JOC The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b01500 • Publication Date (Web): 03 Jul 2017

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Mechanistic Studies of Formal Thioboration Reactions of Alkynes

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ABSTRACT: Several formal heteroborylative cyclization reactions have been recently reported, but little physical-organic and mechanistic data is known. We now investigate the catalyst-free formal thioboration reaction of alkynes to gain mechanistic insight into *B*-chlorocatecholborane (ClBcat) in its new role as an alkynophilic Lewis acid in electrophilic cyclization/dealkylation reactions. In kinetic studies, the reaction is second order globally; first order with respect to both the 2-alkynylthioanisole substrate and the ClBcat electrophile, with activation parameters of $\Delta G^{\ddagger}$ = 27.1 ± 0.1 kcal mol^{-1} at 90 °C, $\Delta H^{\ddagger}$ = 13.8 ± 1.0 kcal mol^{-1} and $\Delta S^{\ddagger}$ = −37 ± 3 cal mol^{-1} K^{-1}, measured over the range of 70–90 °C. Carbon kinetic isotope effects supported a rate-determining Ad_E3 mechanism wherein alkyne activation by neutral ClBcat is concerted with cyclative attack by nucleophilic sulfur. A Hammett study found a ρ^+ of −1.7, suggesting cationic charge buildup during the cyclization and supporting rate-determining concerted cyclization. Studies of the reaction with tris(pentafluorophenyl)borane ($B(C_6F_5)_3$), an activating agent capable of cyclization but not dealkylation, resulted in the isolation of a post-cyclization zwitterionic intermediate. Kinetic studies via UV-vis spectroscopy with this boron reagent found second order kinetics, supporting the likely relevancy of intermediates in this system to the ClBcat system. Computational studies comparing ClBcat with BCl_3 as an activating agent showed why BCl_3, in contrast to ClBcat, failed to mediate the complete the cyclization/demethylation reaction sequence by itself. Overall, the results support a mechanism in which the ClBcat reagent serves a bifunctional role by sequentially activating the alkyne, despite being less electrophilic than other known alkyne-activating reagents, then providing chloride for post-rate-determining demethylation/neutralization of the resulting zwitterionic intermediate.

INTRODUCTION

Addition of boron/sulfur, boron/oxygen, and boron/nitrogen formal equivalents to C–C π bonds is an under-applied area of methodology, despite its promising efficiency in the synthesis of synthetically and biologically useful heterocycles. Substantial recent work has shown that the highly electrophilic $B(C_6F_5)_3$ can activate alkynes towards nucleophilic cyclization.[1–4] The resulting zwitterionic heterocycles, however, contain a carbon–$B(C_6F_5)_3$ bond, which is unreactive for the rich downstream Suzuki cross-coupling reactivity of boron (example, Figure 1a[3]). This limits their utility as synthetic building blocks. The development of methods that effect boron/heteroatom additions while retaining the synthetic versatility of boron would thus be of high impact. We recently reported that the commercially available *B*-chlorocatecholborane (ClBcat) effects boron/oxygen and boron/sulfur heterocyclizations,[5,6] and Fu extended this methodology to boron/nitrogen heterocyclization[7] (Figure 1b). Subsequently, Ingleson found that BCl_3 was sufficiently electrophilic to bring about oxyboration and thioboration reactions of alkynes at 20 °C, albeit with additional reagents to promote thioboration (Figure 1c).[8,9]

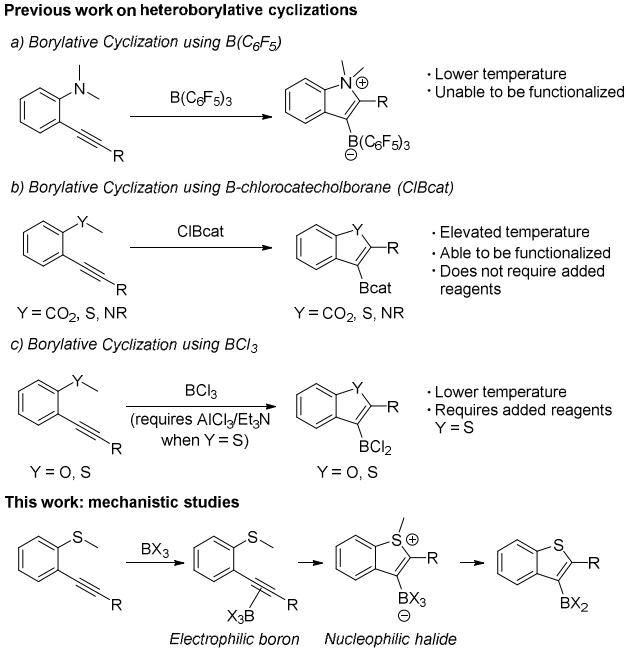
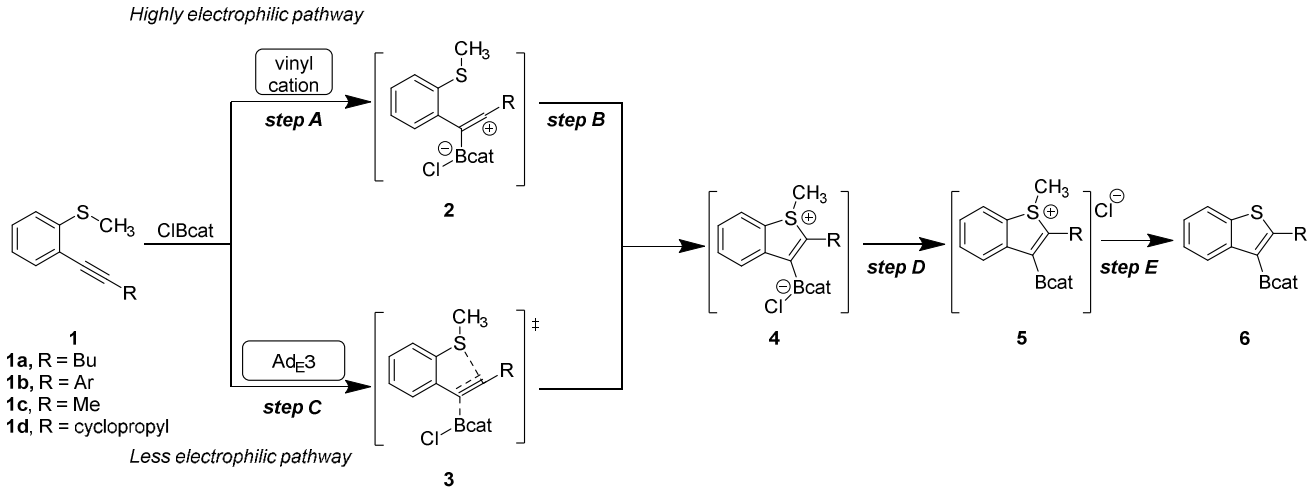


Figure 1. Previous work on catalyst-free borylative cycli-

zations and this work on mechanistic elucidation of the thioboration reaction.

Scheme 1. Two Possible Mechanistic Pathways for Thioboration with ClBcat



In the reactions with ClBcat, we hypothesized that the reagent is bifunctional, first serving as an electrophile to activate the alkyne and second as a source of nucleophilic chloride that demethylates the resulting zwitterion (Scheme 1). This two-step process produces a neutral heterocyclic boron building block primed for subsequent cross-coupling and other synthetically useful reactivity. The success of the ClBcat reagent was surprising in light of the substantially attenuated electrophilicity of ClBcat when compared to the previously reported $B(C_6F_5)_3$. The demethylation in the BCl_3 reactions of Ingleson proceeded without intervention for oxygen nucleophiles. Sulfur nucleophiles, however, required addition of stoichiometric $AlCl_3$ as a Lewis acid and Et_3N as a Lewis base in order to induce chloride release and demethylation, ultimately forming $[Et_3NCH_3][AlCl_4]$. It appears that the balance between the boron reagent's electrophiliciy and its ability to later dissociate chloride is key to the development of a wider family of reactions that access neutral rather than zwitterionic final borylated heterocyles.

These observations open the possibility of a suite of related new reactions employing related boron reagents that may have been previously dismissed as insufficiently electrophilic to effect borylative heterocylizations. Pressing mechanistic questions arise, the answers to which will facilitate the development of optimal reagents for synthetically useful transformations: What is the nature of activation of the alkyne given the lower electrophilicity of ClBcat (and is this nature nevertheless similar to the previously used reagent $B(C_6F_5)_3$), what are the structures and the reactivities of the reaction intermediates, and how do different reagents compare? Here, we present a comprehensive study into ClBcat-induced cyclative thioboration to answer these questions. The results provide guiding principles for developing related borylative cyclization/dealkylation reactions.

RESULTS AND DISCUSSION

Carbophilic Lewis Acid Activation Mechanistic Proposal. The mechanistic pathways considered here for the cyclative thioboration reaction are shown in Scheme 1. Both of these possible reaction routes take advantage of Lewis acidic boron-induced activation of the alkyne in thioanisole **1** to generate zwitterionic intermediate **4**. Previous experiments ruled out alternative mechanistic pathways that proceed through either B–S σ-bond formation/cyclization or haloboration/cyclization routes when ClBcat is the boron electrophile.[6]

The mechanism in Scheme 1 uses monomeric neutral ClBcat as the electrophile, but this was not clear at the beginning of our studies. It also disregards the possible involvement of an alkyne–ClBcat π-complex intermediate. With these simplifications to be evaluated later, a central mechanistic question was whether the addition occurs by a two-step process through vinyl cation intermediate **2** (Scheme 1, top pathway),[10] or by a concerted Ad$_E$3 addition (formally Ad$_E$2, wherein the nucleophilie is intramolecular) via transition state (TS) **3** (Scheme 1, bottom pathway).[11] Qualitatively, it might be anticipated that the choice between mechanisms would depend on the strength of the electrophile; weak electrophiles might be unable to generate the vinyl cation (top) but still accomplish the Ad$_E$3 addition (bottom).

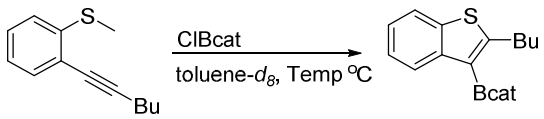
In both pathways, **4** is then demethylated by chloride ion, either via ion pair **5** or by a boron-based chloride shuttle.[7] The demethylation yields the final 3-borylated-benzothiophene product **6**. Both pathways show the key bifunctional reactivity of ClBcat, first as an electrophilic activating agent and second as a source of nucleophilic chloride.

Kinetic Studies. For the first set of kinetic experiments, substrate **1a** was treated with ClBcat. The reaction was run at 90 °C and at 0.05–0.20 M in substrate in toluene-d_8 to allow for the monitoring of the initial reaction rates by ^{1}H NMR spectroscopy using mesitylene as an internal standard. Initial rates were measured over a 3%–8% range of product yield for all conditions. Stand-

ard deviations are reported from triplicate runs. Generation of **6a** exhibited a first-order kinetic dependence with respect to the substrate concentration and a first-order kinetic dependence with respect to ClBcat (Table 1). The reaction exhibited second-order kinetics overall. This dependence on both components rules out a rate-determining preactivition step of the ClBcat (e.g., to generate a borenium[12]), thus, the active carbophilic Lewis acid in this system is assigned as ClBcat.

Eyring Analysis. Additional insight into the mechanism was obtained by an Eyring analysis of the rate constants over a 70–90 °C temperature range. Incorporating the observed bimolecular kinetics, the rate constants k at each temperature were obtained by dividing k_{obs} by the concentration of the reactants. Plotting ln (k/T) versus 1/T yields a $\Delta H^{\ddagger}$ of 13.8 ± 1.0 kcal mol^{-1} and a $\Delta S^{\ddagger}$ of −37 ± 3 cal mol^{-1} K^{-1}, with $\Delta G^{\ddagger}$ at 90 °C being 27.1 ± 0.1 kcal mol^{-1}. The substantially negative $\Delta S^{\ddagger}$ is in a normal range for a bimolecular association reaction with no release of a free molecule (such as Cl$^-$) prior to the rate-limiting step.[13]

Table 1. Observed Reaction Rate Constants at Varying Concentrations and Temperatures[a]



1a **6a**

Entry	Equiv (**1a**)	Equiv (ClBcat)	T (°C)	Rate (10^{-6} M s^{-1})
1	2.0	1.0	90	6.5 ± 0.5
2	0.5	1.0	90	1.8 ± 0.2
3	1.0	2.0	90	8.0 ± 0.1
4	1.0	0.5	90	2.0 ± 0.3
5	1.0	1.0	90	3.7 ± 0.2
6	1.0	1.0	80	1.8 ± 0.1
7	1.0	1.0	70	1.1 ± 0.1

[a]As an example, absolute concentration in entry 5 was 0.1 M **1a** and 0.1 M ClBcat in toluene-d_8.

