FORMATION AND CAPTURE OF THIIRANIUM ION INTERMEDIATES USING LEWIS ACIDS

BY

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THESIS

Submitted in partial fulfillment of the requirements
for the degree of Master of Science in Chemistry
in the Graduate College of the
University of Illinois at Urbana-Champaign, 2015

Urbana, Illinois

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Abstract

The aprotic formation of thiiranium ions and subsequent nucleophilic capture was investigated. It was discovered that β-methoxy and β-acetoxy sulfides could form thiiranium ions in the presences of BF_3•OEt_2, TMSOTf and various organoaluminum reagents. Treatment of β-methoxy and β-acetoxy sulfides with BF_3•OEt_2 or TMSOTf allowed for the capture of thiiranium ions by silyl enol ethers, serving as external nucleophiles. However, treatment with Lewis acid caused a drop in the enantiopurity of the thiiranium ion. Varying the amount of Lewis acid, amount and type of nucleophile, temperature and concentration failed to provide conditions where the reaction could proceed in an enantiospecific manner.

While investigating new Lewis acids that would allow for enantiospecific formation and capture of thiiranium ions, it was serendipitously discovered that trialkylaluminum reagents could form thiiranium ions and transfer an alkyl group. Further investigation showed that dimethyl(phenylethynyl)aluminum could selectively transfer an alkynyl group. A library of β-acetoxy (2,6-diisopropylphenyl) sulfides was synthesized and underwent both methylation and alkynylation with high yields. It was later determined that the installation of a 2,6-diisopropylphenyl group was unnecessary to achieve high yields and 100% enantiospecificity. A library of various β-acetoxy (phenyl) sulfides underwent methylation and alkynylation with very high yields and 100% enantiospecificity in almost all cases. Arylation and alkenylation via organoaluminum reagents were briefly investigated; however, further studies are needed to successfully prepare the organoaluminum reagent and treat it with β-acetoxy (phenyl) sulfides.

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Chapter 1. Introduction and Background of Asymmetric Thiofunctionalization

1.1 Importance and Use of Organosulfur Compounds

Organosulfur compounds are widely present in nature whether in the form of simple amino acids or complex natural products.[1] Nature has inspired the incorporation of sulfur in numerous small molecule drugs; 7 out of the top 10 selling small molecule drugs in 2012 contained sulfur.[2] Low oxidation state sulfur moieties are present in many agrochemicals as sulfur oxygenation is critical to various mechanisms of action.[3] The introduction of sulfur moieties into agrochemicals and pharmaceuticals is increasingly common and new thiofunctionalization methods are necessary to meet rising demand.[4] Many important organosulfur compounds (Figure 1) contain sulfur–bearing stereogenic centers highlighting the importance of asymmetric thiofunctionalizations, which are lacking when compared to existing racemic transformations.[5]

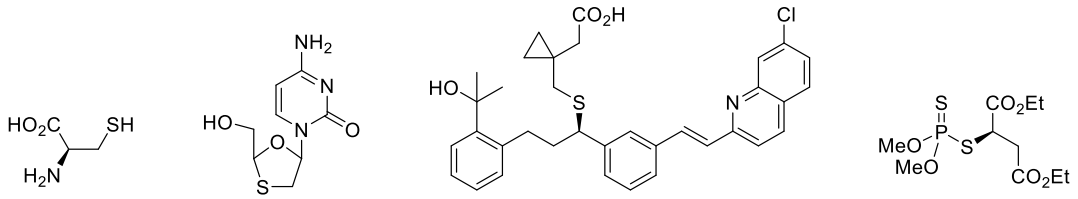
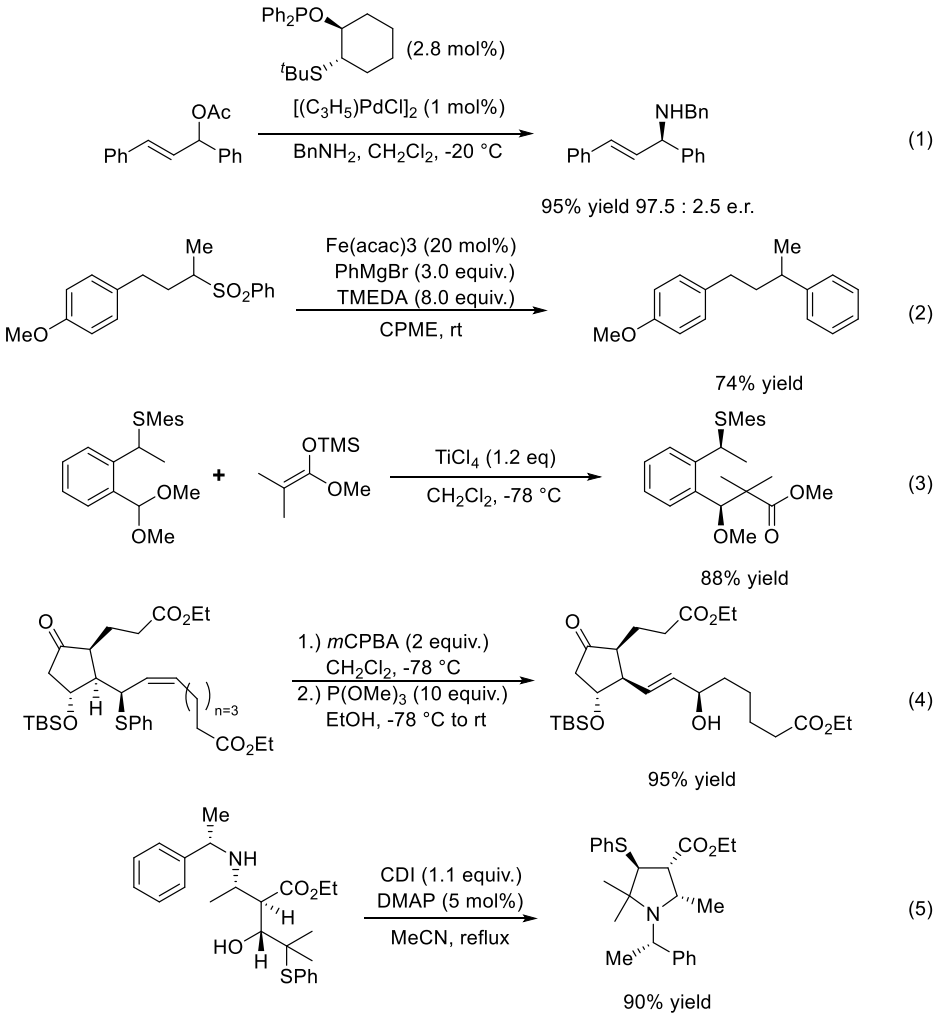


Figure 1. Examples of Sulfur Containing Small Molecules

In addition to applications in pharmaceuticals and agrochemicals, sulfur is a useful synthetic handle for a variety of chemical transformations (Scheme 1). Sulfur can act as a ligand for other transition-metal-catalyzed asymmetric transformations (Scheme 1, 1).[6] Aryl sulfides can act as electrophiles in transition-metal-catalyzed cross-couplings (Scheme 1, 2).[7] Sulfides can provide asymmetric induction via neighboring group participation (Scheme 1, 3).[8] Sulfides can be oxidized to a corresponding sulfoxide when can then undergo a Mislow-Evans rearrangement (Scheme 1, 4).[9] They can also be used for heterocycle synthesis (Scheme 1, 5).[10] Sulfides can be

readily removed via hydrogenation with Raney nickel or radical conditions after their utility as synthetic handles has passed.

Scheme 1

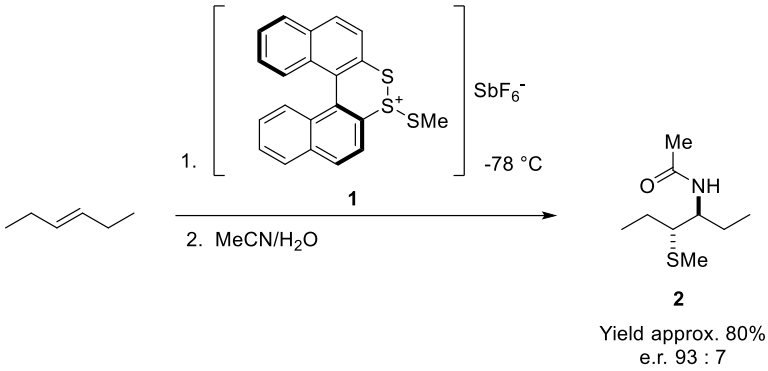


1.2 Current Methods in Asymmetric Thiofunctionalization

Numerous methods are available for the asymmetric construction of organosulfur compounds using both transition-metal catalysis and organocatalysts.[1,11] However, the asymmetric thiofunctionalization of unactivated alkenes is under developed. Until recently, there was only a single report of a stereoselective addition of sulfur to an unactivated alkene (Scheme 2).[12] The

authors formed an enantioenriched thiiranium ion using chiral thiosulfonium salt **1**. The thiiranium ion was opened by acetonitrile which afforded **2** after aqueous work-up.

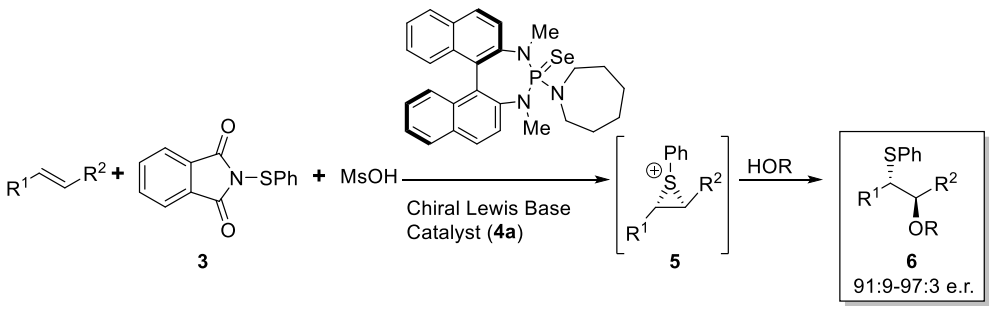
Scheme 2



Thiiranium ions are well-studied intermediates in the transformation of olefins into vicinally functionalized sulfides.[13] Thiiranium ring opening occurs readily with a many nucleophiles and proceeds in a stereospecific manner. The ring opening of thiiranium ions derived from *trans*-alkenes afford *anti*-functionalized sulfides. The stereospecific nature of ring opening ensures complete fidelity in the transfer of stereochemical information of the thiiranium ion to the product.

To access enantioenriched thiiranium ion intermediates, these laboratories have developed catalytic, asymmetric thiofunctionalization reactions of unactivated olefins using the principle of Lewis base activation.[14] However, for intermolecular thiofunctionalizations, the nucleophile scope was limited to alcohols and carboxylic acids. Furthermore, the developed catalytic system is not compatible with acid sensitive nucleophiles. Activation of arylsulfenyl reagent **3** with a strong acid, such as methanesulfonic acid, is required before it can interact with the chiral Lewis base catalyst **4** (Scheme 3). Other sulfenylating reagents have been investigated but still require the use of a Brønsted acid co-catalyst or an activated alkene.[15,16]

Scheme 3



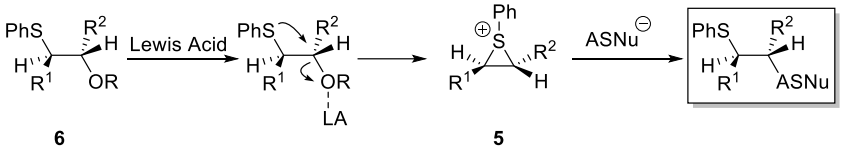
The work presented aims to expand the scope of this asymmetric transformation to include acid sensitive nucleophiles.

Chapter 2. Thiiranium Formation Using Lewis Acids and Capture with Acid Sensitive Nucleophiles

2.1 Introduction and Background

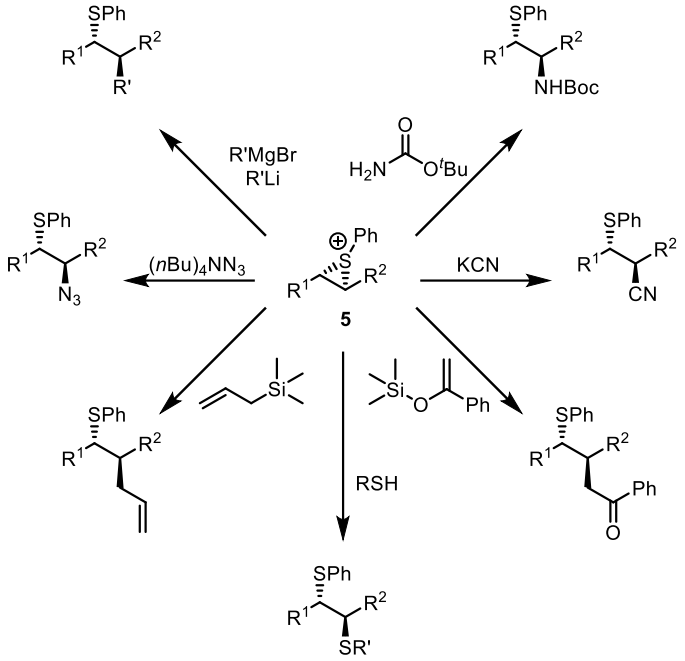
The goal of this project is to develop a method that facilitates the employment of acid sensitive nucleophiles for the vicinal thiofunctionalization of olefins that complements current work by these laboratories. To use acid sensitive nucleophiles, a thiiranium ion must be formed in an aprotic environment. Thiiranium ions can be generated upon displacement of a leaving group with neighboring–group participation by a sulfide group.[17] If done aprotically, the resulting thiiranium ion can be captured with an acid sensitive nucleophile. To aid the displacement of the neighboring leaving group, the sulfide **6** can be exposed to a Lewis acid to generate the desired thiiranium ion **5** in stoichiometric amounts which allows for the capture by an acid sensitive nucleophile ($ASNu^-$) (Scheme 4).

Scheme 4



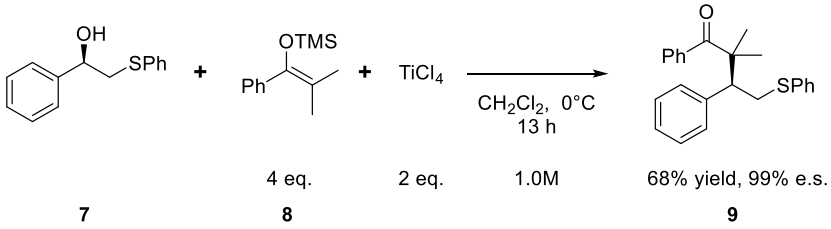
If a general Lewis acid that reforms thiiranium ion **5** can be found, a variety of acid sensitive nucleophiles can be used (Scheme 5).

Scheme 5



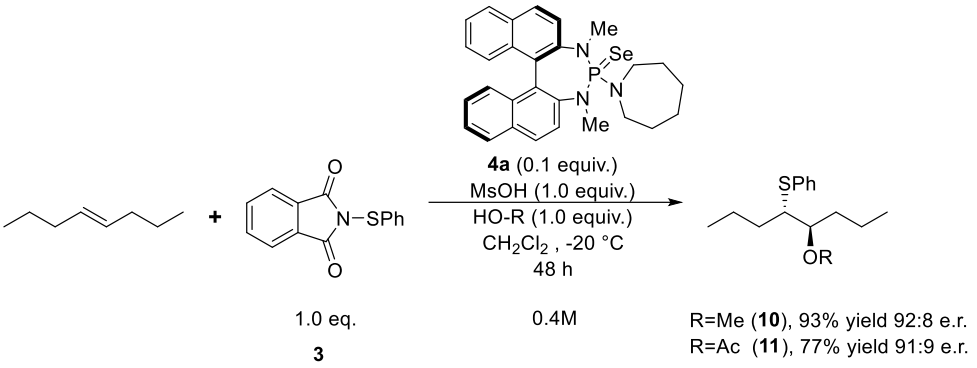
Toshimitsu and co-workers successfully pursued a similar strategy as applied to primary β-hydroxy sulfides using $TiCl_4$ (Scheme 6).[18] The authors treated 2-hydroxyalkyl phenyl sulfide **7** with tetrasubstituted silyl enol ether **8** and $TiCl_4$ which yielded ketone **9** with 99% enantiospecifity.

Scheme 6



The first objective in pursing this strategy was have an easily prepared thiiranium ion precursor. Previous studies by these laboratories showed that AcOH and MeOH were competent nucleophiles in the intermolecular asymmetric thiofunctionalization, affording enantioenriched β-methoxy and β-acetoxy (phenyl) sulfides (**10** & **11**) respectively (Scheme 7).[19] A methoxy or acetoxy group could be displaced by a vicinal sulfide (anchimeric assistance) after coordination to a Lewis acid, forming a thiiranium intermediate in an aprotic environment.

Scheme 7



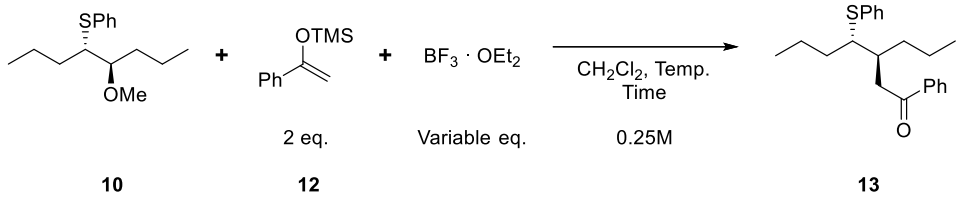
2.2 Results and Discussion

β-Methoxy sulfide **10** was chosen as the thiiranium ion precursor as it could be prepared in a higher yield than the β-acetoxy sulfide **11**. A number of Lewis acids including $TiCl_4$, $SnCl_4$, Et_2AlCl and $BF_3 \bullet OEt_2$ were chosen for an initial survey. Silyl enol ether **12** was chosen as a representative acid sensitive nucleophile of moderate strength.[20] This choice was guided by the desire to develop a general method that can be applied to sensitive nucleophiles of differing nucleophile strength. If a poor-to-fair nucleophile were successful in capturing the thiiranium ion, then the transformation conditions could be applied to stronger nucleophiles without extensive optimization.

No reaction was observed at -20° C using $TiCl_4$ or EtAlCl. $SnCl_4$ promoted the sulfenylation of the silyl enol ether **12** (forming 1-phenyl-2-(phenylthio)ethan-1-one). $BF_3 \bullet OEt_2$ was the only Lewis acid to from the desired ketone **13**, albeit at less than full conversion. To rectify this, a matrix of reaction conditions was created by varying equivalents of $BF_3 \bullet OEt_2$ and reaction temperature (Table 1). The sole metric of this screen was the extent of conversion of the β-methoxy sulfide **10** as measured by ^1H NMR analysis. The product and starting material are inseparable via silica gel column chromatography so it was deemed essential to have full starting material

conversion, so that the product could be easily purified, before any further optimization could be attempted.

Table 1- Screening Variable Amounts of $BF_3 \cdot OEt_2$ at Varying Temperature [a]



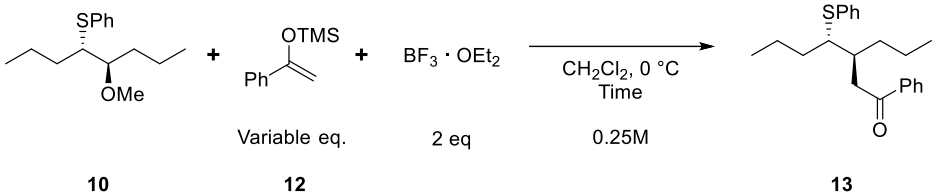
Entry	Equivalents of BF_3•OEt_2	Temperature (ºC)	Full SM Conversion[b]	Time, h[c]
1	1	-20	No	24
2	2	-20	No	24
3	5	-20	Yes	20
4	1	0	No	24
5	2	0	Yes	5
7	1	23	Yes	5.25
8	2	23	Yes	1.75
9	5	23	Yes	1.25

[a] All reactions run on a 0.25 mmol scale. [b]Determined by ^{1}H NMR analysis after work-up procedure. [c]All reactions quenched at 24 h if full SM conversion had not been observed.

Reactions run at room temperature reached full conversion faster than those at 0°C and -20°C, irrespective of equivalents of BF_3•OEt_2 (Table 1, entries 7-9). However, previous research by these laboratories has demonstrated that racemization of the thiiranium ion could occur within the time scale of these reactions at room temperature which is why reactions at 0 °C were selected for further optimization.[21] The conditions of Table 1, entry 5 were selected as the starting point for additional optimization of the equivalents of the nucleophile used.

