LEWIS BASE CATALYZED ENANTIOSELECTIVE OXYSULFENYLATION OF ALKENES

BY

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DISSERTATION

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Abstract

The Lewis base activation of Lewis acids has been harnessed in the development of an enantioselective oxysulfenylation reaction for unactivated alkenes. The weak Lewis acid *N*-(phenylthio)-phthalimide can be activated in the presence of a moderate Brønsted acid and chiral Lewis base donors. The resulting complex is a powerful sulfenylating agent capable of sulfenium transfer to simple mono-, di- and trisubstituted alkenes with high selectivity to form enantioenriched thiiranium ions. Stereospecific and site-selective capture of the thiiranium ions furnish vicinally functionalized thioethers. The nucleophile scope of the reaction encompasses alcohols, carboxylic acids and phenols. Both inter- and intramolecular sulfenylation reactions were realized. The reaction is highly robust and individual substrates usually did not require reoptimization.

Mechanistic, X-ray crystallographic and kinetic investigations enabled a complete catalytic cycle to be formulated. The proposed cycle was supported by both kinetic data and the characterization of reaction intermediates. The turnover-limiting and enantiodetermining steps were identified as thiiranium ion formation. X-ray crystallography of the active sulfenylating agent did not immediately identify a basis for the high selectivity. Instead, the origin of selectivity in the reaction of *trans*-alkenes was determined to be distortion-based with the aid of computational models.

To Jak, Ilona and Serra
Always Were, Always Will Be

Acknowledgements

It takes a village to raise a child, and so it is with doctors. Although a Ph. D. is conferred upon an individual, the efforts of friends, family and colleagues in the minting of a doctor cannot be overstated. In the end, it is only with their support, encouragement and exhortations that the long and windy path over many years can be braved.

I have been graced with a family that loves science, for which I am eternally grateful. The patience both my mother and my father showed to my incessant badgering helped me develop the inquisitive faculties I so very much value today. Serra, your support in discussing occasional flights of fancy are never forgotten.

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The tides of time wait for no man, and thus it was soon that the old guard was replaced with the new. Dr. Lindsey Cullen helped me through the most hopeless days of my career, and I am very much in her debt. I have had the fortune of having excellent lab partners over the years, Zack Matesic, and Dr. Pavel Ryabchuk, with whom discussions were always incredibly stimulating. I also wish to thank Andy Thomas and Scott Barrazza for sharing their love of chemistry, their dry humor, and their positive outlook on life.

Anna, Brian, Sukru, Yonca and Zeynep. Although you did not share lab space with me, without you, this thesis would not have been possible. That is the simple and plain truth.

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Chapter 1: Introduction to Lewis Base Catalysis

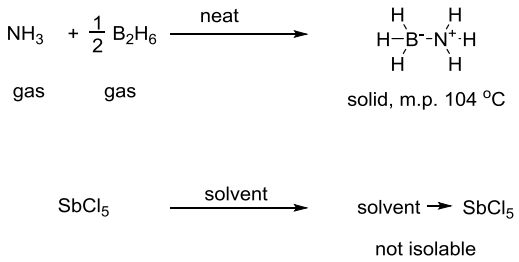
1.1. Overview.

The field of chemistry encompasses the reactivity of atoms, functional groups and molecules. Reactivity is, in turn, dictated by the potential for electrons in atomic and molecular orbitals to achieve lower energy configurations as a result of orbital realignment. In general, the behavior of electrons, and their reorganization to low-energy alignments, constitutes a fundamental principle behind chemical reactivity. Thus, any study of catalysis and catalytic reactions necessitates a deep understanding of the theory underlying reactivity.

The octet rule has been developed as a widely applicable framework for the study of electron rearrangements in molecules.[1] The rule, which states that atoms in molecules attempt to have a filled valence shell of electrons, is based on the observation that in molecules, atoms share electrons and orbitals such that each low-lying atomic orbital is filled. The thermodynamic electron redistribution leading to the octet rule is responsible for a wide variety of phenomena, such as molecular geometry and bond strengths.[2] Stable molecules that are exceptions to the rule are uncommon, but have been isolated and characterized, primarily among group 13 elements.[3] Octet-deficient structures are commonly found in dimeric form to ameliorate the energy penalty associated with their inability to fully delocalize electrons within the available molecular orbitals in monomeric form.[4] In general, molecules that contain octet-deficient electrons greatly desire electron density. Molecules that contain atoms with paired electrons represent the opposite end of the spectrum. The localized electron density in these atoms contain chemical potential that can be used to drive reactivity.

1.1.1. Lewis Acids and Bases. An electron-based approach to explain and categorize reactivity was proposed by G. N. Lewis in his theory of acids and bases.[5] Atomic loci that accept electrons are identified as Lewis acids, and electron donors as Lewis bases. The outcome of the association between Lewis acids with Lewis bases is highly dependent on the nature of the interacting species. Thus, the combination of Lewis acidic BH_3 and Lewis basic NH_3 generates a stable, zwitterionic solid adduct.[4] The delocalization of nitrogen electrons into the empty boron

atomic orbital is highly favorable, which overcomes the penalty associated with formation of charge-separated species. In contrast, the association of polar solvents such as THF or DMF with $SbCl_5$ is dative in nature, and the strength of the interaction varies by the donicity of the solvent. The resulting complexes, while polarized, are not ionized (Scheme 1).[6]



Scheme 1

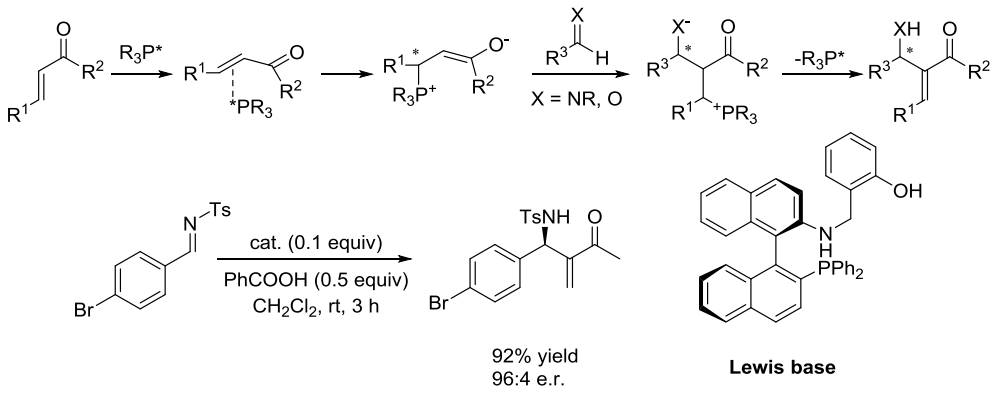
1.1.2. Jensen's Orbital Analysis. The different types of Lewis acid- Lewis base interactions can be classified by the type of orbitals that participate in the bonding scheme. In the classification by Jensen, there are nine possible interactions, from one of either σ, π or n type filled orbitals to one of the σ*, π* or n* type empty orbitals.[7] Of these, the most relevant to catalysis is the interaction of n-type orbitals with π* and σ* orbitals, represented by the green boxes in Table 1.[8]

Table 1. Tabular representation of Lewis base - Lewis Acid interactions by Jensen.

Donor \ Acceptor	n*	π*	σ*
n	n→n*	n→π*	n→σ*
π	π→n*	π→π*	π→σ*
σ	σ→n*	σ→π*	σ→σ*

The importance of the n→π* Lewis base-Lewis acid interaction has been widely recognized in the field of enone functionalizations.[8] A salient example is the catalysis of the Morita-Bayliss-Hillman reaction by phosphine and amine catalysts.[9] The n→π* interaction between the phosphine and the electron-deficient alkene leads to the formation of a charge-separated enolate (Scheme 2). Attack of the enolate onto a second carbonyl compound, followed

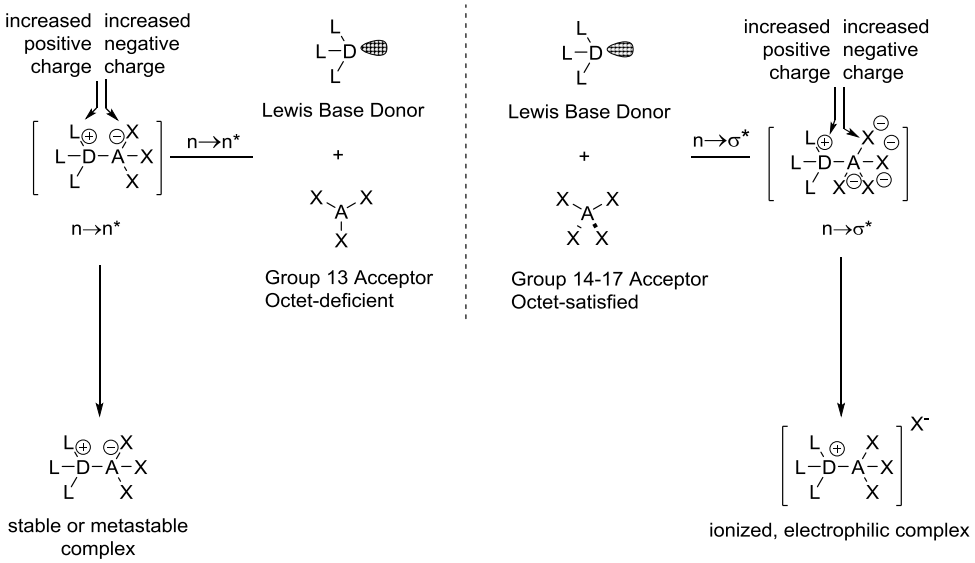
by elimination of the phosphine catalyst, forms the final α-functionalized enone. The use of chiral phosphines in the reaction enables stereocontrol during the enolate addition step, which then leads to the formation of chiral, non-racemic alcohols and amines. The key role of the Lewis base (phosphine) to complex with the Lewis acid (alkene) in promoting reactivity can clearly be recognized from the high enantioselectivities observed in this class of transformations (Scheme 2).[10]



Scheme 2

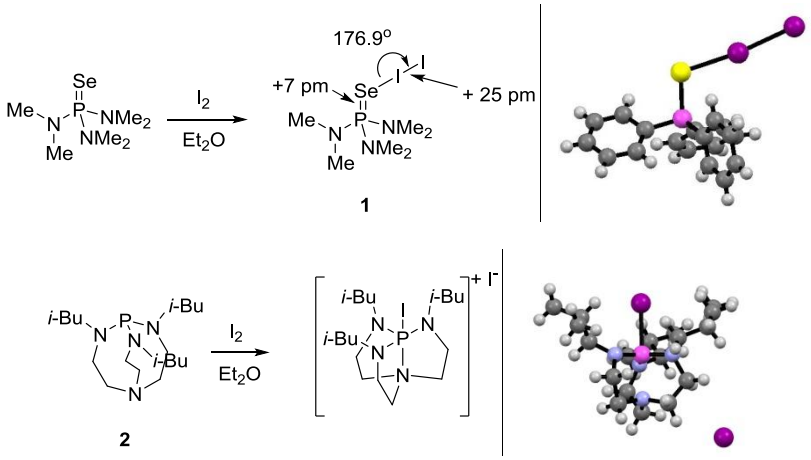
The n→σ* complexation of Lewis bases with Lewis acids leads to bond polarization within the Lewis acidic moiety. Gutmann over 40 years ago identified a "spillover" effect that led to increased bond lengths upon complexation of a Lewis acid with a Lewis base.[6a,11] In his four rules of bonding, Gutmann states that (1) the smaller the intramolecular distance between the donor (D) and the acceptor (A), the greater the induced lengthening of the peripheral bonds (A—X), (2) the longer the bond between D and A, the greater the degree of polarization of electron density across that bond, (3) as the coordination number of an atom increases, so do the lengths of all the bonds originating from that coordination center, and (4) the bonds adjacent to D and A will either contract or elongate to compensate for the changes in electron density at D and A. This last rule was used to explain the variations in bond lengths observed in crystals of stable Lewis base - Lewis acid adducts with respect to their starting materials.

Figure 1. Gutmann Analysis of Donor-Acceptor Pairs



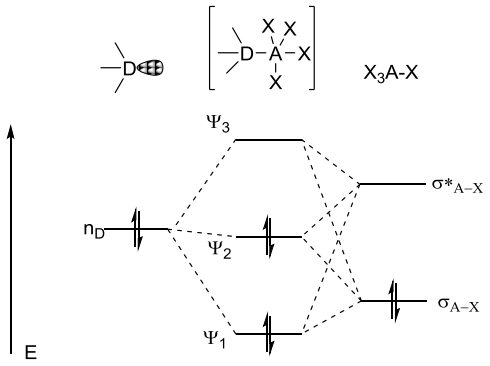
A particular example of this type of interaction can be found in the complexes of I_2 with a variety of Lewis bases. In the HMPA(Se) •I_2 complex **1**, the Se-I-I bond angle is around 176°, displaying the collinear arrangement of the three atoms in the bonding scheme (Figure 2).[12] The I-I bond is lengthened by 0.25 Å as a result of electron density in the $\sigma^*_{I\text{-}I}$ orbital. A 0.065Å lengthening is also observed in the P-Se bond, as the electron density is transferred to the Se center, although the bond retains its double bond character. Stronger Lewis bases such as phosphazanes **2** are capable of inducing halogen bond scission, resulting in formation of I, Br and Cl salts. [13]

Figure 2. Crystal Structures of HMPA(Se)-I_2 and 2-I_2 Adduct



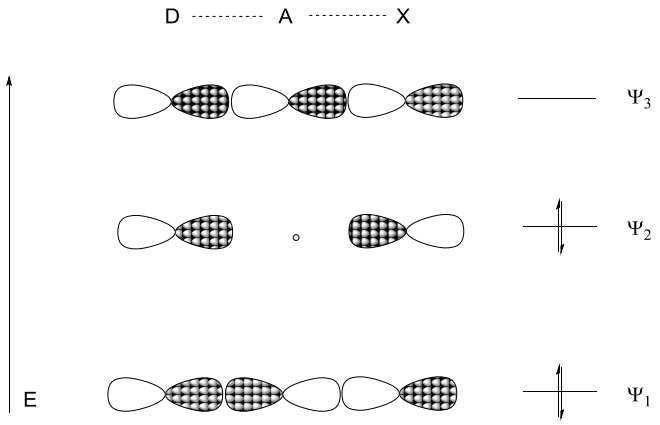
The bonding scheme in a n→σ* type Lewis base - Lewis acid complex has some unusual properties, which are particularly prominent for Group 14-17 Lewis acids bearing ionizable groups. The bonding is hypervalent at the central atom, as the high-lying nature of the *d* orbitals of the central atom preclude them from participating in the bonding.[8] The Lewis base - Lewis acid interaction is then best characterized as a 3-center-4-electron bond, involving the n atomic orbital on the Lewis base component and the σ and σ* orbitals on the Lewis acid component. The resulting MO diagram is shown in Figure 3.

Figure 3. Donor-Acceptor Bonding Analysis for a Group 14 Lewis Acid



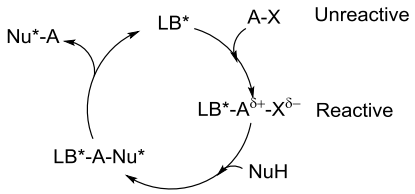
A peculiar characteristic of the 3-center-4-electron bonding scheme is that the terminal atoms are enriched in electron density, whereas the central atom is impoverished in electron density (Figure 4). This conclusion follows from an analysis of the nodes of the molecular orbitals involved in the bonding. For molecular orbital Ψ_1 the electrons are shared equally across all atoms. However, molecular orbital Ψ_2 has a node at the central atom, and increased density at the peripheral atoms. Consequently, the electrons in this orbital are localized at the periphery, increasing the electron density of the ligand atom. The central node results in impoverishment of the Lewis acidic atom above and beyond its starting electron density. This redistribution of electron density in the 3-center-4-electron bond leads to the aforementioned "spillover" phenomenon. As the band gap between Ψ_1 and Ψ_2 increases, the polarization of the bonds becomes greater. At its most extreme, the n→σ* interaction can result in complete ionization of the X ligand, and formation of a highly reactive $[DA]^+$ cation.

Figure 4. Molecular Orbitals of a 3c-4e Bond



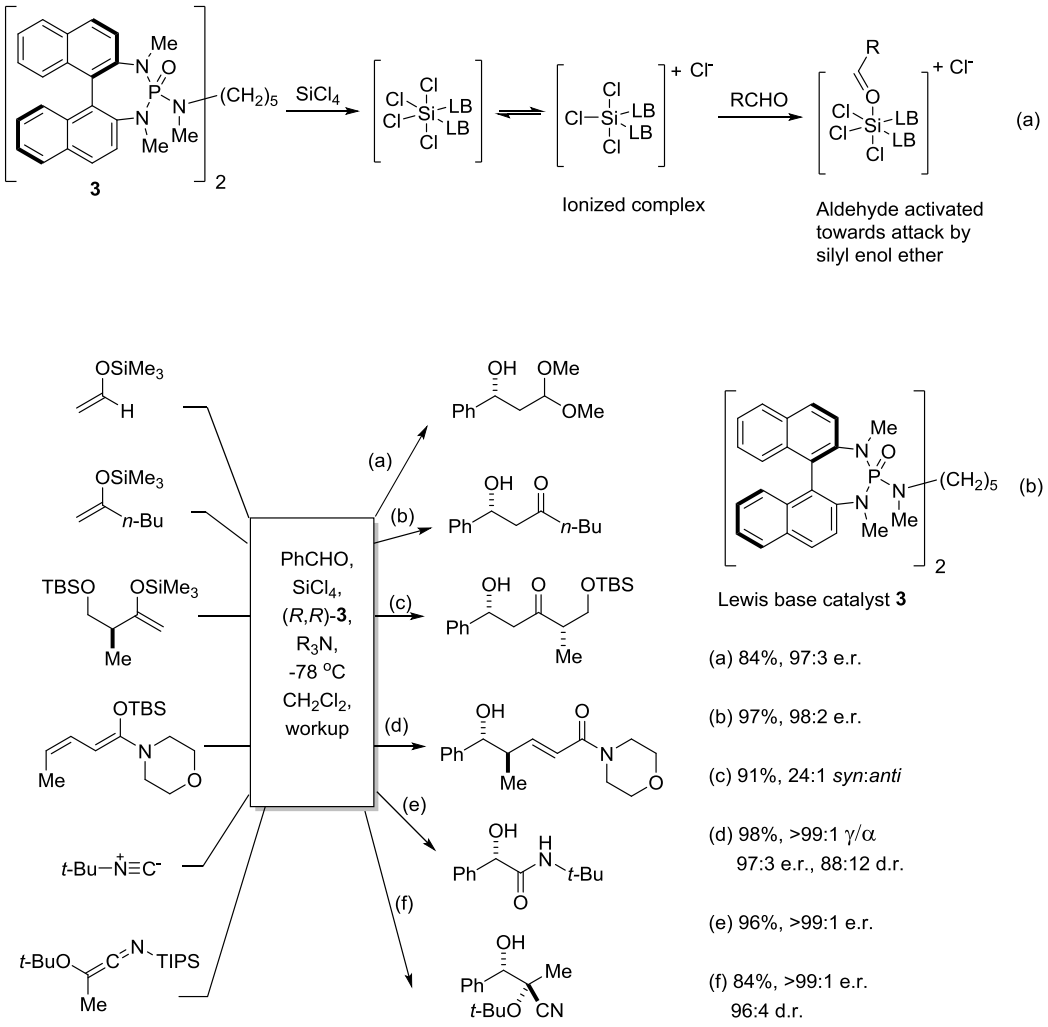
1.1.3. Catalysis by Lewis Bases. The increased Lewis acidity as a consequence of electron redistribution can directly be translated into a catalytic protocol (Figure 5). Group 14, 16 and 17 Lewis acids (generically represented as A-X) can be engaged by Lewis bases to form electron-deficient complexes. Their increased Lewis acidic nature would then promote the complexes' susceptibility to nucleophilic attack. The use of chiral non-racemic Lewis bases would enable the catalytic process to proceed in an enantioselective manner.

Figure 5. A Generic Catalytic Cycle for Lewis Base Catalyzed Enantioselective Functionalization



The n→σ* type activation of Lewis Acids have been extensively developed in these laboratories. In the example of $SiCl_4$, a group 14 Lewis acid, exposure of $SiCl_4$ to a phosphoramide Lewis base **3** results in the formation of a $[SiCl_4LB_2]$ complex, which has increased affinity towards carbonyl groups (Scheme 3a).[14] In the presence of aldehydes, displacement of one of the peripheral chlorines by the aldehyde results in a highly reactive $[SiCl_3LB_2(RCHO)]^+$ electrophile complex which can be nucleophilically attacked by enol ethers.[15] Dissociation of the catalyst from the oxytrichlorosilane product completes the cycle. The application of this technology to diverse classes of enol ethers enabled the formation of

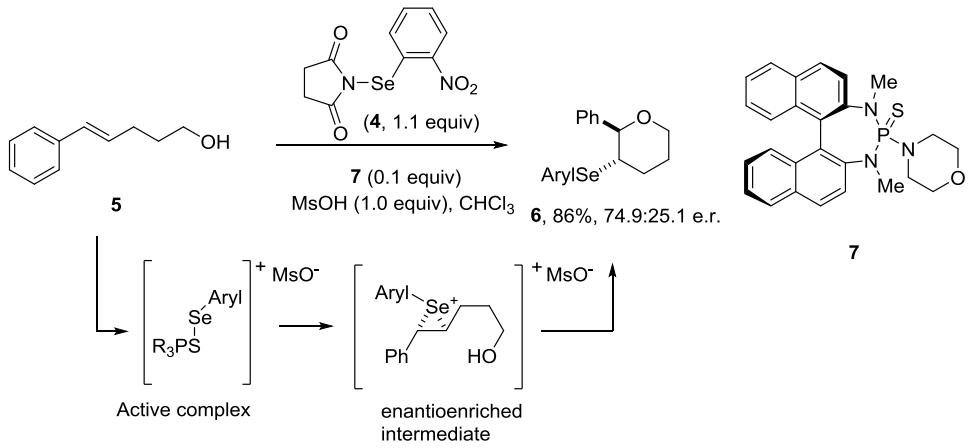
numerous aldol products with excellent yields and selectivities. (Scheme 3b)



Scheme 3

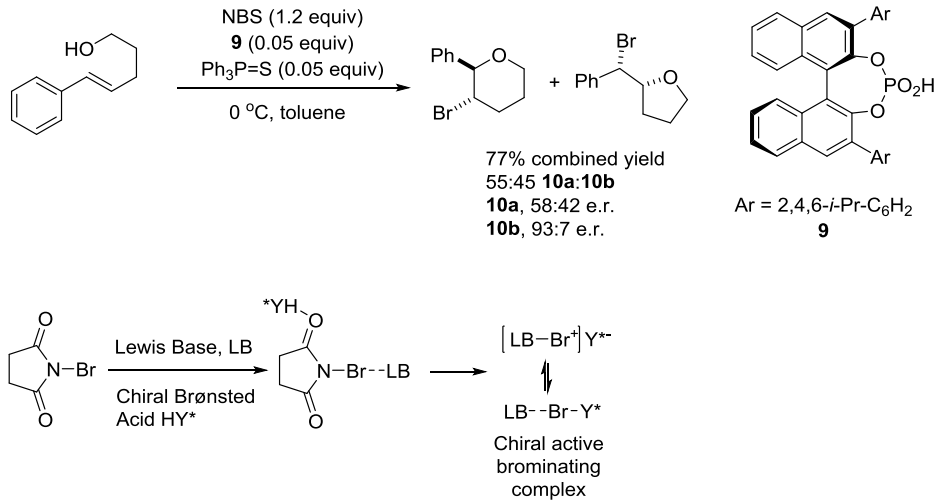
The application of n→σ* activation to group 16 selenium electrophiles enabled an enantioselective selenofunctionalization of alkenes to be realized (Scheme 4).[16] Protonation of benzeneselenyl succinimide creates a highly active Lewis acidic selenenium source. Displacement of succinimide by the phosphoramide catalyst forms the active, chiral, non-racemic selenenylating agent **4**. This complex can be directly attacked by an alkene to form an enantioenriched seleniranium intermediate. Nucleophilic capture of the seleniranium ion inter- or intramolecularly affords selenofunctionalized products. For example, the enantioselective, intramolecular selenofunctionalization of **5** formed 3-selenotetrahydropyran **6** in 86% yield and 75:25 e.r. No reactivity of the selenium electrophile with the alkene was observed when the

catalyst **7** was omitted. The catalyst accelerates the reaction by increasing the reactivity of the Lewis acidic selenium center in accord with the principles of Lewis base activation.



Scheme 4

The n→σ* activation model has also been extended to Group 17 Lewis acids (Scheme 5).[17] Halolactonization and haloetherification reactions of alkenes can be effected by the use of weak electrophilic halogen sources and a variety of Lewis bases. A protic activator is usually added to further promote formation of the active halogenating agent. The family of halogen electrophiles that can be utilized is quite diverse. Unfortunately, the resulting haliranium ions usually suffer from poor stability or undesirable reactivity, and chiral non-racemic Lewis bases that can effect an enantioselective halofunctionalization remain uncommon. Therefore, chiral Brønsted acidic coactivators are used to assist the enantioselectivity. Thus, in an example from these laboratories, the bromoetherification of **8** was accomplished using the Lewis acidic bromine source NBS, Ph_3PS as the Lewis base and phosphoric acid **9** as a chiral Brønsted acidic co-activator.[18] The chiral active brominating complex has not been characterized, but in some way incorporates the conjugate base of **9**. A 55:45 isomer ratio of the 3-bromotetrahydropyran **10a** to the 6-bromo-tetrahydrofuran **10b** was obtained in 77% yield. The enantioenrichment of each product differed significantly, with **10b** being obtained in 93:7 e.r. and **10a** in 58:42 e.r. This difference in selectivity was explained by the participation of the conjugate base of **9** in both the formation and capture steps.

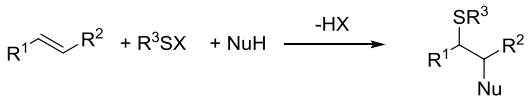


Scheme 5

The common theme of the above-mentioned reactions is the use of alkenes as initial nucleophiles for the Lewis base - Lewis acid complex. In the last few decades, many techniques for the catalytic, enantioselective functionalization of alkenes with O and N electrophiles have been developed, including ones that utilize Lewis base catalysts.[19] However, at the outset of this project, the corresponding catalytic, enantioselective electrophilic alkene sulfenofunctionalization reaction had not been developed.

1.2. Goals of the Project.

The application of Lewis base catalysis to the electrophilic functionalization alkenes has been successful with a wide variety of elements and electrophile families. The development of a Lewis base catalyzed electrophilic sulfenylation reaction seemed possible. The project thus entailed identification of suitable Lewis acids and bases, as well as conditions for an enantioselective, Lewis base catalyzed sulfenofunctionalization (Scheme 6).

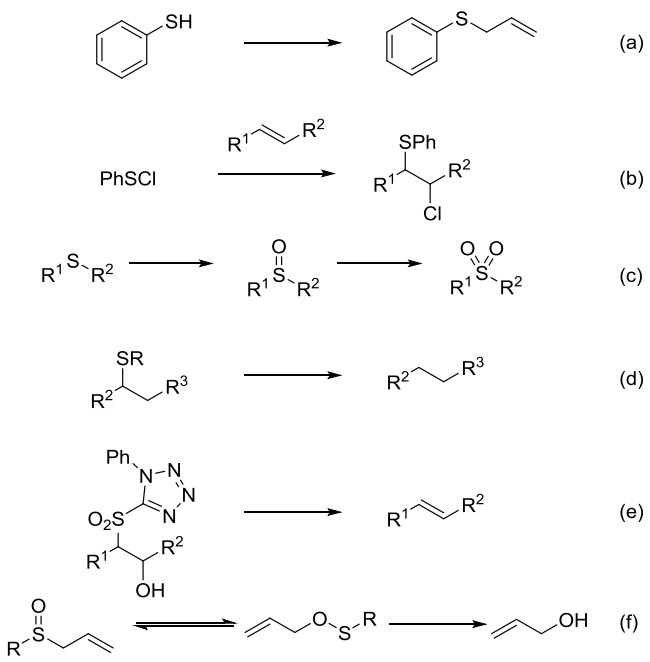


Scheme 6

Chapter 2: Catalyic, Enantioselective Sulfenoetherification of Alkenes

2.1. Introduction.

2.1.1. Sulfenylation. Few elements in the periodic table have as rich and varied participation in chemical reactions as sulfur.[20] Poor overlap between the 3p orbitals of sulfur and the 2p orbitals of the 2nd row elements such as carbon, nitrogen and oxygen leads to a marked decrease in bond strength between these elements. Consequently, molecules containing sulfur can undergo a dazzling variety of chemical transformations.[21] Briefly, sulfur can act both as a nucleophile and an electrophile (Scheme 7, reactions a and b). Oxidation and reduction of the sulfur center is possible, as the -2, 0 and +2 oxidation states of sulfur are all stable under normal conditions (reaction c). Sulfur can also easily be removed from organic molecules under hydrogenative (reaction d) or radical conditions (reaction e). Rearrangements of sulfur moieties are also well-documented, a salient example is the [2,3]-rearrangement of allylic sulfoxides to sulfenic acids which can be cleaved to form allylic alcohols (reaction f). In the same vein, S-H bonds are significantly weaker due to meager 3(sp^n) - 1s overlap This results in the formation of disulfides from thiols under aerobic conditions.[22]



Scheme 7

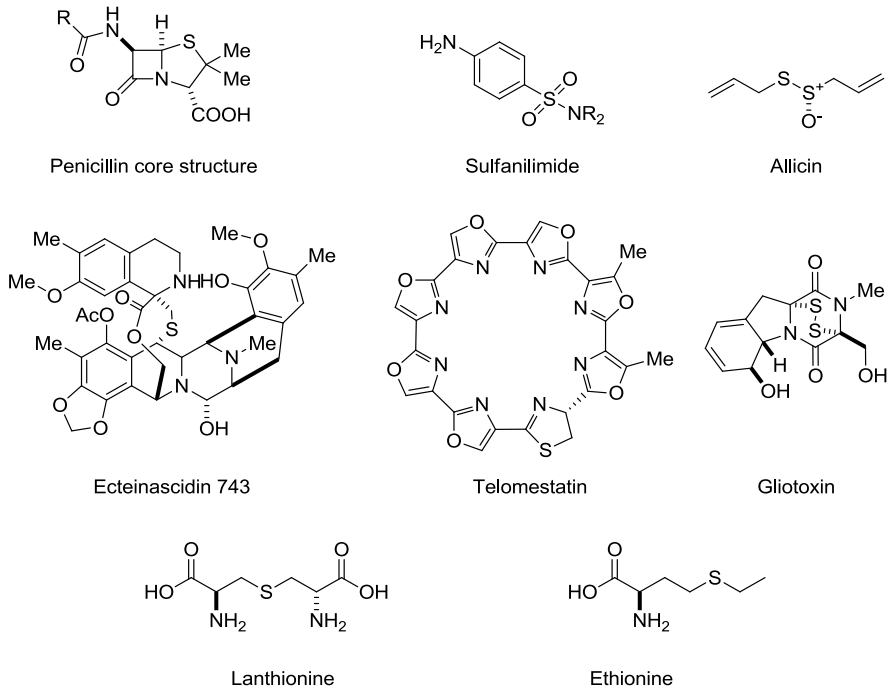
There are numerous applications of sulfur in modern industrial chemistry.[23] Most prominently, sulfurization of polymers leads to the formation of crosslinked polymers with varying mechanochemical and physical properties in the vulcanization process. In addition, the need for removal of sulfurous material from fuel feedstock has promoted substantial research into the behavior of sulfur compounds in refinery environments.[24]

The propensity of sulfur to form strong disulfide linkages, as well as its soft donor nature has resulted in sulfur being the only third-row element that is incorporated into the 20 naturally-occuring amino acids in the form of cysteine and methionine.[22] Disulfides resulting from the oxidative dimerization of two cysteine residues force proteins to adopt specific conformations, playing a key role in the formation of tertiary structures of proteins.[22] Furthermore, sulfur is centrally involved in the protection of biological systems against oxidative stress.[25] Sulfurous compounds also serve as ligands in biological systems; for example many redox-active enzymes in living organisms use Fe-S tetrads as catalytic subunits.[26]

The biological importance of sulfur extends to the level of small molecules (Chart 1). Numerous biologically active compounds containing sulfur have been isolated or prepared; the antibiotics penicillin and sulfanilamide were some of the first drugs used to treat bacterial infections,[27] whereas allicin, which is derived from garlic, is currently being investigated as a

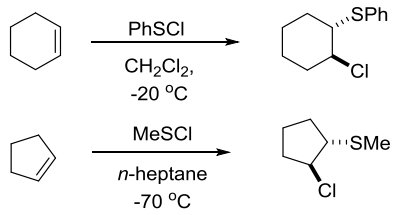
topical antibiotic against methycillin resistant *S. aureus.*[28] Sulfur-containing natural products such as Ecteinascidin 743 and gliotoxin have been employed for their antiproliferative properties.[29] Telomestatin has been shown to suppress telomerase, which leads to Hayflick senescence. Since non-cancerous cells generally do not express telomerase, this differential targeting has led to interest in telomerase-suppressors as anti-cancer therapeutics.[30] There are also numerous nonproteinogenic amino acids derived from cysteine and methionine such as lanthionine, which is present in the lantibiotic peptides, as well as the cytotoxic methionine antagonist ethionine.[31]

Chart 1



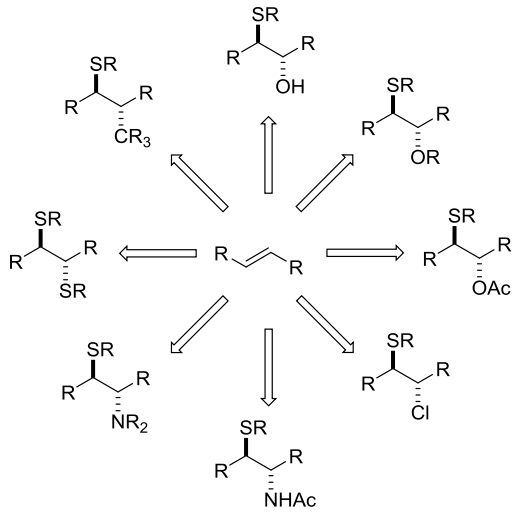
In light of the prevalence of sulfur in biological systems and biologically active small molecules, it would be reasonable to postulate that sulfur should be widely represented in active pharmaceutical ingredients. However, this has unfortunately not been the case. Chemical transformations that incorporate sulfur into organic compounds, specifically ones which do so stereoselectively, have not been well developed.[32] The dearth of robust methods has severely limited the exploration of design space for sulfur-containing molecules. Broadly applicable methods to stereoselectively introduce sulfur into small molecules could speed up the exploitation of this underutilized class of molecules, and furnish new molecules to probe biological systems.

2.1.2. Electrophilic Sulfenylation. A typical method of introducing sulfur into small molecules is through the sulfenofunctionalization of alkenes. This transformation is commonly accomplished through the action of sulfenyl chlorides.[33] The reaction of an alkene and sulfenyl chloride results in stereospecific difunctionalization of the alkene, with both the sulfenyl moiety as well as the chloride group being incorporated. The strongly electrophilic nature of sulfenyl chlorides allow the reaction to proceed at temperatures down to -70 ^{o}C. Both alkyl and aryl sulfenyl chlorides are competent for sulfenium transfer (Scheme 8).[34]



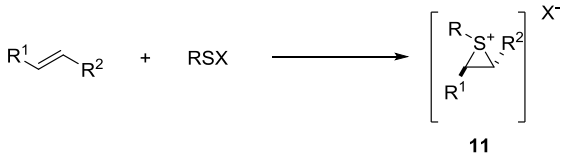
Scheme 8

The difunctionalization of alkenes with nucleophiles other than chloride is also possible. However, the high nucleophilicity of chloride results in undesirable side products, necessitating optimized reaction conditions or superstoichiometric quantities of the desired nucleophile.[35] Thus, the need for sulfur electrophiles with less nucleophilic leaving groups stimulated the development of novel sulfenylating agents, including, but not limited to, sulfenyl acetates, sulfenate esters, and azaheterocycles.[36] These new electrophiles enabled diverse vicinal functionalization products such as sulfeno acetates, sulfeno ethers, sulfeno amides and bisulfides to be obtained in good yields and with high chemoselectivity (Scheme 9). In addition to the extensive use of sulfenyl chlorides in these reactions, sulfenium and sulfonium salts also serve as sulfenyl transfer agents.[37] Unlike sulfenyl chlorides, use of sulfenium and sulfonium salts enable the interception of intermediate thiiranium ions by weak as well as strong external nucleophiles. In all cases the *anti* stereospecific course of the reaction is retained.



Scheme 9

2.1.3. Mechanism of the Sulfenylation Process. The generality and predictable stereochemical course of the electrophilic sulfenylation reaction encouraged extensive studies into the mechanistic and stereochemical aspects the underlie these desirable properties. The *anti* stereospecificity for sulfenofunctionalization of *trans* alkenes was proposed to be the consequence of a bridged intermediate that preserves the stereochemical information of the alkene component (Scheme 10).[38] In this hypothesis, approach of the alkene to the sulfenium ion source results in an $\pi \rightarrow \sigma^*$ interaction that promotes the ionization of the leaving group (X) on the sulfur with simultaneous formation of a three-membered ring intermediate. Subsequent to this proposal, such bridged-ring intermediates (called thiiranium or episulfonium ions) (**11**) have been thoroughly characterized by computational, spectroscopic and crystallographic methods.



Scheme 10

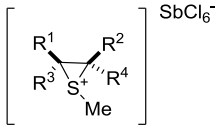
Computational transition state models show a strong directionality in thiiranium formation, in which approach of the alkene spiro with the S-X bond is highly favored (Scheme 11).[39] The sulfenium adopts an approach where the sulfur substituents are oriented orthogonal to the alkene.[40] This type of spiro approach maximizes orbital overlap between the filled sp^3 orbitals on the sulfur atom with the π^* orbital of the alkene component. Notably, the σ^* of the leaving

group X is not directly involved in the formation process. Thus, there are two possible pathways for thiiranium ion formation: (1) C-S bond formation that proceeds synchronously with S-X ionization (pathway A); or (2) S-X bond ionization occurs asynchronously, subsequent to C-S bond formation (pathway B) (Scheme 11). The former would then be similar to the "butterfly mechanism" observed in the epoxidation of alkenes with peracids.[41] In the latter case, the X group may remain either covalently bound to what is now a sulfurane, or form an ion pair. The degree of synchronicity has not been well studied, and likely varies as a result of experimental parameters such as leaving group identity, solvent and temperature.

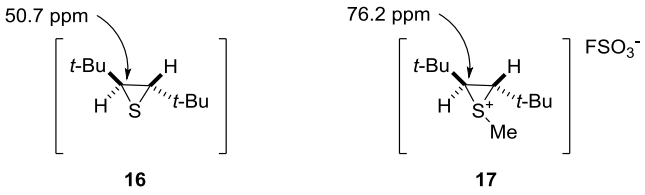
Scheme 11

The ^{1}H NMR spectra of thiiranium ions reveal a wealth of information regarding their structure (Table 2). The protons within the ring system for the thiiranium ion **12** appear at 4.0 ppm (TMS) in SO_2 at -60 ^{o}C (entry 1).[42] These are shifted upfield in the thiiranium ion **14** to 3.56 and 3.85 ppm, clearly showing their anisochronicity which results from the stereogenic sulfur center. Thiiranium **13** derived from a *cis*-alkene showed only one set of signals at 4.32 ppm. Thus, only one of two possible diasteromers is formed, which has been shown to be *cis*-**13**.[42,43] The propensity for formation of *cis*-**13** results from decreased steric clash between the *S*-substituent and the *C*-substituents. The ^{13}C NMR shift of thiiranium ion **17** is at 76.2 ppm ($CDCl_3$), far downfield of the starting thiirane **16** (50.7 ppm) (Scheme 12).[44] This shift is taken as evidence of charge density at the ring carbons of thiiranium ions, in accord with their ambident electrophilic nature. Similar shifts are observed for 1,1- and *trans*-substituted alkenes.[45]

Table 2. Proton NMR Shifts of Thiiranium Ions.



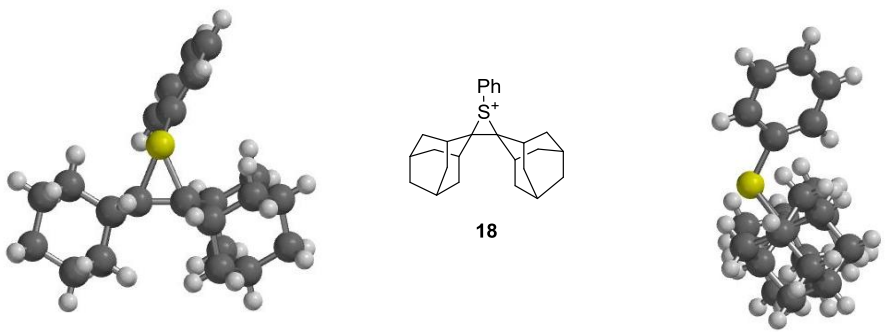
entry	ion	R^1	R^2	R^3	R^4	^{1}H NMR shift of endocyclic protons (TMS)
1	12	Me	H	H	Me	4.0, m, 2H
2	13	Me	Me	H	H	4.32, m, 2H
3	14	Me	H	Me	H	3.56, d, *J* = 6.0 Hz, 1H 3.85 d, 1H
4	15	Me	Me	Me	H	4.09, q, 1H



Scheme 12

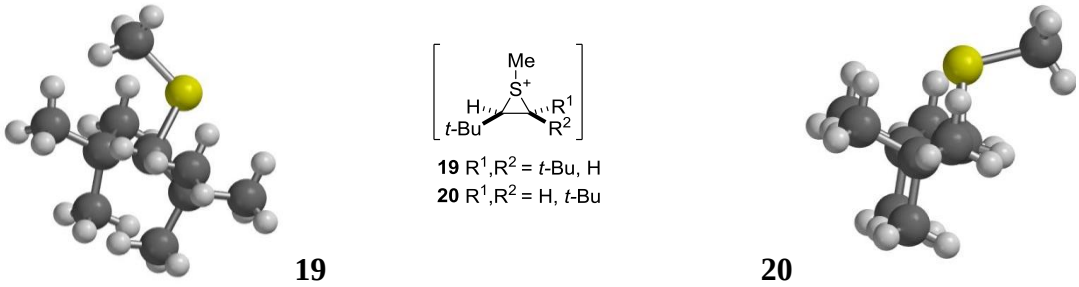
The crystal structures of a number of thiiranium ions have been acquired. Diadamantyl phenyl thiiranium ion **18** shows the classical bent orientation of the sulfur substituent.[46] The acute C-S-C angle of 46.3^o illustrates the deviation of the thiiranium ion from a perfect equilateral triangle as a consequence of the size of the sulfur atom. The C-S bond length is 1.904 Å, which is elongated compared to the average C-S length of 1.82 Å.[47] The C-S-C_{Aryl} bond angle of 117.6^o shows that the sulfur atom is tetrahedrally hybridized.

Figure 6. Crystal Structure of Adamantyl Thiiranium ion 18



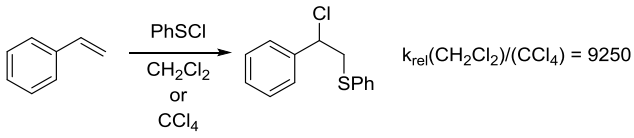
The comparison of methylthiiranium ions derived from *cis*- and *trans*- di-*t*-butylethene is also informative (Figure 7).[43] The $C_{t\text{-Bu}}$-C_S distance is only 3.288 Å for **19**, which is smaller than the sum of the radii for the two methyl groups. The C-C_{ring}-C_{ring}-X dihedral angles also differ substantially between the two structures. For **19**, the dihedral of the opposing substituents is 148.6°. In contrast, **20** has a dihedral angle of 134.6°. There is a similar difference in the dihedrals of the *syn*-substituents. The *t*-butyl substituents eclipse each other for **20**, but the corresponding dihedral in **19** is 15.6° The difference in angles confirms the greater stability of the *cis*-thiiranium ion over the *trans*-thiiranium ion.

Figure 7. Crystal Structures of *cis*- and *trans*-Thiiranium Ions 19 and 20



19 **20**

The rate of sulfenofunctionalization of alkenes has been extensively investigated with a variety of substrates.[34a] The rate of sulfenofunctionalization increases with solvent polarity. The relative rate of the reaction of styrene with PhSCl was 9250 times faster in CH_2Cl_2 than in CCl_4 (Scheme 13). Decreases in reactivity were sometimes observed in highly nonpolar solvents such as cyclohexane.[34a] The polarity of the solvent likely assists in the stabilization of highly charged species like thiiranium ions, lowering the barrier to their formation.



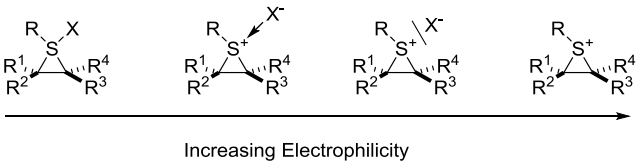
Scheme 13

A comprehensive table of relative reaction rates was compiled by Stirling.[34a] The following general trends could be identified: (1) the reaction of alkyl-substituted alkenes is faster than those of aryl substituted alkenes. (2) increasing numbers of alkyl substituents increase the reaction rate, whereas increasing numbers of aryl substituents decrease it. (3) for cyclic alkenes, the reaction rate increases with alkene strain. (4) the presence of electron-withdrawing groups

conjugated to the alkene severely decreases the reaction rate and (5) inductively electron-withdrawing groups retard the reaction, and correlate with σ* and ρ*. These results are consistent with thiiranium formation being the rate-limiting step. Modest buildup of positive charge on the carbons was inferred, however, these results were not consistent with open carbocation formation.[38]

It is worth noting that the mechanism of thiiranium formation and capture with sulfenyl chlorides appears to be dependent on the sulfenium source. Thus, the reactions with 2,4-dinitrophenylsulfenyl chloride showed different characteristics with respect to phenylsulfenyl chloride, which has led to speculation that the reactions may be proceed through a qualitatively different thiiranium ions.[34a,38] The different intermediates postulated are shown in Figure 8. These are, in increasing order of electrophilicity, a fully bound sulfurane, a datively bound thiiranium, a solvent-associated ion pair, or a fully solvent separated ion pair. The correct view is likely a continuum of reactivity that is dependent on sulfenium ion, solvent, alkene and nucleophile, thus comparisons of the mechanisms of different sulfenylating agents should be done with much care.

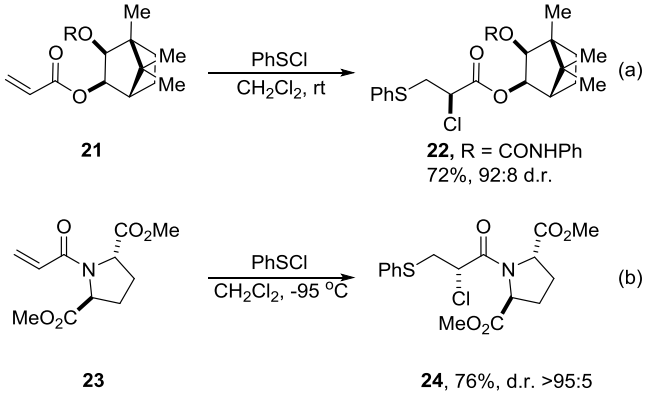
Figure 8. The Types of Possible Thiiranium Ions



A thiiranium ion is an ambident electrophile, and is susceptible to nucleophilic attack at any of its constituents. The bridged nature of thiiranium ions lead to high stereospecificty of addition with sulfur electrophiles. The reaction of *trans*-alkenes with sulfur electrophiles leads to *anti*-functionalization, whereas the reaction of *cis*-alkenes leads to specific *cis*-functionalization. Nucleophilic attack by either X^- or an external nucleophile on the thiiranium ion proceeds stereospecifically, opening either at either carbon to selectively afford *anti*-functionalized products. In electronically biased thiiranium ions, capture follows Markovnikov selectivity.[48] If the thiiranium ion is sterically and electronically unbiased, mixtures of constitutional isomers are obtained.[49] Notably, sulfenyl chlorides are an exception to this rule, occasionally affording some *anti*-Markovnikov product even in biased alkenes.[34a]

2.2. Enantioselective Sulfenylations.

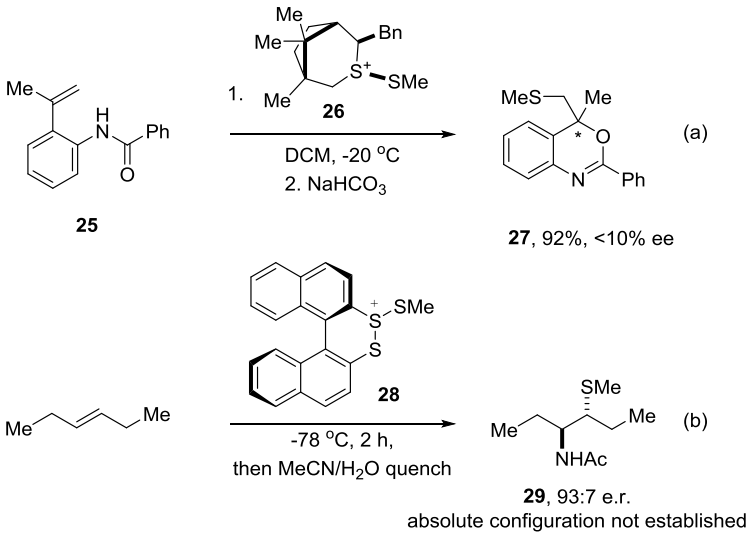
2.2.1. Electrophilic Sulfenylation with Stoichiometric Reagents. The ease with which thiiranium ions can be generated and the valuable products derived from their subsequent reactions has generated broad interest to form them enantioselectively. Although the direct addition of sulfenyl electrophiles to olefins has been known for the better part of a century, enantioselective sulfenofunctionalization remains a young field.[50] Early successes employed diastereoselective reactions of chirally-modified substrates, taking advantage of the stereochemical environment around the alkene to control the selectivity of thiiranium formation. The first such diastereoselective sulfenofunctionalization was accomplished by Effenberger and coworkers using chiral camphor diol derived auxiliaries (Scheme 14a).[51] The auxiliary effectively controls the facial selectivity of thiiranium formation during the sulfenylation of acryloyl ester **21**, even at ambient temperature. Subsequent introduction of amide-based auxiliaries led to higher selectivities.[52] For example, sulfenylation of dimethyl *N*-acryloylpyrrolidine-2,5-dicarboxylate **23** affords thioether **24** in 76% yield and >95:5 d.r (Scheme 14b). However, the reaction is limited to the use of unsubstituted acrylates and acrylamide substrates.



Scheme 14

The auxiliary-based approach described above requires two additional steps to introduce and remove the auxiliary. Enantioselective sulfenylation of prochiral alkenes using chiral sulfenylating agents addresses this challenge. For example, treatment of alkene **25** with camphor-derived sulfonium salt **26** affords thioether **27** in excellent yield albeit with poor enantioselectivity (less than 55:45 e.r.) (Scheme 15a).[37a] The poor selectivity likely arises from initial sulfenylation of the amide moiety followed by intramolecular *S*-methyl group transfer to

afford the final product as a nearly racemic mixture. A more selective sulfenylating agent, *S*-methylthio binaphthyl sulfonium salt **28**, can transfer the *S*-methyl group to 3-hexene and the resulting thiiranium ion is captured by acetonitrile which upon hydrolysis provides methylthio acetamide **29** in 93:7 e.r. (Scheme 15b).[37b] The authors did not present a stereochemical model for the transformation and the absolute configuration of the major enantiomer of the product was not established.

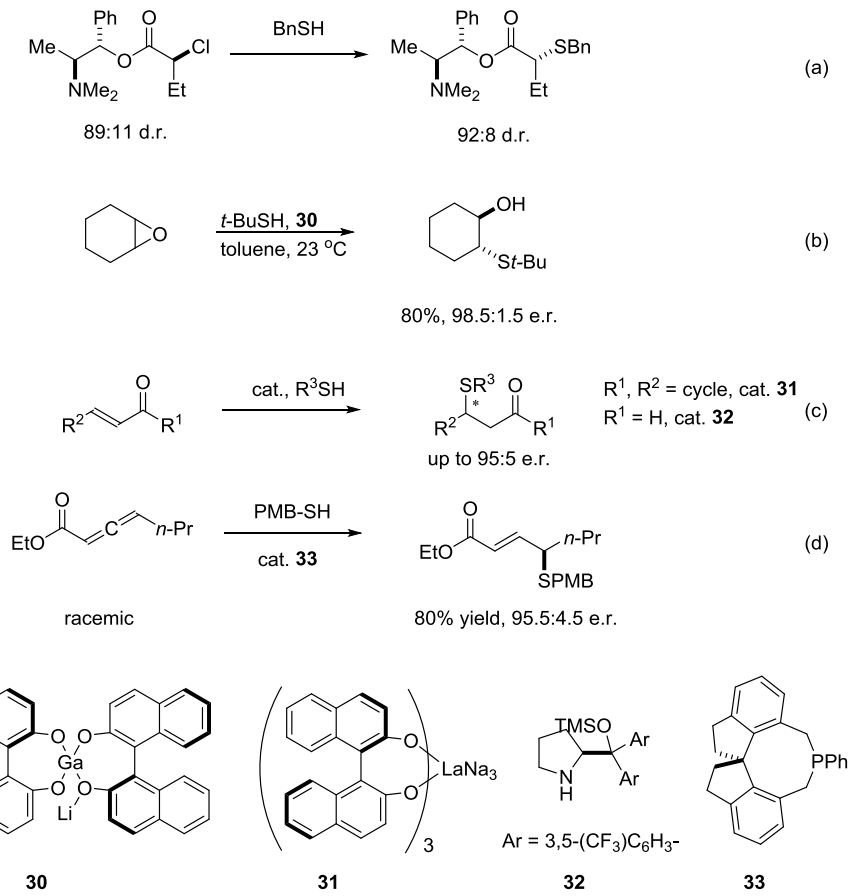


Scheme 15

Although instances of successful enantioselective sulfenofunctionalization occurred in the literature, the lack of a detailed model for enantioinduction hampered the development of more selective chiral sulfenylating reagents. Furthermore, the necessity for use of chiral, stoichiometric reagents is disadvantageous. An ideal strategy would entail the *in situ* formation of enantioenriched thiiranium ions from readily available achiral sulfur electrophiles and substoichiometric amounts of a chiral additive.

2.2.2. Catalytic, Enantioselective Sulfenylation. The stereoselective introduction of sulfur has historically relied on its nucleophilicity, for example the use of sulfur nucleophiles in the invertive displacement of secondary leaving groups and enantioselective opening of epoxides with rare earth catalysts **30** and **31**.(Scheme 16, a and b).[53] The development of a catalytic asymmetric 1,4-addition of thiols to α,β-unsaturated carbonyl compounds was the first catalytic sulfenofunctionalization of an alkene moiety (Scheme 16c).[54] The catalyst for this process was the well known proline derivative **32**. Notably, a catalytic, asymmetric γ-sulfenylation of α,β,γ-

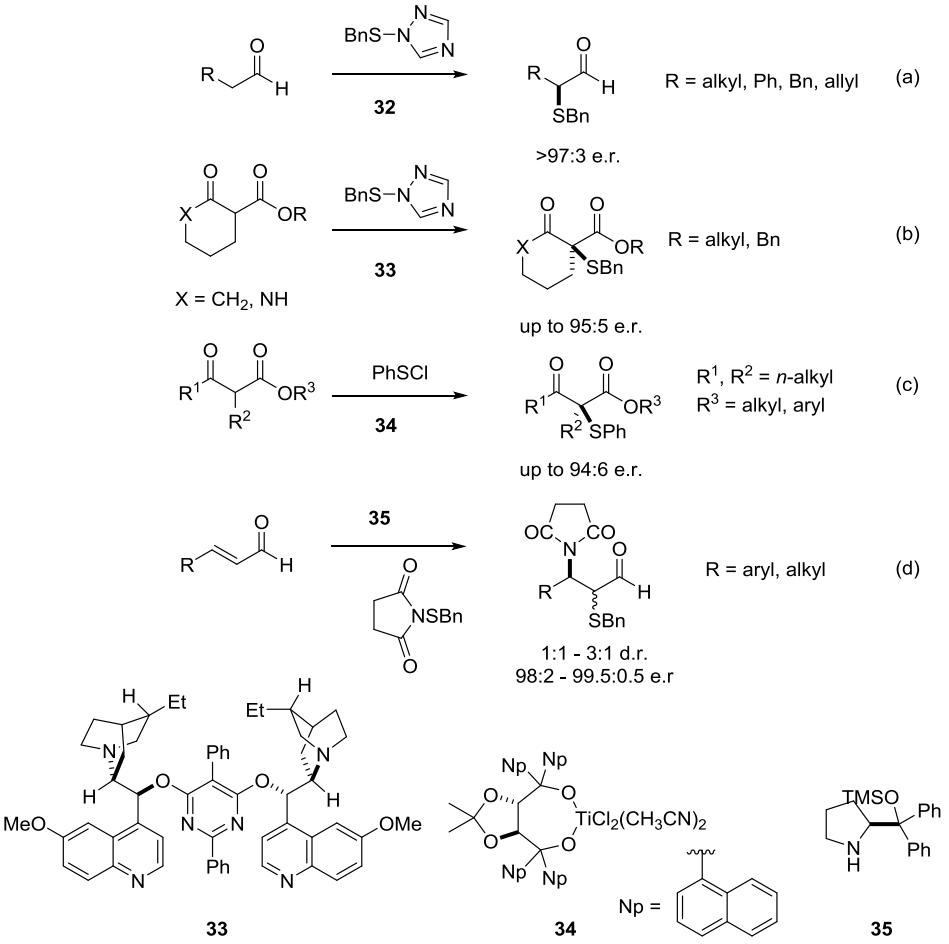
unsaturated carbonyl allenes with a protected thiol which utilizes phosphine **33** as a complement to the aforementioned β-functionalization has also been developed (Scheme 16d).[55]



Scheme 16

The use of electrophilic sulfur reagents for olefin functionalization has been known for many decades.[50a] Weak S-N, S-O and S-halogen bonds can be displaced by π-nucleophiles, leading to Ad_E-type displacements at the sulfur center.[56] Specifically sulfenyl amides, acetates and halides have all been studied in the context of alkene functionalization. In contrast, only recently have examples of catalytic, stereoselective reactions involving electrophilic sulfur species been discovered. In 2005, Jørgensen disclosed a proline-catalyzed asymmetric α-sulfenylation of carbonyl compounds (Scheme 17a).[57] In this transformation, the prolinol enamines formed from prolinol derivatives react with N-benzylsulfenyltriazole to afford benzylsulfenylated aldehydes. Organocatalytic sulfenylation of carbonyl compounds has since been expanded to keto esters and other carbonyl compounds using cinchonine and TADDOL-derived catalysts (Scheme 17b and c).[58] Importantly, Cordova was able to use both the sulfenyl

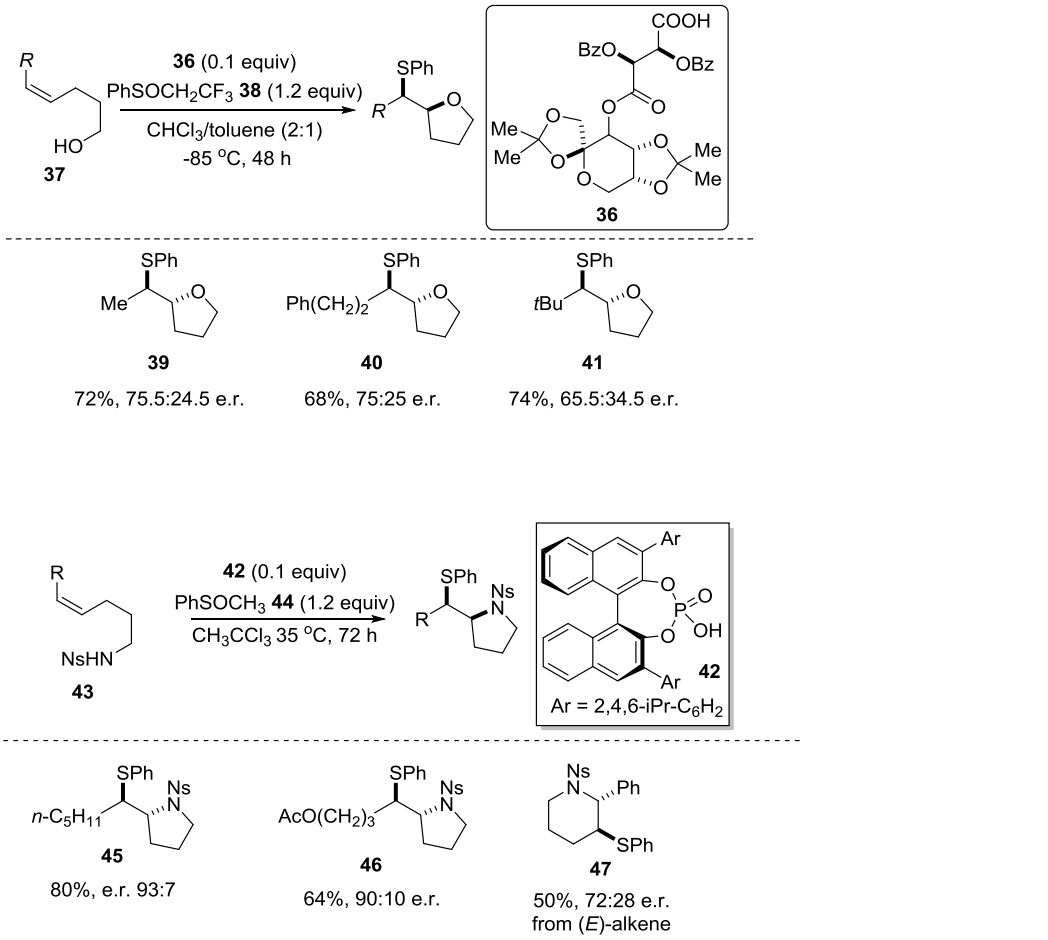
electrophile and the transferring group in the catalytic asymmetric aminosulfenylation of α,β-unsaturated carbonyl compounds (Scheme 17d).[59]



Scheme 17

In the course of this work, other Lewis base catalyzed enantioselective functionalizations have been developed. The Shi group demonstrated the catalytic activity of **36** in the oxysulfenylation of (*Z*)-alkenes **37** with electrophile **38** (Scheme 18).[60] The product tetrahydrofurans **39-41** were obtained with modest enantioselectivity. The chiral acid catalyzed sulfenofunctionalization of alkenes could be extended to nosylamine substrates **43** with electrophile **44** with substantially better enantioselectivity.[61] The increase in enantioselectivity was driven by the use of highly sterically hindered chiral phosphoric acid **42**. The enantioselectivity differed greatly based on alkene configuration, and products of (*Z*)-alkenes (**45,46**) were produced in significantly higher selectivity than (*E*)-alkenes (**47**). Although the

authors postulated a model for selectivity based on data for similar reactions, the unique properties of each sulfenylating agent renders such a comparison ill-advised. Mechanistic experiments or computational simulation to validate the proposed transition state model was not performed.

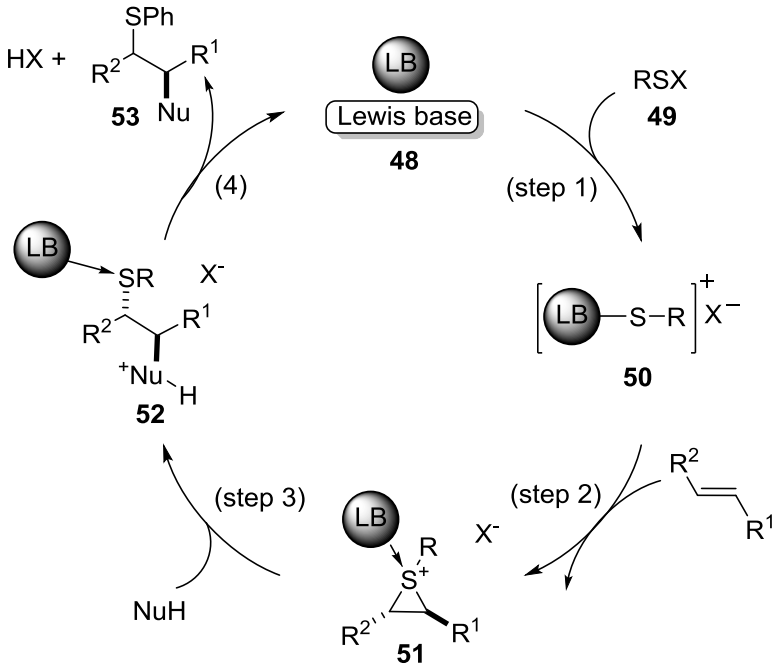


Scheme 18

In all but the last of these transformations, the requirement for an activated alkene to be generated *in situ* limits the overall applicability of the reaction. Thus, the need for a complementary approach was obvious. The conceptual approach of activation of normally unreactive sulfenyl electrophiles towards nucleophilic displacement by electronically unactivated alkenes led to the formulation of a Lewis base catalyzed enantioselective sulfenofunctionalization framework.

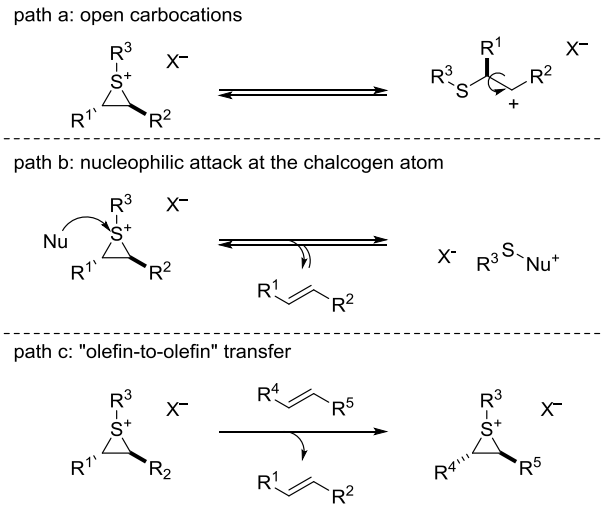
2.2.3. Application of Lewis Base Activation of Lewis Acids to Sulfenofunctionalization. The theoretical formulation of Lewis base activation of sulfur Lewis acids proceeds analogous to those developed for selenium and silicon. Sulfenyl electrophiles are Lewis acidic as a result of their ability to accept electrons into the S-X σ* orbital.[23] Thus, the interaction of a suitable Lewis base with sulfenyl electrophiles is expected to increase their reactivity, ideally to the point where they can be engaged by simple alkenes. If the Lewis base is chiral, the resulting sulfenium source would also be chiral, and potentially able to impart stereochemical information to the nascent thiiranium ion. The ability of the Lewis base to increase the reactivity of the sulfenium moiety is paramount in avoiding a stereoselectively deleterious background reaction. In light of these requirements, a plausible framework for catalytic, enantioselective sulfenylation of alkenes can be formulated. The process commences with the activation of the sulfenylating reagent **49** by a chiral Lewis base (LB) **48** to generate intermediate activated sulfenium source **50 (**Figure 9).[62] Consistent with the principles of Lewis base activation, the redistribution of the electron density from the *S*-atom toward the peripheral ligand (X) enhances the Lewis acidity of the *S*-center. The increased Lewis acidity facilitates the nucleophilic attack of the alkene onto **50** (step 2). The interception of the resulting thiiranium ion **51**, enantioenriched as a consequence of the chirality of **48**, by a nucleophile (step 3) leads to the formation of the product (**53**) and regenerates the Lewis base catalyst (step 4). In the desired reaction framework, both the enantioselectivity of thiiranium formation as well as the stereochemical integrity of the resulting thiiranium ion need to be well controlled. Furthermore, for high selectivity and chemical yield, nucleophilic attack on **51** needs to proceed site selectively among the carbon and sulfur atoms of the thiiranium ion.

Figure 9. Mechanistic Framework for a Lewis Base Catalyzed Sulfenofunctionalization Process



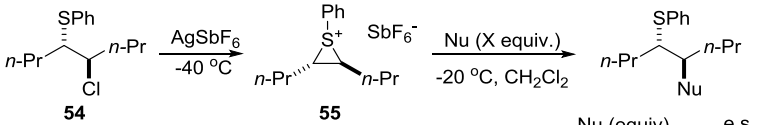
Efforts toward achieving catalytic, enantioselective sulfenylation of alkenes have hinged upon the discovery of conditions that allow for the controlled formation and capture of enantioenriched thiiranium ions. Although the stereoselective, stoichiometric synthesis of thiiranium ions has been accomplished (see Section 2.1.3), these methods did not provide any insights into the configurational stability of thiiranium ions under catalytic conditions.

Mechanistically, three major pathways can result in thiiranium ion racemization (Scheme 19).[63] The first involves the unimolecular racemization of thiiranium ions through equilibrium with an open carbocation (path a). The second mechanism entails nucleophilic attack at the sulfur center followed by addition of the resulting sulfenium moiety to the alkene (path b). Finally, the racemization could occur via a bimolecular alkene-to-alkene transfer mechanism (path c). In a series of studies from these laboratories, each of these issues were separately addressed to provide the foundation for highly-enantioselective, catalytic, sulfenofunctionalization reactions.



Scheme 19

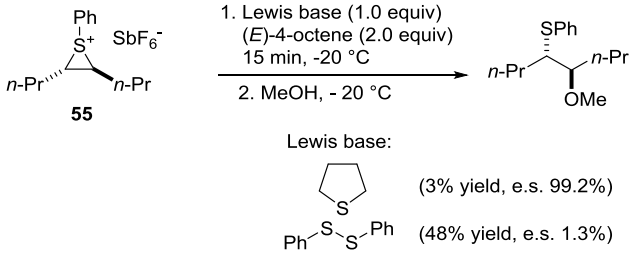
The configurational stability of thiiranium ions in the presence of hard nucleophiles was established by demonstrating high enantiospecificity in the formation and capture of enantiomerically enriched thiiranium ions.[63] Specifically, thiiranium ion **54**, prepared from enantioenriched β-chloro sulfide **55** at -40 °C, undergoes highly stereospecific capture with a variety of nucleophiles at -20 °C to afford the corresponding enantioenriched thioether products (Scheme 20). The use of neutral and anionic oxygen nucleophiles as well as azides results in the formation of β-thioethers, esters, and azides with high enantiospecificity. Thus, thiiranium ions are configurationally stable in the presence of hard nucleophiles at -20 °C. Additionally, the high enantiospecificity observed with all nucleophiles investigated suggests that a unimolecular racemization process does not occur on the timescale of nucleophilic capture (Scheme 19, paths a and b).



Nu (equiv)	e.s.
H_2O (20)	98.9
MeOH (4.0)	99.2
AcOH (4.0)	99.4
NBu_4OAc (1.5)	99.2
NBu_4N_3 (1.5)	99.6

Scheme 20

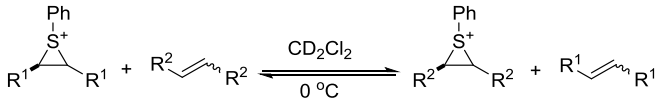
Under catalytic conditions, thiiranium ions (e.g., **55**, Scheme 21) are generated in low concentration in the presence of Lewis bases. Therefore, the configurational stability of thiiranium ions with respect to various Lewis bases is critical. The enantiospecificity for the methanolysis of thiiranium ion **55** is highly dependent on the nature of the Lewis base in the reaction mixture.[63] Whereas complete loss of configurational homogeneity occurs in the presence of diphenyl disulfide, high enantiospecificity is observed for the reaction with tetrahydrothiophene as the Lewis base. These results suggest that the enantiomeric composition of the thiiranium ion in a reaction can be maintained using non-chalcophilic Lewis bases (e.g., tetrahydrothiophene) as catalysts.



Scheme 21

The direct transfer of thiiranium ions between two alkenes has been studied both experimentally and computationally.[40,64] Rapid sulfenium ion transfer between *trans*-thiiranium ions occurs at 0 ^{o}C (Table 3, entries 1 and 2). In addition, the sulfenium ion can be transferred between *cis*- and *trans*- thiiranium ions (entries 3 and 4).

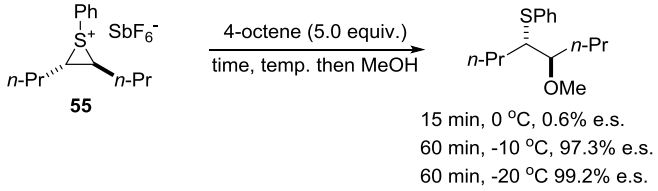
Table 3. Alkene-to-alkene Transfer of Thiiranium Ions.



entry	R^1	R^2	K_{eq}
1	(*E*)-*n*-Pr	Bn	0
2	Bn	(*E*)-*n*-Pr	100
3	(*E*)-*n*-Pr	(*Z*)-*n*-Pr	2
4	(*Z*)-*n*-Pr	(*E*)-*n*-Pr	1[a]

[a] decomposed before equilibrium could be reached.

Consequently complete racemization of enantioenriched thiiranium ion **55** occurs in the presence of an excess of (*E*)-4-octene at 0 ^{o}C as evidenced by the formation of racemic methoxylated product (Scheme 22). However, the olefin-to-olefin transfer process proved to be temperature-dependent, as the racemization of **55** is completely suppressed at -20 ^{o}C. These data implicated that the racemization of thiiranium ions *via path c* can be prevented by judicious choice of reaction conditions.



Scheme 22

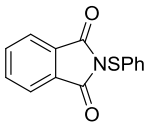
2.3. Goals of the Project.

The detailed mechanistic experiments demonstrated that stereocontrol over thiiranium ion formation is possible. Furthermore, all known major racemization pathways of thiiranium ions can be suppressed for methanol capture. Thus, the challenge lay in identifying a suitable electrophile-Lewis base combination and reaction conditions that would allow for the catalytic formation of thiiranium ions with high stereoselectivity and prevent their racemization.

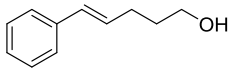
2.4. Results.

2.4.1. Optimization. 2.4.1.1. Background and Initial Survey. To conduct a far-reaching Lewis base survey, a simple and robust test system needed to be determined. An intramolecular cyclization was considered easier to accomplish, due to the high effective concentration of nucleophile in solution, which reduces the necessary lifetime for the thiiranium ion. Furthermore, the existence of a chromophore was considered advantageous with regards to separation and enantiomer determination. Sulfenylating reagent **56** is a crystalline, commercially available, stable solid and was therefore highly suitable for optimization (Chart 2). Unsaturated alcohol **57a**, accessible by a known and scalable procedure in three steps, was selected as the initial substrate.[16] The thiiranium derived from **57a** can cyclize either in *exo*- or *endo*- fashion to afford tetrahydrofurans and tetrahydropyrans respectively. Thus, the choice of **57a** also allows for investigation of the site selectivity of the alcohol nucleophile.

Chart 2



56



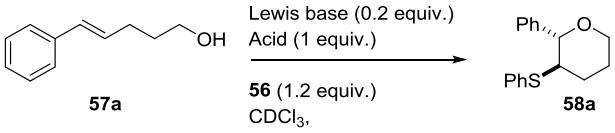
57a

As previosly mentioned, Lewis base activation of Lewis acids requires an ionizable group on the Lewis acidic center. Due to its high pKa, phthalimide is not an ideal leaving group, and attempts to effect the sulfenoetherification with just **56** was not successful.[65] However, protonation of the phthalimide significantly enhances its competence as a leaving group.[16] Trifluoroacetic acid (TFA) was selected initially as a medium-strength acid to protonate the electrophile and enhance its reactivity.[66] Unfortunately, the introduction of a proton source implies that the Lewis base must be tolerant of acidic reaction conditions. Hence the catalyst must balance strong Lewis basicity (to function as a sulfenyl transfer reagent) with weak Brønsted basicity (to be active in acidic reaction media).