Carbon Kinetic Isotope Effects. The ^{13}C kinetic isotope effects (KIEs) for the reaction of **1a** with ClBcat were determined at natural abundance by NMR methodology.[14] Independent reactions of **1a** with ClBcat at 85 °C in toluene were taken to 74% and 75% conversions, and the unreacted **1a** was reisolated by chromatography after a normal workup. The change in the isotopic composition of **1a** was determined by analysis of its ^{13}C NMR spectrum in comparison with **1a** from the same synthetic lot that had not been subjected to the reaction conditions. The arene carbon *para* to the alkynyl group was used as an internal standard for the NMR integrations with the assumption that isotopic fractionation in this position is negligible. From the changes in the isotopic composition at each position and the conversions of the reactions, the KIEs were calculated as previously described.

The results are summarized in Figure 2. The KIEs at the arene carbons are all negligible, while a very small KIE is observed at the methylthio carbon. The key observation is that both alkynyl carbons exhibit a significant ^{13}C KIE. The qualitative interpretation of these KIEs is that both alkynyl carbons are undergoing bonding changes in the rate-limiting TS, as would fit with an Ad$_E$3 mechanism, and the substantial KIE at the external alkynyl carbon appears inconsistent with rate-limiting electrophilic addition to form **2**. A more quantitative interpretation will be possible with the aid of computational studies (vide infra).

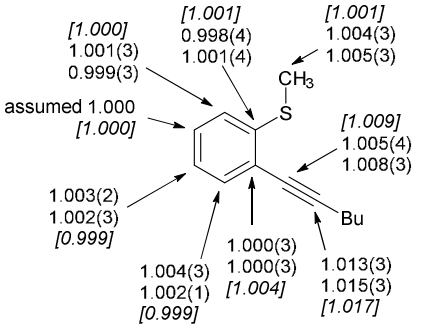


Figure 2. Experimental and B3LYP-D3/6-31+G**/PCM(toluene)-predicted (italicized and in brackets) ^{13}C KIEs (k^{12}/k^{13}) at 85 °C for the thioboration reaction of **1a** with ClBcat. The 95% confidence limits on the last digit are shown in parentheses with the experimental values.

Substituent Effects. A Hammett study was conducted to assess the charge buildup in the TS at the external alkynyl carbon. The relative reaction rates of *para*-substituted arylalkynylthioanisole derivatives (**1** with R = *p*-C$_6$H$_4$X) were assessed via competition experiments in which a solution of ClBcat was added to a solution of 3.0 equiv of a *para*-substituted alkynylthioanisole and 3.0 equiv of a differently substituted alkynylthioanisole in toluene-d_8 (Figure 3). These reactions were monitored by ^{1}H NMR spectroscopy using mesitylene as an internal standard and found to be complete in 2–4 h. The product ratios did not change upon standing.

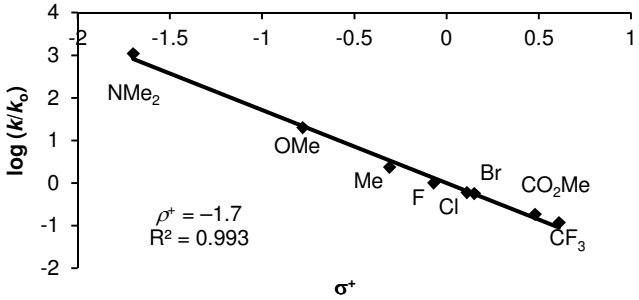


Figure 3. Hammett study showing correlation between log(k/k_o) and σ$^+$ at 100 °C.

A variety of substituents were tested that encompassed the range of electronic possibilities, including electron-withdrawing (*p*-CF$_3$, *p*-CO$_2$Me), slightly donating (*p*-F and *p*-Me), and strongly donating (*p*-NMe$_2$, *p*-OMe) substitu-

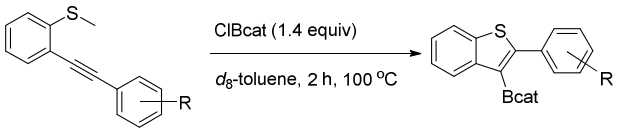
ents. The product ratios obtained through this series of competition experiments were then potted against σ^+ and σ_p. A better fit was obtained when the log of the relative reaction rates were plotted against σ^+ (R^2 = 0.993) than against σ_p (R^2 = 0.957), providing a ρ^+ value of –1.7 (Figure 3). The negative slope indicates that there is positive charge buildup at the external alkynyl carbon in the rate-determining step, and this could not happen unless electrophilic attack by the boron on the internal alkynyl carbon had progressed substantially.

We next considered the magnitude of the ρ^+ value, in order to assess if the rate-determining step involved formation of a formal vinylic cation (top pathway) or a simultaneous boron activation-sulfur ring-closing event to form the sulfonium species (bottom pathway). The low absolute value of ρ^+ suggests that electronic resonance stabilization effects are not as significant as those seen in systems involving the discrete formation of resonance-stabilized carbocations. The ρ^+ values for reactions that generate benzylic carbocations are typically greater than 4.0.[15,16] Assuming that an addition of the ClBcat electrophile to afford vinyl cation **2** would involve a late TS, as expected from Hammond's postulate, a similarly large ρ^+ would be expected for the vinyl cation mechanism (top pathway). The ρ^+ value of –1.7 is then more consistent with the Ad_E3 mechanism, in agreement with the isotope effects.

The substituent location was next varied on the phenyl ring to probe effects on rate of cyclization in the thioboration reaction (Table 2). Two substituents (R = Me, Cl) were selected to incorporate both a moderate electron-donating group and a moderate electron-withdrawing group. These 2-alkynylthioanisole derivatives (**1**) were subjected to standard thioboration conditions (1.3 M toluene-d_8 with respect to starting material, 1.4 equiv ClBcat, 100 °C) and examined by ^{1}H NMR spectroscopy at t = 2 h using mesitylene as an internal standard. Each reaction was run in duplicate and yields are reported with the standard deviation of two runs.

If sterics were the dominating factor on rate of the thioboration reaction, then *ortho*-substituted phenyl rings would result in lower yields at a given reaction time. When R = Me, however, all three substitution patterns provided statistically comparable yields (~82%). This indicates a minimal steric influence in this system or one that is exactly balanced by electronics. When R = Cl, the *p*-Cl provided the highest ^{1}H NMR yield (73 ± 1%), and both *o*-Cl and *m*-Cl provided comparable yields (57 ± 3% and 54 ± 3%, respectively). The higher yield with *p*-Cl versus *m*-Cl is likely due to the lower σ^+ value of *p*-Cl due to its resonance donation. A balance of electronegativity and resonance donation can account for the similar yields obtained with *ortho*-chloro and *meta*-chloro. The σ^+ of *o*-Cl is not defined, but the electron-withdrawing effects of *ortho* halogens are greatly enhanced versus the *meta* and *para* positions (the pK_a of *o*-chlorobenzoic acid is 2.92 versus 3.82 for *m*-chlorobenzoic acid[17]), so the electronic withdrawing ability of *o*-Cl can be balanced by some resonance donation. These observations are consistent with the importance of stabilizing positive charge at the benzylic position.

Table 2. Varying the Substituent Position



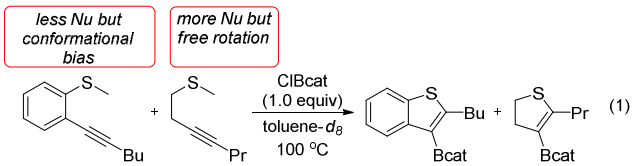
1b **6b**

Entry	R Group	Yield (%)[a] **6b**
1	*o*-Cl	57 ± 3
2	*m*-Cl	54 ± 3
3	*p*-Cl	73 ± 1
4	*o*-Me	85 ± 2
5	*m*-Me	89 ± 3
6	*p*-Me	88 ± 1

[a]Error is reported as standard deviation of two runs.

Nucleophilicity and Heteroatom Competition Experiments. To gain additional insight about the thioboration reaction, a series of competition experiments were conducted. The effects of nucleophilicity and conformational bias were analyzed by comparing the relative reaction rates of alkynylthioanisole **1a** and alkynylthioether **7** via an intermolecular competition experiment. A solution of ClBcat (1.0 equiv) was added to a solution of **1a** and **7** (3.0 equiv each) in toluene-d_8 (eq 1). The reaction was monitored by ^{1}H NMR spectroscopy at t = 2 h and 4 h, using mesitylene as an internal standard.

^{1}H NMR spectroscopic analysis at t = 2 h showed that the relative yields of **6a** and **8** were 7% and 62%, respectively, relative to the limiting ClBcat reagent. Examination at 4 h showed that the product ratios did not change significantly upon standing. The disfavorable formation of **6a** compared to **8** may be due to withdrawal of electron density from sulfur by the phenyl ring in **1a**, which reduces its nucleophilicity and makes it less favorable to attack the alkyne in comparison with the more nucleophilic sulfur in compound **7**. Thus, the enhanced nucleophilicity of the thioether in **7** outweighs the conformational bias towards cyclization of rigid **1a**.

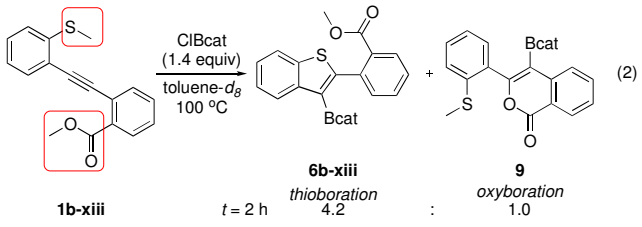


1a	**7**		**6a**	**8**
3.0 equiv	3.0 equiv	t = 2 h	7%	62%
		t = 4 h	8%	64%

In order to examine the nature of the initial alkyne activation step by ClBcat, we next examined an intermolecular competition reaction between thioboration and oxyboration, starting from substrate **1b**. Starting material **1b** was added to a solution of ClBcat (1.4 equiv) in

toluene-d_8 (eq 2) with mesitylene as an internal standard. The reaction was monitored for the formation of products **6b** and **9** by ^{1}H NMR spectroscopy over 2–24 h. At t = 2 h the ratio of **6b** to **9** was 4.2:1.0. This ratio remains approximately the same at t = 4 h, but the ratio at longer reaction times could not be determined due to apparent product decomposition.