When less than two equivalents of **12** were used, full conversion of **13** was not observed (Table 2, entries 2-4). Increasing the number of equivalents of **12** to 2.0 gave full conversion of **10** in five hours. (Table 2, entry 1). In an effort to lower the amount of nucleophile used, the concentration increased to 1M which gave full conversion in 14 hours with 1.5 equivalents of **12**.

Table 2- Screening Variable Amounts of Nucleophile at 0 °C [a]



10 **12** **13**

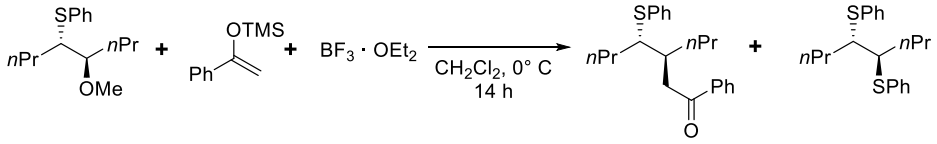
Entry	Equivalents of **12**	Percent **10** Conversion[b]	Time, h[c]
1	2.00	100	5
2	1.50	96	25
3	1.25	87	48
4	1.05	84	48

[a] All reactions run on a 0.25 mmol scale. [b]Determined by ^{1}H NMR analysis after work-up procedure. [c]All reactions quenched at 48 h if full SM conversion had not been observed.

2.2.1 Enantiospecificity of Optimized Reaction Conditions

After preliminary optimization of the reaction conditions, the reaction was performed with enantioenriched **10** to determine if the reaction had proceeded with enantiospecificity (Scheme 8). In addition to the desired product **13**, 20% of the starting material was consumed to form bisphenylsulfane **14** as isolated by preparative TLC, a side product that was formed, but not noticed, in earlier optimizations (Tables 1 and 2). The product **13** had an enantiomeric ratio of 85:15 giving an enantiospecificity of 83%.

Scheme 8

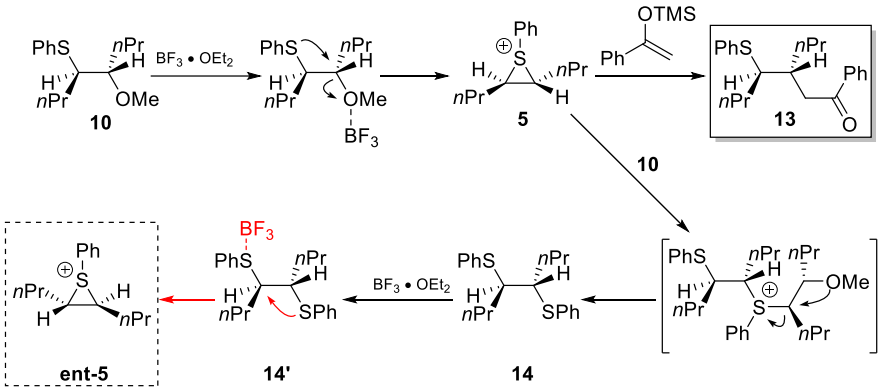


10 **12** **13** **14**

This disappointing drop in enantiopurity was linked to the formation of the bisphenylsulfane **14**, illustrated in the proposed mechanism shown (Scheme 9). The formation of **14** is undesirable as it can lead to racemization when using enantioenriched reagents. The topmost

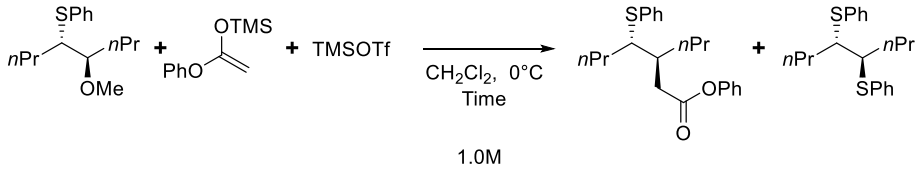
linear sequence, exclusively with black arrows, is the proposed mechanism for the formation of the desired product **18**. The bisphenylsulfane **14** is formed when uncomplexed starting material **10**, opens **5** (intermediate shown in brackets). When **14** is ligated to BF_3•OEt_2 (denoted as **14'**), it can proceed in an undesired pathway were the enantiomeric thiiranium ion, **5'**, is formed (indicated with red arrows). Capture of the thiiranium ion **5'** with silyl enol ether **12** compromises the enantiomeric purity of the product. Since bisphenylsulfane **14** can cause an erosion of enantiopurity, the prevention of its formation was a top priority in all future work.

Scheme 9



Silyl ketene acetals were briefly investigated as nucleophiles. It was thought that a stronger nucleophile would capture thiiranium ion **5** before it underwent racemization. TMSOTf was used as the Lewis acid as it proved to be more compatible than BF_3•OEt_2 with the nucleophile. The bisphenyl sulfane **14** was formed in each reaction (Table 3).

Table 3- Screening Variable Amounts of Silyl Ketene Acetal Nucleophile and TMSOTf



10 **15** **16** **14**

Entry	**15** Equivalents	TMSOTF Equivalents	Yield **16**	Yield **14**	Time, h[b]
1	2.0	5.0	34%	33%	9
2	2.0	1.05	N.D.	N.D.	24
3	1.05	1.05	N.D.	N.D.	8

[a] All reactions run on a 1.0 mmol scale. [b]All reactions quenched at 24 h if full SM conversion had not been observed.

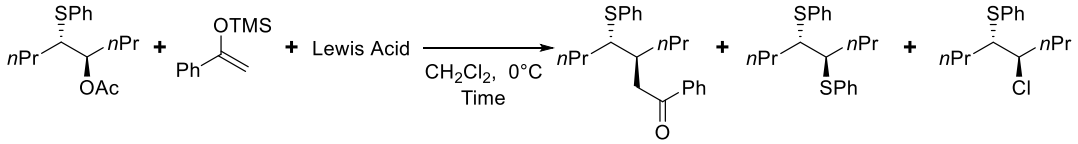
2.2.2 Replacement of the Methoxy Leaving Group with an Acetoxy Group

With extensive work examining effects of the Lewis acid, nucleophile, temperature and concentration, the precursor of the thiiranium ion was examined. As a final point of optimization, investigating the effect of leaving group was performed. Given that the acidity of acetic acid is approximately 10 orders of magnitude greater compared to methanol, the acetoxy group should be a superior leaving group when employing a survey of Lewis acids (Table 3). The facile formation of thiiranium ion **5** would help prevent the formation of bisphenylsulfane **14** as the amount of unreacted starting material would be much smaller. The β-acetoxy sulfide **11** replaced β-methoxy sulfide **10** as the thiiranium ion precursor. Due to the new thiiranium ion precursor, optimization of the reaction had to begin all over again. Silyl enol ether **12** was used for this new optimization survey so that comparisons between **10** and **11** could be made.

To begin the initial screen, a wide scope of Lewis acids were examined including Et_3Al, Et_2AlCl, $SnCl_4$, $TiCl_4$, $Ti(OiPr)_4$, $BF_3 \bullet OEt_2$, TMSOTf, and $TMSNTf_2$. Lewis acids containing a labile chloride ligand (Table 4, entries 2, 3 and 4) provided the β-chloro sulfide **17**. Lewis acids without chloride ligands that were tested yielded varying results. Et_3Al produced ketone **13** (Table 4, entry 1) where Et_2AlCl furnished β-chloro sulfide **17** without formation of **13** (Table 4, entry 2). Formation of **14** indicated that the thiiranium ion was not being generated in a stoichiometric

amount nor was thiiranium ion formation occurring on a time scale as to prevent opening of the thiiranium ion by uncoordinated starting material **10**. Et_3Al is noteworthy as it was the only Lewis acid that produced **13** without side products **14** and/or **17** as such, it was used for further optimization.

Table 4- Screening Lewis Acids with Acetoxy Leaving Group [a]



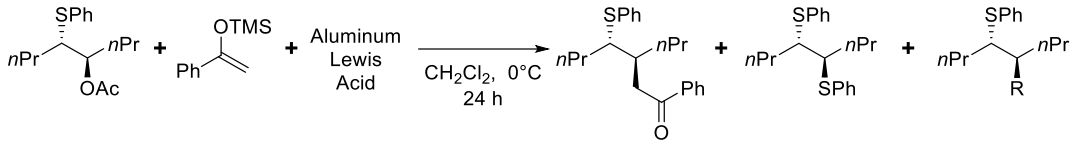
Entry	Lewis Acid	Time, h[c]	Products as a Percentage of **11** Consumed[b], %			
			Unreacted **11**	**13**	**14**	**17**
1	Et_3Al [d]	24	76	24	0	0
2	Et_2AlCl	48	40	0	0	60
3	$SnCl_4$	24	15	0	32	53
4	$TiCl_4$	2.5	0	0	0	100
5	$Ti(OiPr)_4$	6	100	0	0	0
6	$BF_3 \bullet OEt_2$	48	70	18	12	0
7	TMSOTf	48	0	9	91	0
8	$TMSNTf_2$	2	11	0	89	0

[a] All reactions run on a 0.25 mmol scale. [b]Determined by ^1H NMR analysis after work-up procedure. [c]All reactions quenched at 24 h if full SM conversion had not been observed. [d]As a 1M solution in hexane.

Et_3Al and other alkylaluminum reagents were then examined to determine if they could furnish the desired product without the formation of any deleterious side products (Table 5). Starting with conditions obtained in the initial screen (Table 5, entry 1) the amount of nucleophile **12** was increased to two equivalents with a negligible difference in yield (Table 5, entry 2). Increasing Et_3Al to two equivalents (Table 5, entry 3) resulted in the formation of two new side products **18** and **19**. Alkyl substitution product **18** is the result of an alkyl group transfer from the organoaluminum reagent to the thiiranium ion (See Chapter 3 for further discussion on alkyl transfer). Thioether **19** is the result of hydride transfer from Et_2AlH, an impurity present in commercial Et_3Al. Increasing both silyl enol ether **12** and Et_3Al to two equivalents did not result

in full conversion of starting material and afforded the desired product in a 6% yield (Table 5, entry 4).

Table 5- Screening Conditions for Aluminum Assisted Thiiranium Ion Formation [a]



11 **12** **13** **14**

Entry	**12** Equivalents	Lewis Acid Equivalents	Yield **13**[b],%	Recovered **11**, %	Yield **18** [b], %	Yield **19** [b], %	Yield **14** [b], %
1	1.0	1.0 Et_3Al[c]	24	76	0	0	0
2	2.0	1.0 Et_3Al[c]	22	75	0	0	0
3	1.0	2.0 Et_3Al[c]	0	0	70	20	0
4	2.0	2.0 Et_3Al[c]	6	38	33	11	0
5	1.0	1.0 Me_3Al	50	9	40	0	0
6	2.0	1.0 Me_3Al	73	11	4	0	12
7	1.0	2.0 Me_3Al	18	5	50	0	0
8	2.0	2.0 Me_3Al	53	0	21	0	0
9	2.5	1.25 Me_3Al	58	30	6	0	0
10	1.0	1.0 $(iBu)_3Al$	No Reaction				

[a] All reactions run on a 0.25 mmol scale. [b]Determined by ^1H NMR analysis after purification via flash column chromatography. [c]As a 1M solution in hexane.

In an effort to prevent formation of thioether **19**, Me_3Al, which does not have any hydride impurity, was used. Treatment of one equivalent of both silyl enol ether **12** and Me_3Al provided desired product **13** as well as the alkylated side product (Table 5, entry 5). Increasing silyl enol ether **12** to two equivalents formed the undesired bisphenylsulfane **14** (Table 5, entry 6) which was paradoxically not observed when using one equivalent of **12** (Table 5, entry 5). Using two equivalents of both silyl enol ether **12** and Me_3Al allowed for the full conversion of starting material and increased the yield of the desired ketone **13** to 21% (Table 5, entry 8). Further attempts to optimize the reaction conditions to maximize yield of desired product **13** met with failure (Table 5, entry 9). $(iBu)_3Al$ was not competent in forming the thiiranium ion (Table 5, entry 10).

2.3 Conclusions and Outlook

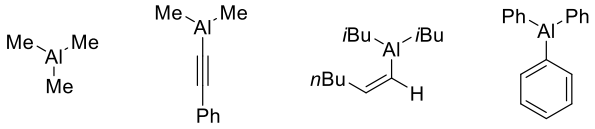
Unfortunately, conditions to reform a thiiranium ion enantiospecifically using Lewis acids to allow capture with an acid-sensitive nucleophile in high yields were not found. Conditions that consumed all starting material typically formed bisphenylsulfane **14**, which is indicative in the racemization of thiiranium ions. Conditions that did not form bisphenylsulfane **14** suffered from poor yields. However, conditions were found for the formation and alkylation of thiiranium ions using organoaluminum reagents.

Chapter 3. Formation and Capture of Thiiranium Ions Using Organoaluminum Reagents

3.1 Introduction and Background

The success of forming the alkyl product **18** stimulated a new direction in method development where the action of forming a thiiranium ion would also result in a nucleophilic aluminate species that could be used to capture the thiiranium ion. Although the scope of possible acid sensitive nucleophiles would be reduced to those that are a part of the aluminum Lewis acid, addition of acid sensitive carbon nucleophiles could be achieved using organoaluminum reagents. It was envisioned that a variety of aluminum reagents could be used to both form and capture thiiranium ions with alkyl, alkenyl, alkynyl and aryl groups (Scheme 10).

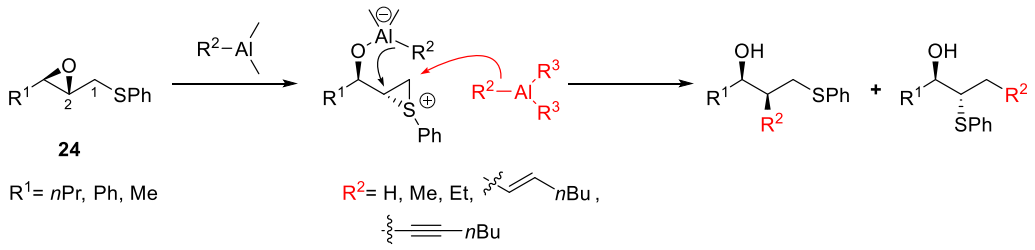
Scheme 10



20 **21** **22** **23**

The opening of thiiranium ions using organoaluminum reagents has been previously explored by Saigo and co-workers.[22] The authors combined 1-phenylthio-2,3-epoxyalkanes (**24**) with various organoaluminum reagents which they believe proceed via a thiiranium ion intermediate (Scheme 11).

Scheme 11



24

R^1= *n*Pr, Ph, Me

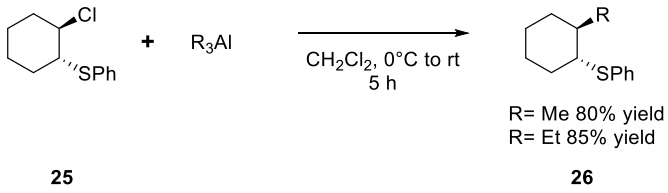
R^2= H, Me, Et, *n*Bu, *n*Bu

The authors propose that the organoaluminum reagent coordinates to the epoxide oxygen and the sulfur atom attacks at the C-2 position from the backside of the C-O bond, breaking it, and

forming a thiiranium ion intermediate. The R^2 group of the aluminum reagent could then attack at either the C-1 or C-2 positions. The authors reported that intramolecular attack at C-2 would occur if Me_3Al were used. However, intermolecular attack would occur at C-1 if alkenyl-, alkynlaluminum, or DiBAl-H were used. The authors rationalized this outcome by citing the fact that alkenyl- alkynylaluminum and DiBAl-H are all more reactive than alkylaluminum and the fact that there is a steric disadvantage with attack at C-2.

The alkylation of racemic β-chloro sulfides was explored by Reetz in 1987.[23] Reetz and co-workers demonstrated that trimethylaluminum and triethylaluminum would add to β-chloro sulfide **25** in a stereospecific manner in moderate to good yields (Scheme 12).

Scheme 12

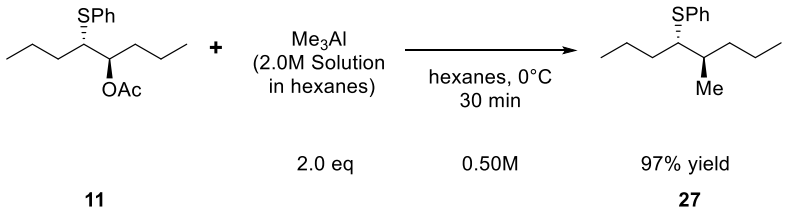


3.2 Results and Discussion

3.2.1 Optimization of Me_3Al- Mediated Capture of Thiiranium Ions

After investigating the use of organoaluminum reagents to form thiiranium ions, it was determined that Me_3Al alone could form and capture a thiiranium ion generated from β-acetoxy sulfide **11,** delivering a methyl group (Scheme 13). Formation of **27** was clean with no other products observed.

Scheme 13

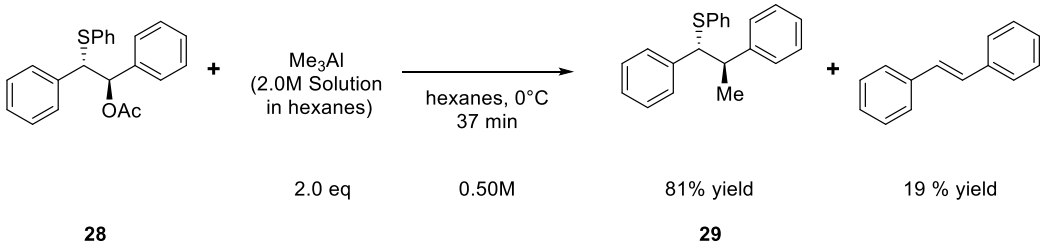


The experimental results demonstrated that it was possible to transfer a methyl group to a thiiranium ion with two equivalents of Me_3Al. When trying to lower the number of equivalents of Me_3Al to 1.0, only an 8% conversion was observed after 24 hours. The additional equimolar amount of Me_3Al is likely required due to the coordination of Me_3Al with the formed acetoxy(dimethyl)aluminum reduces the amount of competent Me_3Al in the reaction mixture.[24]

3.2.2 Effect of Sulfur Aryl Group Substitution

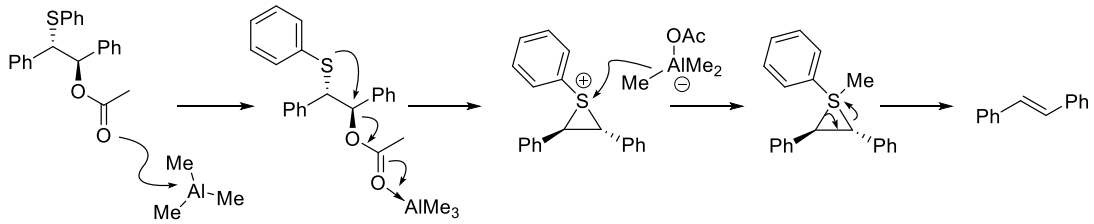
When attempting to transfer these conditions to the stilbene based β-acetoxy sulfide **28**, it was observed that 19% of the starting material was transformed into stilbene due to Me_3Al attack at sulfur (Scheme 14).

Scheme 14



Experimentally, thiiranium ions show ambident electrophilicity with hard nucleophiles preferring attack at carbon. Softer nucleophiles generally prefer attack at the sulfonium sulfur.[25] Therefore, it was unexpected that olefin was formed, the result of nucleophilic attack at sulfur (Scheme 15)

Scheme 15

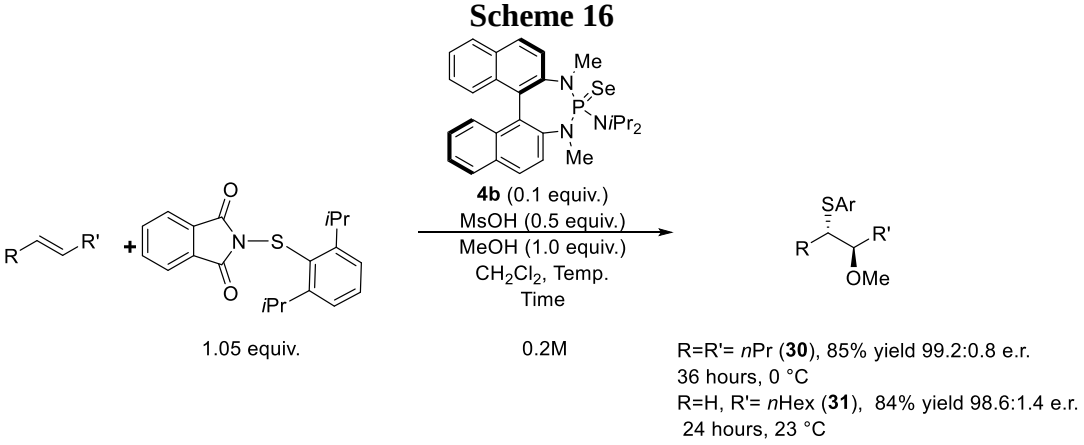


It is possible that the proximity of the aluminate to the sulfonium sulfur allowed nucleophilic attack to occur at sulfur rather than carbon. A similar problem was observed by Reetz

and co-workers.[23] Upon methylating thiiranium ions using $(Me)_2Zn/TiCl_4$, the authors found that modifying the sulfonium aryl group from phenyl to 2,4,6-triisopropylphenyl group resulted in fewer by-products (i.e. reformed olefin and thioanisole). In an attempt to suppress this mechanistic pathway in this work, the steric bulk around sulfur was increased by inserting *iso*-propyl groups on both of the *ortho*-positions of the arylsulfenyl group.