As the soft nature of sulfur favors interactions with easily polarizable groups, and in light of the weak Brønsted basicity of alkyl sulfides, the survey commenced with known transfer catalyst, tetrahydrothiophene (THT).[67] THT, electrophile **56** and alkene **57a** were combined with TFA, yielding thioether **58a** (Table 4, entry 1). A stronger acid, MsOH, was a more potent

activator of **56** (entry 2).[66] No conversion was observed in the absence of acid, which precludes a simple acid-catalyzed cyclization (entries 3 and 4).[68] In light of these results, and the importance of chalcogenides for selenofunctionalization, other sulfur-containing Lewis bases were also tested.[18] DMPU(S) was only a moderately successful catalyst, resulting in 55% conversion after 24 h (entry 5). In contrast, phosphine sulfides $Ph_3P(S)$ and $Cy_3P(S)$ were highly reactive, both reactions giving complete conversion in less than 3 h (entries 6 and 7). No reaction was observed when HMPA was used (entry 8). In contrast, slow conversion was observed with thiophosphoramide HMPA(S) (entry 9). Replacing S with the more polarizable Se resulted in a more active catalyst, with complete conversion observed after 24 h for HMPA(Se) (entry 10). The results confirmed the importance of a soft, polarizable group in the catalyst backbone and optimization studies revolved around phosphorus(V) chalcogenides.

Table 4. Survey of Lewis Base Catalysts for Oxysulfenylation.

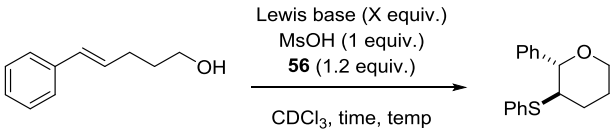


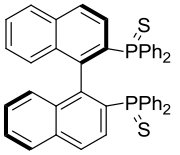
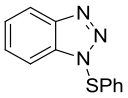
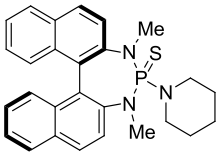
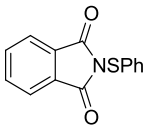
			conversion, %[a]	
entry	acid	Lewis base	3 h	24 h
1	TFA	THT	33	70
2	MsOH	THT	100	100
3	TFA	none	0	0
4	MsOH	none	trace	<10
5	MsOH	DMPU(S)	7	55
6	MsOH	$Ph_3P(S)$	100	100
7	MsOH	$Cy_3P(S)$	100	100
8	MsOH	HMPA	0	0
9	MsOH	HMPA(S)	trace	35
10	MsOH	HMPA(Se)	31	100

[a]Determined by ^1H NMR analysis of quenched mixture.

2.4.1.2. Optimization of Chiral Lewis Base. The initial survey of chiral Lewis bases was conducted mainly by Dr. Thomas Vogler.[63,69] The success of BINAM-phosphoramides in the related selenofunctionalization reaction indicated that the binaphthyl backbone may be a priviliged scaffold for the desired transformation.[16] Selected results from these experiments are displayed in. Thio-BINAP **60** was found to be unselective (Table 5, entry 1). In contrast thiophosphoramide **61** afforded pyran **58a** in 82:18 e.r. (entry 2). Replacing sulfur with selenium slightly lowered the e.r. but significantly increased reactivity (entry 3). Substitution of a hexahydroazepine ring in the place of the piperidine moiety as well as replacing sulfur with selenium resulted in a more active catalyst, **62a**, allowing the reaction to be conducted at low temperature (entry 4). Furthermore, it was also discovered that 10 mol % catalyst was sufficient for this reaction. Under these optimized conditions **58a** was obtained in 91:9 e.r. A heptahydroazocine moiety did not increase selectivity (**62c**, entry 5). Therefore **62b** was chosen as the catalyst for further reaction development. In the course of this work more selective catalysts such as **62d** and **62e** have been developed (entries 6 and 7).[40] They are shown here for comparison purposes.

Table 5. Survey of Chiral, Nonracemic Lewis Bases for Sulfenofunctionalization.



entry	#	catalyst	electrophile	equiv.	time, h	temp, °C	conversion, %[a]	e.r.[b]
1[c,d]	**60**			0.2	3	23	100	46:54
2[d]	**61**			0.2	24	23	100	82:18

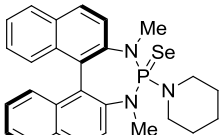
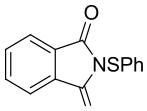
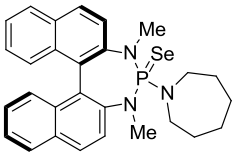
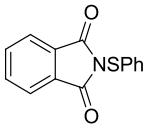
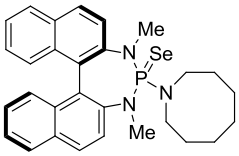
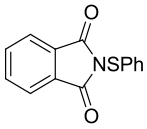
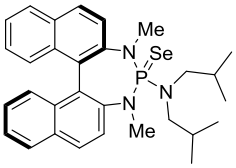
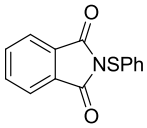
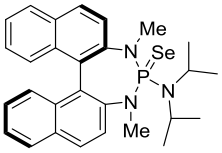
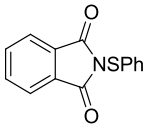
3	**62a**			0.2	4	23	100	79:21

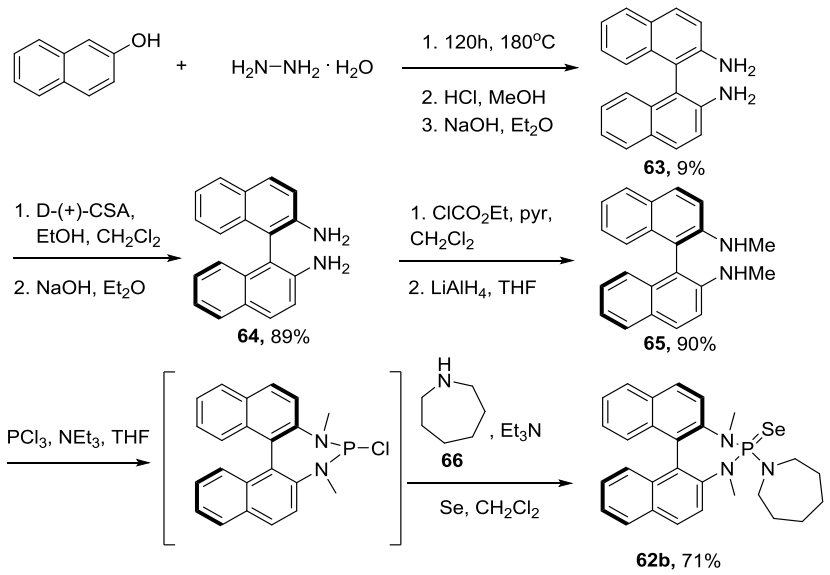
Table 5. (cont.)

4	**62b**			0.1	30	-20	100	91:9
5[c]	**62c**			0.1	48	-20	100	91:9
6	**62d**			0.1	48	-20	100	93:7
7	**62e**			0.1	48	-20	100	95:5

[a]Determined by ^{1}H NMR analysis of crude reaction mixture. [b]Determined by CSP-SFC analysis. [c]TFA was used instead of MsOH. [d]1.2 equiv. of electrophile was used.

On scale, **62b** was prepared from racemic 1,1'-binaphthyl-2,2'-diamine. Condensation of naphthol with hydrazine under high temperature and pressure afforded a tarry mass, from which 1,1'-binaphthyl-2,2'-diamine **63** was isolated in low yield (Scheme 23). The amine was resolved using (*D*)-camphorsulfonic acid, and a second neutralization afforded (*R*)-binaphthylamine **64** in 89% yield over two steps, which was found to have an e.r. of 99.2:0.8 by chiral stationary phase-supercritical fluid chromatography (CSP-SFC). Treatment of **64** with ethyl chloroformate followed by $LiAlH_4$ reduction led to dimethyl derivative **65**.[70] Reaction of **65** with PCl_3 followed by addition of amine **66** and powdered Se to yielded selenophosphoramide **62b** in 5 steps and overall 28% yield from the racemic 1,1'-binaphthyl-2,2'-diamine. The first step in this process

has since been replaced through the use of a Cu-catalyzed coupling oxidative coupling that is more amenable to high throughput.[71]



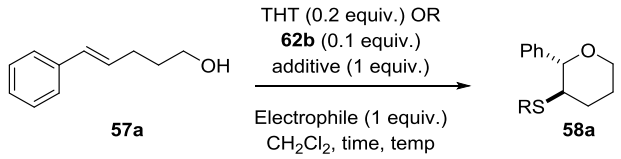
Scheme 23

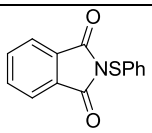
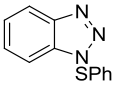
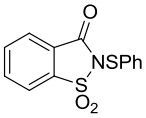
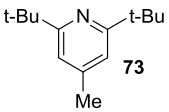
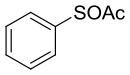
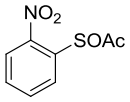
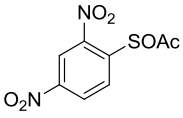
2.4.1.3. Evaluation of Electrophilic Sulfur Sources. The requirement for strong acid activation of **56** meant that many interesting nucleophiles such as cyanide, amines and conjugate bases of carbon acids cannot be used. If a more reactive electrophile/ leaving group combination could be found, this could lead to a significant increase in the nucleophile scope.

The reason behind the low reactivity of **56** is most likely the poor nucleofugality of phthalimide.[23] Thus groups on nitrogen better able to stabilize negative charge should lead to higher reactivity. To test this assumption, a series of electrophiles with increasing conjugate acid strength were tested (Table 6). The e.r. decreased modestly with increasing nucleofugality (entries 2 and 3). Unfortunately the reactions were run under different conditions so a direct comparison of the reactivity was not possible. Weaker Brønsted acids TFA and TCA (trichloroacetic acid) successfuly activated the benzotriazole and saccharin electrophiles respectively, although the overall solution was still highly acidic (pKa (TCA) < 1).[66] Ultimately the highly reactive dimesylamide-derived electrophile **69** successfully effected the cyclization of **57a** in the presence of 2 equiv. of hindered base **73** (entry 4; use of Et_3N and Hünig's base resulted in N-sulfenylation). Unfortunately, the e.r. was significantly lower. More reactive sulfenylating agents were not prepared. Sulfenyl acetate **70**, which corresponds to an intermediate nucleofuge strength was unreactive in the absence of acid (entry 5). Attempts to

decrease the electron density on the sulfur by introducing electron-withdrawing groups, such as in **71** and **72** led to exclusive O-sulfenylation (entries 6 and 7).

Table 6. Survey of Electrophilic Sulfenylating Agents.

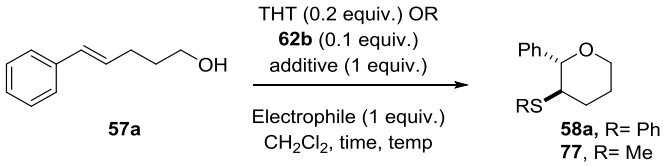


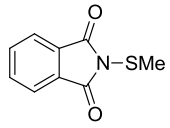
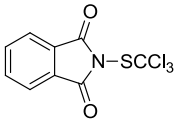
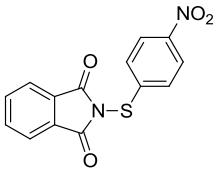
entry	electrophile	#	additive	R	time h	temp °C	conversion %[a]	e.r.[b]
1		**56**	MsOH	Ph	30	-20	100	91:9
2		**67**	TFA	Ph	40	-20	100	84:16
3[c]		**68**	TCA	Ph	1.5	23	89	79:21
4[d]		**69**	 **73**	Ph	48	-20	100	68:32
5		**70**	-	Ph	16	-20	0	-
6		**71**	-	2-NO_2-C_6H_4	16	-20	-[e]	-
7		**72**	-	2,4-NO_2-C_6H_4	16	-20	-[e]	-

[a]Determined by ^{1}H NMR analysis of crude reaction mixture. [b]Determined by CSP-SFC analysis. [c]**62a** was used instead of **62b** [d]2 equiv.of base additive was used. [e]*O*-sulfenylation was observed instead.

The identity of the sulfenyl group was also investigated (Table 7). The use of methyl-derivative **74** resulted in lower e.r. although it is currently unclear whether this is a steric or an electronic effect (entry 1). Trichloromethyl analog **75** proved completely unreactive under the reaction conditions (entry 2). Interestingly **76** was successful in effecting the cyclization, although the e.r. using a chiral Lewis base was not determined (entry 3). Further experimentation in this field was conducted by Dr. Eduard Hartmann.[72]

Table 7. Survey of Sulfur Subsituent of the Sulfenium Source.



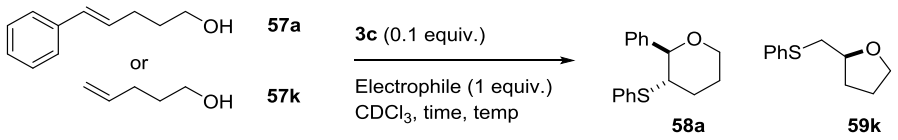
entry	electrophile	#	Lewis base	additive	R	time, h	temp, °C	conversion %[a]	e.r.[b]
1		**74**	**62b**	MsOH	Me	48	-20	100	76:24
2		**75**	THT	MsOH	CCl_3	24	23	0	-
3		**76**	THT	MsOH	4-NO_2-C_6H_4	1	23	50[c]	-

[a]Determined by ^{1}H NMR analysis of crude reaction mixture. [b]Determined by CSP-SFC analysis. [c]Other species were observed as well.

2.4.1.4. Optimization of Temperature. To determine the reactivity profile of the phthalimide electrophile, experiments at a number of different temperatures were performed using the parent substrate **57a**. When conducted at room temperature, the thiofunctionalization of **57a** yielded **58a** with an e.r. of 84:16 (Table 8, entry 1). However, at -10 °C this ratio could be improved to 89:11 (entry 2) and when the reaction was run at -20 °C, where thiiranium ions are

known to be stable, the e.r. was 91:9 (entry 3). Further decrease in the temperature did not affect the enantioselectivity (entry 4). This increase in e.r. was accompanied by a significant increase in reaction time, from 1 h at 23 ^{o}C to 24 h at -10 ^{o}C and 48 h at -20 ^{o}C. The reaction did not reach full conversion even after 66 h at -30 ^{o}C.[69] This trend was confirmed for a second substrate, **57k**: the e.r. of **59k** increased from 78:22 to 83:17 to 84:16 when the reaction temperature was lowered to -10 ^{o}C and -20 ^{o}C respectively (entries 5, 6 and 7). A similar increase in reaction time was observed.

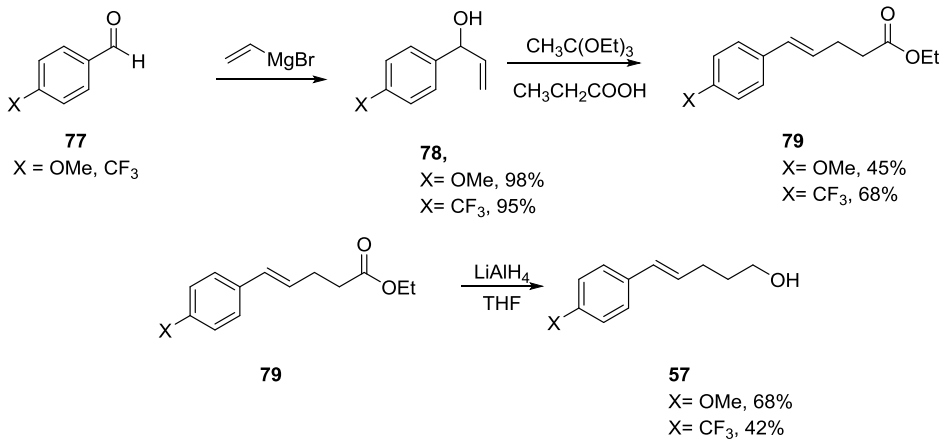
Table 8. Variation of Enantioselectivity as a Function of Temperature.



entry	substrate	temp. ^{o}C	time	product	e.r.[a]
1	**57a**	23	1 h	**58a**	84:16
2	**57a**	-10	24 h	**58a**	89:11
3	**57a**	-20	48 h	**58a**	91:9
4	**57a**	-30	>66 h[b]	**58a**	91:9
5	**57k**	23	2 h	**59k**	78:22
6	**57k**	-10	48 h	**59k**	83:17
7	**57k**	-20	>48 h[b]	**59k**	84:16

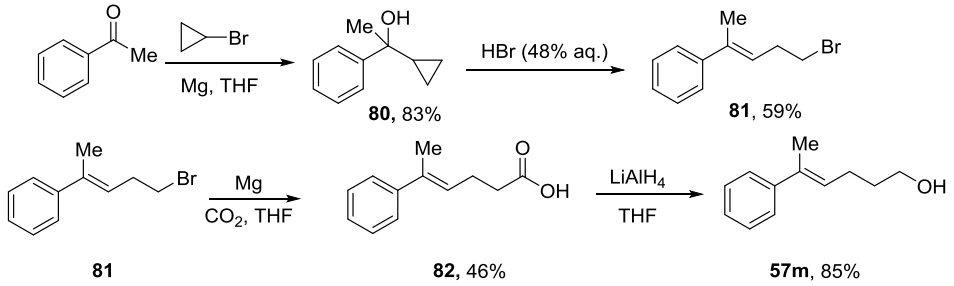
[a]Determined by CSP-SFC analysis [b]full conversion was not achieved at the final data point.

2.4.2. Intramolecular Sulfenoetherification. 2.4.2.1. Preparation of Substrates. The synthesis of γ-alkoxystyrenes followed a 4-step synthetic sequence (Scheme 24). Aldehydes **77** were treated with vinyl magnesium bromide to form secondary alcohol **78**. A Johnson-Claisen rearrangement transformed the secondary alcohols into γ-carboxystyrenes **79**. The ester was then reduced with $LiAlH_4$ to afford the desired substrates **57a-c**. Alkyl substituted **57g** and **57h** were prepared through an identical route.



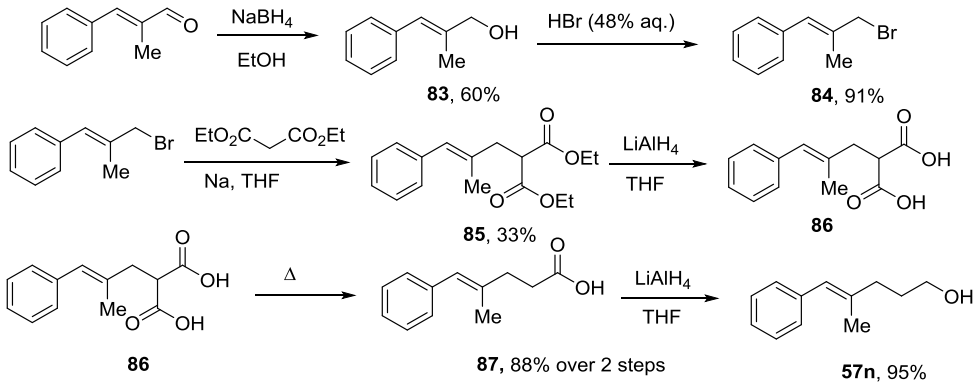
Scheme 24

The synthesis of trisubstituted alkenes was also accomplished over four steps each. The preparation of **57m** commenced with the treatment of benzaldehyde with cyclopropyl magnesium bromide to form secondary alcohol **80** (Scheme 25). Under acidic conditions, rearrangement of the cyclopropane ring resulted in the formation of the (*E*)-alkene **81**. Treatment of the bromide with Mg followed by CO_2 formed acid **82**, which was then transformed into **57m** by exposure to $LiAlH_4$.



Scheme 25

The synthesis of **57n** started with α-methyl-*trans*-cinnamaldehyde. The aldehyde was transformed into the allyl bromide **84** over two steps. Displacement of the allylic bromide with diethyl malonate afforded diester **85**. Hydrolysis of **85** in the presence of LiOH proceeded smoothly, and the product **86** underwent spontaneous decarboxylation upon distillation to the desired acid **87**. Reduction of **87** with $LiAlH_4$ then afforded **57n**.



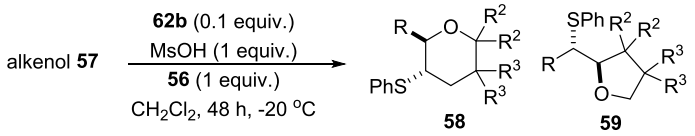
Scheme 26

2.4.2.2. Preparative Intramolecular Sulfenoetherification. A series of alkenes with differing electron density were subjected to the thiofunctionalization conditions. The parent substrate **57a** yielded thioether **58a** in 80% yield and 91:9 e.r. (Table **9**, entry 1). When methoxy-substituted substrate **57c** was used, the product was obtained in 84% yield and 91:9 e.r. (entry 2). In contrast, the reaction of trifluoromethyl-substituted substrate **57b** was found to be quite sluggish, leading to only 45% conversion even at -10 ^{o}C (entry 3). At this temperature **58b** could be obtained in 88:12 e.r. When an even more electron poor α,β-unsaturated ester **57d** was used, no reaction was observed even at elevated temperatures (entry 4). The electron density of the desired alkene appears to have an appreciable effect on reaction rate. Interestingly, even though considerable variation in rate was observed, the e.r. of the products was not affected. Furthermore, all products showed highly selective 6-*endo* closure, in contrast to previous reports suggesting that 5-*exo* closure was kinetically favored for such intramolecular capture reactions.[17]

To determine the importance of substitutents in the carbon tether, substrates bearing tertiary and quaternary carbons were synthesized. Cyclization of tertiary alcohol **57e** afforded pyran **58e** with an e.r. comparable to the parent substrate (Table **9**, entry 5). Substrate **57f** bearing a quaternary carbon also yielded a similar result, indicating that the reaction is insensitive toward substitution in the intervening tether (entry 6). Notably, the *endo*:*exo* selectivity decreased slightly when more hindered substrates were used. The impact of substituents around the carbon-carbon double bond was also investigated. A nonconjugated olefin **57g** was tested first. Under the standard reaction conditions **58g** was obtained in 96:4 e.r., indicating that the reaction of dialkyl olefins is more stereoselective than their styryl counterparts (entry 7). Notably, significant quantitites of the 5-*exo* closure product **59g** were obtained. The e.r. for **59g** was

identical to that of **58g**. The reaction of branched alkene **57h** yielded **58h** in 71% yield and 96:4 e.r. (entry 8). The branched substrate showed similar stereoselectivity but increased *endo* selectivity compared to **57g**. It appears that the introduction of branching at the nucleophile, in the tether, or around the unsaturation does not lead to significant changes in the enantioselectivity of the reaction, and has modest effects on *exo*:*endo* selectivity. No significant trends regarding the constitutional selectivity based on the size and location of the substitution could be determined. All reactions were complete after 48 h at -20 ^{o}C which indicates that any effects on rate are modest at best.

Table 9. Survey of Substrates for Intramolecular Sulfenoetherification.



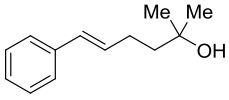
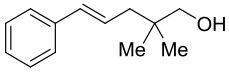
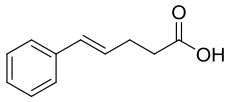
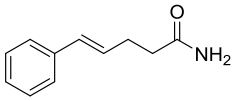
entry	alkenol	R^1	R^2	R^3	temp, ^{o}C	product	yield,[a] %	**58**/**59** [b]	e.r.[c,d]
1	**57a**	Ph	H	H	-20	**58a**	80	49:1	91:9
2	**57b**	4-$CF_3C_6H_4$	H	H	-10	**58b**	36	25:1	88:12
3	**57c**	4-MeO-C_6H_4	H	H	-10	**58c**	84	>10:1	91:9
4	**57d**	COOMe	H	H	rt[d]	**-**	0	-	-
5	**57e**				-20	**58e**	84	13:1	92:8
6	**57f**				-20	**58f**	94	19:1	92:8
7	**57g**	CH_2CH_2Ph	H	H	-20	**58g**, **59g**	88	5:1	96:4 (**58g**) 96:4 (**59g**)
8	**57h**	*i*-Pr	H	H	-20	**58h**	71	17:1	96:4
9[e]	**57i**	H	Ph	H	rt[d]	**58i**	41	N.D.	53:47
10	**57j**	H	$(CH_2)_2Ph$	H	-10	**59j**	72	1:20	54:46

Table 9. (cont.)

11	**57k**	H	H	H	-10	**59k**	72	<1:19	83:17
12	**57l**	H	H	Ph	-20	**59l**	85	<1:99	62:38
13	**57m**	Ph	H	Me	-20	**58m**	82	17:1	70:30
14	**57n**	Ph	Me	H	23	**59n**	24	1:18	60:40
15	**57o**				-10	**59o**	83	1:99	91:9
16	**57p**				rt[d]	-	0	-	-

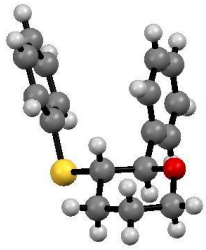
[a]Isolated yield. [b]Determined by ^{1}H NMR analysis of crude reaction mixture. [c]Determined by CSP-SFC analysis. [d]Reaction run at rt for 96 h. [e]Catalyst (*R*)-**62a** and electrophile **67** were used.

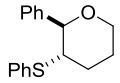
The hallmark of a robust catalyst for alkene functionalization is its ability to engage different alkene substitution patterns. To determine the behavior of the reaction toward the various alkene classes, representatives mono-, di-, and trisubstituted alkenes were used in thiofunctionalizations. Tetrasubstituted alkenes were expected to react sluggishly and were not tested; difficulties with trisubstituted alkenes bore out this expectation. (*Z*)-alkenes were much slower than their (*E*)-alkene counterparts. The cyclization of **57i** took four days at elevated temperature, and afforded nearly racemic product (entry 9). Dialkyl substituted (*Z*)-**57j** was significantly faster, affording thioether **59j** in 72% yield after 48 h at -10 ^{o}C (entry 10). Unfortunately, the product was once again nearly racemic. Terminal olefins are known to be difficult substrates for face-discriminating reactions due to the minimal difference between the enantiotopic faces.[73] Thus, it was pleasing to discover that tetrahydrofuran **59k** could be obtained in 72% yield and 83:17 e.r (Table **9**, entry 11). Higher temperatures (-10 ^{o}C) were necessary for this substrate. In contrast to the cyclizations of (*E*)-alkenes high *exo* selectivity was observed. Disubsituted terminal alkenol **57l** showed good reactivity, and **59l** was obtained with very high *exo*-selectivity albeit with poor enantioselectivity. The use of trisubstituted alkenes did not improve the enantioselectivity significantly, as two different trisubstituted alkenes **57m** and **57n** gave products **58m** and **59n** with 70:30 and 60:40 e.r. respectively. Notably, for **59n** the reaction was quite sluggish, and elevated temperatures were necessary. Many side products were also obtained. Interestingly the constitutional selectivity between **58m** and **59n** were switched. The obtained isomer in each case is consistent with nucleophilic attack at the more substituted carbon.

Other nucleophiles also participated in the opening of thiiranium ions. In addition to alcohols, carboxylic acids were found to be effective nucleophiles, and the cyclization of **57o** yielded **59o** in 83% yield, 99:1 constitutional selectivity and 91:9 enantioselectivity (Table **9**, entry 15). The reaction did require slightly elevated temperatures. When amide **57p** was used, no reaction was observed (entry 16).[74]

The absolute configuration of **58a** was determined by X-ray analysis of single crystals. **58a** was obtained as a viscous oil which crystallized upon standing after distillation. X-ray analysis revealed the absolute configuration to be (2*S*,3*R*)-**58a** (Figure 2). The remaining thioethers are assigned by analogy, assuming the formation of the same configuration at the thiiranium center for the remaining substrates.

Figure 10. X-Ray Crystal Structure of 58a





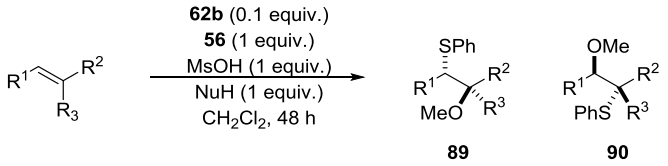
58a

2.4.3. Intermolecular Sulfenoetherification. The intermolecular thiofunctionalization of alkenes represents an important avenue for the development of a general asymmetric sulfenylation reaction. Preparation of substrates for intramolecular thiofunctionalizations may not always be simple, and the obtained products are by necessity cyclic. Thus the functionalization of isolated alkenes with intermolecular nucleophiles introduces sulfur without ring formation, and with a much broader range of functionalized nucleophiles. However, intermolecular functionalizations also present some major challenges. The lifetime of the thiiranium ion in solution is lengthened, which presents greater opportunities for racemization. The lower effective nucleophile concentration may also result in slower reactions. Furthermore, for non-C_2-symmetric alkenes, site selectivity may be an issue. A substrate survey to was initiated to investigate these issues.

The model substrate **88a** was chosen due to its C_{2h}-symmetry and information available regarding its reactivity.[63] Exposing **88a** to the standard thioetherification protocol in the presence of MeOH afforded the difunctionalized product **89a** in 93% yield and 92:8 e.r (Table 10, entry

1). (*Z*)-Olefin **88b** was an interesting substrate as the resulting thiiranium ion would be *meso*. Thus, if enantioinduction were observed, this could be evidence for the continued involvement of the catalyst after thiiranium ion formation. Unfortunately, the products obtained were within experimental error of being racemic (entry 2). Since (*Z*)-Olefins do not give high enantioselectivities with the current catalyst, no conclusions in either direction could be drawn. Terminal alkene **88c** could be functionalized in 77% yield and 82:18 e.r., although constitutional isomers **89c** and **90c** were obtained in a 10:1 ratio (entry 3). The functionalization of unsymmetrically substituted alkene **88d** resulted in 4:1 constitutional ratio of **89d**:**90d** with 58% combined yield and 86:14 e.r. (entry 4). Trends that were apparent in the intramolecular thiofunctionalization reaction transferred well to the intermolecular thiofunctionalization, indicating that the mechanistic pathways may be similar.

Table 10. Survey of Substrates for Intermolecular Sulfenoetherification.



entry	#	R^1	R^2	R^3	temp. ^oC	NuH	yield, %[a]	**89**/**90**[b]	e.r.[c]
1	**88a**	*n*-Pr	*n*-Pr	H	-20	MeOH	93	-	92:8
2	**88b**	*n*-Pr	H	*n*-Pr	-20	MeOH	n.d.	-	52:48
3	**88c**	*n*-Hex	H	H	-20	MeOH	77	10:1	82:18
4	**88d**	*i*-Pr	*n*-Pr	H	-20	MeOH	58	4:1	84:16 (**89**)[d] 84:16 (**90d**)[d]
5	**88a**	*n*-Pr	*n*-Pr	H	-20	AcOH	77	-	91:9
6	**88a**	*n*-Pr	*n*-Pr	H	-20	MeCN[e]	35	-	89:11

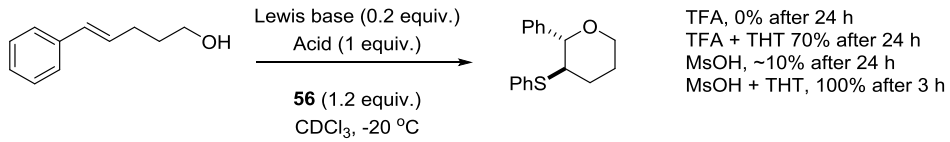
[a]Isolated yield. [b]Determined by ^{1}H NMR analysis of crude reaction mixture. [c]Determined by CSP-SFC analysis. [d]E.r. determined after oxidation to the sulfones **91** and **92**, see experimental section. [e]10 equiv of nucleophile was used.

Nucleophiles other than alcohols were also tested in the intermolecular thiofunctionalization reaction. The thiiranium ion derived from 4-octene could also be captured by acetic acid, which formed **89e** in 77% yield and 91:9 e.r. (Table 10, entry 5). Nitriles have

been shown to react with thiiranium ions to afford nitrilium ions that are hydrolyzed to amides upon workup.[37b] Amide **89f** resulting from nitrile capture was obtained in 89:11 e.r. (entry 6). The yields of the reaction were low, and a significant quantity of material resulting from thiiranium hydrolysis was recovered, even in the presence of excess CH_3CN.

2.5. Discussion.

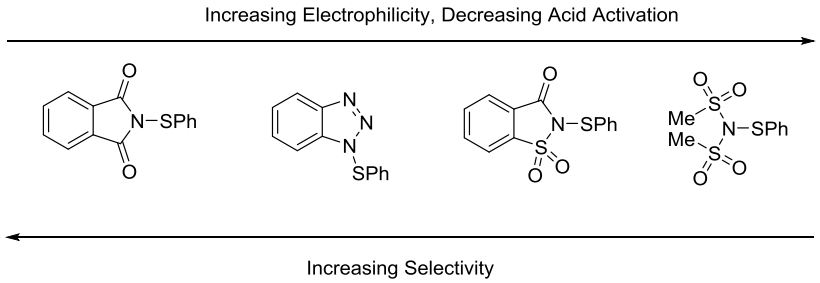
2.5.1. Optimization of Reaction Conditions. The use of Brønsted acids to activate sulfenyl and selenyl electrophiles is well known.[16,23] Protonation of the imide moiety increases its nucleofugality. The increased S-N bond polarization increases Lewis acidity, which is then further bolstered by Lewis base complexation. Only then is the alkene a competent nucleophile for sulfenium transfer. Indeed, the combination of electrophile **56**, alcohol **57a** and Lewis base **62b** did not lead to product formation.[65] However, upon addition of MsOH was clean conversion to **58a** observed. Thus, the reactivity of the sulfenylimides as Lewis acids is modulated by the presence of a Brønsted acidic co-activator (Scheme 27). The decrease in reactivity as a consequence of lower acid strength suggests that the protonated imide fraction needs to be high for efficient turnover.



Scheme 27

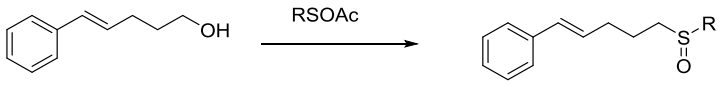
The rate of the reaction for electrophiles **56**, **67** and **68** were comparable at -20 °C. Thus, the rate of the reaction is not a function of electrophile source. For reactions of substrates that are not compatible with strong acids, more reactive sulfenyl agents with less stringent acid requirements can be used. At the most extreme, disulfonylimides **69** allow the reaction to proceed without any acid activation (Table 6, Scheme 28). However, the downside of increasing the reactivity of the sulfenylating agent can be observed in the enantiomeric composition of the resulting products. More reactive sulfenylimides are also more apt to undergo an uncatalyzed sulfenium transfer reaction, leading to the formation of racemic product, polluting the highly enantioenriched material that results from the catalyzed pathway. The influence of the counterion on the facial selectivity for thiiranium formation is also a potential reason for the change in

selectivity, however it would not be expected to monotonically decrease as a function of counterion nucleofugality.



Scheme 28

Sulfenyl acetates represent a different class of electrophile due to the differences between the S-N and S-O bonds.[54b] Sulfenyl acetates displayed σ-electrophilicity as opposed to π-electrophilicity, resulting in preferential O-sulfenylation (Scheme 29). Although the reaction of sulfenyl acetates with alkenes have been well studied, they had been performed in the absence of other nucleophilic groups.[75] Electrophiles with S-O linkages were not studied further as a result of the observed undesirable reactivity.



Scheme 29

The substituent on the sulfur atom can affect the sulfenofunctionalization process in two ways. Functional groups that stabilize positive charge on the sulfur promote ionization of the Lewis base - sulfenium complex, assisting in the formation of the chiral sulfenylating agent. However, they can also donate electron density into the Lewis acidic sulfur atom, decreasing its reactivity as a sulfenylating source. The replacement of the phenyl group by a methyl group did not have a major impact on reactivity, and the reaction proceeded to high conversion. In contrast, the much more electrophilic **75** bearing a trichloromethyl moiety failed to react even at elevated temperatures and with the more active THT catalyst. Thus, thiiranium ion appears to benefit from some stabilization at the sulfur center. This result is in agreement with those from Dr. Matthew Cullen, who observed increased reactivity for sulfenium sources bearing electron-rich arenes.[65] The ability of the arene moiety to modulate the reaction rate is correlated with its

electron density, insofar as its ability to stoichiometrically sulfenylate the Lewis base complex. Therefore, no further sulfenium transfer agents bearing alkyl sulfides were tested. Further modifications to the electrophile were performed by other researchers from these laboratories.[40]

Only a subset of various Lewis bases previously tested in these laboratories are shown. The softness, i.e. polarizability of the Lewis basic atom was extremely important for reactivity.[69] Thus, phospine oxides were poor catalysts, whereas increasing reactivity was observed for the corresponding sulfides and selenides. Thioureas were less effective, potentially due to increased Brønsted basicity or insufficient Lewis basic character. Interestingly, Lewis basic sulfenophosphoramides were less effective than the corresponding alkyl or aryl phosphine sulfides. D_s numbers for the series of Lewis bases (HMPA, 39; THT, 43; HMPA(S), 53, tri-*n*-butylphosphite 56)[76] did not correlate with reactivity, and therefore Lewis basicity may not be the sole factor governing the efficacy of a particular catalyst architecture. Unfortunately, comprehensive donor scales for phosphine sulfides are not available. Comparison with the D_s of the related alkyl phosphines (~80) suggest that they would be substantially more Lewis basic than HMPA(S), potentially contributing to their high reactivity.[76] The D_s numbers of selenophosphoramides and phosphine selenides are unknown, although their increased polarizability would likely also increase their donactity with respect to their corresponding sulfur analogues. It is worth noting that all of these Lewis basic functionalities are poor Brønsted bases and are not protonated under the reaction conditions. Titration of selenophosphoramides with methanesulfonic acid revealed only minor shifts by ^{31}P NMR up to 4 equiv of MsOH.[69]

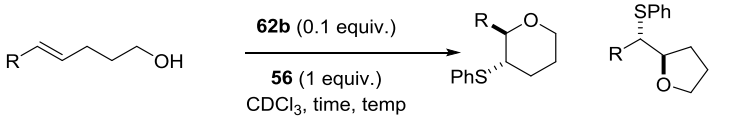
The best catalysts for the sulfenofunctionalization process differed from those for the analogous selenofunctionalization process in one important facet. For sulfenofunctionalization catalysts, selenophosphoramides displayed better catalytic activity than the corresponding sulfenophosphoramides, in contrast to selenofunctionalization for which sulfenophosphoramides were more efficient catalysts.[16] The rate difference is hypothesized to be due to the formation of a strong homonuclear group 16 bond for S-S and Se-Se. In contrast, the S-Se bond is polarized and much weaker due to poor orbital overlap.[77] This trend was confirmed by further X-ray crystallographic studies of reaction intermediates (Chapter 3.2.2).

The catalyst optimization process by researchers in these laboratories, primarily Drs. Thomas Vogler and Matthew Cullen, identified three major families of potential catalysts amenable to modification (1) aryl and alkyl phosphine sulfides, (2) dialkyl sulfides, (3)

selenophosphoramides. Extensive modification of families (1) and (2) were investigated (representative examples are shown in Table 5). The binaphthylphosphoramide backbone proved uniquely selective for the sulfenofunctionalization process. The biaryl moiety is a priviliged ligand, and has been featured in numerous highly selective catalysts, such as **3** for the Lewis base activation of silicon Lewis acids. Structural features of the catalyst architecture that enable the high selectivity will be discussed in Section 3.3.

The temperature-dependent racemization of thiiranium ions has been well documented.[63] Thus, a temperature survey was undertaken to study both rate and enantioselectivity as functions of temperature. The rate of sulfenofunctionalization monotonously and rapidly decreased as a consequence of reaction temperature. A lower bound on reactivity was -20 ^{o}C, at lower temperatures the reaction time was unacceptably long. The enantioselectivity was temperature dependent, however much less so than expected. The e.r. of **58a** decreased from 91:9 to 84:16 when the reaction temperature was increased from -20 ^{o}C to rt (Scheme 30). In contrast, when thiiranium ions were generated stoichiometrically and allowed to equilibriate for 15 min at rt in the presence of excess olefin, complete racemization was observed.[63]

The observed differences in enantioselectivity suggested that the thiiranium ion lifetime is unsurprisingly much shorter in the presence of a nucleophile. Thus, even at elevated temperature, capture is sufficiently fast to protect most of the stereochemical integrity of the thiiranium ion. The stabilization was not solely related to the presence of a stabilizing phenyl group on the alkene. The stereochemical integrity of thiiranium ions derived from terminal olefins was also mostly retained at rt (78:22 vs 84:16, Scheme 30). In the interest of observing the true intrinsic selectivity of the catalyst for the formation of thiiranium ions derived from various alkenes, the optimized reactions were conducted at -20 ^{o}C.

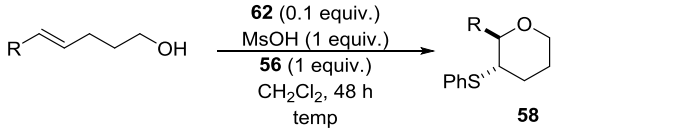


R = Ph, **58a**, rt, 84:16 e.r.,
R = Ph, **58a**, -20 ^{o}C, 91:9 e.r.
R = H, **59k**, rt, 78:22 e.r.
R = H, **59k**, -10 ^{o}C, 84:16 e.r.

Scheme 30

2.5.2. Preparative Intramolecular Sulfenoetherification. The substrate scope for alkene sulfenofunctionalization was designed to investigate the effects on rate, enantio- and site-selectivity as a consequence of alkene parameters. These changes are discussed in turn.

2.5.2.1. Rate. The rate of the sulfenofunctionalization reaction was sensitive to the electronic parameters of the alkene. Increased electron density did not have a measurable effect on rate. In contrast, the presence of an electron-withdrawing -CF_3 moiety resulted in substantially lower reactivity (Scheme 31). Even at elevated temperatures, full conversion was not achieved. The lack of reactivity observed for **58d** bearing an electron-withdrawing ester group is consistent with this hypothesis.



R = Ph, -20 °C, 80%
R = 4-CF_3-C_6H_4, -10 °C, 36%
R = COOMe, rt, 0%

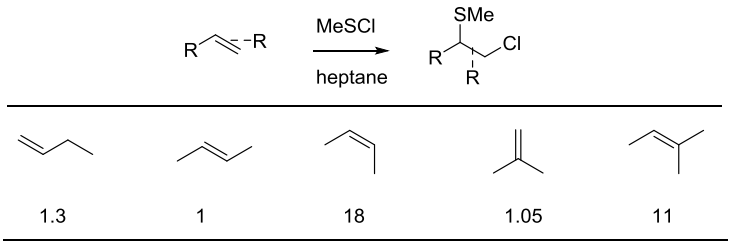
Scheme 31

The electron density of the alkene affects the reaction rate insofar as it affects the nucleophilicity of the alkene towards attack at the thiiranium ion. Thus, substantial changes in rate as a consequence of alkene electron density is consistent with thiiranium formation being turnover-limiting. The high-energy of charge localization on the sulfur as well as the formation of a strained three-membered ring are invoked to explain the high energy barrier towards formation. Comparison with other -iranium functionalizations of Group 16 and Group 17 elements shows that the formation of the three-membered intermediate is uaually turnover-limiting, in agreement with the current results.[62]

The rate of the reaction was not sensitive to steric parameters at the alcohol or along the tether (Table 9, entry 5 and 6). There also appeared to be no discernible difference in rate for aryl, hindered alkyl or unhindered alkyl (*E*)-disubstituted alkenes (Table 9, entries 1, 7 and 8). Thus, the electronic environment of the alkene is a much stronger predictor of cyclization rate than the steric parameter for (*E*)-alkenes.

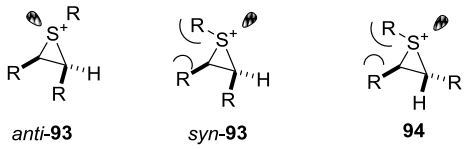
The geometry of the alkene had a very prominent effect on rate. If the alkene geometry changed from (*E*) to (*Z*), the reaction proceeded more slowly. No rate difference was observed

between (*E*)- and 1,1-substituted alkenes. Given the small electronic differences between these alkene classes, steric considerations are likely affecting the rate of cyclization for (*Z*)-alkenes. This result stands in stark contrast with the relative rates of cyclization of *cis*- and *trans*-butene with Cl_2 and MeSCl (Scheme 32).[78] The dichlorination of *cis*-butene with Cl_2 proceeds 1.25 times faster than *trans*-butene, for sulfenochlorination k_{rel} of *cis*-butene to *trans*-butene is 18. In agreement with current results, k_{rel} of *trans*-butene to isobutylene is ~1 when MeSCl is used as the sulfenylating agent. The potential for sulfenyl chlorides to proceed through a qualitatively different thiiranium ion must not be forgotten. The alkene sensitivity may thus also represent differences in carbon charge density between the two thiiranium ions based on counterion.



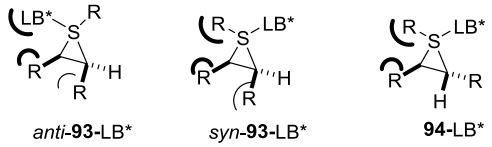
Scheme 32

The barrier to the aforementioned turnover-limiting thiiranium formation will be directly affected by the stability of the resulting thiiranium ion. The following ground-state arguments have been put forth to explain differences in reaction barriers towards thiiranium formation.[43] The reaction of PhSCl and *cis*-butene gives rise to two diastereomers *syn*-**93** and *anti*-**93** (Scheme 33). In *syn*-**93** the substituent on the sulfur atom is in an unfavorable steric interaction with the alkene substituents, whereas the selfsame interaction is avoided in *anti*-**93**. Therefore, formation favors the less hindered *anti*-**93**. The addition of a sulfenium moiety to *trans*-butene results in two enantiomers of **94**, neither of which can escape eclipsing of one of the sulfur substituents. More generally speaking, for *trans*-alkenes the resultant thiiranium ion must necessarily be experiencing steric repulsion with one alkene substituent. Thus, the formation of thiiranium ions from *trans*-alkenes should be slower than *cis*-alkenes, which is borne out by the rate data for MeSCl. The slow reactivity of *cis*-alkenes **57j** and **57k** under the current reaction conditions cannot be explained by an analysis excluding participation of the Lewis base in the transition state.



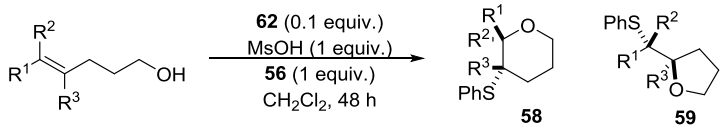
Scheme 33

The steric difference between the sulfenium substituents in the current Lewis-base catalyzed process is much different. The presence of the Lewis base forces the sulfenium moiety to have the equivalent of two large substituents (Scheme 35). The thiiranium ions anti-**93**-LB* and syn-**93**-LB* derived from a *cis*-alkene would then necessarily have at least one large sulfenium substituent eclipsing both alkene arms, disfavoring reaction of the *cis*-alkene. For the corresponding thiiranium ion derived from a *trans*-alkene, each sulfenium substituent eclipses only one alkene arm. The two empty alkene quadrants (occupied by C_{sp3}-H atoms) can accomodate the remaining steric bulk of the substituents. The presence of the Lewis base likely retards the reactivity of the *cis*-alkenes significantly, to the point that *trans*-alkenes are the more reactive substrates.



Scheme 34

Alkene electron density increases monotonically with the number of alkene substituents. The reaction of monosubstituted alkene **57k** was somewhat slower than that of disubstituted **57a** (Scheme 35). No change was observed for **57m**. The corresponding k_{rel} between *trans*-butene and 2-methyl-2-butene is 11 (Scheme 32), again suggesting that the Lewis base appears to be significantly modulating the relative reactivity of alkene isomers for hindered systems. The reaction of trisubsituted alkenes was very sensitive to the location of the methyl group. Altering the position of methyl group led to very slow reactivity, requiring elevated temperatures. Thus, the catalyst appears to be highly selective for *trans*-alkenes over other alkene geometries. The presence of a substituent (*Z*)- to the alkyl chain is also disfavored by the catalyst.



R^1, R^2, R^3 = H,H,H, **57k**, -10 °C, 72%
R^1, R^2, R^3 = Ph,H,H, **57a**, -20 °C, 84%
R^1, R^2, R^3 = H,H,Ph, **57l** -20 °C, 85%
R^1, R^2, R^3 = Ph,Me,H,**57m** -20 °C, 85%
R^1, R^2, R^3 = Ph,H,Me, **57n**, rt, 24%

Scheme 35

Carboxylic acids were competent nucleophiles for the oxysulfenylation reaction. The rates did not deviate from the corresponding alcohols. Thus, even though they are much weaker nucleophiles (pKa ROH_2^+ -2.2, pKa $RCO_2H_2^+$ -6.5)[66] the rate of capture by carboxylic acids still outpaces the rate of thiiranium formation. In contrast, amides were unreactive. The pKa of the conjugate acid for the amide (-0.2)[66,74] is lower than the pKa of MsOH (-2.6)[66], therefore the lack of amide reactivity can be traced back to stoichiometric protonation of the amide (and concomitant decrease in formation of sulfenylation complex **50**).

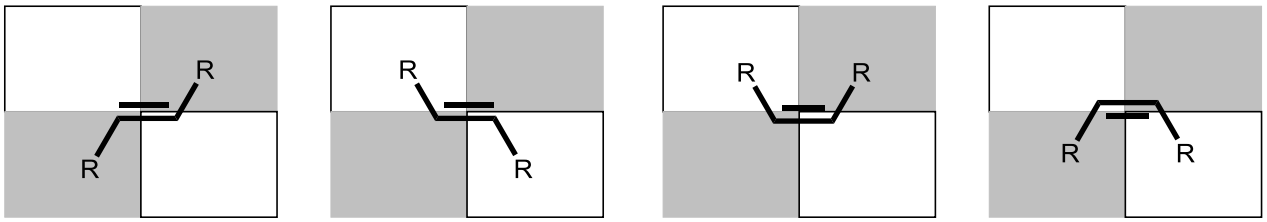
2.5.2.2. Enantioselectivity. The enantioselectivity of the sulfenofunctionalization process was consistently high for (*E*)-styrenes. Changes in the electron density of the alkene did not have a substantial effect on selectivity (Table **9**, entries 1, 2 and 3). Increased steric bulk at the alcohol or in the tether also did not result in changes in enantioselecitivity. In contrast to the reactivity, enantioselectivity for styrenes appears to be well-controlled by the catalyst, and similar selectivities are observed. The similar selectivities observed are in good agreement with a common, configurationally stable thiiranium ion intermediate. The intrinsic selectivity of the catalyst for styrene substrates is directly relayed to the product enantiomeric ratio with little sensitivity to the electronic properties of the thiiranium ion.

Interestingly, sulfenofunctionalization of alkenes with two alkyl substrates resulted in improved enantioselectivity. The effect is not simply related to changes in the steric environment around the alkene, as no change in enantioselectivity was observed between substrates bearing methylene and methine carbons at the α position of the alkene. Thus, the initial thiiranium formation appears to more selective for unconjugated substrates. The position of the conjugated phenyl may have a deleterious effect on selectivity, as the slight increase in selectivity for disubstituted alkenes has been replicated in the amino- and carbosulfenylation reactions.[79,83] For

unconjugated substrates, the alkyl chain could potentially adopt a more selective conformer that is not accessible to the conjugated substrate as a result of planarization of the alkene and arene moieties.

In contrast, changes to the alkene geometry significantly impacted enantioselectivity. Substrate (*Z*)- **57j** of could be sulfenofunctionalized with only 55:45 e.r. in contrast to the result with the (*E*)-**57g** (96:4, Table 9, entries 7 and 10). The lack of a detailed model for enantioselectivity prevents an in-depth analysis of this change. However, a quadrant model of selectivity has been proposed for similar alkene functionalization reactions.[19f] In this model, the catalyst is sterically hindered in two quadrants of the alkene approach, requiring the alkene to orient itself in a manner that places the small substituents in these quadrants (Figure 11, shaded areas are occupied by the catalyst). For (*Z*)-alkenes, no low energy approach is possible, and the transition states leading to the two enantiomers do not have large energy differences, which results in the product being obtained in nearly racemic form. This catalytic model also predicts poor selectivity for other classes of alkenes. Indeed, both 1,1- and trisubstituted alkenes formed sulfenofunctionalization products with diminished e.r. However, the enantioselectivity was much less diminished for a monosubstituted alkene. In the framework of the quadrant model, this result can be explained if the two sterically bulky quadrants contain unequal amounts of space. Thus, the orientation of the monosubstituted alkene is well controlled in terms of which quadrant the alkyl group occupies. While the experimental data does not refute this interpretation, without further data on transition states of less selective alkenes any general model for selectivity remains speculative.

Figure 11. The Quadrant Model for Enantioselectivity.

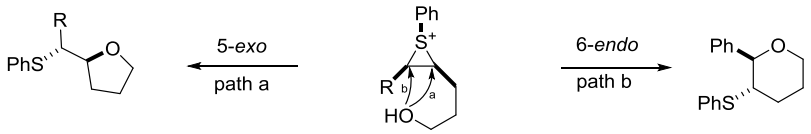


The properties of the nucleophile also did not have a substantial impact on the selectivity. Both hindered alcohol and carboxylic acids resulted in sulfenofunctionalization with similar selectivities (Table 9, entries 5 and 15). Primary amides did not cyclize and therefore the enantioselectivity could not be determined. Interestingly, the intermolecular

sulfenofunctionalization of a nitrile led to the isolation of the secondary amide with an e.r. similar to that of alcohols and acids, which implied that nucleophile identity does not affect product enantioselectivity. Extension of this process to protected amines and amides has since confirmed this observation.[79] Nitrile addition to thiiraniums reversibly forms nitrilium ions, thus the thiiranium ion can be reformed under the reaction conditions.[42] The high configurational stability of the thiiranium ion, in conjunction with the strong preference of hard nucleophiles for C-attack, prevents stereoerosion at this critical juncture.

From this data, the enantioselectivity-determining step is conjectured to be thiiranium formation. The results indicate that the inherent catalyst selectivity is affected by the geometry of the alkene, but not by alkene electron density, steric properties of the tether, nucleophile steric bulk or nucelophile identity. The latter three factors would have all been expected to significantly impact selectivity if the enantioselectivity-determining step were thiiranium capture. The enantioselectivity of the sulfenofunctionalization reaction is thus governed by two primary factors, both involving thiiranium formation: the intrinsic selectivity of the catalyst for sulfenium transfer to a reference alkene and the geometrical configuration of the substrate alkene. The predictable nature of sulfenofunctionalization selectivity on the basis of these factors was then further confirmed in the optimization process for amino- and carbonsulfenylation reactions.

2.5.2.3. Site Selectivity. The three-membered ring of a thiiranium ion is electrophilic at each of its constituent atoms. The propensity of hard nucleophiles to prefer C-attack over S-attack has been covered in Section 2.2.3. However, C-attack can happen at either carbon of the thiiranium ion, leading to constitutional isomers (Scheme 36). For intramolecular cyclizations, the designations *endo* and *exo* are used to signify modes of cyclization in which the sulfur-bearing methylene is endocyclic or exocyclic with respect to ring formation. In the case of sulfenofunctionalization with alcohols, high *endo* selectivity was observed for alkenes displaying an electronic bias. Similarly, sterically biased dialkyl substituted alkene **57h** also cyclized with high *endo* selectivity whereas the unbiased alkene **57g** afforded **58g** and **59g** with only 5:1 *endo*:*exo* selectivity.



Scheme 36

The observed site-selectivity can result from a number of different equilibria. Specifically, the site-selectivity can be under kinetic or thermodynamic control. If under kinetic control, the observed site-selectivities would represent the intrinsic relative rates of *endo* and *exo* cyclization of alcohols. If the site selectivity is instead under thermodynamic control, the relative stability of the tetrahydrofuran and tetrahydropyran products would be responsible for the observed ratios. A different way of phrasing this question would be to state whether the thiiranium capture step is reversible. For reversible capture, the thermodynamically more stable product is expected to be formed, whereas for irreversible capture, the kinetic product should predominate.

The relative kinetic reactivity for the cyclization of seleniranium ions has been established as 5-*exo*>6-*endo*>3-*exo*>4-*endo*.[80] Thus, for a kinetically controlled cyclization of analogous thiiranium ions, the 5-*exo* product is expected to predominate. Instead, the 6-*endo* product was obtained, in accord with Markovnikov rules for nucleophilic attack. Notably, this result is also in accordance with the cyclization of haliranium ions, which generally proceed with high Markovnikov selectivity.[17] The nature of the electrophilic atom in the -iranium ring appears to strongly affect site selectivity.

To ascertain the reversibility of thiiranium capture isomerization studies of *exo*-products **59k**, **59g** and **59j** were conducted (Section 3.2.3). Whereas terminal and (*Z*)-alkene derived thiiranium ions did not isomerize under the reaction conditions, thiiranium ions from (*E*)-alkenes did. Thus the high enantioselectivity appears to be at least partially due to the thermodynamic preference for tetrahydropyrans over tetrahydrofurans. Unfortunately, the *exo*-product could not be obtained in sufficient quantities from the cyclization of styrenes to test whether these substrates also undergo thermodynamic equilibriation. In this case, the Markovnikov and kinetic selectivity are working in conjunction, thus making it difficult to deconvolute their respective contributions.

Interestingly, cyclization of carboxylic acid **57o** proceeded with high *exo* selectivity. There is substantial evidence showing that carboxylic acid cyclizations proceed under different

selection rules than alcohols based on both protonation state and -iranium source.[17] Therefore, no direct comparison with the aforementioned alcohols is drawn.

2.5.3. Preparative Intermolecular Sulfenoetherification. The reactivity trends did not change when intermolecular sulfenylations were tested. Sulfenofunctionalization of 4-octene proceeded within 48 h at the same temperature as **57a**. A larger difference was observed for 1-octene, as the temperature needed to be raised higher for good reactivity. As expected, no rate change was observed as a consequence of increased steric encumbrance around the alkene moiety. This data suggests that thiiranium capture is faster than thiiranium formation during the intermolecular sulfenofunctionalizaiton process, and by extension during the intramolecular sulfenofunctionalization process.

The enantioselectivity for intermolecular sulfenofunctionalizations is mildly diminished compared to the intramolecular case. Thus, whereas **57g** afforded sulfenofunctionalization products with 96:4 e.r., the corresponding intermolecular reaction with 4-octene proceeded with only 92:8 e.r. A similar decrease was observed in the reaction a terminal alkene. An even greater decrease was observed when the alkene was substituted at the α-position. These results suggest that a small amount of racemization may be occurring during the intermolecular sulfenofunctionalization reaction. In the intermolecular pathway, the molecularity of capture changes from unimolecular to bimolecular, resulting in a decrease in effective concentration of the nucleophile. The attendant retardation of the capture step leads to a direct increase in the lifetime of the thiiranium ion, which can then racemize by any of the pathways mentioned in Section 2.2.3 or by other as-yet uncharacterized mechanisms. The overall decrease is minor, which suggests that thiiranium stereointegrity is still retained to a large extent in the course of intermolecular sulfenofunctionalization.

In the intermolecular sulfenofunctionalization of 1-octene, high selectivity for internal capture was observed. There does appear to be a substantial bias towards capture at the more substituted position, as the thermodynamic difference between the two prodcuts is unlikely to account for the high selectivity. There impact of steric bias was modest, with the less hindered position being favored 4:1 in the sulfenofunctionalization of **88d**. It is uncertain whether this is a kinetic or thermodynamic preference. Nitrile capture was found to be reversible as well, and even with excess nitrile in solution, the yield was modest at best. The site selectivity of nitrile capture for substrates other than 4-octene were not investigated. Further experimentation with

amines and amides showed that they, too, show substrate and condition-dependent reversibility of capture.

2.6. Conclusions.

The application of Lewis base catalysis to sulfenofunctionalization enabled the development of the first catalytic, enantioselective version of this venerable reaction. The current system displayed best results for *trans*- or monosubstituted, electron-rich or electron-neutral alkenes. The most relevant factor impacting rate was alkene electron density; impacting enantioselectivity was alkene geometry; and impacting site selectivity was the reversibility of capture and charge stabilization. This initial set of substrates also revealed clues regarding the turnover-limiting and enantiodetermining steps. The ability to observe and characterize reaction intermediates during the course of these studies stimulated a deeper investigation into the mechanism of the oxysulfenylation reaction.

Chapter 3: Formulation of Mechanistic Framework for the Catalytic, Enantioselective Sulfenylation Reaction.

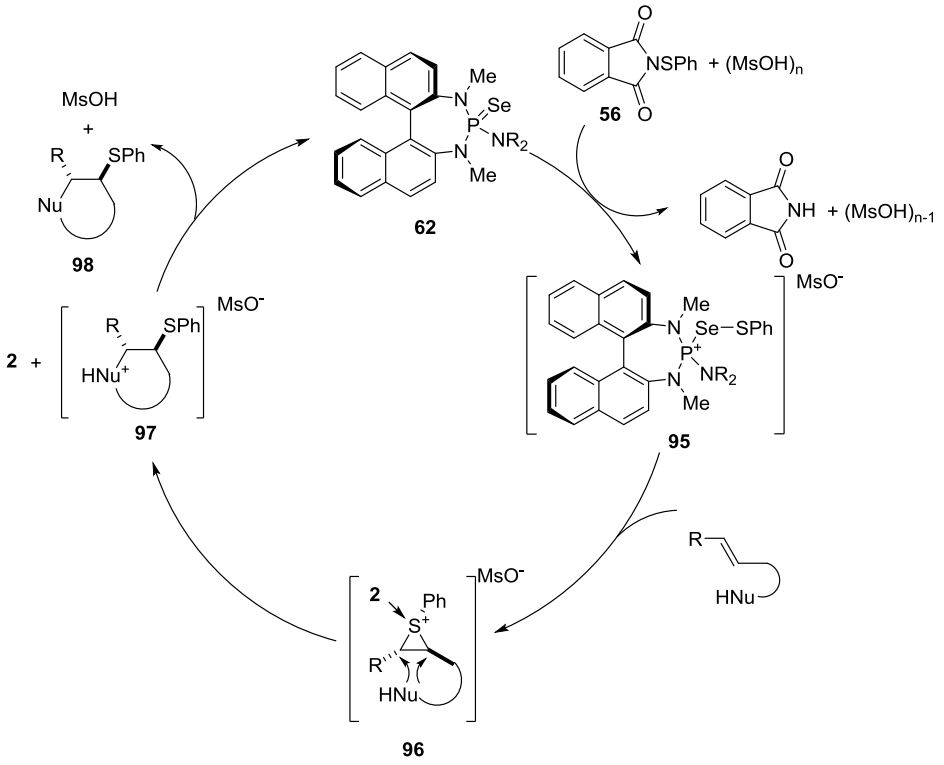
3.1. Introduction.

The experimental results from the sulfenofunctionalization of alkene substrates hinted at the turnover-limiting and enantiodetermining steps. The optimized catalyst was useful with many substitution patterns, and selectivity was diminished as a result of changes in alkene geometry. The reaction was quite selective for *trans*- and monosubstituted alkenes. In an effort to improve catalyst design and to better understand the parameters that govern reactivity and selectivity, a deeper mechanistic investigation of the oxysulfenylation reaction was conducted

There have been extensive kinetic studies on the stoichiometric sulfenofunctionalization reaction.[32] The reaction was found to be second order overall, consistent with an intermolecular rate-determining step. However, the order was not uniform and changed as a consequence of solvent polarity. A Hammett investigation found that the reaction had a negative σ value, which implied substantial buildup of positive charge at the benzylic position of styrenes undergoing sulfenofunctionalization. This evidence led to the conclusion that thiiranium ion formation is rate-determining in stoichiometric sulfenofunctionalization reactions with sulfenyl chlorides.

Based on known mechanisms for electrophilic Ad_E functionalization of alkenes, a catalytic cycle can be formulated and is depicted in Figure 12.[81] The reaction begins with displacement of the ionizable group on the sulfur electrophile by the chiral, non-racemic Lewis base. This results in a chiral, non-racemic sulfenylating reagent **95** that should also be a better electrophile due to increased Lewis acidity on the sulfur atom. The sulfenyl transfer from **95** to an unsaturated species can then proceed to generate thiiranium ion **96**. Species **96** is most likely a high-energy species and will undergo nucleophilic attack by σ-nucleophiles in solution to afford protonated intermediate **97**. Deprotonation of **98** leads to the desired product. Notably, the balanced equation yields only phthalimide as a byproduct, as the acid component solely acts in a cocatalytic manner.

Figure 12. Proposed Mechanistic Cycle for Enantioselective Sulfenofunctionalization.



The postulated mechanism offers a number of testable hypotheses regarding the catalytic cycle to be formulated. There are two microscopic steps that could conceivably be the rate-determining step. Electrophilic addition of the olefin to generate **96** forms a charged, strained species. Due to the high energy of the resulting products, a late transition state where bond breaking is more advanced than bond making can be envisioned, leading to a high barrier. If this step is rate-determining a significant effect of alkene electron density should be observable, as more electron rich alkenes should undergo more facile addition. Capture of **96** by a σ-nucleophile in solution, as well as deprotonation of **95** all appear to be low-barrier processes. Alternatively the formation of **95** could also be rate-determining, with subsequent thiiranium formation being favored due to scission of the weak LB-S dative bond. Identification of the catalyst resting state should be able to differentiate between the two alternatives.

The formation of an enantiomerically enriched product requires an irreversible enantiodetermining step. Either the formation of **96** or **97** can fulfill this requirement. In the former scenario, thiiranium formation is irreversible. This implies that the catalyst, which is most likely thiophilic to some extent, is not sufficiently strong to abstract sulfur from thiiranium ions.

Subsequent stereospecific nucleophilic capture and deprotonation leads to the desired product. In this case the enantioinduction is derived from the catalyst being able to discriminate between enantiotopic olefin faces. In the latter scenario, the catalyst is sufficiently strong to form the thiiranium ion reversibly. Enantioinduction must then necessarily be derived from the relative rates of capture for complex **96** and its diastereomer. This mechanism would require that the catalyst remain associated with the thiiranium ion after formation, as decomplexation before capture would lead to racemic products. These considerations were taken into account during the design of experiments to determine the enantiodetermining step.

3.2. Goals of the Project.

The mechanistic investigations presented here focused on determining the following properties of the sulfenoetherification process: (1) the order of the reaction in each reactant, (2) the physicochemical properties of the active sulfenylating agent, (3) the constitutional and configurational stability of products under the reaction conditions, (4) the turnover-limiting and enantiodetermining steps and (5) the origin of rate differences and enantioselectivity between substrates.

3.3. Results.

3.3.1. Kinetic Experiments. A full investigation of the kinetic parameters was undertaken to identify the rate equation. The conversion of **99** was monitored by ^{19}F NMR (Fig. 2). Catalyst **100** was chosen because the rates of reaction could be followed easily over a wide range of temperatures and concentrations. The order in each component was determined by the method of initial rate kinetics (Figures 12-15). Reactions, done in triplicate, were followed to 10% conversion and the initial rates were plotted against concentration to obtain straight lines. Standard deviations are displayed on the plots. The activation parameters of the reaction were obtained by carrying out the reactions in a temperature range from –20 ^{o}C to 20 ^{o}C (Figure 17).

Figure 13. Dependence of Reaction Rate on Substrate Concentration.

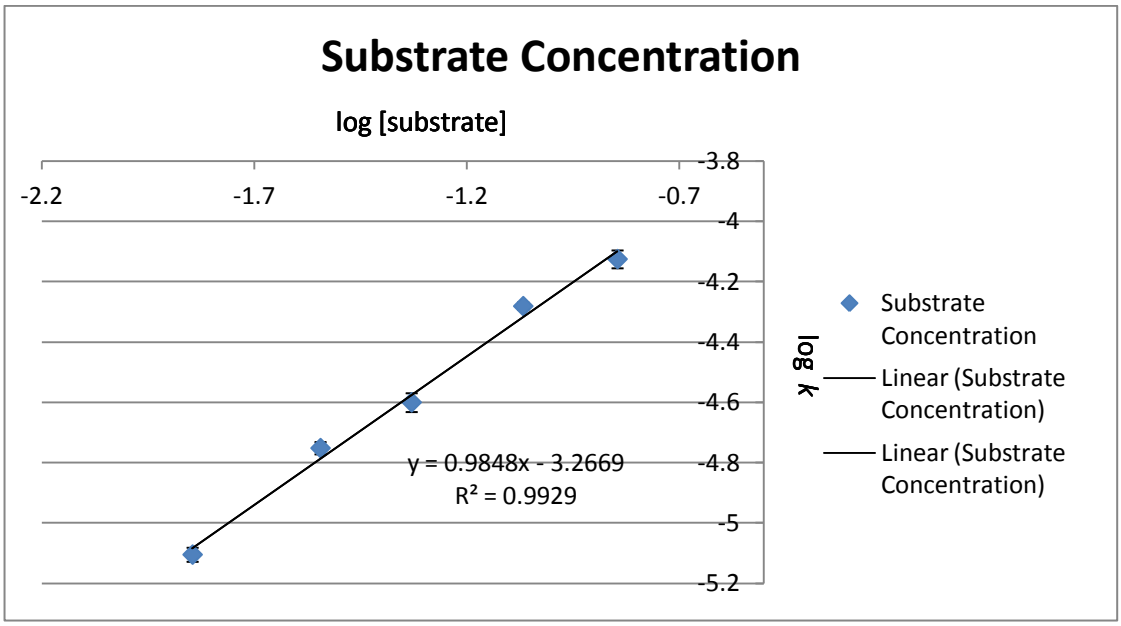


Figure 14. Dependence of Reaction Rate on Electrophile Concentration.

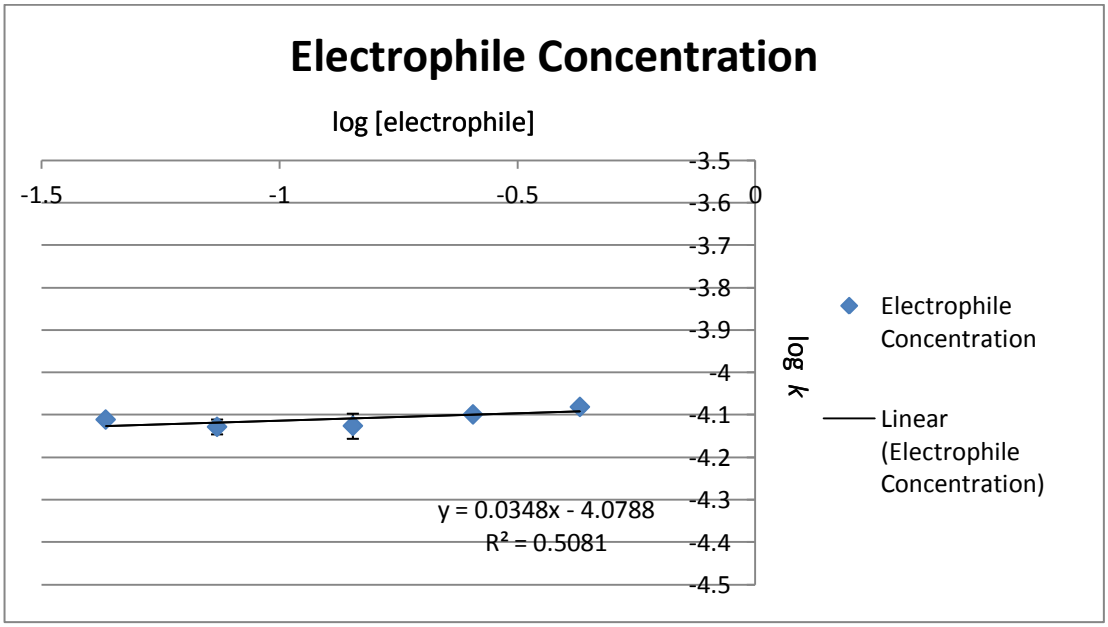


Figure 15. Dependence of Reaction Rate on Catalyst Concentration.

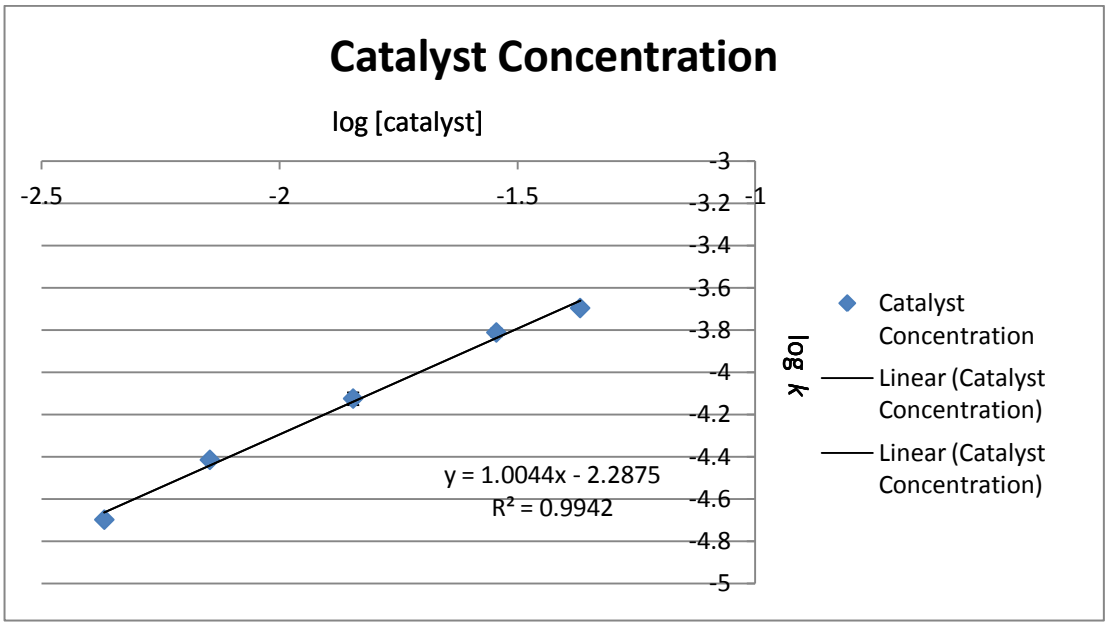


Figure 16. Dependence of Reaction Rate on Acid Concentration.