This data shows a slight preference for thioboration over oxyboration corresponding to $\Delta\Delta G^{\ddagger}$ = 1.1 kcal/mol at 373 K. The similarity in reaction barriers suggests that alkyne activation (plausibly relatively similar for either heterocyclization since the same alkyne is activated) is the dominant contributor to the barrier, rather than the nucleophilic attack (plausibly substantially different for carboxy versus thio since the nature of the attacking nucleophile is different). This suggests that boron–carbon bond formation is more advanced at the TS than carbon–nucleophile bond formation, as would be consistent with the Hammett study. The consistency of this idea with the ^{13}C KIEs is assessed with the aid of computations (vide infra). These results align with the previous observations by Larock, which showed that the cyclization selectivity for SMe vs. COOMe in this substrate is electrophile dependent.[18]

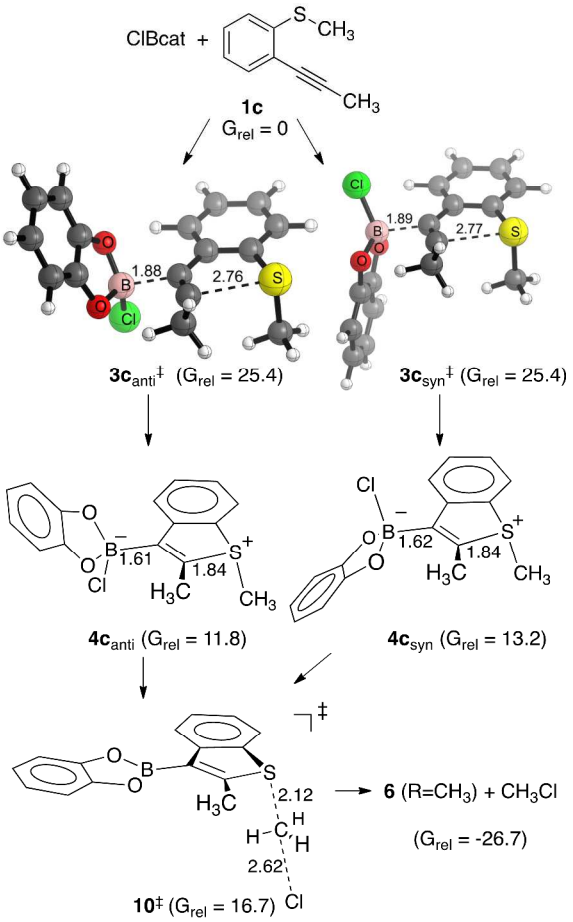


Computational Study of the ClBcat Reaction. The reaction of ClBcat with **1c** was studied with DFT calculations. A series of DFT method and basis set combinations were explored (see SI). Each predicted the same overall mechanism but with some significant variation in the TS geometries. Ordinarily, it would be desirable to choose among the methods based on high-level *ab initio* benchmarking for a tractable simplified reaction model, but the complexity of the reaction leaves us without a satisfactory small model. We will describe here the results of B3LYP/6-31+G** calculations including a PCM solvent model and Grimme's D3 dispersion corrections, then discuss how the predictions of other methods differ.

A second complication in the current reaction is that the key potential energy saddle points (the conventional TSs) for the Ad$_E$3 addition of ClBcat to **1c** lie in relatively flat regions of the energy surface where there is also a relatively rapid decrease in the entropy along the reaction coordinate. When this happens, conventional transition state theory (TST) is subject to significant error. It is then better to use canonical variational transition states (VTSs), i.e. free-energy maxima instead of potential-energy maxima, to predict rates and isotope effects. VTSs were located here using GAUSSRATE / POLYRATE,[19,20] and they are later than the conventional TSs. For the rate constants associated with the VTSs, tunneling was included using the small-curvature tunneling (SCT) approximation.[21]

Two Ad$_E$3 VTSs of approximately equal energy (within 0.1 kcal/mol) were located for the addition of ClBcat to **1c**, depending on whether the Bcat group is anti to the SCH$_3$ group (**3c**$_{anti}^{\ddagger}$) or syn to the SCH$_3$ group (**3c**$_{syn}^{\ddagger}$) (Scheme 2). The free-energy barriers associated with these VTSs using a 1 M standard state are 25.4 kcal/mol, in good agreement with the experimental barriers. This is somewhat misleading because the calculated barriers have not allowed for the entropy of symmetry of the ClBcat, the entropy of mixing of the chiral VTSs, and the kinetic combination of the two VTSs. Together these factors increase the rate by a factor of ~8, lowering the predicted barrier by 1.5 kcal/mol. The phenomenological entropy of activation was calculated from the summed SCT rate constants at 70 and 90 °C, allowing for a 1.0 M standard state and the entropies of mixing and symmetry, giving a $\Delta S^{\ddagger}$ of –37.4 e.u. matching the experimental value. We note that the inclusion of arbitrary entropy "corrections" often employed in the literature[22] would have led to poor predictions of both the free energy barrier and the entropy of activation.

Scheme 2. Calculated mechanism (B3LYP-D3/6-31+G/PCM(toluene)) for the reaction of 1c with ClBcat.**



In **3c**$_{anti}^{\ddagger}$ and **3c**$_{syn}^{\ddagger}$, the bonding between the boron and the internal alkynyl carbon is very advanced while bonding between the sulfur and the external alkynyl carbon has progressed to a much lower extent. The external alkynyl carbon is then moving more at the VTS, and this fits with the larger KIE observed at this carbon. The dif-

ferent degrees of bonding at the two carbons in the VTS also leads to a partial positive charge at the external alkynyl carbon in the VTS, with a gain in charge of 0.63 in Mulliken-charge calculations. This is consistent with the negative ρ^+ seen in the Hammett study.

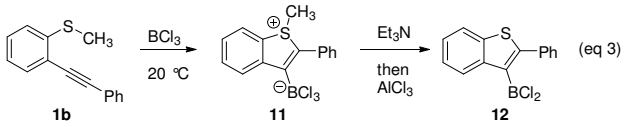
The two Ad_E3 VTSs lead to conformational isomers **4c**$_{anti}$ and **4c**$_{syn}$. The chloride in these zwitterionic heterocycles is predicted to remain bound to the boron; attempts to locate simple ion pairs by dissociating the chloride led back to the **4c** on optimization. The **4c** adducts are uphill from the reactants but they do not go backward because they face a low barrier to their S_N2 demethylation via TS **10**‡ to afford the neutral product **6**. The Ad_E3 addition is thus predicted to be the rate-determining step in the reaction.

A series of alternative mechanistic possibilities were explored. No TS could be located for an addition of ClBcat to **1c** without concomitant nucleophilic attack by the methylthio group. Attempts to optimize the vinyl cation **2** led to C–S bond formation to afford **4c**$_{anti}$ or **4c**$_{syn}$. The Ad_E3 process in the presence of a second molecule of ClBcat was explored with the idea that coordination to the chloride could enhance the reactivity of the electrophile. A structure analogous to **3c**$_{syn}$‡ but with a second ClBcat was located, but it was 3.7 kcal/mol higher in energy. This fits with the experimental kinetics that were unimolecular in ClBcat. Finally, we considered the possible role of an alkyne–boron π-complex as a precursor to the Ad_E3 addition step. A series of loose molecular complexes of **1c** were located, the most stable of which placed the S atom of **1c** in loose coordination with the B atom of the ClBcat. This loose coordination to sulfur was in agreement with weak charge-transfer bands observed at a low temperature in the UV-vis spectrum with large excess of ClBcat (see SI for details). All of the complexes were higher in free-energy than separate starting materials and as a result are not of kinetic significance in the mechanism.

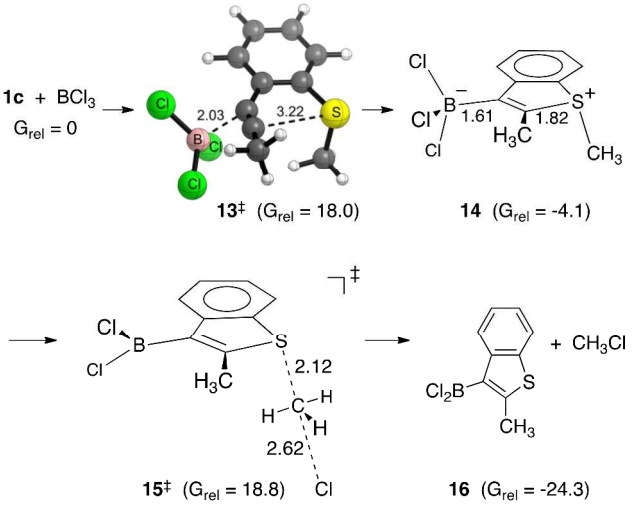
Predicted KIEs. The prediction of the ^{13}C KIEs for VTSs **3c**$_{anti}$‡ and **3c**$_{syn}$‡ could in principle be based on the SCT rate constants, but in practice this requires that POLYRATE rate constants be numerically converged to 4 significant figures (requiring long paths and very small steps along the path) to allow their comparison for KIE calculations. This was judged impractical, so an alternative process of applying the method of Bigeleisen and Mayer[23–25] (designed for TST) to the VTSs was employed. One-dimensional tunneling corrections[26] to the ^{13}C KIEs were negligible (<0.0003) so it was expected that the inclusion of SCT in the KIEs would be unimportant.

The results are summarized alongside the experimental KIEs in Figure 2. The agreement is very good, in that the predicted isotope effects fit well the pattern of isotope effects seen experimentally. However, there is a problem that compromises the significance of this agreement. As alluded to earlier, the geometry of the Ad_E3 transition states varies significantly across a series of calculations (see the SI for details). The forming C–B interatomic distances in the TSs range from 1.86 to 2.13 while the C–S distance varies from 2.70 to 2.96. The effect of this variation is that the predicted KIEs also encompass a relatively large range, from 1.007 to 1.011 and from 1.013 to 1.029 at the internal and external alkynyl carbons, respectively. Because there is no independent way to choose among DFT methods in the current reaction, it would not be correct to say that calculations were able to "predict" the experimental KIEs with good precision. However, it is clear that the experimental KIEs are consistent with the Ad_E3 mechanism. Considering this, along with the consistency of the calculated barrier, entropy, molecularity, and charges with diverse experimental observations, the combination of experiment and computations strongly supports the Ad_E3 addition.

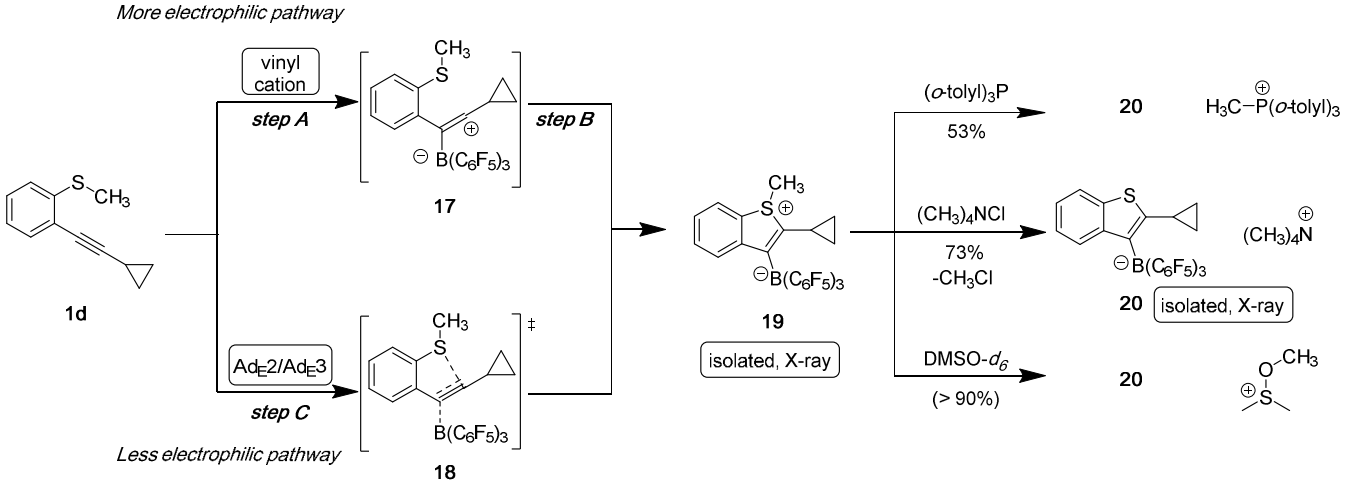
Computational Study of the BCl_3 Reaction. In the reaction of BCl_3 with **1b** (R = phenyl), Ingleson observed by NMR spectroscopy a zwitterionic product that was assigned as having structure **11** (eq 3).[9] Unlike our proposed intermediate **4**, **11** did not spontaneously demethylate. Instead, the neutral product **12** was produced after sequential treatment with Et_3N for demethylation and $AlCl_3$ to remove the chloride. It was of interest to understand why BCl_3 failed to adopt a bifunctional role in this reaction while ClBcat mediates the complete conversion by itself.



To examine this issue, the reaction of BCl_3 with **1c** was investigated computationally. BCl_3 is a much stronger electrophile than ClBcat and this is reflected in its low reaction temperature with **1b**. The B3LYP-D3 calculations mirror this observation, predicting the barrier at 25 °C to be only 18.0 kcal/mol. The TS **13**‡ for the addition is much earlier than the corresponding **3c**$_{anti}$‡ and **3c**$_{syn}$‡ TSs with ClBcat, and only the single TS could be located. The C–S distance for the ring-closing bond in **13**‡ is so long, at 3.22 Å, that the involvement of the sulfur atom as a nucleophile is nearly negligible, but no stepwise intermediate before the cyclized product **14** could be located.



