14o** (15.0 mg, 83%) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.45−7.31 (m, 2H), 6.89−6.74 (m, 2H), 3.80 (s, 3H), 2.18 (tt, J = 7.4, 4.4 Hz, 1H), 1.04−0.93 (m, 2H), 0.74−0.59 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 158.3, 130.1, 128.9, 114.6, 55.5, 14.2, 8.6. Characterization data matched the literature report.[27]

*4-((4-Methoxyphenyl)thio)tetrahydro-2H-pyran (**14p**).* According to the general protocol B, to a solution of 5-chloro-1-aza-5-stannabicyclo[3.3.3]undecane (100 mg, 0.340 mmol) in anhydrous THF (5.00 mL) was added (tetrahydro-2*H*-pyran-4-yl)magnesium chloride solution (3.36 mL, 1.68 mmol, 0.5 M in THF) under N_2 at 0 °C. The mixture was allowed to stir for 15 min and then warmed up to rt. After stirring for 12 h, the reaction was quenched by H_2O (10.0 mL). The resulted mixture was then extracted with EtOAc (3 × 50.0 mL). The combined organic layer was dried over Na_2SO_4, concentrated, and vacuumed to afford the crude product (103.3 mg, 88%) as a yellow solid. The crude alkyl tin reagents were used without further purification. According to the general protocol A, the above crude 5-(tetrahydro-2*H*-pyran-4-yl)-1-aza-5-stannabicyclo-

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[3.3.3]undecane[28] (51.6 mg, 0.150 mmol), 1,2-bis(4-methoxyphenyl)-disulfane (22.8 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 40:1) **14p** (17.5 mg, 78%) as a colorless oil: IR (ATR) ν = 2948, 2840, 1596, 1495, 1465, 1447, 1387, 1290, 1249, 1179, 1134, 1089, 1033, 1011, 985, 888, 832 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50−7.34 (m, 2H), 6.92−6.71 (m, 2H), 4.03−3.90 (m, 2H), 3.80 (s, 3H), 3.38 (ddd, J = 11.6, 10.8, 2.4 Hz, 2H), 3.07 (tt, J = 10.8, 4.1 Hz, 1H), 1.95−1.79 (m, 2H), 1.70−1.49 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 159.8, 136.3, 123.7, 114.6, 67.5, 55.4, 44.7, 33.3; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{12}H_{17}O_2S$ 225.0944; found 225.0941.

*4-((4-Methoxyphenyl)thio)-1-methylpiperidine (**14q**).* According to the general protocol B, to a solution of 5-chloro-1-aza-5-stannabicyclo[3.3.3]undecane (100 mg, 0.340 mmol) in anhydrous THF (5.00 mL) was added (tetrahydro-2*H*-pyran-4-yl)magnesium chloride solution (2.80 mL, 1.68 mmol, 0.6 M in THF) under N_2 at 0 °C. The mixture was allowed to stir for 15 min and then warmed up to rt. After stirring for 12 h, the reaction was quenched by H_2O (10.0 mL). The resulted mixture was then extracted with EtOAc (3 × 50.0 mL). The combined organic layer was dried over Na_2SO_4, concentrated, and vacuumed to afford the crude product (102 mg, 84%) as a yellow solid. The crude alkyl tin reagents were used without further purification. According to the general protocol A, the above crude 5-(1-methylpiperidin-4-yl)-1-aza-5-stannabicyclo[3.3.3]-undecane[24] (53.6 mg, 0.150 mmol), 1,2-bis(4-methoxyphenyl)-disulfane (22.8 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (DCM:MeOH, 15:1) **14q** (19.9 mg, 84%) as a colorless oil: IR (ATR) ν = 3417, 2940, 2840, 2784, 2735, 2672, 2471, 1596, 1495, 1469, 1380, 1287, 1249, 1179, 1130, 1108, 1033, 1000, 978, 832 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ δ 7.44−7.34 (m, 2H), 6.91−6.75 (m, 2H), 3.79 (s, 3H), 2.91−2.84 (m, 3H), 2.31 (s, 3H), 2.23−2.08 (m, 2H), 2.04−1.92 (m, 2H), 1.68 (dtd, J = 13.7, 10.0, 3.7 Hz, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 159.8, 136.1, 124.0, 114.6, 55.5, 54.7, 45.9, 44.6, 31.8; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{13}H_{20}ONS$ 238.1260; found 238.1259.