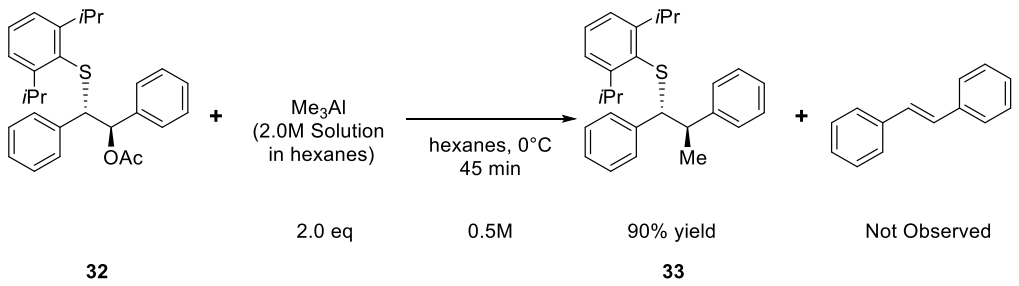
Recent investigations in these laboratories have shown that steric properties of the arylsulfenyl group can impact the stereochemical outcome of the asymmetric thiofunctionalization of alkenes (Scheme 16).[26] Products **30** and **31** were accessed with excellent enantiomeric ratios, 99.2:0.8 and 98.6:1.4 respectively.

Scheme 16



In addition to greater starting material enantiopurity, the installation of *iso*-propyl groups on the arylsulfenyl group suppressed all olefin formation when the stilbene derived β-acetoxy sulfide **32** was treated with Me_3Al (Scheme 17).

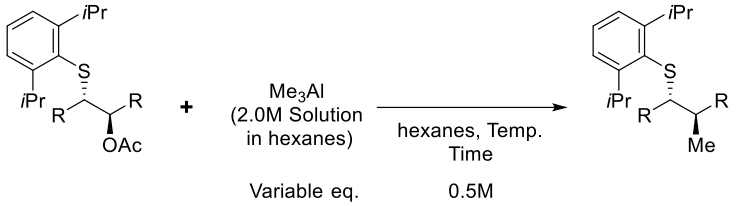
Scheme 17

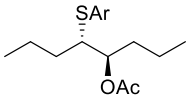
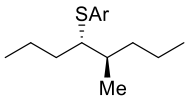
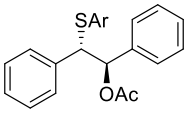
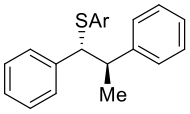
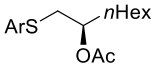
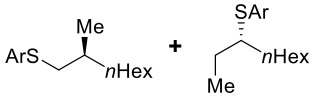
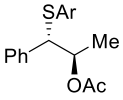
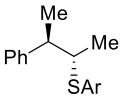


3.2.3 Scope of β-Acetoxy 2,6-Diisopropylphenyl Sulfides

With a viable class of substrate in hand, a variety of organoaluminum reagents were examined. The methylation of **34** using two equivalents of Me_3Al did not did not consume the starting material after 24 hours (Table 6, entry 1). However, once the reaction was run at room temperature all of the starting material was consumed yielding the β-methyl (aryl) sulfide **31** in an 90% yield without any side product formation (Table 6, entry 2). The stilbene based β-acetoxy aryl sulfide **28** underwent efficient methylation at lowered temperatures (0 °C) to obtain a similar yield (Table 6, entry 3).

Table 6- Treatment of β-Acetoxy (diisopropylphenyl) Sulfides with Me_3Al [a]



Entry	Starting Material	Me_3Al Equiv.	Temp, °C	Time, h [c]	Product	Yield[b], %
1	 **34**	2.0	0	24	 **35**	32
2	**34**	2.0	23	15	**35**	90
3	 **32**	2.0	0	0.75	 **33**	90
4	 **36**	2.0	0	24	 **37** **38**	13 ~1:1 Ratio[d]
5	**36**	2.0	23	48	**37** + **38**	65 ~8:7 ratio[d]
6	**36**	4.0	23	24	**37** + **38**	90 ~8:7 ratio[d]
7	 **39**	2.0	23	48	 **40**	81%

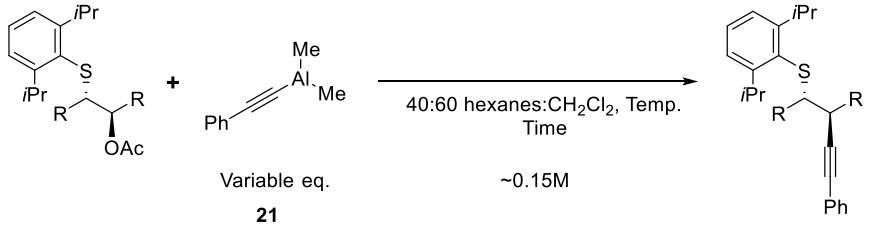
[a] All reactions run on a 0.5 mmol scale. [b]Isolated yield. [c]All reactions quenched at 24 h if full SM conversion had not been observed. [d] Ratio determined by ^1H NMR analysis.

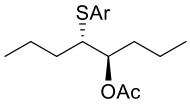
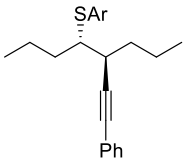
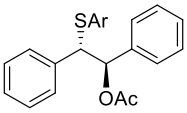
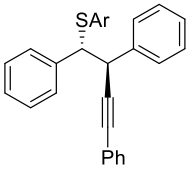
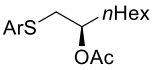
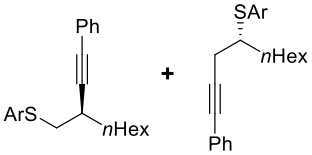
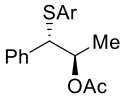
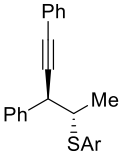
Unsymmetrical β-acetoxy aryl sulfides **36** and **39** were also investigated. Like **34**, the methylation of the 1-octene based β-acetoxy (aryl) sulfide **36** produced higher yields when run at room temperature (Table 6, entries 4 and 5). Increasing the equivalents of Me_3Al further increased the yield to 89.9% (Table 6, entry 6). Unlike **36**, styrene based β-acetoxy (aryl) sulfide **39** formed only one constitutional isomer after treatment with two equivalents of Me_3Al at room temperature

(Table 6, entry 7). Preferential attack at the benzylic position of thiiranium ions is well precedented.[27]

β-Acetoxy (diisopropylphenyl) sulfides underwent efficient alkynylation using dimethyl(phenylethynyl)aluminum (**21**) that was generated *in situ* (Table 7). The alkynylations of **34** and **32** (Table 7, entries 1 and 2) both reached full conversion when treated with two equivalents of **21** at 0 °C. However, the alkynylation of **32** (Table 7, entry 2) was much faster than any other substrate. The 1-octene derived β-acetoxy (aryl) sulfide **36** did not reach full conversion after 24 hours (Table 7, entry 3). Once the reaction was run at room temperature along with four equivalents of **21**, **43** and **44** were afforded in a moderate yield (Table 7, entry 4). The ratio of **43** and **44** is 3 to 2 (Table 6, entry 4) which is similar to the methylation reaction (Table 6, entry 6) with only a slight increase in favoring capture at the terminal position. This may be explained by the larger alkynlaluminum **21** attacking the more accessible terminal carbon. Styrene based β-acetoxy (aryl) sulfide **39** formed only one constitutional isomer after treatment with two equivalents of **21** at room temperature (Table 7, entry 5).

Table 7- Treatment of β-Acetoxy (diisopropylphenyl) Sulfides With Me_2(phenylethynyl)Al [a]



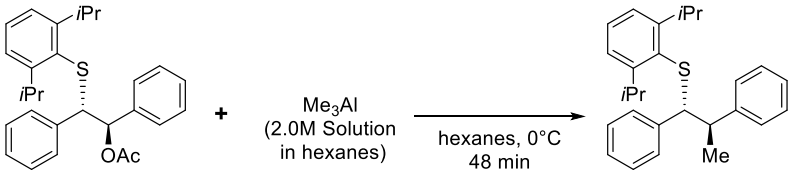
Entry	Starting Material	**11** Equiv.	Temp, °C	Time, h	Product	Yield[b], %
1	 **34**	2.0	23	21.25	 **41**	91
2	 **32**	2.0	0	1.15	 **42**	97
3	 **36**	2.0	23	24	 **43** **44**	50 Ratio 3:2 [d]
4	**36**	4.0	23	24.5	**43** + **44**	79 Ratio 3:2 [d]
5	 **39**	2.0	23	20	 **45**	85

[a] All reactions run on a 0.5 mmol scale. [b]Isolated yield. [c]All reactions quenched at 24 h if full SM conversion had not been observed. [d] Ratio determined by ^{1}H NMR analysis.

3.2.4 Enantiospecificity of Thiiranium Ion Formation and Capture

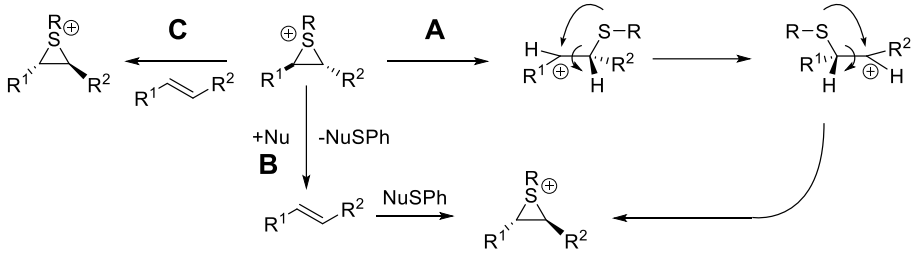
To determine the enantiospecificity of these reactions, enantioenriched **32** was treated with Me_3Al in identical conditions to entry 3 of Table 5 (Scheme 18).

Scheme 18



Under the optimized conditions, erosion of enantioenrichment was observed. Three possible mechanisms of thiiranium ion racemization can be considered, all of which have been studied in these labs.[21] While enantioenriched thiiranium ions can be generated and can captured by a variety of nucleophiles, the configurational integrity can be eroded by a three racemization pathways (Scheme 19).

Scheme 19

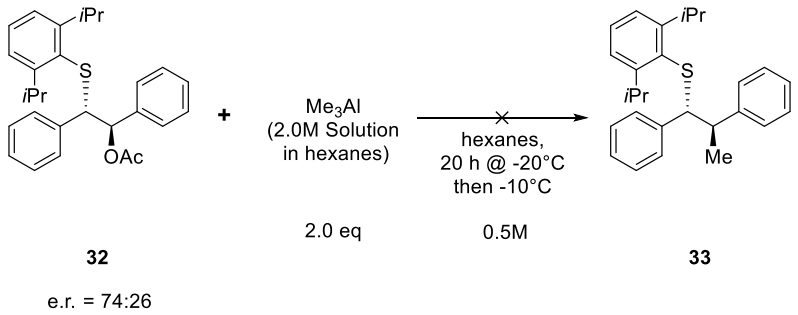


It is possible that **32** might not be intrinsically configurationally stable and could racemize via open carbocation intermediates after thiiranium ion formation but before capture by the aluminate species (Scheme 19, path A). Epimerization of *cis*-substituted thiiranium ions to the thermodynamically more stable *trans*-thiiranium ion has been reported to occur via this pathway.[28] Attack at the sulfonium ion could form a sulfenyl transfer reagent and starting olefin. This achiral sulfenylating reagent could add back to the olefin racemizing the thiiranium ion (path B). Finally, the olefin formed after the attack at sulfur, can erode enantiopurity via sulfenium group transfer (path C). This "olefin-to-olefin" transfer allows the transfer of thiiranium ions to alkene however, this pathway is suppressed at -20 °C.

To determine the cause of the erosion of configuration, the conditions of the experiment were modified. If the methylaluminate reagent is indeed able to attack at the sulfonium sulfur pathways B and C are possible. Fortunately, the resulting methyl aryl sulfide is not a competent sulfenylating reagent therefore pathway B can be eliminated from consideration.[29] This means that simply lowering the temperature to -20 °C should suppress all racemization pathways that come as a result of attack at the sulfonium sulfur.

Unfortunately, the reaction conditions for the methylation of **32** do not allow for any cooling. Consumption of **32** was not observed at either -20 °C or -10 °C (Scheme 20)

Scheme 20



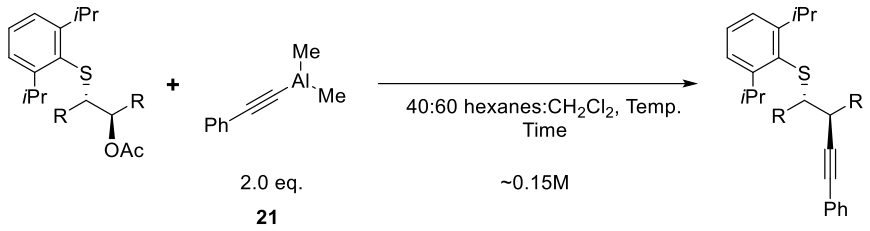
32

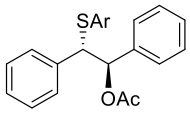
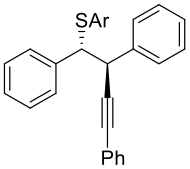
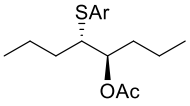
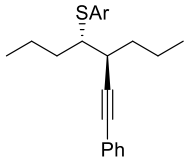
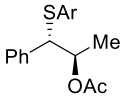
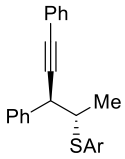
e.r. = 74:26

33

Unable to rule out pathway C, attention was focus was shifted to investigation of pathway A which required a different β-Acetoxy sulfide substrate. The benzylic positions of **32** allow for greater stabilization of a carbocation relative to the alkyl chain of **34**. The methylation of **34** should not favor the formation of carbocations resulting in 100% enantiospecificity if path A is the mechanism of racemization. Separation conditions for **35** could not be found using GC, HPLC, or SFC therefore, investigation of pathway A was continued by observing the enantiospecificity of the alkynylation of the β-acetoxy sulfides (Table 8).

Table 8- Treatment of Enriched β-Acetoxy (diisopropylphenyl) Sulfides With Me_2(phenylethynyl)Al [a]



Entry	Starting Material (e.r.)	Temp, °C	Time, h	Product (e.r.)	Yield[b], %	e.s., %
1	 **32** (74:26)	0	1.15	 **42** (71:29)	90	88
2	 **34** (95:5)	23	16.5	 **41** (95:5)	95	100[c]
3	 **39** (99:1)	23	17	 **45** (99:1)	92	100

[a] All reactions run on a 0.25 mmol scale. [b]Isolated yield. [c]Oxidized to the sulfone for HPLC analysis

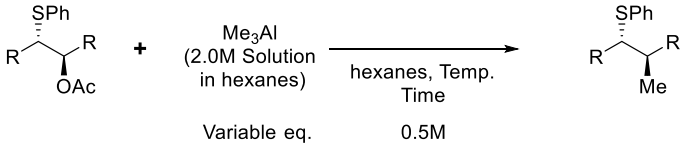
In order to have a benchmark for all alkynylations, enriched **32** was alkynylated giving an e.s. of 88% (Table 8, entry 1). Alkynylation of **34** provided **41** with 100% e.s. suggesting that pathway A is the most likely cause for the racemization of **34**. The benzylic position of **39** did not cause racemization which provides further evidence that pathway A is the cause for the drop in enantiomeric ratio as it would require a carbocation stabilized by a methyl group which is unlikely. Because **32** was the only β-acetoxy sulfide that formed olefin when treated with organoaluminum reagents (Scheme 12) and it was the only substrate that showed a drop in enantiomeric ratio, it was

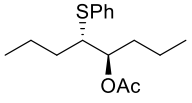
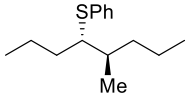
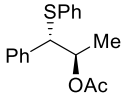
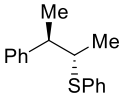
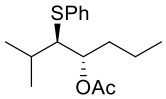
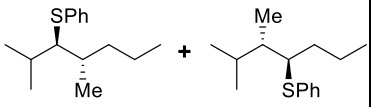
eliminated from any further investigations. The removal of stilbene based β-acetoxy sulfides from further consideration meant there was no reason to install 2,6-diisopropyl groups on the aryl group of sulfur. As such, all further work was performed with β-acetoxy (phenyl) sulfides.

3.2.5 Scope and Enantiospecificity of β-Acetoxy Phenyl Sulfides

After determining that the 2,6-diisopropylphenyl group was not required, conditions were found for the methylation and alkynylation of β-acetoxy (phenyl) sulfides. The methylation of a variety β-acetoxy (phenyl) sulfides was performed (Table 9). Methylation of **11** and **100** both provided products that were 100% enantiospecific (Table 9, entries 1 and 2). Methylation on **48** led to a small drop in enantiospecificity. Only the enantiomeric ratio of the major constitutional isomer, **49**, was taken. It is possible that if the enantiomeric ratio of **50** were found, the specificity may amount to 100%.

Table 9- Treatment of β-Acetoxy (phenyl) Sulfides with Me_3Al [a]

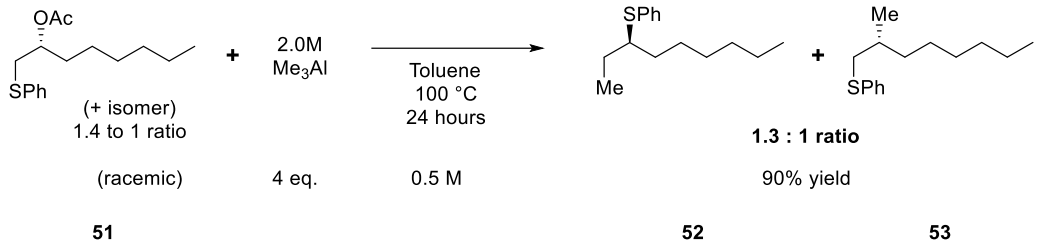


Entry	Starting Material (e.r.)	Me_3Al Equiv.	Temp, °C	Time, h	Product (e.r.)	Yield[b], %	e.s., %
1	 **11** (96.5:3.5)	2.0	23	5	 **27** (96.5:3.5)	94	100 [c]
2	 **46** (99:1)	4.0	23	3	 **47** (99:1)	94	100
3	 **48** 1.9 :1 ratio (91:9)	4.0	23	2	 **49** **50** (90:10)	96 ~3.8:1 Ratio[d]	98 [c]

[a] All reactions run on a 1.0 mmol scale. [b]Isolated yield. [c] Oxidized to the sulfone for HPLC analysis [d] Ratio determined by ^1H NMR analysis.

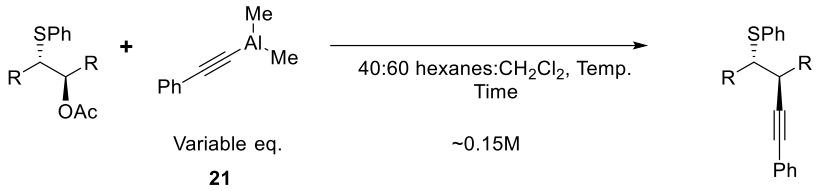
Methylation of 1-octene based β-acetoxy sulfide **51** was high yielding but enantiomeric ratios of the starting material and products was not determined. Separation conditions were sought for **51**, **52, 53** and their corresponding sulfones using GC, HPLC, SFC and by using *R*-BINOL and TFAE as chiral solvating agents. The methylation of **51** did require higher temperatures in toluene to afford full conversion (Scheme 21).

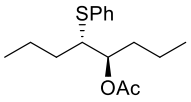
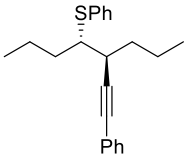
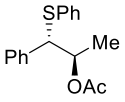
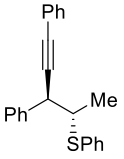
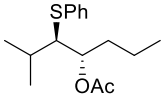
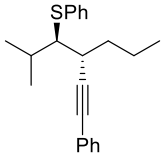
Scheme 21



The alkynylation of a variety β-acetoxy (phenyl) sulfides was also carried out (Table 10). Alkynylation of **11**, **46**, and **48** all provided products that were 100% enantiospecific and with excellent yields (Table 10, entries 1-3). Unlike the methylation of **48**, the alkynylation provided only one constitutional isomer, **56** (Table 10, entry 3).