Scheme 3. Two Possible Mechanisms for Thioboration with $B(C_6F_5)_3$ and Isolation of Intermediates



To proceed on to the neutral product **16** without assistance from additional reagents, a chloride anion would have to dissociate then effect the demethylation via S_N2 TS **15**‡. The free energy of **15**‡ is only modestly above **13**‡ but its starting point, **14**, is more stable, so the barrier for demethylation of **14** once formed is 4.9 kcal/mol higher than the original barrier for its formation. In this way, the high electrophilicity of the BCl_3 works against the overall conversion by making the intermediate zwitterion too stable.

These results qualitatively account for Ingleson's observations, but the calculated barrier for the demethylation of **14**, 22.9 kcal/mol, is quantitatively too low by ~2 kcal/mol. It should be recognized however that DFT calculations tend to underestimate the stability of dative bonds to boron in ate complexes by several kcal/mol,[27] and this would fit with the small discrepancy.

Characterization of Intermediates. In order to investigate reaction intermediates and their fundamental reactivity, as well as to determine how ClBcat compared as a carbophilic electrophile to the previously used highly electrophilic reagent tris(pentafluorophenyl)borane ($B(C_6F_5)_3$), we treated the 2-alkynyl thioanisole substrate **1d** with 1.0 equivalent of $B(C_6F_5)_3$. Notably, this reagent has the potential to display similar reactivity to ClBcat in the initial alkyne activation step, but lacks the bifunctional ability to dissociate an anionic ligand and thus lacks the ability to induce subsequent demethylation. Thus, this reagent may permit "freezing" of the reaction pathway at zwitterionic intermediate **19**,[9] which in turn would permit the study of its structure and of its fundamental reactivity independent of the borylative heterocyclization step. Indeed, after 1 h at 20 °C in CH_2Cl_2 the 1-methyl-1-benzothiophenium borate intermediate **19** was isolated in 81% yield (Scheme 3).

The formation of the zwitterion **19** was monitored by time-resolved UV–vis spectrophotometry at its maximum absorption (λ_{max} = 317 nm) in CH_2Cl_2 at 20 °C under pseudo-first conditions (large excess of $B(C_6F_5)_3$, see SI). These kinetic experiments showed that the reaction is first order with respect to both **1d** and $B(C_6F_5)_3$, thus following an overall second-order behavior with a second-order rate constant of k = 2.00 × 10^{-1} mol L^{-1} s^{-1} ($\Delta G^{‡}$ = 18.1 kcal/mol at 293 K).

The ^{11}B NMR spectrum of the zwitterion **19** showed a singlet at δ = –14.7 ppm, in agreement with previously reported chromone and indole derivatives.[28,29] The complex ^{19}F NMR spectrum of **19** indicated that the rotation around the C–B bond was restricted. Additionally, the presence of two sets of signals in the ^1H, ^{19}F and ^{13}C NMR revealed that **19** existed in solution as two diastereomeric conformations with a 65:35 ratio according to the integrals of the ^1H NMR spectroscopy signals of the two inequivalent S^+–Me groups at 3.08 and 2.90 ppm, respectively. This observation was consistent with restricted bond rotation on the ^1H NMR spectroscopy timescale, likely around the C–B bond connecting the $B(C_6F_5)_3$ group to the benzothiophene core, consistent with the steric crowding observed around the C3-B bond in the crystal structure (Figure 4). This assignment of the origin of restricted rotation is consistent with full lack of symmetry displayed in the ^{19}F NMR spectrum and with previous reports.[29] This ratio was solvent (CD_3CN, CD_2Cl_2, DMSO-d_6) and temperature independent (in CD_3CN) in the range – 40 to + 40 °C). As the ^1H-^1H NOESY experiments in CD_2Cl_2 at 20 °C (mixing time up to 1000 ms) remained inconclusive, the relative configuration and full signal attribution for both diastereomers was not attempted. Single-crystal X-ray diffraction analysis, however, unambiguously confirmed the solid-state structure of intermediate **19** (Figure 4).

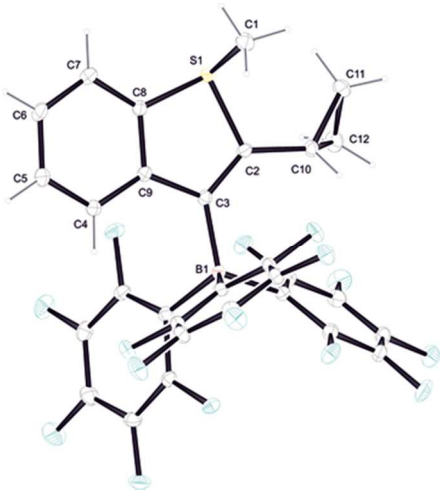


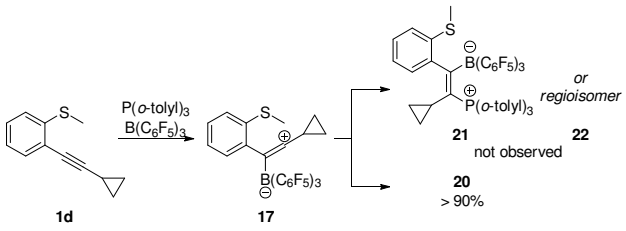
Figure 4. X-ray structure (ellipsoids shown at the 50% probability level) of **19**. Selected interatomic distances (Å) and angles (deg): S1–C2 = 1.805(1), C2–C3 = 1.357(2), C3–B1 = 1.645(2), C3–C9 = 1.483(2), C9–C8 = 1.405(2), C8–S1 = 1.754(1), S1–C1 = 1.805(1), C8–S1–C2 = 92.56(6), S1–C2–C3 = 111.43(9).

The next question was whether now-characterized intermediate **19** was relevant and analogous to the proposed but undetected zwitterionic intermediate **4** derived from ClBcat-induced borylative heterocyclization. Intermediate **4** could not be detected under our conditions, presumably due to its location on the reaction energy surface after rate-determining borylative heterocyclization. To investigate this hypothesis, the reactivity of **19** towards demethlation by chloride was investigated and found to be not only feasible but markedly fast at ambient temperature. This is the analogous demethylation reactivity proposed for unobserved **4** (either direct or via neutral **5**). Specifically, multinuclear NMR spectroscopic monitoring of the demethylation of **19** by various nucleophiles (*o*-tolyl)$_3$P, DMSO and $Me_4N^+Cl^-$) was performed. Whereas demethylation occurred slowly either with (*o*-tolyl)$_3$P or DMSO-d_6 (Scheme 3, top/middle), it proceeded immediately with Et_4N^+Cl (Scheme 3, bottom) to provide **20** in high yield. A crystal structure of **20** was obtained for full characterization and confirmed the formation of this product (See SI).

Demethylation by chloride was sufficiently fast that zwitterion **19** was already fully demethylated after mixing with $Me_4N^+Cl^-$ and immediate recording of the ^{1}H NMR spectrum (< 1 min). The simultaneous formation of CH_3Cl was confirmed by ^{1}H and ^{13}C NMR spectroscopy (δ ^{1}H = 3.03 ppm, δ ^{13}C = 26.0 ppm). Thus, chloride is particularly well-suited for rapid demethylation, supporting demethylation of **4** or **5** to **6** (Scheme 1, Step E) and supporting a bifunctional role for ClBcat as both an alkyne activator and chloride source for post-cyclization demethylation in the synthesis of neutral organoboron building blocks. This observation also shows that free chloride, when and if present, is a rapid demethylation agent. This point is consistent with the previous conclusion that the higher electrophilicity of the BCl_3 unit in zwitterion **11** is preventing demethylation of this zwitterion in the absence of additional reagents.

Carbon KIE studies and the magnitude of the ρ^+ from the Hammett study both indicated a concerted cyclization with ClBcat. To gauge, in contrast, if the more electrophilic $B(C_6F_5)_3$ was sufficiently more reactive to access a formal cation, this reagent was next investigated. When **1d** was reacted with the frustrated Lewis pair $(C_6F_5)_3B$/(*o*-tolyl)$_3$P (Scheme 4), the phosphine-boration product **21** or its regioisomer **22** were not observed, and **20** was formed exclusively. This data suggests that the cyclization pathway is concerted even with this more electrophilic reagent, since an intermediate short-lived vinyl-cation (**17** or its regioisomer), of high electrophilicity,[30] might at least be partially trapped by the phosphine (*o*-tolyl)$_3$P. The phosphine is significantly more nucleophilic in comparison to the sulfur atom in the –SMe ortho substituent as characterized through Mayr nucleophilicity studies, though zwitterion **17** may present a more hindered approach for the bulky phosphine than the standard Mayr substrates[31,32] Thus, the Ad$_E$3 mechanism herein characterized for ClBcat-induced thioboration appears to operate even for this more highly electrophilic boron reagent (Scheme 1, Step C).

Scheme 4. Reaction of 1c with the FLP $(C_6F_5)_3B$/(*o*-tolyl)$_3$P at 20 °C in CH_2Cl_2.



CONCLUSIONS

Thioborylative cyclization reactions with three different boron electrophiles, ClBcat, BCl_3, and $B(C_6F_5)_3$ were investigated by a combined experimental and computational approach. With ClBcat: Hammett studies indicate a concerted reaction pathway, kinetic studies show a bimolecular rate-determining step, ^{13}C KIE studies support a rate-determining Ad$_E$3 mechanism, competition experiments suggest the involvement of sulfur as a nucleophile in the rate-determining step, and DFT studies indicate that a low barrier chloride dissociation enables the reagent to perform the subsequent demethylation in the absence of added reagents. With BCl_3 in contrast, DFT studies indicate a higher barrier chloride dissociation that qualitatively accounts for Ingleson's observation[8] that additional reagents are required to promote demethylation. With $B(C_6F_5)_3$, a methylated zwitterionic reaction intermediate was isolated and characterized by X-ray crystallography, and similar to BCl_3,[9] it required additives for demethylation. With $B(C_6F_5)_3$, UV-vis kinetics demonstrated a bimolecular rate-determining step, and trapping experiments did not support the formation of a long-lived vinyl carbocation despite this reagent's high electrophilicity.

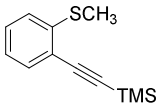
Together, these observations indicate that the commercially available reagent ClBcat serves a bifunctional role as both an electrophilic alkyne activator and a nucle-

ophilic chloride source for demethylation. The alkyne-activation/cyclization process is concerted and rate-determining, followed by rapid demethylation by released chloride. These conclusions are significant for reaction design and improvement because they suggest that increasing the electrophilicity of the boron reagent while keeping its bifunctional ability to release a nucleophile for dealkylation is the key needed feature. This bifunctional reactivity requires a balance of electrophlicity at boron: sufficiently electrophilic to activate the alkyne but insufficiently electrophilic to prevent decoordination of the chloride after alkyne activation. Although less electrophilic than previously reported boron reagents for heteroborylative cyclization reactions, ClBcat is sufficiently electrophilic to participate in the Ad_E3 mechanism. These outcomes provide direction for reaction design through understanding the fundamental reactivity of ClBcat—and by extension, other practical, readily available, and synthetically useful boron reagents—towards alkynes in electrophilic borylation reactions that produce functionalizable organoboron building blocks primed for downstream reactivity.

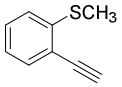
EXPERIMENTAL SECTION

General Information. All chemicals were used as received from commercial sources unless otherwise noted. Triethylamine, acetonitrile, toluene and tetrahydrofuran were purified by passage through an alumina column under argon pressure on a push-still solvent system. Dichloromethane was freshly distilled over CaH_2 prior to use. Et_2O was distilled over sodium/benzophenone. Toluene-d_8 was dried over CaH_2, degassed using three freeze-pump-thaw cycles, and vacuum transferred prior to use. All manipulations were conducted using standard Schlenk techniques unless otherwise specified. Analytical thin layer chromatography (TLC) was performed using Merck F250 plates. Plates were visualized under UV irradiation (254 nm) and/or using a basic aqueous solution of potassium permanganate. Flash chromatography was conducted using a Teledyne Isco Combiflash® Rf 200 Automated Flash Chromatography System, and Teledyne Isco Redisep® 35–70 μm silica gel. All proton, carbon, fluorine, boron and phosphorus nuclear magnetic resonance (^{1}H, ^{13}C, ^{19}F, ^{11}B and ^{31}P NMR) spectra were recorded on a Bruker DRX-500 spectrometer outfitted with a cryoprobe, or a Bruker AVANCE-600 spectrometer outfitted with a cryoprobe, or Varian NMR spectrometers. All chemical shifts (δ) are reported in parts per million (ppm) downfield of tetramethylsilane, and referenced to the residual protiated solvent peak (δ_H = 7.26 ppm for $CDCl_3$, δ_H = 1.94 ppm for CD_3CN, δ_H = 5.32 ppm for CD_2Cl_2 and δ_H = 2.08 ppm for toluene-d_8; δ_C = 77.2 ppm for $CDCl_3$, δ_C = 118.69 ppm for CD_3CN, δ_C = 53.84 ppm for CD_2Cl_2 or δ = 20.4 ppm for toluene-d_8 in ^{13}C NMR spectroscopy experiments).