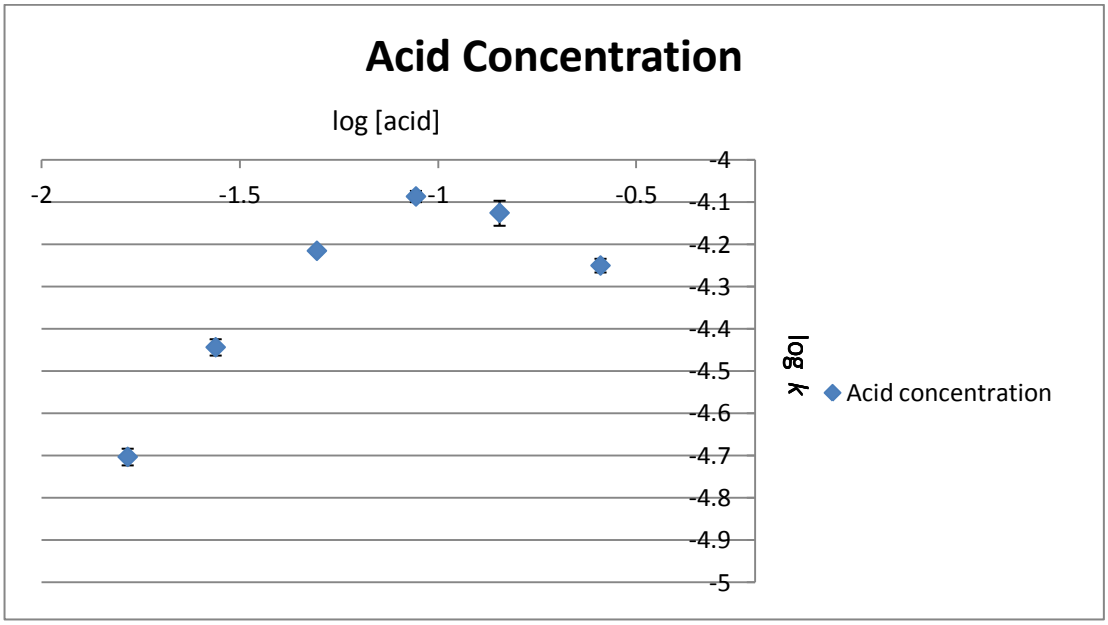
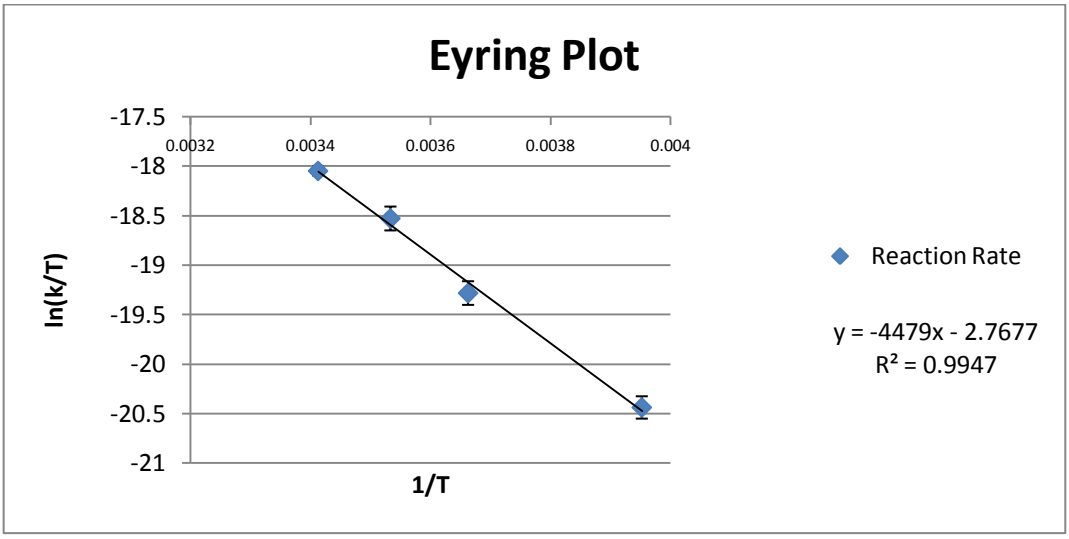
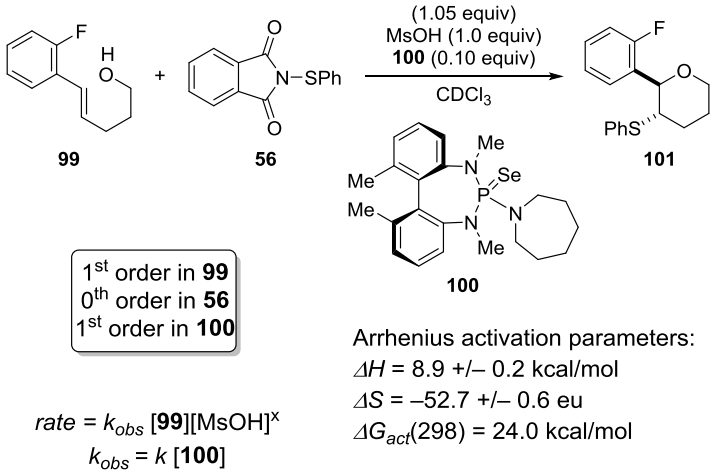


Figure 17. Dependence of Reaction Rate on Temperature.



The reaction was found to be first order in both catalyst and substrate. Zeroth order kinetics was observed for the electrophile. Interestingly, when the acid (MsOH) dependence was investigated, the rate dependence was found to be parabolic with a maximum at ca. 0.6 equiv. The enthalpy of the reaction was 8.9 +/–0.2 kcal/mol and the entropic contribution was 52.7 +/–0.6 e.u. At 298 K, the entropy term is the primary contributor to the free energy of activation of 24 kcal/mol. This data is summarized in Figure 18.

Figure 18. Kinetic study of the Lewis base catalysed sulfenofunctionalisation.



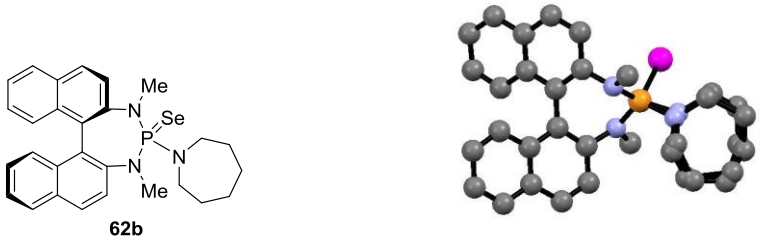
3.3.2. Isolation of the Catalytically Active Species. The proposed catalytically active species $[(R_2N)_3P{=}Se{-}SPh]^+X^-$ is assumed to transfer the sulfenium ion to an alkene, forming a thiiranium ion. Detailed knowledge about the stereostructure of the active species could help to understand the origin of enantioselectivity. Accordingly, the isolation and crystallographic characterisation of $[(R_2N)_3P{=}Se{-}SPh]^+X^-$ was investigated.

The requirement of a Brønsted acid co-activator for **56** is well-documented.[68] Thus, when **56** was combined with **62b**, no change in the ^{31}P spectrum was observed. Upon addition of MsOH, the signal for **62b** at 91.6 ppm is replaced by a signal at 60.4 ppm. The peak at 60.4 ppm can also be observed under the reaction conditions for slower-reacting substrates such as **57d** or **57j**, indicating that the catalyst-resting state is the activated complex (no peak at 91.6 ppm was observed under these conditions). The ^{31}P shift is comparable to other substrates that have the $[P{=}Se{-}C]^+$ moiety.[82]

Other selenophosphoramides that have been synthesized displayed similar upfield shifts in ^{31}P NMR spectra after exposure to sulfenylating agents.[83] The resulting compounds were persistent. After conversion of **62** to **95**, no changes in ^{31}P NMR spectra were observed after 4 d. The remarkable stability of putative complex **95** encouraged studies towards the crystallization and characterization of this species.

First, a crystal structure of the parent species was obtained by crsytallization from CH_2Cl_2/pentane. The Se-P-N_{endo} angle was 109.0° whereas the corresponding Se-P-N_{exo} angle was 111.6°. The P-center is almost completely tetrahedral. The P-Se bond distance is slightly shorter at 2.098 Å compared to HMPA(Se), which has a P-Se bond length of 2.120 Å.[84] The packing of **62b** was disordered at the external amine moiety, which suggests that the amine component can easily rotate. The rate of rotation of the groups on the exocyclic amine is substrate dependent and broadening of ^{31}P NMR spectra was observed for the more hindered **62e**.[79] Notably, electron density for the azepane carbons bound to nitrogen were localized close to the P-Se axis. Thus, it appears that the methyl groups on the endocyclic nitrogens act as gatekeepers, forcing the substituents on the exocyclic amine to adopt an eclipsing conformation with the P-Se bond. The N-Se bond lengths were within a 0.05Å range of each other, elongation was not observed.

Figure 19. Crystal Structure of Selenophosphoramide (*R*)-62b.



Next, crystallization of sulfenylating agent **95** was attempted. Orienting experiments focused on the identification of suitable conditions for generating the active species $[(R_2N)_3P{=}Se{-}SPh]^+X^-$ without any byproducts that would disrupt the crystallization process. The first approach relied on the reaction of a selenophosphoramide with $[PhS(SMe_2)]SbCl_6$[85] which had been used as an of the S-phenyl transfer agent to alkenes (Scheme 37, equation 1). This reagent was also competent in transferring the sulfenyl moiety to the catalyst forming the active species along with volatile Me_2S as the sole byproduct. The formation of the active species was confirmed by the appearance of a diagnostic ^{31}P resonance at 62.4 ppm. Unfortunately, during the crystallization attempts, a disproportionation reaction occurred reducing the sulfenyl group to PhSSPh while oxidizing the selenophosphoramide to the dicationic dimer $[(R_2N)_3P{=}Se{-}Se{=}P(NR_2)_3]^{2+}\ 2SbCl_6^-$ (Scheme 37, equation 2). An X-ray crystal structure of the latter could be obtained, which demonstrated how the groups in the actual active species might be oriented.

$$(R_2N)_3P{=}Se + [PhS(SMe_2)]^+\ SbCl_6^- \xrightarrow[-\ SMe_2]{} [(R_2N)_3P{=}Se{-}SPh]^+\ SbCl_6^- \qquad (a)$$

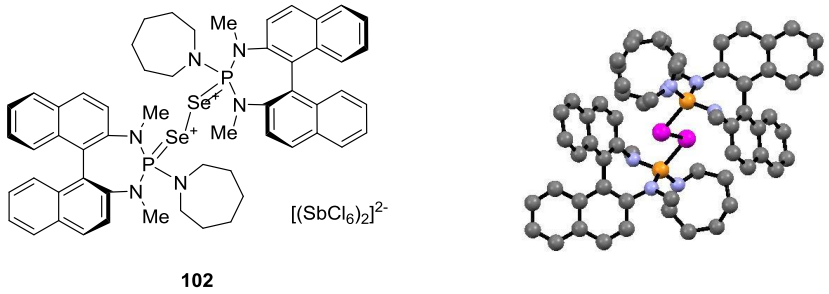
$$2\ [(R_2N)_3P{=}Se{-}SPh]^+\ SbCl_6^- \xrightarrow[-\ PhSSPh]{} [(R_2N)_3P{=}Se{-}Se{=}P(NR_2)_3]^{2+}\ 2SbCl_6^- \qquad (b)$$

Scheme 37

In this complex, the N-P-Se angles are distinct, with the two endo nitrogens having N-P-Se angles of 108.0° and 115.1°. The N_{exo}-P-Se angle is also much more acute, at 105.4°. Thus, in the dimeric complex, all three nitrogens appear to be differentiated, and the phosphorus center is more planarized. The P-Se angle is greatly lengthened to 2.244 Å. The formal bond P-Se bond order is closer to a single bond with positive charge on the phosphorus as opposed to a P-Se double bond with charge on the selenium. The N_{exo}-P distance is 1.618 Å, compared to 1.633 and 1.638 Å for the endocyclic nitrogens. The C_{ring}-N_{exo}-P-Se dihedral is 31°, which suggests some

eclipsing interaction between the N_{exo} substituent and the Se-substituent. The N*exo*-P-Se-Se dihedral is -162.8° and the Se-substituent points directly over the biaryl ring. Experimentally, the disproportionation of sulfenylated selenophosphoramides could not be avoided. Eventually, the crystal structure of a sulfenylated sulfenophosphoramide was isolated by Dr. E. Hartmann, which further assisted the investigation.[40]

Figure 20. Crystal structure of bisselenophosphoramide 102.

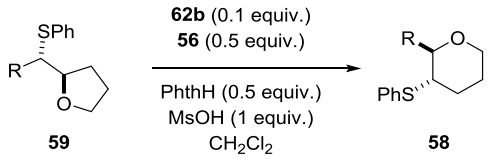


102

3.3.3. Stability of Thioethers. The site-selectivity ratios obtained in the sulfenofunctionalization of alcohols can be the result of kinetic or thermodynamic capture. If capture is reversible, as evidenced in the nitrilium ion case, the observed isomer ratios would be expected to be thermodynamic. However, this possibility also raised the concern that enantioselectivity could be decreased if thiiranium ion stability was impacted as a consequence of reversible capture. In order to determine the configurational and constitutional stability of the products under the reaction conditions, isolated thioethers were resubjected to the reaction mixture. The thioethers under investigation were found to not be configurationally stable, and a range of behavior with regards to *endo*/*exo* interconversion was observed. When **59k** was resubjected to the reaction mixture, no isomerization was observed at 23 °C (Table 11, entry 1). In contrast, **59j** isomerized at 23 °C but not at -10 °C (entries 3 and 4). Furan **59g** was found to isomerize quickly at 23 °C and slowly at -20 °C (entries 5, 6). The constitutional stability of the products appears to be dependent on the nature of the thiiranium intermediate: products that are obtained from the formation of less stable thiiranium ions isomerize slower. This data is consistent with regeneration of the thiiranium ion in solution from the products and reversible capture of the thiiranium ion by the nucleophile.[68] This led to interesting questions regarding the stereochemical stability of the thiiranium ions; if they are accessible in solution, can any racemization of the thioethers be detected? In all cases (**59k**, **59j** and **59g**), the re-isolated

material was obtained with 100% e.s. (entries 2,4 and 6). It can be concluded that the stereochemical purity of the products do not erode under the reaction conditions.[63]

Table 11. Determination of Constitutional and Configurational Stability of Products.



entry	thioether	starting *endo*/*exo*[a]	temp, °C	time, h	final *endo*/*exo*[a]	e.r.[b]	e.s., %[c]
1	**59k**	1:50	23	3	1:50	-	-
2	**59k**	-	-10	48	-	83:17	100
3	**59j**	<1:99	23	3.5	3.5:1	-	-
4	**59j**	<1:99	-10	48	<1:99	-	-
5	**59g**	1:8	23	16	30:1	96:4	100
6	**59g**	1:1	-20	48	5.5:1	96:4	100

[a]Determined by ^{1}H NMR analysis of crude reaction mixture. [b]Determined by CSP-SFC analysis. [c]e.s. = $[ee_{start}/ee_{final}]*100\%$

3.4. Discussion.

3.4.1. Reactant Order. The reaction was found to be first order in catalyst and substrate but zero order in electrophile. Thus, whereas both catalyst and alkene participate in the turnover-limiting step, the electrophile does not. The various ^{1}H and ^{31}P NMR experiments demonstrated that **62b** is quickly converted to complex **95** under the reaction conditions. Conditions where there is less electrophile than catalyst were not tested.

The order in both substrate and catalyst was first order. Thus, the thiiranium ion is not ligated by more than one catalyst at any point before the turnover-limiting step. The reaction was also pseudo-first order overall. The concentraion of sulfenylating agent stays constant throughout the reaction, which implies that neither the Lewis base nor the sulfenylating complex experience product inhibition.

The conversion of **56** and **62b** to **95** is much faster than thiiranium formation. In addition, the equilibrium between **62b** and **95** is very highly in favor of **95**. Consequently, the catalyst is

saturated with electrophile in the initial phase of the reaction. Importantly, the concentration of sulfenylated catalyst does not change as a function of electrophile concentration above 1 equiv of electrophile with respect to catalyst. Thus, with an excess of electrophile over catalyst zero-order kinetics for the electrophile is obserbed. Properly, the electrophile is *pseudo*-zero order, as order in electrophile would be expected to be observable if less **56** than **62b** were present in the reaction mixture.[86]

The order in acid is curved. Curvature in kinetic plots usually results from a change in mechanism. At low concentration, the order in acid appears to be close to 1. At these concentrations, there is likely insufficient acid to fully convert all of the catalyst to the sulfenylating complex. This conclusion agrees with results from these laboratories, which demonstrated that 3-4 equiv of acid with respect to catalyst is necessary for complete formation of **95e** (R = *i*-Pr) from selenophosphoramide **62e**.[87] If this were the entire case, the curvature would be expected to level off and flatten once the catalyst is saturated. Instead, a downward curvature is observed. Excess methanesulfonic acid slows the reaction down. A possible explanation is protonation of the substrate. The presence of positive charge would disfavor the formation of a positively charged species such as a thiiranium ion. Thus, excess acid serves to reduce the effective concentration of substrate in the reaction. The overall rate equation is then shown in Figure 18. Alternatively, the addition of acid may result in changes in the overall dielectric of the solvent mixture. Sulfonic acids strongly hydrogen bond to each other in nonpolar media, and thus may be forming locales of higher dielectric constant.[88] These areas could then potentially sequester acid or substrate, lowering the effective concentration. The current hypothesis based on the study of the related amino- and carbosulfenylation reactions is substrate protonation.[87]

Eyring analysis of the reaction was performed in order to obtain activation parameters for the reaction. The results were in qualitative agreement with calculations performed by Dr. Hao Wang.[40] The activation parameters of $\Delta H^{\ddagger}$ = 8.9 kcal/mol and $\Delta S^{\ddagger}$= 52.7 e.u. imply a highly ordered transition state in which the reaction barrier is primarily entropy-driven. This profile results from the organizational requirement wherein the alkene must approach the catalyst in a highly restricted conformational landscape. In fact, the entropic barrier is comparable to those of other highly-conformationally-restricted, bimolecular transition states such as those of Diels-Alder reactions[89], MBH reactions[90] or the Lewis base promoted aldol addition of trichlorosilyl

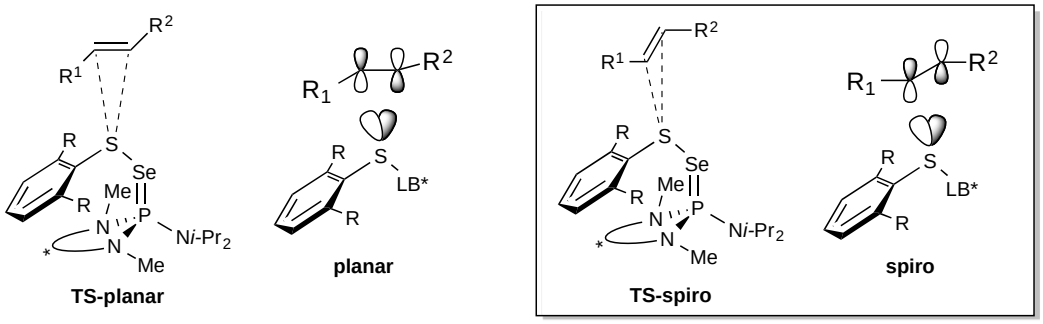
enolates.[91] Notably, the entropic parameter is much larger than that for the simple stoichiometric sulfenofunctionalization of alkenes. Thus, it appears that while the catalyst substantially increases the entropic cost of the reaction, it reduces the enthalpic parameter by an even greater amount.

3.4.2. Turnover-Limiting Step. Transfer of the sulfenium ion to the alkene occurs from the sulfenylated selenophosphoramide $[(R_2N)_3P{=}Se{-}SPh]^+X^-$. First order kinetic behavior in both substrate and catalyst, as well as second-order overall kinetic behavior suggests that thiiranium ion formation is the turnover-limiting step of the reaction. If thiiranium ion capture were turnover-limiting, first order overall kinetic behavior would be expected, and species **95** should not be visible in the reaction. Furthermore, buildup of thiiranium ion **96** over the course of the reaction is not observed, which would have been the case for turnover-limiting thiiranium ion capture. The formation of **95** cannot be turnover-limiting either, as in that case, no order in alkene should be observed. The catalytically active species $[(R_2N)_3P{=}Se{-}SPh]^+X^-$, represents the resting state of the catalyst. Its existence is supported by ^{31}P NMR spectroscopic analysis, in which the diagnostic signal for **62** (80–90 ppm, depending on the catalyst structure) disappears and a new resonance at ca. 60 ppm is observed, which is diagnostic fo **95**. This value is in accord with previously reported, analogous compounds of the type $[(R_2N)_3P{=}Se{-}YAr]^+X^-$.[16,87]

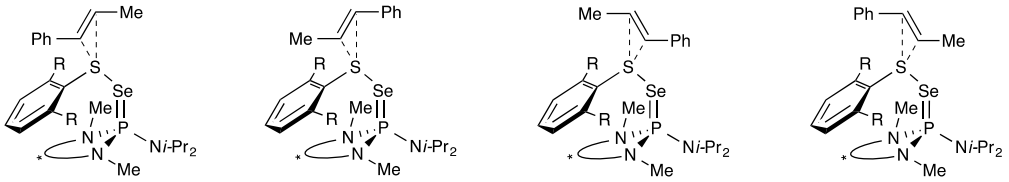
3.4.3. Origins of Selectivity. In the process of catalyst optimization, product enantioenrichment was observed to vary widely with the choice of exocyclic amine. The crystal structures obtained for the first time delivered a structural basis of selectivity. The substituents on the exocyclic amine in **102** serve to orient the Se-S bond over one of the biaryl rings. The approach of the alkene, which occurs orthogonal to the Se-S bond to maximize overlap with the lone pairs on the sulfur, then proceeds in close proximity to the stereogenic axis of **102**.

Table 12. Transition States at the B3LYP/6-31G(d) level with CPCM Correction.[40]

a

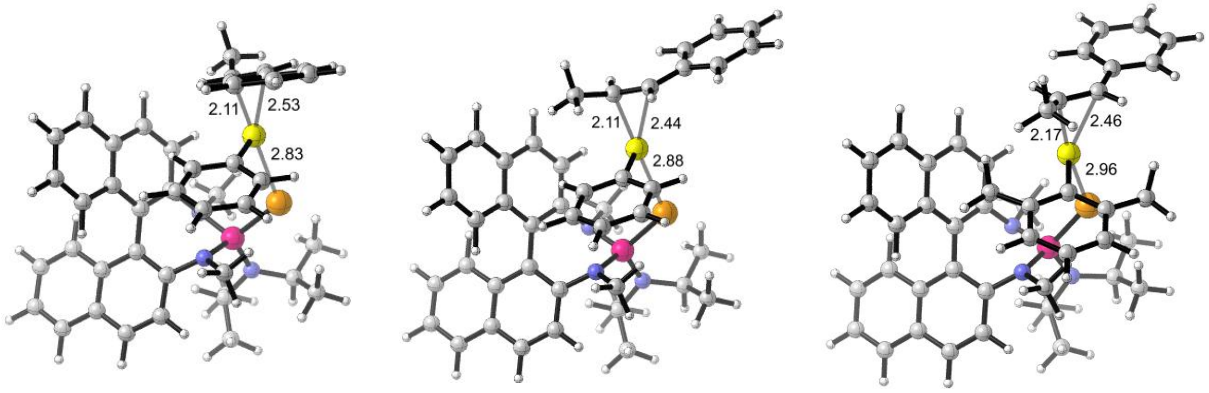


b



R = H	**H-TS-major1**	**H-TS-major2**	**H-TS-minor1**	**H-TS-minor2**
	ΔΔG = 0.0 kcal/mol	ΔΔG = 1.5 kcal/mol	ΔΔG = 1.7 kcal/mol	ΔΔG = 3.0 kcal/mol
R = Me	**Me-TS-major1**	**Me-TS-major2**	**Me-TS-minor1**	**Me-TS-minor2**
	ΔΔG = 0.0 kcal/mol	ΔΔG = 1.8 kcal/mol	ΔΔG = 3.5 kcal/mol	ΔΔG = 5.4 kcal/mol

Table 13. Transition State Models and Distortion Interaction Values for Selected Transition States.[40]



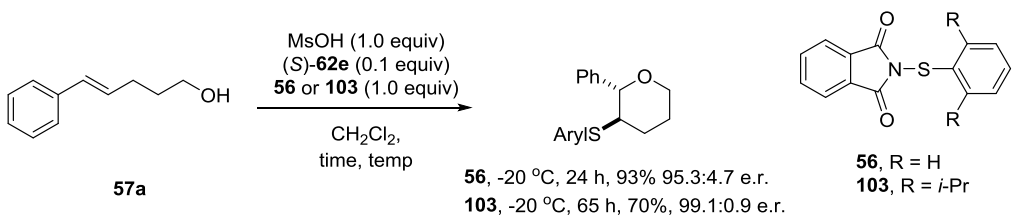
	$\Delta E_{dist\_}\mathbf{A}^a$	$\Delta E_{dist\_}\mathbf{B}^b$	ΔE_d	ΔE_i	$\Delta E_{act}{}^c$	ΔH	ΔG	π(C=C)-σ*(S-Se)^d
H-TS-major1	**9.6**	**26.1**	**35.7**	**-24.8**	**10.9 (0.0)**	**11.9 (0.0)**	**23.9 (0.0)**	**63.3 (6.7)**
H-TS-major2	10.7	27.4	38.1	-25.6	12.5 (1.6)	13.5 (1.6)	25.4 (1.5)	57.5 (0.9)
H-TS-minor1	**10.4**	**28.1**	**38.5**	**-25.9**	**12.6 (1.7)**	**13.6 (1.7)**	**25.6 (1.7)**	**64.2 (7.6)**
H-TS-minor2	13.3	33.5	46.8	-32.2	14.6 (3.7)	15.2 (3.3)	26.9 (3.0)	56.6 (0.0)
Me-TS-major1	**7.8**	**22.8**	**30.7**	**-19.9**	**10.8 (0.0)**	**11.2 (0.0)**	**25.0 (0.0)**	**61.7 (7.3)**
Me-TS-major2	9.0	27.2	36.1	-22.4	13.7 (2.9)	14.7 (3.5)	26.8 (1.8)	55.9 (1.5)
Me-TS-minor1	**9.4**	**28.6**	**38.0**	**-23.0**	**15.0 (4.2)**	**15.3 (4.1)**	**28.5 (3.5)**	**62.1 (7.7)**
Me-TS-minor2	9.1	29.9	39.0	-23.6	15.4 (4.6)	15.5 (4.3)	30.4 (5.4)	54.4 (0.0)

The isolation and crystallization of **102** enabled a more detailed transition state model to be fromulated. The study of the competing transition states resulting from (*Si*) and (*Re*)-face attack of the alkene did not show any steric basis for energy difference. An interaction/distortion analysis identified catalyst distortion as the primary contributor to the energy difference in the transition states.[40] Thus, the favored approach H-TS-major 1 is 1.7 kcal/mol more stable than H-TS-Minor 1 at 253 K. The decomposition of this value into its components shows that the H-TS-Minor 2 has a stronger interaction between sulfenium and alkene, with a difference of -1.1 kcal/mol. However, the total distortion of the individiual components is much worse, at a total of +2.8 kcal/mol. This distortion drives the overall energy gap. The gapi is even bigger for sulfenyl groups with 2,6-substituents. The difference between Me-TS-Major 1 and Me-TS-Minor 1 is 3.5 kcal/mol. The distortion energy in this case is a sizable 7.3 kcal/mol, which dominates the

interaction process. The low reactivity of catalysts of family **62** appears to be partially driven by the problems the catalyst encounters in accomodating the alkene moiety. The alternative transition states leading to the same enantiomer, designated TS-2, are uniformly higher in energy than TS-1 and are not expected to substantially contribute to the enantioselectivity.

Thiiranium ion formation is also likely the enantiodetermining step. The competing hypothesis for the enantiodetermining step in accord with Figure 12 is thiiranium capture. For such a mechanism to be operative two conditions need to be satisfied: (1) the "thiiranium ion" must exist in the form of a charged sulfurane, or at least in very tight association with the Lewis base **62** and (2) the Lewis base must not be able to exchange thiiranium ions once formed. There is no direct evidence that contradicts these requirements. However, in numerous iterations of the sulfenofunctionalization reaction, neither the elemental nature, nor the electronic nor the steric properties of the nucleophile was found to have a significant effect on enantioselectivity.[40,83,87] In the regime of enantiodetermining thiiranium capture, the nucleophile, as opposed to the alkene, would be expected to dominate the selectivity effects, as the transition state for capture is expected to vary with nucleophile properties. The uniform selectivity observed as a consequence solely of alkene geometry is inconsistent with enenatiodetermining capture.

An analysis of the transition state for *cis*-alkenes revealed why selenophosphoramide catalyst family were unsuitable for the functionalization of *cis* alkenes.[83] The competing transition states for *cis* thiiranium ion formation are not differentiated on the basis of their substituent size, and both substituents encounter unfavorable steric clashes with the *S*-aryl moiety. These interactions account for both the low reactivity and low selectivity observed for (*Z*)-alkenes. The combined calculations did not suggest any possible improvements in catalyst architecture for increased selectivity. However, they were successful in predicting increased selectivity as a consequence of increased bulk of the sulfenylating agent. The combination of crystal structures and calculations directly led to the development of electrophile **103**, which showed a significantly improved selectivity profile for the sulfenofunctionalization of alkenes (Scheme 38). Because the energy difference between the competing transition states comes about as a result of catalyst distortion, no simple modifications to increase the selectivity for poorly performing substrate classes were found. The design and synthesis of catalysts to expand the alkene scope for enantioselective sulfenofunctionalization is left to future generations.



Scheme 38

3.4.4. Configurational and Constitutional Stability of Products. Thiiranium ions were found to be uniformly configurationally stable under the reaction conditions. In all cases, no change in enantioselectivity was observed after resubjecting the products to the reaction conditions. For furan **59k** this result is inconclusive, as there were no indications that the thiiranium ion reformed under the reaction conditions. However, in the case of **59g** and **59h**, although isomerization was observed, complete enantiospecificity was retained. Mechanistically, reformation of the thiiranium ion under the reaction conditions essentially significantly prolongs the thiiranium ion lifetime in solution, as it now spends some non-negligible portion of its time in thiiranium ion form. However, the lack of enantioerosion implies that capture still outcompetes racemization processes. Thus, the mechanistic groundwork developed during the intermolecular stoichiometric sulfenylation helped identify conditions where enantioenrichment is retained even in the presence of excess olefin and other potential Lewis bases. Notably, phthalimide incorporation was not observed in this case. The fast intramolecular cyclization outcompetes the intermolecular capture process even when the thiiranium ion can be reformed.

The constitutional integrity of the thiiranium ions was not constant across the substrates. Thiiranium ions isomerized in direct correlation with their reactivity in the reaction, i.e. the more reactive substrates reformed their thiiranium ions faster. Re-formation of the thiiranium ion is the microscopic reverse reaction of thiiranium capture. Thus, the energy barrier to re-formation will be dictated both by the strength of the nucleophile and the stability of the thiiranium ion. Since in all cases the nucleophiles are alcohols, the energy associated with nucleophile departure is close to constant across the thiiranium ions. Consequently, thiiranium ions that are more stable, i.e. have lower ground-state energies can re-form faster. Thus, a direct comparison to the initial thiiranium ion formation can be drawn. And since thiiranium formation is turnover-limiting, a clear downward trend in reactivity (i.e. higher energy to initial formation) can then be translated into a clear downward trend in rate of reformation.

3.5. Conclusions.

The kinetic and crystallographic studies described in this section definitively established both the properties and the behavior of intermediate **95**. The formation of **95** from **62b** proceeds quickly in the presence of MsOH and **56**. Sulfenylating agent **95** was observed and characterized spectroscopically. The reaction of **95** with alkene **57** was established as the turnover-limiting step of the reaction based on the order of the reactants. The turnover-limiting thiiranium ion formation step accounts for the dependence of reaction rate on alkene electron density and its insensitivity to the nucleophile. The enantiodetermining step was assigned as thiiranium ion formation as well, albeit indirectly. The definitive reaction, which is to observe the stereoerosion during the isomerization of products in the presence of the opposite enantiomer of the catalyst, has not yet been performed. However, the insensitivity of enantioselectivity to the nucleophile component, coupled with its high sensitivity to changes in the alkene component, also suggest that thiiranium ion formation is enantiodetermining. A comprehensive model for the enantioselectivity could not be generated from calculation of the transition state. Instead, the diastereomeric transition states leading to the two enantiomers were found to primarily differ in distortion energy. However, in conjunction with X-ray crystallography data, the unique selectivity of the catalysts of family **62** could be explained: the exogenous amine substituent forces the SAr moiety over the biaryl backbone. The approach of the alkene over the biaryl backbone spiro to the SAr group induces conformational changes in the catalyst that then dictate selectivity.

At this juncture, the project diverged in different directions. Development of novel electrophiles for sulfenofunctionalization was performed by Dr. Eduard Hartmann. The use of carbon nucleophiles for thiiranium capture was performed by Drs. Alex Jaunet, Sergio Rossi and Matthew Webster. The aminosulfenylation reaction was taken up by Mr. H. M. Chi. The extension of the sulfenylation to new classes of oxygen-bearing nucleophiles then constitutes the remainder of this thesis.

Chapter 4: Catalytic Enantioselective Functionalization of Alkenes with Phenols

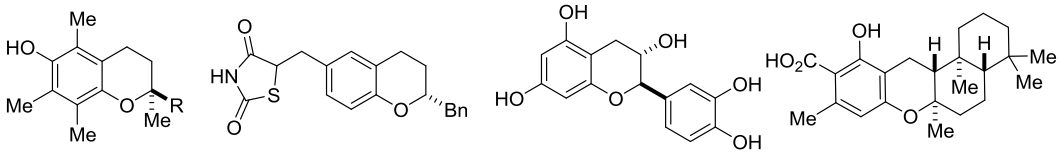
4.1. Introduction.

The initial substrate survey and subsequent mechanistic experiments painted a more complete picture of sulfenofunctionalization. The successful extension of Lewis base catalysis principles to carbosulfenylation and aminosulfenylation has greatly expanded the nucleophile scope of the sulfenofunctionalization reaction.[79,83,134] So far, both alcohols and carboxylic acids proved to be competent nucleophiles. However, phenols, which constitute the other major class of oxygen nucleophile had not been tested so far. Thus, the extension of sulfenofunctionalization chemistry to the functionalization of phenols was undertaken.

4.2. Background.

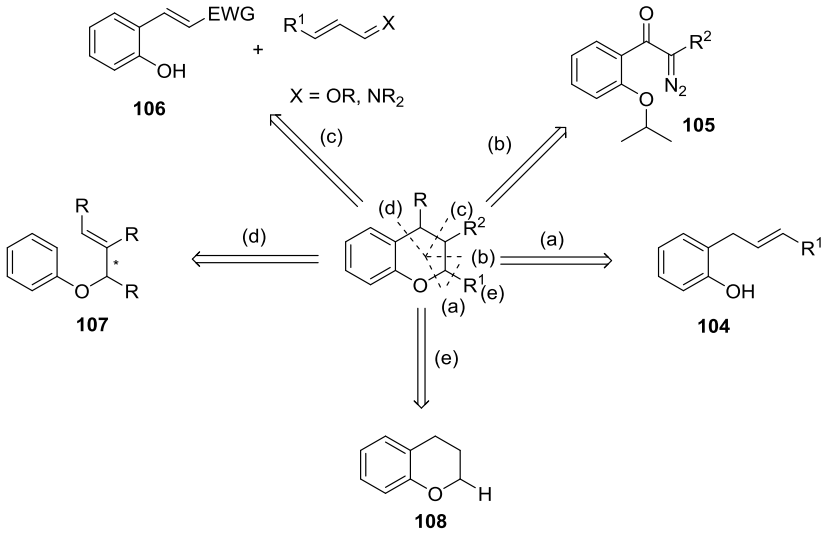
One of the simplest benzofused heterocycles, the chroman core is a privileged scaffold for bioactive compounds, with representatives displaying antioxidant, antitumor, antibacterial, and other therapeutic properties (Chart 3).[92] Its presence in pharmaceutically relevant targets has led to a variety of methods for its enantioselective construction.

Chart 3



The importance of the chroman motif in organic molecules is reflected in the myriad protocols that have been developed for its synthesis. Five major disconnections have been identified, each of which leads to a different starting material (Scheme 39). These are: (a) cyclization of a 2-allylphenol **104**, (b) C-H functionalization of an *O*-alkyl phenol **105**, (c) intermolecular double Michael reaction of a phenol, **106**, with an unsaturated carbonyl

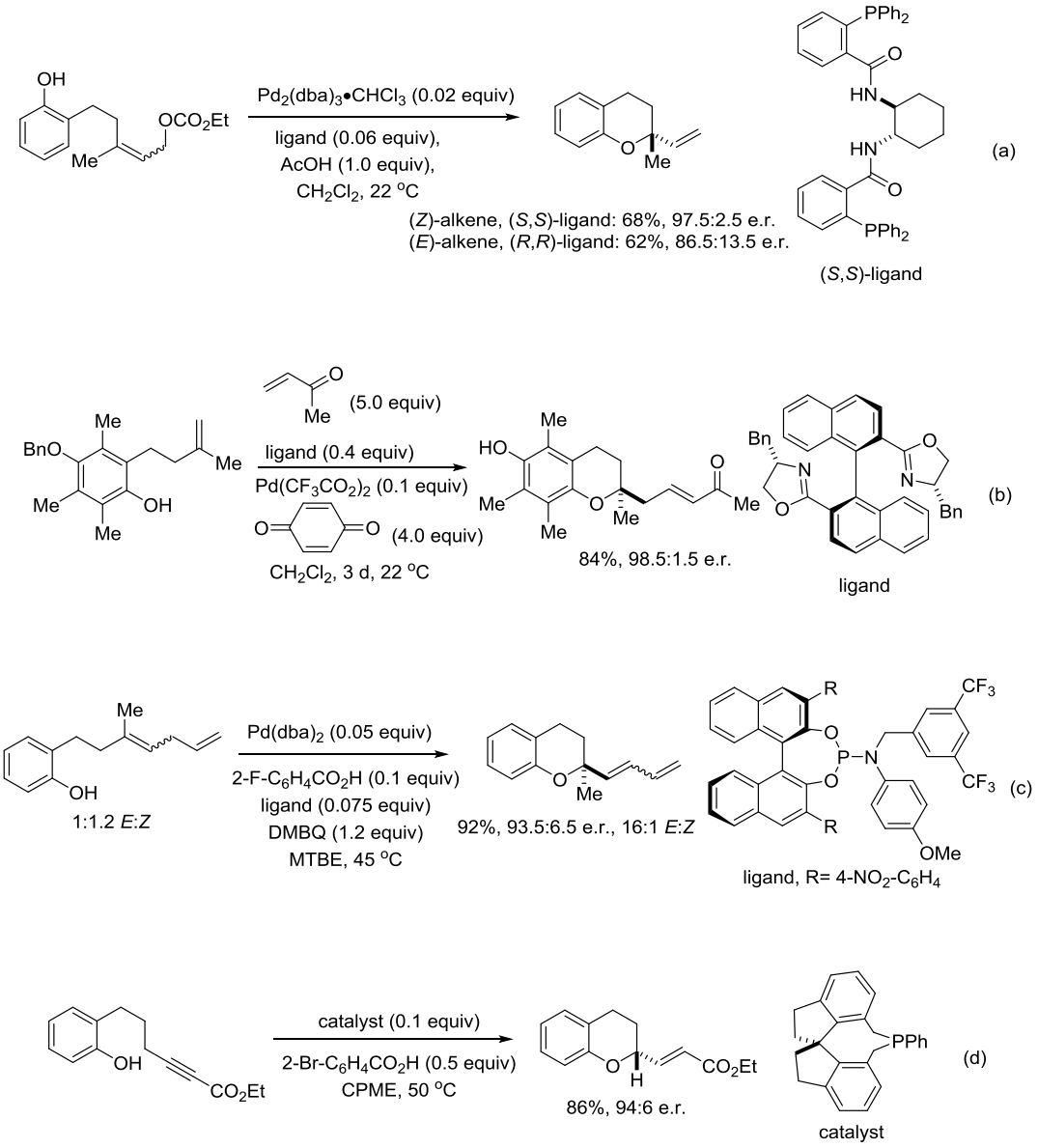
derivative, (d) intramolecular Friedel-Crafts-type cyclization of an *O*-allylphenol **107** and (e) direct functionalization of the 2-position of the parent chroman **108**.



Scheme 39

To date, for each of the pathways (a)-(c), enantioselective versions have been developed, whereas pathway (d) is diastereoselective due to the presence of a stereogenic center. The enantioselective variant of pathway (b) has been accomplished under Rh(II) catalysis,[93] pathway (c) is amenable to enantioselective catalysis by secondary amines,[94] whereas pathway (d) can be accessed either as a two-step epoxidation-ring opening process or in a single step using transition metal catalysis.[95] Each of these pathways have distinct substitution requirements that are reflected in the products they afford. Notably, none of these approaches directly lead to the 2- or 2,3-difunctionalized chromans that are accessible through pathway (a).

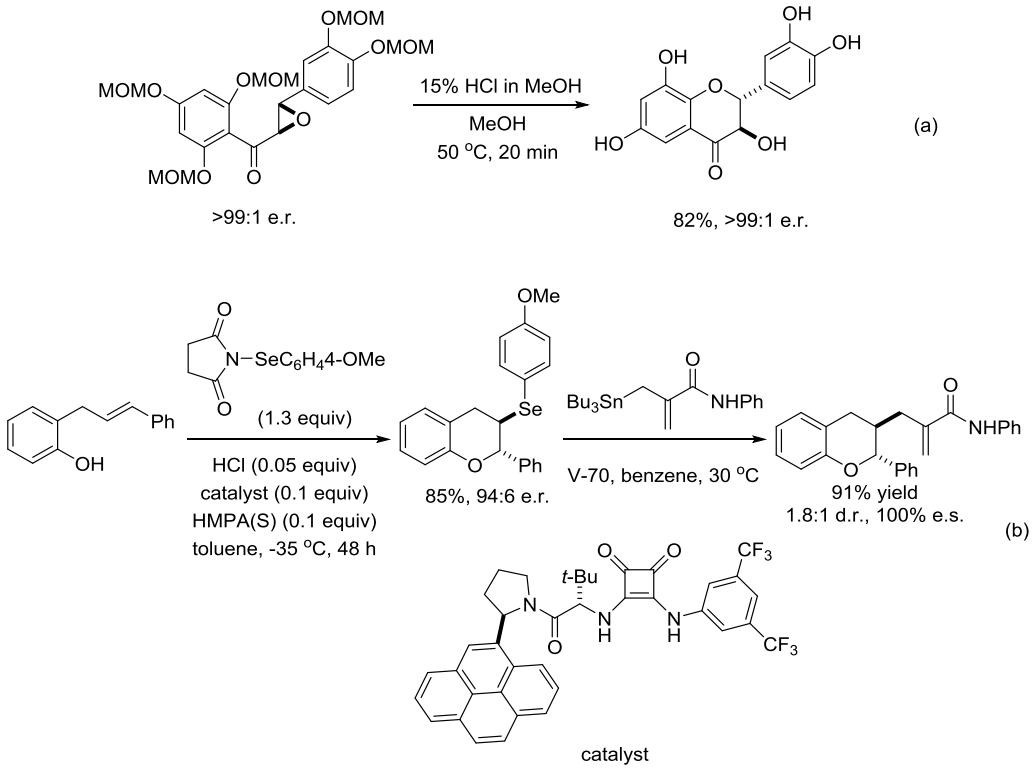
Because many important natural products bear the 2-substituted chroman motif, substantial effort has been devoted to developing enantioselective reactions that proceed through pathway (a).[96] Selected examples include: (1) asymmetric allylic substitution, which proceeds through capture of an allylpalladium intermediate by the phenol oxygen (Scheme 40a);[97] (2) tandem oxidative functionalization/Heck-coupling, wherein a similar allylpalladium intermediate is generated from an isolated alkene (Scheme 40b);[98] (3) oxidative functionalization of a skipped diene precursor to form an allylpalladium complex (Scheme 40c);[99] and (4) Lewis-base catalyzed cyclofunctionalization of the γ-position of an ynoate with a phenolic hydroxyl group (Scheme 40d).[100]



Scheme 40

Despite the impressive selectivities and obvious utility of these methods, they are not applicable to the synthesis of chromans bearing an additional substituent at the 3-position. Hence, direct synthesis of enantioenriched, *anti*-2,3-difunctionalized chromans is usually accomplished diastereoselectively from an acyclic epoxide or diol precursor (Scheme 41a).[101] The difunctionalization of γ-substituted 2-allylphenol to afford chromans with stereocenters at both the 2- and 3- positions remains rare.[102] A recent example involves the stereocontrolled generation and intramolecular opening of a seleniranium ion by a phenolic hydroxyl group to form a 2-seleno-3-arylchroman (Scheme 41b).[103] The reaction proceeds as a DYKAT, since the

seleniranium ion in question is not stable under the reaction conditions. Only aryl substituents were incorporated at the 2-position. The product could be functionalized further by formation of a C-C bond through the intermediacy of a *C*-centered radical. The diastereoselectivity was poor but the stereocenter adjacent to the oxygen atom remained unaffected.



Scheme 41

As part of the ongoing program on enantioselective sulfenofunctionalization of alkenes, extension of the sulfenofunctionalization reaction to the synthesis of chromans represented an appealing target. Sulfenofunctionalization of alkenes is a longstanding strategy for the efficient introduction of sulfur moieties into organic molecules.[62,104] We sought to apply the expertise gained in the study of enantioselective oxysulfenylation of alkenes to the synthesis of difunctionalized chroman derivatives. If both the 2- and the 3-positions of the newly formed ring system are functionalized, the final products can be transformed into a variety of useful compounds, thus constituting a general and selective method for the synthesis of chroman derivatives.

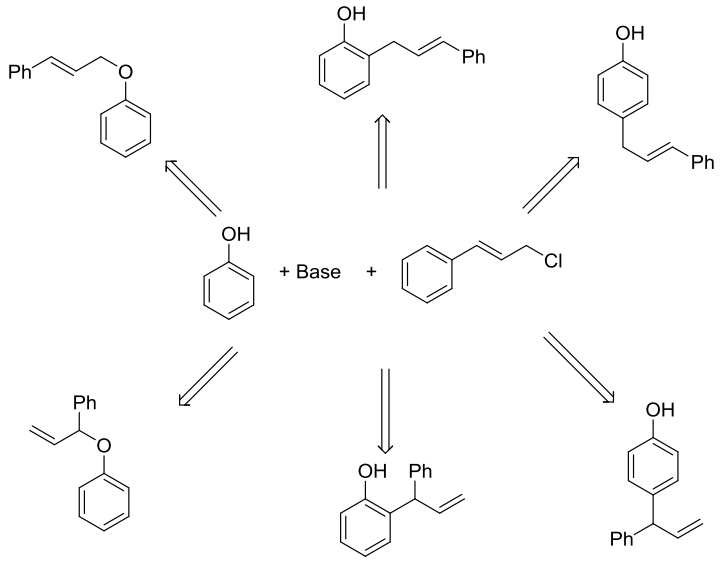
4.3. Goals of the Project.

In the course of previous work from these laboratories, the dependence of rate-, enantio- and site-selectivity of sulfenoetherification on the substitution pattern and electron density of the alkene component have been investigated.[20] However, changes in the reaction outcome as a function of structural variations at the nucleophile were not determined. Furthermore, the tether length was kept constant across the different substrates. The primary goals of this study were to evaluate the influence of: (1) the steric and electronic properties of the nucleophile, in isolation and in competition, (2) the tether length, and (3) the presence of other Lewis basic functional groups for the sulfenoetherification of alkenes with phenolic hydroxyl groups as nucleophiles. To achieve this goal, a study for the synthesis of 2-cinnamylphenols was undertaken.

4.4. Results.

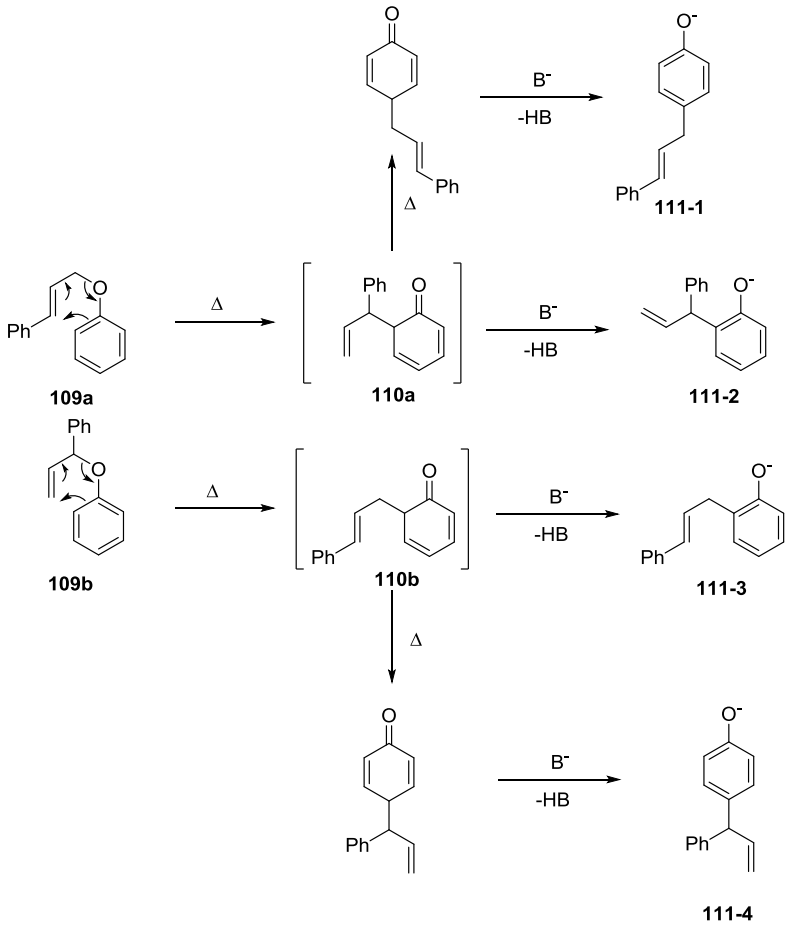
4.4.1. Synthesis of 2-Cinnamylphenols. The direct electrophilic alkylation of phenols is a longstanding method of phenol functionalization.[105] Cinnamyl chloride is a well-known, commonly available and reactive alkylating agent.[106] Thus, the alkylation of phenols or phenolates with cinnamyl chloride promised expedient access to a variety of 2-cinnamylphenols.

Phenols are ambident nucleophiles, and the alkylation of phenols is non-trivial due to the numerous products that can be formed (Scheme 42).[107] The alkylation can take place at the phenol oxygen, termed *O*-alkylation, at the *ortho*-position, or at the *para*-position. Furthermore, an ambident electrophile such as cinnamyl chloride can react in either S_N2 or S_N2' fashion to afford two different sets of products.



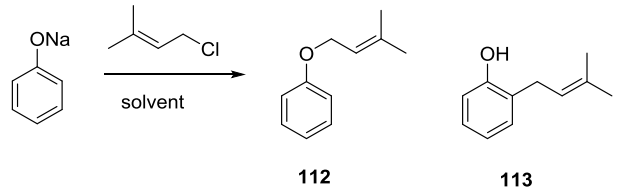
Scheme 42

The *O*-alkylation of cinnamyl chloride results in the formation of an aryl allyl ether, which further complicates the situation (Scheme 43). Aryl allyl ethers can undergo [3,3]-sigmatropic rearrangements at elevated temperature.[108] This has the effect of turning an *O*-alkylation product **109** into *C*-alkylation intermediate **110**. The course of the [3,3]-sigmatropic rearrangement also depends on how quickly the substrate can rearomatize. If rearomatization is slow, the immediate product can undergo a Cope rearrangement, effectively changing the position of *C*-alkylation.[108] Thus, even if the initial alkylation is selective, interconversion of the products is possible under some conditions.



Scheme 43

Clearly, the alkylation of phenols is dependent on a large number of variables. In a lone study, the alkylation of phenol with prenyl chloride was followed by gas chromatographic analysis (Scheme 44).[109] The sterically hindered nature of prenyl chloride enforces high S_N2 selectivity in this transformation. Under the reaction conditions, the alkylation afforded primarily **112** and **113**. The product distribution was highly solvent dependent, and increasing solvent polarity led to higher quantities of *O*-alkylation product. Notably, the solely *para*-alkylation product was not detected in the reaction mixture, which suggested that at least the *para*-alkylation pathway would be disfavored. Reaction conditions for the alkylation of phenols were investigated based on this initial report.

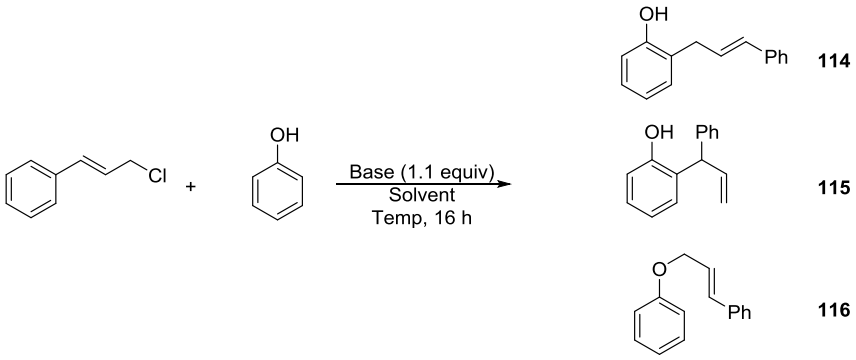


conversion analyzed by GC
yield not reported
ether, **112**:**113**, 2:89
methanol, **112**:**113** 66:9

Scheme 44

The alkylation of phenol in THF using metallic sodium as the base resulted in the formation of three major identifiable components (Table 14). Alkenes **114** and **115** were inseparable from each other under standard purification techniques, and hence the yields provided are for the mixture of materials. In the case of THF, a total yield of 12% was obtained, and significant quantities of *O*-alkylation product **116** was observed (entry 1). The reaction proceeded with greater selectivity in diethyl ether, and afforded the **114** and **115** in 65% combined yield (entry 2). In an effort to increase the site selectivity of the alkylation dichloromethane was employed as a reaction solvent. While the selectivity was still high, the yield suffered. Lithium was not compatible with the reaction conditions (entries 3 and 4). Metallic potassium resulted in a lower ratio (2:1) of **114**:**115** (entry 5). The dissolution of the metallic reagent to form the active alkoxide was visually slow, and therefore sodium hydride was employed as the base. This change resulted in almost immediate deprotonation as evidenced by both gas evolution and an exothermic reaction. Alkylation under these conditions resulted in an improved 7:1 ratio of **114**:**115**, and also restored the high yield observed for the reaction in ether (entry 6). Further optimization of solvents identified both CCl_4 and the more environmentally friendly benzene as appropriate reaction solvents, with **114**:**115** ratio of >9:1 and 68 and 74% yield respectively (entries 7 and 8). The development of a direct *C*-alkylation of phenols thus opened the route to an expedient synthesis of 2-cinnamylphenols.

Table 14. Optimization of *C*-alkylation of Phenols.

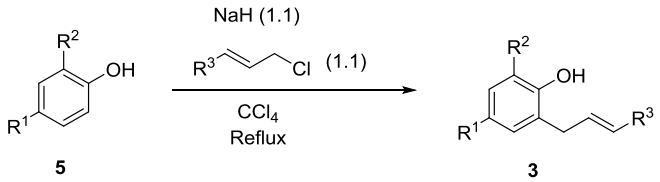


entry	solvent	base	temp, °C	ratio[a] **114**:**115**:**116**	yield of **114**+**115**, %[b]
1	THF	Na	rt	1: trace : 2.5	12
2	Et_2O	Na	rt	4.5 : 1 : 0.3	65
3	CH_2Cl_2	Na	rt	4 : 1 :0	37
4	CH_2Cl_2	Li	rt	Complex mixture	0
5	CH_2Cl_2	K	rt	2 : 1 : 0.4	29
6	CH_2Cl_2	NaH	40 °C	7 : 1 : trace	66
7	CCl_4	NaH	80 °C	9.5:1:0.4	68
8	Benzene	NaH	80 °C	9 : 1 : 1.5	74

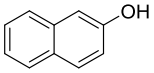
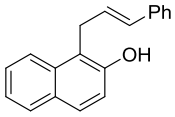
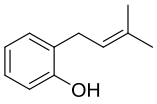
[a]Determined by ^{1}H NMR spectroscopy of crude reaction mixture [b] Isolated yield.

The generality of the cinnamylation reaction was then tested by subjection of a number of 2- and 4- substituted phenols to the optimized conditions. The reaction of phenol with cinnamyl chloride under the optimized conditions produced **114** in 71% yield (Table 15, entry 1). Both 2- and 4-methyl-substituted phenols could be alkylated under the same conditions in 47% and 62% yield respectively (entries 2 and 3). Cinnamylation of 4-hydroxy anisole afforded **114d** in 49% yield (entry 4). Modestly electron-poor phenols such as **116e**, **116f** and **116g** were also reactive under these conditions, albeit with somewhat extended reaction times (entries 5, 6 and 7). The highly electron poor 4-CF_3-substituted **116h** required refluxing toluene to proceed (entry 8). 2-naphthol was alkylated at the 1-position selectively in 79% yield (entry 10). The reaction was not limited to cinnamyl chlorides: phenethyl allyl chloride also reacted with phenol to afford **114i** in 51% yield (entry 9). Isoprenyl chloride could also be used in a similar fashion to afford the desired trisubsituted alkene with 65% yield (entry 11).[110]

Table 15. Alkylation of Substituted Phenols with Cinnamyl Chloride.



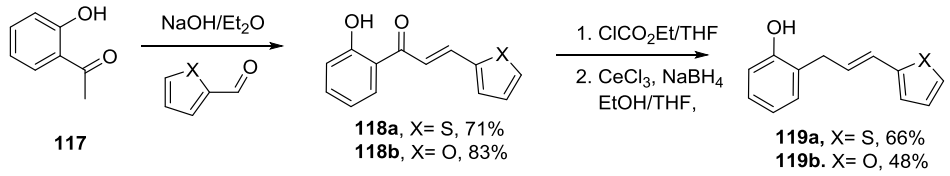
5 3

entry	phenol	R^1	R^2	R^3	time, h	product	yield, %[a]
1	**116a**	H	H	Ph	16	**114**	71%
2	**116b**	Me	H	Ph	16	**114b**	47%
3	**116c**	H	Me	Ph	16	**114c**	62%
4	**116d**	OMe	H	Ph	16	**114d**	49%
5	**116e**	F	H	Ph	24	**114e**	71%
6	**116f**	Cl	H	Ph	24	**114f**	60%
7	**116g**	Br	H	Ph	24	**114g**	56%
8	**116h**	CF_3	H	Ph	24[c]	**114h**	64%
9	**116i**	H	H	CH_2CH_2Ph	16	**114i**	51%
10	**116j**			Ph	16	 **114j**	79%
11	**116k**	H	H	-[b]	20	 **114k**	65%

[a]Isolated yield of pure **114**. [b]Prenyl chloride was used as the electrophile. [c]Toluene was used as the reaction solvent

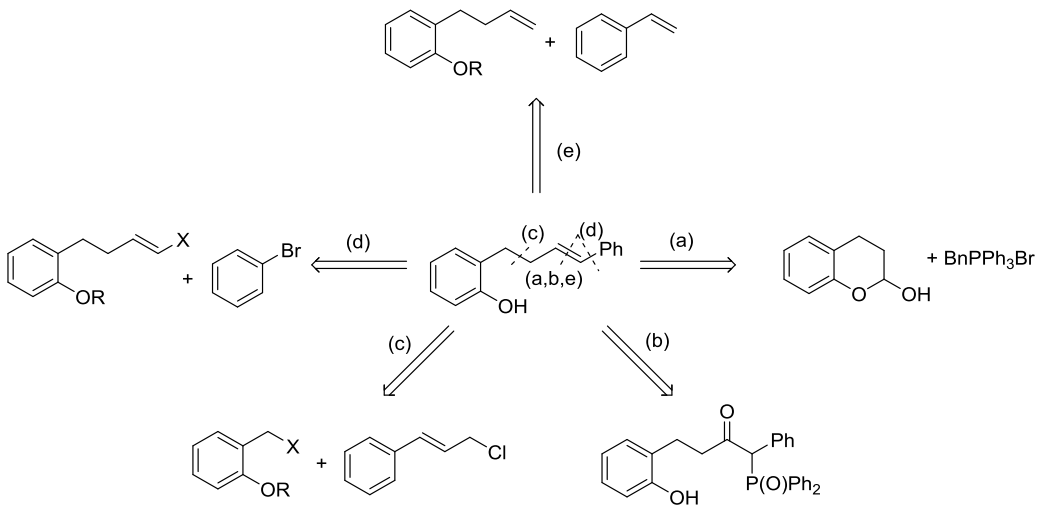
4.4.2. Synthesis of other 2-Substituted Phenols. The extension of the *C*-alkylation method to heterocycles would involve the synthesis of 1-heterocyclic allyl chlorides. These substrates were both difficult to synthesize, as the corresponding alcohols could not be converted into the chloride easily, and prone to decomposition and polymer formation.[111] Therefore an alternative synthesis was devised. The reduction of easily synthesized 2-carbonoylchalcones by sodium borohydride results in the complete reduction of the ketone to the methylene (Scheme 45).[101b,112] Importantly, this route avoids exposure of **119a** and **119b** to acidic reaction conditions, thereby

minimizing the opportunity for decomposition. Chalcones **118a** and **118b** were accessed in one step from 2-hydroxy acetophenone. Formation of the phenol carbonate and subsequent reduction with sodium borohydride afforded **119a** and **119b** in 66 and 48% yield respectively.



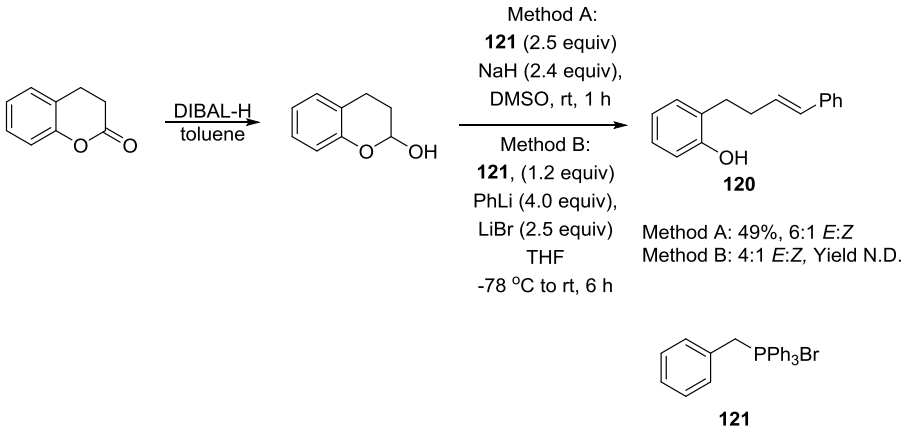
Scheme 45

In previous communications, the sulfenofunctionalization reaction has shown significant changes in both stereo- and site selectivity based on the geometry of the alkene in question as well as the distance between the alkene and the nucleophile (Chapter 2). Therefore, efforts were directed at accessing substrates which could help elucidate these effects with respect to the functionalization with phenolic nucleophiles. The synthesis of geometrically pure (*E*)-alkenes necessary for these reactions was surprisingly difficult. To solve this problem, a number of approaches were considered (Scheme 46). These are (a) Wittig and Schlosser-Wittig reactions, (b) the stereospecific elimination from diastereopure alkyldiphenylphosphine oxides, i.e. Horner-Wittig, (c) the S_N2 and S_N2' displacement of allyl and benzyl halides with organometallic reagents, (d) an intermolecular cross-coupling of alkenyl and aryl halides and (e) olefin metathesis of a terminal alkene and a styrene.



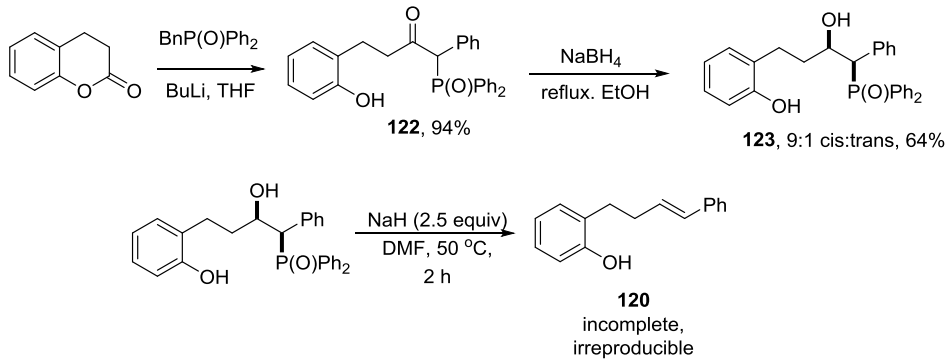
Scheme 46

. *4.4.2.1. Wittig and Schlosser-Wittig Reactions.*[113] The first attempt to form the (*E*)-alkene junction employed benzyltriphenylphosphonium bromide and 2-hydroxy-(4*H*)-dihydrochroman as the reaction partners. With a Na-counterion the *E*:*Z* selectivity was about 6:1. Therefore, the Schlosser modification was tested as an alternative approach. In this case, PhLi was used as the base to equilibriate the intermediate betaine before the final elimination. Unfortunately, under the best conditions tested with the Schlosser modification, the selectivity did not exceed 4:1.



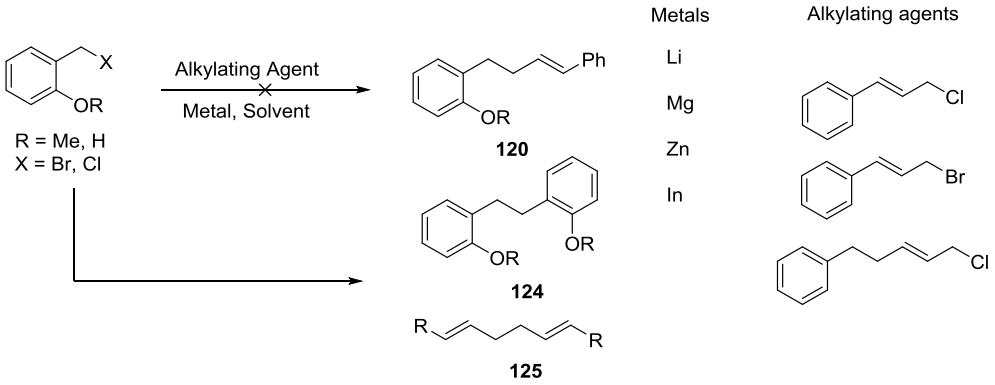
Scheme 47

4.4.2.2. Horner-Wittig Reaction.[114] The disappointing failure of the direct Wittig methodology suggested that the intrinsic *E*:*Z* selectivity for this substrate may not be great. Therefore, an alternative approach that utilizes the Horner method was generated. The α-oxo diphenylphosphines **123** are isolable intermediates, and separation of the diastereomers would lead to diastereopure **123**. The elimination from α-oxo diphenylphosphines is stereospecifically *syn* and therefore **120** should be produced as the geometrically pure (*E*)-isomer. The percursor synthesis began with the nucleophilic attack of benzyldiphenylphosphine anion onto dihydrocoumarin. The resulting ketone was reduced with $NaBH_4$ in 9:1 selectivity favoring the desired *trans*-isomer. However, the final elimination proved problematic. Although only (*E*)-**120** was visible by ^{1}H NMR spectroscopy, the reaction proved to be very irreproducible, with mixtures of starting material, low amounts of alkene and other unidentified products. Although a few conditions were tested, this route, too did not ultimately prove successful.



Scheme 48

4.4.2.3. Organometallic Reagents.[115] The problems encountered setting the (*E*)-alkene geometry led to the investigation of alternative approaches that would take advantage of preformed geometrically pure alkenes. The C-C bond disconnect along the alkene tether led to the consideration of S_N2-type reactions on activated centers. Thus, either the combination of an allyl organometal with a benzyl halide or of a benzyl organometal with an allyl halide would both lead to the desired product. Thus, a wideranging investigation into the possible conditions for such a coupling was performed.

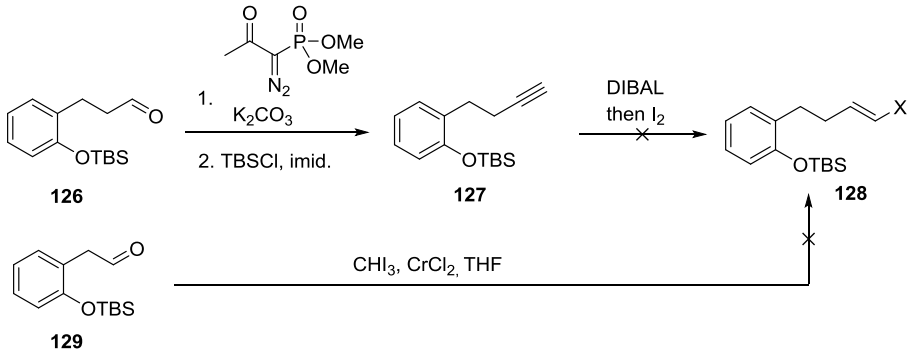


Scheme 49

The Wurtz-type coupling and homocoupling of activated organometallic reagents was an expected side reaction.[116] Unfortunately, in most of the conditions tested, homocoupling to **125** was observed. Primarily, the initial formation of organometallic reagents proved problematic as the organometallic species generated immediately reacted with the remaining reagent leading to homocoupling. Thus, no clean generation of cinnamyl organometallic reagents was possible. The homocoupling was problematic even when the conjugation was interrupted by replacement of the

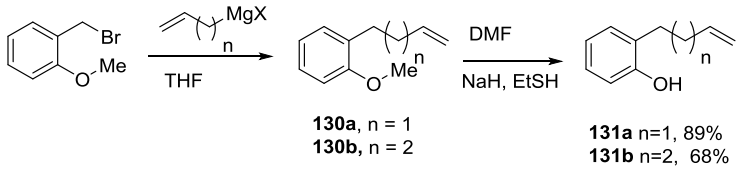
aryl moiety with a phenethyl moiety. The generation of benzyl organometallic species was similarly problematic with predominantly bibenzyl derivative **124** observed as the primary constituent of reaction mixtures. Conditions that employed organometallic reagents with lower reactivities such as In[117] and Zn[118] also did not lead to successful couplings.

4.4.2.4. Synthesis of Vinyl Halogens. The cross coupling of various alkenyl halides and with aryl boronates[119] or aryl silicon reagents[120] is well developed. Therefore, vinyl halides of type **128** were targeted. Treatment of **126** with the Ohira-Bestmann reagent[121] led to the formation of alkyne **127**. However, Al-H reduction of the alkyne followed by I_2 quench primarily afforded the terminal alkene. The Takai reaction[122] of protected aldehyde **129** was also unsuccessful. Further optimization of this route was not attempted based on the success obtained in the cross-metathesis reaction.



Scheme 50

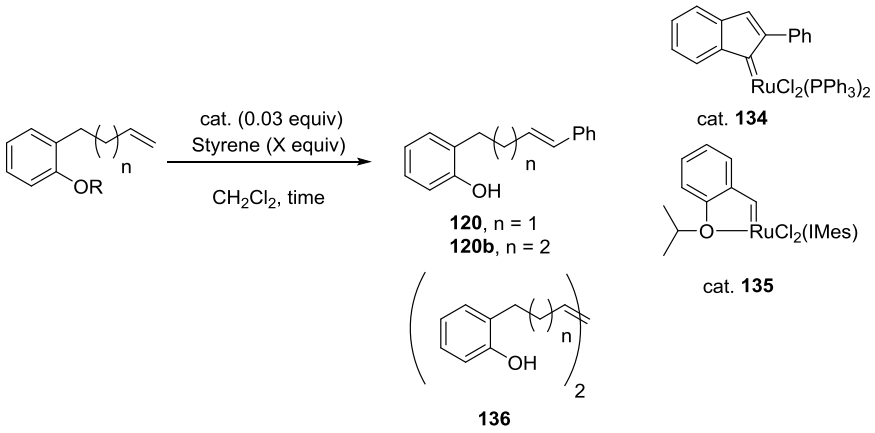
4.4.2.5. Alkene Metathesis. Olefin metathesis reactions that employ Grubbs-I and Grubbs-II type catalysts generally proceed with high (*E*)-selectivity.[123] Thus, metathesis of a styrene with a terminal olefin was seen as a possible answer to the problem of *E*:*Z* selectivity. The requisite terminal alkenes **131** were prepared from 2-methoxybenzyl bromide by displacing the bromide with a preformed Grignard reagent (Scheme 51).[124] Deprotection with sodium ethanethiolate in refluxing DMF produced terminal alkenes **131a** and **131b** in 89 and 68% yield over two steps.[19f]



Scheme 51

The use of Hoveyda-Grubbs II catalyst **135** for the metathesis of alkenes **131** was unsuccessful. No reaction was observed at low temperature. When the temperature was raised to reflux, homocoupling product **136** was observed. The Grubbs-I-indenylidene type catalyst **134** was much more successful at catalyzing the reaction. Metathesis of **130a** and **131a** with excess styrene was found to deliver protected styrenes with high geometrical selectivity.[125] Usually, addition of a second portion of catalyst was necessary for high conversion. Protection of the phenol as the methyl ether led to slightly higher yields in the reaction. Subsequent demethylation under identical conditions resulted in the formation of **120** and **120b** in high yield.

Table 16. Grubbs Metathesis of Butenyl- and Pentenylphenols.

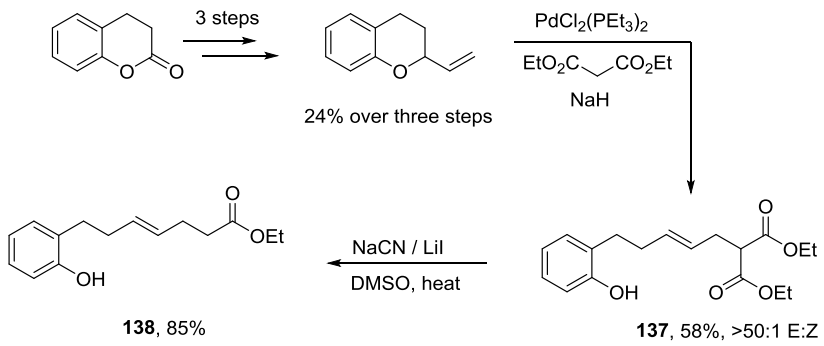


entry	R	n	cat.	styrene	temp, ^{o}C	time, h	yield, %[a]
1	H	1	**135**	1.2	rt	24	0
2	H	1	**135**	1.2	reflux	6	n.d.
3	H	1	**134**	5	rt	36	62%
4	Me	1	**134**	5	rt	36	69%
5	H	2	**134**	5	rt	36	42%

[a]Isolated yield.

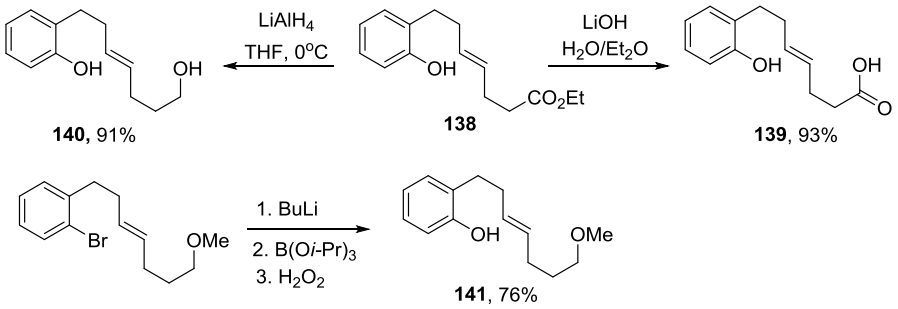
The (*E*)-selectivity of the olefin metathesis reaction does not extend to isolated alkenes under cross-metathesis conditions.[123] Therefore a new route was devised to access substrates with a two-methylene tether but with alkyl substituents. The Pd-mediated opening of 2-vinylchroman by malonate nucleophiles mediated by palladium had been studied by Murahashi in 1986.[126] Under similar conditions, diethylmalonate intermediate **137** could be accessed rapidly (Scheme 52). The decarboxylation of the malonate was effected using Krapcho conditions.[127]

NaCl was sufficient to decarboxylate the diester, but the high temperatures and long reaction times necessary led to uncharacterized polymerization products were observed by ^{1}H NMR spectroscopy. Instead, use of NaCN resulted in rapid decarboxylation at only 160 ^{o}C, with a minimal amount of side products.[128] Under the optimized conditions, the desired ester substrate could be obtained in 85% yield.