Table 10- Treatment of Enriched β-Acetoxy (phenyl) Sulfides With Me_2(phenylethynyl)Al [a]

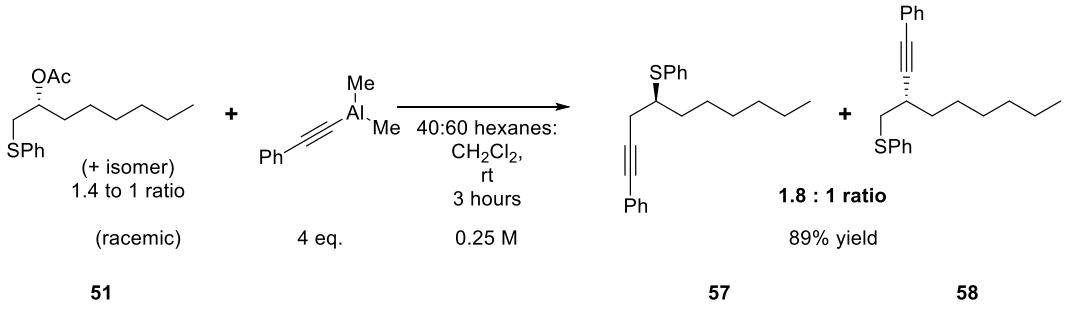


Entry	Starting Material	**11** Equiv.	Temp, °C	Time, h	Product	Yield[b], %	e.s., %
1	 **11** (96.5:3.5)	2	23	3	 **54** (96.5:3.5)	90	100[c]
2	 **46** (99:1)	2	23	6	 **55** (99:1)	96	100
3	 **48** 1.9: 1 ratio (91:9)	4	23	3	 **56** (91:9)	94	100[c]

[a] All reactions run on a 1.0 mmol scale. [b]Isolated yield. [c]Oxidized to the sulfone for HPLC analysis

Methylation of 1-octene based β-acetoxy sulfide **51** was high yielding but enatiomeric ratios of the starting material and products was not determined. (Scheme 22). Separation conditions were sought for **57**, **58**, and their corresponding sulfones using GC, HPLC, SFC and by using *R*-BINOL and TFAE as chiral solvating agents.

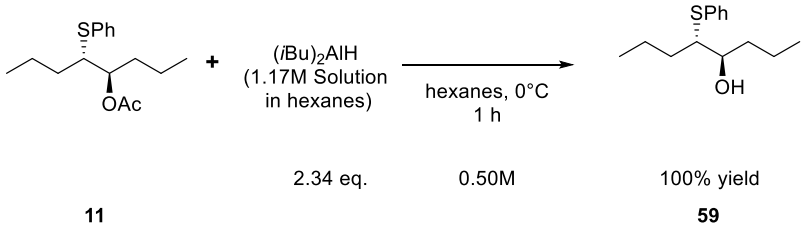
Scheme 22



3.2.6 Reactions with Other Organoaluminum Species

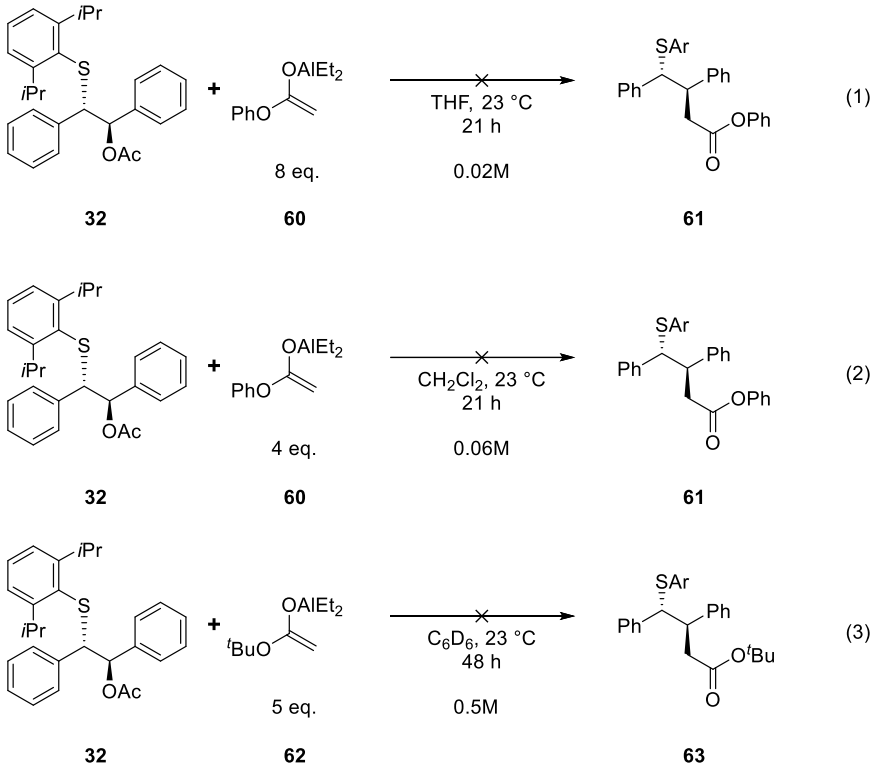
A variety of alkenyl, aryl, and hydride substituted aluminum reagents were probed for reactivity with β-acetoxy (aryl) sulfides. The ability to transfer alkenyl, aryl, and hydride groups has proven to be less robust than the alkynylation and alkylation reactions. Although the capture of thiiranium ions with hydride is known[22], treatment of **34** with DiBAl-H resulted in the reduction of the acetate to the alcohol (Scheme 23).

Scheme 23



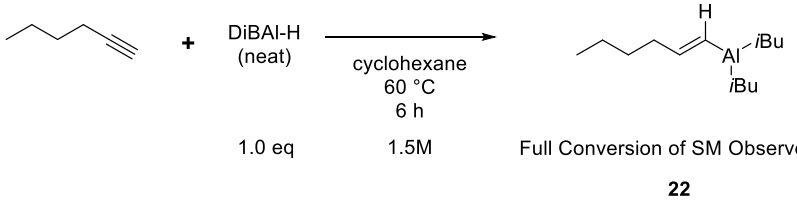
Aluminum enolates were also examined. All attempts were unsuccessful (Scheme 24, 1-3). The formation of **60** was performed in THF which can attenuate the reactivity of aluminum due to coordination of the ether to the vacant p-orbital on aluminum. THF was removed by high vacuum and the reaction was run in CH_2Cl_2 (Scheme 24, 2) but no reaction was observed. When run with a stronger aluminum nucleophile, **62**, and more than ten-fold more concentrated, the reaction also failed to proceed (Scheme 24, 3).

Scheme 24



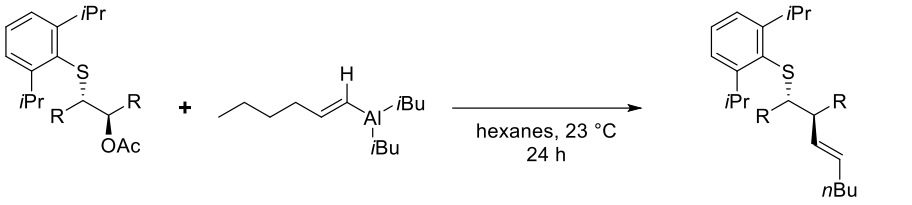
Vinylaluminums were also investigated. The reagents were prepared from the hydrometalation of DiBAl-H with alkyl alkynes. Despite the variety of methods on forming alkyl substituted vinylaluminums, many methods require an excess of DiBAl-H which would consume β-acetoxy sulfides.[30] Vinylaluminum **12** was prepared in cyclohexane, opposed to hexanes, so that the molarity could be calculated in via no-D NMR (Scheme 25).

Scheme 25



β-Acetoxy sulfides **32** and **34** were both treated with **22**. Four equivalents of **22** were required to achieve full conversion of **32**. Under similar conditions, **34** did not go to full conversion (Scheme 26).

Scheme 26



4 eq.

22

0.5M

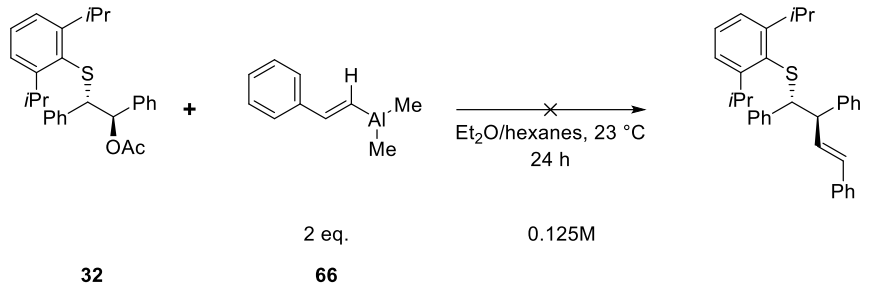
R=Ph (**64**), 73.9% yield*
R=*n*Pr (**65**), 43.5% yield*

The alkenylations of both **32** and **34** provided an intractable mixture; the yields reported are crude. The only evidence that **64** and **65** were formed was the presence of 2 alkene protons in the ^{1}H NMR, a doublet and doublet of triplets. However, those peaks did not integrate correctly with any other peak present in their respective spectrum. High resolution mass spec was taken for **64** which confirmed its formation.

Alkenylation was attempted using the β-acetoxy (phenyl) sulfides **11** and **46** however, after 65 hours neither reaction went to completion and both gave intractable mixtures even after purification via flash column chromatography. ^{1}H NMR showed evidence of *iso*-butyl group transfer. It is unknown why the more sterically encumbered **32** and **34** went to completion after 24 hours when **11** and **46** did not.

Alkenylation was also examined using **66**, which was prepared in a different fashion from **22**. The lithium-halogen exchange from (*E*)-(2-bromovinyl)benzene followed by transmetallation with dimethylaluminum chloride to make an alternative alkenylating reagent was preformed.[31] Treatment with **32** showed no reactivity which is most likely due to the fact **66** was prepared in a solution of diethyl ether (Scheme 27). Coordination of ethers to aluminum can diminish reactivity.

Scheme 27



The viability of phenyl group transfer by $AlPh_3$ has also been examined. Unfortunately, this extension has also been unsuccessful. This endeavor has been made more difficult due to fact that reported preparations are carried out in ethereal solvents and the lack of purification methods. The oxophilicity of aluminum allows coordination of $AlPh_3$ to ethers which will occupy the vacant p-orbital on aluminum preventing coordination to the acetate group. Many preparations of $AlPh_3$ use excess phenylmagnesium bromide or phenyllithium with $AlCl_3$ which is then used without purification. Without purification methods phenyl magnesium bromide or phenyllithium could attack the carbonyl of the acetate. The removal of dibutyl ether from commercially available $AlPh_3$ solutions has been attempted but the removal of coordinated dibutyl ether under 0.05 mmHg and 180 °C did not occur.

3.3 Conclusions and Outlook

The formation and capture by alkyl and alkynyl organoaluminum reagents has been shown to be clean, high yielding reactions. Additionally the methylation and alkynylation of β-acetoxy sulfides are enantiospecific. The incorporation of isopropyl groups on the aryl ring of sulfur was not required either high yields or high enantiospecificity. If separation conditions for 1-octene based starting materials and products can be found it is likely that they would also demonstrate 100% enantiospecificity. Other organoaluminum reagents for the arylation and alkenylation have

been less robust, however further investigation into the facile synthesis of the aluminum reagents could lead to effective transformations with similar levels of enantiospecificity.

Chapter 4. Experimental and Supporting Information

4.1 General Experimental

Reaction Setup: All reactions were performed in flamed-dried glassware under an atmosphere of dry argon unless otherwise indicated. All reported reaction temperatures correspond to internal temperatures measured with a Teflon coated thermocouple. Room temperature (rt) was approximately 23 °C. "Brine" refers to a saturated solution of sodium chloride in H_2O.

NMR Spectroscopy: ^1H and ^{13}C NMR spectra were recorded either a Varian Unity (400 MHz, ^1H; 100 MHz, ^{13}C) or a Inova (500 MHz, ^1H; 126 MHz, ^{13}C) spectrometer. Acquisition times were 4.096 s for ^1H NMR, and 1.024 s for ^{13}C NMR. Spectra are referenced to residual chloroform (δ = 7.26 ppm, ^1H; 77.00 ppm, ^{13}C) or benzene (δ = 7.16 ppm, ^1H; 128.06 ppm, ^{13}C) peaks. Chemical shifts are reported in parts per million (ppm). Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), qu (quintet), and m (multiplet). Coupling constants, *J*, are reported in Hertz. Integration is provided and assignments are indicated. ^1H and ^{13}C assignments are corroborated through 2-D NMR experiments (COSY, HSQC, HMBC).

Enantiomer Separations: Reverse-Phase HPLC was performed on an Agilent 1100 HPLC. Normal-Phase HPLC was performed on the same instrument.

Mass Spectrometry: Mass spectrometry (MS) was performed by the University of Illinois Mass Spectrometry Laboratory. Electron Impact (EI^+) spectra were performed at 70 eV using methane as the carrier gas, with either a double focusing sector field (VSE) or time-of-flight (TOF) mass analyzer. Electrospray Ionization (ESI^+) spectra were performed using a time-of-flight (TOF) mass analyzer. Data are reported in the form of m/z (intensity relative to the base peak = 100).

Liquid Chromatography: Analytical thin-layer chromatography was performed on Merck silica gel 60 F_{254}. Visualization was accomplished with UV light and/or potassium permanganate ($KMnO_4$) solution or ceric ammonium molybdate (CAM) solution. Retention factor (R_f) values reported were measured using a 6 × 2 cm TLC plate in a developing chamber containing the solvent system (10 mL) described. Flash column chromatography was performed using Silicycle SiliaFlash® P60 (40-63 µm particle size, 230-400 mesh) (SiO_2) or Woelm's high porosity grade silica.

Solvents: Reaction solvents tetrahydrofuran (THF) (Fisher, HPLC grade), ether (Et_2O) (Fisher, BHT stabilized ACS grade), and dichloromethane (CH_2Cl_2) (Fisher, unstabilized HPLC grade) were dried by percolation through two columns packed with neutral alumina under a positive pressure of argon. Reaction solvents hexanes and CH_2Cl_2 (ACS grade) was dried by percolation through a column packed with neutral alumina and a column packed with Q5 reactant (supported copper catalyst for scavenging oxygen) under a positive pressure of argon. Reaction solvents acetonitrile (CH_3CN) (ACS grade, amylene stabilized), methanol (MeOH) (ACS grade) and pentane (ACS grade) was distilled from CaH_2 $Mg(OMe)_2$ and Na respectively prior to use.

Solvents for filtration, transfers, chromatography, and recrystallization were dichloromethane (CH_2Cl_2) (ACS grade, amylene stabilized), ether (Et_2O) (Fisher, BHT stabilized ACS grade), ethyl acetate (EtOAc) (Fisher, ACS grade), *tert*-Butyl Methyl Ether (TMBE) (Fisher, ACS grade). and hexane (Fisher, ACS grade).

Chemicals:

The following materials were obtained from commercial suppliers as specified and purified according to the indicated procedure. If no purification method is noted, the compound was used as received from the manufacturer.

Reagent	**Supplier**	**Purification**
Acetonitrile	Aldrich	Distilled (Na)
Acetophenone	Aldrich	Distilled
Boron trifluoride Etherate	Aldrich	Distilled (CaH_2)
Celite	Fischer	
Copper (I) Iodide	Sigma	
Magnesium Sulfate	Fischer	
Methanesulfonic acid	Fischer	
Sodium Chloride	Fischer	
Sodium Iodide	Acros	
Sulfuryl Chloride	Acros	
Thiophenol	Sigma	
Titanium (IV) tetrachloride	Aldrich	Distilled (Cu)
Titanium (IV) isopropoxide	Aldrich	Distilled
Tin (IV) tetrachloride	Alfa-Aesar	
Triethylaluminum	Aldrich	
Triethylaluminum Chloride	Aldrich	
Triethylamine	Aldrich	Distilled (CaH_2)
(E)-2-methyl-3-heptene	ChemSampCo	
β-Methyl Styrene (stabilized)	Sigma	
Trimethylaluminum	Aldrich	
Trimethylsilyl Chloride	Gelest	Distilled
Trimethylsilyl Triflate	Gelest	Distilled
4-E-Octene	GFS Chemicals	
1-Octene	GFS Chemicals	
Stilbene	Sigma	
Styrene	Aldrich	
3-Chloroperoxybenzoic acid	Aldrich	Washed using conditions in *J. Chem. Soc., Perking Trans 1.* **1998**, 2771-2782
Triethylaluminum	Sigma	

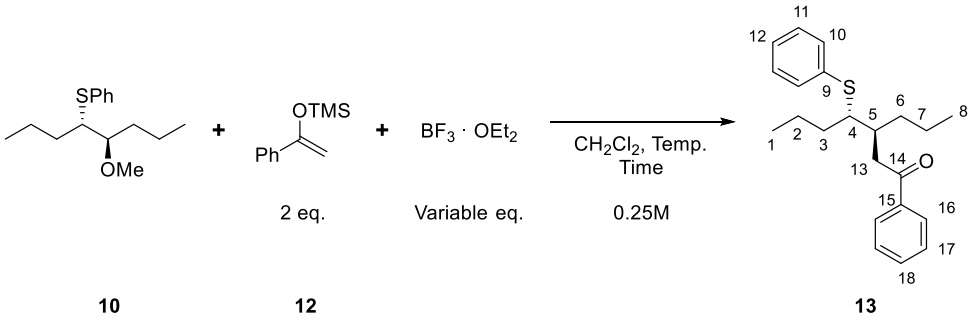
Phenylacetylene	Sigma	Distilled

4.2 Literature Preparations

Silyl enol ether **12**[32], β-methoxy sulfide **10**, β-acetoxy sulfide **11**[19], silyl ketene actetal **15**[33], aluminum enolates **60** and **62**[34], alkenyl aluminum reagents **22** and **66**[31] and alkynl aluminum reagent **21**[35] were reported in the literature and were prepared using the method reported.

4.3 Experimental Procedures

4.3.1 General Procedure 1



10 **12** **13**

To a flame-dried 5-mL Schlenk flask fitted a rubber septum and magnetic stir bar, was charged with 1 mL anhydrous CH_2Cl_2, *rel*-((4*S*,5*R*)-5-methoxyoctan-4-yl)(phenyl)sulfane (**10**) (63 mg, 0.25 mmol, 1.0 equiv.), and trimethyl((1-phenylvinyl)oxy)silane (**12**) (96 mg, 0.5 mmol, 2.0 equiv.), under Ar. Once at the desired temperature, BF_3• OEt_2 (was added dropwise via syringe. The reaction was quenched by diluting the reaction mixture with 30 mL saturated $NaHCO_3$ solution and 20 mL of CH_2Cl_2 in a 60-mL separatory funnel. After thorough mixing the layers were separated. The aqueous layer was extracted 2 x 20 mL of CH_2Cl_2. The organic layers were combined and dried over anhydrous $MgSO_4$ (~5 g) followed by filtration and concentration *in vacuo* (rt, 10 mbar). The residue was then purified via flash column chromatography (SiO_2, Ø 2cm, 0 to 3% EtOAc/hexanes) to yield **13** as a thick yellow oil.

Data for *rel*-(3*S*,4*S*)-1-phenyl-4-(phenylthio)-3-propylheptan-1-one (**13**):

^{1}H NMR: (500 MHz, $CDCl_3$)

7.91 (d, *J* = 7.12 Hz, 2 H HC(16)), 7.54 (t, *J* = 7.40 Hz, 1 H HC(18)), 7.40 (t, *J* = 7.73 Hz, 2 H HC(17)), 7.31 (d, *J* = 7.10 Hz, 2 H HC(10)), 7.18 (t, *J* = 7.5 Hz, 2 H HC(11)), 7.11 (t, *J* = 7.3 Hz 1 H HC(12)), 3.48 (dd, *J* = 16.6, 6.1 Hz, 1 H, H_2C(13)), 3.34 (m, 1 H, CH(4)), 2.80 (dd, *J* = 16.6, 6.9 Hz, 1 H, H_2C(13)), 2.49 (dd qu, J = 9.1, 6.5, 2.7 Hz, 1 H CH(5)), 1.75-1.24 (m, 8 H, HC(2,3,6,7), 0.94 (t, *J* = 7.1 Hz, 3 H, HC(8)), 0.85 (t, *J* = 7.2 Hz, 3 H, HC(1)).