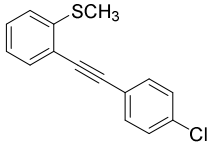
The following abbreviations were used for signal multiplicities: app = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. ^{11}B and ^{19}F NMR spectroscopy experiments are referenced to the absolute frequency of 0 ppm in the ^{1}H dimension according to the Xi scale. NMR spectroscopy signal assignments were based on additional 2D-NMR spectroscopy experiments (COSY, HSQC and HMBC). HRMS ESI mode were performed on a LTQ mass spectrometer and in FAB mode with a Jeol MStation dual focusing sector field mass spectrometer at Ludwig Maximilian University of Munich or at the mass spectroscopy facility at the University of California, Irvine. Melting points were determined on a Büchi B-540 device on capillary tubes and are not corrected. Infrared (IR) spectra of neat compounds were recorded on an IR spectrometer (Spectrum BX from Perkin Elmer) with an ATR unit (attenuated total reflection; Dura Sampler Diamond ATR from Smiths Detection) at Ludwig Maximilian University of Munich.



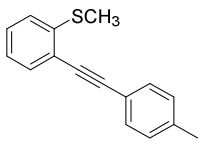
Trimethyl((2-(methylthio)phenyl)ethynyl)silane ***(SI-1)****.* Trimethyl((2-(methylthio)phenyl)ethynyl)silane was synthesized using a literature procedure[34] in 98% yield. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.42 (dd, *J* = 7.6, 0.2 Hz, 1H), 7.27 (td, *J* = 8.0, 1.5 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 1H), 7.06 (td, *J* = 7.6, 1.1 Hz, 1H), 2.48 (s, 3H), 0.30 (s, 9H). This spectrum is in agreement with previously reported spectral data.[34]



(2-Ethynylphenyl)(methyl)sulfane ***(SI-2)****.* (2-Ethynylphenyl)(methyl)sulfane was synthesized using a literature procedure[34] in 99% yield. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.46 (d, *J* = 7.6 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 3.48 (s, 1H), 2.49 (s, 3H). This spectrum is in agreement with previously reported spectral data.[34]

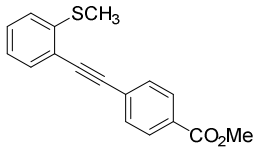


(2-((4-Chlorophenyl)ethynyl)phenyl)(methyl)sulfane ***(1b-i)****.* (2-((4-Chlorophenyl)ethynyl)phenyl)(methyl)sulfane was synthesized using a literature procedure[34] in 99% yield. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.50 (d, *J* = 10.2 Hz, 2H), 7.47 (d, *J* = 9.1 Hz, 1H), 7.33–7.30 (m, 3H), 7.18 (d, *J* = 9.6Hz, 1H), 7.12 (t, *J* = 9.1 Hz, 1H), 2.52 (s, 3H). This spectrum is in agreement with previously reported spectral data.[34]

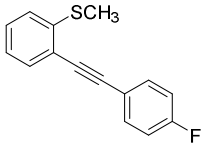


Methyl(2-(p-tolylethynyl)phenyl)sulfane ***(1b-ii)****.* Methyl(2-(p-tolylethynyl)phenyl)sulfane was synthesized

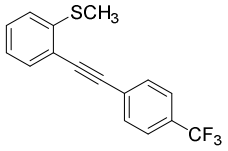
using a literature procedure[35] in 99% yield. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.48–7.46 m, 3H), 7.29 (td, *J* = 7.7, 1.4 Hz, 1H), 7.18–7.15 (m, 3H), 7.11 (td, *J* = 7.5, 1.2 Hz, 1H), 2.51 (s, 3H), 2.37 (s, 3H). This spectrum is in agreement with previously reported spectral data.[35]



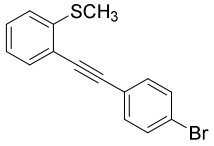
*Methyl 4-((2-(methylthio)phenyl)ethynyl)benzoate (**1b-iii**).* In an N_2-filled glovebox, a 20 mL scintillation vial was charged with methyl 4-iodobenzoate (580 mg, 2.2 mmol, 1.0 equiv), $(PPh_3)_2PdCl_2$ (77 mg, 0.011 mmol, 0.050 equiv), CuI (42 mg, 0.22 mmol, 0.10 equiv), and a stir bar. In a separate dram vial, **SI-2** (420 mg, 2.9 mmol, 1.3 equiv) was dissolved in Et_3N (6.1 mL). This solution was then added to the substrate-containing vial via pipette, and the mixture-containing vial was capped and removed from the glovebox. The solution was stirred for 18 h at ambient temperature. At this time, TLC indicated complete consumption of starting material. The reaction mixture was diluted with 100 mL EtOAc and washed with saturated aqueous NH_4Cl (1 × 20 mL), water (1 × 20 mL), and brine (1 × 20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography using an elution gradient of 0% to 15% EtOAc in hexanes. Product-containing fractions were combined and concentrated in vacuo, and volatiles were removed at c.a. 10 mTorr for 18 h to afford **1b-iii** as a yellow solid (470 mg, 75% yield). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.02 (dt, *J* = 8.4, 1.7 Hz, 2H), 7.63 (dt, *J* = 8.4, 1.7 Hz, 2H), 7.49 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.33 (td, *J* = 8.0, 1.5 Hz, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 7.13 (td, *J* = 7.6, 1.1 Hz, 1H), 3.93 (s, 3H), 2.52 (s, 3H). ^{13}C NMR ($CDCl_3$, 151 MHz): δ 166.7, 142.2, 132.5, 131.6, 129.7, 129.6, 129.4, 128.0, 124.4, 124.3, 120.8, 95.1, 89.9, 52.4, 15.2. HRMS (TOFMS-CI+) m/z Calcd for $C_{17}H_{14}O_2S$ ([M]$^+$): 282.0714; Found 282.0714.



*(2-((4-Fluorophenyl)ethynyl)phenyl)(methyl)sulfane (**1b-iv**).* In an N_2-filled glovebox, a 20 mL scintillation vial was charged with methyl 4-fluoroiodobenzoate (0.24 mL, 2.1 mmol, 1.0 equiv), $(PPh_3)_2PdCl_2$ (77 mg, 0.011 mmol, 0.050 equiv), CuI (40. mg, 0.21 mmol, 0.10 equiv), and a stir bar. In a separate dram vial, **SI-2** (373 mg, 2.5 mmol, 1.2 equiv) was dissolved in Et_3N (6.4 mL). This solution was then added to the substrate-containing vial via pipette, which was capped and removed from the glovebox. The solution was stirred for 18 h at ambient temperature. At this time, TLC indicated complete consumption of starting material. The reaction mixture was diluted with 100 mL EtOAc and washed with saturated aqueous NH_4Cl (1 × 20 mL), water (1 × 20 mL), and brine (1 × 20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography using an elution gradient of 0% to 5% EtOAc in hexanes. Product-containing fractions were combined and concentrated in vacuo, and volatiles were removed at c.a. 10 mTorr for 18 h to afford **1b-iv** as a yellow solid (493 mg, 97% yield). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.56 (ddd, *J* = 8.8, 5.4, 2.2 Hz, 2H), 7.47 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.31 (td, *J* = 7.9, 1.4 Hz, 1H), 7.18 (d, *J* = 7.9 Hz, 1H), 7.11 (td, *J* = 7.6, 1.1 Hz, 1H), 7.05 (tt, *J* = 8.8, 2.1 Hz, 2H), 2.51 (s, 3H). ^{13}C NMR ($CDCl_3$, 151 MHz): δ 162.8 (d, *J* = 249.8 Hz), 141.8, 133.6 (d, *J* = 8.3 Hz), 132.3, 129.0, 124.3 (d, *J* = 28.3 Hz), 121.3, 119.4 (d, *J* = 3.5 Hz), 115.9, 115.7, 94.9, 86.7, 15.2. HRMS (TOFMS-CI+) m/z Calcd for $C_{15}H_{11}FS$ ([M]$^+$): 242.0565; Found 242.0557.

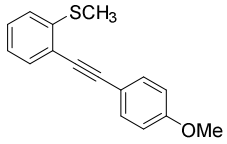


*Methyl(2-((4-(trifluoromethyl)phenyl)ethynyl)phenyl)sulfane (**1b-v**).* In an N_2-filled glovebox, a 20 mL scintillation vial was charged with methyl 4-iodobenzotrifluoride (0.31 mL, 2.1 mmol, 1.0 equiv), $(PPh_3)_2PdCl_2$ (77 mg, 0.011 mmol, 0.050 equiv), CuI (40. mg, 0.21 mmol, 0.10 equiv), and a stir bar. In a separate dram vial, **SI-2** (373 mg, 2.5 mmol, 1.2 equiv) was dissolved in Et_3N (6.4 mL). This solution was then added to the substrate-containing vial via pipette, which was capped and removed from the glovebox. The solution was stirred for 18 h at ambient temperature. At this time, TLC indicated complete consumption of starting material. The reaction mixture was diluted with 100 mL EtOAc and washed with saturated aqueous NH_4Cl (1 × 20 mL), water (1 × 20 mL), and brine (1 × 20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography using an elution gradient of 0% to 5% EtOAc in hexanes. Product-containing fractions were combined and concentrated in vacuo, and volatiles were removed at c.a. 10 mTorr for 18 h to afford **1b-v** as a yellow oil (540 mg, 88% yield). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.68 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.50 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.34 (td, *J* = 7.8, 1.4 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.13 (td, *J* = 7.5, 1.0 Hz, 1H), 2.53 (s, 3H). This spectrum is in agreement with previously reported spectral data.[36]

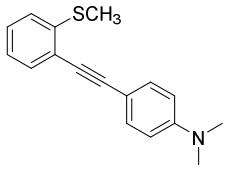


*(2-((4-Bromophenyl)ethynyl)phenyl)(methyl)sulfane (**1b-vi**).* (2-((4-Bromophenyl)ethynyl)phenyl)(methyl)sulfane was synthesized using a literature procedure[34] in 86% yield. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.50–7.46 (m, 3H), 7.44–7.43

(m, 2H), 7.32 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 2.51 (s, 3H). This spectrum is in agreement with previously reported spectral data.[34]



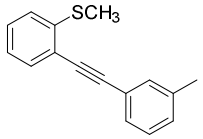
*(2-((4-methoxyphenyl)ethynyl)phenyl)(methyl)sulfane (**1b-vii**).* In an N_2-filled glovebox, a 20 mL scintillation vial was charged with 4-iodoanisole (740. mg, 3.2 mmol, 1.0 equiv), $(PPh_3)_2PdCl_2$ (110 mg, 0.16 mmol, 0.050 equiv), CuI (61 mg, 0.32 mmol, 0.10 equiv), and a stir bar. In a separate dram vial, **SI-2** (570 mg, 3.8 mmol, 1.2 equiv) was dissolved in Et_3N (9.6 mL). This solution was then added to the substrate-containing vial via pipette, which was capped and removed from the glovebox. The solution was stirred for 18 h at ambient temperature. At this time, TLC indicated complete consumption of starting material. The reaction mixture was diluted with 100 mL Et_2O and washed with saturated aqueous NH_4Cl (1 × 20 mL), water (1 × 20 mL), and brine (1 × 20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography using an elution gradient of 0% to 10% EtOAc in hexanes. Product-containing fractions were combined and concentrated in vacuo, and volatiles were removed at c.a. 10 mTorr for 18 h to afford **1b-vii** as a yellow oil (540. Mg, 67% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.54 (d, *J* = 8.8 Hz, 2H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.29 (td, *J* = 7.9 Hz, 1.4 Hz, 1H), 7.17 (d, *J* = 7.9 Hz, 1H), 7.09 (td, *J* = 7.6, 1.0 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 2H), 3.82 (s, 3H), 2.51 (s, 3H). This spectrum is in agreement with previously reported spectral data.[35]