Scheme 52

Ester **138** then served as a linchpin for diversification to study the effects of Lewis basic groups on the reaction. Hydrolysis yielded **139** in 93% yield, and reduction of the ester afforded **140** in 91% yield (Scheme 53). Ether **141** was synthesized from the corresponding bromoarene.

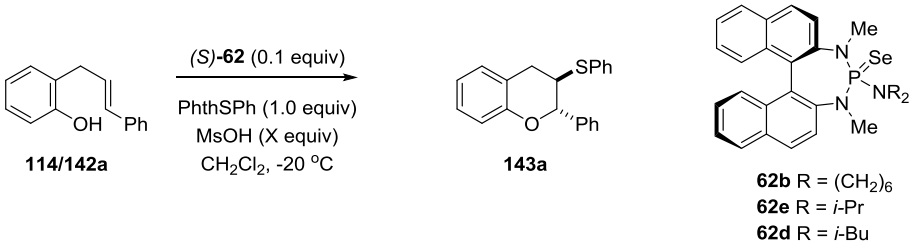


Scheme 53

4.4.3. Optimization of the Phenoxysulfenylation Reaction. The use of a phenolic hydroxyl group as the nucleophile afforded a unique opportunity to systematically vary both the steric and the electronic properties of the nucleophile. The reaction temperature was chosen as -20 ^{o}C to avoid any potential enantioerosion of the thiiranium ion.[63] Previous studies suggested that only 1.0 equiv of **56** was necessary for the reaction.[20] The initial-rate experiments revealed that an excess amount of acid was detrimental to the reaction rate, thus 0.75 equiv was chosen as

the starting point for optimization. Solvent and concentration were unchanged from the previous conditions for sulfenoetherification reactions. For catalysts of type **62**, exocyclic amine substituent strongly affects the enantioselectivity of the sulfenofunctionalization process. Thus, catalyst **62b** afforded the desired product with poor selectivity (Table 17, entry 1). Catalyst **62e** formed product **143a** in 46% yield and with an e.r. of 95.1:4.9 (entry 2). Changing to catalyst **62d** resulted in slightly lower enantioselectivity of 93.1:6.9 e.r (entry 3). Reducing the concentration of the reaction using catalyst **62e** allowed the product to be obtained in 95% yield (entry 4).

Table 17. Optimization of the Sulfenocyclization Reaction.[a]



entry	substrate	[**3**], M	acid, equiv	catalyst	time, h	yield, %[b]	e.r.[c]
1	**142a**	0.4	0.75	**62b**	24	35[d]	65.6:34.4
2	**142a**	0.4	0.75	**62e**	24	46[e]	95.1:4.9
3	**142a**	0.4	0.75	**62d**	24	27[f]	93.1:6.9
4	**142a**	0.15	0.75	**62e**	24	95	-[i]
5	**142a**	0.15	0.5	**62e**	24	95	95.3:4.7
6	**142a**	0.15	0.25	**62e**	24	94	95.7:4.3
7	**142a**	0.15	0.1	**62e**	24[h]	32	94.9:5.1
8	**142a**	0.15	0.5[g]	**62e**	24	96	94.3:5.7

[a] Reactions run on 0.1 mmol scale. [b] Yield of isolated, purified product. [c] Determined by CSP-SFC. [d] Also isolated product contaminated with **2a**. [e] Also isolated product contaminated with **2b**. [f] Also isolated product contaminated with **2c**. [g] $EtSO_3H$ was used. [h] Incomplete conversion. [i] Not determined.

In all preceding sulfenofunctionalization studies, the loading of the Brønsted acid proved to greatly affect the rate and selectivity of the reaction.[18,20] In the sulfenoetherification with alcohols, maximum reactivity was reached at 0.6 equiv of methanesulfonic acid. Cyclization of substrate **114** (hereforth referred to as **142a**) using 0.75 equiv of acid was complete within 24 h.

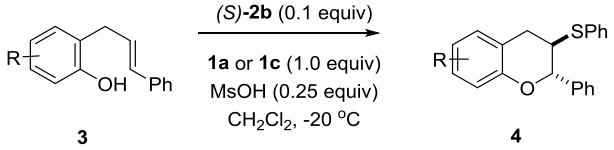
Decreasing the amount of acid to 0.5 equiv or even 0.25 equiv did not decrease the yield in the same time frame (entries 5 and 6). In all cases, high selectivity (>30:1) for *endo* capture to form the chroman was observed. Further decrease in the acid loading resulted in reduced yield (entry 7). The use of ethanesulfonic acid did not affect the enantioselectivity and was not pursued further (entry 8).

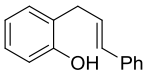
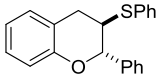
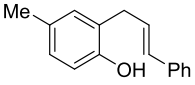
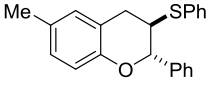
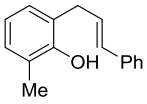
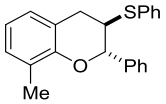
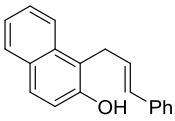
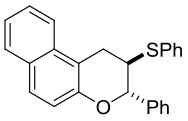
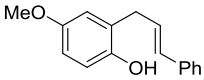
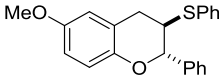
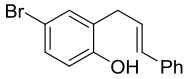
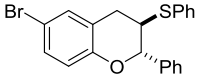
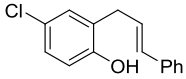
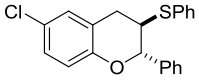
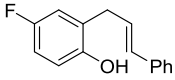
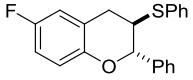
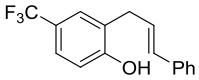
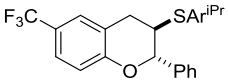
4.4.4. Sulfenocyclizations of Substituted (E)-2-Cinnamylphenols: Influence of Phenol Ring Substituents. The nucleophilicity of phenolic hydroxyl groups is influenced by both steric and electronic properties of ring substituents.[129] Accordingly, a series of substituted (*E*)-2-cinnamylphenols was prepared and evaluated (Table 2). The parent substrate, **142a**, which afforded **143a** in 84% yield, 94.9:5.1 e.r. and >30:1 *endo*-selectivity was used as a benchmark (Table 2, entry 1). Methyl substituents at the 4- and 6- positions on the ring did not alter the reaction outcome meaningfully (entries 2 and 3). The presence of an extended π-system resulted in no change in yield and a very small decrease in e.r. (entry 4). In all cases high (>30:1) consitutional selectivity was observed.

Next, the influence of heteroatom substituents on reaction outcome was evaluated. Electron-donating groups had little influence, for example **142e** bearing a 4-methoxy group cyclized to form **143e** in 84% yield and 94.4:5.6 selectivity (entry 5). Bromophenol **142f** cyclized to afford **143f** in 81% yield and 93.8:6.2 e.r (entry 6), albeit with slightly extended reaction time. The more electronegative chloro- and fluoro-substituted substrates reacted in the same time frame, **143g** and **143h** being produced in 70 and 82% yields respectively (entries 7 and 8). The enantioselectivity of the reactions remained high with these substrates.

Phenol **142i,** bearing a highly electron-withdrawing 4-CF_3 group, was insufficiently reactive at -20 ^oC. When the reaction temperature was increased to 22 ^oC, significant enantioerosion was observed (e.r. 70.7:29.3, SI). Sterically bulky *N*-2,6-diisopropylphenylthiophthalimide electrophile **103** prevents erosion at elevated reaction temperatures by shielding the intermediate thiiranium ion.[40] Cyclization of **142i** at room temperature using **103** proceeded smoothly, and **143i** was isolated with 89% yield and 95.2:4.8 e.r (entry 9).

Table 18. Sulfenocyclizations of Substituted (*E*)-2-Cinnamylphenols.[a]



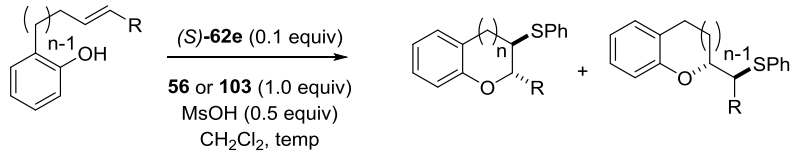
entry	phenol		time, h	product		yield, %[b]	e.r.[c]
1		**3a**	24		**4a**	84	94.9:5.1
2		**3b**	24		**4b**	82	95.0:5.0
3		**3c**	24		**4c**	78	96.0:4.0
4		**3d**	24		**4d**	79	93.2:6.8
5		**3e**	24		**4e**	84	94.4:5.6
6		**3f**	36		**4f**	81	93.8:6.2
7		**3g**	36		**4g**	70	93.8:6.2
8		**3h**	36		**4h**	86	93.2:6.8
9		**3i**	12[d,e]		**4i**	89	95.2:4.8[f]

[a] Reactions run on 1.0 mmol scale. [b] Yield of isolated, purified product. [c] Determined by CSP-SFC. [d] Electrophile **1c** was used, Ar^{iPr} = 2,6-(*i*-Pr)-C_6H_3 [e] Reaction run at 22 °C [f] Determined after oxidation to the sulfone.

4.4.5. Sulfenocyclization of 2-Substituted Phenols. Changes in the alkene substitution pattern have been documented to dramatically alter selectivity for the sulfenofunctionalization process.[18,20,79,83] (*E*)-substituted alkenes were the most selective substrates for sulfenoetherification, whereas terminal alkenes were only slightly less so. Trisubstituted, (*Z*)-

and 1,1-substituted alkenes reacted with poor selectivity. Thus, primarily (*E*)- and terminal alkenes were employed in this study. Initially, the (*E*)-phenyl substituent was varied. Furan-substituted benzopyran **143j** was produced in 88% yield and 92.7:7.5 e.r, whereas thiophene-substituted substrate **142k** produced the desired product in 86% yield and 93.9:6.1 e.r.(Table 3, entries 1 and 2). Changing the alkene substituent to an aliphatic group as in substrate **142l** led to a 74% combined yield of a 1.5:1.0 mixture of isomers **143l** and **144l** with 96.6:3.4 e.r. for **143l** (entry 3). Trisubstituted alkenes generally lead to less selective cyclizations with **56**.[83] To increase selectivity, electrophile **103**, which has an improved selectivity profile, was tested with substrate **142m**.[40] In this case, use of **103** led to the formation of gem-disubstituted benzopyran **143m** in 93% yield and 95.4:4.6 e.r. (entry 4).

Table 19. Sulfenocyclizations of 2-Substituted Phenols.[a]



142 143 144

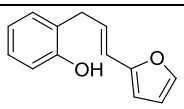
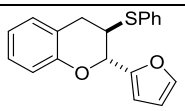
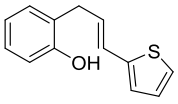
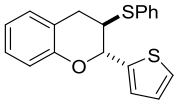
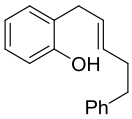
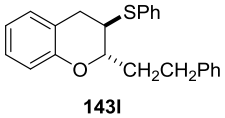
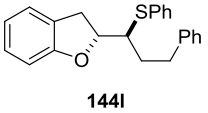
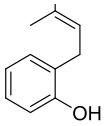
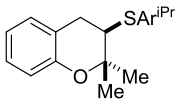
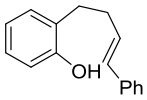
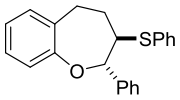
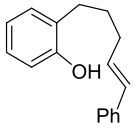
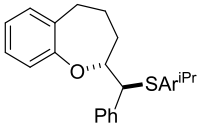
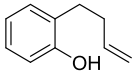
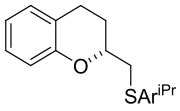
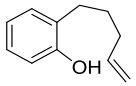
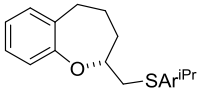
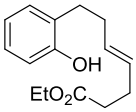
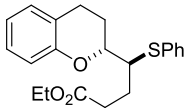
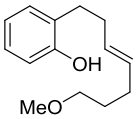
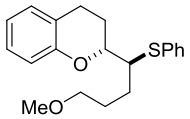
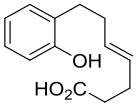
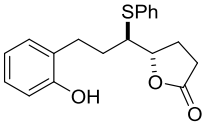
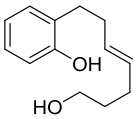
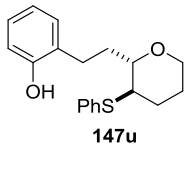
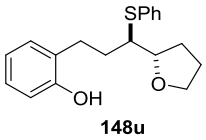
entry		substrate	sulf. agent	time h	temp °C	product[c]		yield %[b]	*endo:exo*[d]	e.r.[e]
1[f]	**142j**		**56**	24	-20		**143j**	88	>30:1	92.5:7.5
2[f]	**142k**		**56**	24	-20		**143k**	86	>30:1	93.9:6.1
3[f]	**142l**		**56**	24	-20	 **143l**  **144l**	**143l, 144l**	74	1.5:1	96.6:3.4 (**143l**) 96.3:3.7 (**144l**)

Table 19. (cont.)

4[f]	**142m**		**103**	24	0		**143m**	93	>30:1	95.4:4.6[g]
5	**142n**		**56**	18	-20		**143n**	92	>30:1	94.4:5.6
6	**142o**		**103**	24	0		**144o**	76	<1:30	92.6:7.4[g]
7	**142p**		**103**	12	0		**144p**	91	<1:30	97.2:2.8[g]
8	**142q**		**103**	48	0		**144q**	84	<1:30	97.7:2.3[g]
9	**142r**		**56**	24	-20		**144r**	80	1:12	93.2:6.8
10	**142s**		**56**	24	-20		**144s**	85	<1:30	96.7:3.3
11	**145t**		**56**	24	-20		**147t**	92	<1:30	92.2:7.8
12	**146u**		**56**	24	-20	 **147u**  **148u**	**147u, 148u**	88	1.1:1[h]	96.9:3.1 (**8u**) 97.1:2.9 (**9u**)

[a] Reactions run on 1.0 mmol scale. [b] Yield of isolated product. [c] Ar^{iPr} = 2,6-(*i*-Pr)-C_6H_3. [d] Determined by ^{1}H NMR analysis of crude reaction mixtures. [e] Determined by CSP-SFC. [f] 0.25 equiv MsOH was used. [g] Determined after oxidation to the sulfone. [h] *endo:exo* ratio for alcohol capture.

The site-selectivity of thiiranium ion capture during intramolecular sulfenocyclization is expected to be strongly influenced by the relative rates of formation of different size rings. The preparation of substrates with varying tether length enabled for a systematic study of ring size

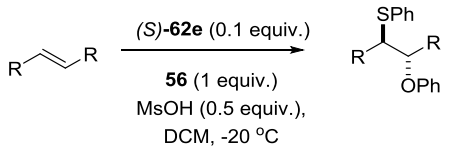
effects (Table 3). Substrate **142n**, which contains an (*E*)-2-styryl group at the end of a two carbon tether, afforded the 7-*endo* cyclization product benzoxepane **143n** in 92% yield and 94.4:5.6 e.r (entry 5). Further extending the tether to three methylene groups in substrate **142o** proved problematic: under the optimized conditions using electrophile **56**, no desired product was observed. Gratifyingly, use of electrophile **103** led to the surprising formation of *exo* cyclization product **144** in 76% yield and 92.6:7.4 e.r (entry 6). Next, the electronic bias imparted by the phenyl group was removed to evaluate the site-selectivity of closure with a terminal alkene in the reaction with electrophile **103**. Substrate **142p** reacted via a 6-*exo*-mode cyclization to afford **144p** with high site-selectivity, 91% yield and 97.2:2.8 e.r (entry 7). Extension of the tether length by one more methylene group, as in substrate **142q**, was gratifyingly successful, as the cyclization proceeded in a 7-*exo* mode to afford product **144q**, with 84% yield and 97.7:2.3 e.r (entry 8).

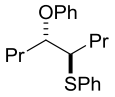
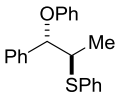
The Lewis basic nature of the selenophosphoramide moiety prompted an investigation into the compatibility of the reaction conditions with other Lewis basic functional groups in the substrate. Substrate **142r**, containing a carboxylic ester group three carbons removed from the reacting olefin, afforded **144r** in good yield albeit with somewhat diminished enantioselectivity compared to **142a** (c.f. entry 9 and Table 2, entry 1). Replacement of the ester by the corresponding ether in **142s** restored the enantioselectivity in comparable yield (entry 10). The relative reactivity of other oxygen nucleophiles with respect to phenolic hydroxyl groups was also tested. Both carboxylic acids and alcohols outcompeted phenols for thiiranium ion capture. Substrate **142t**, bearing a carboxylic acid moiety, preferentially afforded lactone **147t** in 92% yield and 92.2:7.8 e.r. (entry 11). In the presence of a remote hydroxyl group, such as in substrate **142u**, saturated oxacycles **147u** and **148u** were formed as a 1.1:1 mixture of constitutional isomers in 88% combined yield and with 96.9:3.1 e.r. (entry 12).

4.4.6. Intermolecular Sulfenylation of Alkenes with Phenols. The intermolecular sulfenofunctionalization of alkenes with phenols would greatly extend the potential applications of the reaction. Thus, the functionalization of representative alkenes with phenols were tested. The cyclization of 4-octene with phenol under the standard reaction conditions afforded **149** in 75% yield and 93:7e.r. However, when β-methylstyrene was tested, both the yield and the enantioselectivity for **150** were much lower (44% and 86:14). High site selectivity for capture at

the benzylic position was observed. Stilbene was completely unreactive under the standard conditions, even at elevated temperature.

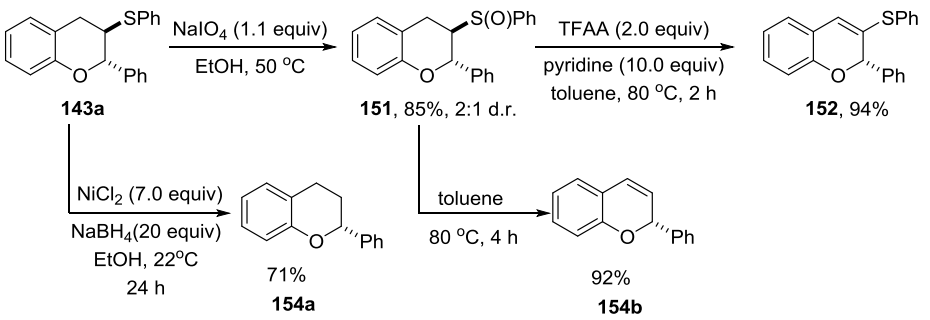
Table 20. Intermolecular Sulfenofunctionalization with Phenol Nucleophiles.



entry	R,R	product	time, h	temp, °C	yield[a]	site selectivity[b]	e.r.[c]
1	*n*-Pr,*n*-Pr	 **149**	24	-20	75	N/A	93:7
2	Ph, Me	 **150**	48	-20	44	<1:30	86:14
3	Ph,Ph	-	48	23	0	-	-

[a]Isolated yield. [b]Determined by ^{1}H NMR analysis of crude mixture. [c]Determined by CSP-SFC.

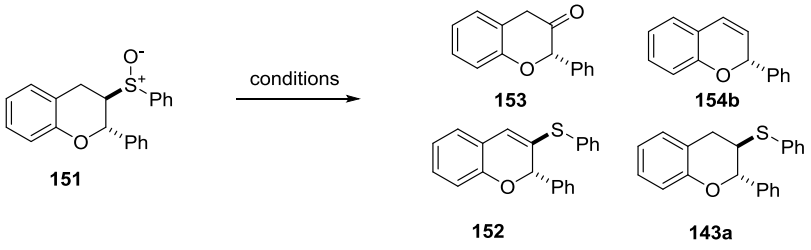
4.4.7. Transformations of Sulfenofunctionalization Products. The sulfenyl moiety in the product thioether can act as a functional handle for further transformations. Thus, a series of manipulations to explore the reactivity of the thioether group were carried out (Scheme 54). Reductive cleavage of **143a** with nickel boride formed 2-phenylchroman in 35% yield. Oxidation of **143a** with sodium metaperiodate led to sulfoxide **151** in 85% yield and in a 2:1 diastereomer ratio. Both diastereomers underwent thermal elimination in toluene, leading to the formation of 2-phenylchromene in 92% yield. Attempts to engage the sulfoxide in a Pummerer process was not successful. Instead, vinyl thioether **152**, which results from elimination of the thiocarbenium intermediate, was formed under a variety of conditions (see experimental section). In the presence of trifluoroacetic anhydride and pyridine, **152** was obtained in 94% yield.



Scheme 54

Conversion of sulfoxide **151** to ketone **153** under other Pummerer conditions were attempted. Representative examples of conditions are shown in (Table 21). Treatment of the sulfoxide with acetic anhydride in the presence and absence of acetate led to the exclusive formation of chromene **154**. Interestingly, other dehydrating agents such as thionyl and oxalyl chlorides resulted in the formation of the sulfide, formally oxidizing the reagent. The addition of both soluble and insoluble bases did not lead to product formation. Other activating agents such as PIDA and TBSOTf were also ineffective at promoting the Pummerer rearrangement.

Table 21. Survey of Pummerer Rearrangement Conditions for 151.



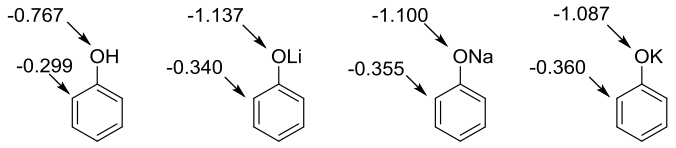
entry	solvent	reagent	base	temp, °C	time, h	**153**:**154**:**152**:**143a**[a]
1	Ac_2O	-	-	110	2	0:1:0:0
2	Ac_2O	AcOH	-	110	2	0:1:0:0
3	CH_2Cl_2	$SOCl_2$	-	rt	1	0:0:1:7.5
4	CH_2Cl_2	$(COCl)_2$	-	rt	1	0:0:1:1
5	CH_2Cl_2	$(COCl)_2$	K_2CO_3	rt	2	0:0:1:3.5
6	CH_2Cl_2	$(COCl)_2$	KOAc	rt	2	0:0:1:4.8
7	CH_2Cl_2	$(COCl)_2$	Pyr	rt	2	0:0:1.25:1
8	DCE	PIDA	-	rt	12	No Reaction
9	CH_2Cl_2	TBSOTf	Et_3N	rt	3	0:0:1:0

[a] Determined by ^{1}H NMR spectroscopy of crude reaction mixture.

4.5. Discussion.

The synthesis and reactivity of phenolic substrates was unexpectedly difficult. Phenols with one and two-carbon methylene tethers each had unique challenges associated with their synthesis. In the first section of the discussion some of the challenges related to geometrical and constitutional purity will be discussed.

4.5.1. Optimization of the Phenol Alkylation Process. The selectivity of phenolate alkylation is affected by both reaction solvent and counterion. Therefore, these variables will be treated sequentially. Alkylation of sodium phenolate was slightly more selective for **114** than with potassium phenolate. Lithium phenolates reacted slower than their sodium counterparts. Interestingly, the use of potassium in polar media with allyl chloride results in clean ether formation.[130] In contrast, sodium phenolates were more problematic substrates for the reaction with an allyl halide. Calculation of charge densities for phenol and its alkali metal salts at the B3LYP level shows that the partial negative charge at C(2) increases monotonically moving down the group (Scheme 55). Greater *O*-alkylation over ether formation would be expected as a consequence, in contrast to the observed trend. However, these calculations were performed in the gas phase. The aggregation of phenols in nonpolar media may alter the relative reactivities of these enolates. The strongly coodinating nature of Li-ate complexes in nonpolar media probably attenuates the reactivity of the phenolate anion. Furthermore, coordination of the oxygen can both sterically encumber and electronically deactivate it, favoring *C*- over *O*-alkylation.



Scheme 55

Indeed, changes in the solvent had a great effect on the site of alkylation. Thus, whereas high selectivity for **114** was observed in ether, the reaction in THF afforded primarily the undesired isomer **115**. These results were in agreement with previous results for ethereal solvents.[109] Thus, the alkylation was performed in highly nonpolar solvents. Under these conditions the reaction is usually heterogenous, as the phenoxide ion can crash out of solution.

NaH was significantly more effective at deprotonating the phenol. Deposition of phenolate on the metal surface can retard the further formation of anions in dissolving metal deprotonations. Alkali metals can also undergo SET reactions with chlorinated and aromatic solvents. The clean reactivity profile of NaH led to it being the best choice for this reaction.

The alkylation of phenols under these conditions resulted in the formation of two major isomers. High selectivity for the desired isomer **114** was observed, the S_N2' alkylation product was difficult to remove from the reaction mixture. Although a number of conditions were tested, its production could not be fully suppressed. The relative ratio of **114**/**115** appears to be better in highly nonpolar solvents. The S_N2' alkylation of cinnamyl chloride would require the phenolate to approach a secondary methine as opposed to a primary methylene for S_N2 alkylation. Thus, the formation of aggregates may actually be beneficial. Increased nucleophile size as a consequence of aggregation would then favor attack at the less hindered position of cinnamyl chloride. Unfortunately, even under the optimized conditions, the production of isomer **115** could not be fully suppressed. The separation of **114** and **115** was not possible on silica. Thus, new purification techniques needed to be developed. Unfortunately, the sacrificial reaction with K_2OsO_4/NMO, which had previously been successfully employed in these laboratories did not fully remove the minor isomer.[131] Finally, $AgNO_3$ on SiO_2 (10% w/w) was found to separate the two isomers. The operational overhead on the direct alkylation of phenols proved to be considerable.

4.5.2. Synthesis of 2-Substituted Phenols. The synthesis of phenols with more than one methylene linker was successful only after numerous different attempts. The initial failure of 2nd generation Hoveyda-Grubbs led fruitless efforts at either geometrically constructing the (*E*)-alkene in a geometrically pure manner or disconnecting somewhere else in the tether. After much effort, the efforts came full circle, and the alkene could be constructed in >50:1 *E*/Z selectivity using 1st generation Grubbs catalyst **134**

The success of **134** over **135** is comment worthy. NHC ligands are known to decrease the reactivity of the Ru center, while substantially increasing catalyst stability. In the current system, no reactivity was observed with **130** at room temperature. If the Ru center is insufficiently reactive, the initial [2+2] addition to form the [Ru(substrate)] complex can not take place. As a result, starting material is recovered. The selectivity of the two catalysts was also different. Whereas **135** gave a mixture of homo- and heterocoupling products, **134** afforded

primarily the heterocoupling product. The reactivity of terminal alkenes in cross-metathesis reactions is greater than styrenes, therefore an initial addition to form the homocoupling product is plausible. However, the carbene complex derived from **134** can add back into the dimer **136** to reform starting material and the [Ru(substrate)] complex. The mixture observed for **135** suggests that the carbene derived from **135** can either not add back into the internal alkene or that this addition is much slower than the initial rate of reaction with the terminal alkene in solution. Either way, catalyst **134** was much better suited to the reaction. However, the low stability of **134** required two portions of catalyst to be added over the timeframe of the reaction. Since the overall total catalyst loading is still 3-4 mol %, this was not particularly problematic. The effect of the hydroxyl group was not prominent.

The low selectivity of intermolecular metathesis reactions is a result of the low energy difference between alkyl substituted (*E*)- and (*Z*)-alkenes. In light of the difficulties encountered with the aforementioned methods of making geometrically pure (*E*)-alkenes, a different approach was tested. The palladium catalyzed opening of 2-vinylchroman proceeded with very high (*E*)-selectivity. The original proposal for the selectivity is the preference for the Pd-allyl complex that forms upon opening of vinyl chroman to adopt a preferentially *trans* configuration. Subsequent displacement of the Pd-allyl complex by malonate preserves the high (*E*)-selectivity on account of an outer-shell S_E2-type transition state that is formally related to the Tsuji-Trost process.[132]

4.5.3. Optimization of the Phenoxysulfenylation Reaction. The systematic variation of reaction conditions, phenol substituents, tether length and functional groups enabled a more thorough understanding of the factors governing the sulfenofunctionalization process. In this section, the influences of each of these components on observable reaction outcomes such as rate, enantioselectivity and site-selectivity will be discussed in turn.

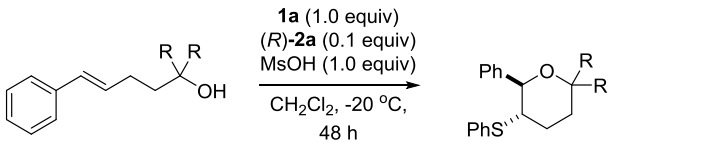
4.5.3.1. Catalyst. The optimization of the sulfenofunctionalization reaction focused on two main variables, the catalyst and the loading of the Brønsted acid. Of the three best catalysts for sulfenofunctionalization, optimum selectivity was achieved with **62e**. The high selectivity for this catalyst can be traced to the increased steric encumbrance provided by the *N*,*N*-diisopropyl substituents, accentuating the degree to which the catalyst backbone must distort to accommodate the alkene.[40] Conversion across all catalysts was comparable.

4.5.3.2. Brønsted Acid. The kinetic studies established that for an alcohol nucleophile, the υ_{max} was reached with 0.6 equiv of methanesulfonic acid (MsOH).[40] Further increases in the Brønsted acid loading led to decreases in reaction rate. Two major factors need to be considered for optimal MsOH loading: (1) the amount of acid necessary to fully transform the catalyst into active complex **95**, (2) the effective acidity of the reaction mixture as a result of solvation effects in nonpolar reaction media. In the proposed mechanistic cycle, the acid is present only in cocatalytic amounts, therefore only 1.0 equiv of acid *with respect to catalyst* should be necessary. However, titration studies with ethanesulfonic acid together with **56** and **62d** established that up to 4 equiv of acid are needed before full conversion to the sulfenylated species is observed.[87] In the case of cyclizations of phenolic hydroxyl groups, high conversion could be achieved with as little as 2.5 equiv of MsOH with respect to catalyst. Small differences in the pK_a values of MsOH and ethanesulfonic acid as well as the pK_b values of **62d** and **62e** may account for the reduced acid loading necessary for good reactivity. In contrast to alcohols, the phenolic hydroxyl group does not appear to act as a proton buffer.

The cyclization of **142a** was complete within 24 h at -20 ^oC, compared to 93% after 24 h at the same temperature for the corresponding alcohol substrate.[20] Thus, the rate of phenol cyclization is comparable to that of the alcohols. In the prior set of experiments a large excess (10 equiv with respect to catalyst) of MsOH was employed, which led to rates slower than υ_{max}. The decrease in rate at high MsOH concentrations was ascribed to protonation of the substrate by excess acid.[40] In the case of phenols, no substantial changes in rate were observed as a result of increased acid concentration in the range of 2.5 to 7.5 equiv of MsOH *with respect to catalyst*. The substantially lower Brønsted basicity of phenols (pK_a of $PhOH_2^+$: -6.5, pK_a $EtOH_2^+$: -2.2)[66] implies that a much smaller fraction of substrate is protonated even in the presence of an excess of acid. Thus similar reaction rates are observed over a much broader range of acid stoichiometry.

4.5.4. Structural Effects on Rate and Selectivity. 4.5.4.1. Influence of the Nucleophile. The rate, enantio- and site-selectivity of sulfenofunctionalization of any alkene with a pendant nucleophile is dependent on a multitude of structural factors. The initial studies showed a substantial impact of alkene environment on all three of these observables.[20] However, no such systematic investigation for the nucleophile was undertaken. In an isolated example, the cyclization of a tertiary alcohol was comparable with that of a primary alcohol (Scheme 56, c.f.

Table 9). A previous study regarding the rate of sulfenocyclization of a number of protected amines did not identify specific reactivity trends.[79] Thus, the cyclization of (*E*)-2-cinnamylphenols provided an opportunity to understand how the aforementioned observables are impacted by the steric and electronic properties of the nucleophile.



R = H, 80%, 50:1 *endo:exo*, 91:9 e.r.
R = Me, 84%, 13:1 *endo:exo* 92:8 e.r.

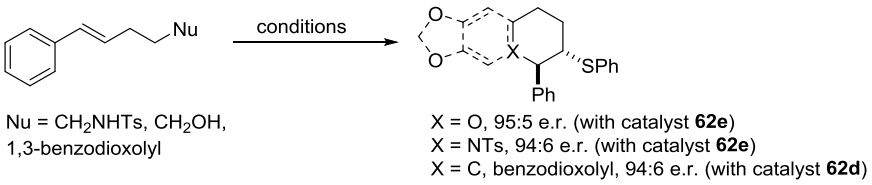
Scheme 56

4.5.4.2. Reaction Rate. The turnover-limiting step of the sulfenofunctionalization reaction for alcohols is thiiranium ion formation, hence for these substrates thiiranium ion capture is fast. (Chapter 3). As mentioned previously, phenols are substantially weaker nucleophiles than alcohols.[66] However, the rates of cyclization of **142a, 142b, 142c** and **142e** were comparable. Thus, the turnover-limiting step does not change for electron-neutral or -rich phenol nucleophiles. Naphthols are slightly stronger nucleophiles than phenols, and, in agreement with the aforementioned turnover-limiting thiiranium ion formation, the rate of cyclization of **142d** was not affected.[66]

Introduction of weakly electron-withdrawing substituents led to slightly slower overall rates. The electron-withdrawing properties of substituents on phenols is a composite effect of the inductive (σ_I) and resonance (σ_R) contributions of the substituent to the electron density on the phenol.[133] Chlorine and bromine both strongly withdraw electron density inductively (σ_I Br, 0.49; Cl, 0.43) but also donate electron density through π-resonance (σ_R Br, -0.16; Cl, -0.16).[133] Fluorine is a strongly withdrawing substituent inductively, but also a much better π-donor (σ_I F, 0.57; σ_R F, -0.33) such that its overall effect is comparable. In contrast, a trifluoromethyl group is both inductively and mesomerically electron-withdrawing (σ_I CF_3, 0.46; σ_R CF_3, 0.09). The reaction of Br, Cl and F-substituted phenols (**142f**, **142g**, **142h**, respectively) were all only slightly slower at -20 °C compared to parent substrate **142a**. The reaction does not appear to be sensitive to either of these parameters. However, for CF_3-bearing substrate **142i** the reaction needed to be performed at room temperature.

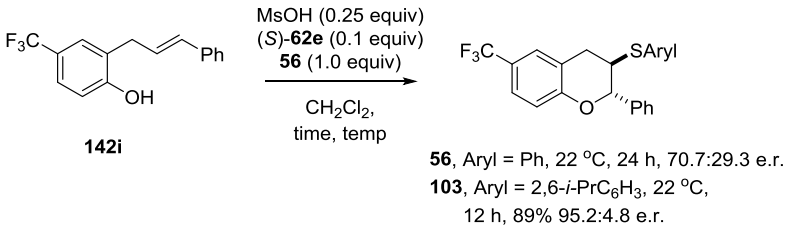
The substantial difference in rate between **142a** and **142i** (c.f. Table 18, entries 1 and 9) suggests that the turnover-limiting step may change from formation to capture of the thiiranium ion for electronically deactivated nucleophiles. Although the lifetime of the thiiranium ion intermediate derived from **142i** likely increases as a result of slow capture, the high chemical yield implies that the thiiranium ion is stable when **103** is used as the electrophile.

4.5.4.3. Enantioselectivity. The configurational stability of thiiranium ions at -20 ^{o}C in dichloromethane has been established.[63] Thus, the enantiomeric composition of the thiiranium ion upon its genesis is retained throughout the remaining reaction steps.[40] Notably, capture of thiiranium ions derived from styrenes by C, N and O-nucleophiles resulted in the same absolute configuration and comparable levels of product enantioenrichment (Scheme 57).[20,79,83]



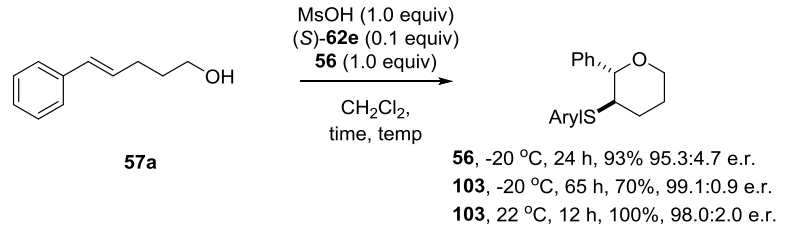
Scheme 57

For the participation of phenolic hydroxyl groups, the enantioselectivity of sulfenocyclization remained uniformly high for electron-rich phenols. However, the change in mechanism from turnover-limiting formation to turnover-limiting capture raises the possibility of erosion of enantioselectivity as a consequence of increased thiiranium ion lifetime and attendant racemization. Previous studies on the intermolecular sulfenoetherification reaction showed that under the optimized conditions at -20 ^{o}C, the configurational integrity of the thiiranium ion is retained.[63] No decrease in enantioselectivity is observed for substrates bearing halogen substituents, confirming the overall stereochemical stability of the thiiranium ion for slightly extended lifetimes at -20 ^{o}C For the trifluoromethyl-substituted phenol, the lack of reactivity required that the reaction be run at 23 ^{o}C, leading to decreased product enantioselectivity with electrophile **56** (Scheme 58).



Scheme 58

To attenuate the racemization, electrophile **103**, bearing a bulky 2,6-diisopropylphenyl group was used. The 2,6-substituents impart both slightly higher intrinsic selectivity to **103** as well as increased stability to the resulting thiiranium ions (Scheme 59).[40] The use of **103** in the reaction of **142i** resulted in a dramatic increase in selectivity, albeit not to the level observed with alcohol **57a** (Scheme 58).[40] Thus, configurational erosions of thiiranium ions can be ameliorated through increased steric shielding of the sulfur atom.

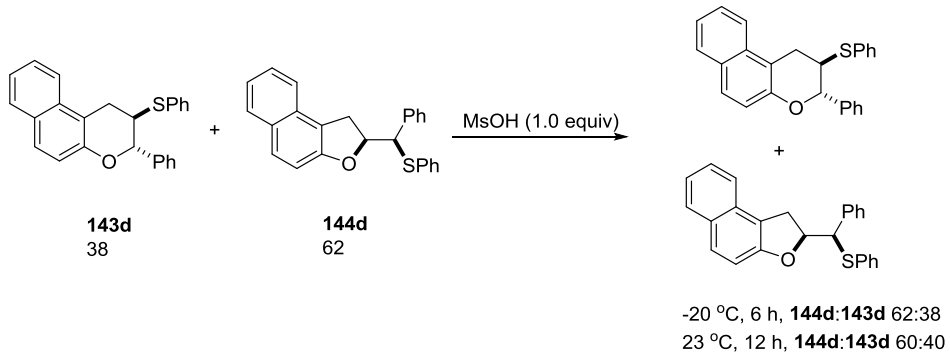


Scheme 59

4.5.4.4. Site-selectivity. The site-selectivity for the sulfenoetherification follows the established Markovnikov rule.[48] Reaction of (*E*)-2-cinnamylphenols can proceed through either a 5-*exo* cyclization to afford a benzofuran or a 6-*endo* cyclization to afford a chroman. Only chromans were observed as reaction products in the cyclization of (*E*)-2-cinnamylphenols. Changes in the electron density or steric bulk of the nucleophile had no effect on site-selectivity. Opening of the thiiranium ion through a Friedel-Crafts-type process (i.e. *C*-aryl cyclization) was not observed, demonstrating that the chemoselectivity of capture is high, irrespective of arene electron density. [83,95c]

The reversible capture observed for alcohol cyclizations prevented conclusions about the intrinsic site selectivity of the sulfenoetherification process. Therefore, an isomerization experiment with product **143d** was set up. Even at elevated temperature, only a minute amount of isomerization was observed (Scheme 60). Thus, in the case of phenoxysulfenylation at

subambient temperatures and substoichiometric acid concentrations, no product isomerization is expected. Therefore, the observed ratios represent the kinetic site selectivity of thiiranium ion functionalization.



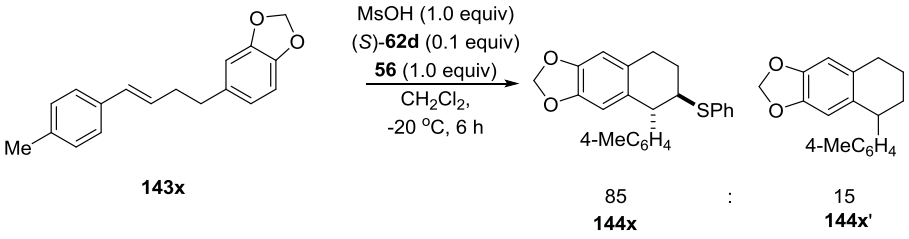
Scheme 60

4.5.5. Influence of Alkene Environment. The alkene environment represents the most important variable that can influence both the rate and the selectivity of the sulfenocyclization process.[40] This sensitivity has been evident in numerous sulfenofunctionalizations.[20,79,83,134] In general, higher alkene electron density leads to increased reactivity. Enantioselectivity is most sensitive to the alkene substitution pattern, whereas site-selectivity is governed by the aforementioned Markovnikov selectivity, albeit complicated by the potential for isomerization of certain sets of constitutional isomers under the reaction conditions.

4.5.5.1. Rate. The rate of cyclization was expected to follow a well-defined trend of alkene electron density. The reaction times of substrates with disubstituted alkenes demonstrated that the reactivity difference between heteroaryl, aryl and alkyl substituents was not substantial for disubstituted alkenes (**142a**, **142k**, **142l**, **142s** 24 h at -20 °C). However, because both mono- and trisubstituted alkenes required electrophile **103** for high selectivity, direct comparison of the rate of cyclization for terminal alkene **142p** and trisubsituted alkene **142m** with their respective analogs **142s** and **142l** is not possible.

The strongly acidic nature of the reaction conditions raised the possibility of cationic alkene cyclization or polymerization as a competitive side reaction, especially for substrates with electron-rich alkenes.[135] For example, in the cyclization of a 4-tolyl substituted alkene **143x** in the absence of Lewis basic functionality, a proton initiated cyclization was observed (Scheme

61).[87] No evidence of acid-catalyzed polymerization or cyclization was observed for the current set of styrenes.



Scheme 61

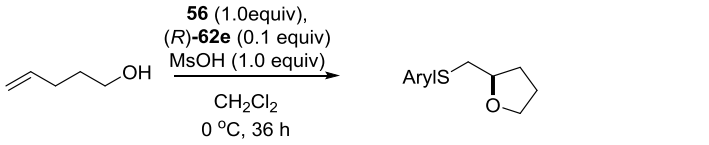
Conjugated electron-rich heteroarenes are significantly more susceptible to polymerization. Thus, when MsOH was added to a mixture of **142j**, **62e**, and **56** in dichloromethane at -20 ^{o}C, rapid polymerization was observed and no identifiable product was obtained. If the order of addition was changed to introduce **142j** last, the desired reaction pathway was restored. The effective acid concentration in solution clearly has a substantial impact on the rate of polymerization for sensitive alkenes. Incubation of the methanesulfonic acid with the remaining reagents solubilizes MsOH, removing local concentrations of acid.[87]

4.5.5.2. Enantioselectivity. The enantiomeric composition of the final products in sulfenofunctionalizations is determined by the enantioenrichment of their precursor thiiranium ions.[20,79] The enantioselectivity of thiiranium ion formation is, in turn, determined by the transition state complex consisting of alkene and intermediate **95**. Computation of the energies of the diastereomeric transition states revealed that catalyst distortion as the most important contributor to the difference in transition state free energies.[40] Thus, changes in alkene substitution pattern and consequently the degree of distortion that the catalyst experiences to accomodate the substituents, are expected to substantially impact the stereoselectivity of the process. Indeed, foregoing studies have demonstrated that the enantiotopic faces of (*Z*)- and 1,1-disubstituted alkenes were poorly differentiated by the active sulfenylating agent derived from **62e**.[20,40]

The enantioselectivity of the sulfenoetherifications herein was consistent among aryl, heteroaryl and alkyl-substituted *(E)*-alkenes (**143a**, 94.9:5.1; **143k**, 93:9:6.1; **143l**, 96.6:3.4). The nature of the oxygen nucleophile played only a minor role as phenols, alcohols and carboxylic acids cyclized with comparable enantioselectivities (**143a**, 94.9:5.1; **147u**, 96.9:3.1; **147t**,

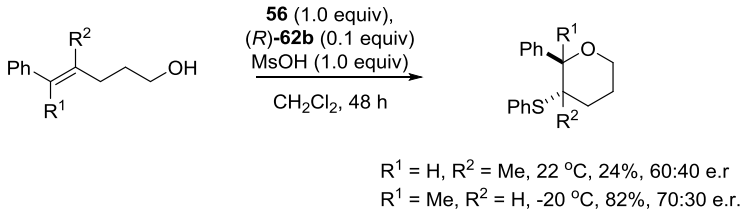
92.2:7.8). The high enantioselectivities observed independent of nucleophile parameters is in good agreement with the current hypothesis of stereodetermining thiiranium ion formation.

Terminal alkenes are usually difficult substrates for enantioselective alkene functionalizations due to absence of steric differentiation at the terminus.[136] Lower enantioselectivities have been observed previously for sulfenofunctionalization with this class of substrates (Scheme 62).[20,83] Therefore, more selective electrophile **103** was employed for the cyclization of terminal alkenes **142p** and **142q**. Thus, when **1c** was used for the cyclization of **142p**, the enantioselectivity was found to be 97.2:2.8. (c.f. Table 19, entries 5 and 7). Similarly, cyclization of **142q** proceeded with high enantioselectivity even at elevated temperature (97.7:2.3).



Scheme 62

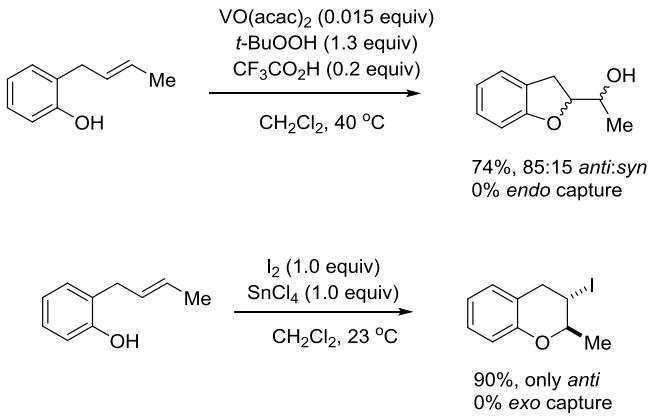
Trisubstituted alkenes are challenging substrates for selective sulfenofunctionalization. In the cyclization of pendant alcohols, both (*E*)- and (*Z*)-trisubstituted alkenes afford the corresponding products with poor enantioselectivities (60:40 and 70:30 respectively, Scheme 63). The higher intrinsic selectivity of sulfenylating agent **103** was beneficial to this class of substrates as well, as benzopyran **143m** was produced with 95.4:4.6 e.r. The stereochemical model for enantioselectivity posits that bulky electrophiles accentuate the difference in catalyst distortion during the transition state for thiiranium ion formation. Thus, the respective position of the (*Z*)-methyl group to the enantiotopic faces of **142m** appears to cause a much greater distortion in the complex **95** derived from **103** than that from **56**.[40]



Scheme 63

4.5.5.3. Site-selectivity. The Markovnikov rule for site-selectivity holds well for the cyclization of alkenes wherein the nucleophile is three atoms removed (Section 4.5.4.4). The investigation of constitutional site-selectivity of the reaction alcohols to thiiranium ions derived from biased alkenes demonstrated that cyclization preferentially occurs at the stabilized position. For unbiased alkenes, a mixture of isomers is obtained, although an *in situ* isomerization process from the 5-*exo* isomer to the 6-*endo* isomer precluded analysis of kinetically controlled selectivity (Table 11).[18] In contrast, high 5-*exo* selectivity is observed for carboxylic acid cyclizations. The cyclization of phenolic hydroxyl groups proceeds similarly to the alcohols, with high Markovnikov site-selectivity being observed. The presence of resonance stabilization (presence of a Ph substituent, c.f. Table 19, entry 5) or inductive stabilization (disubsituted carbon atom of the thiiranium ion, Table 19, entry 4) is sufficient for high selectivity. Moreover, a mixture of isomers is observed in the absence of electronic bias (Table 19, entry 3). The presence of a phenolic hydroxyl group did not otherwise impact selectivity, as the cyclization of **142u** proceeded to give a mixture of isomers, whereas carboxylic acid **145t** displayed very high 5-*exo* selectivity, confirming previous trends (Table 19, entries 11 and 12).[137]

For capture of an electronically unbiased thiiranium ion by a phenolic hydroxyl group three atoms away, the Markovnikov rule predicts poor selectivity. Instead, the controlling factor is the relative rate of 5-*exo* to *6-endo* cyclization. For epoxides, *exo* opening to afford furans is preferred.[141b] In the case of substrate **142l**, a 1.5:1 ratio of **143l**/**144l** from *endo* vs. *exo* cyclization respectively was obtained. Direct comparison to the corresponding alcohol substrate, which afforded a 5:1 ratio of *endo*/*exo* isomers, is not warranted due to the presence of C_{sp2} atoms in the tether.[20] Instead, comparisons can be drawn to intramolecular phenol capture of other tethered three-membered rings. The opening of a disubstituted alkyl epoxide by a phenolic hydroxyl proceeds exclusively *exo*, whereas the iodine-mediated cyclization of 2-crotylphenol, which proceeds through an iodonium intermediate, affords solely the *endo* product (Scheme 64).[138] The intrinsic selectivity of phenol capture is therefore highly dependent on the nature of the electrophilic moiety, wherein increased charge and larger atoms in the three-membered ring result in higher formation of the *endo* product. Thiiranium ions are between these two extremes, and consequently low selectivity is observed.



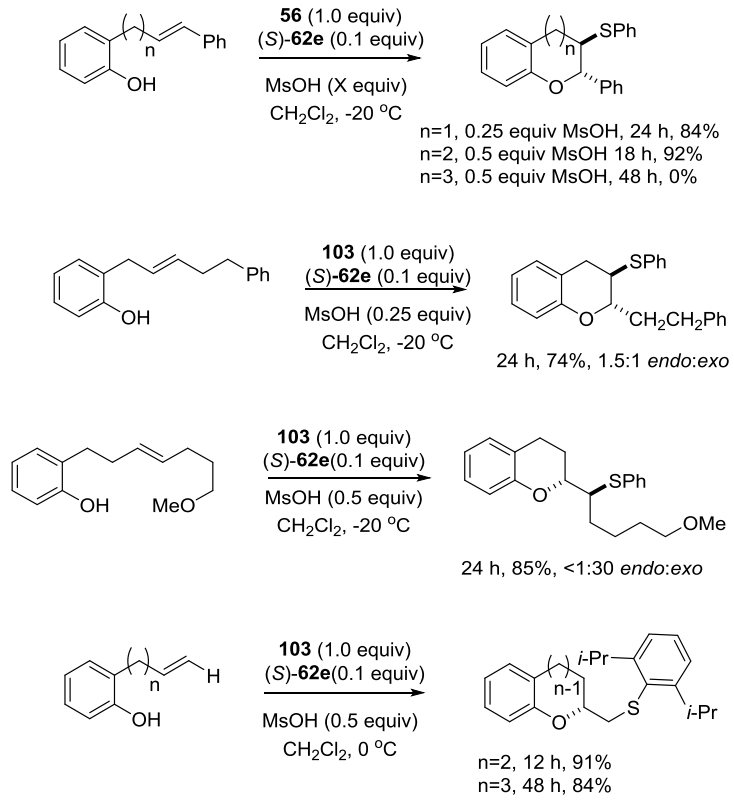
Scheme 64

The ratio **143l**/**144l** is independent of conversion. In this particular case, the reduced basicity of a benzopyran oxygen compared to a pyran, as well as the reduced MsOH loading likely retard isomerization, leading to poor site selectivity that represents kinetic control.

4.5.6. Influence of Tether Length. On the basis of the observed characteristics of the sulfenofunctionalization reaction, changes in the tether length were primarily expected to affect the rate- and site-selectivity of the process. As the alkene environment is constant among the various substrates, the enantioselectivity was not expected to vary. Indeed, comparable substrates displayed similar enantioselectivities irrespective of tether length (**142a** and **142n**, **142p** and **142q**).

4.5.6.1. Rate. The free energy barrier to cyclization for medium sized rings is highly dependent on ring size.[139] Consequently, the relative rates of *endo* and *exo* capture of the thiiranium ions are dependent on the sizes of the rings being formed. The rate of cyclization of substrate **142n**, bearing one more atom in the tether than **142a**, is similar to the rate of **142a** (c.f. Table 18, entry 1 and Table 19, entry 5, Scheme 65a). Similarly, the rates of cyclization of dialkyl-substituted substrates **142l** and **142s** are comparable (Table 19, entries 3 and 10, Scheme 65b and Scheme 65c). Overall, for 5-*exo*, 6-*endo*, 6-*exo* and 7-*endo* capture, thiiranium ion formation appears to be turnover-limiting, and no effect on rate as a function of tether length is observed. In contrast, substantially different rates are observed for the cyclization of **142p** and **142q** (12 h vs 48 h) which have, respectively, two and three methylene units in their tethers (Table 19, entries 7 and 8, Scheme 65d). The cyclization of **142o**, also bearing a three carbon tether, with **1c**, required elevated temperature compared to the shorter **142n** (22 ^{o}C vs -20 ^{o}C, Table 3, entries 5 and 6). Attempts to cyclize **142o** with **56** for comparison purposes failed, with

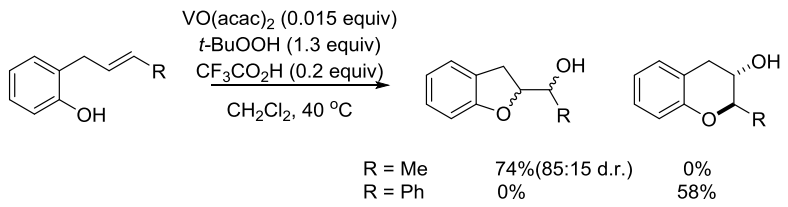
primarily decomposition products being formed (Scheme 65a). Thus, both 7-*exo* and 8-*endo* cyclizations are generally disfavored in comparison to the aforementioned modes. The overall relative rates as a function of cyclization mode can then be expressed as 8-*endo* << 7-*exo* < 7-*endo* ~ 6-*exo* ~ 6-*endo* ~ 5-*exo*. In conjunction with these rates, a regime for change of the rate-determining step can be established. For 7-*endo* and more facile closures, thiiranium formation remains turnover-limiting, however, for less favored closures such as 7-*exo* and 8-*endo*, capture becomes turnover-limiting. The importance of sterically shielding the thiiranium ion reactions with turnover-limiting capture is clearly illustrated by the failure of **56** to promote the cyclization of **142o**.



Scheme 65

4.5.6.2. Site-selectivity. Changing the tether length introduces substantial bias into the cyclization due to the higher energy associated with forming 7-membered and larger rings.[139,140] The cyclization of electronically unbiased alkenes with two-carbon tethers (**142s** and **142r**) show that the intrinsic selectivity for 6-*exo* over 7-*endo* highly favors the 6-*exo* product. However, **142n**, which bears a phenyl substituent, cyclized selectively to the less favored benzoxepane

143n. Thus, there exists a kinetic preference for cyclization following the Markovnikov rule. Surprisingly, the cyclization of **142o** did not follow the expected trend. Under standard reaction conditions, decomposition was observed. The increased kinetic barrier to either 8-*endo* or 7-*exo* cyclization likely extends thiiranium lifetime to the point where decomposition processes intervene. The use of the electrophile **103** led to preferential 7-*exo* cyclization. Electrophile **103** has been known to substantially increase thiiranium lifetime, enabling intramolecular sulfenofunctionalization reactions to be run at ambient temperature.[18,40] In this case, the increased stability imparted to the thiiranium ion is sufficient to prevent decomposition, whereupon successful phenol capture can take place. The observed site-selectivity is dominated by the kinetic preference for formation of a seven- vs. eight-membered ring. The subtle interplay between enthalpic and entropic contributions is similar to that exhibited with epoxide substrates wherein the cyclization of an electronically-unbiased epoxide affords the 5-*exo* isomer vs. the 6-*endo* isomer with high selectivity whereas an electronically biased epoxide opens with opposite selectivity (Scheme 66).[141]



Scheme 66

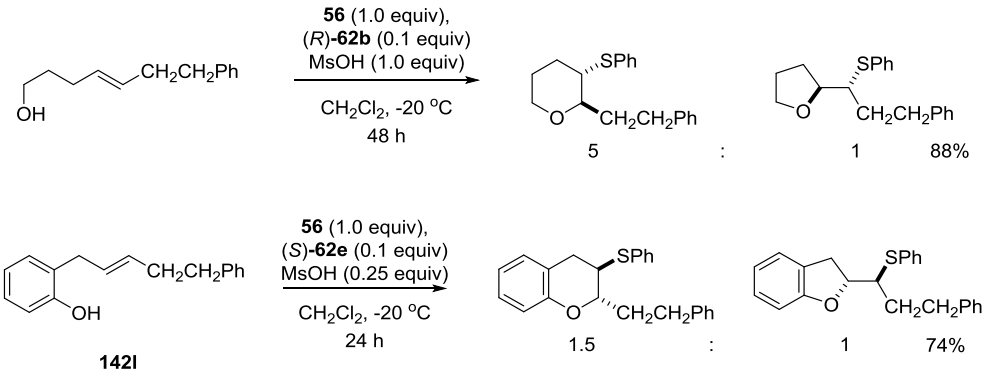
4.5.7. Influence of Lewis Basic Functional Groups. The sulfenofunctionalization process relies on a moderately Lewis basic selenophosphoramide to promote the catalytic process. Therefore, the sensitivity of the reaction to other Lewis basic functional groups that may be present in the reaction was of interest. In comparison with the reaction of **142a,** no effect on rate was observed for any of the four Lewis basic groups tested (alcohol, acid, ester, ether), although in these cases 0.5 equiv acid was used to counteract any potential buffering effects.

The enantioselectivity of the reactions were consistently high except for **143r** and **147t** which showed a slight erosion. The interaction of the carbonyl group either directly with the thiiranium ion during its formation or with the complex during its capture may lead to this erosion. Given the small magnitude of the change, the interaction appears to be weak. The site

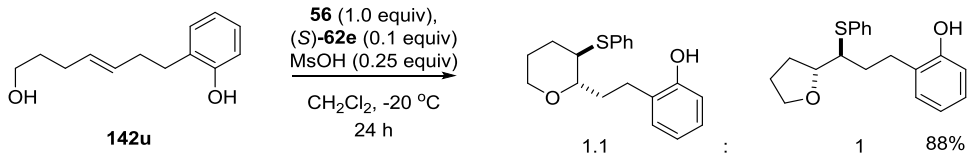
selectivity for ester **143r** was slightly lower than for **142s**, which also suggests an interaction not present with the ether functional group.

If two competent nucleophiles are present in the molecule, such as in **145t** and **146u**, capture with either nucleophile is possible. The chemoselectivity of the reaction is then dependent on, in addition to the ring size as discussed, the relative rates of cyclization for either nucleophile. Both a carboxylic acid and an alcohol outcompeted the phenolic hydroxyl group for thiiranium capture. Clearly, the deactivation of the phenolic hydroxyl group, a consequence of electron delocalization, with respect to other oxygen nucleophiles is sufficient to disfavor aryl ether formation.[129] Interestingly, the chemoselectivity does not correlate with proton affinity, as the pKa of a protonated carboxylic acid is somewhat higher than a protonated phenol ($pK_{a,aq.}$ $PhCO_2H_2^+$: -7.8 vs $PhOH_2^+$: -6.5).[66] The discrepancy suggests the existence of a secondary interaction that favors capture by the carboxylic acid, similar to what was observed during the cyclization of ester **142r**.

The site-selectivity for the formation of lactone **147t** was consistent with high 5-*exo* preference for cyclization of carboxylic acid substrates with phosphoramides.[20] In contrast, the alcohol **142u** formed **147u** and **148u** in almost equimolar ratio, compared to previous results where a 5:1 isomer ratio favoring the pyran was observed (Scheme 67a).[20] There appears to be no intrinsic kinetic preference for 5-*exo* vs. 6-*endo* cyclization for alcohols with three carbon tethers, in agreement with the low kinetic preference observed in the cyclization of phenol **142l** (Scheme 67b and Scheme 67c).



Scheme 67



Scheme 67 (cont.)

4.5.8. Intermolecular Sulfenylation. The phenoxysulfenylation reaction could also be performed intermolecularly. The production of **149** ensued in comparable yield and selectivity to **143a**. Although the selectivity was slightly lower (93:7 compared to 95:5), such small decreases were also observed in the comparison of inter- and intramolecular sulfenylation. However, the sulfenofunctionalization of β-methylstyrene was much less successful. The lower nucleophilicity of phenols with respect to alcohols now allows substantial racemization to take place. Stilbene was completely unreactive. Increased conjugation is known to decrease reactivity with respect to thiiranium ions, and the result was not particularly unexpected. The applicability of intermolecular sulfenylation remains limited based on the current substrate scope.

4.6. Conclusions.

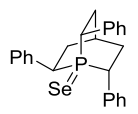
The highly enantioselective sulfenocyclization of alkenes with tethered phenolic hydroxyl groups to afford substituted chromans has been accomplished. A systematic variation of the nucleophile component and tether length allowed further trends in sulfenofunctionalization to be identified. The reaction was insensitive to changes in the steric properties of the nucleophile. The nucleophile electron density only made a difference for highly electron-deficient phenols. The reaction rate did not change for one- and two-methylene tethers, and both benzopyrans and benzoxepanes were readily prepared, whereas further increases in tether length resulted in slower reactions. Enantioselectivity was unaffected by changes in the nucleophile component or tether length. Nucleophilic capture occurred at the more electronically biased location of the thiiranium ion. In the absence of electronic bias, the intrinsic site selectivity of sulfenofunctionalization was low for one-methylene tethers but high for two-methylene tethers. Carboxylic acids and alcohols were more reactive towards thiiranium ions than phenolic hydroxyl groups, and high chemoselectivity was observed in competition experiments. Substrates which displayed low reactivity at -20 ^{o}C were amenable to sulfenofunctionalization with hindered **103** at higher temperatures. The increased thiiranium ion stability as a result of

shielding prevented enantioerosion that had previously plagued reactions at such elevated temperature.

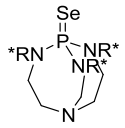
4.7. Outlook.

The sulfenofunctionalization of alkenes has enabled the rapid synthesis of diverse sulfenylated heterocycles. In the presence of oxygen based nucleophiles pyrans, benzopyrans and lactones can be formed. The enantioselectivity of the reaction remained high throughout a diverse set of modifications, a result of the configurational stability of the thiiranium ion. Only changes in the alkene geometry were not well tolerated.

The development of new sulfenofunctionalization catalysts is necessary for the extension of the reaction to other alkene geometries such as *cis*- or 1,1-substituted. Steric differentiation of *cis*-alkenes usually requires catalysts of ungerade symmetry, thus, these catalysts will likely not exhibit the C_2 symmetry present in the current catalyst architecture. Some architectures that have been proposed so far are the C_3 symmetric propellane architectures **155** and **156 (**Scheme 68**)**.



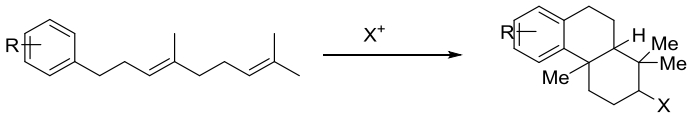
155



156

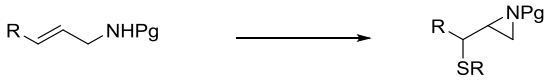
Scheme 68

The thiiranium ion that results from initial alkene sulfenofunctionalization remains a strong electrophile. Thus, other alkenes of sufficient electron density may be able to engage the thiiranium ion in C-C bond formation. The resulting carbocation would then serve as a locus for further ring formation or rearrangement. These well known polyene cyclization processes have been triggered by the formation of other -iranium ions before, however current enantioselective polyene cyclization methods remain limited (Scheme 69).[142] The broad nucleophile and substituent tolerance of the sulfenofunctionalization process and high selectivity independent of substrate are well suited towards this type of cyclization.



Scheme 69

The highly selective functionalization of terminal alkenes remains an area of active research, and the sulfenofunctionalization reaction could be employed to synthesize terminal aziridines with high selectivity in a Payne-type reaction.[143] The sulfenofunctionalization of an allyl amine would lead to the formation of a thiiranium ion with an α-amine. Anchimeric opening of the thiiranium ion would lead to α-thioaziridine formation (Scheme 70).



Scheme 70

The deprotection of the thioether moiety has remained problematic throughout the course of these investigations. Attempts at cross coupling with an Fe-based system were met with mixed success, and, as detailed above, the direct deprotection also proved difficult.[144] Conversion of the sulfoxide to the ketone failed as well. Thus, changes to the aryl group that make it easier to deprotect are necessary. These may be either increasing electron density on the arene, to better undergo oxidative deprotection, or completely changing the electrophile to better accommodate deprotection strategies. These approaches remain active areas of research in these laboratories.

Chapter 5: Experimental Procedures

5.1. General Experimental.

All reactions were performed in oven- (160 °C) and/or flame-dried glassware under an atmosphere of dry argon unless otherwise noted. Reaction solvents tetrahydrofuran (Fisher, HPLC grade), ether (Fisher, BHT stabilized ACS grade), and dichloromethane (Fisher, unstabilized HPLC grade), were dried by percolation through two columns packed with neutral alumina under a positive pressure of argon. Reaction solvents hexanes (Fisher, OPTIMA grade) and toluene (Fisher, ACS grade) were 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. Solvents for filtration, transfers, and chromatography were certified ACS grade. "Brine" refers to a saturated solution of sodium chloride in water. All reaction temperatures correspond to internal temperatures measured with Teflon coated thermocouples. A ThermoNesLab CC-100 or a ThermoNesLab IBC-4A cryocool with an attached cryotrol was used for reactions at subambient temperatures.

^{1}H and ^{13}C NMR spectra were recorded on Varian Unity (400 MHz, ^{1}H; 101 MHz, ^{13}C) or Inova (500 MHz, ^{1}H; 126 MHz, ^{13}C) spectrometers. ^{31}P NMR and ^{19}F spectra were recorded on Inova (202 MHz) and Inova (470 MHz) spectrometers respectively. Acquisition times were 4.096 s for ^{1}H NMR, 1.024 s for ^{13}C NMR, 0.655 s for ^{31}P NMR, and 0.328 s for ^{19}F NMR. Spectra are referenced to residual chloroform (δ = 7.26 ppm, ^{1}H; 77.0 ppm, ^{13}C). Chemical shifts are reported in parts per million, multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), sept (septet), m (multiplet), and br (broad). Coupling constants, *J*, are reported in Hertz, and integration is provided and assignments are indicated. Assignments were confirmed through 2-D COSY and HMQC experiments. Elemental analysis was performed by the University of Illinois Microanalysis Laboratory or Robertson Microlit Laboratories. 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 on a Finnegan-MAT C5 spectrometer. Chemical Ionization (CI) spectra were performed with methane reagent gas on a Micromass 70-VSE spectrometer. Electrospray Ionization (ESI) spectra were performed on a Micromass Q-Tof Ultima spectrometer. Data are reported in the

form of m/z (intensity relative to the base peak = 100). Infrared spectra (IR) were recorded on a Perkin-Elmer FT-IR system and peaks are reported in cm^{-1} with indicated relative intensities: s (strong, 0–33% T); m (medium, 34–66% T), w (weak, 67–100% %), and br (broad). Melting points (mp) were determined on a Thomas-Hoover capillary melting point apparatus in sealed tubes under vacuum and are corrected.

Analytical thin-layer chromatography (TLC) was performed on Merck silica gel 60 F254 or Merck silica gel 60 RP-18 F254s plates. Silver impregnated silica was prepared by first dissolving 5 g of $AgNO_3$ in 30 mL of deionized water. The resulting homogenous solution was added to 50 g of SiO_2 in a mortar. The clumpy silica was ground with a pestle until free-flowing. The mortar was then covered in aluminium foil and placed in an oven (160 ^oC) for 3 h. The vessel was then removed from the oven, and allowed to cool in a dessicator. No special precautions were necessary during the chromatography process, however, prolonged (>6 h) exposure to visible light resulted in the formation of black Ag nanoparticles and a loss of column separation power. Visualization was accomplished with UV light and/or Ceric Ammonium Molybdenate (CAM) solution. R_f values reported were measured using a 10 × 2 cm TLC plate in a developing chamber containing the solvent system described. Flash chromatography was performed using Merck silica gel 60 230–400 mesh (60–63 μ, 60 Å pore size). Analytical chiral stationary phase supercritical fluid chromatography (CSP-SFC) was performed on an Agilent 1100 HPLC equipped with an Aurora Systems A-5 supercritical CO_2 adapter for supercritical fluid chromatography and a UV detector (220 nm or 254 nm) using Daicel Chiralcel OD, OJ, OB or Chiralpak AD, and AS columns as well as a Regis Whelk-O1 column. Normal Phase HPLC was performed on an Agilent 1100 HPLC equipped with AD-H, OJ-H, IB-3, Naphtholeucine and *R,R*-Beta-Gem columns. Reverse-Phase HPLC was performed on an Agilent 1100 HPLC using a Chiralpak AD-RH or Chiralcel OJ-RH column.

Commercial reagents were purified by distillation or recrystallization prior to use unless noted. Solvents for chromatography, filtration and recrystallization were toluene (Fisher, ACS grade), dichloromethane (Aldrich, ACS grade), ethyl acetate (Fisher, ACS grade), and hexane (Fisher, Optima). Isopropylamine (Aldrich), triethylamine (Alfa-Aesar) and pyridine (Fisher) were distilled from CaH_2.

5.2. Literature Preparations.

Literature Preparations for Chapter 2:

Electrophiles *N*-(phenylthio)-phthalimide **56**[145], *N*-(phenylthio)-benzotriazole **67**[69], *N*-(phenylthio)saccharin **68**[146]**,** *N*-(phenylthio)bismethylsulfonamide **69**[147]**,** phenylsulfenyl acetate **70**[75]**,** 2-nitrophenylsulfenyl acetate **71**[75]**,** 2,4-dinitrophenylsulfenylacetate **72**[75]**,** *N*-(methylthio)-phthalimide **74**[148]**,** *N*-(trichloromethylthio)-phthalimide **75**[149]**,** *N*-(4-nitrophenylthio)phthalimide **76**[148] and *N*-(2,6-diisopropylphenylthio) phthalimide **103**[40] were prepared as decribed.

Alkenes (*E*)-5-phenyl-pent-4-en-1-ol **57a**[20]**,** (*E*)-5-(4-trifluoromethylphenyl)-pent-4-en-1-ol **57b**[20]**,** (*E*)-5-(4-methoxyphenyl)-pent-4-en-1-ol **57c**[20]**,** methyl (E)-6-hydroxyhex-2-enoate **57d**[20]**,** (*E*)-2-methyl-6-phenylhex-5-en-2-ol **57e**[150]**,** (*E*)-2,2-dimethyl-5-phenylpent-4-en-1-ol **57f**[20]**,** (*E*)-7-phenylhept-4-en-1-ol **57g**[20]**,** (*E*)-6-methylhept-4-en-1-ol **57h**[20]**,** (*Z*)-5-phenyl-pent-4-en-1-ol **57i**[20]**,** (*Z*)-7-phenylhept-4-en-1-ol **57j**[151]**,** pent-4-en-1-ol **57k**[20]**,** 4-phenylpent-4-en-1-ol **57l**[20]**,** (*E*)-5-phenylhex-4-en-1-ol **57m**[20]**,** (*E*)-4-methyl-5-phenylpent-4-en-1-ol **57n**[20]**,** (*E*)-5-phenylpent-4-enoic acid **57o**[20]**,** (*E*)-5-phenylpent-4-enamide **57p**[152] were prepared as described.

Catalysts **61**[69], (*R*)-4-(piperidin-1-yl)-3,5-dimethyl-4,5-dihydro-3*H*-dinaphtho[2,1-*d*:1',2'-*f*][1,3,2]diazaphosphepine-4-selenide **62a**[16], (*R*)-4-(diisobutyl)-3,5-dimethyl-4,5-dihydro-3*H*-dinaphtho[2,1-*d*:1',2'-*f*][1,3,2]diazaphosphepine-4-selenide **62d**[83], di-Me-BINAM[71]**,** (*R*)-4-(diisopropyl)-3,5-dimethyl-4,5-dihydro-3*H*-dinaphtho[2,1-*d*:1',2'-*f*][1,3,2]diazaphosphepine-4-selenide **62e**[40]**,** and azocane[153] were prepared according to their published procedures.

Literature Preparations for Chapter 3:

(*E*)-5-(2-fluorophenyl)-pent-4-en-1-ol **99**[154], (*R*)-6,6- dimethyl-2,2-di(methylamino)-1,1-biphenyl[155], benzenesulfenyl chloride[156], 1,1-dimethyl-2-phenyldisulfan-1-ium hexachloroantimonate ($[PhS(SMe_2)]SbCl_6$)[85] were prepared according to their published procedures.

Literature Preparations for Chapter 4:

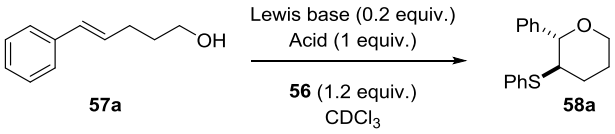
2-((*E*)-3-thiophenylprop-2-en-1-yl)phenol **119a**[157], 2-(but-3-en-1-yl)phenol[96b], **142p**[158], 2-(pent-4-en-1-yl)phenol **142q**[96b], (*E*)-3-(furan-2-yl)-1-(2-hydroxyphenyl)prop-2-en-1-one

118b[159] and diethyl (*E*)-2-(5-(2-hydroxyphenyl)pent-2-en-1-yl)malonate **138**[160] were prepared as described.

5.3. Experimental Procedures for Chapter 2.

Survey of Achiral Lewis Bases (Table 4)

General Procedure 1



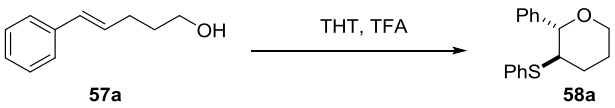
An oven-dried, 5-mm NMR tube was charged with *N*-phenylthiophthalimide (**56**, 1.2 equiv) in a glovebox and capped with a septum. Outside of the glovebox, 5-phenyl-4-penten-1-ol (**57a**), the indicated amount of catalyst and 0.62 mL of $CDCl_3$ was added and the mixture was shaken well. Subsequently, the corresponding amount of acid was added and the mixture was shaken again. Spectra were recorded at 3 h and 24 h time points. Conversion to product was measured by the appearance of the diagnostic ^{1}H NMR resonance for the product at 4.14 ppm with respect to the substrate peaks at 6.23 ppm and 3.72 ppm. Generally, no other products were observed in the ^{1}H NMR spectra. Formation of phthalimide byproduct was visually confirmed by the precipitation out of the solution.