*(Bicyclo[2.2.1]heptan-2-yl)(4-methoxyphenyl)sulfane (**14r**).* According to the general protocol B, to a solution of 5-chloro-1-aza-5-stannabicyclo[3.3.3]undecane (100 mg, 0.340 mmol) in anhydrous THF (5.00 mL) was added *exo*-2-norbornylzinc bromide solution (3.36 mL, 1.68 mmol, 0.5 M in THF) under N_2 at 0 °C. The mixture was allowed to stir for 15 min and then heated at 80 °C. After stirring for 12 h, the reaction was quenched by H_2O (10.0 mL). The resulted mixture was then extracted with EtOAc (3 × 50.0 mL). The combined organic layer was dried over Na_2SO_4, concentrated, and vacuumed to afford the crude product (118 mg, 98%) as a light-yellow oil. The crude alkyl tin reagents were used without further purification. According to the general protocol A, the above crude 5-(exo-2-norbornyl)-1-aza-5-stannabicyclo[3.3.3]undecane (53.1 mg, 0.150 mmol), *N*,*N*′-(disulfanediylbis(4,1-phenylene))diacetamide (33.2 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 3:1) **14r** (17.5 mg, 67%) as a colorless oil: IR (ATR) ν = 3298, 3178, 3104, 3048, 2951, 2869, 1666, 1596, 1536, 1495, 1454, 1398, 1376, 1320, 1261, 1182, 1097, 1019, 970, 832, 736 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ δ 7.57−7.26 (m, 5H), 3.11 (ddd, J = 8.3, 4.5, 1.7 Hz, 1H), 2.34−2.19 (m, 2H), 2.16 (s, 3H), 1.84−1.09 (m, 10H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 168.4, 136.2, 132.8, 130.9, 120.5, 77.2, 49.3, 42.4, 38.6, 36.7, 35.6, 29.0, 28.8, 24.7; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{15}H_{19}ONSNa$ 284.1080; found 284.1075.

*1-Methylpropyl(4-acetylaminophenyl)sulfane (**14s**).* According to the general protocol B, to a solution of 5-chloro-1-aza-5-stannabicyclo[3.3.3]undecane(300 mg, 1.02 mmol) in anhydrous THF (5.00 mL) was added *s*-butyllithum solution (3.60 mL, 5.10 mmol, 1.40 M in hexane) under N_2 at 0 °C. The mixture was allowed to stir for 15 min and then warmed up to rt. After stirring for 12 h, the reaction was quenched by H_2O (10.0 mL). The resulted mixture was then extracted with EtOAc (3 × 50.0 mL). The combined organic layer was dried over Na_2SO_4, concentrated, and vacuumed to afford the crude product (290 mg, 92%) as a yellow oil. The crude alkyl tin reagents were used without further purification. According to the general protocol A, the above crude 5-(1-methylpropyl)-1-aza-5-stannabicyclo[3.3.3]undecane[25] (63.2 mg, 0.200 mmol), 1,2-bis(4-acetylaminophenyl)disulfane (33.2 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (19.8 mg, 0.200 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 100:1) **14s** (18.3 mg, 82%) as a yellow oil: IR (ATR) ν = 3301, 3178, 3104, 3048, 2966, 2925, 2877, 1670, 1596, 1532, 1499, 1462, 1398, 1376, 1316, 1294, 1261, 1019, 832 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51−7.27 (m, 4H), 3.06 (h, J = 6.7 Hz, 1H), 2.17 (s, 3H), 1.67−1.56 (m, 1H), 1.49 (dt, J = 14.1, 7.1 Hz, 1H), 1.24 (d, J = 6.7 Hz, 3H), 0.99 (t, J = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 168.4, 137.1, 133.8, 130.4, 120.2, 45.8, 29.5, 24.8, 20.6, 11.6; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{12}H_{17}ONSNa$ 246.0923; found 249.0926.