^{13}C NMR: (125 MHz, $CDCl_3$)

200.55 (C(14)), 137.40 (C(15)), 136.66 (C(9)), 132.97 (C(18)), 131.21(C(17)), 128.99, (C(16)), 128.60 (C(11)), 128.25 (C(10)), 126.49 (C(12)), 53.31(C(4)), 40.60 (C(13)), 37.77(C(5)), 34.23(C(3/5)), 32.81(C(3/5)), 21.28 (C(2/7)), 20.90 (C(2/7)), 14.29(C(1/8)), 14.09(C(1/8)).

MS: (EI)

340.2, 309.1, 220.1, 105 (100), 77.1 [Values not provided].

HRMS: Calcd For: 340.18544 Found: 340.18609

4.3.2 Experimental Procedures Contained in "Table 1-Screening Variable Equivalents of BF_3•OEt_2 at Varying Temperatures" and "Table 2-Screening Variable Amount of Nucleophile at 0 °C)"

Table 1 Entry 1

Following General Procedure 1, a flame-dried Schlenk flask was charged with 1 mL CH_2Cl_2, **10** (63 mg, 0.25 mmol), and **12** (96 mg, 0.5 mmol, 2.0 equiv.). Once at -20°C, BF_3• OEt_2 (35.5 mg, 0.25 mmol, 1.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched. After stirring for 24 hours, full consumption of **10** was not observed via ^{1}H NMR.

Table 1 Entry 2

Following General Procedure 1, a flame-dried Schlenk flask was charged with 1 mL CH_2Cl_2, **10** (63 mg, 0.25 mmol), and **12** (96 mg, 0.5 mmol, 2.0 equiv.). Once at -20°C, BF_3• OEt_2 (71 mg, 0.5 mmol, 2.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched. After stirring for 24 hours, full consumption of **10** was not observed via ^{1}H NMR.

Table 1 Entry 3

Following General Procedure 1, a flame-dried Schlenk flask was charged with 1 mL CH_2Cl_2, **10** (63 mg, 0.25 mmol), and **12** (96 mg, 0.5 mmol, 2.0 equiv.). Once at -20°C, BF_3• OEt_2 (178 mg, 1.25 mmol, 5.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 20 hours before the reaction was quenched. Full consumption of **10** was observed after 20 hours via ^{1}H NMR.

Table 1 Entry 4

Following General Procedure 1, a flame-dried Schlenk flask was charged with 1 mL CH_2Cl_2, **10** (63 mg, 0.25 mmol), and **12** (96 mg, 0.5 mmol, 2.0 equiv.). Once at 0°C, BF_3• OEt_2 (35.5 mg, 0.25 mmol, 1.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched. After stirring for 24 hours, full consumption of **10** was not observed via ^{1}H NMR.

Table 1 Entry 5 and **Table 2 Entry 1**

Following General Procedure 1, a flame-dried Schlenk flask was charged with 1 mL CH_2Cl_2, **10** (63 mg, 0.25 mmol), and **12** (96 mg, 0.5 mmol, 2.0 equiv.). Once at 0°C, BF_3• OEt_2 (71 mg, 0.50 mmol, 2.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 20 hours before the reaction was quenched. Full consumption of **10** was observed after 5 hours via ^{1}H NMR.

Table 1 Entry 6

Following General Procedure 1, a flame-dried Schlenk flask was charged with 1 mL CH_2Cl_2, **10** (63 mg, 0.25 mmol), and **12** (96 mg, 0.5 mmol, 2.0 equiv.). Once at room temperature, BF_3• OEt_2 (178 mg, 1.25 mmol, 5.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 5.25 hours before the reaction was quenched. Full consumption of **10** was observed after 5.25 hours via ^{1}H NMR.

Table 1 Entry 7

Following General Procedure 1, a flame-dried Schlenk flask was charged with 1 mL CH_2Cl_2, **10** (63 mg, 0.25 mmol), and **12** (96 mg, 0.5 mmol, 2.0 equiv.). Once at room temperature, BF_3• OEt_2 (71 mg, 0.50 mmol, 2.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 1.75 hours before the reaction was quenched. Full consumption of **10** was observed after 1.75 hours via ^{1}H NMR.

Table 1 Entry 8

Following General Procedure 1, a flame-dried Schlenk flask was charged with 1 mL CH_2Cl_2, **10** (63 mg, 0.25 mmol), and **12** (96 mg, 0.5 mmol, 2.0 equiv.). Once at room temperature, BF_3• OEt_2 (178 mg, 1.25 mmol, 5.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 1.25 hours before the reaction was quenched. Full consumption of **10** was observed after 1.25 hours via ^{1}H NMR.

Table 2 Entry 2

Following General Procedure 1, a flame-dried Schlenk flask was charged with 1 mL CH_2Cl_2, **10** (63 mg, 0.25 mmol), and **12** (72 mg, 0.375 mmol, 1.50 equiv.). Once at room temperature, BF_3• OEt_2 (71 mg, 0.50 mmol, 2.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 25 hours before the reaction was quenched and worked up. 96% conversion was observed after 25 hours via ^{1}H NMR.

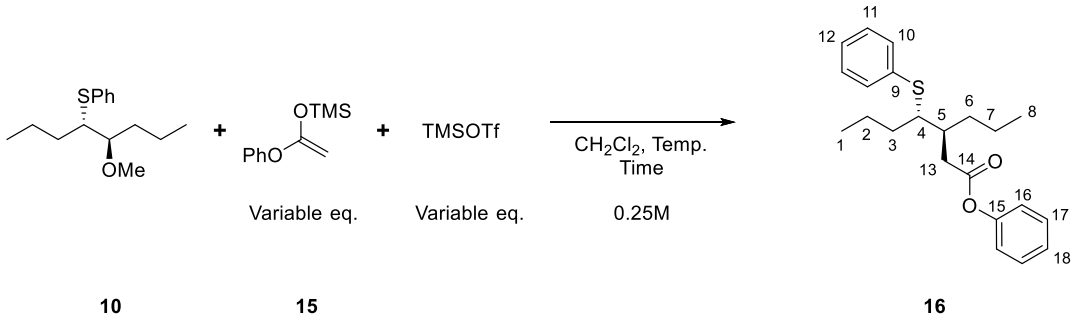
Table 2 Entry 3

Following General Procedure 1, a flame-dried Schlenk flask was charged with 1 mL CH_2Cl_2, **10** (63 mg, 0.25 mmol), and **12** (60 mg, 0.313 mmol, 1.25 equiv.). Once at room temperature, BF_3• OEt_2 (71 mg, 0.50 mmol, 2.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 48 hours before the reaction was quenched and worked up. 87% conversion was observed after 48 hours via ^{1}H NMR.

Table 2 Entry 4

Following General Procedure 1, a flame-dried Schlenk flask was charged with 1 mL CH_2Cl_2, **10** (63 mg, 0.25 mmol), and **12** (50 mg, 0.26 mmol, 1.05 equiv.). Once at room temperature, BF_3• OEt_2 (71 mg, 0.50 mmol, 2.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 48 hours before the reaction was quenched and worked up. 84% conversion was observed after 48 hours via ^{1}H NMR.

4.3.3 Experimental Procedures Contained in "Table 3- Screening Variable Amounts of Silyl Ketene Acetal Nucleophile and TMSOTf"



10 **15** **16**

Data for *rel*-phenyl (3S,4S)-4-(phenylthio)-3-propylheptanoate (**16**):

^{1}H NMR: (400 MHz, $CDCl_3$)

7.43 (d, *J* = 8.3 Hz, 2 H HC(10)), 7.28-7.16 (m, 6 H HC(17/18/11/12)), 6.99 (d, *J* = 8.6 Hz, 2 H HC(16)), 3.30 (m, 1 H, CH(4)), 3.01 (dd, *J* = 15.8, 7.1 Hz, 1 H, H_2C(13)), 2.48 (dd, *J* = 15.8, 7.1 Hz, 1 H, H_2C(13)), 2.31 (m, 1 H CH(5)), 1.75-1.25 (m, 8 H, HC(2,3,6,7), 0.87 (m, 3 H, H_3C(1/8)),

TLC: R_f 0.714 (5% EtOAc/hexanes) [UV]

Table 3 Entry 1

Following a modified General Procedure 1, a flame-dried Schlenk flask was charged with 1 mL CH_2Cl_2, **10** (252 mg, 1.0 mmol), and **15** (417 mg, 2.0 mmol, 2.0 equiv.). Once at 0°C, TMSOTf (1.1 g, 5.0 mmol, 5.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 9 hours before the reaction was quenched. Following work-up the residue was purified via Chromatatron (4mm silica plate, flow of 8.4 mL/min). Ran 275 mL 1% EtOAc/hexanes followed by 100 mL 1.5% EtOAc/hexanes.

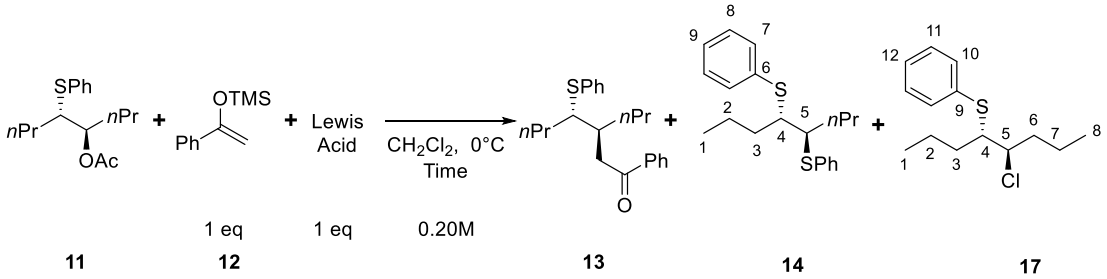
Table 3 Entry 2

Following a modified General Procedure 1, a flame-dried Schlenk flask was charged with 1 mL CH_2Cl_2, **10** (252 mg, 1.0 mmol), and **15** (417 mg, 2.0 mmol, 2.0 equiv.). Once at 0°C, TMSOTf (233 mg, 1.05 mmol, 1.05 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched. After 24 hours, full consumption of **10** was not observed via ^{1}H NMR.

Table 3 Entry 3

Following a modified General Procedure 1, a flame-dried Schlenk flask was charged with 1 mL CH_2Cl_2, **10** (252 mg, 1.0 mmol), and **15** (229 mg, 1.05 mmol, 1.05 equiv.). Once at 0°C, TMSOTf (233 mg, 1.05 mmol, 1.05 equiv.was added dropwise via syringe. The reaction was allowed to stir for 8 hours before the reaction was quenched.

4.3.4 General Procedure 2



To a flame-dried, 5-mL Schlenk flask fitted a rubber septum and magnetic stir bar, was charged with 1.25 mL anhydrous CH_2Cl_2, *rel*-(4*R*,5*S*)-5-(phenylthio)octan-4-yl acetate (**11**) (70 mg, 0.25 mmol), and trimethyl((1-phenylvinyl)oxy)silane (**12**) (48 mg, 0.25 mmol, 1.0 equiv.), under Ar. The flask was cooled to 0 °C via an isopropanol cryo-cool bath. Once at the desired temperature, 1 equiv. Lewis acid was added dropwise. The reaction was quenched by adding 3 mL 0 °C saturated sodium bicarbonate solution. The reaction mixture was diluted with 20 mL saturated $NaHCO_3$ solution and 20 mL of CH_2Cl_2 in a 60-mL separatory funnel. After thorough mixing, the layers were separated. The aqueous layer was extracted 1 x 20 mL of CH_2Cl_2. The organic layers were combined and dried over anhydrous $MgSO_4$ followed by filtration and concentration *in vacuo* (rt, 10 mbar).

Data for *rel*-((4*R*,5*S*)-octane-4,5-diyl)bis(phenylsulfane)one (**14**):

^{1}H NMR: (500 MHz, C_6D_6)

7.43 (d, *J* = 6.46 Hz, 4 H, HC(7)), 6.99 (t, *J* = 8.01 Hz, 4 H HC(8)), 6.93 (t, *J* = 6.46 Hz, 2 H HC(9)), 3.41(dq, *J* = 4.07, 4.07, 4.07, 8.83 Hz, 2 H H_2C(4&5)), 1.82-1.70 (m, 4 H H_2C(3)), 1.64-1.53 (m, 2 H H_2C(2)), 1.42-1.32 (m, 2H H_2C(2)), 0.76 (t, *J* = 7.22 Hz, 6 H H_3C(1)).

^{13}C NMR: (125 MHz, C_6D_6)

137.53 (C(6)), 132.20 (C(7)), 129.14 (C(8)), 126.83 (C(9)), 55.75 (C(4)), 35.41 (C(3)), 21.10 (C(2)), 13.99 (C(1))

MS: (EI)

330.1, 221.1 (100), 165.0, 123.0, 109.0, 69.1, 54.9 [Values not provided]

TLC: R_f 0.786 (5% EtOAc/hexanes) [UV]

Data for *rel*-((4*R*,5*S*)-5-Chlorooctan-4-yl)phenylsulfide (**17**):

^{1}H NMR: (500 MHz, $CDCl_3$) 7.45 (d, *J* = 7.5 Hz, 2 H, HC(10)), 7.31 (t, *J* = 7.5 Hz, 2 H, HC(11)), 7.26 (t, *J* =7.5 Hz, 1 H, HC(12)), 4.03 (qu, *J* = 4.5 Hz, 1 H, HC(5)), 3.22 (qu, *J* = 4.5 Hz, 1 H, HC(4)), 1.86-1.35 (m, 8 H, H_2C(2,3,6,7)), 0.95 (t, *J* = 7 Hz, 3 H, H_3C(8)), 0.88 (t, *J* = 7 Hz, 3 H, H_3C(1))

TLC: R_f 0.80 (5% EtOAc/hexanes) [UV]

4.3.5 Experimental Procedures Contained in "Table 4- Screening Lewis Acids with Acetoxy Leaving Group"

Table 4 Entry 1

Following General Procedure 2, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12**. Once at 0 °C, Et_3Al (28.5 mg, 0.25 mmol, 1.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched and worked up. After stirring for 24 hours, full conversion of **11** was not observed via TLC. Ratios of **11**, **13**, **14**, and **17** were calculated via ^{1}H NMR taken after running the reaction for 24 hours.

Table 4 Entry 2

Following General Procedure 2, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12**. Once at 0 °C, Et_2AlCl (30 mg, 0.25 mmol, 1.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 48 hours before the reaction was quenched and worked up. After stirring for 24 hours, no full conversion of **16** was not observed via TLC. Ratios of **11**, **13**, **14**, and **17** were calculated via ^{1}H NMR taken after running the reaction for 48 hours.

Table 4 Entry 3

Following General Procedure 2, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12**. Once at 0 °C, $SnCl_4$ (65 mg, 0.25 mmol, 1.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched and worked up. After stirring for 24 hours, full conversion of **11** was not observed via TLC. Ratios of **11**, **13**, **14**, and **17** were calculated via ^{1}H NMR taken after running the reaction for 24 hours.

Table 4 Entry 4

Following General Procedure 2, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12**. Once at 0 °C, $TiCl_4$ (47.4 mg, 0.25 mmol, 1.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 2.5 hours before the reaction was quenched and worked up. After stirring for 1 hour, full conversion of **11** was observed via TLC. Ratios of **11**, **13**, **14**, and **17** were calculated via ^{1}H NMR.

Table 4 Entry 5

Following General Procedure 2, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12**. Once at 0 °C, $Ti(O\textit{i}Pr)_4$ (71 mg, 0.25 mmol, 1.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 5 hours before the reaction was quenched and worked up. After stirring for 5 hours, it appeared the reaction had stalled and was making no further progress via TLC. Ratios of **11**, **13**, **14**, and **17** were calculated via ^{1}H NMR taken after running the reaction for 5 hours.

Table 4 Entry 6

Following General Procedure 2, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12**. Once at 0 °C, $BF_3 \bullet OEt_2$ (35.5 mg, 0.25 mmol, 1.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 48 hours before the reaction was quenched and worked up. After stirring for 24 hours, full conversion of **11** was not observed via TLC Ratios of **11**, **13**, **14**, and **17** were calculated via ^{1}H NMR taken after running the reaction for 48 hours.

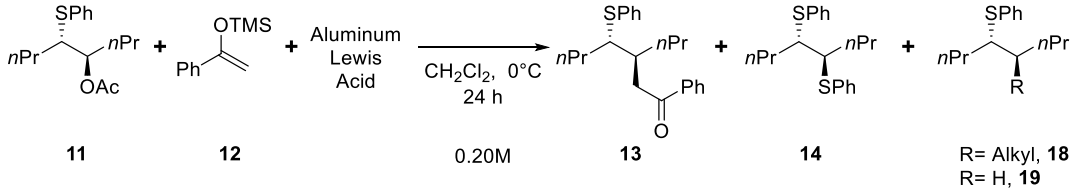
Table 4 Entry 7

Following General Procedure 2, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12**. Once at 0 °C, TMSOTf (55.5 mg, 0.25 mmol, 1.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 48 hours before the reaction was quenched and worked up. After stirring for 24 hours, full conversion of **11** was not observed via TLC. Ratios of **11**, **13**, **14**, and **17** were calculated via ^{1}H NMR taken after running the reaction for 48 hours.

Table 4 Entry 8

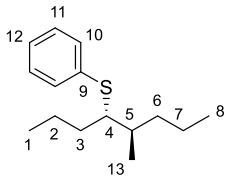
Following General Procedure 2, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12**. Once at 0 °C, $TMSNTf_2$ (Provided by Yusuke Ueki. 88.3 mg, 0.25 mmol, 1.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 2 hours before the reaction was quenched and worked up. After stirring for 2 hours, it appeared that full conversion of **11** had occurred (observed via TLC) however, the ^{1}H NMR showed that **11** was still present. Ratios of **11**, **13**, **14**, and **17** were calculated via ^{1}H NMR taken after running the reaction for 2 hours.

4.3.6 General Procedure 3



11 **12** **13** **14**

To a flame-dried, 5-mL Schlenk flask fitted a rubber septum and magnetic stir bar, was charged with 1.25 mL anhydrous CH_2Cl_2, *rel*-(4*R*,5*S*)-5-(phenylthio)octan-4-yl acetate (**11**) (70 mg, 0.25 mmol), and trimethyl((1-phenylvinyl)oxy)silane (**12**), under Ar. The flask was cooled to 0 °C via an isopropanol cryo-cool bath. Once at the desired temperature, the aluminum Lewis acid was added dropwise. The reaction was quenched by adding 1 mL 0 °C saturated sodium bicarbonate solution. The reaction mixture was diluted with 20 mL saturated $NaHCO_3$ solution and 20 mL of CH_2Cl_2 in a 60-mL separatory funnel. After thorough mixing, the layers were separated. The aqueous layer was extracted 1 x 20 mL of CH_2Cl_2. The organic layers were combined and dried over anhydrous $MgSO_4$ followed by filtration and concentration *in vacuo* (rt, 10 mbar). The residue was then purified by column chromatograph (high resolution SiO_2, 35 g, *tert*-butyl methyl ether/hexanes 1-3%, 100 mL solvent for each percent).

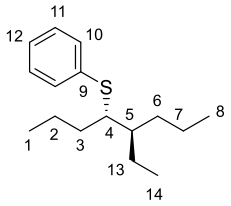


27

Data for *rel*-((4*S*,5*R*)-5-methyloctan-4-yl)(phenyl)sulfane (**27**):

^{1}H NMR: (500 MHz, $CDCl_3$)

7.42 (d, *J* = 7.2 Hz, 2 H HC(10)), 7.31 (t, *J* = 7.5 Hz, 2 H HC(11)), 7.21 (t, *J* = 7.4 Hz, 1 H HC(12)), 3.15 (dt, *J* = 8.9, 3.5 Hz, 1 H, HC(4)), 1.83 (ddt, *J* = 11.7, 8.3, 4.0 Hz, 1 H, CH(5)), 1.65 (m, 2H, H_2C(3/2), 1.47 (m, 2H, H_2C(3/2) 1.40 (m, 2H, H_2C(6/7), 1.27 (m, 2H, H_2C(6/7), 1.02 (d, J = 6.8 Hz, 3 H, H_3C(13)), 0.95 (t, *J* = 6.8 Hz, 3 H, H_3C (1)), 0.90 (t, *J* = 6.8 Hz, 3 H, H_3C (8)).