Data for **58a**:

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

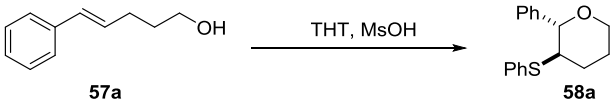
7.32 (m, 2 H, H(C-aryl)), 7.28 – 7.16 (m, 3 H, H(C-aryl)), 7.14 – 7.03 (m, 5 H, H(C-aryl)), 4.14 (d, *J* = 10.1 Hz, 1 H, HC(2)), 4.09 – 4.00 (m, 1 H, HC(6)), 3.53 (td, *J* = 11.9, 2.2 Hz, 1 H, HC(6)), 3.20 (ddd, *J* = 11.5, 10.2, 4.0 Hz, 1 H, HC(3)), 2.32 – 2.17 (m, 1 H, HC(4)), 1.93 – 1.73 (m, 1 H, HC(5)), 1.66 (m, 2 H, HC(4), HC(5)).

Sulfenocyclization with Tetrahydrothiophene and TFA (Table 4, Entry 1) [DJK-3-34A]



Following General Procedure 1, an oven-dried NMR tube was charged with **56** (20 mg, 0.078 mmol 1.2 equiv), **57a** (9.9 mg, 0.062 mmol), THT (Tetrahydrothiophene, 1.2 µL, 0.013 mmol, 0.22 equiv) and $CDCl_3$ (0.62 mL). Trifluoroacetic acid (4.7 µL, 0.061 mmol, 1.0 equiv) was added and the tube was shaken well. Spectral analysis revealed 33% and 70% conversion after 3 h and 24 h respectively.

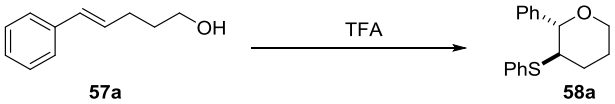
Sulfenocyclization with Tetrahydrothiophene and MsOH (Table 4 Entry 2) [DJK-3-34B]



57a **58a**

Following General Procedure 1, an oven-dried NMR tube was charged with **56** (20 mg, 0.078 mmol 1.2 equiv), **57a** (9.7 mg, 0.062 mmol), THT (1.2 µL, 0.013 mmol, 0.23 equiv) and $CDCl_3$ (0.62 mL). Methanesulfonic acid (4.0 µL, 0.061 mmol, 1.0 equiv) was added and the tube was shaken well. Spectral analysis revealed 100% conversion after 3 h.

Background Sulfenofunctionalization with TFA (Table 4 Entry 3) [DJK-3-34D]



57a **58a**

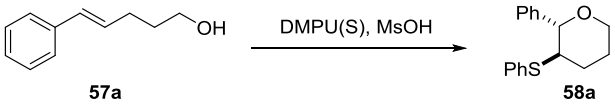
Following General Procedure 1, an oven-dried NMR tube was charged with **56** (20 mg, 0.078 mmol 1.2 equiv), **57a** (10.2 mg, 0.063 mmol) and $CDCl_3$ (0.62 mL). Trifluoroacetic acid (4.7 µL, 0.061 mmol, 1.0 equiv) was added and the tube was shaken well. Spectral analysis revealed no conversion after 24 h.

Background Sulfenofunctionalization with MsOH (Table 4 Entry 4) [DJK-3-34E]

57a **58a**

Following General Procedure 1, an oven-dried NMR tube was charged with **56** (20 mg, 0.078 mmol 1.2 equiv), **57a** (10.0 mg, 0.062 mmol) and $CDCl_3$ (0.62 mL). Methanesulfonic acid (4.0 µL, 0.062 mmol, 1.0 equiv) was added and the tube was shaken well. Spectral analysis revealed trace and 10% conversion after 3 and 24 h respectively.

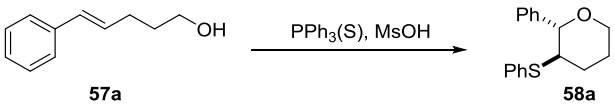
Sulfenofunctionalization with 1,3-Dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinthione (DMPU(S)) (Table 4 Entry 5) [DJK-3-25-M]



57a **58a**

Following General Procedure 1, an oven-dried NMR tube was charged with **56** (20 mg, 0.078 mmol 1.2 equiv), **57a** (10.2 mg, 0.063 mmol), 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinethione (1.9 mg, 0.013 mmol, 0.21 equiv) and $CDCl_3$ (0.62 mL). Methanesulfonic acid (4.0 µL, 0.062 mmol, 1.0 equiv) was added and the tube was shaken well. Spectral analysis revealed 7% and 55% conversion after 3 and 24 h respectively.

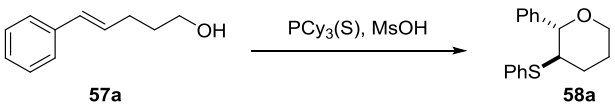
Sulfenofunctionalization with Triphenylphosphine sulfide (Table 4 Entry 6) [DJK-3-25-G]



57a **58a**

Following General Procedure 1, an oven-dried NMR tube was charged with **56** (20 mg, 0.078 mmol 1.2 equiv), **57a** (10.2 mg, 0.063 mmol), triphenylphosphine sulfide (3.63 mg, 0.012 mmol, 0.20 equiv) and $CDCl_3$ (0.62 mL). Methanesulfonic acid (4.0 µL, 0.062 mmol, 1.0 equiv) was added and the tube was shaken well. Spectral analysis revealed 100% conversion after 3 h.

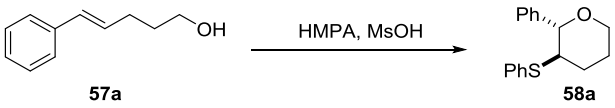
Sulfenofunctionalization with Tricyclohexylphosphine sulfide (Table 4 Entry 7) [DJK-3-25-L]



57a **58a**

Following General Procedure 1, an oven-dried NMR tube was charged with **56** (20 mg, 0.078 mmol 1.2 equiv), **57a** (10.1 mg, 0.062 mmol), tricyclohexylphosphine sulfide (3.89 mg, 0.012 mmol, 0.20 equiv) and $CDCl_3$ (0.62 mL). Methanesulfonic acid (4.0 µL, 0.062 mmol, 1.0 equiv) was added and the tube was shaken well. Spectral analysis revealed 100% conversion after 3 h.

Sulfenofunctionalization with Hexamethylphosphoramide (Table 4 Entry 8) [DJK-3-25-I]



57a **58a**

Following General Procedure 1, an oven-dried NMR tube was charged with **56** (20 mg, 0.078 mmol 1.2 equiv), **57a** (10.1 mg, 0.062 mmol), hexamethylphosphoramide (2.1 µL, 0.012 mmol, 0.20 equiv) and $CDCl_3$ (0.62 mL). Methanesulfonic acid (4.0 µL, 0.062 mmol, 1.0 equiv) was added and the tube was shaken well. Spectral analysis revealed 0% conversion after 24 h.

Sulfenofunctionalization with Hexamethylsulfenophosphoramide (Table 4 Entry 9) [DJK-3-25-H]

57a **58a**

Following General Procedure 1, an oven-dried NMR tube was charged with **56** (20 mg, 0.078 mmol 1.2 equiv), **57a** (9.8 mg, 0.061 mmol), hexamethylthiophosphoramide (2.42 mg, 0.012 mmol, 0.2 equiv) and $CDCl_3$ (0.62 mL). Methanesulfonic acid (4.0 µL, 0.062 mmol, 1.0 equiv) was added and the tube was shaken well. Spectral analysis revealed 35% conversion after 24 h.

Sulfenofunctionalization with Hexamethylselenophosphoramide (Table 4 Entry 10) [DJK-3-25-J]

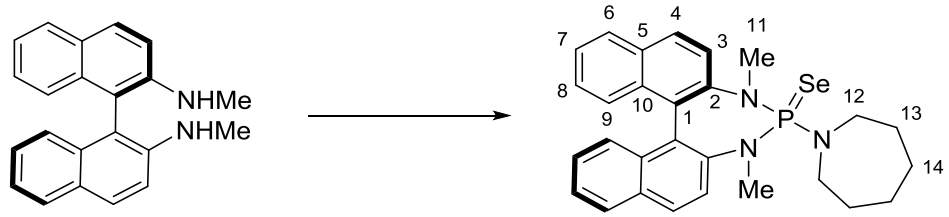
57a **58a**

Following General Procedure 1, an oven-dried NMR tube was charged with **56** (20 mg, 0.078 mmol 1.2 equiv), **57a** (10.2 mg, 0.063 mmol), hexamethylselenophosphoramide (3.06 mg, 0.012 mmol, 0.2 equiv) and $CDCl_3$ (0.62 mL). Methanesulfonic acid (4.0 µL, 0.062 mmol, 1.0 equiv) was added and the tube was shaken well. Spectral analysis revealed 31% and 100% conversion after 3 and 24 h respectively.

Survey of Chiral, Nonracemic Lewis Bases for Sulfenofunctionalization

Preparation of Catalysts for Table 5:

Preparation of (*R*)-4-(Azepan-1-yl)-3,5-dimethyl-4,5-dihydro-3*H*-dinaphtho[2,1-*d*:1',2'-*f*][1,3,2]diazaphosphepine-4-selenide (62b) [DJK-2-27]



65 **62b**

To a flame-dried, 50-mL Schlenk flask equipped with a magnetic stir bar and septum were added amine **65** (1.048 g, 3.35 mmol) and anhydrous toluene (10.0 mL) via syringe under argon. The solvent was removed under high vacuum (30 °C, 0.05 mm Hg) for 30 min. Anhydrous THF (30.0 mL) and Et_3N (1.167 mL, 8.38 mmol, 2.5 equiv) were added via syringe and the homogeneous mixture was cooled to 0 °C. Phosphorus trichloride (880 µL, 10.0 mmol, 3.0 equiv) was added dropwise via syringe whereupon a colorless precipitate formed immediately. The reaction mixture was stirred at 0 °C for 1.5 h, then was allowed to warm to room temperature and was stirred for another 3 h. The volatiles were removed under high vacuum (30 °C, 0.05 mm Hg) and anhydrous Et_2O (10.0 mL) was added via syringe and the mixture was stirred for 5 min. The supernatant was cannula filtered into a tared, flame-dried, argon filled, 50-mL Schlenk flask equipped with a rubber septum. The remaining precipitate in the reaction flask was washed with anhydrous Et_2O (5.0 mL) and then was filtered into the receiver Schlenk flask. The volatiles were removed under high vacuum (30 °C, 0.05 mm Hg) to afford 1.262 g of a colorless foam. The solid was redissolved in anhydrous Et_2O (10.0 mL) and the volatiles were again removed under high vacuum (30 °C, 0.05 mm Hg) to remove traces of HCl. The solid was then dried for 2.5 h at reduced pressure (23 ^{o}C, 0.05 mm Hg) to give a colorless foam. Anhydrous CH_2Cl_2 (30.0 mL) was added via syringe and the mixture was cooled to 0 °C. Triethylamine (560 µL, 4.0 mmol, 1.2 equiv) and hexahydro-1*H*-azepine (411 µL, 3.65 mmol, 1.1 equiv) were added via syringe and the reaction mixture was allowed to warm to room temperature and then was stirred for 24 h. Powdered selenium (796 mg, 10.1 mmol, 3.0 equiv)

was added and the mixture was stirred for 50 h, whereupon the mixture was filtered through a pad of Celite (5 g, 35 mm). The pad was washed with EtOAc (50 mL) and the filtrate was concentrated in vacuo (40 °C, 10 mm Hg) and the residue was purified by silica gel flash column chromatography (SiO_2, 15 g, 20 mm Ø, hexanes/EtOAc, 60:1 to 40:1) to afford 1.233 g (71%) of **62b** as an off-white solid.Data for (*R*)-**62b**:

mp: 252-253 °C (decomposition)

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

8.06 (d, *J* = 8.8 Hz, 1 H, HC(4,4')), 8.01 (d, *J* = 8.8 Hz, 1 H, HC(4,4')), 7.96 (d, *J* = 8.1 Hz, 1 H, HC(6)), 7.93 (d, *J* = 8.2 Hz, 1 H, HC(6')), 7.72 (d, *J* = 8.2 Hz, 1 H, HC(3,3')), 7.71 (d, *J* = 8.4 Hz, 1 H, HC(3,3')), 7.47 (t, *J* = 7.2 Hz, 1 H, HC(7)), 7.41 (t, *J* = 7.2 Hz, 1 H, HC(7')), 7.34 (d, *J* = 8.4 Hz, 1 H, HC(9)), 7.27 (t, *J* = 7.4 Hz, 1 H, HC(8)), 7.18 (t, *J* = 7.4 Hz, 1 H, HC(8')), 7.14 (d, *J* = 8.4 Hz, 1 H, HC(9')), 3.46 - 3.36 (m, 2 H, H_2C(12) and H_2C(12')), 3.33 (d, *J* = 12.3 Hz, 3 H, H_3C(11,11')), 3.17 - 3.02 (m, 2 H, H_2C(12) and H_2C(12')), 2.95 (d, *J* = 13.4 Hz, 3 H, H_3C(11,11')), 1.72 (bs, 8 H, H_2C(13), H_2C(14))

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

142.9 (d, *J* = 11.3 Hz, C(2,2')), 141.8 (C(2,2')), 132.4 (C(aryl)), 132.2 (C(aryl)), 131.2 (C(aryl)), 130.9 (C(aryl)), 129.3 (C(4,4')), 128.7 (C(6)), 128.5 (C(1,1')), 128.0 (C(4,4')), 2 × 127.8 (C(6') and C(8')), 127.4 (d, *J* = 2.5 Hz, C(1,1')), 127.1 (C(9')), 126.0 (C(9)), 125.7 (C(8')), 125.1 (C(7)), 124.7 (C(7')), 123.0 (C(3,3')), 122.1 (C(3,3')), 49.6 (C(12)), 37.9 (d, *J* = 11.3 Hz, C(11,11')), 35.2 (d, *J* = 6.3 Hz, C(11,11')), 30.3 (d, *J* = 3.8 Hz, C(13)), 26.7 (C(14))

^{31}P NMR: (202 MHz, $CDCl_3$)

91.64

IR: (KBr)

3046 (w), 2993 (w), 2929 (m), 2858 (w), 1618 (m), 1593 (s), 1506 (s), 1466 (s), 1329 (s), 1274 (s). 1147 (s), 1090 (s), 1052 (s), 934 (s), 815 (s), 753 (s)

MS: (ESI)

522 (25), 521 (34), 520 (100, $M+H^+$), 518 (57), 517 (24), 516 (21)

HRMS: calcd for $C_{28}H_{31}N_3PSe^+$: 520.1415, found: 520.1422

TLC: R_f 0.17 (hexanes/EtOAc, 20:1) [CAM]

Opt Rot. : $[\alpha]_D^{24}$ -318.1 (c = 0.25, $CHCl_3$)

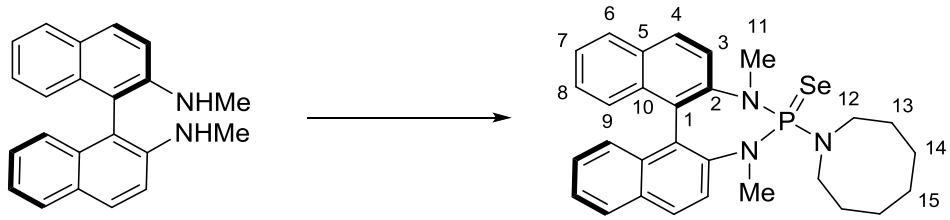
SFC: (*R*)-***3c***, t_R, 15.75 min (99.2%); (*S*)-3c, t_R 19.42 min (0.8%) (Chiralpak AD, 15% MeOH in CO_2, 2 mL/min, 220 nm.)

Analysis: $C_{28}H_{30}N_3PSe$ (518.49)

Calcd: C, 64.86; H, 5.83% N, 8.10%

Found: C, 64.88; H, 5.83% N, 7.98%

Preparation of (*R*)-4-(Azocin-1-yl)-3,5-dimethyl-4,5-dihydro-3*H*-dinaphtho[2,1-*d*:1',2'-*f*][1,3,2]diazaphosphepine-4-selenide (62c) [DJK-1-56]



65 **62c**

To a flame-dried, 50-mL Schlenk flask equipped with a magnetic stir bar and septum were added amine **65** (161.2 mg, 0.5 mmol) and anhydrous toluene (10.0 mL) via syringe under argon. The solvent was removed under high vacuum (30 °C, 0.05 mm Hg) for 30 min. Anhydrous THF (30.0 mL) and Et_3N (174 µL, 1.25 mmol, 2.5 equiv) were added via syringe and the homogeneous mixture was cooled to 0 °C. Phosphorus trichloride (131 µL, 1.5 mmol, 3.0 equiv) was added dropwise via syringe whereupon a colorless precipitate formed immediately. The reaction mixture was stirred at 0 °C for 1.5 h, then was allowed to warm to room temperature and was stirred for another 24 h. The volatiles were removed under high vacuum (30 °C, 0.05 mm Hg) and anhydrous Et_2O (15.0 mL) was added via syringe and the mixture was stirred for 5 min. The supernatant was cannula filtered into a tared, flame-dried, argon filled, 50-mL Schlenk flask equipped with a rubber septum. The remaining precipitate in the reaction flask was washed with anhydrous Et_2O (5.0 mL) and then was filtered into the receiver Schlenk flask. The volatiles were removed under high vacuum (30 °C, 0.05 mm Hg). The solid was redissolved in anhydrous Et_2O (10.0 mL) and the volatiles were again removed under high vacuum (30 °C, 0.05 mm Hg) to remove traces of HCl. The solid was then dried for 2.5 h at reduced pressure (23 °C, 0.05 mm Hg) to give 188.4 mg of a colorless foam. Anhydrous CH_2Cl_2 (10.0 mL) was added via syringe and the mixture was cooled to 0 °C. Triethylamine (90 µL, 0.63 mmol, 1.2 equiv)

and heptahydro-1*H*-azocine (80 mg, 0.58 mmol, 1.1 equiv) were added via syringe and the reaction mixture was allowed to warm to room temperature and then was stirred for 24 h. Powdered selenium (120 mg, 1.5 mmol, 3.0 equiv) was added and the mixture was stirred for 50 h, whereupon the mixture was filtered through a pad of Celite (5 g, 35 mm). The pad was washed with EtOAc (50 mL) and the filtrate was concentrated in vacuo (40 °C, 10 mm Hg) and the residue was purified by silica gel flash column chromatography (SiO_2, 15 g, 20 mm Ø, hexanes/EtOAc, 60:1 to 40:1) to afford 223.1 mg (71%) of **62c** as an off-white solid.Data for **62c:**

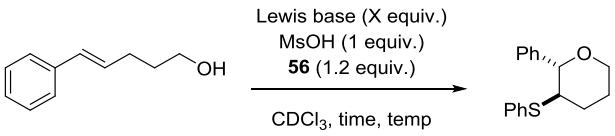
^{1}H NMR: (500 MHz, $CDCl_3$)

δ 8.01 – 7.97 (d, *J* = 8.9 Hz, 1H, HC(4,4')), 7.97 – 7.92 (d, *J* = 8.8 Hz, 1H, HC(4,4')), 7.93 – 7.88 (d, *J* = 8.2 Hz, 1H, HC(6)), 7.89 – 7.85 (d, *J* = 8.1 Hz, 1H, HC(6')), 7.70 – 7.65 (d, *J* = 9.0 Hz, 1H, HC(3,3')), 7.65 – 7.61 (dd, *J* = 8.9, 1.3 Hz, 1H, HC(3,3')), 7.46 – 7.40 (ddd, *J* = 8.1, 6.4, 1.5 Hz, 1H, HC(7)), 7.39 – 7.34 (t, *J* = 7.5 Hz, 1H, HC(7')), 7.30 – 7.20 (m, 2H, HC(8,9)), 7.17 – 7.10 (ddd, *J* = 8.1, 6.7, 1.2 Hz, 1H, HC(8')), 7.09 – 7.02 (d, *J* = 8.5 Hz, 1H, HC(9')), 3.33 – 3.18 (d, *J* = 12.2 Hz, 4H, HC(11,11',12)), 3.04 – 2.91 (tdd, *J* = 14.5, 8.1, 4.0 Hz, 2H, HC(12')), 2.91 – 2.84 (d, *J* = 13.4 Hz, 3H, HC(11,11')), 1.79 – 1.70 (m, 2H, HC(13,14,15), 1.70 – 1.63 (m, 6H, HC(13,14,15)), 1.62 – 1.55 (m, 2H, HC(13,14,15)).

^{31}P NMR: (202 MHz, $CDCl_3$)

92.44

Sulfenofunctionalization with Chiral Nonracemic Lewis Bases (Table 5)



General Procedure

An oven-dried 5-mm NMR tube was charged with **56** in a glovebox. The tube was taken out of the box and the Lewis base, **57a**, and 0.7 mL $CDCl_3$ was added. If indicated, the tube was cooled to the appropriate temperature in a -20 ^oC freezer or cryocool unit. The acid was added at the indicated temperature and the mixture was shaken well. The reaction was quenched after the indicated time with excess Et_3N, and the product was purified by silica gel flash column

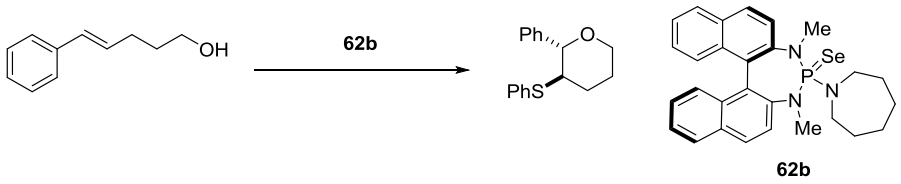
chromatography prior to SFC analysis.

Data for **58a**:

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

7.32 (m, 2 H, H(C-aryl)), 7.28 – 7.16 (m, 3 H, H(C-aryl)), 7.14 – 7.03 (m, 5 H, H(C-aryl)), 4.14 (d, *J* = 10.1 Hz, 1 H, HC(2)), 4.09 – 4.00 (m, 1 H, HC(6)), 3.53 (td, *J* = 11.9, 2.2 Hz, 1 H, HC(6)), 3.20 (ddd, *J* = 11.5, 10.2, 4.0 Hz, 1 H, HC(3)), 2.32 – 2.17 (m, 1 H, HC(4)), 1.93 – 1.73 (m, 1 H, HC(5)), 1.66 (m, 2 H, HC(4), HC(5)).

Sulfenofunctionalization with (*R*)-4-(1-Azepano)-3,5-dimethyl-4,5-dihydro-3H-dinaphtho[2,1-d:1',2'-f][1,3,2]diazaphosphepine-4-selenide (62b) (Table 5 Entry 4) [DJK-1-17]



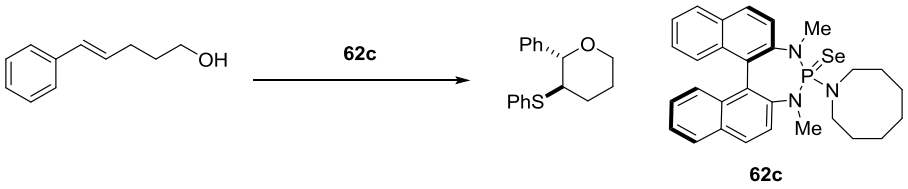
62b

Following General Procedure 2, an oven-dried NMR tube was charged with **56** (25.5 mg, 0.1 mmol, 1 equiv), and **57a** (16.2 mg, 0.1 mmol). To this was added (*R*)-**62b** (5.2 mg, 0.01 mmol, 0.1 equiv), $CDCl_3$ (0.7 mL). The reaction was cooled to -20 ^oC in a freezer and MsOH (6.5 µL, 0.1 mmol, 1.0 equiv) was added. After 30 h, the reaction was quenched with Et_3N (10 µL). Purification by flash chromatography (SiO_2, 20 g, 20 mm Ø, hexanes/EtOAc, 30:1) afforded 16 mg (59%) of **58a** as a white solid**.**

Data for **58a**:

SFC: (2*R*,3*S*)-**58a,** t_R 4.29 min (90.6%); (2*S*,3*R*)-**58a,** t_R 5.35 min (9.4%) (Chiralpak AD, 5% MeOH in CO_2, 3 mL/min, 220 nm, 40 ^oC)

Sulfenofunctionalization with (*R*)-4-(1-Azocano)-3,5-dimethyl-4,5-dihydro-3H-dinaphtho[2,1-d:1',2'-f][1,3,2]diazaphosphepine-4-selenide (62c) (Table 5 Entry 5) [DJK-1-66]



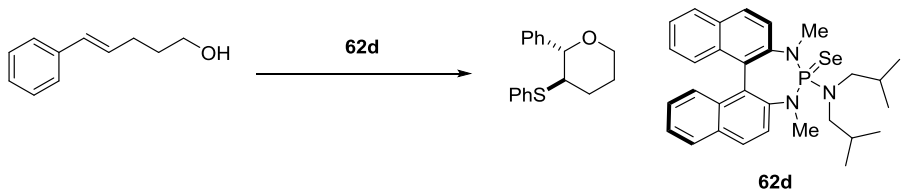
62c

Following General Procedure 2, an oven-dried NMR tube was charged with **56** (30.6 mg, 0.12 mmol, 1.2 equiv), and **57a** (16.2 mg, 0.1 mmol). To this was added (*R*)-**62c** (5.4 mg, 0.01 mmol, 0.1 equiv), $CDCl_3$ (0.7 mL) and the reaction was cooled to -20 ^oC in a freezer. MsOH (6.6 µL, 0.1 mmol, 1.0 equiv) was added and the tube was shaken well. After 96 h, the reaction was quenched with Et_3N (10 µL). Purification by silica gel flash column chromatography (SiO_2, 20 g, 20 mm Ø, hexanes/EtOAc, 40:1) afforded 12 mg (44%) of **58a** as a white solid**.**

Data for **58a**:

SFC: (2*R*,3*S*)-**58a,** t_R 4.29 min (90.7%); (2*S*,3*R*)-**58a,** t_R 5.35 min (9.3%) (Chiralpak AD, 5% MeOH in CO_2, 3 mL/min, 220 nm, 40 ^oC)

Sulfenofunctionalization with (*R*)-4-(Diisobutylamino)-3,5-dimethyl-4,5-dihydro-3H-dinaphtho[2,1-d:1',2'-f][1,3,2]diazaphosphepine-4-selenide (62d) (Table 5 Entry 6) [DJK-3-75]



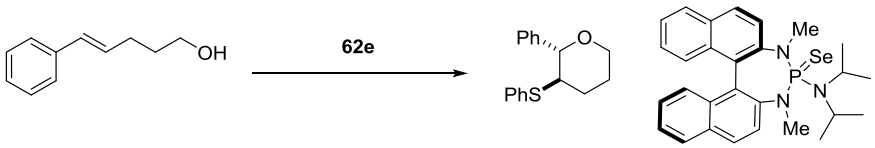
62d

An oven-dried Schlenk flask was charged with **56** (64 mg, 0.25 mmol, 1 equiv), and **57a** (40.6 mg, 0.25 mmol). To this was added (*S*)-**62d** (13.7 mg, 0.025 mmol, 0.1 equiv), $CDCl_3$ (0.7 mL). The reaction was cooled to -20 ^oC in an *i*-Pr bath with stirring and MsOH (17 µL, 0.25 mmol, 1.0 equiv) was added. After 48 h, the reaction was quenched with Et_3N (50 µL). Purification by silica gel flash chromatography (SiO_2, 20 g, 20 mm Ø, hexanes/EtOAc, 40:1) afforded 25 mg (37%) of **58a** as a white solid**.**

Data for **58a**:

SFC: (2*R*,3*S*)-**58a,** t_R 4.29 min (7.1%); (2*S*,3*R*)-**58a,** t_R 5.35 min (92.9%) (Chiralpak AD, 5% MeOH in CO_2, 3 mL/min, 220 nm, 40 ^oC)

Sulfenofunctionalization with (*R*)-4-(Diisopropylamino)-3,5-dimethyl-4,5-dihydro-3H-dinaphtho[2,1-d:1',2'-f][1,3,2]diazaphosphepine-4-selenide (62e) (Table 5 Entry 7) [DJK-10-55]



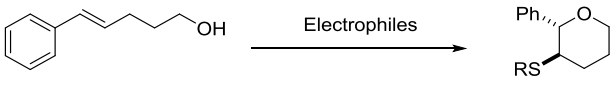
62e

An oven-dried Schlenk flask was charged with **56** (26 mg, 0.1 mmol, 1 equiv), and **57a** (16.2 mg, 0.1 mmol). To this was added (*S*)-**62e** (5.2 mg, 0.01 mmol, 0.1 equiv), $CDCl_3$ (0.7 mL). The reaction was cooled to -20 ^oC in an *i*-Pr bath with stirring and MsOH (4.8 µL, 0.75 mmol, 0.75 equiv) was added. After 48 h, the reaction was quenched with Et_3N (50 µL). Purification by flash chromatography (SiO_2, 20 g, 20 mm Ø, hexanes/EtOAc, 40:1) afforded 14 mg (52%) of **58a** as a white solid**.**

Data for **58a**:

SFC: (2*R*,3*S*)-**58a,** t_R 4.29 min (5.3%); (2*S*,3*R*)-**58a,** t_R 5.35 min (94.7%) (Chiralpak AD, 5% MeOH in CO_2, 3 mL/min, 220 nm, 40 ^oC)

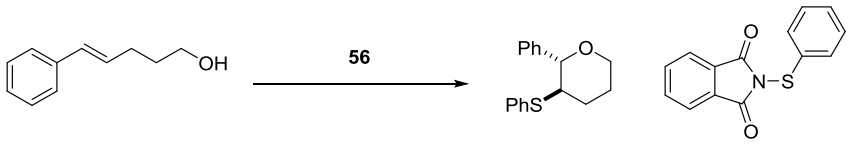
Sulfenofunctionalization with Electrophilic Sulfenium Sources (Table 6)



General Procedure

An oven-dried NMR tube was charged with **56, 57a** and catalyst. To this was added $CDCl_3$, followed by MsOH. If necessary, the reaction was cooled to the appropriate reaction temperature. The reaction was monitored by ^1H NMR spectroscopy. After the specified time, the reaction was quenched with excess Et_3N, and purified by silica gel flash column chromatography.

Sulfenofunctionalization with *N*-Phenylthiophthalimide 56 (Table 6 Entry 1) [DJK-1-17]



56

An oven-dried NMR tube was charged with **56** (25.5 mg, 0.1 mmol, 1 equiv), and **57a** (16.2 mg, 0.1 mmol). To this was added (*R*)-**62b** (5.2 mg, 0.01 mmol, 0.1 equiv) and $CDCl_3$ (0.7 mL). The reaction was cooled to -20 ^oC in a freezer and MsOH (6.5 µL, 0.1 mmol, 1.0 equiv) was added. After 30 h, the reaction was quenched with Et_3N (10 µL). Purification by silica gel flash column chromatography (SiO_2, 20 g, 20 mm Ø, hexanes/EtOAc, 30:1) afforded 6 mg (22%) of **58a** as a white solid**.**

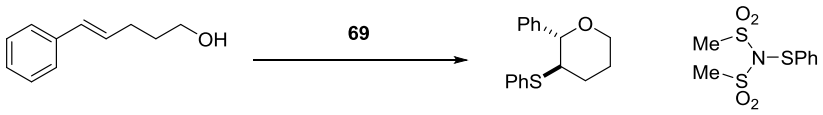
Data for **58a**:

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

7.32 (m, 2 H, H(C-aryl)), 7.28 – 7.16 (m, 3 H, H(C-aryl)), 7.14 – 7.03 (m, 5 H, H(C-aryl)), 4.14 (d, *J* = 10.1 Hz, 1 H, HC(2)), 4.09 – 4.00 (m, 1 H, HC(6)), 3.53 (td, *J* = 11.9, 2.2 Hz, 1 H, HC(6)), 3.20 (ddd, *J* = 11.5, 10.2, 4.0 Hz, 1 H, HC(3)), 2.32 – 2.17 (m, 1 H, HC(4)), 1.93 – 1.73 (m, 1 H, HC(5)), 1.66 (m, 2 H, HC(4), HC(5)).

SFC: (2*R*,3*S*)-**58a,** t_R 4.29 min (90.6%); (2*S*,3*R*)-**58a,** t_R 5.35 min (9.4%) (Chiralpak AD, 5% MeOH in CO_2, 3 mL/min, 220 nm, 40 ^oC)

Sulfenofunctionalization with *N*-Phenylthiobismethanesulfonamide 69 (Table 6 Entry 4) [DJK-4-10]



69

An oven-dried NMR tube was charged with **69** (60 mg, 0.2 mmol, 2 equiv), and **57a** (16.2 mg, 0.1 mmol). To this was added (*R*)-**62b** (10.3 mg, 0.02 mmol, 0.2 equiv) and $CDCl_3$ (0.7 mL). The reaction was cooled to -20 ^oC in a freezer and 2,6-di-*t*-butyl-4-methylpyridine (44 mg, 0.2 mmol, 2 equiv) was added. After 18 h, the reaction was quenched with Et_3N (50 µL). Purification by silica gel flash column chromatography (SiO_2, 20 g, 20 mm Ø, hexanes/EtOAc, 30:1) afforded 5 mg (19%) of **58a** as a white solid**.**

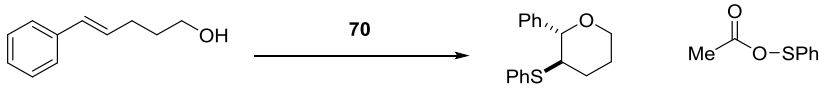
Data for **58a**:

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

7.32 (m, 2 H, H(C-aryl)), 7.28 – 7.16 (m, 3 H, H(C-aryl)), 7.14 – 7.03 (m, 5 H, H(C-aryl)), 4.14 (d, *J* = 10.1 Hz, 1 H, HC(2)), 4.09 – 4.00 (m, 1 H, HC(6)), 3.53 (td, *J* = 11.9, 2.2 Hz, 1 H, HC(6)), 3.20 (ddd, *J* = 11.5, 10.2, 4.0 Hz, 1 H, HC(3)), 2.32 – 2.17 (m, 1 H, HC(4)), 1.93 – 1.73 (m, 1 H, HC(5)), 1.66 (m, 2 H, HC(4), HC(5)).

SFC: (2*R*,3*S*)-**58a,** t_R 4.29 min (68.3%); (2*S*,3*R*)-**58a,** t_R 5.35 min (31.7%) (Chiralpak AD, 5% MeOH in CO_2, 3 mL/min, 220 nm, 40 ^{o}C)

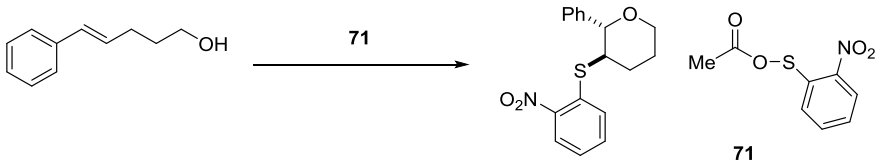
Attempted Sulfenofunctionalization with Phenylsulfanyl ethanoate (Table 6 Entry 5) [DJK-3-80]



70

An oven-dried Schlenk flask was charged with PhSCl (14.5 mg, 0.1 mmol, 1 equiv) and CH_2Cl_2 (0.7 mL). AgOAc (16.7 mg, 0.1 mmol, 1 equiv.) was added and the reaction was cooled to -20 ^{o}C and stirred 16 h. Afterwards, **57a** (16.2 mg, 0.1 mmol) and (*R*)-**62b** (2.6 mg, 0.005 mmol, 0.05 equiv) were added. After 12 h, no change was visible by ^{1}H NMR. No further manipulations were done.

Attempted Sulfenofunctionalization with 2-Nitrophenylsulfanyl ethanoate (Table 6 Entry 6) [DJK-3-79]

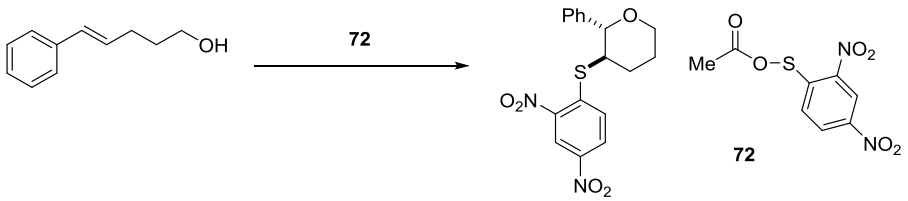


71

An oven-dried Schlenk flask was charged with 2-NO_2-C_6H_4-SCl (19 mg, 0.1 mmol, 1 equiv) and CH_2Cl_2 (0.7 mL). AgOAc (16.7 mg, 0.1 mmol, 1 equiv.) was added and the reaction was cooled to -20 ^{o}C and stirred 16 h. Afterwards, **57a** (16.2 mg, 0.1 mmol) and (*R*)-**62b** (2.6 mg, 0.005 mmol, 0.05 equiv) were added. After 16 h, no desired product was visible by ^{1}H

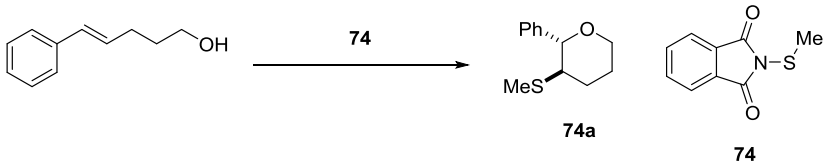
NMR. No further manipulations were done.

Attempted Sulfenofunctionalization with 2,4-Dinitrophenylsulfanyl ethanoate (Table 6 Entry 7) [DJK-3-77]



An oven-dried NMR tube was charged with 2,4-NO_2-C_6H_3-SOAc (10.4 mg, 0.04 mmol, 1 equiv) and $CDCl_3$ (0.7 mL). **57a** (16.2 mg, 0.1 mmol) was added and after 2h, (*R*)-**62b** (1 mg, 0.002 mmol, 0.05 equiv) were added. After 16 h, no desired product was visible by ^{1}H NMR. No further manipulations were done.

Sulfenofunctionalization with *N*-methylthiophthalimide (Table 7 Entry 1) [DJK-4-14]



An oven-dried Schlenk flask was charged with **74** (19.3 mg, 0.1 mmol, 1 equiv) and CH_2Cl_2 (0.7 mL). **57a** (16.2 mg, 0.1 mmol) was added and (*R*)-**62b** (5.1 mg, 0.01 mmol, 0.1 equiv) were added. The reaction was cooled to -20 ^{o}C and MsOH (6.4 µL, 0.1 mmol, 1 equiv) was added. After 48 h, the reaction was quenched with Et_3N (50 µL Et_3N). Purification by flash chromatography (SiO_2, 8 g, 10 mm Ø, hexanes/EtOAc, 60:1) afforded 5 mg (24%) of pure **77.**

Data for **74a**:

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

7.45 – 7.39 (m, 2H), 7.39 – 7.26 (m, 83), 4.14 (m, 2H), 3.61 (td, *J* = 11.9, 2.4 Hz, 1H), 2.92 (s, 3H), 2.68 (ddd, *J* = 12.3, 10.2, 4.0 Hz, 1H), 2.01 (m, 1H), 1.89 (tdd, *J* = 17.1, 8.7, 4.2 Hz, 1H), 1.76 (dddd, *J* = 11.3, 9.5, 6.6, 4.6 Hz, 1H), 1.62 (m, 1H).

SFC: (2*R*,3*S*)-**74a,** t_R 3.43 min (76.3%); (2*S*,3*R*)-**74a,** t_R 4.95 min (23.7%) (Chiralpak AD, 5% MeOH in CO_2, 2 mL/min, 220 nm, 40 ^{o}C)

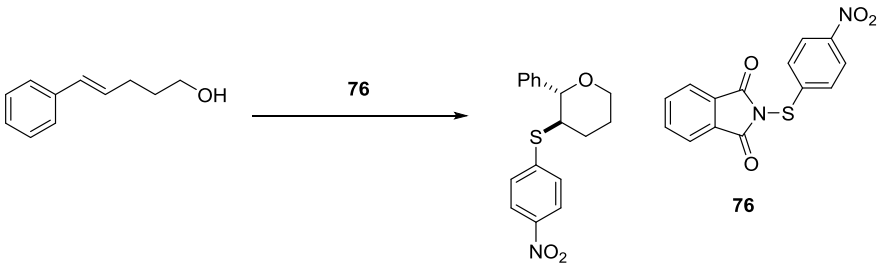
Attempted Sulfenofunctionalization with *N*-Trichloromethylthiophthalimide (Table 7

Entry 2) [DJK-4-21]

75

An oven-dried 5-mm NMR tube was charged with **75** (29.6 mg, 0.1 mmol, 1 equiv) and $CDCl_3$ (0.7 mL). **57a** (16.2 mg, 0.1 mmol), THT (1.8 µL, 0.02 mmol, 0.2 equiv) and MsOH (6.4 µL, 0.1 mmol, 1 equiv) were added. After 24 h, no reaction was observed. No further manipulations were made.

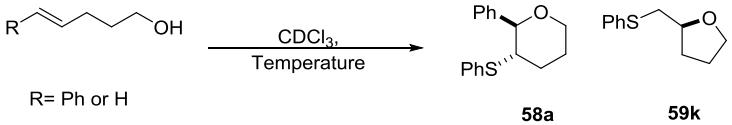
Attempted Sulfenofunctionalization with *N*-(4-Nitrophenyl)thiophthalimide (Table 7 Entry 3) [DJK-4-17]



76

An oven-dried 5-mm NMR tube was charged with **76** (29.9 mg, 0.1 mmol, 1 equiv) and $CDCl_3$ (0.7 mL). **57a** (16.2 mg, 0.1 mmol), THT (1.8 µL, 0.02 mmol, 0.2 equiv) and MsOH (6.4 µL, 0.1 mmol, 1 equiv) were added. After 2 h, substantial conversion was observed by ^{1}H NMR. However, no product was isolated from the reaction.

Evaluation of Enantioselectivity as a Function of Temperature (Table 8)



R= Ph or H

58a **59k**

General Procedure

An oven-dried 5-mm NMR tube was charged with **1** in a glovebox. The tube was taken out of the box and the Lewis base, **57a**, and 0.7 mL $CDCl_3$ was added. If indicated, the tube was cooled to the appropriate temperature in a cryocool unit. The acid was added at the indicated temperature and the mixture was shaken well. The reaction was quenched after the indicated time with excess Et_3N, and the product was purified by silica gel column chromatography prior

to SFC analysis.

Data for **58a**:

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

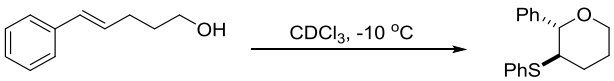
7.32 (m, 2 H, H(C-aryl)), 7.28 – 7.16 (m, 3 H, H(C-aryl)), 7.14 – 7.03 (m, 5 H, H(C-aryl)), 4.14 (d, *J* = 10.1 Hz, 1 H, HC(2)), 4.09 – 4.00 (m, 1 H, HC(6)), 3.53 (td, *J* = 11.9, 2.2 Hz, 1 H, HC(6)), 3.20 (ddd, *J* = 11.5, 10.2, 4.0 Hz, 1 H, HC(3)), 2.32 – 2.17 (m, 1 H, HC(4)), 1.93 – 1.73 (m, 1 H, HC(5)), 1.66 (m, 2 H, HC(4), HC(5)).

Data for **59k**:

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

7.37 (d, *J* = 7.9 Hz, 2 H, HC(9)), 7.28 (t, *J* = 7.7 Hz, 2 H HC(10)), 7.17 (t, *J* = 7.4 Hz, 1 H, HC(11)), 4.11 – 4.00 (tt, *J* = 6, 7 Hz, 1 H, HC(2)), 3.91 (dd, *J* = 14.4, 7.3 Hz, 1 H, HC(5)), 3.77 (dd, *J* = 14.4, 7.8 Hz, 1 H, HC(5)), 3.16 (dd, *J* = 13.0, 5.8 Hz, 1 H, HC(6)), 2.97 (dd, *J* = 13.0, 6.8 Hz, 1 H, HC(6)), 2.06 (m, 1 H, HC(3)), 1.91 (m, 2 H, HC(4)), 1.66 (m, 1 H, HC(3)).

Evaluation of Enantioselectivity for the Sulfenofunctionalization of 57a at -10 °C (Table 8 Entry 2) [DJK-1-80]



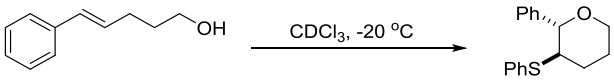
Following General Procedure 4, an oven-dried NMR tube was charged with **56** (64 mg, 0.25 mmol, 1 equiv), and **57a** (40.0 mg, 0.25 mmol). To this was added (*R*)-**62b** (13 mg, 0.025 mmol, 0.1 equiv), $CDCl_3$ (0.7 mL)**.** The reaction was cooled to -10 °C in a cryocool. MsOH (17 µL, 0.25 mmol, 1.0 equiv) was added. After 24 h, the reaction was quenched with Et_3N (50 µL). Purification by silica gel flash column chromatography (SiO_2, 20 g, 20 mm Ø, hexanes/EtOAc, 30:1) afforded 42 mg (63%) of **58a** as a white solid**.**

Data for **58a**:

SFC: (2*R*,3*S*)-**58a,** t_R 4.29 min (89.4%); (2*S*,3*R*)-**58a,** t_R 5.35 min (10.6%) (Chiralpak AD, 5% MeOH in CO_2, 3 mL/min, 220 nm, 40 °C)

Evaluation of Enantioselectivity for the Sulfenofunctionalization of 57a at -20 °C (Table 8

Entry 3) [DJK-1-84]

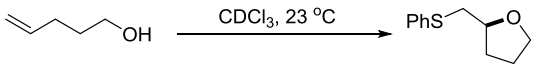


Following General Procedure 4, an oven-dried NMR tube was charged with **56** (64 mg, 0.25 mmol, 1 equiv), and **57a** (40.0 mg, 0.25 mmol). To this was added (*R*)-**62b** (13 mg, 0.025 mmol, 0.1 equiv), $CDCl_3$ (0.7 mL)**.** The reaction was cooled to -20 °C in a cryocool. MsOH (17 µL, 0.25 mmol, 1.0 equiv) was added. After 48 h, the reaction was quenched with Et_3N (50 µL). Purification by silica gel flash column chromatography (SiO_2, 20 g, 20 mm Ø, hexanes/EtOAc, 30:1) afforded 50 mg (74%) of **58a** as a white solid**.**

Data for **58a**:

SFC: (2*R*,3*S*)-**58a,** t_R 4.29 min (91.1%); (2*S*,3*R*)-**58a,** t_R 5.35 min (8.9%) (Chiralpak AD, 5% MeOH in CO_2, 3 mL/min, 220 nm, 40 °C)

Evaluation of Enantioselectivity for for the Sulfenofunctionalization of 57k at 23 °C (Table 8 Entry 5) [DJK-1-21]

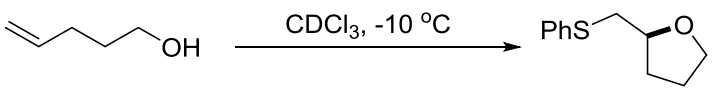


Following General Procedure 4, an oven-dried NMR tube was charged with **56** (28.4 mg, 0.11 mmol, 1.2 equiv), and **57k** (8.2 mg, 0.09 mmol). To this was added (*R*)-**62b** (4.8 mg, 0.009 mmol, 0.1 equiv), $CDCl_3$ (0.7 mL). MsOH (6 µL, 0.09 mmol, 1.0 equiv) was added. After 16 h the reaction was judged to be complete by ^1H NMR. After 24 h, the reaction was quenched with Et_3N (50 µL). Purification by silica gel flash column chromatography (SiO_2, 20 g, 20 mm Ø, hexanes/EtOAc, 75:1) afforded 6 mg (34%) of **59k** as a white solid**.**

Data for **59k**:

SFC: (2*S*)-**59k**, t_R 4.97 min (21.8%); (2*R*)-**59k**, t_R 6.07 min (78.2%) (Chiralpak AD, 5 % MeOH in CO_2, 2 mL/min, 220 nm, 40 °C)

Evaluation of Enantioselectivity for for the Sulfenofunctionalization of 57k at -10 °C (Table 8 Entry 6) [DJK-2-31]



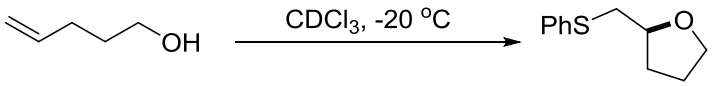
Following General Procedure 4, an oven-dried Schlenk flask was charged with **56** (64 mg, 0.25 mmol, 1 equiv), and **57k** (21.8 mg, 0.25 mmol). To this was added (*R*)-**62b** (13.1 mg,

0.025 mmol, 0.1 equiv), $CDCl_3$ (0.7 mL). The reaction was cooled to -10 °C in a cryocool. MsOH (17 µL, 0.25 mmol, 1.0 equiv) was added. After 48 h the reaction was quenched with Et_3N (50 µL). Purification by silica gel flash column chromatography (SiO_2, 20 g, 20 mm Ø, hexanes/EtOAc, 75:1) afforded 41 mg (85%) of **59k** as a white solid.

Data for **59k**:

SFC: (2*S*)-**59k**, t_R 4.97 min (16.8%); (2*R*)-**59k**, t_R 6.07 min (83.2%) (Chiralpak AD, 5 % MeOH in CO_2, 2 mL/min, 220 nm, 40 °C)

Evaluation of Enantioselectivity for for the Sulfenofunctionalization of 57k at -20 °C (Table 8 Entry 7) [DJK-2-13]



Following General Procedure 4, an oven-dried Schlenk flask was charged with **56** (66 mg, 0.26 mmol, 1.04 equiv), and **57k** (21.2 mg, 0.25 mmol). To this was added (*R*)-**62b** (13 mg, 0.025 mmol, 0.1 equiv), $CDCl_3$ (0.7 mL). The reaction was cooled to -20 °C. MsOH (17 µL, 0.25 mmol, 1.0 equiv) was added. After 72 h, the reaction was quenched with Et_3N (50 µL). Purification by flash chromatography (SiO_2, 20 g, 20 mm Ø, hexanes/EtOAc, 75:1) afforded 49 mg (98%) of **59k** as a white solid.

Data for **59k**:

SFC: (2*S*)-**59k**, t_R 4.97 min (13.9%); (2*R*)-**59k**, t_R 6.07 min (86.1%) (Chiralpak AD, 5 % MeOH in CO_2, 2 mL/min, 220 nm, 40 °C)

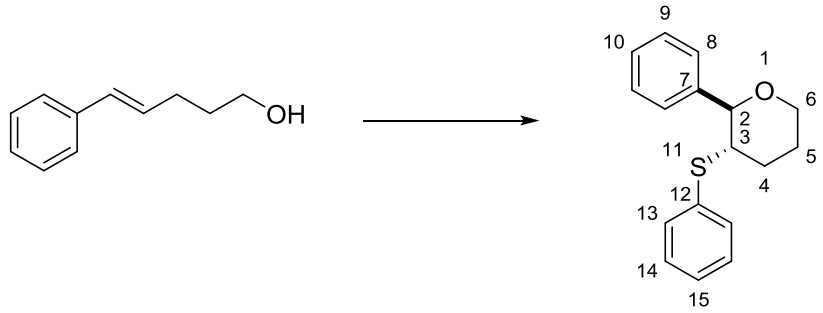
Preparative Sulfenofunctionalization of Alkenes (Table 9)

General Procedure

In a glovebox, a 5-mL Schlenk flask equipped with a stirbar was charged with **1** (255 mg, 1.0 mmol, 1.0 equiv). The flask was transferred to a vacuum manifold and the corresponding alkene (1.0 mmol, 1.0 equiv), catalyst (*R*)-**3c** (52 mg, 0.1 mmol, 0.1 equiv), nucleophile (if indicated, 1.0 mmol, 1.0 equiv) and CH_2Cl_2 (2.5 mL) were added. The flask was placed into either a 1:1 ethylene glycol/water or isopropyl alcohol bath, and the bath was cooled to the appropriate temperature via a cryocool unit. The temperature of the mixture was monitored via a

thermocouple digital temperature probe. After the temperature stabilized, MsOH (65 µL, 1.0 mmol, 1.0 equiv) was added and the mixture was allowed to stir for the indicated time. The reaction was quenched while cold by the addition of 150 µL of Et_3N. The resulting mixture was poured into 20 mL of 1 M HCl in a separatory funnel, 30 mL of CH_2Cl_2 was added and the layers were thoroughly mixed. The organic layer was poured into 20 mL of 1 M NaOH and the layers were thoroughly mixed and then separated. The acidic layer was back-extracted with 30 mL CH_2Cl_2, which was then poured into the basic layer and used to extract that layer as well. Both organic portions were combined, dried over $MgSO_4$, filtered through glass wool and then concentrated on a rotavap (20-23 ^oC, 3 mm Hg). The product thioethers were purified by silica gel flash chromatography.

Preparation of (2*R*,3*S*)-Tetrahydro-2-phenyl-3-(phenylthio)-2*H*-pyran (58a) (Table 9 Entry 1) [DJK-3-67]



57a **58a**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv), **57a** (162 mg, 1.0 mmol), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -20 ^oC in an *i*-PrOH bath. Methanesulfonic acid (65 µL, 1.0 mmol, 1.0 equiv) was added and the mixture was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product **58a** was purified by flash chromatography (SiO_2, 26 g, 20 mm Ø, hexanes/EtOAc, 80:1 to 40:1) to afford 216.1 mg, (80%) of a pale yellow oil. Kugelrohr distillation afforded 171 mg of analytically pure **58a** which crystallized upon standing. The crystals were of suitable quality for single crystal X-ray diffraction, which unambiguously established relative and absolute configurations (see pp. 266)

Data for **58a** :

bp: 100 ^{o}C (ABT), 2 x 10^{-4} mm Hg

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

7.32 (m, 2 H, H(C-aryl)), 7.28 – 7.16 (m, 3 H, H(C-aryl)), 7.14 – 7.03 (m, 5 H, H(C-aryl)), 4.14 (d, *J* = 10.1 Hz, 1 H, HC(2)), 4.09 – 4.00 (m, 1 H, HC(6)), 3.53 (td, *J* = 11.9, 2.2 Hz, 1 H, HC(6)), 3.20 (ddd, *J* = 11.5, 10.2, 4.0 Hz, 1 H, HC(3)), 2.32 – 2.17 (m, 1 H, HC(4)), 1.93 – 1.73 (m, 1 H, HC(5)), 1.66 (m, 2 H, HC(4), HC(5)).

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

139.9 (C(7)), 133.7 (C(12)), 133.0 (C-aryl), 128.5 (C-aryl), 128.2 (C-aryl), 128.1 (C-aryl), 127.7 (C-aryl), 127.0 (C-aryl), 85.1 (C(2)), 68.5 (C6)), 50.7 (C(3)), 32.3 (C(4)), 27.0 (C(5))

IR: 3033 (s), 2937 (s), 2850 (s), 2720 (m), 1951 (m), 1872 (m), 1809 (w), 1741 (w), 1583 (s), 1493 (s), 1473 (s), 1436 (s), 1369 (s), 1346 (m), 1325 (s), 1308 (m), 1256 (s), 1230 (m), 1213 (m), 1179 (s), 1077 (s), 1024 (s), 1002 (s), 968 (s), 941 (s), 909 (s), 883 (m), 851 (m), 819 (m), 780 (s), 755 (s), 696 (s), 636 (m)

MS: (EI)

270 (65), 161 (35), 160 (40), 149 (24), 136 (100), 135 (43), 91 (52), 77 (19)

TLC: R_f 0.27 (hexanes/EtOAc, 20:1) [CAM]

Opt Rot. : $[\alpha]_D^{24}$ -35.1 (c = 0.42, $CHCl_3$)

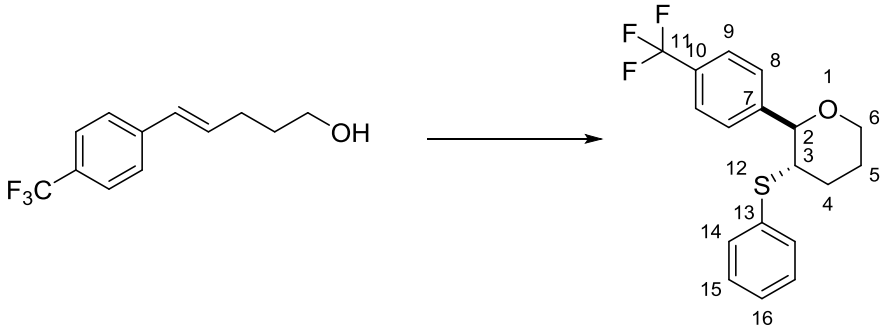
SFC: (2*R*,3*S*)-**58a,** t_R 5.53 min (91.1%); (2*S*,3*R*)-**58a,** t_R 7.49 min (8.9%) (Chiralpak AD, 5% MeOH in CO_2, 2 mL/min, 220 nm, 40 ^{o}C)

Analysis: $C_{17}H_{18}OS$ (270.11)

Calcd: C, 75.51; H, 6.71%

Found: C, 75.73; H, 6.55%

Preparation of (2*R*,3*S*)-Tetrahydro-3-(phenylthio)-2-(4-(trifluoromethyl)phenyl)-2H-pyran (58b) (Table 9 Entry 2) [DJK-3-43]



57b **58b**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv), **57b** (230 mg, 1.0 mmol), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -10 ^oC in a glycol/water bath. Methanesulfonic acid (65 µL, 1.0 mmol, 1.0 equiv) was added and the mixture was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product **58b** was purified by flash chromatography (SiO_2, 27 g, 20 mm Ø, hexanes/dichloromethane, 9:1 to 4:1 to 0:100) to afford 120.1 mg (36%) of **58b** along with 125.5 mg (55%) of unreacted **57b.** Recrystallization from hot hexanes (5 mL) followed by sublimation (refluxing ethanol) yielded 30.2 mg (9%) of analytically pure **58b** as a white solid.

Data for **58b** :

mp: 86-88 ^oC (hexane)

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

7.44 (m, 4 H, H(C-aryl)), 7.10 (m, 3 H, H(C-aryl)), 7.02 (m, 2 H, H(C-aryl)), 4.24 (d, 1 H, *J* = 10.2 Hz, HC(2)), 4.09 (m, 1 H, HC(6)), 3.57 (dt, 1 H, *J* = 2.3, 12 Hz, HC(6)), 3.18 (ddd, 1 H, *J* = 10.1, 4, 12 Hz, HC(3)), 2.34 (m, 1 H, HC(4)), 1.89 (m, 1H, HC(5)), 1.72 (m, 2 H, HC(4), HC(5))

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

143.77 (C(7)), 133.64 (C(13)), 132.65 (C-aryl), 130.17 (q, *J* = 32 Hz, C(10)), 128.58 (C-aryl), 128.15 (C-aryl), 127.12 (C-aryl), 124.96 (q, *J* = 3.8 Hz, C(9)), 124.06 (q, *J* = 272 Hz, C(11)), 85.02 (C(2)), 68.50 (C(6)), 50.98 (C(3)), 32.07 H(C(4)), 27.05 (HC(5)).

^{19}F NMR: (470 MHz, $CDCl_3$)

-63.04

IR: (KBr)

2975 (m), 2952 (m), 2925 (m), 2863 (m), 1618 (w), 1572 (w), 1481 (w), 1439 (m), 1425 (m), 1326 (s), 1261 (m), 1161 (s), 1134 (s), 1118 (s), 1095 (s), 1068 (s), 1018 (s), 943 (m), 844 (m), 824 (m), 782 (m), 739 (s), 688 (m), 666 (m), 604 (m)

MS: (EI)

338 (81), 229 (27), 228 (28), 173 (20), 159 (29), 149 (40), 136 (100), 135 (40), 91 (19), 71 (17)

TLC: R_f 0.31 (hexanes/EtOAc, 20:1) [CAM]

Opt Rot. : $[\alpha]_D^{24}$ -19.6 (c = 0.16, $CHCl_3$)

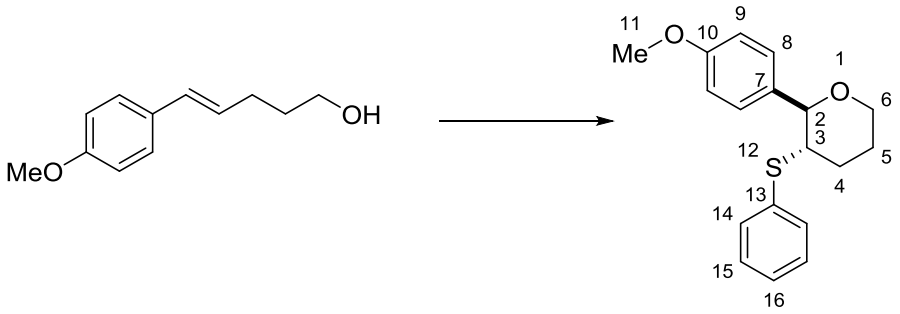
SFC: (2*R*,3*S*)-**58b,** t_R 4.77 min (88.1%); (2*S*,3*R*)-**58b,** t_R 5.79 min (11.9%) (Chiralpak AD, 4% MeOH in CO_2, 2 mL/min, 220 nm, 40 ^oC)

Analysis: $C_{18}H_{17}F_3OS$ (338.42)

Calcd: C, 63.89; H, 5.06%

Found: C, 63.59; H, 4.91%

Preparation of (2*R*,3*S*)-Tetrahydro-2-(4-methoxyphenyl)-3-(phenylthio)-2H-pyran (57c) (Table 9 Entry 3) [DJK-3-41]



57c **58c**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv), **57c** (192 mg, 1.0 mmol, 1.0 equiv), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -20 ^oC in a glycol/water bath. Methanesulfonic acid (65 µL, 1.0 mmol, 1.0 equiv) was added and the mixture was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product **58c** was purified by flash

chromatography (SiO_2, 27 g, 20 mm Ø, hexanes/dichloromethane, 9:1) to afford 250 mg (84%) of **58c** as a white solid. Recrystallization from hot pentane provided 220 mg (73%) of analytically pure **58c** as a white solid.

Data for **58c** :

mp: 71-73 °C (pentane)

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

7.26 (d, 2 H, *J* = 8.6 Hz, HC(8)), 7.15 (m, 5 H, H(C-aryl)), 6.80 (d, 2 H, *J* = 8.7Hz, HC(9)), 4.14 (d, 1 H, *J* = 10.1Hz, HC(2)), 4.07 (m, 1 H, HC(6)), 3.78 (s, 3 H, HC(12)), 3.55 (dt, 1 H, *J* = 2.2Hz, *J* = 12.1Hz, HC(6)), 3.23 (ddd, 1 H, *J* = 4.0Hz, 10.2Hz, 12.0Hz, HC(3)), 2.26 (m, 1 H, HC(4)), 1.83 (m, 1 H, HC(5)), 1.67 (m, 2 H, HC(4), HC(5))

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

159.39 (C(10)), 133.67 (C(14)), 133.07 (C-aryl), 132.27 (C-aryl), 128.73 (C-aryl), 128.49 (C-aryl), 127.01 (C(7)), 113.56 (C(9)), 84.56 (C(2)), 68.57 (C(6)), 55.24 (C(12)). 51.76 (C(3)), 32.21 (C(4)), 27.04 (C(5))

IR: (KBr)

2955 (s), 2935 (m), 2914 (m), 2843 (s), 1612 (s), 1583 (m), 1560 (m), 1542 (w), 1518 (s), 1499 (m), 1491 (m), 1474 (s), 1459 (s), 1450 (m), 1440 (s), 1370 (m), 1330 (w), 1303 (m), 1267 (m), 1245 (s), 1176 (s), 1115 (m), 1092 (s), 1074 (s), 1030 (s), 962 (s), 949 (s), 940 (s), 922 (m), 829 (s), 817 (s), 778 (s), 748 (s), 693 (s)

MS: (EI)

300 (40, M+), 191 (28), 190 (41), 136 (100), 135 (45), 121 (42), 91 (18)

TLC: R_f 0.17 (hexanes/EtOAc, 10:1) [CAM]

Opt Rot. : $[\alpha]_D^{24}$ -45.5 (c = 0.2, $CHCl_3$)

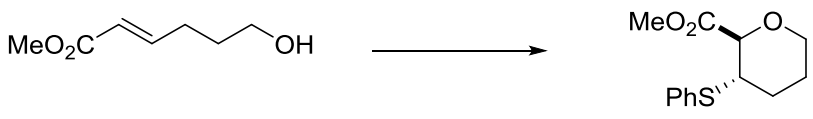
SFC: (2*R*,3*S*)-**58c,** t_R 6.28 min (91.4%); (2*S*,3*R*)-**58c,** t_R 9.88 min (8.6%) (Chiralpak AD, 5% MeOH in CO_2, 2.5 mL/min, 220 nm, 40 °C)

Analysis: $C_{18}H_{20}O_2S$ (300.41)

Calcd: C, 71.96; H, 6.71%

Found: C, 71.64; H, 6.90%

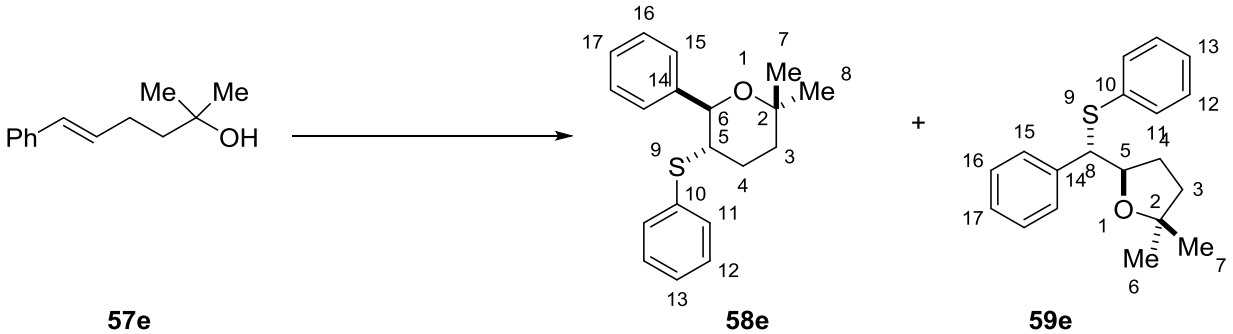
Attempted Sulfenofunctionalization of (*E*)-Methyl 6-hydroxyhex-2-enoate (57d) (Table 9 Entry 4) [DJK-1-98]



57d **58d**

An oven-dried NMR tube was charged with **56** (25.6 mg, 0.1 mmol, 1 equiv), and **57d** (14.6 mg, 0.1 mmol). To this was added (*R*)-**62b** (5.2 mg, 0.01 mmol, 0.1 equiv), $CDCl_3$ (0.7 mL). MsOH (6.7 µL, 0.1 mmol, 1.0 equiv) was added. After 96 h, only **57d** was detectable by ^1H NMR. No further manipulations were done.

Preparation of (5*S*,6*R*)-Tetrahydro-2,2-dimethyl-6-phenyl-5-(phenylthio)-2H-pyran (58e) and (5*S*,8*R*)-Tetrahydro-2,2-dimethyl-5-(phenyl(phenylthio)methyl)furan (59e) (Table 9 Entry 5) [DJK-2-45]



57e **58e** **59e**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv)**, 57e** (190 mg, 1.0 mmol), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -20 ^oC in a *i*-PrOH bath. Methanesulfonic acid (65 µL, 1.0 mmol, 1.0 equiv) was added and the mixture was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product was purified by flash chromatography (SiO_2, 35 g, 20 mm Ø, hexanes/EtOAc, 100:1) to afford 181.4 mg (61%) of **58e** and 70.2 mg (24%, combined yield 84%) of a mixture of **58e** and **59e** as white solids. Partial separation of isomers was accomplished by silica gel flash chromatography (SiO_2, 3 g, 10 mm Ø, hexanes/dichloromethane, 4:1).

Data for isomer mixture :

IR: 3061 (m), 3028 (m), 2969 (s), 2936 (s), 2860 (s), 1583 (m), 1493 (m), 1471 (s), 1452 (s), 1437 (s), 1380 (m), 1369 (s), 1354 (s), 1333 (m), 1309 (m), 1259 (m), 1227 (m), 1180 (s), 1159 (s), 1124 (m), 1072 (s), 1065 (s), 1023 (s), 952 (m), 924 (m), 911 (s), 892 (s), 819 (w), 784 (m), 757 (s), 744 (s), 701 (s), 628 (m)

MS: (EI)

298 (M+), 136 (100), 135 (23), 91 (15)

TLC: R_f **58e**, 0.39 (hexanes/EtOAc, 10:1) [CAM]

Analysis: $C_{19}H_{22}OS$ (298.44)

Calcd. : C: 76.46; H: 7.43

Found : C: 76.33; H: 7.62

Data for **58e** :

mp: 58-61 ^{o}C

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

δ 7.4 (m, 2 H, H(C-aryl)), 7.26 (m, 3 H, H(C-aryl)), 7.13 (m, 5 H, H(C-aryl)), 4.48 (d, *J* = 10.2 Hz, 1 H, HC(6)), 3.11 (ddd, *J* = 12.1, 10.5, 4.3 Hz, 1 H, HC(5)), 2.08 (ddd, *J* = 13.5, 7.6, 4.0 Hz, 1 H, HC(4)), 1.87 (m, 1 H, HC(4)), 1.77 – 1.56 (m, 2 H, HC(3)), 1.32 (s, 3 H, HC(7)), 1.28 (s, 3 H, HC(8)).

^{13}C NMR: (100 MHz, $CDCl_3$)

δ 140.6 (C(14)), 133.9 (C(10)), 132.7 (C-aryl), 128.5 (C-aryl), 128.1 (C-aryl), 128.0 (C-aryl), 127.8 (C-aryl), 126.9 (C-aryl), 77.8 (C(6)), 72.4 (C(2)), 51.2 (C(5)), 37.2 (C(3)), 31.4 (C(8)), 28.7 (C(4)), 21.7 (C(7)).

Opt Rot. : $[\alpha]_D^{24}$ -4.6 (c = 0.56, $CHCl_3$)

SFC: (5*S*,6*R*)-**58e**, t_R 4.08 min (92.4%); (6*S*,5*R*)-**58e**, t_R 4.66 min (7.6%) (Chiralpak AD, 5 % MeOH in CO_2, 2.5 mL/min, 220 nm, 40 ^{o}C)

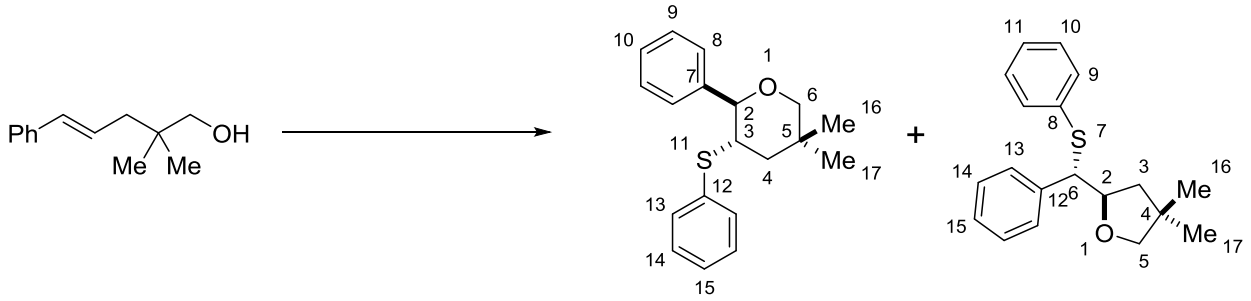
Data for **59e** :

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

δ 7.4 (m, 2 H, H(C-aryl)), 7.26 (m, 5 H, H(C-aryl)), 7.13 (m, 3 H, H(C-aryl)), 4.43 (app q, *J* = 6.6 Hz, 1 H, HC(5)), 4.25 (d, *J* = 5.4 Hz, 1 H, HC(8)), 2.08 (m, 1

H, HC(4)), 1.87 (m, 1 H, HC(4)), 1.77 – 1.56 (m, 2 H, HC(3)), 1.20 (s, 3 H, HC(7)), 1.18 (s, 3 H, HC(6)).

Preparation of (2*R*,3*S*)-Tetrahydro-5,5-dimethyl-2-phenyl-3-(phenylthio)-2H-pyran (58f) and (2*R*,6*S*)-Tetrahydro-4,4-dimethyl-2-(phenyl(phenylthio)methyl)furan (59f) (Table 9 Entry 6) [DJK-2-46]



57f **58f** **59f**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv), **57f** (190 mg, 1.0 mmol), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -10 ^oC in a *i*-PrOH bath. Methanesulfonic acid (65 µL, 1.0 mmol, 1.0 equiv) was added and the mixture was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product was purified by flash chromatography (SiO_2, 30 g, 20 mm Ø, hexanes/EtOAc, 40:1) to afford 281 mg (94%) of a 19:1 mixture of **58f**:**59f** as a pale yellow oil. Further, partial separation of isomers was accomplished by silica gel flash chromatography (SiO_2, 15 g, 20 mm Ø, hexanes/dichloromethane, 4:1).

Data for isomer mixture :

IR: 3063 (m), 3033 (m), 2942 (s), 2927 (m), 2866 (m), 2842 (m), 1949 (w), 1581 (w), 1495 (w), 1473 (s), 1455 (m), 1438 (s), 1390 (m), 1372 (m), 1301 (w), 1280 (m), 1209 (w), 1079 (s), 1026 (s), 993 (s), 963 (m), 921 (w), 894 (m), 814 (m), 759 (s), 743 (s), 699 (s), 655 (w)

MS: (EI)

298 (M+), 188 (19), 177 (84), 136 (100), 135 (38), 91 (65)

TLC: R_f **58f**, 0.42; **59f**, 0.35 (hexanes/EtOAc, 10:1) [CAM]

Analysis: $C_{19}H_{22}OS$ (298.44)

Calcd. :	C: 76.46;	H: 7.43
Found :	C: 76.22;	H: 7.49

Data for **58f** :

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

7.41 (m, 2 H, H(C-aryl)), 7.29 (m, 3 H, H(C-aryl)), 7.14 (m, 3 H, H(C-aryl)), 7.08 (m, 2 H, H(C-aryl)), 4.12 (d, *J* = 10.4 Hz, 1 H, HC(2)), 3.62 (dd, *J* = 11.1, 2.6 Hz, 1 H, HC(6)), 3.42 (ddd, *J* = 12.6, 10.4, 4.2 Hz, 1 H, HC(3)), 3.35 (d, *J* = 11.2 Hz, 1 H, HC(6)), 2.04 (ddd, *J* = 13.3, 4.1, 2.7 Hz, 1 H, HC(4)), 1.58 (app t, *J* = 13 Hz, 1 H, HC(4)), 1.23 (s, 3 H, HC(16)), 0.92 (s, 3 H, HC(16')).

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

δ 139.9 (C(7)), 133.9 (C(12)), 132.5 (C-aryl), 128.5 (C-aryl), 128.2 (C-aryl), 127.7 (C-aryl), 126.9 (C-aryl), 85.3 (C(2)), 78.2 (C(6)), 48.0 (C(3)), 45.6 (C(4), 32.6 (C(5)), 26.8 (C(16')), 23.8 (C(16)).