N,N-Dimethyl-4-((2-(methylthio)phenyl)ethynyl)aniline (**1b-viii**). N,N-Dimethyl-4-((2-(methylthio)phenyl)ethynyl)aniline was synthesized using a literature procedure[34] in 97% yield. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.47 (d, *J* = 10.9 Hz, 3H), 7.26 (t, *J* = 9.5 Hz, 1H), 7.16 (d, *J* = 9.3 Hz, 1H), 7.10 (t, *J* = 9.0 Hz, 1H), 6.66 (d, *J* = 10.7 Hz, 2H), 2.99 (s, 6H), 6.51 (s, 3H). This spectrum is in agreement with previously reported spectral data.[34]

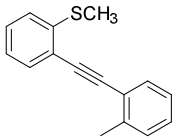
*Procedure for Reference Cyclizations of Thionasioles **1b (i–viii)**.* In order to monitor the competition reactions by ^{1}H NMR spectroscopy, it was necessary to run the individual substrates **1b(i–viii**) under thioboration conditions to determine product resonances. This procedure was performed in an N_2-filled glovebox. A dram vial was charged with *B*-chlorocatecholborane (42 mg, 0.27 mmol, 1.4 equiv) and 0.15 mL of d_8-toluene. A separate dram vial was charged with **1b(i–viii)** (0.20 mmol, 1.0 equiv). The ClBcat/d_8-toluene containing solution was then transferred via pipette to the vial containing compound **1**. The vial was capped and placed in a pre-heated aluminum block at 100 °C. The mixture was heated for 4 h. The mixture was then cooled to room temperature before the contents of this vial were then transferred to a J. Young NMR tube and 0.3 mL of d_8-toluene was added. The tube was then sealed and removed from the glovebox. ^{1}H NMR spectroscopy was used to identify the resonances corresponding to the desired thioboration products **6b (i–viii)**.

Procedure for Competition Experiments to Determine the Hammett Plot. This procedure was performed in an N_2-filled glovebox. A dram vial was charged with *B*-chlorocatecholborane (13 mg, 0.087 mmol, 1.0 equiv) and 0.4 mL of d_8-toluene. A separate dram vial was charged with mesitylene (6.0 μL, 0.043 mmol, 0.50 equiv), **1b-A** (0.26 mmol, 3.0 equiv) and **1b-B** (0.26 mmol, 3.0 equiv). The ClBcat/d_8-toluene containing solution was then transferred via pipette to the vial containing compounds **1b-A** and **1b-B**. The contents of this vial were then transferred to a J. Young NMR tube, which was capped, and removed from the glovebox. The tube was then placed in a preheated oil bath at 100 °C. Single-scan ^{1}H spectra were taken at time points *t* = 0 h (before heating), and at *t* = 2 h and 4 h, for which the tube was briefly removed from the heating bath. The resonances corresponding to **6b-A** and **6b-B** were compared to the internal standard to determine the relative reaction rates (k) for each competition experiment. The product ratios did not change upon standing.

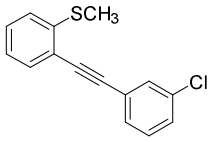


*Methyl(2-(m-tolylethynyl)phenyl)sulfane (**1b-ix**).* In an N_2-filled glovebox, a 20 mL scintillation vial was charged with 3-iodotoluene (0.27 mL, 2.1 mmol, 1.0 equiv), $(PPh_3)_2PdCl_2$ (73 mg, 0.010 mmol, 0.050 equiv), CuI (39 mg, 0.20 mmol, 0.10 equiv), and a stir bar. In a separate dram vial, **SI-2** (365 mg, 2.50 mmol, 1.2 equiv) was dissolved in Et_3N (12 mL). This solution was then added to the substrate-containing vial via pipette, which was capped and removed from the glovebox. The solution was stirred for 18 h at ambient temperature. At this time, TLC indicated complete consumption of starting material. The reaction mixture was diluted with 100 mL Et_2O and washed with saturated aqueous NH_4Cl (1 × 20 mL), water (1 × 20 mL), and brine (1 × 20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography using an elution gradient of 0% to 5% EtOAc in hexanes. Product-containing fractions were combined and concentrated in vacuo, and volatiles were removed at c.a. 10 mTorr for 18 h to afford **1b-ix** as a yellow oil (475 mg, 95% yield). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.48 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.41–7.38 (m, 2H), 7.30 (td, *J* = 7.9, 1.5 Hz, 1H), 7.25 (t, *J* = 7.6 Hz, 1H), 7.19 (d, *J* = 7.7 Hz, 1H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.11 (td, *J* = 7.5, 1.1 Hz, 1H),

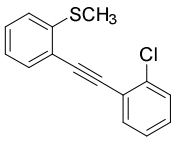
2.52 (s, 3H), 2.36 (s, 3H). ^{13}C NMR ($CDCl_3$, 151 MHz): δ 141.8, 138.1, 132.4, 132.3, 129.5, 128.83, 128.82, 128.4, 124.4, 124.2, 123.1, 121.6, 96.2, 86.7, 21.4, 15.2. HRMS (TOFMS-CI+) m/z Calcd for $C_{16}H_{14}S$ ([M]$^+$): 238.0816; Found 238.0821.



*Methyl(2-(o-tolylethynyl)phenyl)sulfane (**1b-x**).* In an N$_2$-filled glovebox, a 20 mL scintillation vial was charged 2-iodoanisole (0.49 mL, 3.5 mmol, 1.0 equiv), $(PPh_3)_2PdCl_2$ (120. mg, 0.180 mmol, 0.050 equiv), CuI (67 mg, 0.35 mmol, 0.10 equiv), and a stir bar. In a separate dram vial, 2-ethynyltoluene (0.57 mL, 4.6 mmol, 1.3 equiv) was diluted in Et_3N (11 mL). This solution was then added to the substrate-containing vial via pipette, which was capped and removed from the glovebox. The solution was stirred for 18 h at ambient temperature. At this time, TLC indicated complete consumption of starting material. The reaction mixture was diluted with 100 mL Et_2O and washed with saturated aqueous NH_4Cl (1 × 20 mL), water (1 × 20 mL), and brine (1 × 20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography using an elution gradient of 0% to 5% EtOAc in hexanes. Product-containing fractions were combined and concentrated in vacuo, and volatiles were removed at c.a. 10 mTorr for 18 h to afford **1b-x** as a yellow liquid (420. mg, 50% yield). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.55 (d, *J* = 7.4 Hz, 1H), 7.51 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.31 (td, *J* = 7.7, 1.4 Hz, 1H), 7.24 (dd, *J* = 4.8, 1.0 Hz, 2H), 7.19–7.16 (m, 2H), 7.12 (td, *J* = 7.5, 1.1 Hz, 1H), 2.58 (s, 3H), 2.52 (s, 3H). ^{13}C NMR ($CDCl_3$, 151 MHz): δ 141.6, 140.5, 132.5, 132.2, 129.6, 128.8, 128.6, 125.7, 124.4, 124.2, 123.1, 121.7, 95.0, 90.8, 21.2, 15.2. HRMS (TOFMS-CI+) m/z Calcd for $C_{16}H_{14}S$ ([M]$^+$): 238.0816; Found 238.0815.



*(2-((3-Chlorophenyl)ethynyl)phenyl)(methyl)sulfane (**1b-xi**).* In an N$_2$-filled glovebox, a 20 mL scintillation vial was charged with 3-chloro-iodobenzene (0.15 mL, 1.2 mmol, 1.0 equiv), $(PPh_3)_2PdCl_2$ (42 mg, 0.060 mmol, 0.050 equiv), CuI (23 mg, 0.12 mmol, 0.10 equiv), and a stir bar. In a separate dram vial, **SI-2** (231. mg, 1.60 mmol, 1.3 equiv) was dissolved in Et_3N (3.6 mL). This solution was then added to the substrate-containing vial via pipette, which was capped and removed from the glovebox. The solution was stirred for 18 h at ambient temperatures. At this time, TLC indicated complete consumption of starting material. The reaction mixture was diluted with 100 mL Et_2O and washed with saturated aqueous NH_4Cl (1 × 20 mL), water (1 × 20 mL), and brine (1 × 20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography using an elution gradient of 0% to 3% EtOAc in hexanes. Product-containing fractions were combined and concentrated in vacuo, and volatiles were removed at c.a. 10 mTorr for 18 h to afford **1b-xi** as a yellow oil (390 mg, 94% yield). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.57–7.56 (m, 1H), 7.48 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.45 (dt, *J* = 7.4, 1.4 Hz, 1H), 7.34–7.27 (m, 3H), 7.19 (d, *J* = 7.8 Hz, 1H), 7.12 (td, *J* = 7.5, 1.1 Hz, 1H), 2.52 (s, 3H). ^{13}C NMR ($CDCl_3$, 151 MHz): δ 142.1, 134.3, 132.5, 131.5, 129.8, 129.7, 129.3, 128.8, 125.1, 124.4, 124.3, 120.9, 94.4, 88.2, 15.1. HRMS (TOFMS-CI+) m/z Calcd for $C_{15}H_{11}SClNH_4$ ([M+NH_4]$^+$): 276.0614; Found 276.0602.

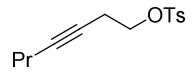


*(2-((2-Chlorophenyl)ethynyl)phenyl)(methyl)sulfane (**1b-xii**).* In an N$_2$-filled glovebox, a 20 mL scintillation vial was charged with 2-chloro-iodobenzene (0.16 mL, 1.3 mmol, 1.0 equiv), $(PPh_3)_2PdCl_2$ (46 mg, 0.065 mmol, 0.050 equiv), CuI (25 mg, 0.13 mmol, 0.10 equiv), and a stir bar. In a separate dram vial, **SI-2** (250 mg, 1.70 mmol, 1.3 equiv) was dissolved in Et_3N (3.9 mL). This solution was then added to the substrate-containing vial via pipette, which was capped and removed from the glovebox. The solution was stirred for 18 h at ambient temperature. At this time, TLC indicated complete consumption of starting material. The reaction mixture was diluted with 100 mL Et_2O and washed with saturated aqueous NH_4Cl (1 × 20 mL), water (1 × 20 mL), and brine (1 × 20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography using an elution gradient of 0% to 3% EtOAc in hexanes. Product-containing fractions were combined and concentrated in vacuo, and volatiles were removed at c.a. 10 mTorr for 18 h to afford **1b-xii** as a yellow oil (329 mg, 98% yield). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.62–7.61 (m, 1H), 7.54 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.44–7.43 (m, 1H), 7.33 (td, *J* = 7.9, 1.4 Hz, 1H), 7.28–7.23 (m, 2H), 7.20 (d, *J* = 7.7 Hz, 1H), 7.13 (td, *J* = 7.5, 1.1 Hz, 1H), 2.53 (s, 3H). ^{13}C NMR ($CDCl_3$, 151 MHz): δ 142.0, 136.0, 133.6, 132.8, 129.5, 129.5, 129.3, 126.6, 124.4, 124.4, 123.3, 121.2, 92.6, 92.0, 15.3. HRMS (TOFMS-CI+) m/z Calcd for $C_{15}H_{11}SCl$ ([M]$^+$): 258.0270; Found 258.0262.

*Procedure for Cyclizations of Thionasioles **1b-i**, **1b-ii** and **1b(ix–xii)**.* This procedure was performed in an N$_2$-filled glovebox. A dram vial was charged with *B*-chlorocatecholborane (99 mg, 0.64 mmol, 1.4 equiv) and 0.35 mL of d_8-toluene. A separate dram vial was charged with **1b(ix–xii)** (0.46 mmol, 1.0 equiv) and mesitylene (20. μL, 0.14 mmol, 0.33 equiv). The ClBcat/d_8-toluene containing solution was then transferred via pipette to the vial containing compound **1b(ix–xii)**. The contents of the vial were then transferred to a J. Young NMR tube. The tube was then capped, removed from the glovebox, and placed into a preheated 100 °C oil bath.