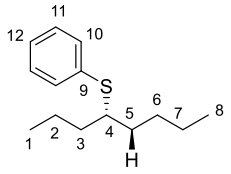


18

Data for *rel*-((4*S*,5*R*)-5-ethyloctan-4-yl)(phenyl)sulfane (**18**):

^{1}H NMR: (500 MHz, $CDCl_3$)

7.40 (d, *J* = 7.8 Hz, 2 H HC(10)), 7.28 (t, *J* = 7.5 Hz, 1 H HC(11)), 7.19 (t, *J* = 7.4 Hz, 2 H HC(10)), 3.25 (ddd, *J* = 8.3, 4.9 3.1 Hz, 1 H, HC(4)), 1.60-1.19 (m, 8 H, H_2C(2,3,5,6,7), 0.92-0.89 (t, 9 H, H_3C(1,8,4))



19

Data for *rel*-(S)-octan-4-yl(phenyl)sulfane (**19**):

^{1}H NMR: (500 MHz, $CDCl_3$)

7.40 (d, *J* = 7.8 Hz, 2 H HC(10)), 7.28 (t, *J* = 7.5 Hz, 1 H HC(11)), 7.19 (t, *J* = 7.4 Hz, 2 H HC(10)), 3.25 (ddd, *J* = 8.3, 4.9 3.1 Hz, 1 H, HC(4)), 3.10 (qu, *J*=6.4 Hz, 2 H, H_2C(5)), 1.60-1.19 (m, 8 H, HC(2,3,6,7), 0.92-0.89 (t, 6 H, H_3C(1/8))

4.3.7 Experimental Procedures Contained in "Table 4- Screening Lewis Acids with Acetoxy Leaving Group"

Table 5 Entry 1

Following General Procedure 3, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12** (48 mg, 0.25 mmol, 1.0 equiv.). Once at 0 °C, Et_3Al (28.5 mg, 0.25 mmol, 1.0 equiv.) was added

dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched and worked up. After stirring for 24 hours, full conversion of **11** was not observed via TLC. Ratios of **11**, **13**, **14**, **18** and **18** were calculated via ^{1}H NMR after purification via flash column chromatography.

Table 5 Entry 2

Following General Procedure 3, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12** (96 mg, 0.50 mmol, 2.0 equiv.). Once at 0 °C, Et_3Al (28.5 mg, 0.25 mmol, 1.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched and worked up. After stirring for 24 hours, full conversion of **11** was not observed via TLC. Ratios of **11**, **13**, **14**, **18** and **18** were calculated via ^{1}H NMR after purification via flash column chromatography.

Table 5 Entry 3

Following General Procedure 3, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12** (48 mg, 0.25 mmol, 1.0 equiv.). Once at 0 °C, Et_3Al (57 mg, 0.50 mmol, 2.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched and worked up. After stirring for 24 hours, full conversion of **11** was not observed via TLC. Ratios of **11**, **13**, **14**, **18** and **18** were calculated via ^{1}H NMR after purification via flash column chromatography.

Table 5 Entry 4

Following General Procedure 3, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12** (96 mg, 0.50 mmol, 2.0 equiv.). Once at 0 °C, Et_3Al (57 mg, 0.50 mmol, 2.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched and worked up. After stirring for 24 hours, full conversion of **11** was not observed via TLC. Ratios of **11**, **13**, **14**, **18** and **18** were calculated via ^{1}H NMR after purification via flash column chromatography.

Table 5 Entry 5

Following General Procedure 3, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12** (48 mg, 0.25 mmol, 1.0 equiv.). Once at 0 °C, Me_3Al (18 mg, 0.25 mmol, 1.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched and worked up. After stirring for 24 hours, full conversion of **11** was not observed via TLC. Ratios of **11**, **13**, **14**, **18** and **18** were calculated via ^{1}H NMR after purification via flash column chromatography.

Table 5 Entry 6

Following General Procedure 3, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12** (96 mg, 0.50 mmol, 2.0 equiv.). Once at 0 °C, Me_3Al (18 mg, 0.25 mmol, 1.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched and worked up. After stirring for 24 hours, full conversion of **11** was not observed via TLC. Ratios of **11**, **13**, **14**, **18** and **18** were calculated via ^{1}H NMR after purification via flash column chromatography.

Table 5 Entry 7

Following General Procedure 3, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12** (48 mg, 0.25 mmol, 1.0 equiv.). Once at 0 °C, Me_3Al (36 mg, 0.50 mmol, 2.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched and worked up. After stirring for 24 hours, full conversion of **11** was not observed via TLC. Ratios of **11**, **13**, **14**, **18** and **18** were calculated via ^{1}H NMR after purification via flash column chromatography.

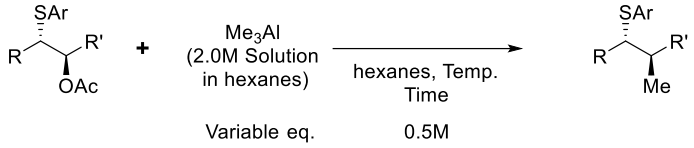
Table 5 Entry 8

Following General Procedure 3, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12** (96 mg, 0.50 mmol, 2.0 equiv.). Once at 0 °C, Me_3Al (36 mg, 0.50 mmol, 2.0 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched and worked up. After stirring for 24 hours, full conversion of **11** was not observed via TLC. Ratios of **11**, **13**, **14**, **18** and **18** were calculated via ^{1}H NMR after purification via flash column chromatography.

Table 5 Entry 9

Following General Procedure 3, a flame-dried Schlenk flask was charged with CH_2Cl_2, **11,** and **12** (120 mg, 0.63 mmol, 2.0 equiv.). Once at 0 °C, Me_3Al (45 mg, 0.31 mmol, 1.25 equiv.) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched and worked up. After stirring for 24 hours, full conversion of **11** was not observed via TLC. Ratios of **11**, **13**, **14**, **18** and **18** were calculated via ^{1}H NMR after purification via flash column chromatography.

4.3.8 General Procedure 4



To a flame-dried, 5-mL Schlenk flask fitted a rubber septum and magnetic stir bar, was charged the trimethylaluminum solution under Ar. The flask was cooled to 0 °C via an isopropanol cryo-cool bath or run at room temperature. Once at the desired temperature, the β-acetoxy (aryl) sulfide was added dropwise. Once judged complete by TLC, the reaction was quenched by adding 1.5 mL EtOAc followed by 2.5 mL 3M HCl. The reaction was allowed to sitr until two distinct layers had formed. The reaction mixture was then transferred a 60-mL separatory funnel containing 15 mL EtOAc and 15 mL 3M HCl. After thorough mixing, the layers were separated. The aqueous layer was extracted 2 x 15 mL + 1 x 10 mL of EtOAc. The organic layers were combined, washed 1 x 10 mL brine and dried over anhydrous $MgSO_4$ followed by filtration and concentration *in vacuo* (rt, 10 mbar). The residue was then purified by flash column chromatograph (high resolution SiO_2, 35 g, *tert*-butyl methyl ether/hexanes 1-3%, 100 mL solvent for each percent).

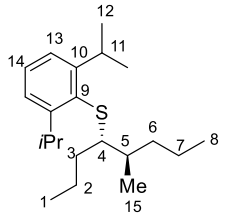
4.3.9 Experimental Procedures for Methylations Using Trimethylaluminum

Table 6 Entry 1

Following General Procedure 4, a flame-dried Schlenk flask was charged with hexanes and Me_3Al (144 mg, 1.0 mmol, 2 equiv.) and cooled to 0°C. Once at 0 °C, **34** (182mg, 0.5 mmol) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched and worked up. After 24 hours, full conversion of **34** was not observed via TLC.

Table 6 Entry 2

Following General Procedure 4, a flame-dried Schlenk flask was charged with hexanes and Me_3Al (144 mg, 1.0 mmol, 2 equiv.) and cooled to 0°C. Once at 0 °C, **34** (182mg, 0.5 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was was quenched after 15 hours when **34** had been consumed (monitored via TLC) and worked up. After purification via chromatography, **35** was obtained in a 90% yield.



35

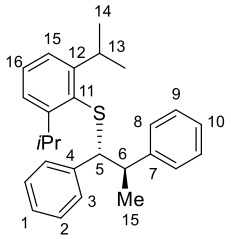
Data for *rel*-(2,6-diisopropylphenyl)((4*S*,5*R*)-5-methyloctan-4-yl)sulfane (**35**):

^{1}H NMR: (400 MHz, $CDCl_3$)

7.28 (t, 1 H HC(14)), 7.13 (d, *J* = 7.7 Hz, 2 H HC(13)), 3.99 (hept, *J* = 6.8 Hz, 2 H, HC(11)), 2.72 (dt, *J*= 9.0, 3.7 Hz, 1 H, H_2C(4)), 1.60-1.19 (m, 9 H, HC(2,3,5, 6,7), 1.22 (d, J=6.9 Hz, 6H H_3C(12)), 1.20 (d, J=6.9 6H H_3C(12)), 1.01 (d, *J*=6.8 Hz, 3 H, H_3C(5)), 0.90 (t, *J* = 7.2 Hz 3 H, H_3C(1/8)), 0.72 (t, *J* = 6.8 Hz 3 H, H_3C(1/8))

Table 6 Entry 3

Following General Procedure 4, a flame-dried Schlenk flask was charged with hexanes and Me_3Al (144 mg, 1.0 mmol, 2 equiv.) and cooled to 0°C. Once at 0 °C, **32** (216 mg, 0.5 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was was quenched after 45 minutes when **32** had been consumed (monitored via TLC) and worked up. After purification via chromatography, **33** was obtained in a 90% yield.



33

Data for *rel*-(2,6-diisopropylphenyl)((1*R*,2*R*)-1,2-diphenylpropyl)sulfane (**33**):

^{1}H NMR: (400 MHz, $CDCl_3$)

7.35-6.95 (m, 12 H HC(1, 2, 3, 8, 9, 10, 15, 16)), 3.69 (d, *J* = 10.4 Hz, 1 H HC(5)), 3.29 (m, 3 H, HC(6, 13)), 1.12 (d, *J* = 7.0 Hz 6H H_3C(14)), 1.09 (d, *J* = 7.0 Hz 6H H_3C(14)), 0.72 (d, *J* = 6.8 Hz 3 H, H_3C(15))

Table 6 Entry 4

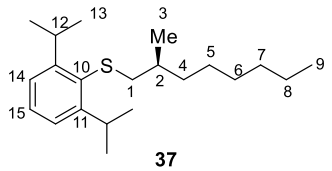
Following General Procedure 4, a flame-dried Schlenk flask was charged with hexanes and Me_3Al (144 mg, 1.0 mmol, 2 equiv.) and cooled to 0°C. Once at 0 °C, **36** (182 mg, 0.5 mmol) was added dropwise via syringe. The reaction was allowed to stir for 24 hours before the reaction was quenched and worked up. After 24 hours, full conversion of **36** was not observed via TLC.

Table 6 Entry 5

Following General Procedure 4, a flame-dried Schlenk flask was charged with hexanes and Me_3Al (144 mg, 1.0 mmol, 2 equiv.) and cooled to 0°C. Once at 0 °C, **36** (182 mg, 0.5 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was allowed to stir for 48 hours before the reaction was quenched and worked up. After purification via chromatography, **37** and **38** were obtained as an inseparable mixture in a 65% yield with a ratio of 8:7.

Table 6 Entry 6

Following General Procedure 4, a flame-dried Schlenk flask was charged with hexanes and Me_3Al (288 mg, 2.0 mmol, 4 equiv.) and cooled to 0°C. Once at 0 °C, **36** (182 mg, 0.5 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was quenched after 24 hours when **36** had been consumed (monitored via TLC) and worked up. After purification via chromatography, **37** and **38** were obtained as an inseparable mixture in a 90% yield with a ratio of 8:7.

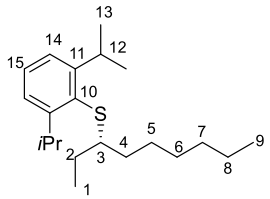


37

Data for *rel*-(*S*)-(2,6-diisopropylphenyl) (2-methyloctyl)sulfane (**37**):

^{1}H NMR: (400 MHz, $CDCl_3$)

7.31 (t, *J* = 7.7 Hz 1 H HC(15)), 7.17 (d, *J* = 7.7 Hz, 2 H HC(14)), 4.00 (ddt, *J* = 10.4, 6.8, 3.6 Hz, 2 H, HC(12)), 2.65-2.48 (ddd, *J*= 38, 6.5, 6.5 Hz, 2 H, H_2C(1)), 1.69 (m, 1 H, HC(2), 1.62-1.38 (m, 10 H H_2C(4, 5, 6, 7, 8)), 1.05 (d, *J* = 6.6 Hz 3 H, H_3C(3)), 0.90 (t, 3 H, H_3C(9)).



38

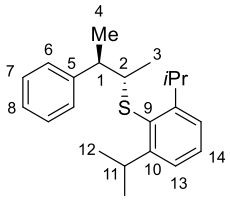
Data for *rel*-(*S*)-(2,6-diisopropylphenyl)(nonan-3-yl)sulfane (**38**):

^{1}H NMR: (400 MHz, $CDCl_3$)

7.31 (t, *J* = 7.7 Hz 1 H HC(15)), 7.17 (d, *J* = 7.7 Hz, 2 H HC(14)), 4.00 (ddt, *J* = 10.4, 6.8, 3.6 Hz, 2 H, HC(12)), 2.65-2.48 (m, 2 H, HC(3)), 1.69 (m, 1 H, HC(2), 1.62-1.38 (m, 11 H H_2C and HC(2, 4, 5, 6, 7, 8)), 0.98 (t, *J* = 7.4 Hz 3 H, H_3C(1)), 0.90 (t, 3 H, H_3C(9)).

Table 6 Entry 7

Following General Procedure 4, a flame-dried Schlenk flask was charged with hexanes and Me_3Al (144 mg, 1.0 mmol, 2 equiv.) and cooled to 0°C. Once at 0 °C, **39** (185 mg, 0.5 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was quenched after 48 hours when **39** had been consumed (monitored via TLC) and worked up. After purification via chromatography, **40** was obtained in a 81% yield.



40

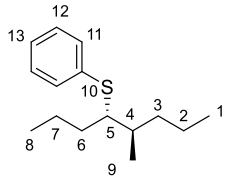
Data for *rel*-(2,6-diisopropylphenyl)((2*S*,3*R*)-3-phenylbutan-2-yl)sulfane (**40**):

^{1}H NMR: (400 MHz, C_6D_6) **Note:** $CDCl_3$ provides better separation of aryl peaks

7.23-7.0 (m, 8H HC(6, 7, 8, 13, 14)), 4.00 (hept, *J* = 6.8 Hz, 2H, HC(11)), 3.10 (qu, *J* = 7.1 Hz 1H, HC(1/2)), 2.99 (qu, *J* = 7.1 Hz, 1H, HC(1/2)), 1.33 (d, *J* = 7.1 Hz 3H, H_3C(3/4)), 1.22 (dd, *J* = 4.7 Hz 6H H_3C(12)) 1.05 (d, *J* = 7.1 Hz 3H, H_3C(3/4)).

Table 9, Entry 1

Following General Procedure 4, a flame-dried Schlenk flask was charged with hexanes and Me_3Al (144 mg, 2.0 mmol, 2 equiv.) and cooled to 0°C. Once at 0 °C, (4*R*,5*S*)-**11** (280 mg, 1.0 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was quenched after 5 hours when **11** had been consumed (monitored via TLC) and worked up. The residue was purified by column chromatography (High Resolution SiO_2, 32g, Ø 2cm, TBME/hexanes 1 to 2%) to afford 221 mg (94%) of **27** as a foul smelling colorless oil.



27

Data for ((4*S*,5*R*)-5-methyloctan-4-yl)(phenyl)sulfane (**27**):

^{1}H NMR: (500 MHz, $CDCl_3$)

7.42 (d, *J* = 7.2 Hz, 2H HC(11)), 7.31 (t, *J* = 7.5 Hz, 2H HC(12)), 7.21 (t, *J* = 7.4 Hz, 1H HC(13)), 3.15 (dt, *J* = 8.9, 3.5 Hz, 1H, HC(5)), 1.83 (ddt, *J* = 11.7, 8.3, 4.0 Hz, 1H, CH(4)), 1.65 (m, 2H, H_2C(6,7), 1.47 (m, 2H, H_2C(6,7) 1.40 (m, 2H, H_2C(2,3), 1.27 (m, 2H, H_2C(2,3), 1.02 (d, J = 6.8 Hz, 3 H, H_3C(9)), 0.95 (t, *J* = 6.8 Hz, 3 H, H_3C (8)), 0.90 (t, *J* = 6.8 Hz, 3 H, H_3C (1)).

^{13}C NMR: (101 MHz, $CDCl_3$)

137.42 (C(10)), 131.04 (C(11)), 128.88 (C(12)), 126.15 (C(13)), 55.13 (C(5)), 36.47 (C(4)), 36.16 (C(3)), 32.84 (C(6)), 21.20 (C(7)), 20.56 (C(2)), 15.91 (C(9)), 14.39 (C(8)), 14.18 (C(1))

IR: (neat)

3074 (w), 2957 (s), 2929 (s), 2872 (m), 1583 (m), 1478 (m), 1464 (m), 1438 (m), 1378 (m), 1089 (m), 1025 (m), 738 (s), 691 (s), 478 (w)

MS: (EI)

236.2 (M^+), 165.1 (53), 126.1 (24), 123.0 (84), 110.0 (100), 109.0 (32), 85.1 (85), 84.1 (17), 71.1 (44)

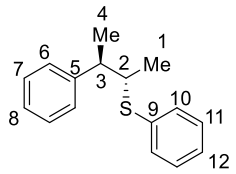
HRMS: calcd for 236.1599, found: 236.1597

TLC: R_f 0.909 (5% TBME/hexanes) [UV]

Opt. Rot.: $[\alpha]_D^{24}$ -25 (c=0.91, Ethanol)

Table 9, Entry 2

Following General Procedure 4, a flame-dried Schlenk flask was charged with hexanes and Me_3Al (288 mg, 4.0 mmol, 4 equiv.) and cooled to 0°C. Once at 0 °C, (1*S*,2*R*)-**46** (280 mg, 1.0 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was quenched after 2 hours when **46** had been consumed (monitored via TLC) and worked up. The residue was purified by column chromatography (High Resolution SiO_2, 30g, Ø 2cm, 1 to 2% TBME/hexanes) to afford 228 mg (94%) of **47** as a foul smelling colorless oil.



47

Data for phenyl((2*S*,3*R*)-3-phenylbutan-2-yl)sulfane(**47**):

^{1}H NMR: (500 MHz, $CDCl_3$)

7.47 (d, *J* = 7.1 Hz, 2H HC(10)), 7.36 (m, 4H, HC(8, 12, 11), 7.27 (m, 4H, HC(6,7), 3.55 (qd, *J*= 6.8, 5.0 Hz, 1H HC(2)), 3.09 (qd, *J*= 7.1, 4.9 Hz, 1H HC(3), 1.44 (d, *J*=7.1 Hz, 3H, H_3C(4)), 1.26 (d, *J*=6.9 Hz, 3H, H_3C(1))

^{13}C NMR: (126 MHz, $CDCl_3$)

144.48, (C(9)), 135.99 (C(5)), 131.96 (C(10)), 128.99 (C(8/12)), 128.36 (C(8/12)), 127.88 (C(11)), 126.83(C(6/7)), 126.56 (C(6/7)), 50.07 (C(2)), 43.38 (C(3)), 16.58 (C(1)), 15.21 (C(4)).

IR: (neat)

2969 (w), 1583 (w), 1494 (w), 1450 (w), 1090 (w), 1075 (w), 781 (w), 739 (w), 739 (m), 699 (s), 691 (s), 543 (w).

MS: (EI)

242.1 (M^+), 137.0 (100), 109.0 (12), 91.1 (16)

HRMS: Calcd for 242.1129 Found: 242.1128

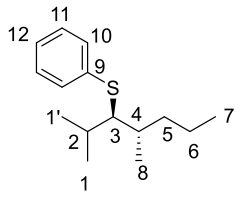
TLC: R_f 0.78 (5% TBME/hexanes) [UV]

Opt. Rot.: $[\alpha]_D^{24}$ 65.6 (c=0.72, Ethanol)

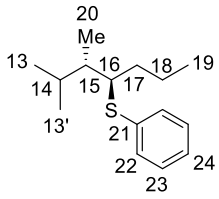
HPLC: (2*S*, 3*R*)-(**47**), t_R 11.176 min (99%); (2*R*, 3*S*)-(**47**), t_R 10.505 min (1%), (Chiralcel OJ-H, 25 °C, 1% *i*PrOH in hexanes, 1.0 mL/min, 220 nm)

Table 9, Entry 3

Following General Procedure 4, a flame-dried Schlenk flask was charged with hexanes and Me_3Al (288 mg, 4.0 mmol, 4 equiv.) and cooled to 0°C. Once at 0 °C, (3*R*,4*S*)-**48** (280 mg, 1.0 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was quenched after 2 hours when **48** had been consumed (monitored via TLC) and worked up. The residue was purified by column chromatography (High Resolution SiO_2, 36g, Ø 2cm, 1% TBME/hexanes) to afford 227 mg (69%) an inseparable mixture of **49** and **50** in a 3.8 to 1 ratio as a foul smelling colorless oil.