Opt Rot. : $[\alpha]_D^{24}$ -27.1 (c = 0.35, $CHCl_3$)

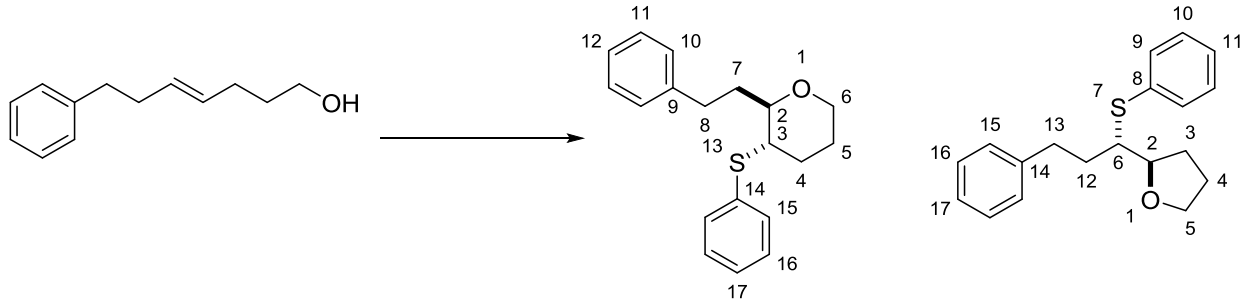
SFC: (2*R*,3*S*)-**58f** t_R 2.88 min (92.4%); (2*S*,3*R*)-**58f** t_R 5.46 min (7.6%) (Chiralpak AD, 5% MeOH in CO_2, 2.5 mL/min, 220 nm, 40 ^oC)

Data for **59f** :

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

δ 4.52 (dd, *J* = 16.0, 6.6 Hz, 1 H, HC(2)), 4.25 (d, *J* = 7.1 Hz, 1 H, HC(5)), 3.51 (s, 1 H, HC(6)), 1.94 (dd, *J* = 12.4, 6.3 Hz, 1 H, HC(3)), 1.73 (dd, *J* = 12.4, 9.2 Hz, 1 H, HC(3)), 1.12 (s, 3 H, HC(16)), 1.07 (s, 3 H, HC(16')).

Preparation of (2*R*,3*S*)-Tetrahydro-2-phenethyl-3-(phenylthio)-2H-pyran (58g) and (2*S*,6*R*)-Tetrahydro-2-(3-phenyl-1-(phenylthio)propyl)furan (59g) (Table 9 Entry 7) [DJK-2-48]



57g **58g** **59g**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0mmol, 1.0 equiv), **57g** (190 mg, 1.0 mmol), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -20 ^oC in a bath. Methanesulfonic acid (65 µL, 1.0 mmol, 1.0 equiv) was added and the mixture was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product was purified by flash chromatography (SiO_2, 28 g, 20 mm Ø, hexanes/EtOAc, 50:1) to afford 263.4 mg (88%) of a 5:1 mixture of **58g**:**59g** as a pale yellow oil. Partial separation of isomers was accomplished by flash chromatography (SiO_2, 3 g, 10 mm Ø, hexanes/dichloromethane, 2:1, then SiO_2, 4 g, 10 mm Ø, hexanes/EtOAc, 40:1)

Data for isomer mixture :

IR: 3060 (m), 3025 (s), 2940 (s), 2848 (s), 2729 (w), 1946 (w), 1876 (w), 1804 (w), 1602 (m), 1583 (m), 1496 (s), 1479 (s), 1454 (s), 1438 (s), 1377 (m), 1344 (m), 1288 (m), 1256 (m), 1233 (m), 1179 (m), 1118 (s), 1087 (s), 1065 (s), 1038 (s), 1025 (m), 1010 (m), 982 (m), 931 (m), 869 (m), 844 (w), 804 (w), 777 (w), 743 (s), 700 (s)

MS: (EI)

298 (M+), 189 (24), 136 (60), 135 (28), 117 (24), 91 (100), 71 (35)

TLC: R_f **58g**, 0.30; **59g**, 0.24 (hexanes/EtOAc, 20:1)[CAM]

Analysis: $C_{19}H_{22}OS$ (298.44)

Calcd. : C: 76.46; H: 7.43

Found : C: 76.58; H: 7.49

Data for **58g**:

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

7.46 (d, *J* = 7.4 Hz, 2 H, H(C-aryl)), 7.26 (m, 5 H, H(C-aryl), 7.18 (t, 3 H, *J* = 7.4 Hz, H(C-aryl)) , 4.00 (ddd, *J* = 9.5, 5.0, 3.1 Hz, 1 H, HC(6)), 3.36 (td, *J* = 11.8, 2.5 Hz, 1 H, HC(6)), 3.20 (td, *J* = 9.5, 2.4 Hz, 1 H, HC(2)), 2.91 (ddd, *J* = 11.9, 10.0, 4.1 Hz, 1 H, HC(3)), 2.82 (ddd, *J* = 14.3, 9.9, 4.8 Hz, 1 H, HC(8)), 2.69 (ddd, *J* = 13.6, 9.5, 7.3 Hz, 1 H, HC(8)), 2.46 – 2.31 (m, 1 H, HC(7)), 2.19 – 2.09 (m, 1 H, HC(5)), 1.87 – 1.77 (ddt, *J* = 14, 4.8, 9.3 Hz, 1 H, HC(7)), 1.77 – 1.66 (m, 1 H, HC(4)), 1.66 – 1.58 (m, 1 H, HC(4)), 1.50 (app qd, *J* = 13.0, 4.2 Hz, 1 H, HC(5)).

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

142.2 (C(9)), 133.5 (C(14)), 133.2 (C-aryl), 128.8 (C-aryl), 128.6 (C-aryl), 128.2 (C-aryl), 127.3 (C-aryl), 125.6 (C-aryl), 80.3 (C(2)), 67.9 (C(3)), 49.0 (C(8)), 35.3 (C(4)), 31.9 (C(8)), 31.3 (C(5)), 27.2 (C(7)),

Opt Rot. : $[\alpha]_D^{24}$ 48.9 (c = 0.44, $CHCl_3$)

SFC: (2*S*,3*R*)-**58g**, t_R 7.42 min (4.1%); (2*R*,3*S*)-**58g**, t_R 8.19 min (95.9%) (Chiralcel OJ, 4 % MeOH in CO_2, 2 mL/min, 220 nm, 40 ^{o}C)

Data for **59g**:

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

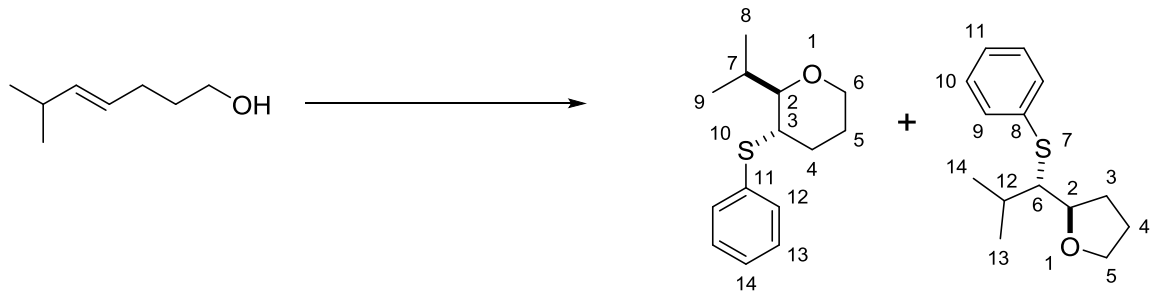
7.43 (m, 2 H, H(C-aryl)), 7.24 (m, 5 H, H(C-aryl)), 7.15 (m, 3 H, H(C-aryl)), 3.94 (q , *J* = 7.0 Hz, 1 H, HC(2)), 3.82 (dt, *J* = 14.0, 6.9 Hz, 1 H, HC(5)), 3.73 (td, *J* = 7.7, 5.9 Hz, 1 H, HC(5)), 3.14 – 3.05 (m, 1 H, HC(6)), 3.04 – 2.94 (m, 1 H, HC(8)), 2.78 (ddd, *J* = 13.7, 9.7, 6.8 Hz, 1 H, HC(8)), 2.17 – 2.06 (m, 1 H, HC(7)), 2.06 – 1.96 (m, 1 H, HC(7)), 1.93 – 1.64 (m, 4 H, H_2C(3) and H_2C(4)).

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

141.83 (C(14)), 135.56 (C(8)), 132.03 (C-aryl), 128.80 (C-aryl), 128.54 (C-aryl), 128.30 (C-aryl), 126.75 (C-aryl), 125.79 (C-aryl), 81.77 (C(2)), 68.34 (C(5)), 53.73 (C(6)), 33.52 (C(3)), 33.00 (C(13)), 29.73(C(4)), 26.01 (C(12))

SFC: (2*R*,6*S*)-**59g**, t_R 6.89 min (4.1%); (2*S*,6*R*)-**59g**, t_R 8.16 min (95.9%) (Chiralcel OD, 5 % MeOH in CO_2, 2 mL/min, 220 nm, 40 ^{o}C)

Preparation of (2*R*,3*S*)-Tetrahydro-2-isopropyl-3-(phenylthio)-2H-pyran (58h) and (2*R*,6*S*)-Tetrahydro-2-(2-methyl-1-(phenylthio)propyl)furan (59h) (Table 9 Entry 8) [DJK-2-66]



57h **58h** **59h**

Following General Procedure 5 a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv), **57h** (128 mg, 1.0 mmol), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -20 ^oC in an *i*-PrOH bath. Methanesulfonic acid (65 µL, 1.0 mmol, 1.0 equiv) was added and the mixture was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product was purified by flash chromatography (SiO_2, 28 g, 20 mm Ø, hexanes/EtOAc, 40:1) to afford 168 mg (71%) of a 17:1 mixture of **58h**:**59h** as a pale yellow oil. Further partial separation of isomers was accomplished by silica gel flash chromatography (SiO_2, 3 g, 10 mm Ø, hexanes/dichloromethane, 4:1)

Data for isomer mixture :

IR: 3073 (m), 2958 (s), 2842 (s), 1949 (m), 1735 (m), 1583 (s), 1474 (s), 1438 (s), 1378 (s), 1365 (s), 1303 (m), 1264 (s), 1229 (w), 1185 (m), 1085 (s), 1026 (s), 1001 (s), 925 (s), 873 (m), 853 (w), 805 (m), 775 (s), 744 (s), 691 (s)

MS: (EI)

236 (M+), 193 (61), 175 (57), 136 (100), 127 (29), 109 (35), 91 (29), 83 (26), 71 (83), 65 (24), 54 (45)

TLC: R_f **58h**, 0.38; **59h**, 0.26 (hexanes/EtOAc, 20:1) [CAM]

Analysis: $C_{14}H_{20}OS$ (236.37)

Calcd. : C: 71.14; H: 8.53

Found : C: 71.42; H: 8.55

Data for **58h** :

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

7.43 (d, 2 H, *J* = 6.9 Hz, HC(12)), 7.28 (m, 3 H, HC(13,14)), 3.95 (m, 1 H, HC(6)), 3.34 (dt, 1 H, *J* = 3.0, 11.3 Hz, HC(6)), 3.09 (dd, 1 H, *J* = 2.2, 10.0 Hz, HC(2)), 3.02 (ddd, 1 H, *J* = 3.9, 10.0, 11.0 Hz, HC(3)), 2.34 (dsept, 1 H, *J* = 2.0, 7.0 Hz, H C(7)), 2.12 (m, 1 H, HC(4)), 1.59 (m, 3 H, HC(4,5)), 1.00 (d, 3 H, *J*=7.0 Hz, HC(8)) 0.83 (d, 3 H, *J*= 6.8Hz, H(C9))

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

133.7 (C11)), 133.2 (C(12)), 128.8 (C(13)), 127.3 (C(14)), 85.2 (C(2)), 68.2 (C6)), 46.9 (C(3)), 32.1 (C(4)), 28.8 (C(7)), 27.2 (C(5)), 20.3 (C(8)), 14.5 (C(9))

Opt Rot. : $[\alpha]_D^{24}$ 85.5 (c = 0.14, $CHCl_3$)

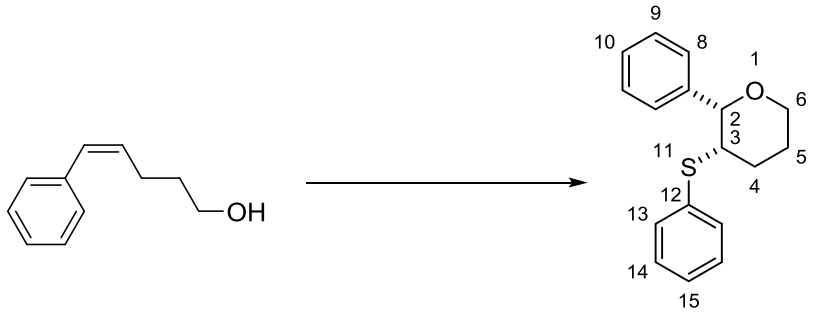
SFC: (2*R*,3*S*)-**4i**, t_R 3.02 min (96.4%); (2*S*,3*R*)-**4i**, t_R 3.49 min (3.6%) (Chiralpak AD, 1 % MeOH in CO_2, 3 mL/min, 220 nm, 40 ^{o}C),

Data for **59h** :

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

7.44 (d, 2 H, *J*= 7.6 Hz, HC(9)), 7.28 (t, 2 H, *J* = 8 Hz, HC(10)), 7.18 (d, 2 H, *J* = 7.4 Hz, HC(11), 4.05 (app q, *J* =7.4 Hz, 1 H, HC(2)), 3.84 (app q, 1 H, *J*= 7.2 Hz, HC(5)), 3.76 (app q, 1 H, *J*= 7.2 Hz, HC(5)), 3.06 (dd, 1 H, *J*= 3.4, 8.6 Hz, HC(6)), 2.31 (m, 1 H, HC(12)), 2.08 (m, 1 H, HC(4,5)), 1.83 (m, 2 H, HC(4,5)), 1.58 (m, 1 H, HC(4,5), 1.11 (d, 3 H, *J*= 6.9 Hz, HC(13,14)), 0.99 (d, 3 H, *J*= 6.9 Hz, H(C13,14))

Preparation of (2*S*,3*S*)-Tetrahydro-2-phenyl-3-(phenylthio)-2*H*-pyran (58i) (Table 9 Entry 9) [DJK-1-11]



57i **58i**

An oven-dried 5-mm NMR tube was charged with **67** (34 mg, 0.15 mmol, 1.2 equiv), **57i** (20 mg, 0.12 mmol), (*R*)-**62a** (11.5 mg 0.025 mmol, 0.2 equiv) and $CDCl_3$ (0.7 mL). Trifluoroacetic acid (9.5 µL, 0.12 mmol, 1.0 equiv) was added and the mixture was allowed to stir for 96 h. The product was purified by flash chromatography (SiO_2, 27 g, 20 mm Ø, hexanes/EtOAc, 40:1) to afford 13.7 mg (41%) of **58i** as a pale yellow oil.

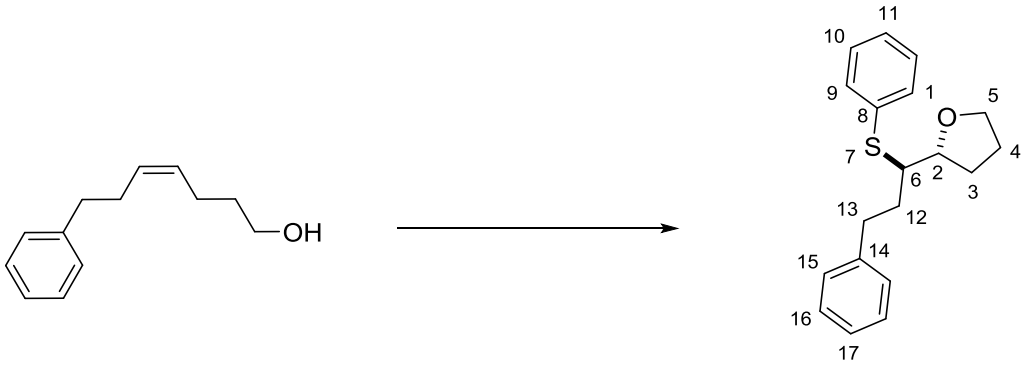
Data for **58i**:

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

δ 7.51 (m, 2H, HC(Aryl)), 7.36 (m, 4H HC(Aryl)), 7.25, (m, 1H, HC(Aryl)), 7.14 (m, 3H, HC(Aryl)), 4.81 (s, 1H, HC(2)), 4.30 (ddt, *J* = 11.2, 3.5, 1.9 Hz, 1H, HC(6)), 3.72 (m, 1H, HC(6')), 3.61 (s, 1H, HC(3)), 2.32 (m, 1H, HC(4,5)), 2.21 (m, 1H, HC(4,5)), 2.09 (m, 1H, HC(4,5)), 1.51 (m, 1H, HC(4,5)).

SFC: (2*S*,3*S*)-**58i**, t_R 9.05 min (47.2%); (2*R*,3*R*)-**58i**, t_R 11.86 min (52.8%) (Chiralpak AD, 5 % MeOH in CO_2, 2 mL/min, 220 nm, 40 ^oC)

Preparation of (2*R*,6*R*)-Tetrahydro-2-(3-phenyl-1-(phenylthio)propyl)furan (59j) (Table 9 Entry 10) [DJK-2-73]



57j **59j**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv), **59j** (190 mg, 1.0 mmol), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -10 ^oC in an *i*-PrOH bath. Methanesulfonic acid (65 µL, 1.0 mmol, 1.0 equiv) was added and the mixture was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product was purified by flash chromatography (SiO_2, 23 g, 20 mm Ø, hexanes/EtOAc, 70:1) to afford 240 mg (81%) of **59j** as a pale yellow oil.

Data for **59j** :

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

7.42 (d, *J* = 7.1 Hz, 2 H, H(C-aryl)), 7.28 (app t, *J* = 7.4 Hz, 4 H, H(C-aryl)), 7.24 – 7.14 (m, 4 H, H(C-aryl)), 4.08 (dt, *J* = 11.3, 5.6 Hz, 1 H, HC(2)), 3.93 (dd, *J* = 14.8, 6.6 Hz, 1 H, HC(5)), 3.78 (dd, *J* = 14.3, 7.1 Hz, 1 H, HC(5)), 3.23 (dt, *J* = 9.1, 4.4 Hz, 1 H, HC(6)), 2.99 (ddd, *J* = 14.7, 9.9, 5.3 Hz, 1 H, HC(13)), 2.81 (ddd, *J* = 13.8, 9.7, 6.7 Hz, 1 H, HC(13)), 2.11 (m, 1 H, HC(12)), 2.04 – 1.96 (m, 1 H, HC(3)), 1.94 – 1.73 (m, 4 H, HC(12), H(C3), HC(4)).

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

141.6 C(14), 135.7 C(8), 131.2 (C-aryl), 128.8 (C-aryl), 128.4 (C-aryl), 128.3 (C-aryl), 126.4 (C-aryl), 125.8 (C-aryl), 80.7 (C(2)), 68.7 (C(6)), 52.3 (C(5)), 33.3 (C(13)), 32.8 (C(12)), 28.3 (C(3)), 26.1 (C4)).

IR: 3060 (s), 3025 (s), 2945 (s), 2860 (s), 1947 (m), 1873 (w), 1805 (w), 1603 (m), 1583 (s), 1496 (s), 1480 (s), 1454 (s), 1438 (s), 1357 (m), 1302 (m), 1242 (m), 1181 (m), 1057 (s), 1025 (s), 925 (m), 869 (w), 741 (s), 699 (s)

MS: (EI)

298 (M+), 135 (18), 117 (35), 91 (100), 71 (53), 64 (36)

TLC: R_f 0.18 (hexanes/EtOAc, 20:1), [CAM]

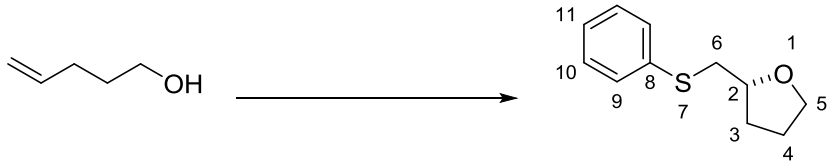
SFC: (2*R*,6*R*)-**59j**, t_R 7.70 min (46.3%); (2*S*,6*S*)-**59j**, t_R 8.50 min (53.7%) (Chiralpak OD, Gradient 1 % MeOH in CO_2 to 10% MeOH in CO_2 over 10 min, 2.5 mL/min, 220 nm, 40 ^oC),

Analysis: $C_{19}H_{20}OS$ (298.44)

Calcd. : C: 76.47; H: 7.43

Found : C: 76.58; H: 7.40

Preparation of (2*R*)-Tetrahydro-2-((phenylthio)methyl)furan (59k) (Table 9 Entry 11) [DJK-2-53]



57k **59k**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv), **57k** (86 mg, 1.0 mmol), (*R*)-**62b** (52 mg 0.1 mmol, 0.1 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -10 ^oC in an *i*-PrOH bath. Methanesulfonic acid (65 µL, 1.0 mmol, 1.0 equiv) was added and the mixture was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product was purified by flash chromatography (SiO_2, 27 g, 20 mm Ø, hexanes/EtOAc, 80:1 to 60:1) to afford 140 mg (72%) of **59k** as a pale yellow oil. The spectroscopic data match those published in the literature.[56a]

Data for **59k**:

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

7.37 (d, *J* = 7.9 Hz, 2 H, HC(9)), 7.28 (t, *J* = 7.7 Hz, 2 H HC(10)), 7.17 (t, *J* = 7.4 Hz, 1 H, HC(11)), 4.11 – 4.00 (tt, *J* = 6, 7 Hz, 1 H, HC(2)), 3.91 (dd, *J* = 14.4, 7.3 Hz, 1 H, HC(5)), 3.77 (dd, *J* = 14.4, 7.8 Hz, 1 H, HC(5)), 3.16 (dd, *J* = 13.0, 5.8 Hz, 1 H, HC(6)), 2.97 (dd, *J* = 13.0, 6.8 Hz, 1 H, HC(6)), 2.06 (m, 1 H, HC(3)), 1.91 (m, 2 H, HC(4)), 1.66 (m, 1 H, HC(3)).

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

136.3 (C(8)), 129.0 (C(9)), 128.7 (C(10)), 125.82 (C(11)), 77.46 (C(2)), 68.19 (C(5)), 38.71 (C(6)), 30.82 (C(3)), 25.64 (C(4)).

Opt Rot. : $[\alpha]_D^{24}$ 13.1 (c = 0.89, $CHCl_3$)

SFC: (2*S*)-**59k**, t_R 4.97 min (17.0%); (2*R*)-**59k**, t_R 6.07 min (83.0%) (Chiralpak AD, 5 % MeOH in CO_2, 2 mL/min, 220 nm, 40 ^oC)

Preparation of (2*R*)-Tetrahydro-2-phenyl-2-((phenylthio)methyl)furan (59l) (Table 9 Entry 12) [DJK-2-49]

57l **59l**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv), **57l** (162 mg, 1.0 mmol), (*R*)-6**2b** (52 mg, 0.1 mmol, 0.1 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -20 ^{o}C in an *i*-PrOH bath. Methanesulfonic acid (65 µL 1.0 mmol, 1.0 equiv) was added and the mixture was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product was purified by flash chromatography (SiO_2, 24 g, 20 mm Ø, hexanes/EtOAc, 80:1) to afford 228 mg (85%) of **59l** as a pale yellow oil.

Data for **59l** :

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

7.47 (d, *J* = 8.1, 2 H, H(C-aryl)), 7.37 (m, 2 H, H(C-aryl)), 7.32 (m, 2 H, H(C-aryl)), 7.26 (m, 3 H, H(C-aryl)), 7.16 (t, 1 H, *J* = 6.7 Hz, H(C-aryl)), 4.08 (dt, *J* = 14.4, 7.1 Hz, 1 H, HC(5)), 3.95 (td, *J* = 8.0, 5.8 Hz, 1 H, HC(5)), 3.48 (d, *J* = 12.9 Hz, 1 H, HC(10)), 3.38 (d, *J* = 12.9 Hz, 1 H, HC(10)), 2.43 (dt, *J* = 12.3, 8.2 Hz, 1 H, HC(3)), 2.28 (ddd, *J* = 12.5, 7.9, 5.1 Hz, 1 H, HC(3)), 2.13 – 2.00 (m, 1 H, HC(4)), 1.85 (m, 1 H, HC(4)).

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

145.9 (C(6)), 138.0 (C(12)), 129.5 (C-aryl), 128.9 (C-aryl), 128.4 (C-aryl), 127.2 (C-aryl), 125.9 (C-aryl), 125.6 (C-aryl), 86.4 (C(2)), 68.4 (C(5)), 47.0 (C(10)),

37.1 (C(3)), 26.2 (C(4)).

IR: 3058 (m), 3023 (m), 2975 (m), 2872 (m), 1952 (w), 1881 (w), 1582 (w), 1480 (s), 1446 (m), 1439 (m), 1300 (m), 1211 (m), 1120 (m), 1088 (m), 1052 (s), 1026 (s), 979 (m), 921 (w), 880 (w), 739 (s), 702 (s)

MS: (EI)

270 (M+), 147 (100), 105 (40), 77 (21)

TLC: R_f 0.42 (hexanes/EtOAc, 10:1) [CAM]

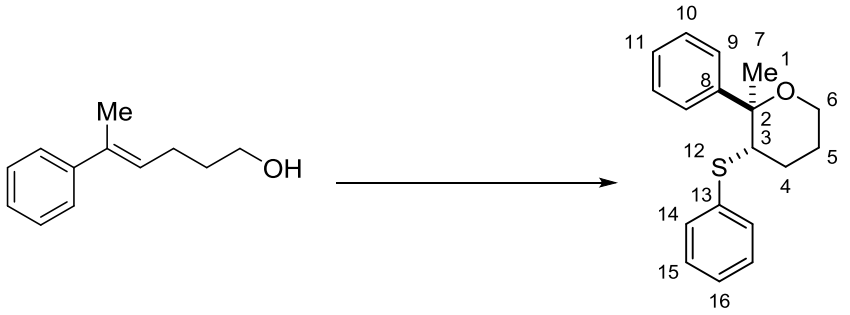
Opt Rot. : $[\alpha]_D^{24}$ -8.5 (c = 0.51, $CHCl_3$)

SFC: (2*R*)-**59l**, t_R 5.96 min (61.7%); (2*S*)-**59l**, t_R 7.25 min (38.3%) (Chiralpak AD, 5 % MeOH in CO_2, 2.5 mL/min, 220 nm, 40 ^oC)

Analysis: $C_{17}H_{18}OS$ (270.11)

Calcd. :	C: 75.51;	H: 6.71
Found :	C: 75.53;	H: 6.52

Preparation of (2*R*,3*S*)-Tetrahydro-2-methyl-2-phenyl-3-(phenylthio)-2H-pyran (58m) (Table 9 Entry 13) [DJK-3-33]



57m **58m**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv), **57m** (176 mg, 1.0 mmol), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -20 ^oC in a glycol/water bath. Methanesulfonic acid (65 µL 1.0 mmol, 1.0 equiv) was added at -20 ^oC and the reaction was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product was purified by silica gel flash chromatography (SiO_2, 18 g, 20 mm Ø, hexanes/EtOAc, 60:1) to afford 233 mg (82%) of **58m** as a white solid. Recrystallization from hot MeOH (5 mL) followed by partial sublimation (refluxing ether) yielded 17 mg (6%) of analytically pure needle-like crystals.

Data for **58m** :

mp: 46-48 °C (MeOH)

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

7.55 (d, 2 H, *J* = 7.3 Hz, H(C-aryl)), 7.35 (t, 2 H, *J* = 7.7Hz, H(C-aryl)), 7.25 (t, 1H, *J* = 7.2 Hz, H(C-aryl)), 7.18 (m, 5H, H(C-aryl)), 3.85 (ddd, 1 H, *J* = 3.7, 8.0, 11.7 Hz, HC(6)), 3.77 (m, 1 H, HC(6)), 3.57 (dd, 1 H, *J* = 3.9, 8.7 Hz, HC(3)), 2.05 (m, 1 H, HC(4)), 1.94 (m, 2 H, HC(4), HC(5)), 1.67 (s, 3 H, HC(7)), 1.57 (m, 1 H, HC(5)).

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

145.3 (C(8)), 135.9 (C(13)), 131.7 (C-aryl), 128.8 (C-aryl), 128.1 (C-aryl), 127.1 (C-aryl), 126.7 (C-aryl), 126.1 (C-aryl), 78.5 (C(2)), 61.8 (C(6)), 55.3 (C(3)), 27.8 (C(4)), 24.6 (C(5)), 22.5 (C(7)).

IR: (KBr)

3069 (m), 2994 (m), 2941 (s), 2868 (m), 1578 (m), 1570 (m), 1492 (m), 1479 (s), 1438 (s), 1377 (s), 1286 (m), 1247 (m), 1155 (m), 1099 (s), 1076 (s), 1059 (s), 1019 (m), 975 (s), 940 (m), 850 (w), 827 (w), 777 (w), 755 (s), 732 (s), 699 (s), 615 (w)

MS: (EI)

284 (52, M+), 164 (25), 136 (100), 135 (41), 93 (45), 91 (17)

TLC: R_f 0.42 (hexanes/EtOAc, 20:1) [CAM]

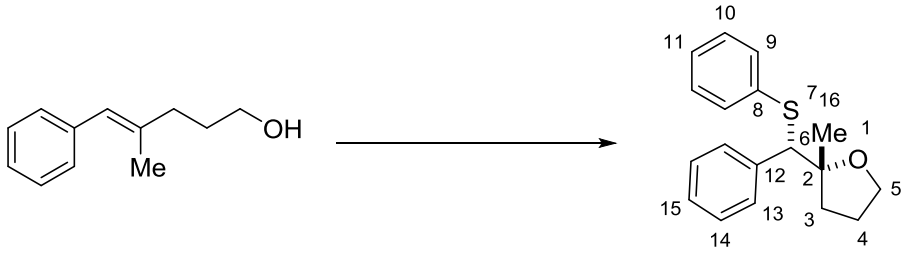
SFC: (2*R*,3*S*)-**58m**, t_R 5.82 min (69.8%); (2*S*,3*R*)-**58m**, t_R 6.29 min (30.2%) (Chiralpak AD, gradient 1% MeOH to 10% MeOH in CO_2 over 10 min, 2.5 mL/min, 220 nm, 40 °C)

Analysis: $C_{18}H_{20}OS$ (284.41)

Calcd. : C: 76.01; H: 7.09

Found : C: 75.62; H: 7.03

Preparation of (2*R*,6*S*)-Tetrahydro-2-methyl-2-(phenyl(phenylthio)methyl)furan (59n) (Table 9 Entry 14) [DJK-3-56]



57n **59n**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv), **57n** (176 mg, 1.0 mmol), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv) and CH_2Cl_2 (2.5 mL). Methanesulfonic acid (65 µL 1.0 mmol, 1.0 equiv) was added at 23 ^oC and the reaction was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product was purified by silica gel flash chromatography (SiO_2, 19 g, 20 mm Ø, hexanes/EtOAc, 40:1 then SiO_2, 8 g, 10 mm Ø, hexanes/EtOAc, 60:1) to afford 69 mg (24%) of **59n** as a clear liquid which solidified at -20 ^oC.

Data for **59n** :

bp: 120 ^oC, 0.15 mm Hg

mp: 34-36 ^oC

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

δ 7.42 (d, *J* = 7.5 Hz, 2 H, H(C-aryl)), 7.30 – 7.20 (m, 5 H, H(C-aryl)), 7.14 (m, 3 H, H(C-aryl)), 4.29 (s, 1 H, HC(6)), 3.96 – 3.87 (m, 2 H, HC(5)), 2.31 – 2.21 (m, 1 H, HC(3)), 2.00 – 1.89 (m, 1 H, HC(4)), 1.86 – 1.77 (m, 2 H, HC(3), HC(4)), 1.32 (s, 3 H, HC(16)).

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

δ 140.2 (C(12)), 136.3 (C(8)), 130.8 (C-aryl), 129.6 (C-aryl), 128.6 (C-aryl), 127.8 (C-aryl), 127.0 (C-aryl), 126.3 (C-aryl), 85.2 (C(2)), 68.3 (C(5)), 63.6 (C(6)), 36.4 (C(3)), 26.3 (C(4)), 25.4 (C(16)).

IR: (KBr)

3058 (m), 2987 (s), 2965 (s), 2943 (m), 2924 (m), 2853 (s), 1584 (m), 1570 (m), 1560 (w), 1491 (m), 1481 (s), 1451 (s), 1372 (m), 1353 (m), 1303 (m), 1252 (m), 1155 (m), 1095 (s), 1072(m), 1042 (s), 910 (m), 885 (m), 834 (m), 789 (w), 764

(m), 746 (m), 733 (s), 703 (s), 686 (s), 650 (w)

MS: (EI)

284 (4, M+), 199 (5), 105 (6), 85 (100)

TLC: R_f 0.34 (hexanes/EtOAc, 20:1) [CAM]

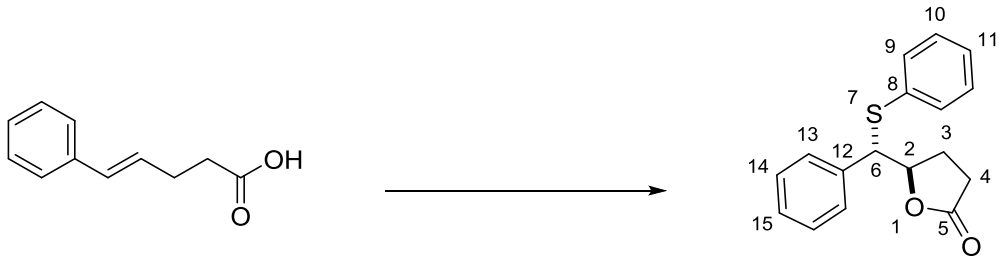
SFC: (2*R*,6*S*)-**59n**, t_R 6.28 min (60.0%); (2*S*,6*R*)-**59n**, t_R 9.68 min (40.0%) (Chiralpak OD, 5 % MeOH in CO_2, 2 mL/min, 220 nm, 40 ^oC),

Analysis: $C_{18}H_{20}OS$ (284.41)

Calcd. : C: 76.01; H: 7.09

Found : C: 75.95; H: 7.03

Preparation of (5*R*,6*S*)-Dihydro-5-(phenyl(phenylthio)methyl)furan-2(3*H*)-one (59o) (Table 9 Entry 15) [DJK-2-58]



57o **59o**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv), **57o** (176 mg, 1.0 mmol), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -10 ^oC in an *i*-PrOH bath. Methanesulfonic acid (65 µL 1.0 mmol, 1.0 equiv) was added and the reaction was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product was purified by flash chromatography (SiO_2, 21 g, 20 mm Ø, hexanes/EtOAc, 6:1) to afford 237.2 mg (84%) of **59o** as a white solid. Analytically pure material was obtained by recrystallization from hot hexane.

Data for **59o** :

mp: 92-93 ^oC (hexane)

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

δ 7.28 (m, 10 H, H(C-aryl)), 4.89 (dt, *J* = 6.3, 6.7 Hz, 1 H, HC(5)), 4.27 (d, *J* = 5.8 Hz, 1 H, HC(6)), 2.49 – 2.34 (m, 2 H, HC(3), H(C4)), 2.25 (tt, *J* = 14.0, 6.8 Hz, 1 H, HC(3)), 2.18 – 2.06 (m, 1 H, HC(4)).

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

δ 176.5 C(2), 137.3 C(12), 133.5 C(8), 133.0 (C-aryl), 129.0 (C-aryl), 128.8 (C-aryl), 128.6 (C-aryl), 128 (C-aryl), 127.9 (C-aryl), 81.3 C(6), 58.1 C(5), 28.4 C(3), 25.9 C(4).

IR: (KBr)

3071 (w), 3058 (m), 3030 (w), 2989 (w), 2944 (w), 1778 (s), 1470 (m), 1454 (m), 1439 (m), 1408 (w), 1381 (w), 1346 (m), 1303 (w), 1279 (w), 1253 (w), 1226 (m), 1184 (s), 1141 (w), 1111 (m), 1055 (m), 1021 (s), 994 (m), 923 (s), 870 (w), 803 (w), 789 (w), 753 (m), 718 (m), 694 (s), 654 (w)

MS: (EI)

284 (M+), 199 (100), 175 (16), 91 (34)

TLC: R_f 0.12 (hexanes/EtOAc, 4:1) [CAM]

Opt Rot. : $[\alpha]_D^{24}$ 113.8 (c = 0.46, $CHCl_3$)

SFC: (2*R*,3*S*)-**59o**, t_R 11.35 min (90.7%); (2*S*,3*R*)-**59o**, t_R 13.86 min (9.3%) (Chiralpak AS, 3 % MeOH in CO_2, 2.5 mL/min, 220 nm, 40 ^oC)

Analysis: $C_{17}H_{16}O_2S$ (284.37)

Calcd. : C: 71.80 H: 5.67

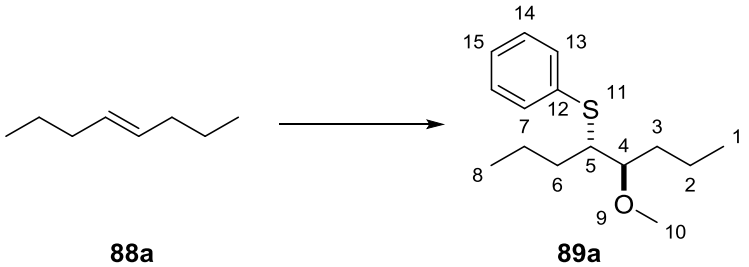
Found : C: 71.83 H: 5.71

Attempted Sulfenofunctionalization of (*E*)-5-Phenylpent-4-enamide (57p) (Table 9 Entry 16) [DJK-2-55]

57p **59p**

An oven-dried 5 mL Schlenk flask was charged with **56** (64.1 mg, 0.25 mmol, 1 equiv), and **57p** (43.8 mg, 0.25 mmol). To this was added (*R*)-**62b** (13 mg, 0.025 mmol, 0.1 equiv), CH_2Cl_2 (0.7 mL). MsOH (17 µL, 0.25 mmol, 1.0 equiv) was added. After 48 h, the reaction was quenched with Et_3N (50 µL). No desired product was observed. No further manipulations were done.

Preparation of (4*S*,5*R*)-5-(Methoxyoctan-4-yl)(phenyl)sulfide (89a) (Table 10 Entry 1) [DJK-3-74]



88a **89a**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv), 4-octene, **88a**, (112 mg, 1.0 mmol), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv), MeOH (32 mg, 1.0 mmol, 1.0 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -20 ^oC in an *i*-PrOH bath. Methanesulfonic acid (65 µL 1.0 mmol, 1.0 equiv) was added and the mixture was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product was purified by silica gel flash chromatography (SiO_2, 20 g, 20 mm Ø, hexanes/EtOAc, 40:1) to afford 234.7 mg (93%) of **89a** as a pale yellow oil. The spectroscopic data match those published in the literature.[63]

Data for **89a** :

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

7.42 (d, *J* = 7.3 Hz, 2 H, HC(13)), 7.27 (t, *J* = 7.3 Hz, 2 H, HC(14)), 7.20 (t, *J* = 7.4 Hz, 1 H, HC(15)), 3.37 (s, 3 H, H_3C(10)), 3.29 (dt, *J* = 8.2, 4.2 Hz, 1 H, HC(4)), 3.19 (m, 1 H, HC(5)), 1.57 (m, 8 H, H_2C(2), H_2C(3), H_2C(6) and H_2C(7)), 0.91 (t, *J* = 7.2 Hz, 3 H, H_3C(1,8)), 0.89 (t, *J* = 7.2 Hz, 3 H, H_3C(1,8))

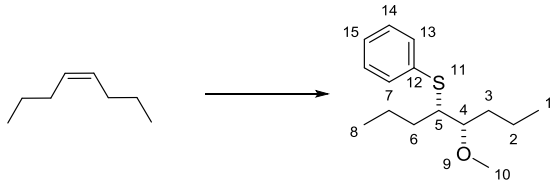
MS: (EI)

252 (M+), 166 (42), 165 (35), 123 (43), 87 (100), 55 (25)

Opt Rot. : $[\alpha]_D^{24}$ -13.1 (c = 0.41, $CHCl_3$)

SFC: (4*R*,5*S*)-**89a**, t_R 6.93 min (8.2%), (4*S*,5*R*)-**89a**, t_R 7.72 min (91.8%) (Chiralpak OD, 1% 95:5 hexanes/*i*-PrOH in CO2 , 1 mL/min, 220 nm, 40 ^oC)

Preparation of ((4*S*,5*S*)-5-Methoxyoctan-4-yl)(phenyl)sulfane (Table 10 Entry 2) [DJK-1-29]



88b **89b**

An oven-dried NMR tube was charged with **1** (30.6 mg, 0.12 mmol, 1.2 equiv), **88b** (11.5 mg, 0.1 mmol), (*R*)-**62b** (5.2 mg, 0.01 mmol, 0.1 equiv), MeOH (4.1 µL, 0.1 mmol, 1 equiv) and $CDCl_3$. The reaction was cooled to -20 ^oC and MsOH (6.6 µL, 0.1 mmol, 1 equiv) was added. The reaction was stirred for 20h and then quenched with Et_3N (10 µL). Silica gel flash column chromatography (SiO_2, 5 g, 10 mm Ø, hexanes/EtOAc 40:1) afforded 5 mg (20%) of **89b** as a thin film**.**

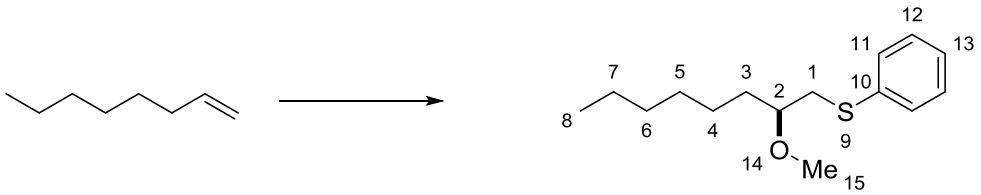
Data for **89b**:

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

7.41 (d, *J* = 7.3 Hz, 2 H, HC(13)), 7.27 (t, *J* = 7.3 Hz, 2 H, HC(14)), 7.20 (t, *J* = 7.4 Hz, 1 H, HC(15)), 3.32 (s, 3 H, H_3C(10)), 3.28 (m, 1 H, HC(4)), 3.22 (m, 1 H, HC(5)), 1.8 – 1.2(m, 8 H, H_2C(2), H_2C(3), H_2C(6) and H_2C(7)), 0.94 (m, 6 H, H_3C(1,8))

SFC: (4*R*,5*R*)-**89b**, t_R 4.12 min (47.9%), (4*S*,5*S*)-**89b**, t_R 4.45 min (52.1%) (Chiralpak OD, 0.8% MeOH in CO_2 , 2.3 mL/min, 220 nm, 40 °C)

Preparation of (*R*)-(2-Methoxyoctyl)(phenyl)sulfide (89c) and (*S*)-(1-Methoxyoctan-2-yl)(phenyl)sulfide (90c) (Table 10 Entry 3) [DJK-2-74]



88c **89c**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv), 1-octene, **88c**, (112 mg, 1.0 mmol), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv) MeOH (32 mg, 1.0 mmol, 1.0 equiv) and CH_2Cl_2 (2.5 mL). Methanesulfonic acid (65 µL 1.0 mmol, 1.0 equiv) was added at room temperature and the reaction was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product was purified by flash chromatography (SiO_2, 20 g, 20 mm Ø, hexanes/*t*-BuOMe, 60:1) to afford 193 mg (77%) of **89c** as a pale yellow oil. Kugelrohr distillation (130 °C ABT, 3 mm Hg) afforded 123.4 mg (49%) of analytically pure **89c** as a clear oil. Isomer separation was achieved by flash chromatography (SiO_2, 5 g, 10 mm Ø, hexanes/dichloromethane, 9:1).

Data for isomer mixture :

bp: 116 °C (ABT), 3 mm Hg

IR: 3059 (m), 2928 (s), 2859 (s), 1584 (s), 1480 (s), 1461 (s), 1438 (s), 1377 (m), 1185 (m), 1096 (s), 1025 (s), 738 (s), 690 (s)

MS: (EI)

252 (M+), 129 (100), 124 (20), 123 (19), 109 (18), 97 (78), 69 (19), 55 (83)

TLC: R_f **89c**, 0.27; **90c**, 0.31 (hexanes/EtOAc, 20:1) [CAM]

Analysis: $C_{15}H_{24}OS$ (252.42)

Calcd. : C: 71.37 H: 9.58

Found : C: 71.12 H: 9.32

Data for **89c**:

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

7.37 (d, 2 H, *J* = 7.2 Hz, HC(11)), 7.28 (t, 2 H, *J* = 7.3 Hz, HC(12), 7.18 (t, 1 H, *J* =7.3 Hz, HC(13)), 3.34 (s, 3 H, HC(15)), 3.34 (m, 1 H, HC(2)), 3.11 (dd, 1 H, *J* = 5.6, 13.1Hz, HC(1)), 2.99 (dd, 1 H, *J* = 6.1, 13.1 Hz, HC(1)), 1.59 (m, 2 H, $H_2C(3)$), 1.29 (m, 8 H, $H_2C(4)$, $H_2C(5)$, $H_2C(6)$, $H_2C(7)$), 0.88 (t, 3 H, *J* = 6.8 Hz, $H_3C(8)$)

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

136.9 (C(10)), 129.2 (C(11)), 128.8 (C(12)), 125.9 (C(13)), 79.9 (C(2)), 57.1 (C(15)), 37.6 (C(1)), 33.3 (C(3)), 31.7 (C-alkyl), 29.3 (C-alkyl), 25.1 (C-alkyl), 22.6 (C-alkyl), 14.1 (C(8))

Opt Rot. : $[\alpha]_D^{24}$ 5.9 (c = 0.11 , $CHCl_3$)

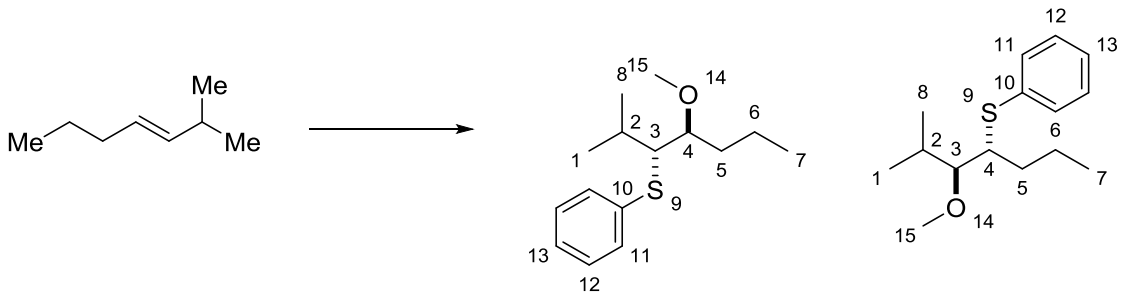
HPLC: (*S*)-**89c**, t_R 14.13 min (17.8%), (*R*)-**89c**, t_R 16.92 min (82.2%) (Chiralpak AD-RH, 45 % MeCN in H_2O, 1 mL/min, 220 nm, 40 ^oC)

Data for **90c**:

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

Diagnostic Signals : 7.42 (d, *J* = 7.2 Hz, HC(11)), 3.51 (m, 1H, HC(1)), 3.23 (m, 1H, HC(2))

Preparation of (3*R*,4*S*)-4-(Methoxy-2-methylheptan-3-yl)(phenyl)sulfide (89d) and (3*S*,4*R*)-3-(Methoxy-2-methylheptan-4-yl)(phenyl)sulfide (90d) (Table 10 Entry 4) [DJK-3-49]



88d **89d** **90d**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv)**,** (*E*)-2-methyl-3-heptene, **88d**, (112 mg, 1.0 mmol), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv), MeOH (32 mg, 1.0 mmol, 1.0 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -20 ^oC in a glycol/water bath. Methanesulfonic acid (65 µL 1.0 mmol, 1.0 equiv) was added

and the reaction was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product was purified by flash chromatography (SiO_2, 20 g, 20 mm Ø, hexanes/dichloromethane, 9:1) followed by Kugelrohr distillation to afford 144 mg (58%) of a pale yellow oil, determined to be an inseparable 4:1 mixture of **89d**:**90d**.

Data for mixture :

bp: 100 °C (ABT, 0.3 mm Hg)

IR: 3073 (s), 2959 (s), 2872 (s), 2823 (s), 1583 (s), 1478 (s), 1438 (s), 1383 (s), 1364 (s), 1329 (m), 1313 (m), 1237 (m), 1179 (s), 1151 (s), 1093 (s), 1025 (s), 983 (m), 932 (m), 827 (m), 736 (s), 690 (s)

MS: (EI)

252 (19, M+), 164 (31), 165 (43), 123 (18), 87 (100), 55 (26)

TLC: R_f 0.67 (hexanes/EtOAc, 20:1) [CAM]

Analysis: $C_{15}H_{24}OS$ (252.37)

Calcd. : C: 71.37 H: 9.58

Found : C: 71.57 H: 9.50

Data for **89d**:

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

7.45 (d, *J* = 7.2 Hz, 2 H, HC(11)), 7.33 – 7.22 (t, *J* = 7.6 Hz, 2 H, HC(12)), 7.19 (t, *J* = 7.4 Hz, 2 H, HC(13), 3.42 – 3.35 (m, 1 H, HC(4)), 3.37 (s, 3 H, HC(15)), 3.09 (dd, *J* = 6.8, 4.5 Hz, 1 H, HC(3)), 2.25 (dsept, *J* = 6.7 Hz, 4.4 Hz, 1 H, HC(2)), 1.70 – 1.62 (m, 2 H, HC(5)), 1.41 – 1.27 (m, 2 H, HC(6)), 1.12 (d, *J* = 6.8 Hz, 3 H, HC(7)), 1.06 (d, *J* = 6.7 Hz, 3 H, HC(8)), 0.85 (t, *J* = 7.4 Hz, 3 H, HC(1)).

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

138.0 (C(10)), 131.0 (C(11)), 128.8 (C(12)), 126.1 (C(13)), 82.5 (C(4)), 60.9 (C(3)), 57.6 (C(15)), 33.5 (C(5)), 29.1 (C(2)), 21.7 (C(7/8)), 18.9 (C(7/8)), 18.6 (C(6)), 14.1 (C(1))

Data for **90d**:

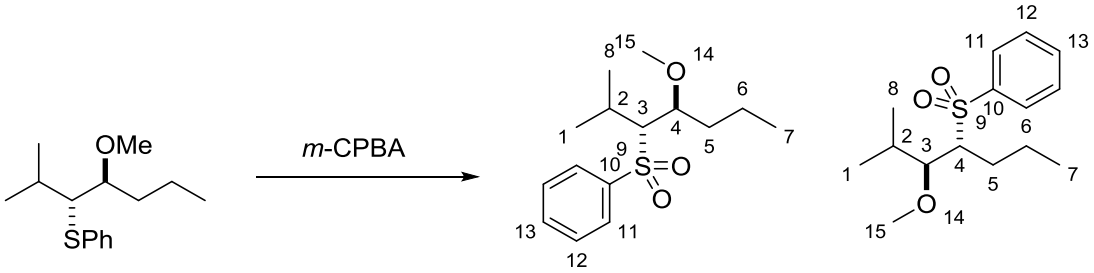
^{1}H NMR: (500 MHz, $CDCl_3$)

7.42 (d, *J* = 7.2 Hz, 2 H, HC(11)), 7.33 – 7.29 (m, 2 H, HC(12)), 7.24-7.21 (m, 1 H, HC(13)), 3.56 (s, 3 H, H(C15)), 3.25 (ddd, *J* = 11.2, 6.0, 3.4 Hz, 1 H, HC(4), 2.99 (dd, *J* = 6.9, 4.2 Hz, 1 H, HC(3), 2.01 (dsept, *J* = 6.8, 6.8 Hz, 1 H, HC(2)), 1.82 – 1.70 (m, 1 H, HC(5)), 1.62 – 1.44 (m, 3 H, HC(5)), 0.93 (m, 9 H, HC(7/8), HC(1))

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

136.6 (C(10)), 131.4 (C(11)), 128.8 (C(12)), 126.4 (C(13)), 89.4 (C(4)), 61.9 (C(15)), 52.2 (C(3)), 31.6 (C(2)), 31.3 (C(5)), 20.8 (C(7/8)), 20.0 (C(7/8)), 18.4 (C(6)), 14.0 (C(1)).

Preparation of (3*R*,4*S*)-4-(Methoxy-2-methylheptan-3-yl)(phenyl)sulfone (91) and (3*S*,4*R*)-3-(Methoxy-2-methylheptan-4-yl)(phenyl)sulfone (92) (Table 10 Entry 4) [DJK-3-58]



A 5-mL flame-dried Schlenk flask was charged with a 4:1 mixture of **89d**:**90d** (25 mg, 0.1 mmol), and CH_2Cl_2 (1.5 mL). *m*-Chloroperbenzoic acid (48 mg, 0.28 mmol, 2.8 equiv) was added portionwise. The reaction was stirred at 23 ^{o}C for 2 h. Thereupon, the reaction was poured into a separatory funnel containing 10 mL of a 4:1 mixture of sat. aq. $Na_2S_2O_3$:H_2O. The reaction was diluted with 9 mL CH_2Cl_2. The layers were separated and the organic layer was poured into 10 mL of 1 M NaOH. The aqueous layers were then individually extracted with 10 mL CH_2Cl_2. The organic layers were combined, dried over Mg_2SO_4, filtered and concentrated. Passage through a plug of SiO_2 (100% EtOAc) gave 27.0 mg (95%) of a 4:1 mixture of **91**:**92**. The crude NMR showed no other products. The constitutional isomers were separated by silica gel flash chromatography (SiO_2, 7 g, 10 mm Ø, hexanes/EtOAc, 25:1).

Data for mixture:

HRMS (ESI): Calcd. for $C_{12}H_{25}O_3S$ ($M+H^+$) : 285.1524, found : 285.1524

Data for **91**:

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

7.91 (d, *J* = 7.2 Hz, 2H, HC(11)), 7.63 (t, *J* = 7.4 Hz, 1H, HC(13)), 7.55 (t, *J* = 7.6 Hz, 2H HC(12)), 3.70 (ddd, *J* = 7.7, 5.4, 2.5 Hz, 1H, HC(3)), 3.33 (s, 3H, HC(15)), 3.07 (t, *J* = 2.7 Hz, 1H, HC(4), 2.37 (septd, *J* = 6.9, 2.8 Hz, 1H, HC(2)), 1.77 (dddd, *J* = 13.3, 9.9, 7.6, 5.4 Hz, 1H, HC(5)), 1.51 (ddt, *J* = 14.2, 9.9, 5.7 Hz, 1H, H(C(5)), 1.37 – 1.23 (m, 2H, HC(6)), 1.21 (d, *J* = 7.1 Hz, 3H, HC(1)), 1.15 (d, *J* = 7.1 Hz, 3H, HC(8)), 0.84 (t, *J* = 7.4 Hz, 3H, HC(7)).

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

133.2 (C(13)), 128.9 (C-aryl), 128.5 (C-aryl), 78.8 (C(4), 72.1 (C(3)), 58.1 (C(15)), 35.7 (C-alkyl), 26.9 (C-alkyl), 21.7 (C-alkyl), 20.9 (C-alkyl), 19.3 (C-alkyl), 13.8 (C-alkyl).

SFC: (3*R*,4*S*)-**91**, t_R 6.90 min (84.0%), (3*S*,4*R*)-**91**, t_R 7.74 min (16.0%), (Welk-O, 1% MeOH in CO_2, 3.0 mL/min, 220 nm, 40 ^oC)

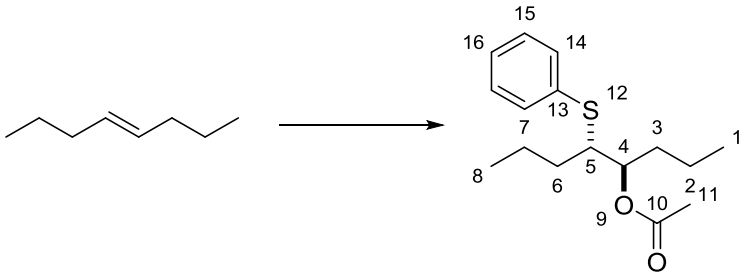
Data for **92**:

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

7.91 (d, *J* = 7.2 Hz, 2H, HC(11)), 7.65 (t, *J* = 7.4 Hz, 1H, HC(13)), 7.57 (t, *J* = 7.6 Hz, 2H, HC(12)), 3.59 (dd, *J* = 7.7, 1.7 Hz, 1H, HC(3)), 3.44 (s, 3H, HC(15)), 3.06 (td, *J* = 5.7, 1.6 Hz, 1H, HC(4)), 1.77 (m, 3H, H-alkyl), 1.38 – 1.26 (m, 1H, H-alkyl), 1.24 – 1.09 (m, 2H, H-alkyl), 0.95 (d, *J* = 6.7 Hz, 3H, HC(1)), 0.84 (d, *J* = 6.8 Hz, 3H, HC(8)), 0.78 (t, *J* = 7.3 Hz, 3H, HC(7)).

SFC: (3*S*,4*R*)-**92**, t_R 5.64 min (84.0%), (3*R*,4*S*)-**92**, t_R 6.56 min (16.0%) (Welk-O, 5% hexane:*i*-PrOH, 95:5 in CO_2, 2.0 mL/min, 220 nm, 40 ^oC)

Preparation of (4*R*,5*S*)-5-(Phenylthio)octan-4-yl acetate (89e) (Table 10 Entry 5) [DJK-2-65]



88a **89e**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **1** (255 mg, 1.0 mmol, 1.0 equiv), 4-octene, **88a**, (112 mg, 1.0 mmol), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv) acetic acid (60 mg, 1.0 mmol, 1.0 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -20 ^oC in an *i*-PrOH bath. Methanesulfonic acid (65 µL 1.0 mmol, 1.0 equiv) was added and the reaction was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product was purified by flash chromatography (SiO_2, 24 g, 20 mm Ø, hexanes/EtOAc, 40:1) to afford 217 mg (77%) of **89e** as a clear liquid. The spectroscopic data match those published in the literature.[63a]

Data for **89e** :

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

7.44 (d, 2 H, *J* = 7.5 Hz, H(C14)), 7.29 (t, 2 H, *J* = 7.4 Hz, HC(15)), 7.22 (t, 1 H, *J* = 7.3 Hz, H(C16)), 5.01 (td, 1 H, *J* = 3.7, 9.5 Hz, H(C4)), 3.29 (td, 1 H, *J* = 4.2Hz, 8.5Hz, HC(5)), 1.84 (s, 3 H, HC(11)), 1.76 (m, 2 H, H(C-alkyl)) 1.63 (m, 1 H, H(C-alkyl)), 1.52 (m, 3 H, H(C-alkyl)), 1.35 (m, 1 H, H(C-alkyl)), 1.26 (m, 1 H, H(C-alkyl)), 0.96 (t, 3 H, *J* =7.1Hz, HC(1,8)), 0.90 (t, 3 H, *J* =7.4Hz, HC(1,8))

^{13}C NMR: 170.8 (C(10)), 136.1 (C(13)), 132.2 (C(15)), 128.8 (C(14)), 126.8 (C(16)), 75.9 (C(4)), 53.4 (C(5)), 33.1 (C(3,6)), 32.4 (C(3,6)), 20.8 (C(2,7,11)), 20.7 (C(2,7,11)), 18.9 (C(2,7,11)), 13.9 (C,1,8)), 13.8 (C(1,8)).

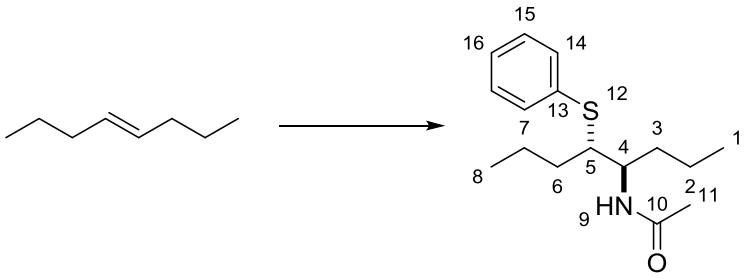
MS: (EI)

280 (M+), 220 (93), 191 (44), 165 (69), 123 (100), 69 (38), 55 (35)

Opt Rot. : $[\alpha]_D^{24}$ -13.8 (c = 0.46, $CHCl_3$)

HPLC: (4*S*, 5*R*)-**89e**, t_R 5.23 min (8.6%), (4*R*, 5*S*)-**89e**, t_R 5.82 min (91.4%) (Chiralpak AD-RH, 45 % MeCN in H_2O, 1 mL/min, 220 nm, 40 ^oC)

Preparation of *N*-((4*R*,5*S*)-5-(Phenylthio)octan-4-yl)acetamide (89f) (Table 10 Entry 6) [DJK-2-91]



88a **89f**

Following General Procedure 5, a 5-mL Schlenk flask was charged with **56** (255 mg, 1.0 mmol, 1.0 equiv), 4-octene (112 mg, 1.0 mmol), (*R*)-**62b** (52 mg, 0.1 mmol, 0.1 equiv), acetonitrile (525 µL, 10.0 mmol, 10 equiv) and CH_2Cl_2 (2.5 mL). The mixture was cooled to -20 ^oC in an *i*-PrOH bath. Methanesulfonic acid (65 µL 1.0 mmol, 1.0 equiv) was added and the reaction was allowed to stir for 48 h. The reaction was worked up following the General Procedure. The product was purified by flash chromatography (SiO_2, 24 g, 20 mm Ø, hexanes/EtOAc, 3:1) to afford 91 mg (35%) of **89f** as a clear liquid. This compound was not characterized for publication.

Data for **89f**:

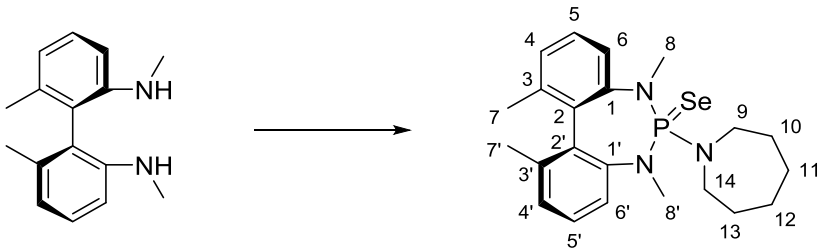
^{1}H NMR: (500 MHz, $CDCl_3$)

7.39 (m, 2H, HC(15)), 7.27 (m, 2H, HC(14)), 7.19 (m, 1H, HC(16)), 5.50 (d, *J* = 9.3 Hz, 1H, HN(9)), 4.20 (m, 1H, HC(4)), 3.39 (m, 1H, HC(5)), 1.73 (s, 3H, HC(11), 1.68 – 1.21 (m, 8H, HC(2,3,7,8)), 0.95 (m, 6H, HC(1,8)).

SFC: (3*R*,4*S*)-**89f**, t_R 3.08 min (89.1%), (3*S*,4*R*)-**89f**, t_R 3.81 min (10.9%), (AD, 5% MeOH in CO_2, 2.5 mL/min, 220 nm, 40 ^oC)

5.4. Experimental Procedures For Chapter 3.

Preparation of (*R*)-6-(Azepan-1-yl)-1,5,7,11-tetramethyl-5,7-dihydrodibenzo[d,f][1,3,2]-diazaphosphepine 6-selenide (100)



100

To a dry, 20-mL Schlenk flask under argon was added 6,6-dimethyl-2,2-di(methylamino)-1,1-biphenyl[134] (580 mg, 2.45 mmol), THF (9 mL) and Et_3N (780 µL, 5.63 mmol, 2.30 equiv). The solution was cooled to 0 °C. Neat, distilled PCl_3 (630 µL, 7.36 mmol, 3.00 equiv) was added via syringe, and the reaction was allowed to stir for 3 h at room temperature. The resulting precipitate was filtered off via cannula with the filtrate being transferred to a 100-mL Schlenk flask. The THF was removed by stirring under vacuum. Azepane (310 µL, 2.80 mmol, 1.10 equiv), CH_2Cl_2 (15 mL) and Et_3N (500 µL, 3.60 mmol, 1.48 equiv) were added and the reaction allowed to stir for 16 h. Selenium powder (580 mg, 7.36 mmol, 3.00 equiv) was added and the reaction stirred at room temperature for 24 h. The excess selenium was filtered off through a pad of Celite and the filtrate was concentrated to yield an orange foam. The material was dissolved in a minimal amount CH_2Cl_2 and purified by chromatography (SiO_2, 140 g, 20 mm ×18 cm, hexane/CH_2Cl_2, 6:1). The resulting off-white powder was filtered through a silica plug washing with hexane/Et_2O (1:1) to yield 880 mg (82%) of (*R*)-**100** (Note: The use of ether is important to remove all traces of selenium). An analytically pure sample was obtained by recrystallization from hexane (ca. 10 mL/g).

Data for (*R*)-**100**:

mp: 105–107 °C (hexane)

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

δ 7.27 (t, *J* = 7.8 Hz, 1H, H(C5)), 7.22 (t, *J* = 7.7 Hz, 1H, H(C5')), 7.15 (dd, *J* = 8.1, 3.1 Hz, 2H, HC(4), HC(4')), 7.09 (d, *J* = 7.5 Hz, 1H, H(C6)), 7.06 (d, *J* = 7.6 Hz, 1H, H(C6')), 3.18 (tt, *J* = 9.5, 4.6 Hz, 2H, HC(9)), 3.07 (d, *J* = 12.5 Hz, 3H, H(C8)), 2.95 (ddd, *J* = 14.3, 10.3, 4.6 Hz, 2H, H(C9')), 2.75 (d, *J* = 13.4 Hz, 3H, H(C8')), 2.13 (s, 3H, HC(7)), 2.03 (s, 3H, H(C7')), 1.59 (s, 8H, HC(10), C(11)).

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

δ 144.6 (d, *J* = 5.5 Hz, C(1)), 143.6 (C(1')), 137.4 (C(3)), 136.8 (C(3')), 134.6 (C(2)), 132.5 (d, *J* = 2.6 Hz, C(2')), 127.8 (d, *J* = 2.1 Hz, C(5)), 127.4 (C(5')), 127.2 (C(6)), 126.9 (d, *J* = 2.5 Hz, C(6')), 122.0 (C(4)), 120.3 (d, *J* = 3.6 Hz, C(4')), 49.6 (d, *J* = 2.0 Hz, C(9)), 38.7 (d, *J* = 10.1 Hz, C(8)), 35.5 (d, *J* = 6.3 Hz, C(8')), 30.3 (d, *J* = 4.7 Hz, C(7)), 26.7 (C(7)), 20.0 (C(10)), 19.8 (C(11))

^{31}P NMR: (202 MHz, $CDCl_3$)

δ 89.4, J_{P-Se} = 818 Hz

IR: (ATR, cm^{-1})

2 934 (w), 2858 (w), 1665 (m), 1590 (w), 1510 (w), 1451 (m), 1380 (w), 1278 (s), 1239 (s), 1223 (s), 1155 (s), 1088 (m), 1055(m), 1027 (s), 1001 (m), 920 (m), 892 (w), 846 (w), 819 (s), 784 (m), 755 (m), 734 (m), 701 (s), 688 (m), 636 (s), 615 (s)

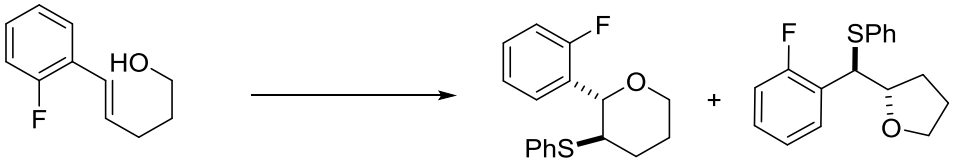
HRMS: calcd for $C_{22}H_{31}N_3PSe$: 448.1425, found: 448.1421

TLC: R_f = 0.52 (hexane/EtOAc, 4:1)

Analysis: $C_{22}H_{30}N_3PSe$ (446.44)

Calcd:	C, 59.19;	H, 6.77;	N, 9.41
Found:	C, 59.50;	H, 6.65;	N, 9.12

Preparation of (2*S*,3*R*)-2-(2-Fluorophenyl)-3-(phenylthio)tetrahydro-2H-pyran (101) and (*S*)-2-((*R*)-(2-Fluorophenyl)(phenylthio)methyl)tetrahydrofuran (101') [DJK-11-17]



101 **101'**

To a 10-mL Schlenk flask was added 5-(2-fluorophenyl)-pent-4-en-1-ol (**99**)[3] (180 mg, 1.00 mmol), sulfenylating agent **56** (256 mg, 1.00 mmol, 1.00 equiv), (*S*)-**100** (52.2 mg, 0.100 mmol, 0.100 equiv). To this was added CH_2Cl_2 (7 mL) and the flask was cooled to 0 °C. Neat, dry MsOH (48 μL, 0.75 mmol, 0.75 equiv) was added via syringe. The reaction was stirred for 24 h at 0 °C and then was quenched with Et_3N (200 μL). The resulting white suspension was concentrated in vacuo (20–23 °C, 20 mmHg). The residue was taken up in a minimal amount of chloroform and the compound was purified by column chromatography (SiO_2, 140 g, 20 mm, 22 cm, hexane/EtOAc, 20:1) to afford 227 mg (79%) of a 20:1 mixture of **101** and **101'**. An analytically pure sample was obtained by Kugelrohr distillation.

Data for **101**:

bp: 130 °C (ABT), 0.4 mmHg

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

δ 7.36 (td, *J* = 7.4, 1.8 Hz, 1H, HC(11)), 7.25–7.10 (m, 6H, HC(9), HC(13), HC(14), HC(15)), 7.05 (td, *J* = 7.6, 1.2 Hz, 1H, H(C(10)), 6.96 (ddd, *J* = 9.6, 8.3, 1.2 Hz, 1H, HC(8)), 4.57 (d, *J* = 10.3 Hz, 1H, HC(1)), 4.08 (ddt, *J* = 11.4, 4.8, 1.7 Hz, 1H, HC(5)), 3.57 (td, *J* = 11.8, 2.2 Hz, 1H, HC(5)), 3.33 (ddd, *J* = 12.0, 10.3, 4.0 Hz, 1H, HC(2)), 2.33 (dtd, *J* = 12.9, 4.7, 2.7 Hz, 1H, HC(3)), 1.91–1.82 (m, 1H, HC(4)), 1.75–1.71 (m, 1H, HC(4)), 1.68 (dd, *J* = 12.5, 4.1 Hz, 1H, HC(3))

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

δ 160.5 (d, *J* =247 Hz, C(7)), 133.5 (C(12)), 133.2 (C(14)), 129.6 (d, *J* = 8.7 Hz, HC(11)), 128.8 (d, *J* = 4.2 Hz, HC(10)), 128.5 (C(13)), 127.3 (d, *J* = 11.3 Hz, C(6)) 127.2 (C(15)), 124.0 (d, *J* = 3.8 Hz, C(9)), 115.3 (d, *J* = 22.5 Hz, C(8)), 78.4 (C(1)) , 68.6 (C(5)) , 50.0 (C(2)) , 32.2 (C(3)) , 27.0 (C(4))

^{19}F NMR: (476 MHz, $CDCl_3$)

δ 117.4

IR: (NaCl plate)
3059 (w), 2941 (m), 2850 (m), 1619 (w), 1584 (m), 1493 (s), 1453 (m), 1438 (m), 1371 (w), 1300 (w), 1260 (w), 1232 (s), 1190 (m), 1076 (s), 1025 (s), 970 (m), 959 (m), 829 (m), 798 (m), 757 (s)

HRMS: calcd for $C_{17}H_{18}FOS$: 289.1062, found: 289.1062

TLC: R_f = 0.46 (hexane/EtOAc, 4:1)

Opt. Rot. : $[\alpha]_D^{24}$ +14.2 (c = 0.97, $CHCl_3$)

Analysis: $C_{17}H_{17}FOS$ (288.38)
Calcd: C, 70.80; H, 5.94;
Found: C, 70.56; H, 5.96;

SFC: (2*S*,3*R*)-**101**, t_R 5.88 min (90.4%); (2*R*,3*S*)-**101**, t_R 5.33 min (9.6%) (Chiralpak AD, 5% MeOH in CO_2, 2 mL/min, 200 bar, 40 °C)

Data for **101'**:

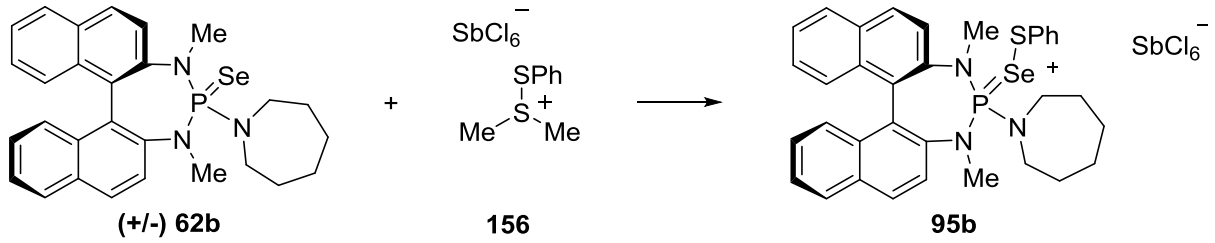
^{1}H NMR: (500 MHz, $CDCl_3$)
Diagnostic signals: δ 4.62 (d, *J* = 6.9 Hz, 1H), 4.38 (dq, *J* = 0.8, 6.7 Hz, 1H), 3.87–3.68 (m, 2H), 2.21–2.12(m, 2H), 1.90–1.82 (m, 2H)

^{19}F NMR: (476 MHz, $CDCl_3$)
δ 118.90

Crystallization of (*R*)-62b [DJK-6-5]

To a 1-dram vial was added **62b** (52 mg, 0.1 mmol). CH_2Cl_2 (0.5 mL) was added. The vial was then placed in a closed container in the presence of a 4-dram vial containing 10 mL of pentanes. White spindles were obtained after 48 h which were harvested and submitted for X-ray analysis.

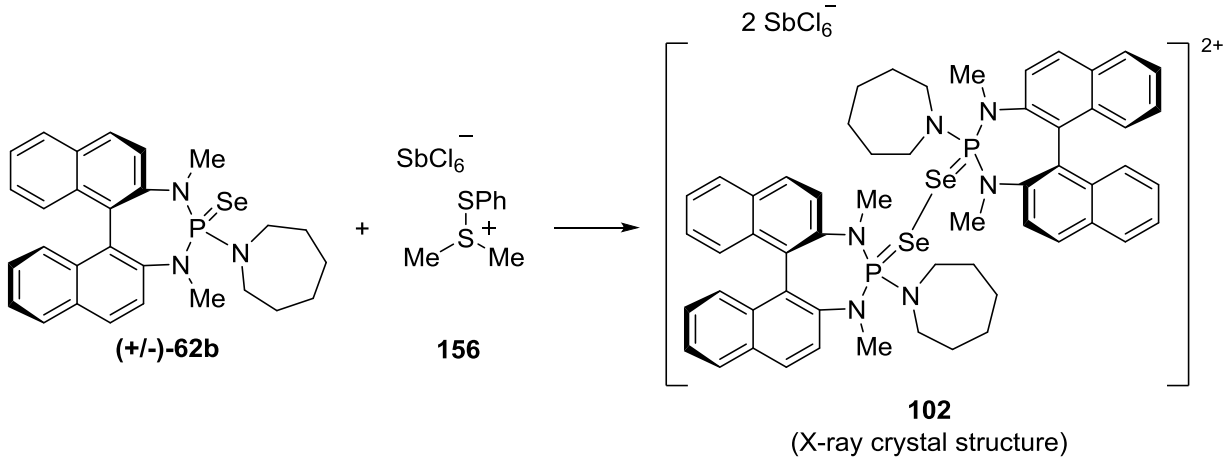
Reaction of Selenophosphoramide 62b with [PhS(SMe$_2$)]SbCl$_6$ 95b [DJK-6-46]



(+/-) 62b **156** **95b**

To a solution of **62b** (30 mg 0.06 mmol) in DME (200 μL) was added **156** [PhS(SMe$_2$)]SbCl$_6$ (30 mg, 0.058 mmol). The solution was layered with benzene (1 mL). Precipitation was observed. The solids were partially dissolved in $CDCl_3$. A 4:1 ratio of two ^{31}P NMR resonances at 62.4 ppm and 58.3 ppm respectively was observed.