*n-Butyl(4-acetylaminophenyl)sulfane (**14t**).* According to the general protocol B, to a solution of 5-chloro-1-aza-5-stannabicyclo-[3.3.3]undecane (150 mg, 0.510 mmol) in anhydrous THF (5.00 mL) was added *n*-BuLi (0.410 mL, 1.02 mmol, 2.5 M in hexane) under N_2 at 0 °C. The mixture was allowed to stir for 15 min and then warmed up to rt. After stirring for 12 h, the reaction was quenched by H_2O (10.0 mL). The resulted mixture was then extracted with EtOAc (3 × 50.0 mL). The combined organic layer was dried over Na_2SO_4, concentrated, and vacuumed to afford the crude product (147 mg, 91%) as a dark yellow oil. The crude alkyl tin reagents were used without further purification. According to the general protocol B, the above crude 5-butyl-1-aza-5-stannabicyclo[3.3.3]undecane (47.6 mg, 0.150 mmol), 1,2-bis(4-acetylaminophenyl)disulfane (33.2 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 100:1) **14t** (10.0 mg, 45%) as a white foam: IR (ATR) ν = 3309, 3108, 3056, 2959, 2929, 2873, 1670, 1599, 1536, 1499, 1397, 1376, 1320, 1261, 1097, 1019, 825 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.52−7.39 (m, 2H), 7.30 (td, J = 6.7, 3.2 Hz, 3H), 2.93−2.80 (m, 2H), 2.16 (s, 3H), 1.65−1.50 (m, 2H), 1.48−1.33 (m, 2H), 0.90 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 168.4, 136.3, 132.1, 130.7, 120.5, 34.3, 31.4, 24.7, 22.0, 13.8; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{12}H_{17}ONSNa$ 246.0923; found 249.0922.

*tert-Butyl(3,4-dimethoxyphenyl)sulfane (**14u**).* According to the general protocol A, to a solution of 5-chloro-1-aza-5-stannabicyclo-[3.3.3]undecane (200 mg, 0.680 mmol) in anhydrous THF (5.00 mL) was added *tert*-butylmagnesium chloride (1.70 mL, 3.40 mmol, 2.0 M in diethyl ether) under N_2 at 0 °C. The mixture was allowed to stir for 15 min and then warmed up to rt. After stirring for 12 h, the reaction was quenched by H_2O (10 mL). The resulted mixture was then extracted with EtOAc (3 × 50.0 mL). The combined organic layer was dried over Na_2SO_4, concentrated, and vacuumed to afford the crude product (159 mg, 74%) as white foam. The crude alkyl tin reagents were used without further purification. According to the general protocol B, the above crude 5-(*tert*-butyl)-1-aza-5-stannabicyclo[3.3.3]undecane (47.7 mg, 0.150 mmol), 1,2-bis(3,4-dimethoxyphenyl)disulfane (33.8 mg, 0.100 mmol), KF (11.6 mg, 0.200 mmol), and CuCl (14.9 mg, 0.150 mmol) were added to anhydrous 1,4-dioxane (2.00 mL). The reaction mixture was stirred at 120 °C for 48 h and afforded after chromatographic purification on SiO_2 (Hexanes/EtOAc, 100:1) **14u** (11.5 mg, 51%) as a colorless oil: IR (ATR) ν = 2962, 2933, 2862, 1737, 1588, 1506, 1462, 1395, 1320, 1257, 1235, 1179, 1141, 1030, 862, 814, 769, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.11 (dd, J = 8.2, 2.1 Hz, 1H), 7.03 (d, J = 2.0 Hz, 1H), 6.83 (d, J = 8.2 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 1.28 (s,

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9H); $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 150.0, 148.5, 130.6, 124.0, 120.5, 111.0, 56.1, 56.0, 45.9, 31.0; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{12}H_{18}O_2SNa$ 249.0925; found 249.0923.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c01399.

Experimental procedures, characterization data of all new compound, and copies of NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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