49



50

Data for ((3*R*,4*S*)-2,4-dimethylheptan-3-yl)(phenyl)sulfane (**49**) and ((3*S*,4*R*)-2,3-dimethylheptan-4-yl)(phenyl)sulfane (**50**):

^{1}H NMR: (500 MHz, $CDCl_3$)

7.45 (d, *J* = 8.2 Hz, 2H HC(10)), 7.29 (t, *J*= 7.7 Hz, 2H HC(11)), 7.19 (t, *J*= 7.4 Hz, 1H HC(12)), 2.86 (t, *J*= 5.8 Hz, 1H HC(3)), 2.13 (dq, *J*=12.8, 6.6 Hz, 1H HC(2)), 1.90 (ddp, *J*= 12.7, 10.2, 3.2 Hz, 1H CH(4)), 1.64 (m, 1H $H_2C(5)$), 1.45 (m, 2H, $H_2C(6)$), 1.27 (m, 1H, $H_2C(5)$), 1.10 (d, *J*=3.7 Hz, $H_3C(1/1')$), 1.08 (d, *J*=3.5 Hz, $H_3C(1/1')$), 1.07 (d, *J*=6.1 Hz, $H_3C(8)$), 0.93 (t, 3H, $H_3C(7)$)

7.42 (d, *J*=9.4, 2H HC(22)), 7.31 (m, 2H, HC(23)), 7.23 (t, *J*=7.4 Hz, 1H, HC(24)), 3.35 (dt, *J*= 9.8, 3.5 Hz, 1H, HC(16)), 1.78 (dt, *J*=13.4, 6.9 Hz, 1H HC(14)), 1.64 (m, 2H, H_2C(17), HC(15)), 1.50 (m, 2H H_2C(18)), 1.45 (m, 1H, H_2C(17)), 1.07 (d, *J*=6.1 Hz, 3H, H_3C(20)), 0.98 (t, *J*= 7.2 Hz, 3H, H_3C(19)), 0.95(d, *J*=6.3 Hz, 3H, H_3C(13/13')), 0.89 (d, *J*= 6.9 Hz, 3H, H_3C(13/13')

^{13}C NMR: (126 MHz, $CDCl_3$)

139.49, (C(9)), 130.45 (C(10)), 128.82 (C(11)), 125.74 (C(12)), 64.83 (C(3)), 36.20 (C(4)), 35.56 (C(5)), 31.09 (C(2)), 22.10 (C(1/1')), 20.66 (C(6)), 19.88 (C(8)), 18.33 (C(1/1')), 14.43 (C(7))

137.21 (C(21)), 131.19 (C(22)), 128.87 (C(23)), 126.23 (C(24)), 52.73 (C(16)), 43.31 (C(18)), 31.73 (C(17)), 30.44 (C(16)), 21.57, (C(14/15)), 20.88 (C(14/15)), 20.16 (C(13/13')), 14.25 (C(13/13')), 12.34 (C(19))

IR: (neat)

2957 (s), 2928 (w), 1583 (w), 1478 (m), 1438 (m), 1380 (w), 1155 (w), 1088 (w), 739 (s), 690 (s), 485 (w)

MS: (EI)

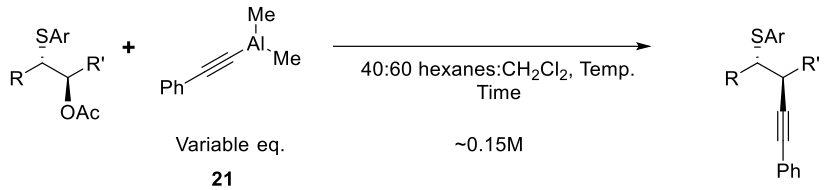
236.2 (M^+), 193.1 (23), 165.1 (82), 137.0 (13), 126.1 (24), 123.0 (72), 110.0 (100), 109.0 (40), 85.1 (25), 83.1 (44), 71.1 (52)

HRMS: Calcd for 236.1599 Found: 236.1600

TLC: R_f 0.931 (5% TBME/hexanes) [UV]

Opt. Rot.: $[\alpha]_D^{24}$ -23 (c=0.68, Ethanol)

4.3.10 General Procedure 5



Phenylacetylene was purified immediately before use via kugelrohr distillation at 0.05 torr with ABT of 50 °C yielding a clear colorless liquid.

To a flame-dried, 10-mL Schlenk flask fitted a rubber septum and magnetic stir bar, was charged the phenylacetylene (204 mg, 220 μL, 2.0 mmol, 2.0 equiv.) and 3mL CH_2Cl_2 under Ar. The reaction was stirred in a 0 °C ice bath for 5 minutes when 2.54M *n*BuLi in hexanes (787 μL,

2.0 mmol, 2.0 equiv) was added resulting in an opaque yellow solution. Following *n*BuLi addition, the reaction was stirred for 15 minutes at 0 °C when 1.0M Me_2AlCl in hexanes (2.0 mL, 2.0 mmol, 2.0 equiv.) was added over 40 seconds. The reaction was stirred at 0 °C for 5 minutes and then room temperature for 25 minutes. The reaction was re-cooled to 0 °C and β-acetoxy (aryl) sulfide (1.0 mmol) was added as a solution in 1.0 mL CH_2Cl_2 via syringe. After the addition was complete the ice bath was removed and the reaction was allowed to warm to room temperature. Once judged complete by TLC, the reaction was quenched by adding 1.5 mL EtOAc followed by 2.5 mL 3M HCl. The reaction was allowed to sitr until two distinct layers had formed. The reaction mixture was then transferred a 60-mL separatory funnel containing 15 mL EtOAc and 15 mL 3M HCl. After thorough mixing, the layers were separated. The aqueous layer was extracted 2 x 15 mL + 1 x 10 mL of EtOAc. The organic layers were combined, washed 1 x 10 mL brine and dried over anhydrous $MgSO_4$ followed by filtration and concentration *in vacuo* (rt, 10 mbar). The residue was then purified by flash column chromatograph (high resolution SiO_2, 35 g, *tert*-butyl methyl ether/hexanes 1-3%, 100 mL solvent for each percent).

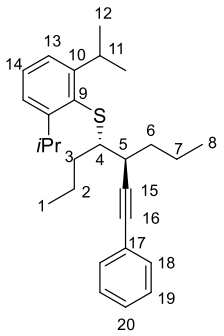
4.3.11 Experimental Procedures for Alkenylations

Table 7 Entry 1

Following General Procedure 5, a flame-dried Schlenk flask containing an *in situ* prepared dimethyl(phenylethynyl)Al (1.0 mmol, 2.0 equiv.) was cooled 0 °C. Once at 0 °C, **34** (182mg, 0.5 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was quenched after 21 hours when **34** had been consumed (monitored via TLC) and worked up. The residue was purified by column chromatography (High Resolution SiO_2,Ø 2cm, 1 to 2% TBME/hexanes) to afford **41** in a 91% yield.

Table 8 Entry 2

Following General Procedure 5, a flame-dried Schlenk flask containing an *in situ* prepared dimethyl(phenylethynyl)Al (0.5 mmol, 2.0 equiv.) was cooled 0 °C. Once at 0 °C, (4*R*,5*S*)-**34** (91mg, 0.25 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was quenched after 16.5 hours when **34** had been consumed (monitored via TLC) and worked up. The residue was purified by column chromatography (High Resolution SiO_2,Ø 2cm, 1 to 2% TBME/hexanes) to afford **41** in a 95% yield with 100% enantiospecificity.



41

Data for (2,6-diisopropylphenyl)((4*S*,5*S*)-5-(phenylethynyl)octan-4-yl)sulfane (**41**):

^{1}H NMR: (400 MHz, $CDCl_3$)

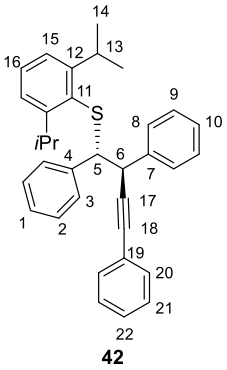
7.50 (m, 1 H HC(14)), 7.43 (m, 2 H HC(18)), 7.37 (d, *J* = 7.8 2 H HC(13)), 7.32-7.27 (m, 2 H HC(19, 20)) 4.28 (hept, *J* = 6.6 Hz, 2 H, HC(11)), 3.33 (m, 1 H, HC(5)), 3.06 (td, *J* = 6.1, 2.3 Hz, 1H, HC(4)), 2.10 (m, 2H H_2C(6)), 1.80-1.39 (m, 6 H, H_2C(2, 3, 7)), 1.29 (dd, 6H H_3C(12)), 0.92 (t, *J* = 7.3 Hz 3 H, H_3C(1/8)), 0.87 (t, *J* = 7.2 Hz 3 H, H_3C(1/8)).

Table 7 Entry 2

Following General Procedure 5, a flame-dried Schlenk flask containing an *in situ* prepared dimethyl(phenylethynyl)Al (1.0 mmol, 2.0 equiv.) was cooled 0 °C. Once at 0 °C, **32** (216 mg, 0.5 mmol) was added dropwise via syringe. The reaction was quenched after 75 minutes when **32** had been consumed (monitored via TLC) and worked up. The residue was purified by column chromatography (High Resolution SiO_2,Ø 2cm, 1 to 2% TBME/hexanes) to afford **42** in a 97% yield.

Table 8 Entry 2

Following General Procedure 5, a flame-dried Schlenk flask containing an *in situ* prepared dimethyl(phenylethynyl)Al (0.5 mmol, 2.0 equiv.) was cooled 0 °C. Once at 0 °C, (1*R*,2*S*)-**32** (1.08 mg, 0.25 mmol) was added dropwise via syringe. The reaction was quenched after 75 minutes when **32** had been consumed (monitored via TLC) and worked up. The residue was purified by column chromatography (High Resolution SiO_2,Ø 2cm, 1 to 2% TBME/hexanes) to afford **42** in a 90% yield with 88% enantiospecificity.



42

Data for (2,6-diisopropylphenyl)((1*R*,2*S*)-1,2,4-triphenylbut-3-yn-1-yl)sulfane (**42**):

^{1}H NMR: (400 MHz, $CDCl_3$)

7.31-7.09 (m, 18 H HC(1, 2, 3, 8, 9, 10, 15, 16, 20, 21, 22)), 4.29 (d, J = 6.6 Hz, 1 H HC(5/6)), 3.85 (d, J = 6.6 Hz, 1 H HC(5/6)), 3.72 (hept, J = 7.0 Hz, 2 H, HC(13)), 1.15 (d, J = 6.8 Hz 3H H_3C(14)), 0.93 (d, J = 6.8 Hz 3H H_3C(14)).

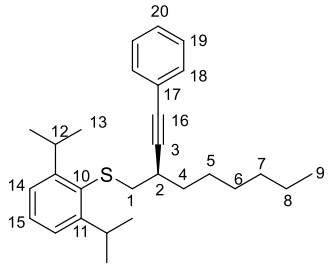
HPLC: ((1*R*,2*S*)-(**42**), t_R 5.787 min (88.2%); ((1*S*,2*R*)-(**42**), t_R 7.251 min (11.8%), (Chiralpak AD-H, 5 °C, 1% *i*PrOH in hexanes, 0.7 mL/min, 220 nm).

Table 7 Entry 3

Following General Procedure 5, a flame-dried Schlenk flask containing an *in situ* prepared dimethyl(phenylethynyl)Al (1.0 mmol, 2.0 equiv.) was cooled 0 °C. Once at 0 °C, **36** (182 mg, 0.5 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was quenched after 24 hours and worked up. Full conversion of **36** was not observed. The residue was purified by column chromatography (High Resolution SiO_2,Ø 2cm, 1 to 2% TBME/hexanes) to afford inseparable mixture of **43** and **44** in a 3 to 2 ratio in a 50% yield.

Table 7 Entry 4

Following General Procedure 5, a flame-dried Schlenk flask containing an *in situ* prepared dimethyl(phenylethynyl)Al (2.0 mmol, 4.0 equiv.) was cooled 0 °C. Once at 0 °C, **36** (182 mg, 0.5 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was quenched after 24 hours when **36** had been consumed (monitored via TLC) and worked up. The residue was purified by column chromatography (High Resolution SiO_2,Ø 2cm, 1 to 2% TBME/hexanes) to afford inseparable mixture of **43** and **44** in a 3 to 2 ratio in a 79% yield.

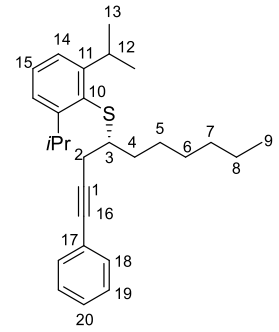


43

Data for *rel*-(*R*)-(2,6-diisopropylphenyl)(2-(phenylethynyl)octyl)sulfane (**43**):

^{1}H NMR: (500 MHz, $CDCl_3$)

7.50 (m, 4 H HC(14, 18)), 7.41 (m, 2 H HC(19)), 7.28 (d, *J* = 4.7 Hz, 2 H HC(15/20)), 7.27 (d, *J* = 4.7 Hz, 2 H HC(15/20)), 4.17 (qu, *J* = 4.7 Hz, 2 H, HC(12)), 3.08 (qu, *J* = 6.9 Hz, 2 H, HC(2)), 2.69 (ddd, *J* = 4.8, 4.7, 7.1 Hz, 2 H $H_2C(1)$), 1.82-1.42 (m, 10 H $H_2C(4, 5, 6, 7, 8)$), 1.36 (dd, J = 6.9, 2.1 Hz, 12H $H_3C(13)$), 1.00 (t, J = 6.5 Hz 3 H, $H_3C(9)$).



44

Data for *rel*-(R)-(2,6-diisopropylphenyl)(1-phenyldec-1-yn-4-yl)sulfane (**44**):

^{1}H NMR: (500 MHz, $CDCl_3$)

7.50 (m, 4 H HC(14, 18)), 7.41 (m, 2 H HC(19)), 7.28 (d, *J* = 4.7 Hz, 2 H HC(15/20)), 7.27 (d, *J* = 4.7 Hz, 2 H HC(15/20)), 4.17 (qu, *J* = 4.7 Hz, 2 H, HC(12)), 2.99 (dd, *J* = 12.0, 7.4 Hz, 2 H, $H_2C(2)$), 2.85 (m, 1 H HC(3)), 1.82-1.42 (m, 10 H $H_2C(4, 5, 6, 7, 8)$), 1.36 (dd, J = 6.9, 2.1 Hz, 12H $H_3C(13)$), 1.00 (t, *J* = 6.5 Hz 3 H, $H_3C(9)$).

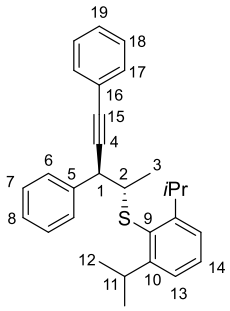
Table 7 Entry 5

Following General Procedure 5, a flame-dried Schlenk flask containing an *in situ* prepared dimethyl(phenylethynyl)Al (1.0 mmol, 2.0 equiv.) was cooled 0 °C. Once at 0 °C, **39** (185 mg, 0.5 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was quenched after 20 hours when **39** had been consumed (monitored via TLC) and

worked up. The residue was purified by column chromatography (High Resolution SiO_2,Ø 2cm, 1 to 2% TBME/hexanes) to afford **45** in a 85% yield.

Table 8 Entry 3

Following General Procedure 5, a flame-dried Schlenk flask containing an *in situ* prepared dimethyl(phenylethynyl)Al (0.5 mmol, 2.0 equiv.) was cooled 0 °C. Once at 0 °C, (1*S*,2*R*)-**39** (93 mg, 0.25 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was quenched after 17 hours when **39** had been consumed (monitored via TLC) and worked up. The residue was purified by column chromatography (High Resolution SiO_2,Ø 2cm, 1 to 2% TBME/hexanes) to afford **45** in a 92% yield with 100% enantiospecificity.



45

Data for (2,6-diisopropylphenyl)((2*S*,3*S*)-3,5-diphenylpent-4-yn-2-yl)sulfane (**45**):

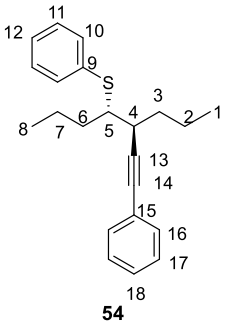
^{1}H NMR: (400 MHz, $CDCl_3$)

7.54 (m, 2 H HC(17)), 7.35-7.18 (m, 11 H HC(6, 7, 8, 13, 14, 18, 19)), 4.11 (hept, *J* = 13.6, 6.5 Hz, 2 H, HC(11)), 4.00 (d, *J* = 3.9 Hz 1 H, HC(1)), 3.08 (m, 1 H, HC(2)), 1.26 (d, *J* = 6.8 Hz 15 H, H_3C(12, 3)).

HPLC: ((1*S*,2*S*)-(**45**), t_R 3.806 min (99.0%); ((1*R*,2*R*)-(**45**), t_R 4.065 min (1.0%), (Chiralpak AD-H, 20 °C, 2% *i*PrOH in hexanes, 1.0 mL/min, 220 nm).

Table 10 Entry 1

Following General Procedure 5, a flame-dried Schlenk flask containing an *in situ* prepared dimethyl(phenylethynyl)Al (2.0 mmol, 2.0 equiv.) was cooled 0 °C. Once at 0 °C, (4*R*,5*S*)-**11** (280 mg, 1.0 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was quenched after 3 hours when **11** had been consumed (monitored via TLC) and worked up. The residue was purified by column chromatography (High Resolution SiO_2, 36g, Ø 2cm, 1 to 2% TBME/hexanes) to afford **54** in a 90% yield with 100% enantiospecificity.



54

Data for phenyl((4S,5S)-5-(phenylethynyl)octan-4-yl)sulfane (**54**):

^{1}H NMR: (500 MHz, $CDCl_3$)

7.52 (d, *J*= 7.3 Hz, 2H, HC(16)), 7.48-7.42 (m, 2H, HC(10)), 7.37-7.31 (m, 5H, HC(11, 17, 18)), 7.27 (t, *J*=7.3 Hz, 1H, HC(12)), 3.21 (ddd, *J*= 9.0, 5.4, 3.6 Hz, 1H, HC(5)), 2.91 (dt, *J*= 8.1, 56 Hz, 1H, HC(4)), 1.96-1.86 (m, 1H H_2C(6)), 1.84-1.74 (m, 2H, H_2C(6,7)), 1.74-1.67 (m, 2H, H_2C(3)), 1.67-1.60 (m, 2H, H_2C(2)), 1.57 (tdd, *J*= 12.4, 5.6, 4.1 Hz, 1H, H_2C(7)), 1.52-1.42 (m, 1H, H_2C(2)), 1.01 (t, J=7.2 Hz, 3H, H_3C(1/8)), 0.97 (t, *J*=7.2 Hz, 3H, H_3C(1/8))

^{13}C NMR: (126 MHz, $CDCl_3$)

136.22 (C(9)), 132.13 (C(16)), 131.78 (C(10)), 128.99 (C(11/17)), 128.27 (C(11/17)), 127.72 (C(18)), 126.87 (C(12)), 124.03 (C(15)), 91.13 (C(14)), 83.49 (C(13)), 53.56 (C(5)), 38.11 (C(4)), 35.22 (C(3)), 34.28 (C(6)), 22.06 (C(2)), 21.03 (C(7)), 14.18 (C(1/8)), 14.04 (C(1/8))

IR: (neat)

3057 (w), 2956 (m), 2931(m), 1597 (w), 1583 (w), 1490 (m), 1479 (m), 1465 (m), 1303 (w), 1176 (w), 754 (s), 691(s), 525 (w), 497 (w)

MS: (EI)

322.2 (M^+), 245.1 (19), 212.2 (23), 183.1 (20), 165.1 (88), 155.1 (17), 141.1 (27), 123.0 (78), 115.1 (100), 91.0 (18)

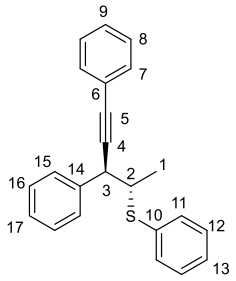
HRMS: Calcd for 322.1755 Found: 322.1754

TLC: R_f 0.818 (5% TBME/hexanes) [UV]

Opt. Rot.: $[\alpha]_D^{24}$ -166 (c=0.65, Ethanol)

Table 10 Entry 2

Following General Procedure 5, a flame-dried Schlenk flask containing an *in situ* prepared dimethyl(phenylethynyl)Al (2.0 mmol, 2.0 equiv.) was cooled 0 °C. Once at 0 °C, (1*S*,2*R*)-**46** (280 mg, 1.0 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was quenched after 6 hours when **46** had been consumed (monitored via TLC) and worked up. The residue was purified by column chromatography (High Resolution SiO_2, 34g, Ø 2cm, 1 to 2% TBME/hexanes) to afford **55** in a 96% yield with 100% enantiospecificity.