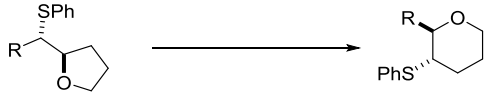
Disproportionation Upon Attempted Crystallization of Active Species 95b [DJK-6-52]



(+/-)-62b **156** **102**
(X-ray crystal structure)

In a glovebox, **62b** (50 mg, 0.098 mmol) and **156** (48 mg, 0.097 mmol) were added to a 5-mm NMR tube. The material was dissolved in DME (250 μL) and layered with benzene (1 mL). Upon standing for 24 h, orange, air-stable crystals of **102** were observed. These were harvested and submitted for X-ray analysis.

Isomerization Studies of Tetrahydrofuran Products 59

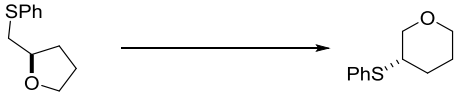


59 **58**

General Procedure

To an oven dried 5-mm NMR-tube was added substrate, catalyst, electrophile and phthalimide as solids. Phthalimide was included to simulate the effect of byproduct formation during the reaction. MsOH was added to the side of the NMR tube via syringe. The NMR tube was capped with a septa and shaken well. The solution was homogenous. The NMR tube was then kept at the appropriate temperature for the specified time. A cryocool bath filled with 2-propanol and a NESLAB IBC-4A cryocool was used to keep constant temperature for low temperature reactions. Furthermore, for low temperature reactions, a Dewar was filled with 2-propanol and cooled to below -50 ^{o}C with dry ice. The NMR tube was placed in the cold Dewar during transport to and from the NMR spectrometer. The reactions were followed by routine ^{1}H NMR spectroscopy.

Isomerization of 59k into 58k (Table 11, entry 1) [DJK-3-31]



59k **58k**

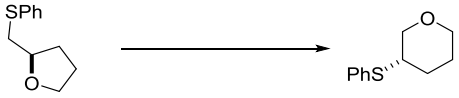
Following General Procedure 7, to an oven-dried NMR tube was added **59k** (9.7 mg, 0.05 mmol), **62b** (5.3 mg, 0.01 mmol, 0.2 equiv), **56** (12.9 mg, 0.05 mmol, 1 equiv) and $CDCl_3$ (0.7 mL). Methanesulfonic acid (3.3 µL, 0.05 mmol, 1 equiv) was added at room temperature and the mixture was shaken. NMR monitoring revealed no isomerization of **59 k** after 3h.

Data for **59k**:

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

7.37 (d, *J* = 7.9 Hz, 2 H, HC(9)), 7.28 (t, *J* = 7.7 Hz, 2 H HC(10)), 7.17 (t, *J* = 7.4 Hz, 1 H, HC(11)), 4.11 – 4.00 (tt, *J* = 6, 7 Hz, 1 H, HC(2)), 3.91 (dd, *J* = 14.4, 7.3 Hz, 1 H, HC(5)), 3.77 (dd, *J* = 14.4, 7.8 Hz, 1 H, HC(5)), 3.16 (dd, *J* = 13.0, 5.8 Hz, 1 H, HC(6)), 2.97 (dd, *J* = 13.0, 6.8 Hz, 1 H, HC(6)), 2.06 (m, 1 H, HC(3)), 1.91 (m, 2 H, HC(4)), 1.66 (m, 1 H, HC(3)).

Isomerization of 59k (Table 11, entry 2) [DJK-3-36]



59k **58k**

Following General Procedure 7,to an oven-dried NMR tube was added **5k**(19 mg, 0.1 mmol), (*R*)-**62b** (5.3 mg, 0.01 mmol, 0.1 equiv), **56** (12.8 mg, 0.05 mmol, 0.5 equiv), phthalimide (9.1 mg, 0.06 mmol, 0.6 equiv) and $CDCl_3$ (0.7 mL). The mixture was cooled to -10 ^{o}C in a glycol/water bath. Methanesulfonic acid (3.3 µL, 0.05 mmol, 1 equiv) was added at -10 ^{o}C. The mixture was shaken and kept at -10^{o}C for 48 h and then quenched with Et_3N (5 µl). NMR spectroscopy revealed no isomerization of **59k** after 48 h. The product was purified by passage through a silica plug (hexane/EtOAc, 1:1). **59k** was recovered with 100% enantiospecificity.

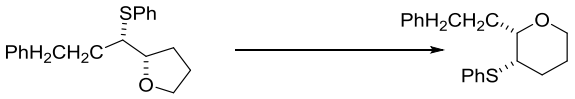
Data for **59k**:

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

7.37 (d, *J* = 7.9 Hz, 2 H, HC(9)), 7.28 (t, *J* = 7.7 Hz, 2 H HC(10)), 7.17 (t, *J* = 7.4 Hz, 1 H, HC(11)), 4.11 – 4.00 (tt, *J* = 6, 7 Hz, 1 H, HC(2)), 3.91 (dd, *J* = 14.4, 7.3 Hz, 1 H, HC(5)), 3.77 (dd, *J* = 14.4, 7.8 Hz, 1 H, HC(5)), 3.16 (dd, *J* = 13.0, 5.8 Hz, 1 H, HC(6)), 2.97 (dd, *J* = 13.0, 6.8 Hz, 1 H, HC(6)), 2.06 (m, 1 H, HC(3)), 1.91 (m, 2 H, HC(4)), 1.66 (m, 1 H, HC(3)).

SFC: (2*S*)-**5j**, t_R 4.97 min (16.6%); (2*R*)-**5j**, t_R 6.07 min (83.4%) (Chiralpak AD, 5 % MeOH in CO_2, 2 mL/min, 220 nm, 40 ^{o}C)

Isomerization of 59j at 23 °C (Table 11 entry 3) [DJK-3-32]



59j **58j**

Following General Procedure 7, to an oven-dried NMR tube was added **59j** (15.1 mg, 0.05 mmol), (*R*)-**62b** (5.3 mg, 0.01 mmol, 0.2 equiv), **56** (12.9 mg, 0.05 mmol, 1 equiv) and $CDCl_3$ (0.7 mL). Methanesulfonic acid (3.3 µL, 0.05 mmol, 1 equiv) was added at room temperature and the mixture was shaken. After 3h, NMR spectra showed a 3.5:1 ratio of **58j**:**59j**, after 4 d at room temperature the ratio was >19:1 **58j**:**59j**.

Data for **59j** :

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

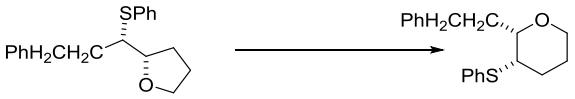
7.42 (d, *J* = 7.1 Hz, 2 H, H(C-aryl)), 7.28 (app t, *J* = 7.4 Hz, 4 H, H(C-aryl)), 7.24 – 7.14 (m, 4 H, H(C-aryl)), 4.08 (dt, *J* = 11.3, 5.6 Hz, 1 H, HC(2)), 3.93 (dd, *J* = 14.8, 6.6 Hz, 1 H, HC(5)), 3.78 (dd, *J* = 14.3, 7.1 Hz, 1 H, HC(5)), 3.23 (dt, *J* = 9.1, 4.4 Hz, 1 H, HC(6)), 2.99 (ddd, *J* = 14.7, 9.9, 5.3 Hz, 1 H, HC(13)), 2.81 (ddd, *J* = 13.8, 9.7, 6.7 Hz, 1 H, HC(13)), 2.11 (m, 1 H, HC(12)), 2.04 – 1.96 (m, 1 H, HC(3)), 1.94 – 1.73 (m, 4 H, HC(12), H(C3), HC(4)).

Data for **58j:**

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

4.09 (ddt, *J* = 11.3, 4.3, 1.9 Hz, 1H), 3.60 (ddd, *J* = 8.6, 4.8, 2.2 Hz, 1H), 3.51 (td, *J* = 11.6, 2.6 Hz, 1H), 2.83 – 2.71 (m, 1H), 2.67 (ddd, *J* = 13.7, 9.2, 7.2 Hz, 1H), 2.27 – 2.13 (m, 2H), 2.09 – 1.99 (m, 1H), 1.95 – 1.81 (m, 2H).

Isomerization of 59j at -10 °C (Table 11 entry 4) [DJK-3-35]



59j **58j**

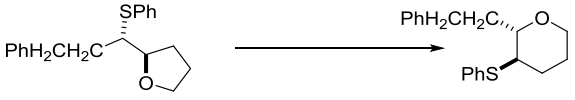
Following General Procedure 7, to an oven-dried NMR tube was added **5h** (75 mg, 0.25 mmol), **62b** (13.1 mg, 0.025 mmol, 0.1 equiv), **1** (31.7 mg, 0.125 mmol, 0.5 equiv), phthalimide (18.5 mg, 0.125 mmol, 0.5 equiv.) and $CDCl_3$ (0.7 mL). Methanesulfonic acid (17 µL, 0.25 mmol, 1 equiv) was added at -10 °C and the mixture was shaken. After 48 h the reaction was quenched with Et_3N (5 µL). NMR spectroscopy revealed pure **59j**.

Data for **59j** :

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

7.42 (d, *J* = 7.1 Hz, 2 H, H(C-aryl)), 7.28 (app t, *J* = 7.4 Hz, 4 H, H(C-aryl)), 7.24 – 7.14 (m, 4 H, H(C-aryl)), 4.08 (dt, *J* = 11.3, 5.6 Hz, 1 H, HC(2)), 3.93 (dd, *J* = 14.8, 6.6 Hz, 1 H, HC(5)), 3.78 (dd, *J* = 14.3, 7.1 Hz, 1 H, HC(5)), 3.23 (dt, *J* = 9.1, 4.4 Hz, 1 H, HC(6)), 2.99 (ddd, *J* = 14.7, 9.9, 5.3 Hz, 1 H, HC(13)), 2.81 (ddd, *J* = 13.8, 9.7, 6.7 Hz, 1 H, HC(13)), 2.11 (m, 1 H, HC(12)), 2.04 – 1.96 (m, 1 H, HC(3)), 1.94 – 1.73 (m, 4 H, HC(12), H(C3), HC(4)).

Isomerization of 59g at 23 °C (Table 11 entry 5) [DJK-3-50]



59g **58g**

Following General Procedure 7, to an oven-dried NMR tube was added **59g** (7.3 mg, 0.025 mmol), **56** (3.3 mg, 0.0125 mmol, 0.5 equiv), (*R*)-**62b** (1.2 mg, 0.0025 mmol), phthalimide (1.8 mg, 0.0125 mmol, 0.5 equiv.) and $CDCl_3$ (0.7 mL). Methanesulfonic acid (1.6 µL, 0.025 mmol, 1 equiv) was added at room temperature and the mixture was shaken. After 16 h, NMR spectra showed 30:1 ratio of **58g**:**59g**. The reaction was quenched with Et_3N (5 µL), and the product was purified by flash chromatography (SiO_2, 3 g, 10 mm Ø, hexanes:EtOAc, 20:1) to yield 3.1 mg (42%) of **58g**. **58g** was formed with 100% enantiospecificity.

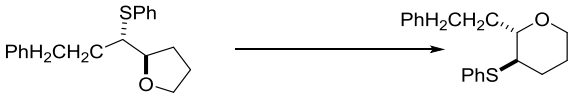
Data for **58g**:

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

7.46 (d, *J* = 7.4 Hz, 2 H, H(C-aryl)), 7.26 (m, 5 H, H(C-aryl), 7.18 (t, 3 H, *J* = 7.4 Hz, H(C-aryl)) , 4.00 (ddd, *J* = 9.5, 5.0, 3.1 Hz, 1 H, HC(6)), 3.36 (td, *J* = 11.8, 2.5 Hz, 1 H, HC(6)), 3.20 (td, *J* = 9.5, 2.4 Hz, 1 H, HC(2)), 2.91 (ddd, *J* = 11.9, 10.0, 4.1 Hz, 1 H, HC(3)), 2.82 (ddd, *J* = 14.3, 9.9, 4.8 Hz, 1 H, HC(8)), 2.69 (ddd, *J* = 13.6, 9.5, 7.3 Hz, 1 H, HC(8)), 2.46 – 2.31 (m, 1 H, HC(7)), 2.19 – 2.09 (m, 1 H, HC(5)), 1.87 – 1.77 (ddt, *J* = 14, 4.8, 9.3 Hz, 1 H, HC(7)), 1.77 – 1.66 (m, 1 H, HC(4)), 1.66 – 1.58 (m, 1 H, HC(4)), 1.50 (app qd, *J* = 13.0, 4.2 Hz, 1 H, HC(5)).

SFC: (2*S*,3*R*)-**58g**, t_R 7.42 min (3.9%); (2*R*,3*S*)-**58g**, t_R 8.19 min (96.1%) (Chiralcel OJ, 4 % MeOH in CO_2, 2 mL/min, 220 nm, 40 ^{o}C)

Isomerization of 59g at -20 ^{o}C (Table 11 entry 6) [DJK-3-57]



59g **58g**

Following General Procedure 7, to an oven-dried NMR tube was added a 1:1 mixture of **58g**:**59g** (15 mg, 0.05 mmol), (*R*)-62b (2.4 mg, 0.005 mmol), **56** (6.5 mg, 0.025 mmol, 0.5 equiv), phthalimide (3.7 mg, 0.025 mmol, 0.5 equiv.) and $CDCl_3$ (0.15 mL). The mixture was cooled to -20 ^{o}C in an *i*-PrOH bath. Methanesulfonic acid (3.2 µL, 0.05 mmol, 1 equiv) was added at -20 ^{o}C, and the mixture was shaken. After 48 h, the reaction was quenched with Et_3N (5 µL) and 0.55 mL of $CDCl_3$ was added. NMR spectroscopy revealed a 5.5:1 mixture of **58g**:**59g**. The product was purified by flash chromatography (SiO_2, 5 g, 10 mm Ø, hexane/EtOAc, 50:1) to afford 8.9 mg of a mixture of **58g** and **59**g and 4.4 mg of **59g** (89% combined recovery).

Data for **58g**:

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

7.46 (d, *J* = 7.4 Hz, 2 H, H(C-aryl)), 7.26 (m, 5 H, H(C-aryl), 7.18 (t, 3 H, *J* = 7.4 Hz, H(C-aryl)) , 4.00 (ddd, *J* = 9.5, 5.0, 3.1 Hz, 1 H, HC(6)), 3.36 (td, *J* = 11.8, 2.5 Hz, 1 H, HC(6)), 3.20 (td, *J* = 9.5, 2.4 Hz, 1 H, HC(2)), 2.91 (ddd, *J* = 11.9, 10.0, 4.1 Hz, 1 H, HC(3)), 2.82 (ddd, *J* = 14.3, 9.9, 4.8 Hz, 1 H, HC(8)), 2.69 (ddd, *J* = 13.6, 9.5, 7.3 Hz, 1 H, HC(8)), 2.46 – 2.31 (m, 1 H, HC(7)), 2.19 – 2.09 (m, 1 H, HC(5)), 1.87 – 1.77 (ddt, *J* = 14, 4.8, 9.3 Hz, 1 H, HC(7)), 1.77 – 1.66 (m, 1 H, HC(4)), 1.66 – 1.58 (m, 1 H, HC(4)), 1.50 (app qd, *J* = 13.0, 4.2 Hz, 1 H, HC(5)).

SFC: (2*S*,3*R*)-**58g**, t_R 7.42 min (3.8%); (2*R*,3*S*)-**58g**, t_R 8.19 min (96.2%) (Chiralcel OJ, 4 % MeOH in CO_2, 2 mL/min, 220 nm, 40 ^oC)

Data for **59g**:

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

7.43 (m, 2 H, H(C-aryl)), 7.24 (m, 5 H, H(C-aryl)), 7.15 (m, 3 H, H(C-aryl)), 3.94 (q , *J* = 7.0 Hz, 1 H, HC(2)), 3.82 (dt, *J* = 14.0, 6.9 Hz, 1 H, HC(5)), 3.73 (td, *J* = 7.7, 5.9 Hz, 1 H, HC(5)), 3.14 – 3.05 (m, 1 H, HC(6)), 3.04 – 2.94 (m, 1 H, HC(8)), 2.78 (ddd, *J* = 13.7, 9.7, 6.8 Hz, 1 H, HC(8)), 2.17 – 2.06 (m, 1 H, HC(7)), 2.06 – 1.96 (m, 1 H, HC(7)), 1.93 – 1.64 (m, 4 H, $H_2C(3)$ and $H_2C(4)$).

Determination of Reactant Order in the Sulfenofunctionalization Reaction

General Procedure

To a dried 5-mm NMR tube, electrophile **56** and substrate **101** were added. To this was added 300 μL of a freshly prepared stock solution of a measured amount of catalyst **100** and fluorobenzene standard (1.0 equiv of standard with respect to substrate) in $CDCl_3$, followed by 400 μL of neat $CDCl_3$. The sample was then inserted into a 400 MHz spectrometer that had been pre-cooled to the appropriate temperature and then allowed to equilibrate for 20 minutes. The sample was then ejected, the corresponding amount of MsOH was added, the sample was shaken for ca. 10 s, reinserted and ^{19}F data collection was begun immediately. Data acquisition

parameters were as follows:

Spectral Window : –100 ppm to –130 ppm
pw = 16 μs
Acquisition Time: 1 s
Delay Time: 9 s
Scans per data point: 4

A delay parameter of 20 s was introduced after each data point such that one data point was collected every minute. For brevity, data here is presented in 15 minute intervals. The reactions were followed to a minimum of 12% conversion, of which the initial 10% was used to determine the initial rate of the reaction. Each experiment was repeated three times and the rates and standard deviations were calculated. Uncertainties are given to one standard deviation.

Determination of Rate for 1.0 equiv. of substrate- Run 1 [DJK-5-20-1]

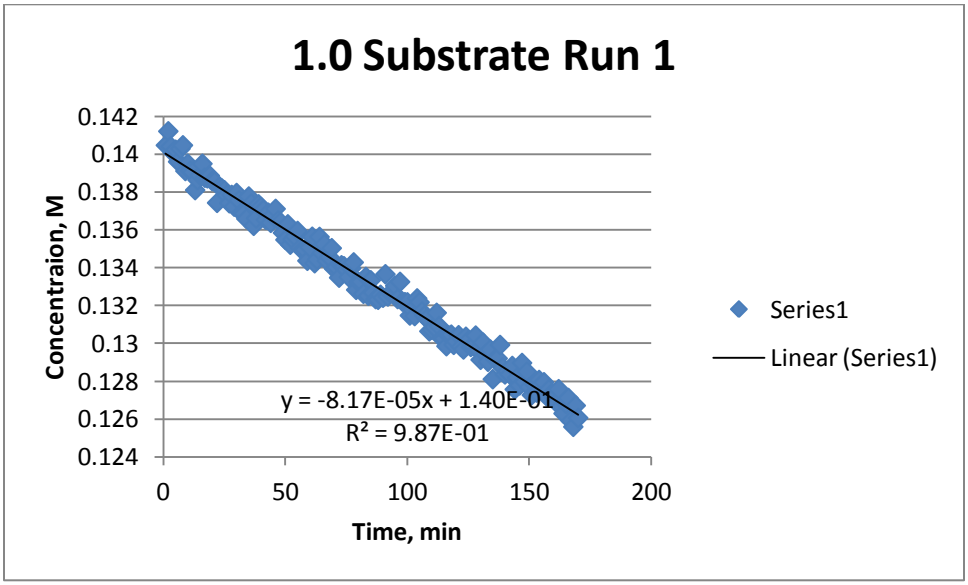
Following the General Procedure, **56 (**25.5 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.1 equiv) and MsOH (6.5 μL, 0.1 mmol, 1.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^oC. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 8.17E-05 M/min

[**101**] = 0.14 M
[**56**] = 0.14 M
[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	19297.7	22228.2	0.142857
16	19207.5	21687.6	0.140037
31	19204.7	21577.1	0.139344

46	19457.6	21638.5	0.137924
61	19350.8	21279.1	0.136382
76	19249.5	21073.9	0.135778
91	19309.3	20996.3	0.134859
106	19222	20736.6	0.133796
121	19094.3	20523.5	0.133306
136	19488.5	20758.1	0.132103
151	19192.6	20264.5	0.13095
166	19402.9	20421.2	0.130532
181	19366	20080.3	0.128598
196	19218.4	19945.7	0.128717
211	19142.7	19666.6	0.127418
226	19230.4	19610.6	0.126475
241	19142.6	19375.1	0.12553
256	19049.9	19154.7	0.124706



Determination of Rate for 1.0 equiv. of substrate- Run 2 [DJK-5-20-2]

Following the General Procedure, **56 (**25.5 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 1.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} =

7.81E-05 M/min

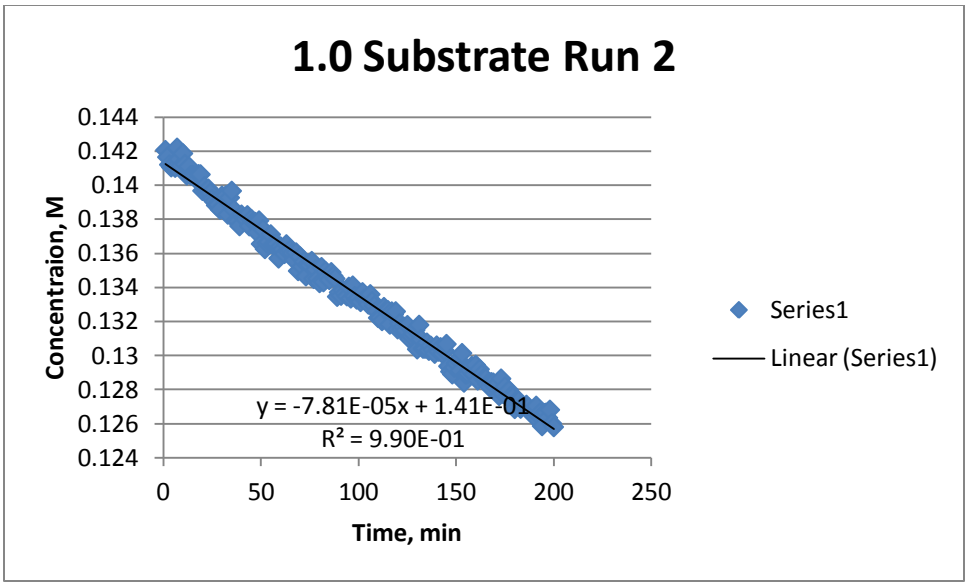
[**101**] = 0.14 M

[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	17254.8	19621.1	0.140476
16	17627.1	19905.3	0.139501
31	17521.1	19509.6	0.137555
46	17478	19399.4	0.137115
61	17137.5	18817.2	0.135643
76	17228.6	18619.6	0.133509
91	17372.4	18796.3	0.13366
106	17489.5	18643	0.131682
121	17126.1	18082.9	0.130436
136	17331.5	18122	0.129169
151	17221.4	17742.2	0.127271
166	17284.2	17785.7	0.127119
181	17168.8	17528	0.126119
196	17216.2	17394.9	0.124817
211	17072.7	17020.5	0.123157
226	17257.6	17118.6	0.12254



Determination of Rate for 1.0 equiv. of substrate- Run 3 [DJK-5-20-3]

Following the General Procedure, **56 (**25.5 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 1.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 6.52E-05 M/min

[**101**] = 0.14 M

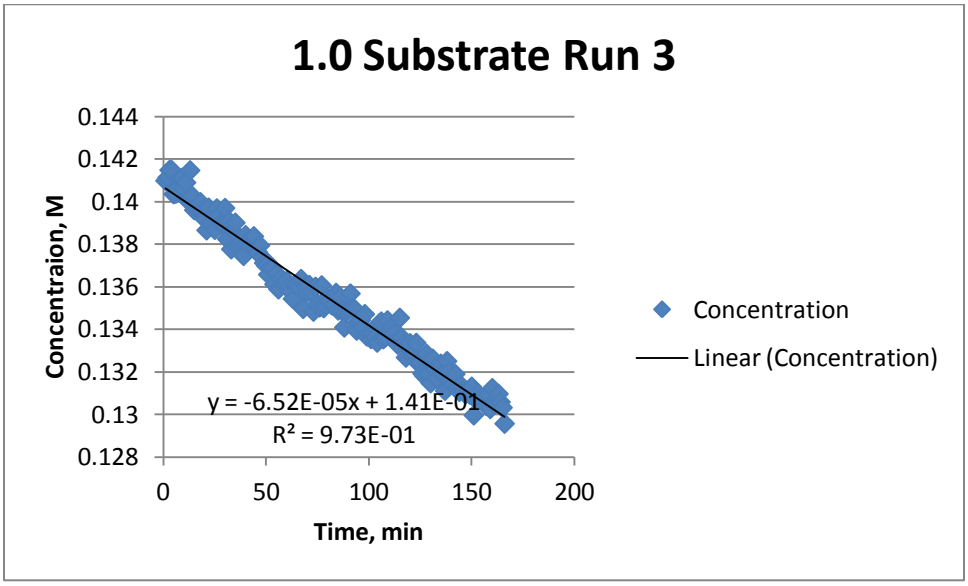
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	17254.8	19621.1	0.140476
16	17627.1	19905.3	0.139501
31	17521.1	19509.6	0.137555
46	17478	19399.4	0.137115
61	17137.5	18817.2	0.135643
76	17228.6	18619.6	0.133509

91	17372.4	18796.3	0.13366
106	17489.5	18643	0.131682
121	17126.1	18082.9	0.130436
136	17331.5	18122	0.129169
151	17221.4	17742.2	0.127271
166	17284.2	17785.7	0.127119
181	17168.8	17528	0.126119
196	17216.2	17394.9	0.124817
211	17072.7	17020.5	0.123157
226	17257.6	17118.6	0.12254



Determination of Rate for 0.2 equiv. of substrate- Run 1 [DJK-5-21-1]

Following the General Procedure, **56 (**25.5 mg, 0.1 mmol, 5.0 equiv), **101** (3.6 mg, 0.02 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.5 equiv) and MsOH (6.5 µL, 0.1 mmol, 5.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.73E-05 M/min

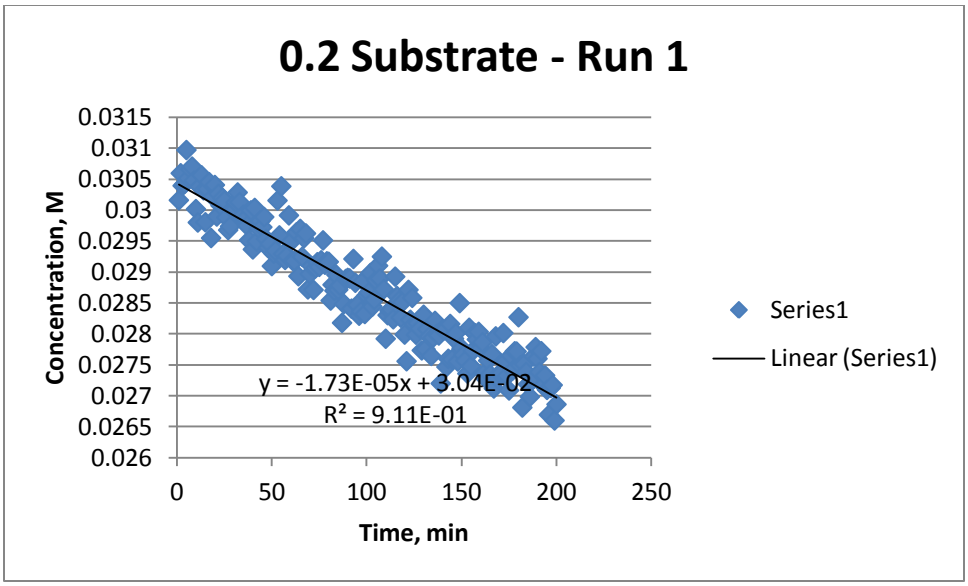
[**101**] = 0.028 M

[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	10351.8	4602.83	0.030159
16	10347.9	4628.25	0.030337
31	10308.4	4578	0.030122
46	10243.3	4513.6	0.029887
61	10301.3	4431.66	0.02918
76	10200	4389.33	0.029188
91	10272.8	4376.3	0.028895
106	10219.4	4384.53	0.029101
121	10361.6	4209.74	0.027557
136	10334.6	4298.13	0.028209
151	10249.2	4179.5	0.027659
166	10229.7	4173.67	0.027673
181	10229	4145.93	0.027491
196	10300.4	4053.65	0.026693
211	10132.1	4035.01	0.027012
226	10247.7	4022.88	0.026627
241	10193.8	3974.25	0.026444
256	10243.5	3950.94	0.026161
271	10223.1	3927.23	0.026056
286	10221.9	3774.96	0.025049
301	10171.7	3745.46	0.024976
316	10224.6	3739.16	0.024805
331	10264.8	3749.75	0.024777
346	10191.5	3756.95	0.025004
361	10256.3	3681.87	0.024349
376	10126.2	3588.08	0.024034
391	10229.7	3627	0.024049
406	10238.9	3533.67	0.023409
421	10141.7	3532.63	0.023626
436	10177.5	3470.67	0.02313
451	10193.3	3532.63	0.023506
466	10248.4	3416.93	0.022614
481	10249.9	3301.25	0.021846
496	10369.6	3473.14	0.022718



Determination of Rate for 0.2 equiv. of substrate- Run 2 [DJK-5-21-2]

Following the General Procedure, **56 (**25.5 mg, 0.1 mmol, 5.0 equiv), **101** (3.6 mg, 0.02 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.5 equiv) and MsOH (6.5 µL, 0.1 mmol, 5.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.93E-05 M/min

[**101**] = 0.028 M

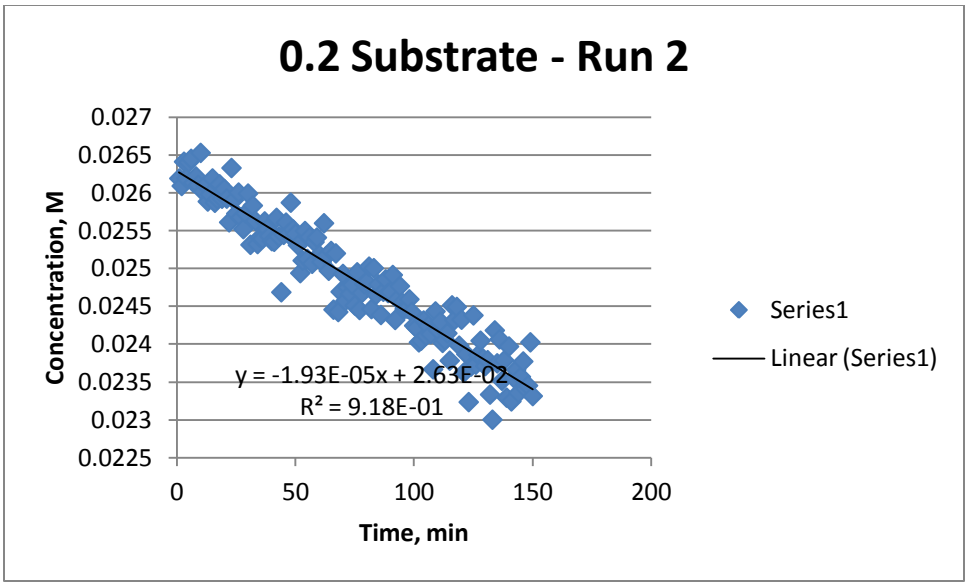
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	9026.41	4012.4	0.02619
16	8988.09	3946.27	0.025869
31	9064.36	3894.25	0.025313
46	9081.38	3946.81	0.025606
61	9039.12	3848.57	0.025086
76	8990.63	3807.15	0.02495

91	9027.9	3817.54	0.024914
106	8988.36	3697.96	0.02424
121	9046.63	3627.46	0.023625
136	8943.41	3652.61	0.024063
151	8969.39	3540.14	0.023255
166	8944.07	3416.44	0.022506
181	8923.69	3454.11	0.022806
196	8950.07	3438.87	0.022638
211	9054.26	3453.97	0.022476
226	8935.37	3377.87	0.022273
241	9026.12	3383.39	0.022085
256	8934.23	3213.64	0.021193
271	8989.68	3221.75	0.021116
286	8848.51	3147.9	0.020961
301	8939.57	3142.65	0.020713
316	9081.41	3135.43	0.020342
331	8974.48	3018.45	0.019817
346	9018.71	2973.68	0.019427
361	8946.08	2930.68	0.019301
376	8957.99	2915.54	0.019176
391	8922.59	2833.7	0.018712
406	8983.35	2776.98	0.018213
421	9032.4	2798.19	0.018253
436	8926.65	2745.64	0.018122
451	8972.7	2690.03	0.017664
466	8897.56	2540.26	0.016821
481	8920.09	2583.62	0.017065
496	8940.66	2667.57	0.017579
511	8833.85	2524.29	0.016836
526	8936.04	2444.12	0.016115



Determination of Rate for 0.2 equiv. of substrate- Run 3 [DJK-5-21-3]

Following the General Procedure, **56 (**25.5 mg, 0.1 mmol, 5.0 equiv), **101** (3.6 mg, 0.02 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.5 equiv) and MsOH (6.5 µL, 0.1 mmol, 5.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.65E-05 M/min

[**101**] = 0.028 M

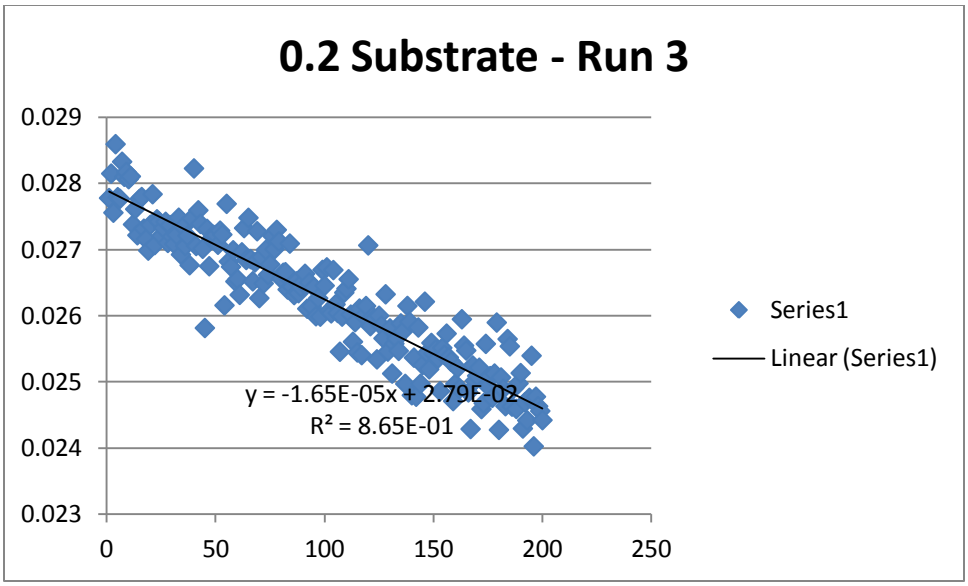
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	10433.8	3247.82	0.027778
16	10269.2	3198.37	0.027793
31	10342.2	3138.71	0.027082
46	10391.1	3180.31	0.027312
61	10409.4	3069.53	0.026314
76	10333.8	3150.39	0.027205

91	10257.2	3061.27	0.026633
106	10340.2	3017.41	0.026041
121	10450.2	3026.2	0.025842
136	10327.7	2981.53	0.025762
151	10388.7	2967.07	0.025487
166	10342	2878.88	0.024841
181	10316.7	2897.85	0.025066
196	10295.4	2771.8	0.024025
211	10254.7	2739.3	0.023838
226	10390	2785.99	0.023928
241	10316.9	2793.42	0.024162
256	10336.5	2778.54	0.023988
271	10298.7	2721.48	0.023581
286	10457.2	2708.39	0.023112
301	10284.8	2612.9	0.022671
316	10360.6	2659.21	0.022904
331	10285.2	2534.92	0.021994
346	10405.1	2559.95	0.021955
361	10294.9	2501.15	0.02168
376	10305.8	2450.44	0.021218
391	10263.7	2408.26	0.020939
406	10265.2	2390.41	0.02078
421	10241.1	2438.83	0.021251
436	10300.7	2369.27	0.020526
451	10249	2329.19	0.02028
466	10250	2156.45	0.018774
481	10277	2253.95	0.019572
496	10250.7	2188.88	0.019055
511	10236.6	2075.83	0.018096



Determination of Rate for 0.33 equiv. of substrate- Run 1 [DJK-5-24-1]

Following the General Procedure, **56 (**25.5 mg, 0.1 mmol, 3.0 equiv), **101** (6 mg, 0.033 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.3 equiv) and MsOH (6.5 µL, 0.1 mmol, 3.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 2.3E-05 M/min

[**101**] = 0.045 M

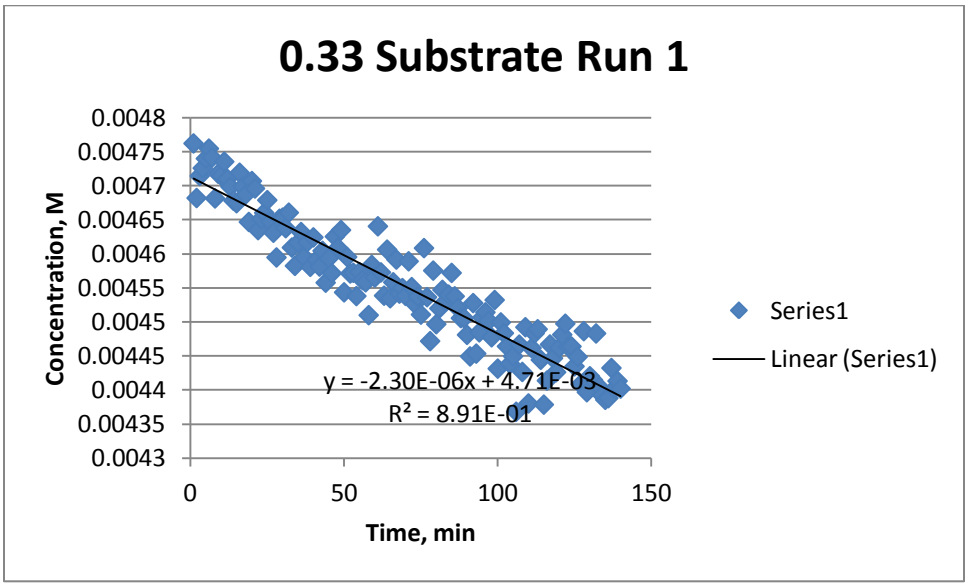
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	10275.6	7687.94	0.004762
16	10225.2	7581.16	0.004719
31	10331.5	7527.74	0.004637
46	10398.8	7468.9	0.004571
61	10360.5	7553.31	0.00464
76	10316.8	7469.57	0.004608
91	10366.1	7246.15	0.004449

106	10356.8	7107.42	0.004368
121	10263.7	7226.15	0.004481
136	10420.5	7183.87	0.004388
151	10357.8	7154.04	0.004396
166	10288.5	7002.15	0.004332
181	10185.6	6974.49	0.004358
196	10254.3	6961.55	0.004321
211	10134.5	6782.09	0.004259
226	10264.4	6822.62	0.004231
241	10237.2	6769.8	0.004209
256	10256.8	6766.76	0.004199



Determination of Rate for 0.33 equiv. of substrate- Run 2 [DJK-5-24-2]

Following the General Procedure, **56 (**25.5 mg, 0.1 mmol, 3.0 equiv), **101** (6 mg, 0.033 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.3 equiv) and MsOH (6.5 µL, 0.1 mmol, 3.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 2.41E-05 M/min

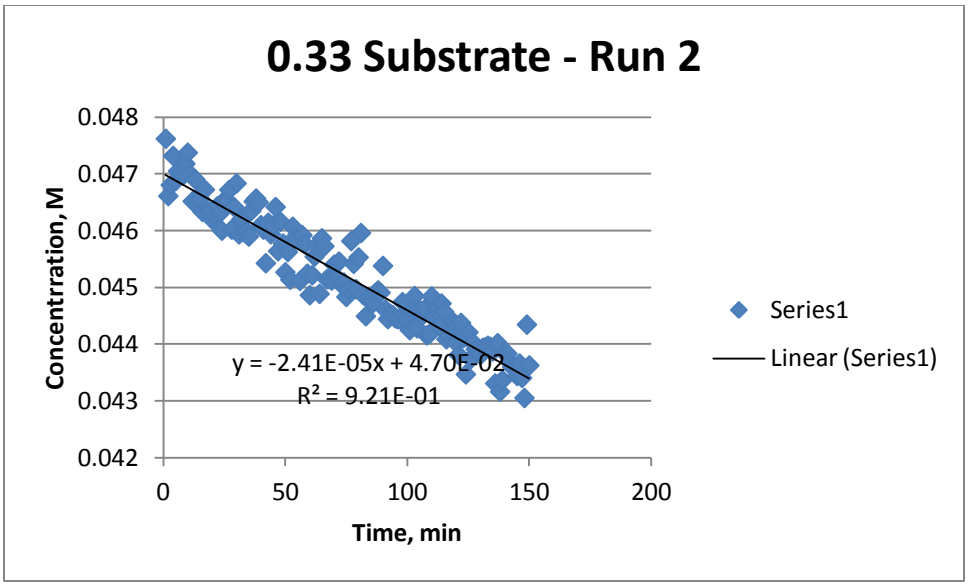
[**101**] = 0.045 M

[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	9993.4	8446.41	0.047619
16	10033.9	8251.56	0.046333
31	10007.2	8158.9	0.045935
46	9920.41	8172.94	0.046416
61	9959.23	7992.45	0.045214
76	9936.76	7928.88	0.044956
91	10019.5	7933.09	0.044609
106	9923.51	7837.48	0.044497
121	10015	7787.27	0.043808
136	9995.63	7683.35	0.043307
151	9955.83	7682.62	0.043476
166	9931.44	7648.62	0.04339
181	9911.4	7502.03	0.042645
196	9917.41	7481.08	0.0425
211	9961.64	7479.11	0.0423
226	10004.9	7475.35	0.042096
241	9914.63	7260.81	0.04126
256	9912.3	7195.83	0.0409
271	9979.76	7220.15	0.040761
286	9912.9	7163.52	0.040714
301	9955.09	7123.25	0.040314
316	9964.23	7024.42	0.039718
331	9973.77	7038.52	0.03976
346	9887.14	6979.61	0.039772
361	9965.61	6873.82	0.038861
376	9929.93	6851.09	0.038872
391	9833.89	6797.05	0.038942
406	9818.74	6651.6	0.038167
421	9910.96	6645.56	0.037778
436	9802.82	6611.23	0.037997
451	9845.6	6472.2	0.037037
466	9799.86	6486.67	0.037293
481	9801.99	6379.07	0.036666
496	9958.57	6471.34	0.036612
511	9987.07	6342.19	0.035779
526	9893.13	6308.6	0.035927



Determination of Rate for 0.33 equiv. of substrate- Run 3 [DJK-5-24-3]

Following the General Procedure, **56 (**25.5 mg, 0.1 mmol, 3.0 equiv), **101** (6 mg, 0.033 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.3 equiv) and MsOH (6.5 µL, 0.1 mmol, 3.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 2.68E-05 M/min

[**101**] = 0.045 M

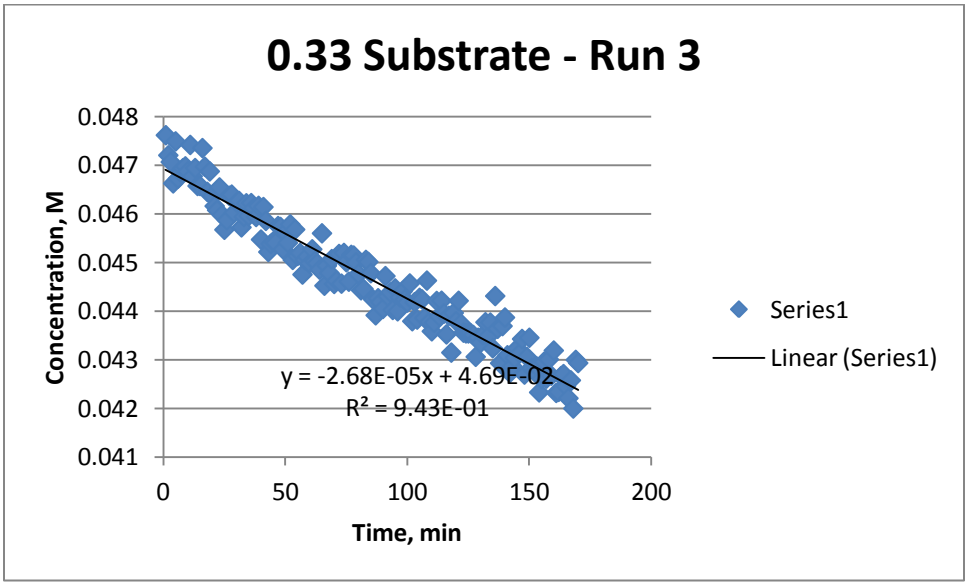
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	9856.83	7077.35	0.047619
16	9821.55	7012.79	0.047354
31	9800.34	6837.27	0.046269
46	9894.93	6774.54	0.045406
61	9811.66	6697.89	0.045273
76	9868.1	6637.3	0.044607
91	9902.04	6677.22	0.044722
106	9883.71	6593.63	0.044244

121	9932.07	6621.58	0.044215
136	9871.09	6595.42	0.044312
151	9867.38	6372.14	0.042828
166	9813.94	6246.19	0.04221
181	9779.49	6326.62	0.042905
196	9767.99	6172.65	0.04191
211	9982.19	6196.44	0.041168
226	9925.37	6203.28	0.04145
241	9941.44	6070.14	0.040495
256	9904.36	6061.91	0.040591



Determination of Rate for 0.6 equiv. of substrate- Run 1 [DJK-5-26-1]

Following the General Procedure, **56 (**25.5 mg, 0.1 mmol, 1.7 equiv), **101** (10.8 mg, 0.06 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.017 equiv) and MsOH (6.5 µL, 0.1 mmol, 1.7 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 5.53E-05 M/min

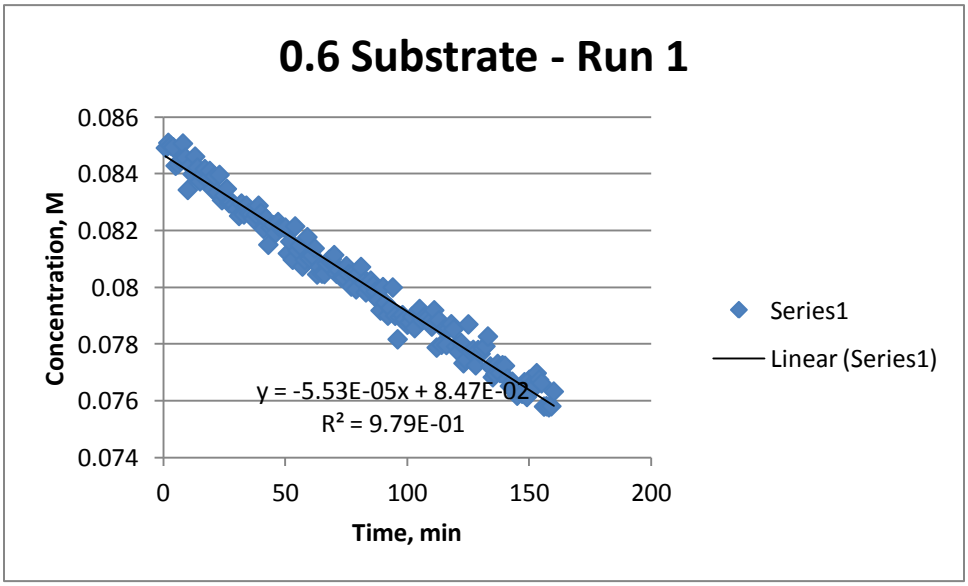
[**101**] = 0.085 M

[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	13257.5	12996.8	0.084921
16	13179.1	12774.6	0.083965
31	13211.7	12586.3	0.082524
46	13149.4	12435.7	0.081922
61	13228.4	12388.8	0.081126
76	13248.3	12307.1	0.08047
91	13199.4	12108.2	0.079463
106	13221.2	12033.5	0.078842
121	13163	11812	0.077733
136	13156.6	11686.5	0.076945
151	13078.4	11564.1	0.076594
166	13145.7	11512.4	0.075861
181	13173	11398.6	0.074956
196	13142	11329.9	0.07468
211	13105.6	11097.4	0.07335
226	13074.4	11109.1	0.073603



Determination of Rate for 0.6 equiv. of substrate- Run 2 [DJK-5-26-2]

Following the General Procedure, **56 (**25.5 mg, 0.1 mmol, 1.7 equiv), **101** (10.8 mg, 0.06 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.017 equiv) and MsOH (6.5 µL, 0.1 mmol, 1.7 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an

NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 5.05E-05 M/min

[**101**] = 0.085 M

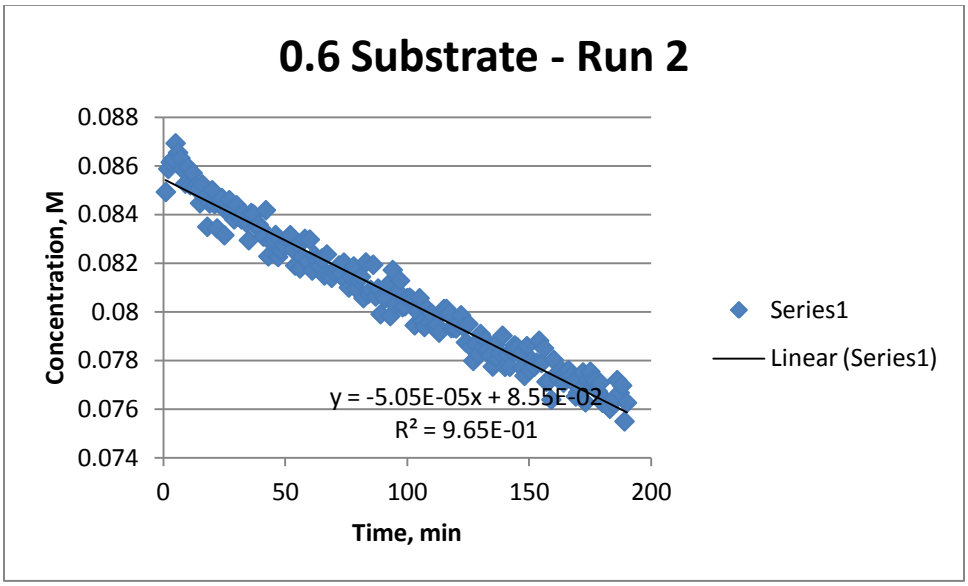
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	11883.6	12266.3	0.084921
16	11937.4	12366.8	0.085231
31	11926.4	12172.7	0.08397
46	11792.9	11919.2	0.083152
61	11841.9	11758.3	0.08169
76	11984.6	11798.1	0.080991
91	11768.8	11521.6	0.080543
106	11987.7	11600.6	0.079615
121	11774.5	11380.8	0.07952
136	11738.5	11220.4	0.07864
151	11780.7	11168.9	0.077999
166	11778.4	11109.4	0.077598
181	11813.1	10967.1	0.076379
196	11827.6	10720.7	0.074572
211	11782.3	10807.9	0.075467
226	11745.1	10505	0.073585
241	11694.9	10509.6	0.073933
256	11733.1	10320	0.072363
271	11677.2	10371.6	0.073073
286	11805.3	10175.3	0.070912
301	11815.1	10109.7	0.070396
316	11668.2	10047	0.07084
331	11652.6	9793.79	0.069147
346	11739.6	9817.01	0.068798
361	11818.6	9856.03	0.068609
376	11657.3	9648.64	0.068095
391	11692.5	9552.7	0.067215
406	11714.4	9670.85	0.067919
421	11726.2	9443.92	0.066259
436	11653.9	9323.91	0.065823
451	11731.4	9207.34	0.06457
466	11792.9	9198.6	0.064172

481	11720.4	9078.99	0.06373
496	11676.2	8937.52	0.062974
511	11720.9	8899.81	0.062469



Determination of Rate for 0.6 equiv. of substrate- Run 3 [DJK-5-26-3]

Following the General Procedure, **56 (**25.5 mg, 0.1 mmol, 1.7 equiv), **101** (10.8 mg, 0.06 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.017 equiv) and MsOH (6.5 µL, 0.1 mmol, 1.7 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 5.12E-05 M/min

[**101**] = 0.085 M

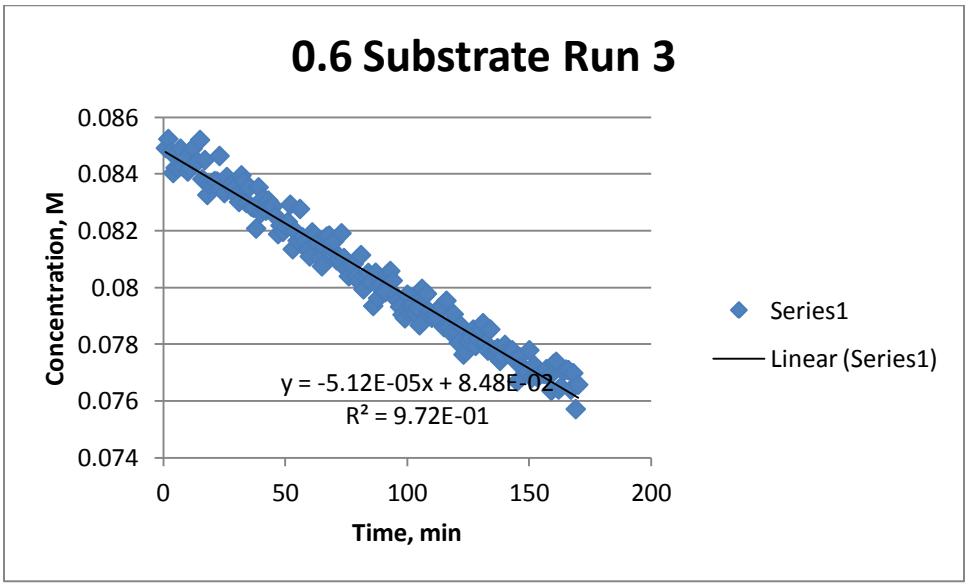
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	433.599	424.951	0.084921
16	435.414	421.24	0.083828

31	435.183	416.971	0.083023
46	432.401	411.786	0.082518
61	432.667	409.197	0.081949
76	435.503	404.114	0.080404
91	431.978	398.054	0.079844
106	428.372	395.296	0.079958
121	431.857	389.041	0.078058
136	428.547	384.8	0.077804
151	432.99	383.905	0.076826
166	432.059	384.416	0.077094
181	430.659	378.087	0.076071
196	430.673	376.276	0.075704
211	427.165	365.308	0.074101
226	430.099	369.489	0.074438
241	431.305	361.696	0.072664
256	430.016	360.771	0.072696



Determination of Rate for 2.0 equiv. of substrate- Run 1 [DJK-5-48-1]

Following the General Procedure, **56 (**25.5 mg, 0.1 mmol, 0.5 equiv), **101** (36 mg, 0.2 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.05 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.5 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.11E-04 M/min

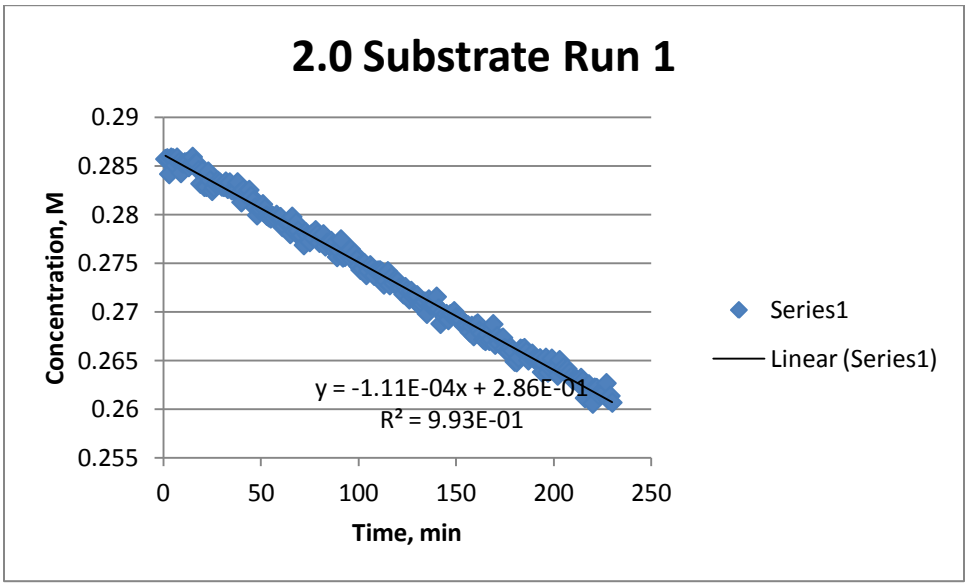
[**101**] = 0.28 M

[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	16554.9	20355.8	0.285714
16	16540.5	20302	0.285207
31	16457.9	20034.2	0.282858
46	16374.6	19828.3	0.281375
61	16434.3	19713.8	0.278734
76	16514.2	19758.2	0.27801
91	16540.2	19749.2	0.277446
106	16507.2	19520.8	0.274786
121	16457.1	19297	0.272463
136	16469.3	19227	0.271273
151	16376.4	18979.8	0.269304
166	16452.6	18953	0.267679
181	16448.4	18747.3	0.264841
196	16426.5	18753.3	0.265279
211	16341.3	18499.2	0.263049
226	16325	18387.9	0.261727
241	16398.7	18322.6	0.259626
256	16474.4	18349.2	0.258808
271	16301	18006.8	0.25668
286	16400.6	17925.6	0.253971
301	16495.5	17935.2	0.252645
316	16406.4	17787.2	0.251921
331	16371.6	17630.2	0.250228
346	16354	17542.9	0.249257
361	16353	17390.3	0.247104
376	16370.3	17321.7	0.245869
391	16288.3	17148.4	0.244635
406	16358.4	17050.3	0.242193
421	16401.4	17117.6	0.242511
436	16165	16736.8	0.240584
451	16314.2	16761.7	0.238739
466	16288.2	16564	0.236299
481	16327.1	16613	0.236434
496	16147.3	16238.8	0.233682
511	16287.4	16361.5	0.233422
526	16245.1	16178.2	0.231408



Determination of Rate for 2.0 equiv. of substrate- Run 2 [DJK-5-48-2]

Following the General Procedure, **56 (**25.5 mg, 0.1 mmol, 0.5 equiv), **101** (36 mg, 0.2 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.05 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.5 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.17E-04 M/min

[**101**] = 0.28 M

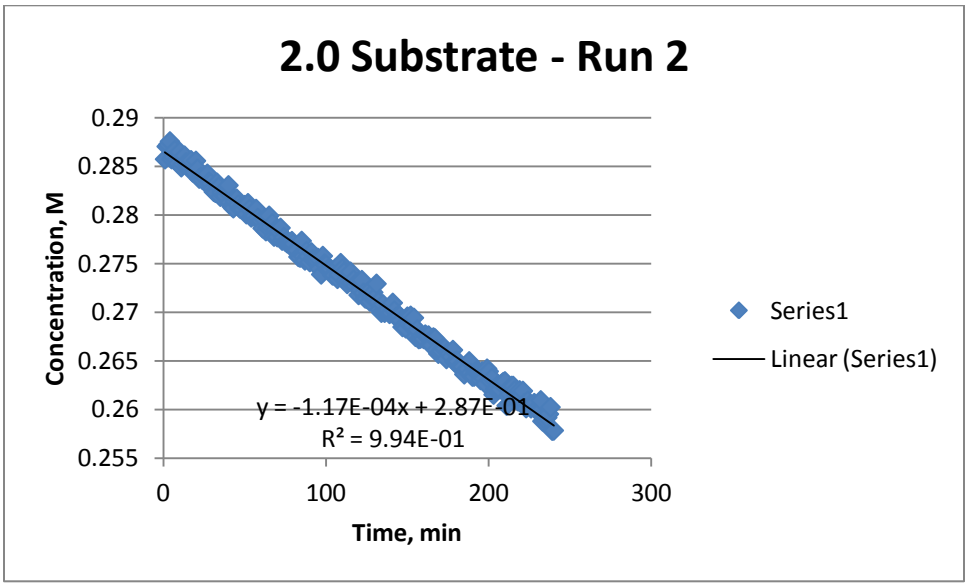
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	17650.1	20153.7	0.285714
16	17810.7	20279.4	0.284904
31	17467.1	19710.4	0.282357
46	17486.1	19639.8	0.28104
61	17727	19738.4	0.278613

76	17491	19368.8	0.277085
91	17636.7	19463	0.276132
106	17575.6	19281.6	0.274509
121	17517.7	19059.8	0.272249
136	17341.5	18707.2	0.269927
151	17749.7	19064.6	0.268758
166	17512.4	18713.5	0.267383
181	17608	18642.6	0.264924
196	17600.4	18561.9	0.263891
211	17363.4	18067.8	0.260372
226	17331.1	18015.6	0.260104



Determination of Rate for 2.0 equiv. of substrate- Run 3 [DJK-5-48-3]

Following the General Procedure, **56 (**25.5 mg, 0.1 mmol, 0.5 equiv), **101** (36 mg, 0.2 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.05 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.5 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.16E-04 M/min

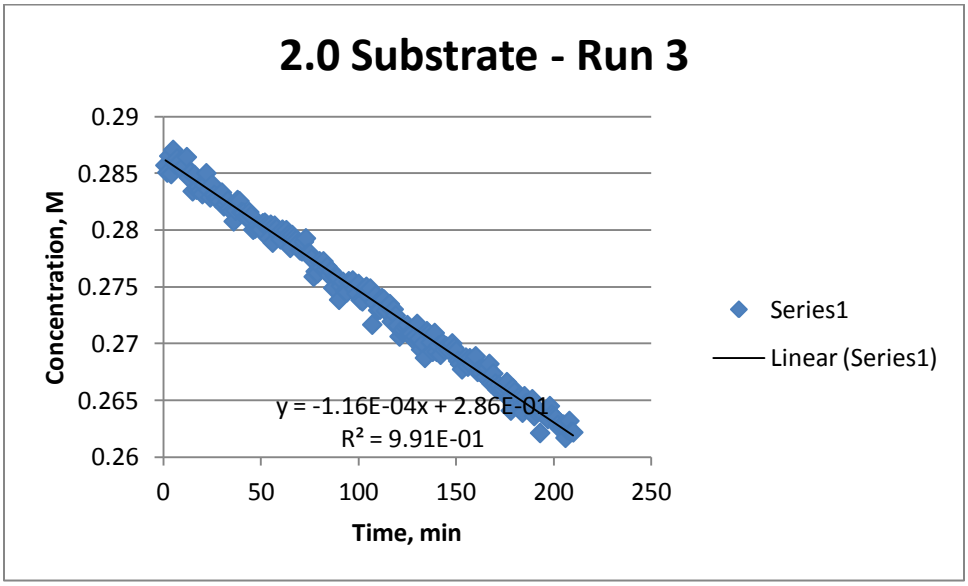
[**101**] = 0.28 M

[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	18958.3	21815.2	0.285714
16	18826.9	21599.7	0.284866
31	18669.7	21211.6	0.282103
46	18744.3	21140.8	0.280043
61	18733.9	21129.5	0.280048
76	18802.1	21011.1	0.277469
91	18671.9	20685.8	0.275078
106	18745.3	20750.6	0.274859
121	18619.1	20293.7	0.270629
136	18629.1	20323.4	0.27088
151	18575	20085.2	0.268485
166	18548.5	20007	0.267821
181	18648.1	19879.9	0.264699
196	18658	19844.6	0.264088
211	18668.9	19701.4	0.26203



Determination of Rate for 0.3 equiv. of electrophile- Run 1 [DJK-5-34-1]

Following the General Procedure, **56 (**7.6 mg, 0.03 mmol, 0.3 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an

NMR spectrometer at room 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 6.43E-05 M/min

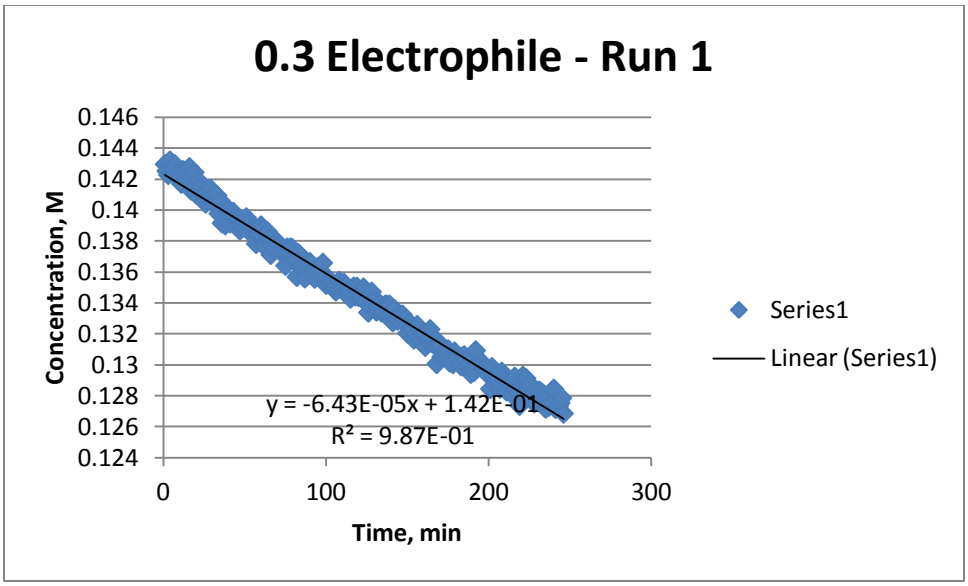
[**101**] = 0.14 M

[**56**] = 0.042 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	20577.1	22405	0.142857
16	20451.8	22223.6	0.142569
31	20632	22108.3	0.14059
46	20439.7	21790.5	0.139873
61	20543.8	21580.2	0.137821
76	20544	21498.4	0.137297
91	20513.3	21199.4	0.13559
106	20393.1	21046.7	0.135407
121	20355.9	20951.5	0.135041
136	20422.4	20810.9	0.133698
151	20516.2	20833.3	0.13323
166	20420	20483.3	0.131609
181	20357.8	20210	0.13025
196	20359.4	20316.1	0.130923
211	20345.2	19920.7	0.128465
226	20414.4	19900.7	0.127901
241	20344.7	19739.9	0.127302
256	20409.1	19867.6	0.127721



Determination of Rate for 0.3 equiv. of electrophile- Run 2 [DJK-5-34-2]

Following the General Procedure, **56 (**7.6 mg, 0.03 mmol, 0.3 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 5.30E-05 M/min

[**101**] = 0.14 M

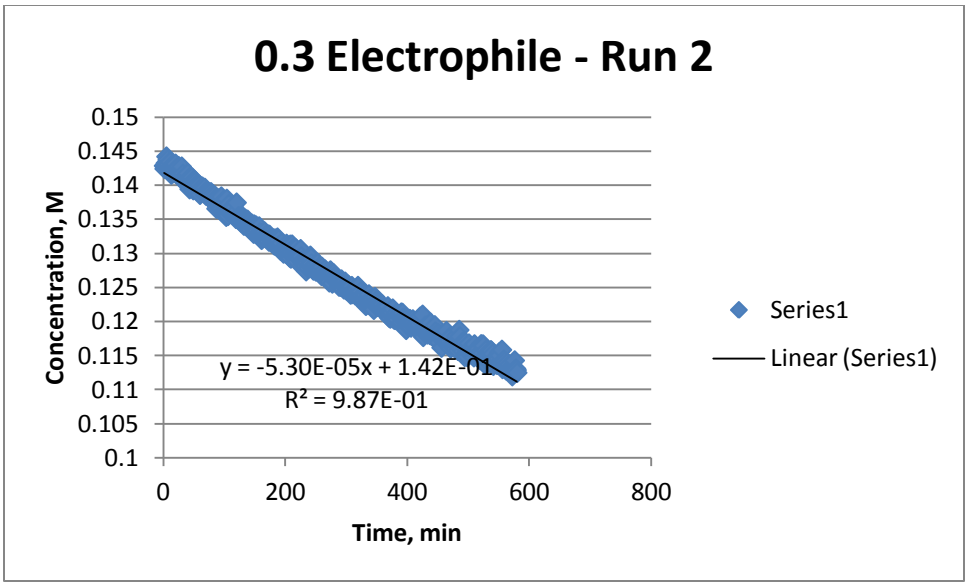
[**56**] = 0.042 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	19785.3	20881.9	0.142857
16	19979.1	21021.1	0.142414
31	19736.8	20538.7	0.140855
46	19740.7	20508.6	0.14062
61	20111.2	20733.6	0.139544
76	19575.2	19967	0.138064
91	19730.4	20124.8	0.138061

106	19575	19598.8	0.13552
121	19689.1	19646.3	0.135061
136	19554.2	19401	0.134295
151	19698.1	19378.7	0.13316
166	19784.3	19467.9	0.13319
181	19663.9	19074.8	0.1313
196	19479.9	18792.6	0.130579
211	19461.9	18875.1	0.131274
226	19626.3	18781.7	0.12953
241	19601.2	18774.1	0.129644
256	19529.4	18360.4	0.127253
271	19472.4	18230.9	0.126725
286	19574.7	18191.9	0.125793
301	19494.8	17933.2	0.124513
316	19612	18079.1	0.124776
331	19463.2	17807.1	0.123838
346	19365.8	17578.2	0.122861
361	19564.1	17590	0.121697
376	19560.8	17613	0.121877
391	19542.6	17303.7	0.119848
406	19444.6	17112.2	0.119119
421	19768.3	17625.8	0.120685
436	19343.4	16921.3	0.118406
451	19482.6	17013.4	0.1182
466	19578	16926.9	0.117026
481	19537.7	16813.5	0.116482
496	19473.3	16702.3	0.116094
511	19229.2	16365.2	0.115195
526	19414.4	16431	0.114555
541	19352.1	16226.4	0.113493
556	19312.4	16127.3	0.113032
571	19464.3	16282.7	0.11323
586	19464.2	16056.3	0.111656



Determination of Rate for 0.3 equiv. of electrophile- Run 3 [DJK-5-34-3]

Following the General Procedure, **56 (**7.6 mg, 0.03 mmol, 0.3 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 7.13E-05 M/min

[**101**] = 0.14 M

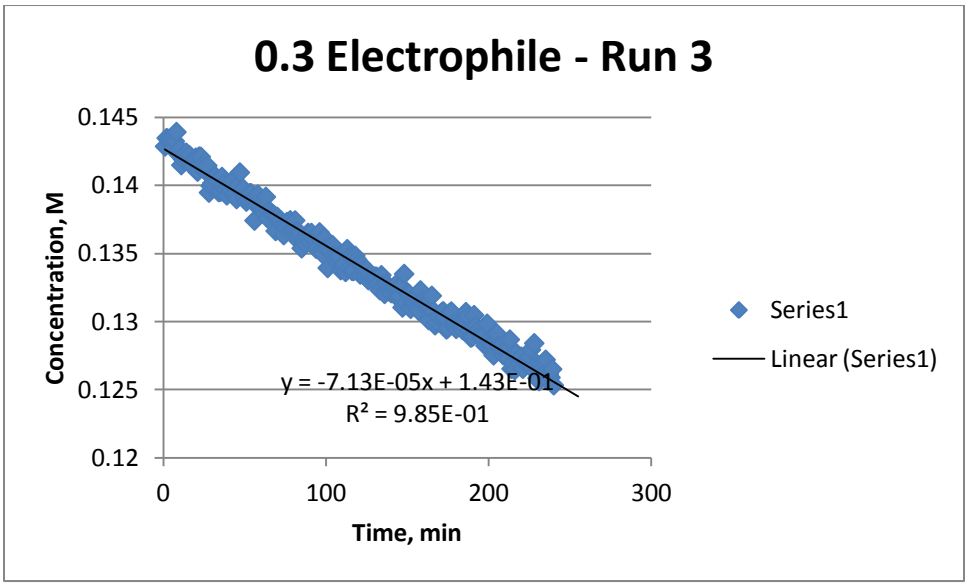
[**56**] = 0.042 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	18383.4	21323.6	0.142857
16	18718.9	21614	0.142207
31	18368.3	20982.2	0.140685
46	18225.9	20718.4	0.140002
61	18280	20513.7	0.138209
76	18383.7	20495.1	0.137304
91	18464.1	20464.6	0.136503

106	18215.4	19905.5	0.134587
121	18276.6	19804	0.133452
136	18154.6	19461.7	0.132027
151	18184.5	19492.8	0.13202
166	18134.3	19251.8	0.130749
181	18076.8	19048.7	0.129781
196	18256.7	19079.8	0.128712
211	18126.9	18818.6	0.127859
226	18231.8	18936.8	0.127922



Determination of Rate for 0.5 equiv. of electrophile- Run 1 [DJK-5-33-1]

Following the General Procedure, **56 (**12.8 mg, 0.05 mmol, 0.5 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 7.22E-05 M/min

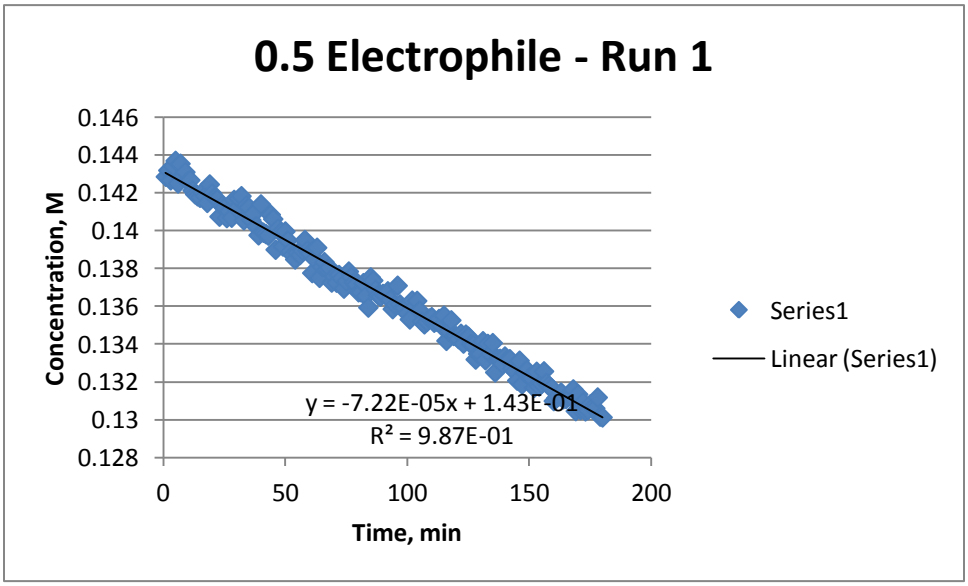
[**101**] = 0.14 M

[**56**] = 0.07 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	19863	22121.4	0.142857
16	19694.2	21807.8	0.142039
31	19638.1	21692.6	0.141692
46	19720	21369.2	0.139
61	19776.3	21240	0.137767
76	19669.1	21137	0.137846
91	19658.7	20937.7	0.136618
106	19629.3	20689.6	0.135201
121	19548	20462.8	0.134276
136	19702.6	20354	0.132514
151	19631.7	20234.2	0.132209
166	19614.1	20066.1	0.131229
181	19517.3	19777	0.12998
196	19564	19670.2	0.128969
211	19660.8	19599.7	0.127874
226	19579.3	19392.2	0.127047