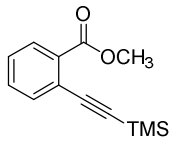
Single-scan ^{1}H spectra were taken at time points t = 0 h (before heating), and t = 2 h, for which the tube was briefly removed from the heating bath. The resonances corresponding to thioboration products **6b(ix–xii)** were compared to the internal standard to determine ^{1}H NMR spectroscopy yields. Each experiment was replicated. The yield and error are reported as the average and standard deviation of two runs, respectively.

*(2-(Hex-1-yn-1-yl)phenyl)(methyl)sulfane (**1a**).* (2-(Hex-1-yn-1-yl)phenyl)(methyl)sulfane was synthesized using a literature procedure[34] in 92% yield. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.36 (d, J = 7.6 Hz, 1H), 7.24 (t, J = 7.9 Hz, 1H), 7.12 (d, J = 7.5 Hz, 1H), 7.05 (t, J = 7.5 Hz, 1H), 2.50 (t, J = 7.0 Hz, 2H), 2.47 (s, 3H), 1.64 (quin, J = 7.9 Hz, 2H), 1.60–1.50 (m, 2H), 1.25 (t, J = 7.4 Hz, 3H). This spectrum is in agreement with previously reported spectral data.[34]

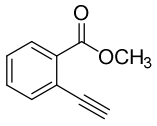


*Hept-3-yn-1-yl 4-methylbenzenesulfonate (**SI-4**).* Hept-3-yn-1-yl 4-methylbenzenesulfonate was synthesized using a literature procedure[37] in 58% yield. ^{1}H NMR (CDCl3, 600 MHz): δ 7.80 (d, J = 7.8 Hz, 2H), 7.34 (d, J = 7.7 Hz, 2H), 4.06 (q, J = 7.3 Hz, 2H), 2.51 (d, J = 7.1 Hz, 2H), 2.45 (s, 3H), 2.5 (d, J = 7.9 Hz, 2H), 1.44 (quin, J = 7.2 Hz, 2H), 0.92 (t, J = 7.4 Hz, 3H). This spectrum is in agreement with previously reported spectral data.[37]

*Hept-3-yn-1-yl(methyl)sulfane (**7**).* Hept-3-yn-1-yl(methyl)sulfane was synthesized using a literature procedure[34] in 14% yield. ^{1}H NMR (CDCl3, 600 MHz): δ 2.63 (t, J = 8.0 Hz, 2H), 2.47–2.44 (m, 2H), 2.14–2.11 (m, 5H), 1.50 (sext., J = 7.3 Hz, 2H), 0.96 (t, J = 7.3 Hz, 3H). This spectrum is in agreement with previously reported spectral data.[34]



*Methyl 2-((trimethylsilyl)ethynyl)benzoate (**SI-6**).* Methyl 2-((trimethylsilyl)ethynyl)benzoate was synthesized using a literature procedure[38] in 79% yield. ^{1}H NMR (CDCl3, 600 MHz): δ 7.90 (app d, J = 7.6 Hz, 1H), 7.58 (app d, J = 7.5 Hz, 1H), 7.44 (td, J = 7.6, 0.8 Hz, 1H), 7.36 (app t, J = 7.6 Hz, 1H), 3.92 (s, 3H), 0.27 (s, 9H). This spectrum is in agreement with previously reported spectral data.[38]



*Methyl 2-ethynylbenzoate (**SI-7**).* Methyl 2-ethynylbenzoate was synthesized using a literature procedure[38] in 83% yield. ^{1}H NMR (CDCl3, 600 MHz): δ 7.94 (d, J = 7.8 Hz, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 3.93 (s, 3H), 3.40 (s, 1H). This spectrum is in agreement with previously reported spectral data.[38]

*Methyl 2-((2-(methylthio)phenyl)ethynyl)benzoate (**1b-xiii**).* Methyl 2-((2-(methylthio)phenyl)ethynyl)benzoate was synthesized using a literature procedure according to a literature procedure[38] in 79% yield. ^{1}H NMR (CDCl3, 600 MHz): δ 7.94 (dd, J = 7.9, 1.4 Hz, 1H), 7.73 (dd, J = 7.6, 1.1 Hz, 1H), 7.54 (dd, J = 7.6, 1.2 Hz, 1H), 7.49 (dt, J = 7.5, 1.4 Hz, 1H), 7.39 (dt, J = 7.7, 1.3 Hz, 1H), 7.31 (dt, J = 7.9, 1.4 Hz, 1H), 7.19 (d, J = 7.9 Hz, 1H), 7.13 (dt, J = 7.5, 0.9 Hz, 1H), 3.93 (s, 3H), 3.39 (s, 3H). This spectrum is in agreement with previously reported spectral data.[38]

*Procedure for Competitive Cyclization of Thioanisole **1a** and Thioether **7**.* This procedure was performed in an N_2-filled glovebox. A dram vial was charged with *B*-chlorocatecholborane (13 mg, 0.087 mmol, 1.0 equiv) and 0.2 mL of d_8-toluene. Another dram vial was charged with **1a** (0.26 mmol, 3.0 equiv) and 0.1 mL of d_8-toluene. A third dram vial was charged with **7** (0.26 mmol, 3.0 equiv) and 0.1 mL of d_8-toluene. The **1a**/d_8-toluene containing solution was then transferred via pipette to the vial containing **7**/d_8-toluene, which was then transferred via pipette to the vial containing ClBcat/d_8-toluene. The final solution was then charged with mesitylene (6.0 μL, 0.043 mmol, 0.50 equiv) and then transferred to a J. Young NMR tube, sealed and removed from the glovebox. The tube was then placed in a preheated oil bath at 100 °C. Single-scan ^{1}H spectra were taken at time points t = 0 h (before heating), and t = 2 h and 4 h, for which the tube was briefly removed from the heating bath. The resonances corresponding to **6a** and **8** were compared to the internal standard to determine the relative yields of **6a** and **8**.

*Procedure for Intramolecular Competitive Cyclization of **6b-xiii** and **9**.* This procedure was performed in an N_2-filled glovebox. A dram vial was charged with *B*-chlorocatecholborane (141 mg, 0.91 mmol, 1.4 equiv) and 0.4 mL of d_8-toluene. A separate dram vial was charged with **1b-xiii** (0.65 mmol, 1.0 equiv). The ClBcat/d_8-toluene containing solution was then transferred via pipette to the vial containing compounds **1b-xiii**, and the solution was charged with mesitylene (30 μL, 0.217 mmol, 0.30 equiv). The contents of this vial were then transferred to a J. Young NMR tube. The vial was rinsed once with 0.1 mL of d_8-toluene and it was added to the J. Young NMR tube. The tube was then sealed and removed from the glovebox. The tube was placed in a preheated oil bath at 100 °C. Single-scan ^{1}H spectra were taken at time points t = 0 h, 2 h, and 4 h for which the tube was briefly removed from the heating bath. The resonances corresponding to **6b-xiii** and **9** were compared to the internal standard to determine the relative product ratios for the competition experiment.

*Preparation of Substrates **1a** and **6a** for ^{13}C KIE Measurements.* This procedure was performed in an N_2-filled glovebox. A 20 mL scintillation vial was charged sequentially with compound **1a** (2.75 g, 12.3 mmol, 1.00 equiv),

toluene (11.5 mL), *B*-chlorocatecholborane (2.65 g, 17.2 mmol, 1.40 equiv), and a stir bar. The vial was then sealed and placed in a preheated aluminum block at 85 °C and stirred. The mixture was vented by removing the cap briefly every 20 minutes to prevent pressure build up from the CH_3Cl byproduct. After 134 min, a small aliquot (~10 μL) of the reaction mixture was removed, diluted in d_8-toluene, and analyzed by single scan ^{1}H NMR to determine reaction conversion (75% conversion was detected at t = 134 min). In order to recover unreacted starting material for isotopic analysis, a flask was charged with MeOH (10 mL) and Et_3N (10 mL), and then cooled to 0 °C. The reaction mixture-containing vial was removed from the glovebox and added to this flask. The mixture was then stirred for 15 min at 0 °C. The mixture was then transferred to a separatory funnel, diluted with Et_2O (150 mL), washed with water (3 × 30 mL), and brine (1 × 30 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography using an elution gradient of 0% to 5% EtOAc in hexanes. Starting material (**1a**)-containing fractions were combined and concentrated in vacuo, and volatiles were removed at c.a. 10 mTorr for 18 h to recover 617 mg of starting material **1a**. Spectral data were identical to those previously obtained for this compound. This experiment was repeated on the 2.75 g scale, stopped at 74% conversion, and 664 mg was recovered of **1a**.

*(2-cyclopropyl-1-methyl-1H-benzo[b]thiophenium-3-yl)tris(pentafluoro)phenylborate (**19**).* *In* a flame-dried Schlenk flask under Ar, the 2-alkynyl thioanisole substrate **1d** (55 mg, 0.29 mmol, 1.0 equiv.) was dissolved in 2 mL of CH_2Cl_2, and a solution of $B(C_6F_5)_3$ (150. mg, 0.293 mmol, 1.01 equiv) in 2 mL of CH_2Cl_2 was added dropwise. After stirring 1 hour at 20 °C in CH_2Cl_2, the clear solution became a white suspension, and 10 mL of *n*-pentane was added to ensure full precipitation of a white solid. After filtration under nitrogen and washing the solid twice with 10 mL of a *n*-pentane:CH_2Cl_2 (8:2) mixture, and drying under high vacuum (10^{-3} mbar) for 6 h, the 1-methyl-1-benzothiophenium borate intermediate **19** was isolated in 81% yield (165 mg, 0.236 mmol). ^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.83 (app. d, J = 8.1 Hz, 1H, major rotamer), 7.72 (app. t, J = 8.0 Hz, 3H, minor + major rotamer), 7.50–7.57 (m, 2H, minor + major rotamer), 7.43 (app. t, J = 7.6 Hz, 2H, minor + major rotamer), 3.10 (s, 3H, S^+Me of minor rotamer), 2.91 (s, 3H, S^+Me of major rotamer), 1.98 (p, J = 7.9 Hz, 1H, cyclopropyl-CH of minor rotamer), 1.75 (p, J = 8.1 Hz, 1H, cyclopropyl-CH of major rotamer), 1.37–0.58 (m, 8H, cyclopropyl-CH_2 of minor and major rotamers). ^{19}F NMR (376 MHz, CD_2Cl_2): δ -127.2 (bs, 1F, *o*-F, major rotamer), -129.1 – -129.4 (m, 1F, *o*-F, minor + major rotamers), -129.6 (app. t., $^3J_{F\text{-}F}$ = 26.1 Hz, 1F, *o*-F, minor rotamer), -129.9 – -130.1 (m, 1F, *o*-F, minor + major rotamers), -131.0 (bs, 1F, *o*-F, major rotamer), -131.6 (bs, 1F, *o*-F, minor rotamer), -132.5 – -132.6 (m, 1F, *o*-F, minor rotamer), -133.8 – -133.9 (m, 1F, *o*-F, major rotamer), -134.9 (bs, 1F, *o*-F, minor rotamer), -136.4 (bs, 1F, *o*-F, major rotamer), -162.2 – -162.4 (m, 2F, 2 × *p*-F, minor + major rotamers), -162.6 (app. t, $^3J_{F\text{-}F}$ = 19.9 Hz, 1F, *p*-F, minor + major rotamers), -166.7 – -167.9 (m, 6F, *m*-F, minor + major rotamers). ^{13}C NMR (101 MHz, CD_2Cl_2): δ 133.5, 133.5, 128.7, 128.6, 127.6, 126.2, 126.1, 118.3, 33.8, 33.5, 11.3, 11.2, 10.6, 10.5, 10.0, 9.9, 9.3. (Only partial assignment, full attribution not attempted because of low resolution and low solubility.) ^{11}B NMR (128 MHz, CD_2Cl_2) δ -15.1. HRMS (FAB^-) m/z Calcd. for $C_{30}H_{11}BF_{15}S^-$ ([M-H]$^-$): 699.0440; Found 699.0450. IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3027, 1642, 1515, 1457, 1445, 1272, 1091, 1083, 970, 968, 775, 691. UV-Vis (CH_2Cl_2, 20 °C): λ_{max} = 231 nm (ε = 2.52 × 10^4 L mol^{-1} cm^{-1}), 268 nm (ε = 5.43 × 10^3 L mol^{-1} cm^{-1}) and 320 nm (ε = 3.22 × 10^3 L mol^{-1} cm^{-1}). Mp: 192–194 °C.