55

Data for ((2*S*,3*S*)-3,5-diphenylpent-4-yn-2-yl)(phenyl)sulfane (**55**):

^{1}H NMR: (500 MHz, $CDCl_3$)

7.69 (d, *J*=7.4 Hz, 4H, HC(7, 11)), 7.56 (d, *J*=7.7 Hz, 2H, HC(15)), 7.48 (m, 7H, HC(9, 13, 17, 8, 12)), 7.41 (d, *J*=7.3 Hz, 2H, HC(16)), 4.39 (d, *J*=4.4 Hz, 1H, HC(3)), 3.71 (qd, *J*= 6.8, 4.4 Hz, 1H, HC(2)), 1.53 (d, *J*=6.8 Hz, 3H, H_3C(1))

^{13}C NMR: (101 MHz, $CDCl_3$)

139.37 (C(14)), 135.20 (C(10)), 132.46 (C(7/11)), 131.86 (C(7/11)), 129.09 (C(8, 12, 16)), 128.48 (C(8, 12, 16)), 128.30 (C(8, 12, 16)), 128.18 (C(15)), 128.04 (C(9)), 127.31 (C(13/17)), 127.25 (C(13/17)), 123.56 (C(6)), 87.69 (C(5)), 85.72 (C(4)), 49.78 (C(2)), 44.01 (C(3)), 16.21 (C(1))

IR: (neat)

2969 (w), 1598 (w), 1583 (w), 1489 (m), 1480 (w), 1439 (w), 1346 (w), 1178 (w), 1091 (w), 914 (w), 754 (s), 702 (m), 690 (s), 610 (m), 529 (m)

MS: (EI)

328.1(M^+), 243.1 (13), 242.1 (75), 218.1 (23), 202.1 (15), 138.0 (14), 137.0 (100), 135.0 (67), 117.1 (29), 115.1 (31), 109.0 (77), 91.0 (73), 77.0 (39)

HRMS: Calcd for 328.1286 Found: 328.1282

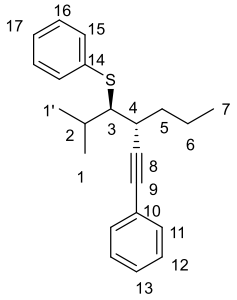
TLC: R_f 0.677 (5% TBME/hexanes) [UV]

Opt. Rot.: $[\alpha]_D^{24}$ -119 (c=1.4, Chloroform)

HPLC: ((2*R*,3*R*)-(**55**), t_R 8.319 min (1.0%); ((2*S*,3*S*)-(**55**), t_R 10.384 min (99.0%), (Chiralcel OJ-H, 25 °C, 1% *i*PrOH in hexanes, 1.2 mL/min, 220 nm).

Table 10 Entry 3

Following General Procedure 5, a flame-dried Schlenk flask containing an *in situ* prepared dimethyl(phenylethynyl)Al (4.0 mmol, 4.0 equiv.) was cooled 0 °C. Once at 0 °C, (3*R*,4*S*)-**48** (280 mg, 1.0 mmol) was added dropwise via syringe and then allowed to return to room temperature. The reaction was quenched after 3 hours when **48** had been consumed (monitored via TLC) and worked up. The residue was purified by column chromatography (High Resolution SiO_2, 36g, Ø 2cm, 1 to 2% TBME/hexanes) to afford **56** in a 94% yield with 100% enantiospecificity.



56

Data for ((3*R*,4*R*)-2-methyl-4-(phenylethynyl)heptan-3-yl)(phenyl)sulfane (**56**):

^{1}H NMR: (500 MHz, $CDCl_3$)

7.53 (d, *J*= 8.2 Hz, 2H, HC(11/15)), 7.47-7.41 (m, 2H, HC(11/15)), 7.37-7.29 (m, 5H, HC(12, 13, 16)), 7.23 (t, *J*=7.4 Hz, HC(17)), 3.15 (dd, *J*= 8.7, 3.9 Hz, 1H, HC(3)), 2.94 (td, *J*= 9.5, 3.8 Hz, 1H, HC(4)), 2.63 (heptd, *J*=6.9, 3.9 Hz, 1H, HC(2)), 1.99 (m, 1H, H_2C(5), 1.65 (m, 2H, H_2C(5,6)), 1.52 (m, 1H, H_2C(6)), 1.20 (d, *J*= 6.7 Hz, 3H, H_3C(1/1')), 1.14 (d, *J*= 6.7 Hz, 3H, H_3C(1/1')), 0.96 (t, *J*= 7.3, 3H, H_3C(7))

^{13}C NMR: (126 MHz, $CDCl_3$)

138.45 (C(14)), 131.68 (C(11/15), 130.96 (C(11/15)), 128.96 (C(12/16)), 128.30 (C(12/16)), 127.77 (C(13)), 126.28 (C(17)), 123.95 (C(10), 91.72 (C(9)), 83.73 (C(8)), 62.20 (C(3)), 37.83 (C(4)), 35.16 (C(5)), 31.28 (C(2)), 22.19 (C(1/1')), 20.82 (C(6)), 17.83 (C(1/1')), 14.04 (C(7))

IR: (neat)

2959 (m), 2929 (w), 2870 (w), 1583 (w), 1489 (m), 1478 (m), 1463 (m), 1085 (w), 1068 (w), 754 (s), 690 (s), 527 (w)

MS: (EI)

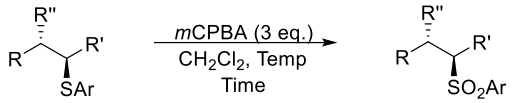
322.2 (M^+), 245.1 (38), 220.1 (100), 205.1 (42), 177.0 (63), 165.1 (38), 149.0 (68), 135.0 (72), 115.0 (39), 91.0 (16)

HRMS: Calcd for 322.1755 Found: 322.1754

TLC: R_f 0.864 (5% TBME/hexanes) [UV]

Opt. Rot.: $[\alpha]_D^{24}$ 18 (c=0.9, Ethanol)

4.3.12 General Procedure 6: Oxidation of Sulfides for HPLC Analysis

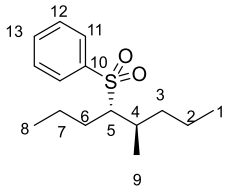


0.05M

To a 25-mL "tear-drop" flask fitted with a magnetic stir bar, was charged with a solution of sulfide in CH_2Cl_2 under air. The sulfide was massed in a 1-dram vial and dissolved with half the required CH_2Cl_2. The flask was fitted with a glass funnel and the *m*CPBA was added with the remaining CH_2Cl_2 used to rinse the funnel and sides of the flask. The funnel was removed and replaced with a Teflon cap. Once judged complete by TLC, the reaction was quenched with 20 mL of a solution of $Na_2S_2O_3$ (sat. aq. $Na_2S_2O_3$: H_2O, 3:1) and allowed to stir for 0.5-2 hours. The biphasic mixture was transferred to a 60-mL separatory funnel containing 10 mL CH_2Cl_2 and 10 mL 1M NaOH. After thorough mixing the phases were separated. The organic layer was washed with an additional 10 mL 1M NaOH. The aqueous layers were combined and washed 3 x 10 mL CH_2Cl_2. The organic layers were combined, washed 1 x 10 mL brine, dried over anhydrous $MgSO_4$ followed by filtration and concentration *in vacuo* (rt, 10 mbar). The resulting residue was of sufficient purity for HPLC analysis.

Synthesis of (((4*S*,5*R*)-5-methyloctan-4-yl)sulfonyl)benzene (67**)**

Following general procedure 6, a solution of **27** (47 mg, 0.2 mmol) in 1.0 mL CH_2Cl_2 was added to a 25-mL flask containing a magnetic stir bar. *meta*-chloroperoxybenzoic acid (103 mg, 0.6 mmol, 3 equiv.) was added with the aid of a glass funnel. The remaining 3.0 mL CH_2Cl_2 was used to rinse the funnel and flask. The reaction was quenched after 5 hours when **27** had been consumed (monitored via TLC). The biphasic mixture was allowed to stir for 40 minutes before being worked up. The extraction afforded sulfone **67** as a clear, colorless, foul smelling oil in a quantitative yield.



67

Data for(((4*S*,5*R*)-5-methyloctan-4-yl)sulfonyl)benzene (**67**):

^{1}H NMR: (400 MHz, $CDCl_3$)

7.87 (d, *J*=7.5 Hz, 2H, HC(11)), 7.62 (t, *J*=7.4 Hz, 1H, HC(13)), 7.54 (t, *J*=7.6 Hz, 2H, HC(12)), 2.93 (m, 1H HC(5)), 2.14 (q, *J*=6.7 Hz, 1H, HC(4)), 1.87 (m, 1H, H_2C(6)), 1.58 (m, 1H, H_2C(6)), 1.31 (m, 2H, H_2C(3)), 1.21 (m, 4H, H_2C(2,7)), 0.97 (t, *J*=6.9 Hz, 3H, H_3C(9)), 0.82 (t, *J*=7.3 Hz, 3H, H_3C(1/8)), 0.77 (t, *J*=7.0 Hz, 3H, H_3C(1/8))

^{13}C NMR: (101 MHz, $CDCl_3$)

139.34 (C(10), 133.47 (C(13)), 129.18 (C(11/12)), 128.57 (C(11/12)), 67.82 (C(5)), 38.08 (C(4)), 31.55 (C(3/6)), 25.79 (C(3/6)), 22.37 (C(2/7)), 20.43 (C(2/7)), 14.82 (C(9)), 14.17 (C(1/8)), 13.87 (C(1/8))

IR: (neat)

2960 (m), 2931 (m), 2873 (w), 1586 (w), 1446 (m), 1303 (s), 1292 (s), 1144 (s), 1084 (s), 1072 (m), 930 (w), 753 (m), 724 (s), 691 (s), 624 (m), 605 (m)

MS: (ESI)

269.2 (M+H), 238.0 (35), 174.0 (36), 143.0 (77), 125.0 (51), 97.0 (13)

HRMS: Calcd for 269.1575 Found: 269.1577

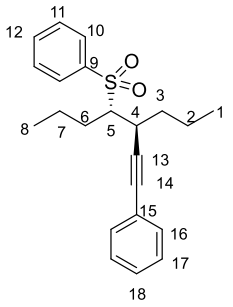
TLC: R_f 0.553 (20% TBME/hexanes) [UV]

HPLC: ((4*R*,5*S*)-(**67**), t_R 8.085 min (3.5%); ((4*S*,5*R*)-(**67**), t_R 7.435 min (96.5%), (Chiralpak AD-H, 20 °C, 1% *i*PrOH in hexanes, 1.0 mL/min, 220 nm).

Synthesis of (((4*S*,5*S*)-5-(phenylethynyl)octan-4-yl)sulfonyl)benzene (68**)**

Following general procedure 6, a solution of **54** (51 mg, 0.16 mmol) in 1.0 mL CH_2Cl_2 was added to a 25-mL flask containing a magnetic stir bar. *meta*-chloroperoxybenzoic acid (82 mg, 0.47 mmol, 3 equiv.) was added with the aid of a glass funnel. The remaining 2.2 mL CH_2Cl_2 was used to rinse the funnel and flask. The reaction was quenched after 5 hours when **54** had been consumed

(monitored via TLC). The biphasic mixture was allowed to stir for 55 minutes before being worked up. The extraction afforded sulfone **68** as a thick yellow oil in a quantitative yield.



68

Data for (((4*S*,5*S*)-5-(phenylethynyl)octan-4-yl)sulfonyl)benzene (**68**):

^{1}H NMR: (400 MHz, $CDCl_3$)

7.95 (d, *J*=7.4 Hz, 2H, HC(10)), 7.58 (t, *J*=7.3 Hz, 1H, HC(12)), 7.51 (t, *J*=7.5 Hz, 2H, HC(11)), 7.28-7.17 (m, 3H, HC(17,18)), 7.14 (d, *J*=7.7 Hz, 2H, HC(16)), 3.44 (ddd, *J*=9.7, 5.2, 2.1 Hz, 1H, HC(5)), 2.99 (td, *J*=6.0, 1.7 Hz, 1H, HC(4)), 2.05-1.93 (m, 1H, H_2C(6)), 1.81 (ddt, *J*= 15.1, 9.6 6.4 Hz, 1H, H_2C(6)), 1.72-1.40 (m, 6H, H_2C(7, 3, 2), 0.93 (t, *J*= N.D., 3H, H_3C(1/8)), 0.91 (t, *J*=N.D., 3H, H_3C(1/8))

^{13}C NMR: (101 MHz, $CDCl_3$)

137.70 (C(9)), 133.77 (C(12)), 131.59 (C(10)), 129.63 (C(11/16/17)), 128.99 (C(11/16/17)), 128.13 (C(11/16/17)), 127.95 (C(16)), 123.21 (C(15)), 87.64 (C(13)), 84.58 (C(14)), 68.01 (C(5)), 37.56 (C(3)), 32.36 (C(4)), 28.97 (C(6)), 21.82 (C(2/7)), 20.84 (C(2/7)), 14.21 (C(1/8)), 13.68 (C(1/8))

IR: (neat)

2959 (w), 2933 (w), 1490 (w), 1465 (w), 1446 (w), 1134 (s), 1081 (m), 999 (w), 797 (w), 755 (s), 727 (s), 690 (s), 584 (s), 557 (m), 535 (s), 526 (m), 508 (w)

MS: (ESI)

355.2 (M+H, 100), 214.2 (14), 213.2 (83), 157.1 (11)

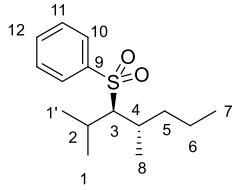
HRMS: Calcd for 355.1732 Found: 355.1737

TLC: R_f 0.518 (20% TBME/hexanes) [UV]

HPLC: ((4*S*,5*S*)-(**68**), t_R 8.705 min (96.5%); ((4*R*,5*R*)-(**68**), t_R 10.073 min (3.5%), (Chiralcel OJ-H, 20 °C, 1% *i*PrOH in hexanes, 1.0 mL/min, 220 nm).

Synthesis of (((3*R*,4*S*)-2,4-dimethylheptan-3-yl)sulfonyl)benzene (69**):**

Following general procedure 6, a solution of **49**/**50** (50 mg, 0.21 mmol) in 1.2 mL CH_2Cl_2 was added to a 25-mL flask containing a magnetic stir bar. *meta*-chloroperoxybenzoic acid (110 mg, 0.63 mmol, 3 equiv.) was added with the aid of a glass funnel. The remaining 3.0 mL CH_2Cl_2 was used to rinse the funnel and flask. The reaction was quenched after 2 hours when **49**/**50** had been consumed (monitored via TLC). The biphasic mixture was allowed to stir for 65 minutes before being worked up. The extraction afforded sulfone **69** as a clear, colorless thick oil in a 68% yield.



69

Data for (((3*R*,4*S*)-2,4-dimethylheptan-3-yl)sulfonyl)benzene (**69**):

(Note: the data for the sulfone resulting from sulfide **50** is not reported and separations conditions could not be found).

^{1}H NMR: (400 MHz, $CDCl_3$)

7.88 (d, *J*= 8.5 Hz, 2H, HC(10)), 7.61 (t, *J*=7.4 Hz, 1H, HC(12)), 7.54 (t, *J*=7.4 Hz, 2H, HC(11)), 2.92 (d, *J*=1.7 Hz, 1H HC(3)), 2.20 (dqd, *J*= 14.1, 7.1, 2.0 1H, HC(3)), 1.92 (m, 1H HC(2)), 1.33 (q, *J*= 7.5 Hz, 2H H_2C(5)), 1.25 (d, *J*=5.3 Hz, 3H, H_3C(1/1')), 1.23 (d, *J*=5.3 Hz, 3H, H_3C(1/1')), 1.08 (dq, *J*=14.7, 7.4 Hz, 2H, H_2C(6)), 0.68 (t, *J*= 7.3 Hz, 3H, H_3C(7))

^{13}C NMR: (101 MHz, $CDCl_3$)

140.65 (C(9)), 133.26 (C(12)), 129.12 (C(10/11)), 128.42 (C(10/11)), 72.43 (C(3)), 37.36 (C(5)), 32.24 (C(2/4)), 26.87 (C(2/4)), 23.04 (C(6)), 20.92 (C(1/1'), 20.71 (C(1/1')), 17.12 (C(8)), 13.82 C(7))

IR: (neat)

2960 (m), 2874 (w), 1585 (w), 1463 (m), 1301 (s), 1139 (s), 1083 (s), 1024 (w), 815 (w), 763 (m), 719 (s), 690 (s), 596 (m), 569 (m), 547 (m), 497 (w)

MS: (ESI)

269.16 (M+H), 237.96 (18), 174.00 (19), 143.02 (83), 125.01 (53), 97 (14), 291.1 (100)

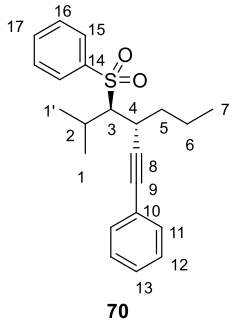
HRMS: Calcd for 269.1575 Found: 269.1575

TLC: R_f 0.516 (20% TBME/hexanes) [UV]

HPLC: ((3*R*,4*S*)-(**69**), t_R 6.643 min (90.0%); ((3*S*,4*R*)-(**69**), t_R 7.000 min (10.0%), (Chiralpak AD-H, 20 °C, 1% *i*PrOH in hexanes, 1.0 mL/min, 220 nm).

Synthesis of (((3*R*,4*R*)-2-methyl-4-(phenylethynyl)heptan-3-yl)sulfonyl)benzene (70**):**

Following general procedure 6, a solution of **56** (50 mg, 0.16 mmol) in 1.2 mL CH_2Cl_2 was added to a 25-mL flask containing a magnetic stir bar. *meta*-chloroperoxybenzoic acid (80 mg, 0.47 mmol, 3 equiv.) was added with the aid of a glass funnel. The remaining 2.0 mL CH_2Cl_2 was used to rinse the funnel and flask. The reaction was quenched after 10.5 hours when **56** had been consumed (monitored via TLC). The biphasic mixture was allowed to stir for 35 minutes before being worked up. The extraction afforded sulfone **70** as thick yellow oil in a quantitative yield.



70

Data for (((3*R*,4*R*)-2-methyl-4-(phenylethynyl)heptan-3-yl)sulfonyl)benzene (**70**):

^{1}H NMR: (400 MHz, $CDCl_3$)

7.97 (d, *J*=7.3 Hz, 2H, HC(15)), 7.61 (t, *J*=7.3 Hz, 2H, HC(17)), 7.53 (t. *J*=7.5 Hz, 2H, HC(16)), 7.34-7.23 (m, 5H, HC(11, 12, 13)), 3.32 (dt, *J*=9.7, 3.6 Hz, 1H, HC(4)), 3.02 (t, *J*=3.4 Hz, 1H, HC(3)), 1.73 (q, *J*=9.7 Hz, 1H, H_2C(5)), 1.50 (m, 3H, H_2C(5, 6)), 1.38 (d, *J*=7.0 Hz, 3H, H_3C(1/1')), 1.23 (d, *J*=7.0 Hz, 3H, H_3C(1/1')), 0.84 (t, *J*=7.1 Hz, 3H, H_3C(7))

^{13}C NMR: (101 MHz, $CDCl_3$)

139.74 (C(14)), 133.61 (C(17)), 131.54 (C(15)), 129.12 (C(16)), 128.92 (C(11/12)), 128.25 (C(11/12)), 127.97 (C(13)), 123.48 (C(10), 89.03 (C(9)), 84.31 (C(8)), 72.86 (C(3)), 37.49 (C(5)), 31.58 (C(4)), 28.51 (C(2)), 22.01 (C(1/1'), 21.44 (C(1/1'), 20.83 (C(6)), 13.59 (C(7))

IR: (neat)

2690 (m), 2932 (w), 2873 (w), 1598 (w), 1490 (m), 1303 (s), 1145 (s), 1083 (s), 1024 (w), 755 (s), 719 (s), 690 (s), 611 (s), 597 (s), 536 (s)

MS: (ESI)

355.2 (M+H, 100), 229.1 (24), 213.2 (46), 157.1 (31), 125.0 (14)

HRMS: Calcd for 355.1735 Found: 355.1733

TLC: R_f 0.506 (20% TBME/hexanes) [UV]

HPLC: ((3*S*,3*S*)-(**70**), t_R 9.926 min (9.0%); ((4*R*,5*R*)-(**70**), t_R 8.797 min (91.0%), (Chiralpak AD-H, 20 °C, 1% *i*PrOH in hexanes, 1.0 mL/min, 220 nm).

Chapter 5. References

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