*Tetramethylammonium (2-cyclopropylbenzo[b]thiophen-3-yl)tris(pentafluoro)phenylborate (**20**).* The 2-alkynyl thioanisole substrate **1d** (100. mg, 0.531 mmol, 1.0 equiv.) was dissolved in 5 mL of CH_2Cl_2, and a solution of $B(C_6F_5)_3$ (273 mg, 0.533 mmol, 1.00 equiv) in 5 mL of CH_2Cl_2 was added with a syringe. After stirring for 1 hour at 20 °C in CH_2Cl_2 a white suspension was formed and a white solid precipitated (compound **19**). Compound **19** was treated by adding tetramethylammonium chloride $Me_4N^+Cl^-$ as a solid (60. mg, 0.55 mmol, 1.0 equiv.) and 5 mL of CH_3CN were added to the suspension (low solubility of $Me_4N^+Cl^-$ in CH_2Cl_2). After vigorous stirring overnight, approximately half of the solvent was removed under vacuum and 20 mL of Et_2O were added to the Schlenk flask, which resulted in the immediate precipitation of a white solid. Filtration under nitrogen and washing the solid twice with 15 mL of Et_2O and drying under high vacuum (10^{-3} mbar) for 10 h gave the benzothiophene **20** Me_4N^+ in 78% yield (316 mg, 0.416 mmol). ^{1}H NMR (400 MHz, CD_3CN): δ 7.60 – 7.63 (m, 1H, H-4), 7.52 (app. d, $^3J_{H\text{-}H}$ = 8.0 Hz, 1H, H-7), 6.95-7.03 (m, 2H, H-5 and H-6), 3.07 (app. t, $^2J_{N\text{-}H}$ = 0.6 Hz, 12H, Me_4N^+), 1.94 – 1.99 (m, 1H, H-10, signal overlapped with CD_3CN residual solvent peak), 0.74 – 0.81 (m, 1H, H-11 or H-12), 0.64 – 0.72 (m, 3H, H-11 and H-12). ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.60 (d, $^3J_{H\text{-}H}$ = 7.4 Hz, 1H, H-4), 7.40 (d, $^3J_{H\text{-}H}$ = 7.6 Hz, 1H, H-7), 6.93 – 7.00 (m, 2H, H-5 and H-6), 3.09 (br. s, 12H, Me_4N^+), 1.83 (p, $^3J_{H\text{-}H}$ = 6.4 Hz, 1H, H-10), 0.85 – 0.73 (m, 1H, H-11 or H-12), 0.69 – 0.46 (m, 3H, H-11 and H-12). ^{19}F NMR (376 MHz, CD_3CN): δ -127.80 (app. t, $^3J_{F\text{-}F}$ = 27.6 Hz, 1F, *o*-F), -129.23 – -129.40 (m, 1F, *o*-F), -130.29 (app. d, $^3J_{F\text{-}F}$ = 24.2 Hz, 1F, *o*-F), -131.19 (br. s, 1F, *o*-F), -132.55 (app. d, $^3J_{F\text{-}F}$ = 24.5 Hz, 1F, *o*-F), -134.58 (br. s, 1F, *o*-F), -164.36 (t, $^3J_{F\text{-}F}$ = 19.7 Hz, 2F, 2 × *p*-F), -165.04 (t, $^3J_{F\text{-}F}$ = 19.8 Hz, 1F, *p*-F), -168.00 – -168.38 (m, 3F, *m*-F), -168.46 – -169.07 (m, 3F, *m*-F). ^{13}C NMR (101 MHz, CD_3CN): δ 151.1 (m, C_6F_5), 149.9 (m, C_6F_5), 149.0 (s, C9), 148.4 (m, C_6F_5), 147.5 (m, C_6F_5), 146.3 (s, C2), 143.4 (m, C_6F_5), 142.8 (m, C_6F_5), 142.2 (m, C_6F_5), 141.6 (m, C_6F_5), 140.4 (m, C_6F_5), 139.6 (m, C_6F_5), 138.5 (m, C_6F_5), 138.2 (m, C_6F_5), 137.8 (s, C8), 137.2 (m, C_6F_5), 136.1 (m, C_6F_5), 127.2 (br. s, C3),124.5 (d, J = 9.0 Hz, C4), 123.2 (s, C5 or C6), 122.3 (s, C5 or C6), 122.0 (s, C7), 56.1 (s, Me_4N^+), 14.0 (d, J = 9.9 Hz, C10), 12.1 (C11 or C12), 10.9 (C11 or C12). Attribution for quaternary carbons of C_6F_5 rings not attempted. ^{11}B NMR (128 MHz, CD_3CN): δ –14.8. HRMS (ESI^-) m/z Calcd. for $C_{29}H_9BF_{15}S^-$ ([M-H]$^-$): 685.02840; Found

685.02935. IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3010, 1644, 1511, 1455, 1448, 1266, 1073, 974, 961, 948, 767, 685. UV-Vis (CH_2Cl_2, 20 °C): λ_{max} = 237 nm (ε = 2.64 × 10^4 L mol^{-1} cm^{-1}), 283 nm (ε = 8.86 × 10^3 L mol^{-1} cm^{-1}). Mp: 313–314 °C.

*Methyl(tris)(o-tolyl)phosphonium (2-cyclopropylbenzo[b]thiophen-3-yl)tris(pentafluoro)phenylborate (**20**).* The 2-alkynyl thioanisole substrate **1d** (100. mg, 0.531 mmol, 1.0 equiv.) was dissolved in 5 mL of CH_2Cl_2, and a solution of $B(C_6F_5)_3$ (273 mg, 0.533 mmol, 1.00 equiv) in 5 mL of CH_2Cl_2 was added with a syringe. After stirring for 1 hour at 20 °C in CH_2Cl_2 a white suspension is formed and a white solid precipitated. Tri(*o*-tolyl)phosphine was added as a solid (162 mg, 0.532 mmol, 1.00 equiv.) the solution was stirred overnight. Approximately half of the solvent was remove under vacuum and 20 mL of *n*-pentane were introduced, which resulted in the precipitation of a pale-brown solid. Filtration under nitrogen, washing the solid three times with 10 mL of *n*-pentane, and drying under high vacuum (10^{-3} mbar) for 48 h, gave **20**, $MeP^+(o\text{-tolyl})_3$ in 53% yield (281 mg, 0.280 mmol). Despite extensive drying under high vacuum, traces of *n*-pentane remained in the final product. ^{1}H NMR (600 MHz, CD_2Cl_2): δ 7.75 – 7.71 (m, 3H, 17-H), 7.58 – 7.48 (m, 5H, 18-H and 4-H and 7-H), 7.40 (app. t, J = 7.3 Hz, 3H, 16-H), 7.14 (app. dd, J = 15.7, 7.9 Hz, 3H, 15-H), 6.99 – 6.91 (m, 2H, 5-H and 6-H), 2.67 (d, $^1J_{P\text{-}H}$ = 12.8 Hz, 3H, 13-H), 2.28 (d, $^3J_{P\text{-}H}$ = 1.4 Hz, 9H, 20-H), 1.99 – 1.87 (m, 1H, 10-H), 0.79 – 0.57 (m, 4H, 11-H and 12-H, signal overlapped with traces of *n*-pentane, see description above). ^{19}F NMR (376 MHz, CD_2Cl_2): δ -127.01 (t, $^3J_{F\text{-}F}$ =27.7 Hz, 1F, *o*-F), -128.54 – -128.88 (m, 1F, *o*-F), -130.08 (d, $^3J_{F\text{-}F}$ = 24.0 Hz, 1F, *o*-F), -130.48 (t, $^3J_{F\text{-}F}$ = 22.2 Hz, 1F, *o*-F), -132.28 (dt, $^3J_{F\text{-}F}$ = 25.4, 7.5 Hz, 1F, *o*-F), -133.63 – -133.88 (m, 1F, *o*-F), -136.18 (br. d, $^3J_{F\text{-}F}$ = 20.5 Hz, 1F, *o*-F), -164.03 (app. q., $^3J_{F\text{-}F}$ = 17.2 Hz, 2 F, 2 × *p*-F), -164.82 (t, $^3J_{F\text{-}F}$ = 20.6 Hz, 1F, *p*-F). -167.1 (dddd, J = 24.6, 20.3, 8.4, 4.2 Hz, 1F, *m*-F), -167.27 (dddd, J = 24.9, 20.5, 8.2, 4.4 Hz, 1F, *m*-F), -167.44 (dddd, J = 25.1 Hz, 20.7, 7.9, 4.4 Hz, 1F, *m*-F), -167.68 (dddd, J = 25.0, 20.7, 8.7, 4.2 Hz, 1F, *m*-F), -167.10 – -168.00 (m, 2 F, 2 *m*-F). ^{13}C NMR (151 MHz, CD_2Cl_2): δ 150.2 (m, C_6F_5), 149.8 (m, C_6F_5), 148.9 (m, C_6F_5), 148.7 (s, C9), 148.2 (m, C_6F_5), 147.3 (m, C_6F_5), 145.6 (s, C9), 143.4 (d, J = 8.8 Hz, C-19), 139.4 (m, C_6F_5), 138.7 (m, C_6F_5), 137.7 (m, C_6F_5), 137.2 (s, C-8), 136.11 (bs, C-17), 135.8 (m, C_6F_5), 134.7 (d, J = 12.5 Hz, C-15), 134.4 (d, J = 11.0 Hz, C-18), 128.4 (d, J = 13.2 Hz, C-16) 124.2 (d, J = 5.9 Hz, C-4), 122.5 (s, C-5 or C-6), 121.4 (s, C-5 or C-6), 121.3 (s, C-7), 117.3 (d, J = 85.1 Hz, C-14), 22.9 (s) 14.55 (d, J = 57.3 Hz, C-20), 13.6 (d, J = 9.6 Hz, C-10), 11.8 (C11 or C12), 10.6 (C11 or C12). Full attribution for quaternary carbons of C_6F_5 rings not attempted. Contains traces of *n*-pentane at 14.2, 22.8 and 34.6 ppm, see description above). ^{31}P NMR (162 MHz, CD_2Cl_2): δ –14.8. ^{11}B NMR (128 MHz, CD_2Cl_2): δ 21.6. IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2927, 1640, 1510, 1455, 1269, 1079, 975, 747. Mp: 144–148 °C.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Plots of kinetic data analysis, UV-Vis, IR, ^{1}H NMR and ^{13}C NMR spectra and crystal structure for compound characterization and details of computational analyses (PDF)

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Notes

The authors declare the following competing financial interests: U.S. patent 9,238,661 and provisional patent application no. 61/906,040 have been filed by the University of California.

Author Contributions

The manuscript was written through contributions of all authors. / All authors have given approval to the final version of the manuscript. / #These authors contributed equally.

ACKNOWLEDGMENT

This work was supported by a grant from the NIH (1R01GM098512-01), by the Alexander von Humboldt Foundation through a fellowship to S.A.B., and by the University of California, Irvine. We thank Dr. Phillip R. Dennison for NMR spectroscopy assistance. G.B. thanks Prof. Dr. Herbert Mayr and Dr. Armin R. Ofial for helpful discussions and for invaluable support via the Deutsche Forschungsgemeinschaft (SFB 749, project B1). J.O.B. and D.A.S. thank the NIH (GM 45617) for their financial support.

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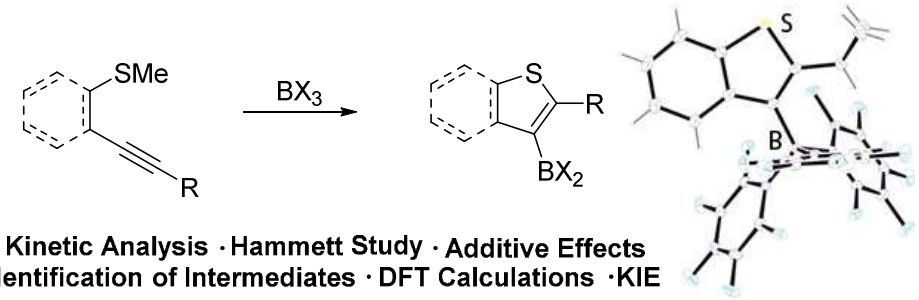

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· Identification of Intermediates · DFT Calculations ·KIE