Determination of Rate for 0.5 equiv. of electrophile- Run 2 [DJK-5-33-2]

Following the General Procedure, **56 (**12.8 mg, 0.05 mmol, 0.5 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an

NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 7.04E-05 M/min

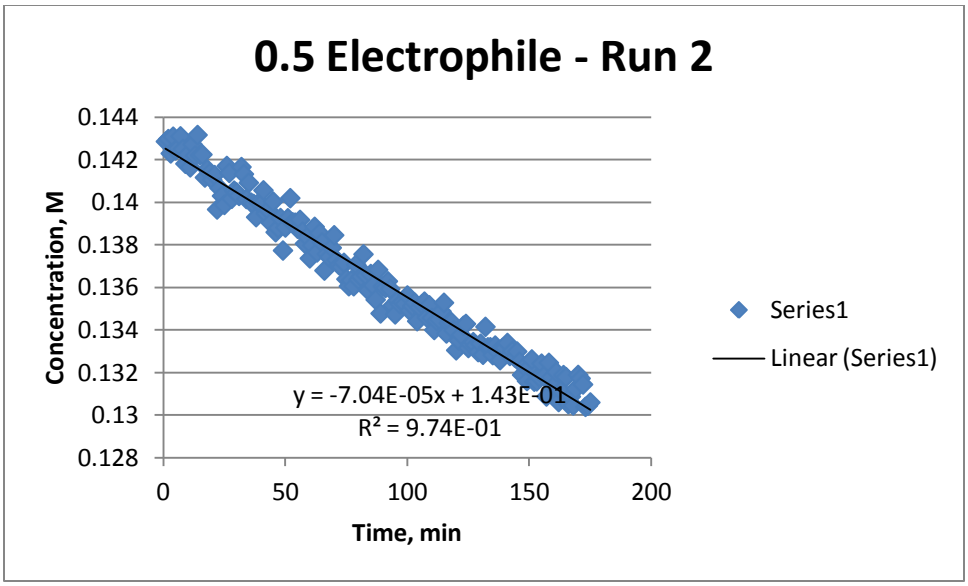
[**101**] = 0.14 M

[**56**] = 0.07 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	14342.6	16649.4	0.142857
16	14429	16677.6	0.142242
31	14233.1	16226.6	0.140301
46	14475.9	16302.7	0.138594
61	14284.6	16014.9	0.137971
76	14379.4	15897.5	0.136057
91	14306.4	15807	0.135972
106	14331.2	15745.7	0.135211
121	14135	15334.4	0.133506
136	14560.9	15768.2	0.133268
151	14344.5	15457.8	0.132615
166	14267	15130.4	0.130512
181	14311	15070.4	0.129594
196	14249.9	15026.5	0.129771
211	14415.2	15123.1	0.129107
226	14310.9	14809.4	0.127351



Determination of Rate for 0.5 equiv. of electrophile- Run 3 [DJK-5-33-3]

Following the General Procedure, **56 (**12.8 mg, 0.05 mmol, 0.5 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 7.96E-05 M/min

[**101**] = 0.14 M

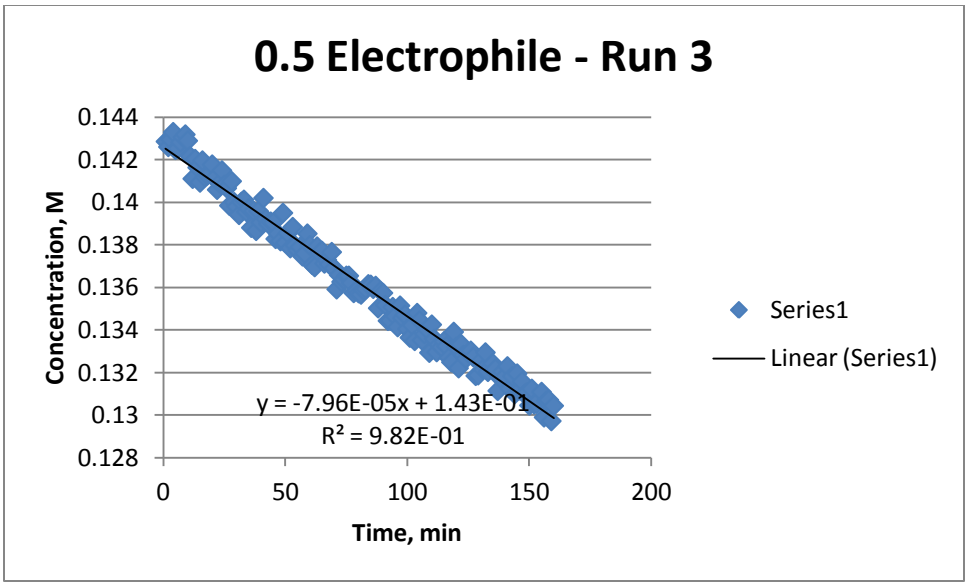
[**56**] = 0.07 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	19273.8	21606.7	0.142857
16	19354.2	21560.9	0.141962
31	19389.8	21212.1	0.139409
46	19292.2	20934.5	0.138281
61	19268	20723.8	0.137061
76	19325.1	20707.1	0.136546
91	19371	20546.9	0.135168

106	19396.8	20322.6	0.133515
121	19209.8	19929	0.132204
136	19406	20127.3	0.132169
151	19308.1	19883.8	0.131232
166	19370.7	19707.7	0.12965
181	19349.4	19570.2	0.128887
196	19360.8	19365.4	0.127463
211	19419.5	19327.3	0.126828
226	19278.3	19007.6	0.125643
241	19300.5	18797.4	0.124111
256	19361.4	18680.5	0.122951
271	19309.9	18604.3	0.122776
286	19438.2	18533.8	0.121504
301	19394.1	18343.2	0.120528
316	19490.1	18350.5	0.119982
331	19324.3	17978.6	0.118559
346	19505.9	18070.1	0.118053
361	19626.9	18119.3	0.117644
376	19391.7	17794.7	0.116938
391	19310	17575.7	0.115988
406	19409.3	17413.9	0.114332
421	19220.2	17137.2	0.113622
436	19402.5	17179.4	0.112832
451	19488.2	17041.4	0.111433
466	19364.1	16986.4	0.111785
481	19374.3	16748.6	0.110162
496	19489.2	16868.8	0.110299
511	19418.1	16610	0.109004
526	19258.9	16362.5	0.108268
541	19534.6	16388.8	0.106911
556	19399.4	16224.9	0.10658
571	19506.6	16159.8	0.105569
586	19447.8	16063.4	0.105256



Determination of Rate for 1.8 equiv. of electrophile- Run 1 [DJK-5-27-1]

Following the General Procedure, **56 (**46 mg, 0.18 mmol, 1.8 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 7.78E-05 M/min

[**101**] = 0.14 M

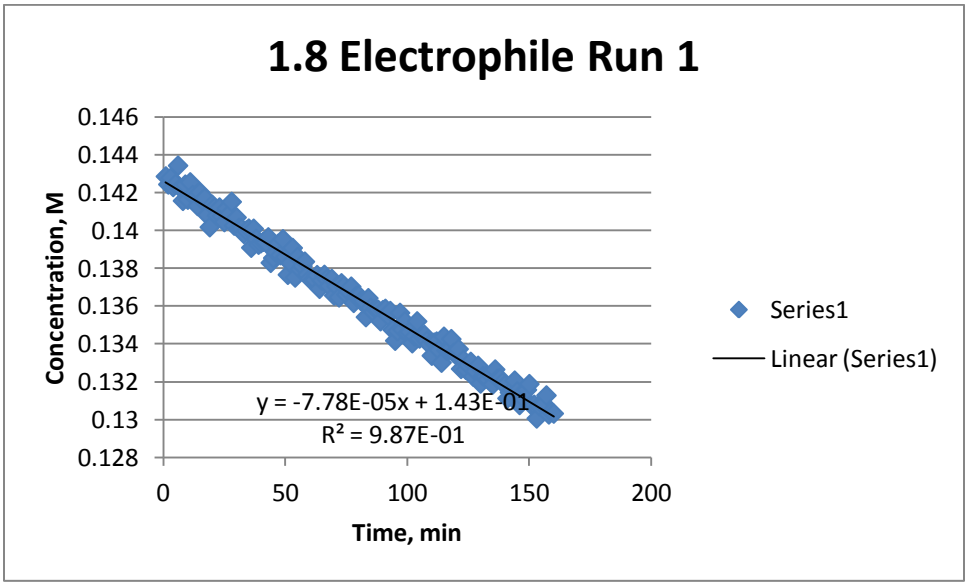
[**56**] = 0.26 M

[**MsOH**] = 0.14

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	19445.7	23603.9	0.142857
16	19345	23274.1	0.141594
31	19170.7	22827.2	0.140138
46	19251	22710.5	0.13884
61	19235.8	22450.1	0.137357
76	19221.2	22338.7	0.136779
91	19294.7	22273.1	0.135858

106	19341	22090.1	0.134419
121	19151.3	21761.4	0.13373
136	19289	21740.5	0.132648
151	19271.5	21409.8	0.130749
166	19244.8	21240.1	0.129893
181	19209.2	21038.2	0.128896
196	19198.3	20800.3	0.127511
211	19261.9	20837.3	0.127316
226	19106.8	20503	0.126291
241	19208.5	20343.1	0.124642
256	19147	20268	0.124581
271	19152.1	19971.5	0.122726
286	19121.1	19808.5	0.121922
301	19033.1	19598	0.121184
316	19150.4	19615.9	0.120551
331	19267.4	19579.5	0.119597
346	19302.5	19299.4	0.117672
361	19186.2	19142	0.117419
376	19038.1	18842.2	0.11648
391	19110	18882.8	0.116291
406	19128.4	18684.9	0.114962
421	19080.5	18483.1	0.114006
436	19082.7	18476.7	0.113953
451	19185.2	18215.7	0.111743
466	19106.6	18047.3	0.111166
481	19092.3	17859.6	0.110092
496	19068.8	17650.1	0.108935
511	19157.6	17674	0.108576



Determination of Rate for 1.8 equiv. of electrophile- Run 2 [DJK-5-27-2]

Following the General Procedure, **56 (**46 mg, 0.18 mmol, 1.8 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.1 equiv) and MsOH (6.5 μL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^oC. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 7.92E-05 M/min

[**101**] = 0.14 M

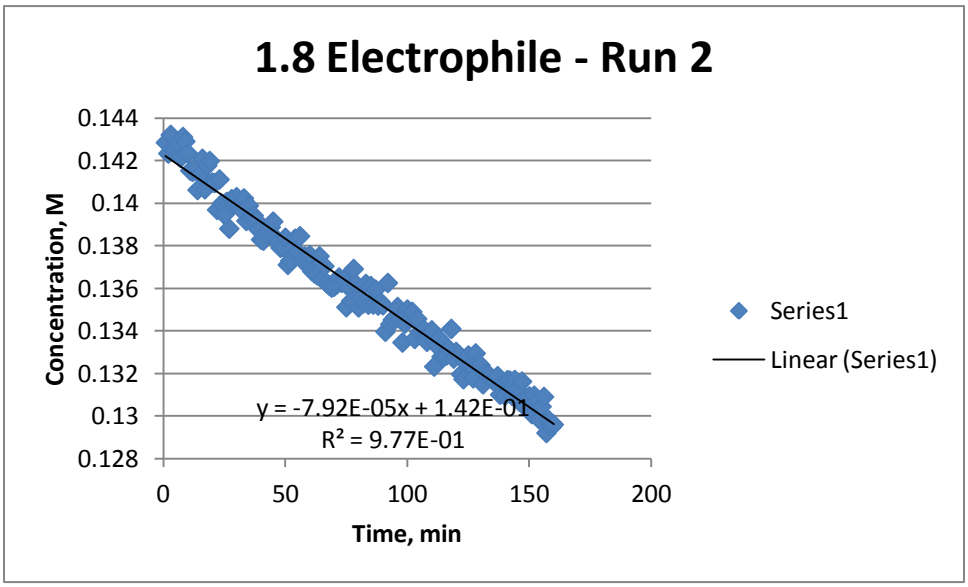
[**56**] = 0.26 M

[**MsOH**] = 0.14

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	18351.5	21274	0.142857
16	18046.1	20808.6	0.142097
31	17982.8	20414.2	0.139894
46	18299.6	20546.5	0.138363
61	18111	20105.8	0.136805
76	18304.6	20209.6	0.136057
91	18119.8	19698.1	0.133966
106	18062	19634.9	0.133964
121	17999.1	19408.3	0.13288
136	18032.2	19258.5	0.131613
151	17809.2	18801.6	0.130099
166	17846.6	18862.8	0.130249
181	17844.9	18648.2	0.12878
196	18347.4	18822.8	0.126425
211	17749.9	18153.3	0.126033
226	18137.2	18365.5	0.124783
241	18035.4	18108.9	0.123734
256	17961.2	18050.3	0.123844
271	18068.2	17841.5	0.121686
286	18086.6	17762.2	0.121022
301	18075.3	17531.2	0.119523
316	18043.5	17488.4	0.119441
331	17848.9	17181.3	0.118623
346	18224.1	17332.1	0.117201

361	18116	17047	0.11596
376	17977.5	16740.2	0.114751
391	17911.1	16587.7	0.114127
406	18222.2	16703	0.112958
421	17929	16392.4	0.112671
436	18214.3	16340.3	0.110553
451	18108	16204.8	0.11028
466	17854.9	15812.3	0.109134
481	17968.3	15925.2	0.10922
496	18020.7	15669.4	0.107153
511	18104.5	15681.8	0.106742
526	17814.7	15283.4	0.105722



Determination of Rate for 1.8 equiv. of electrophile- Run 3 [DJK-5-27-3]

Following the General Procedure, **56 (**46 mg, 0.18 mmol, 1.8 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 8.21E-05 M/min

[**101**] = 0.14 M

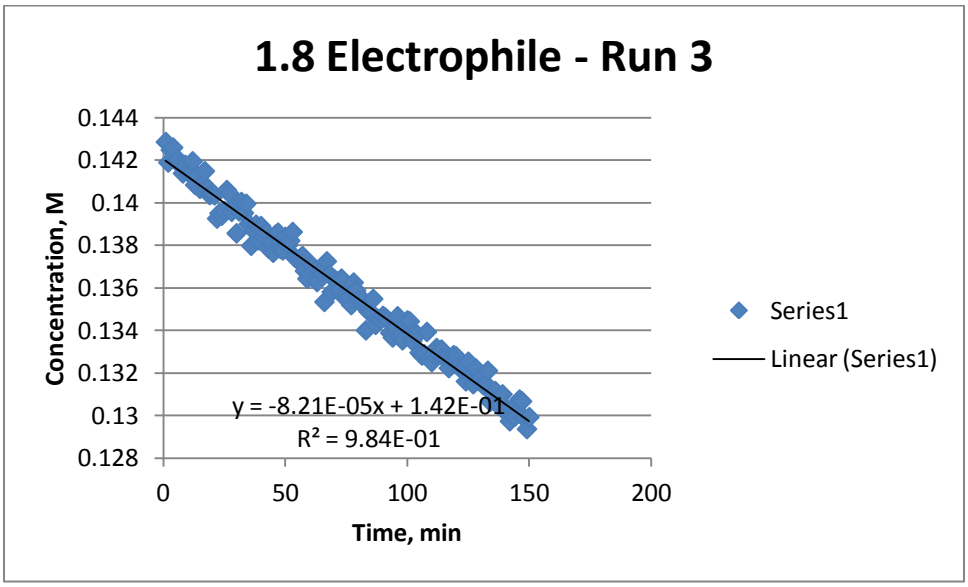
[**56**] = 0.26 M

[**MsOH**] = 0.14

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	17815.6	21628.9	0.142857
16	17686.6	21177.4	0.140895
31	17868.8	21198.9	0.1396
46	17670.5	20799.4	0.138506
61	17697.8	20610.7	0.137038
76	17709.2	20398.1	0.135537
91	17663.4	20205.7	0.134607
106	17692.1	19970.3	0.132823
121	17664.5	19861.2	0.132304
136	17607.6	19625.5	0.131156
151	17682.2	19444.5	0.129398
166	17689.6	19226	0.127891
181	17691.5	19179.7	0.127569
196	17753.5	19036.1	0.126172
211	17692.8	18787.1	0.124949
226	17594.1	18559	0.124124
241	17636.4	18347.2	0.122413
256	17567.6	18266.7	0.122353
271	17618.3	18050.1	0.120555
286	17580.2	17895.3	0.11978
301	17677.3	17760.1	0.118222
316	17511.9	17619.1	0.118391
331	17495.9	17456.9	0.117408
346	17462.1	17192.2	0.115852
361	17608.3	17109.6	0.114338
376	17494.4	16867	0.113451
391	17689.4	16759.6	0.111486
406	17584.3	16497.7	0.110399
421	17521.9	16495.3	0.110776
436	17479.9	16270.6	0.10953
451	17596.9	16243.8	0.108622
466	17512.8	16011.8	0.107585
481	17542.4	15880	0.10652
496	17552.4	15790.4	0.105858
511	17575.3	15721.3	0.105258
526	17498.5	15485	0.104131
541	17523.2	15280.2	0.102609
556	17582.9	15194.3	0.101685
571	17526.4	15045	0.101011

586	17561	14997.6	0.100494



Determination of Rate for 3.0 equiv. of electrophile- Run 1 [DJK-5-29-1]

Following the General Procedure, **56** (76.6 mg, 0.3 mmol, 3.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.1 equiv) and MsOH (6.5 μL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 8.26E-05 M/min

[**101**] = 0.14 M

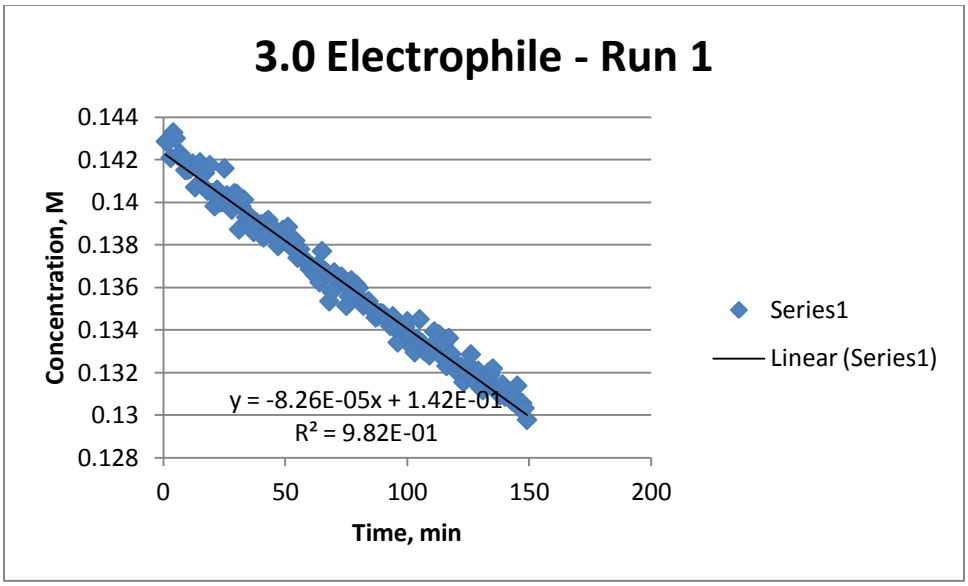
[**56**] = 0.42 M

[**MsOH**] = 0.14

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	18605.1	19509.4	0.142857
16	18481.4	19098	0.140781
31	18469.7	18806.8	0.138722

46	18214.1	18483.7	0.138252
61	18402.3	18501.9	0.136973
76	18297.8	18209.1	0.135575
91	18469.4	18241.6	0.134555
106	18456	18069.8	0.133385
121	18658.4	18113.4	0.132256
136	18256.8	17580.5	0.131189
151	18119.8	17385.1	0.130712
166	18346.3	17330.9	0.128695
181	18352.5	17342.9	0.128741
196	18285.1	17048.3	0.12702
211	18554.4	17153.2	0.125947
226	18933.8	17366.7	0.12496



Determination of Rate for 3.0 equiv. of electrophile- Run 2 [DJK-5-29-2]

Following the General Procedure, **56** (76.6 mg, 0.3 mmol, 3.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.1 equiv) and MsOH (6.5 μL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 8.58E-05 M/min

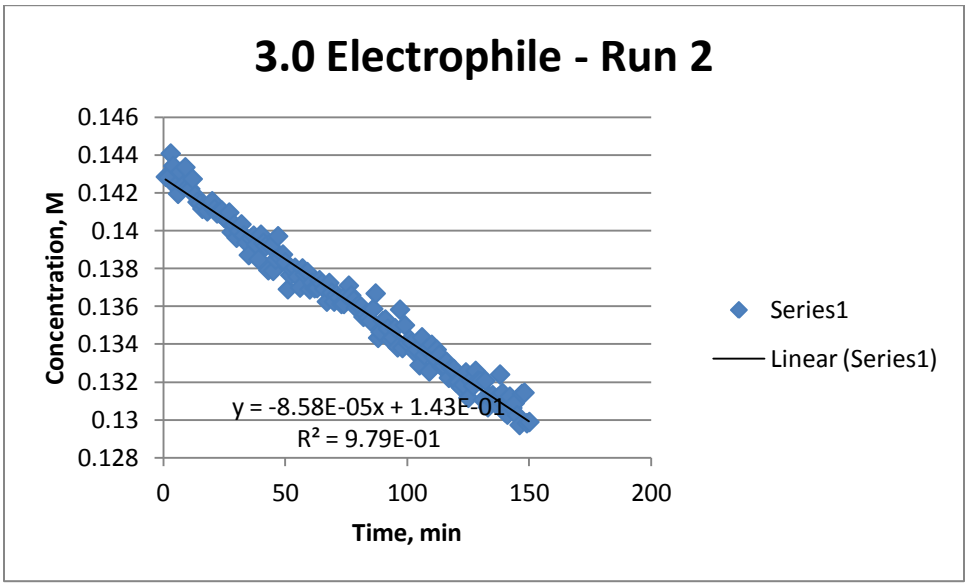
[**101**] = 0.14 M

[**56**] = 0.42 M

[**MsOH**] = 0.14

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	18060.7	19782.1	0.142857
16	18220.6	19721	0.141166
31	18231.3	19568.8	0.139994
46	18118	19237	0.138481
61	18227.7	19183	0.137262
76	18065	18989.7	0.137102
91	18247.9	18931.3	0.135311
106	18154.8	18704.1	0.134372
121	18196	18415	0.131996
136	18146	18208.8	0.130877
151	18166.6	18087.9	0.129861
166	18181.6	17910	0.128478
181	18159.7	17799.3	0.127838
196	18107.5	17562.3	0.126499
211	18277.5	17562.9	0.125327
226	18203.3	17386.2	0.124571
241	18342	17326.6	0.123206
256	18150.7	16957	0.121848
271	17924.6	16901.2	0.122979
286	18230.7	16798	0.120176
301	17946.4	16553.3	0.120302
316	18128.5	16361.9	0.117716
331	18133.1	16276.6	0.117073
346	18174.8	16042.4	0.115123
361	18080.8	15872.4	0.114496
376	18202.9	15916.8	0.114046
391	18185.2	15752.9	0.112981
406	18199.1	15672.6	0.11232
421	18085.6	15437.5	0.111329
436	18135.4	15366	0.110509
451	18073.3	15116.1	0.109085
466	18185.1	15063.3	0.108036
481	18164.4	15020.9	0.107855
496	18116.7	14784.5	0.106437
511	18296.9	14803	0.10552
526	18093.7	14567.5	0.105008
541	18122	14456.7	0.104046
556	18149.8	14315	0.102869
571	18155.3	14187.3	0.10192



Determination of Rate for 3.0 equiv. of electrophile- Run 3 [DJK-5-29-3]

Following the General Procedure, **56** (76.6 mg, 0.3 mmol, 3.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.01 mmol, 0.1 equiv) and MsOH (6.5 μL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 8.06E-05 M/min

[**101**] = 0.14 M

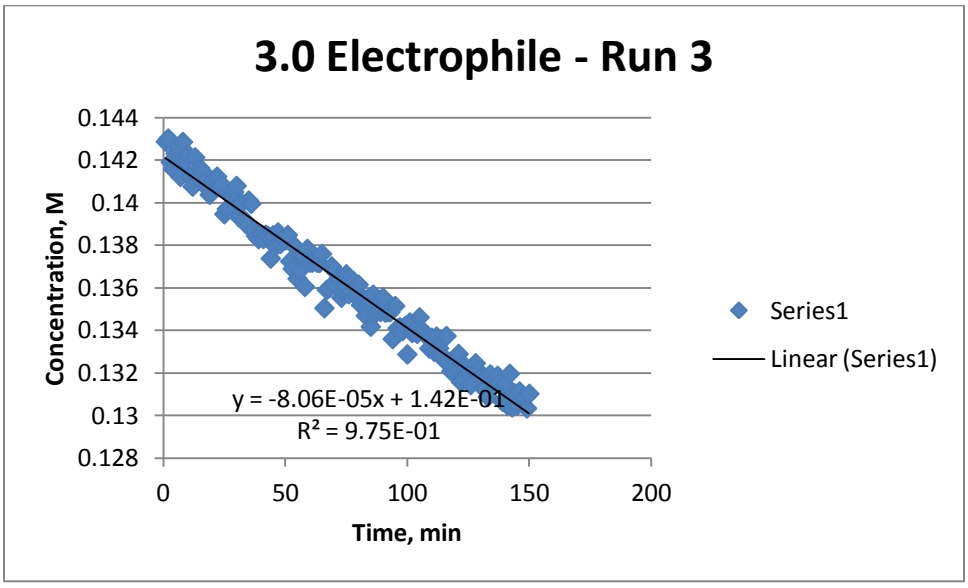
[**56**] = 0.42 M

[**MsOH**] = 0.14

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	15007.5	19915.5	0.142857
16	14861.2	19527.9	0.141456
31	14996.9	19408.1	0.139316
46	14946.9	19151.8	0.137936
61	15053.5	19182.7	0.13718

76	15028.8	18944.2	0.135697
91	15085.7	18894	0.134827
106	14882.2	18526	0.134009
121	14957.2	18463	0.132884
136	15164.9	18517.1	0.131448
151	14971.4	18077.5	0.129986
166	14924.6	17946.9	0.129451
181	15064.5	17890	0.127842
196	14894.8	17619.6	0.127345
211	14877.1	17446.3	0.126242
226	14952.4	17519.6	0.126134



Determination of Rate for 0.03 equiv. of catalyst- Run 1 [DJK-5-43-1]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (1.4 mg, 0.01 mmol, 0.03 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 2.04E-05 M/min

[**101**] = 0.14 M

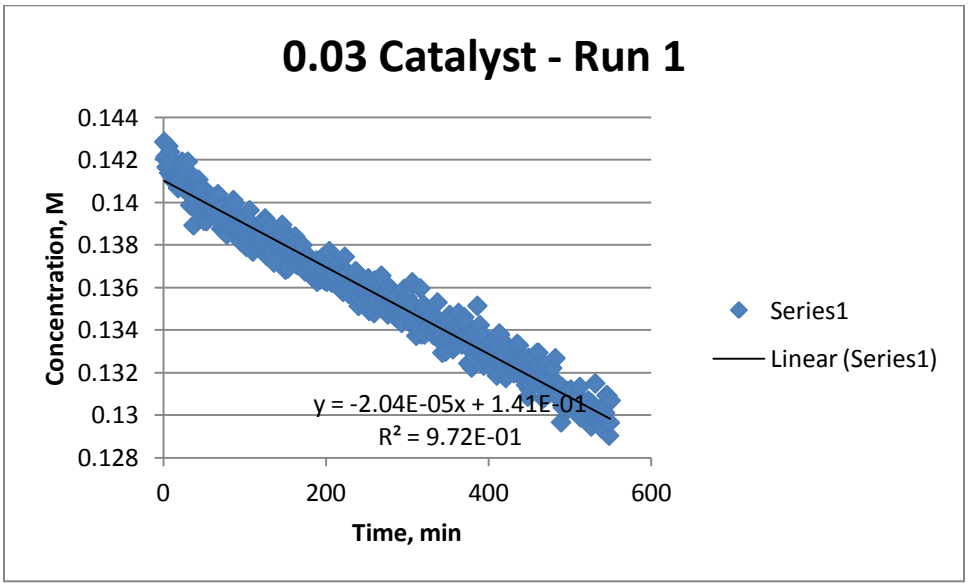
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	17522.5	21089.3	0.142857
16	17528.6	20860.1	0.141255
31	17485.9	20686.1	0.140419
46	17471.3	20553.7	0.139637
61	17302.8	20444.8	0.14025
76	17523	20524.4	0.139027
91	17461	20486.3	0.139261
106	17420.1	20493.7	0.139639
121	17457.3	20301.2	0.138032
136	17513.5	20240.9	0.137181
151	17435.2	20236.9	0.137769
166	17428.5	20172.5	0.137384
181	17536.4	20242.8	0.137014
196	17446.1	20202.1	0.137447
211	17408.1	20027.9	0.136559
226	17517.4	20167.6	0.136653
241	17559	20046.9	0.135514
256	17455.2	19974.5	0.135827
271	17412.3	19880.4	0.13552
286	17398	19809.4	0.135147
301	17384.3	19807.3	0.13524
316	17544.2	20097.1	0.135968
331	17261.2	19577.6	0.134625
346	17398.7	19573.3	0.133531
361	17359	19494.2	0.133296
376	17365.8	19476.8	0.133125
391	17312.2	19426.7	0.133193
406	17399.9	19466.2	0.132792
421	17394.5	19308.6	0.131757
436	17592.8	19664.7	0.132675
451	17368.7	19232.6	0.131434
466	17341.2	19196	0.131392
481	17401.4	19275.9	0.131482
496	17303.1	19046.4	0.130655
511	17394	19176.1	0.130857
526	17436.8	19021.2	0.129481
541	17381.2	19043.2	0.130046
556	17423.9	19177.7	0.130643
571	17287	18943.4	0.130069
586	17435.9	18942.8	0.128954
601	17394.7	18873.8	0.128789

616	17433.7	18937	0.128931
631	17221.3	18648.2	0.128531
646	17326.4	18676.5	0.127945
661	17379.6	18652	0.127386
676	17295.7	18562.9	0.127392
691	17351.2	18521.6	0.126702



Determination of Rate for 0.03 equiv. of catalyst- Run 2 [DJK-5-43-2]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (1.4 mg, 0.01 mmol, 0.03 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 2.04E-05 M/min

[**101**] = 0.14 M

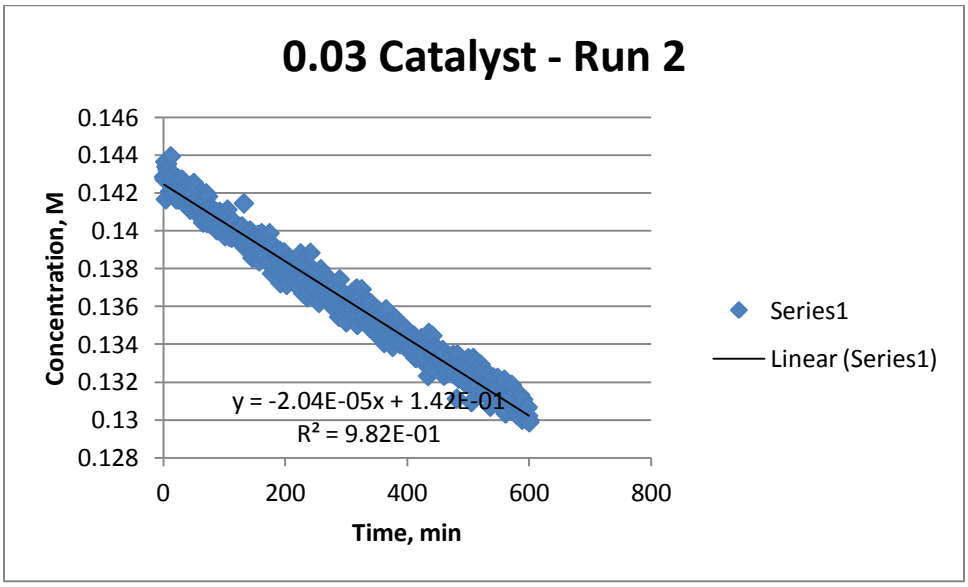
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	17393.3	22103.9	0.142857
16	17243.3	21780.9	0.141994
31	17193.1	21824.6	0.142694
46	17144.9	21593.9	0.141583
61	17234.6	21665.1	0.141311
76	17396.6	21872.6	0.141335
91	17227.9	21528.1	0.140472
106	17156.6	21483.6	0.140764
121	17218.2	21403	0.139734
136	17135.6	21244.4	0.139367
151	17518.2	21693.1	0.139203
166	17415.3	21499.6	0.138776
181	17310.6	21260.3	0.138061
196	17205.2	21151.6	0.138197
211	17159.5	21066.2	0.138006
226	17355.9	21319.4	0.138084
241	16978.9	20970.3	0.138839
256	17161.6	20949.5	0.137224
271	17134.5	20933.6	0.137337
286	17216.5	20872	0.136281
301	17008.4	20597.3	0.136133
316	17146.1	20787.7	0.136288
331	17325.3	20931.2	0.135809
346	17160.2	20577.8	0.134801
361	17222.5	20693.2	0.135066
376	17225.4	20513.5	0.133871
391	17059.1	20369.4	0.134226
406	17110	20422.2	0.134174
421	17159.3	20394.3	0.133605
436	17260.3	20520.5	0.133646
451	17097.4	20293.6	0.133427
466	17040.8	20117.3	0.132707
481	17208.6	20074	0.13113
496	17157.6	20161.1	0.132091
511	17088.8	20029.1	0.131754
526	17087.6	19975	0.131408
541	17069.7	20082.7	0.132255
556	17115.9	19968.7	0.131149
571	17051.4	20002.1	0.131865
586	17090.9	19791.1	0.130173
601	17079.4	19705.9	0.1297
616	17106.5	19782.3	0.129996

631	17105.5	19834.4	0.130346
646	17074.1	19696.1	0.129675
661	17049	19620.2	0.129366
676	17150.3	19529	0.128004
691	17102.2	19563.7	0.128592
706	17021.9	19346	0.127761
721	17159.1	19563.6	0.128165
736	17062.2	19442.7	0.128096
751	17035.5	19304.3	0.127384
766	17158.1	19408.4	0.127156
781	17183.3	19371.8	0.12673
796	17076.6	19349.6	0.127375
811	17155.4	19450.2	0.12745
826	16876.6	19015	0.126656
841	17038.9	19098.8	0.126003
856	16942.4	18891.4	0.125344



Determination of Rate for 0.03 equiv. of catalyst- Run 3 [DJK-5-43-3]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (1.4 mg, 0.01 mmol, 0.03 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.90E-05 M/min

[**101**] = 0.14 M

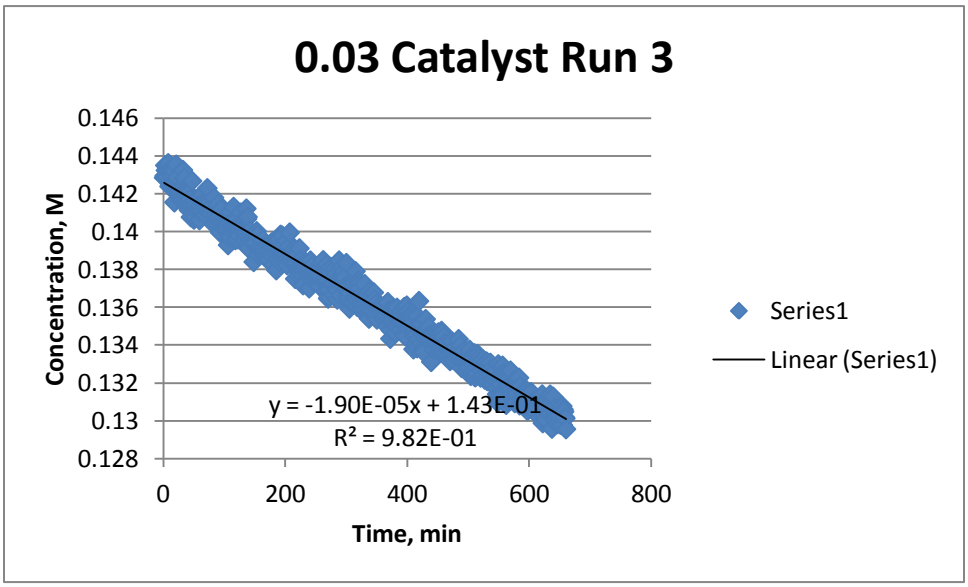
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	19753.4	22001.6	0.142857
16	19604.9	21904.2	0.143302
31	19806.4	21976	0.142309
46	19746.4	21775.8	0.141441
61	19817	21834.7	0.141318
76	19717.5	21713	0.14124
91	19704.1	21674.9	0.141088
106	19782.8	21485.5	0.139299
121	19663.9	21472.9	0.140059
136	19768.4	21766.5	0.141223
151	19790.6	21507	0.139383
166	19829.2	21471	0.138879
181	19857.8	21405.7	0.138257
196	19843.2	21530.2	0.139164
211	19645.7	21237.6	0.138652
226	19658.6	21164.1	0.138082
241	19697.5	21266.4	0.138475
256	19699	21060.6	0.137125
271	19626.4	20893.2	0.136538
286	19516	20830.6	0.136899
301	19568.1	20905.3	0.137024
316	19598.1	20850.6	0.136456
331	19594.1	20835.6	0.136386
346	19654.6	20906.7	0.13643
361	19674	20793.9	0.13556
376	19583.5	20663.5	0.135333
391	19592.4	20645.4	0.135153
406	19732.8	20776.4	0.135043
421	19566.3	20625.7	0.135204
436	19782.5	20753.5	0.134555
451	19559.3	20538.1	0.134678
466	19655.2	20490.6	0.133711
481	19688.5	20516.5	0.133653
496	19716.7	20442.7	0.132982
511	19644.9	20265.5	0.132311
526	19569.2	20269.1	0.132847

541	19634	20261.1	0.132356
556	19696.4	20411.4	0.132915
571	19568.8	20086.2	0.131651
586	19633.7	20070.2	0.131111
601	19721.9	20089	0.130647
616	19666	20084.6	0.13099
631	19531.3	19958.5	0.131065
646	19640	19881.1	0.129834
661	19543.2	19866	0.130378
676	19570.4	19791.8	0.129711
691	19594.4	19824.9	0.129768
706	19518.7	19701.9	0.129463



Determination of Rate for 0.05 equiv. of catalyst- Run 1 [DJK-5-36-1]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (2.3 mg, 0.01 mmol, 0.05 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 3.72E-05 M/min

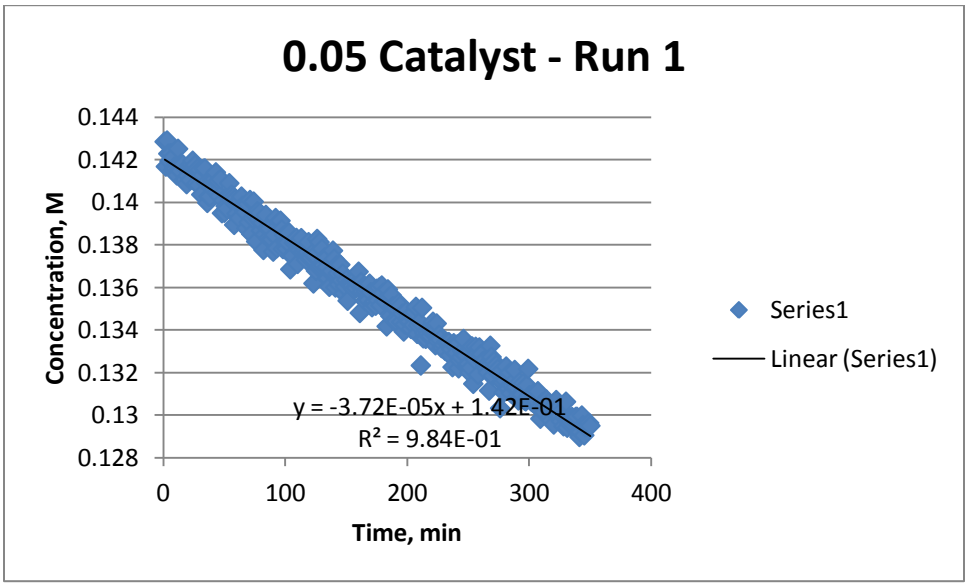
[**101**] = 0.14 M

[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	19390.9	20728.4	0.142857
16	19437.9	20621	0.141773
31	19492.6	20474.5	0.140371
46	19489.5	20460	0.140294
61	19617.2	20555	0.140028
76	19646	20311.9	0.138169
91	19335.5	20034.3	0.138469
106	19437	19998	0.137496
121	19337.5	19882.9	0.137408
136	19368.3	19716.2	0.13604
151	19414.2	19667.5	0.135383
166	19432.1	19748.2	0.135813
181	19456.2	19711.5	0.135393
196	19408.3	19572.6	0.134771
211	19623.9	19433.2	0.132341
226	19514.9	19534.7	0.133775
241	19418.7	19374	0.133332
256	19338.4	19277.2	0.133216
271	19439.6	19278	0.132528
286	19441.4	19114.3	0.131391
301	19326.5	18901.4	0.1307
316	19538.6	19092.3	0.130587
331	19405	18792	0.129418
346	19288.3	18683.6	0.12945
361	19366.2	18733.3	0.129272
376	19347	18635.9	0.128727
391	19397.3	18575.2	0.127975
406	19333.1	18440.1	0.127466
421	19327	18414.1	0.127327
436	19424	18302.2	0.125921
451	19325.3	18198.9	0.12585
466	19451.5	18246.7	0.125362
481	19501.3	18352.8	0.125769
496	19404.2	18050.2	0.124314
511	19359.6	17945.1	0.123875
526	19489.4	17914	0.122837
541	19445.8	17796.6	0.122305
556	19440.3	17886.3	0.122957
571	19382.3	17746.9	0.122363



Determination of Rate for 0.05 equiv. of catalyst- Run 2 [DJK-5-36-2]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (2.3 mg, 0.01 mmol, 0.05 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 3.72E-05 M/min

[**101**] = 0.14 M

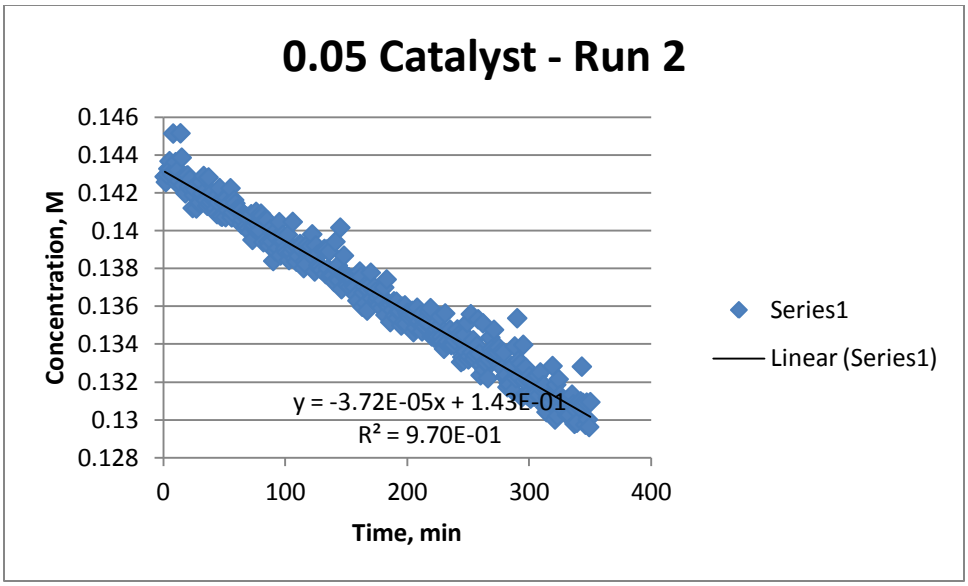
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	18509.5	20850.5	0.142857
16	18454.7	20723.3	0.142407
31	18155.6	20410.6	0.142569
46	18596.3	20860	0.142255
61	18377	20451.9	0.141136

76	18248.9	20288.8	0.140994
91	18159.4	20035.2	0.139918
106	18302.5	20271.9	0.140464
121	18558.1	20368.2	0.139187
136	18651.4	20428	0.138898
151	18330.2	19818.5	0.137115
166	18126.8	19464.1	0.136174
181	18244	19708.7	0.136999
196	18243.1	19561.2	0.135981
211	18159.2	19409.4	0.135549
226	18394.1	19569.9	0.134924
241	18245.7	19390.9	0.134778
256	18459.8	19421.4	0.133424
271	18143.2	19279.3	0.134759
286	18113.8	18968.8	0.132804
301	18151.2	18766.8	0.131119
316	18035.8	18638.8	0.131058
331	18357.6	18854.3	0.130249
346	18191.9	18611.4	0.129742
361	18122.5	18438.9	0.129032
376	17810.3	18055.2	0.128562
391	17871.2	18168.4	0.128927
406	18383.9	18781.2	0.129558
421	18377	18682.7	0.128927
436	17945.8	18128.3	0.128107
451	18062.8	18193.1	0.127733
466	18167.6	18199.8	0.127043
481	18088	17792.6	0.124747
496	18170.5	18020.7	0.125772
511	18238	17815.3	0.123879
526	18531.6	18273.8	0.125054
541	18241.7	17680.7	0.122918
556	18374.8	17858.1	0.123252
571	18051.4	17424.4	0.122413
586	18059.4	17492.4	0.122836



Determination of Rate for 0.05 equiv. of catalyst- Run 3 [DJK-5-36-3]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (2.3 mg, 0.01 mmol, 0.05 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 4.07E-05 M/min

[**101**] = 0.14 M

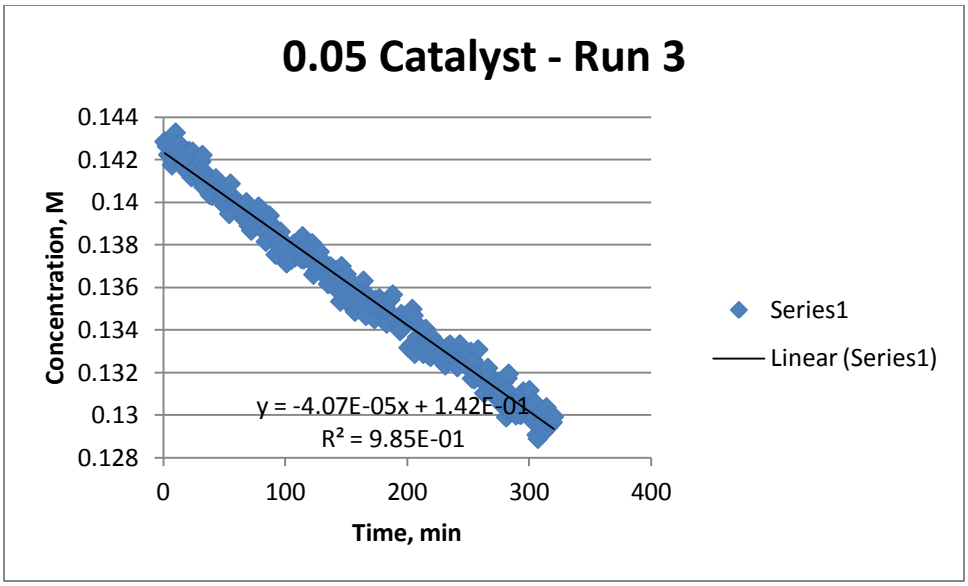
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	19009.1	20905.4	0.142857
16	18968.1	20752	0.142115
31	18936.6	20688.7	0.141918
46	18974.2	20527.1	0.14053
61	18996.8	20466.7	0.13995
76	18994.6	20398.1	0.139497
91	18910.1	20179.3	0.138617

106	18960	20098.6	0.1377
121	18960.3	20031.2	0.137236
136	18886.3	19879.4	0.136729
151	18945.8	19732.2	0.135291
166	18939.9	19635.5	0.13467
181	18766.8	19496.6	0.13495
196	18794.4	19398.4	0.134073
211	18920.9	19428.1	0.133381
226	18892.8	19365.7	0.13315
241	18893.4	19236.7	0.132259
256	18832.7	19131.5	0.13196
271	18856.3	19063.3	0.131325
286	18891.9	18955.9	0.130339
301	18795.8	18840.5	0.130208
316	18770.2	18739.9	0.129689
331	18670.4	18589.1	0.129333
346	18771.9	18621.7	0.128859
361	18641.8	18435.1	0.128458
376	18654.4	18369.1	0.127912
391	18805.6	18314.3	0.126505
406	18868.6	18269.1	0.125772
421	18860.6	18256.8	0.12574
436	18853.1	18013.3	0.124113
451	18840.3	18045	0.124415
466	18784.6	17953.8	0.124154
481	18640.5	17815.8	0.124152
496	18683.9	17687.2	0.122969
511	18709.4	17634.9	0.122439
526	18824.5	17687.1	0.12205
541	18741.3	17465	0.121053
556	18755.7	17406.4	0.120554



Determination of Rate for 0.18 equiv. of catalyst- Run 1 [DJK-5-39-1]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (8 mg, 0.018 mmol, 0.18 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.50E-04 M/min

[**101**] = 0.14 M

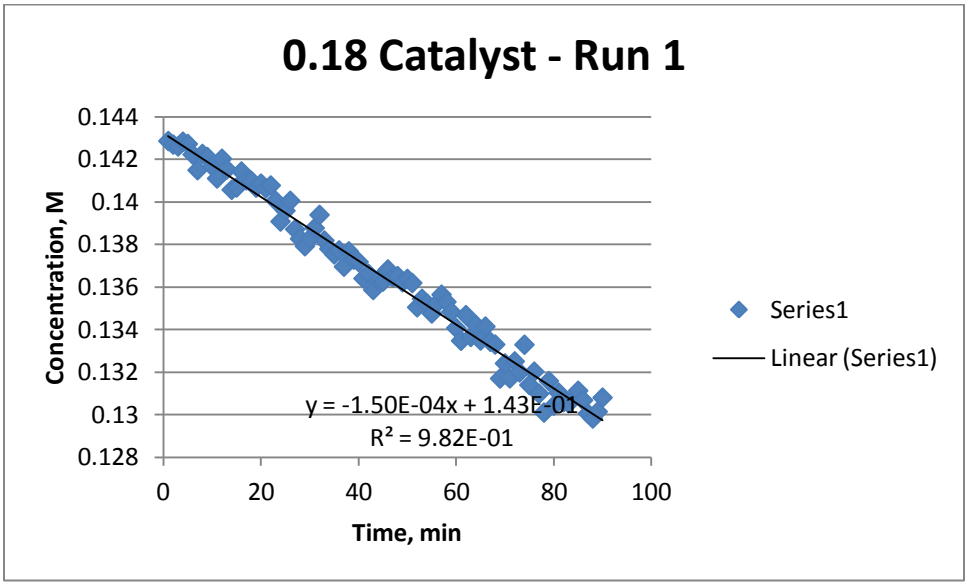
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	17696.8	21730.4	0.142857
16	17770.7	21602.1	0.141423
31	17428.9	20788.7	0.138767
46	17368.2	20425.4	0.136818
61	17420.1	19985.1	0.13347
76	17477.7	19832.9	0.132017
91	17427.9	19370.6	0.129308

106	17619.3	19101.5	0.126127
121	17327.1	18721.6	0.125703
136	17401.7	18501.1	0.12369
151	17470.6	18264.2	0.121625
166	17653.2	17984.8	0.118525



Determination of Rate for 0.18 equiv. of catalyst- Run 2 [DJK-5-39-2]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (8 mg, 0.018 mmol, 0.18 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.71E-04 M/min

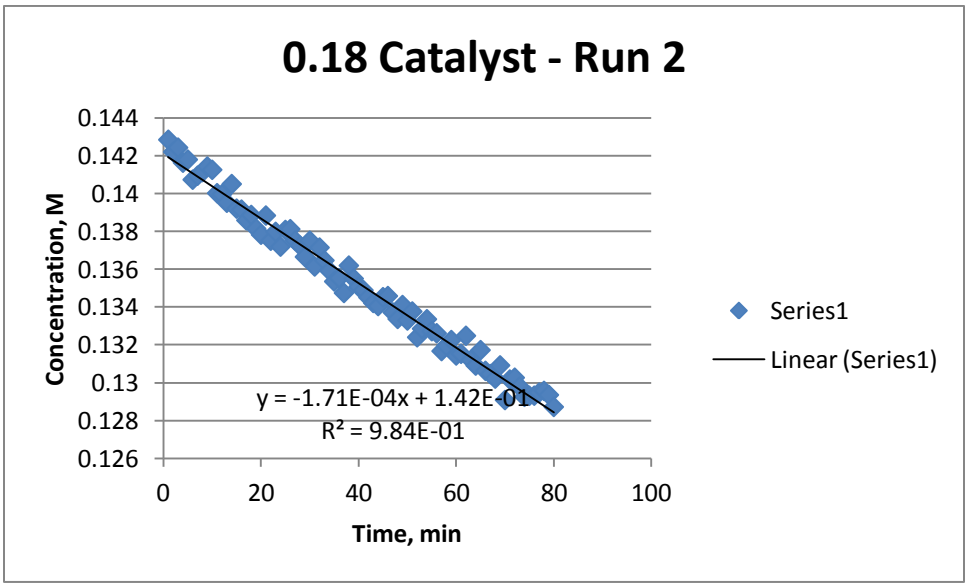
[**101**] = 0.14 M

[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	18995.9	20420.1	0.142857
16	19208.1	20114.4	0.139164
31	19001.2	19467.9	0.136158
46	18763.3	19003.4	0.134594
61	18926.6	18734.1	0.131542
76	19034.5	18523.6	0.129327
91	19190	18290.1	0.126662
106	19117.4	17887.2	0.124342
121	19141.4	17619.3	0.122326
136	19031.8	17258.9	0.120514
151	19046.8	16996.8	0.11859
166	18883.9	16532.4	0.116345



Determination of Rate for 0.18 equiv. of catalyst- Run 3 [DJK-5-39-3]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (8 mg, 0.018 mmol, 0.18 equiv) and MsOH (6.5 µL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.38E-04 M/min

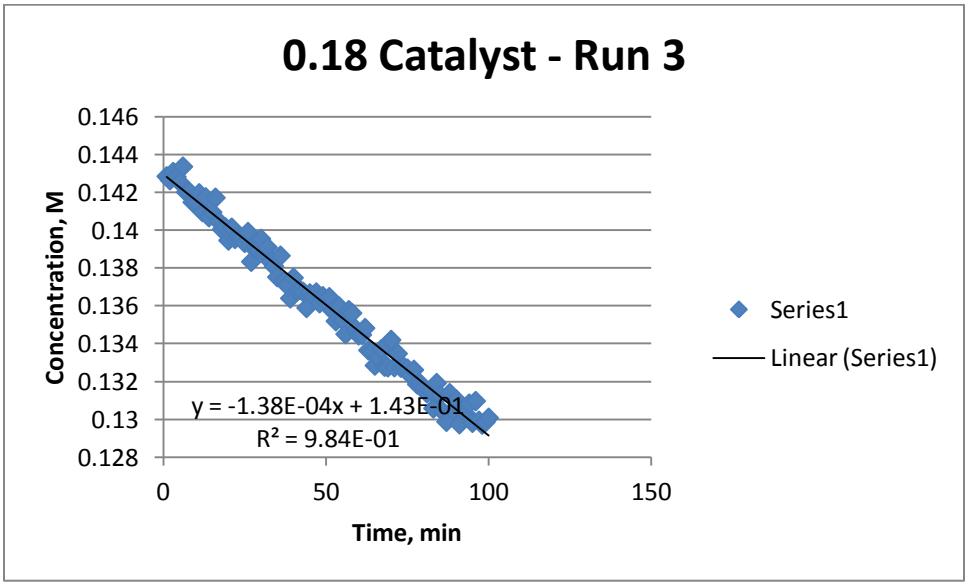
[**101**] = 0.14 M

[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	19088	22538.6	0.142857
16	18883.6	22120.5	0.141725
31	18832.2	21603.9	0.138793
46	18896.3	21325.8	0.136541
61	19203.5	21345	0.134478
76	18946	20722.8	0.132332
91	18920.7	20292.1	0.129755
106	18898.3	20000.4	0.128042
121	18888.8	19845.4	0.127113
136	18930.8	19441.4	0.124249
151	18862.1	19120.8	0.122645
166	18977.6	18983.6	0.121024



Determination of Rate for 0.3 equiv. of catalyst- Run 1 [DJK-5-79-1]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (13.2 mg, 0.3 mmol, 0.3 equiv) and MsOH (6.5 μL, 0.1 mmol, 0.1 equiv)

were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 2.05E-04 M/min

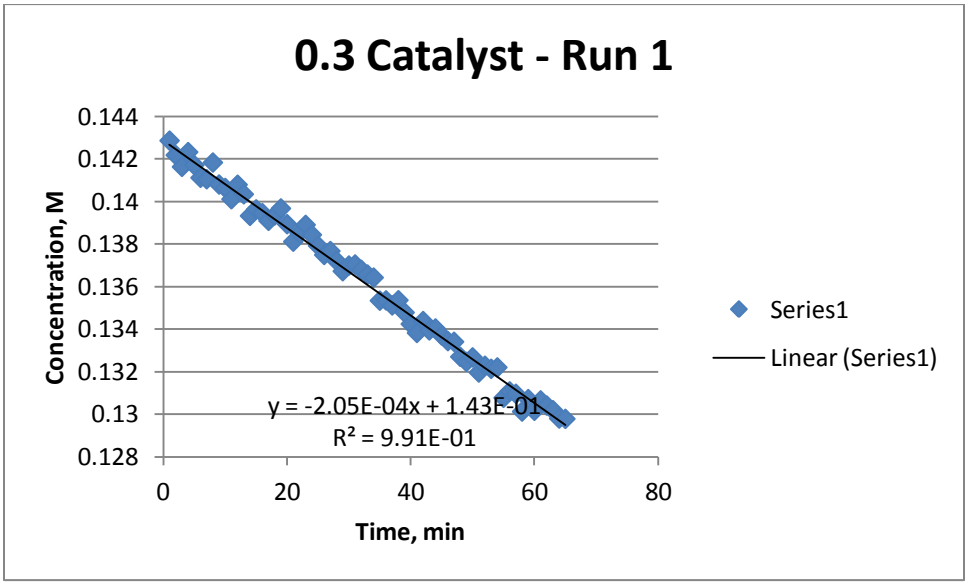
[**101**] = 0.14 M

[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	19078.3	21697.3	0.142857
16	18989.6	21081.1	0.139448
31	18886.4	20603.9	0.137036
46	18918.3	20096.3	0.133435
61	18953.1	19712.8	0.130648
76	19027.1	19317.9	0.127533
91	18856.4	18686.4	0.124481
106	18937.7	18288.2	0.121305
121	18972	17884.5	0.118413



Determination of Rate for 0.3 equiv. of catalyst- Run 2 [DJK-5-79-2]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (13.2 mg, 0.3 mmol, 0.3 equiv) and MsOH (6.5 μL, 0.1 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^oC. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 2.04E-04 M/min

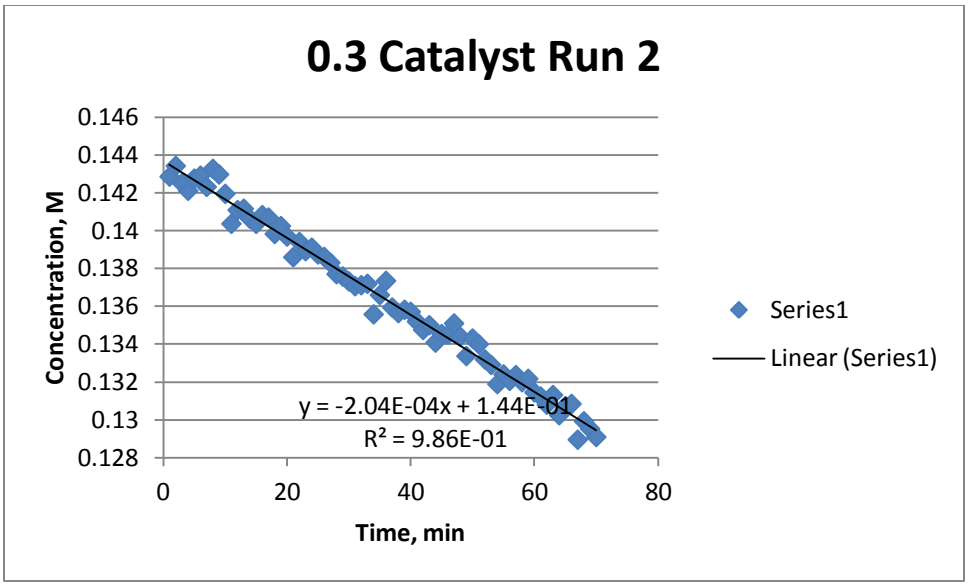
[**101**] = 0.14 M

[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	19107.6	21243.4	0.142857
16	18980.5	20801.5	0.140822
31	18989.7	20256.3	0.137065
46	18614.1	19484	0.134499
61	19040.3	19446.4	0.131235
76	18537.8	18633.6	0.129158
91	18804.9	18230.4	0.124569
106	18672.7	17882.2	0.123055



Determination of Rate for 0.3 equiv. of catalyst- Run 3 [DJK-5-79-3]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (13.2 mg, 0.3 mmol, 0.3 equiv) and MsOH (6.5 μL, 0.1 mmol, 1.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.93E-04 M/min

[**101**] = 0.14 M

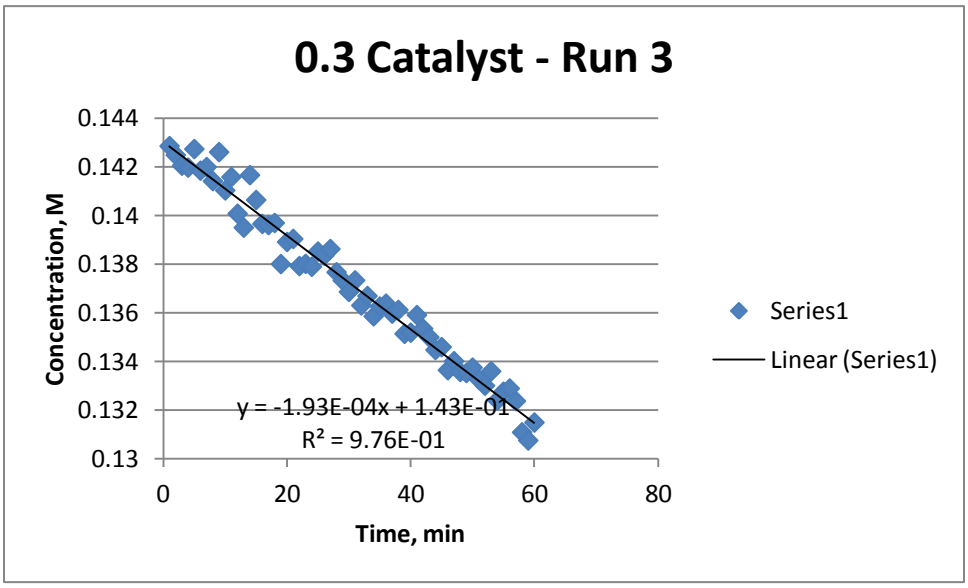
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	17635.7	20259.8	0.142857
16	17740	19923.2	0.139658
31	17606.3	19444.2	0.137335
46	17479.4	18785.1	0.133643
61	17329.6	18424.4	0.13221
76	17397.4	17884.5	0.127836
91	17494.6	17864.8	0.126985

106	17642.2	17634.6	0.1243
121	17119.8	16714.2	0.121408



Determination of Rate for 0.1 equiv. of acid - Run 1 [DJK-5-59-1]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (0.7 μL, 0.01 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 2.16E-05 M/min

[**101**] = 0.14 M

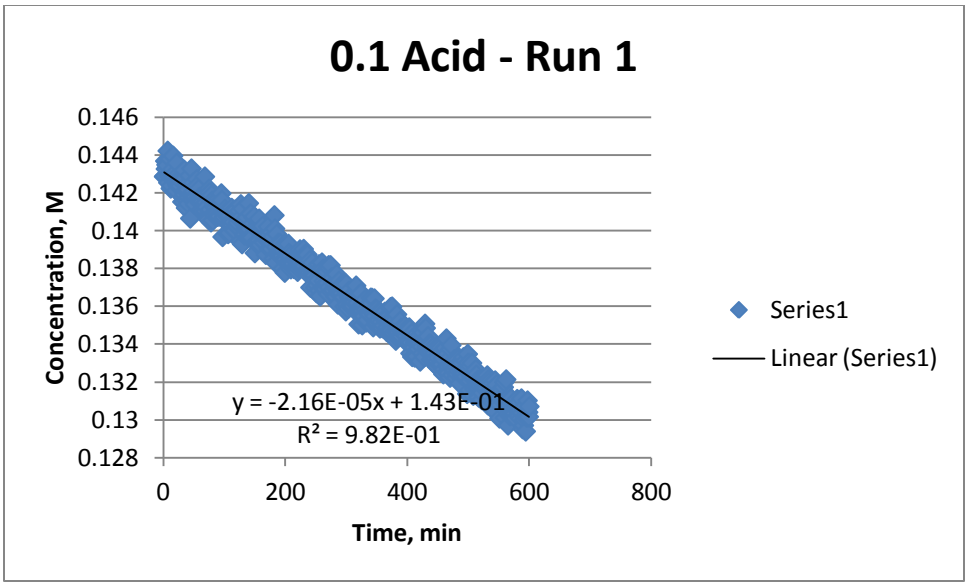
[**56**] = 0.14 M

[**MsOH**] = 0.014 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	627.378	666.39	0.142857
16	623.49	667.361	0.143957
31	627.327	660.121	0.141525

46	618.85	659.277	0.14328
61	627.972	658.727	0.141081
76	623.293	658.158	0.142017
91	621.958	655.155	0.141673
106	625.505	650.303	0.139826
121	624.075	650.722	0.140237
136	623.127	648.864	0.140049
151	621.72	647.686	0.140111
166	621.306	645.462	0.139723
181	626.197	644.926	0.138517
196	627.882	644.217	0.137993
211	621.169	638.252	0.138193
226	623.732	640.212	0.138048
241	621.689	633.261	0.136997
256	623.963	634.79	0.136828
271	615.936	632.762	0.138168
286	623.924	631.39	0.136103
301	619.433	626.694	0.13607
316	617.34	629.259	0.137091
331	620.466	629.077	0.136361
346	613.274	622.005	0.136409
361	622.464	624.745	0.134987
376	619.61	622.861	0.1352
391	618.982	618.543	0.134399
406	619.987	618.123	0.13409
421	619.418	612.943	0.133088
436	619.115	615.621	0.133735
451	621.744	616.133	0.13328
466	616.497	611.883	0.133487
481	616.854	609.047	0.132792
496	619.44	609.228	0.132277
511	621.426	608.868	0.131776
526	619.459	607.164	0.131825
541	621.997	605.456	0.130917
556	617.626	601.592	0.131002
571	617.96	598.489	0.130256
586	617.963	597.603	0.130063
601	619.541	600.27	0.13031
616	614.048	594.107	0.130126
631	616.909	592.507	0.129174
646	614.421	591.115	0.129392
661	614.28	589.645	0.1291
676	618.188	587.988	0.127924
691	614.95	585.781	0.128114
706	614.193	585.697	0.128254



Determination of Rate for 0.1 equiv. of acid - Run 2 [DJK-5-59-2]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (0.7 µL, 0.01 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.92E-05 M/min

[**101**] = 0.14 M

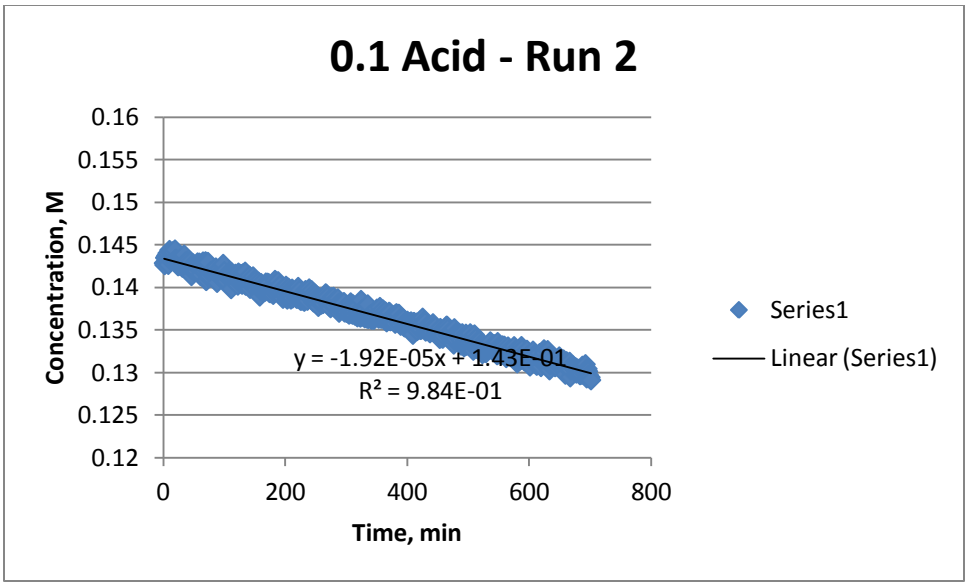
[**56**] = 0.14 M

[**MsOH**] = 0.014 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	17787.2	21886.2	0.142857
16	17983.8	22191.1	0.143264
31	18084.7	22172.2	0.142343
46	18025.4	21945.8	0.141353
61	18151.1	22097.8	0.141347
76	17879.4	21764.9	0.141333
91	17956.9	21891.1	0.141539

106	17882.3	21765.6	0.141314
121	17834.2	21693.1	0.141224
136	17645.3	21403.1	0.140827
151	17846.4	21632.3	0.140731
166	17892.2	21533	0.139727
181	17913.5	21543	0.139626
196	17885.5	21364.3	0.138684
211	17772.1	21405	0.139835
226	17845.6	21370.1	0.139032
241	17842.1	21343.2	0.138884
256	17757	21170.2	0.138419
271	17809.4	21152.2	0.137894
286	17772.5	21229.9	0.138688
301	17876.8	21185.4	0.13759
316	17751.5	21033.3	0.137566
331	17830.1	20991.1	0.136685
346	17907.1	21049	0.136473
361	17689	20817.2	0.136634
376	17800.9	20933.5	0.136533
391	17690.2	20764.9	0.136281
406	17656.6	20680	0.135982
421	17832.6	20738.9	0.135024
436	17885.8	20792.2	0.134968
451	17609.7	20474.3	0.134988
466	17730.1	20633.7	0.135115
481	17653.9	20478.2	0.134676
496	17647	20449.4	0.134539
511	17695.3	20308.5	0.133248
526	17779	20372.4	0.133037
541	17619.4	20208.4	0.133162
556	17592.8	20178.8	0.133168
571	17691.4	20113.3	0.131996
586	17678.5	20023.5	0.131502
601	17835.6	20083.8	0.130737
616	17695.4	20129.1	0.13207
631	17636.7	19976.8	0.131507
646	17513.2	19851.7	0.131605
661	17556.4	19855.4	0.131305
676	17771.9	19987.5	0.130576
691	17648	19813.3	0.130347
706	17704.3	19800.6	0.129849
721	17643.4	19725.3	0.129802



Determination of Rate for 0.1 equiv. of acid - Run 3 [DJK-5-59-3]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (0.7 µL, 0.01 mmol, 0.1 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.85E-05 M/min

[**101**] = 0.14 M

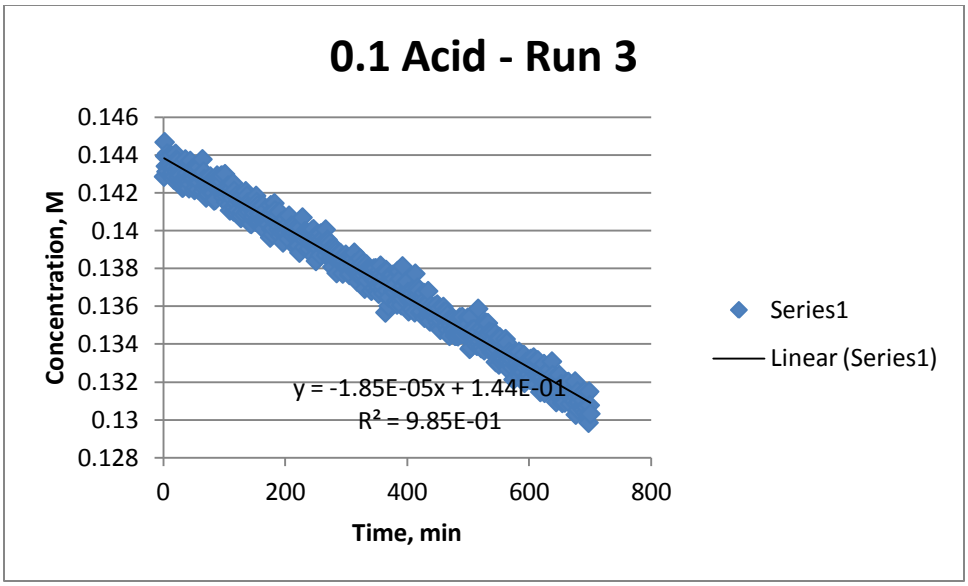
[**56**] = 0.14 M

[**MsOH**] = 0.014 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	19261.1	22082.3	0.142857
16	19156.3	21998.2	0.143092
31	19164.2	21882.2	0.142278
46	18933.3	21714.1	0.142907
61	18978.2	21775.5	0.142972
76	19082.9	21780.3	0.142219
91	18908.8	21650.4	0.142673

106	19031.6	21746.7	0.142383
121	19056.1	21545.6	0.140885
136	19059.5	21562.3	0.140969
151	19029	21452.7	0.140477
166	19019.2	21480.9	0.140734
181	18823.5	21321.9	0.141145
196	19087.3	21350.2	0.139379
211	18915.5	21235.1	0.139886
226	18882.4	21171.6	0.139712
241	19071.5	21328.2	0.13935
256	18866.8	21153.3	0.139707
271	18865.9	21027.8	0.138885
286	18827.8	20923.5	0.138476
301	18885.8	20996.1	0.138529
316	18916	20939.5	0.137935
331	19005.6	21026.4	0.137855
346	19000.8	20884.2	0.136957
361	18890.3	20721.7	0.136686
376	18922.2	20905.1	0.137664
391	18745.1	20586.2	0.136844
406	18856.6	20688	0.136708
421	18872.7	20548.8	0.135672
436	18817.6	20476	0.135587
451	18789.7	20440.3	0.135552
466	18700	20341.7	0.135545
481	18754.2	20339.3	0.135138
496	18903.1	20458.6	0.13486
511	18739.2	20224.7	0.134484
526	18733.7	20097.5	0.133677
541	18862.7	20218	0.133559
556	18865.2	20176.5	0.133267
571	18887.4	20154.6	0.132966
586	18824.8	20021.9	0.13253
601	18783	19915.8	0.132121
616	18705.6	19850.6	0.132233
631	18742	19822.7	0.131791
646	18866.8	20001.7	0.132101
661	18675.2	19728.5	0.131634
676	18856.4	19714.1	0.130274
691	18735.3	19770.4	0.13149
706	18671.2	19560.2	0.130539



Determination of Rate for 0.2 equiv. of acid - Run 1 [DJK-5-56-1]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (1.3 µL, 0.02 mmol, 0.2 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 3.87E-05 M/min

[**101**] = 0.14 M

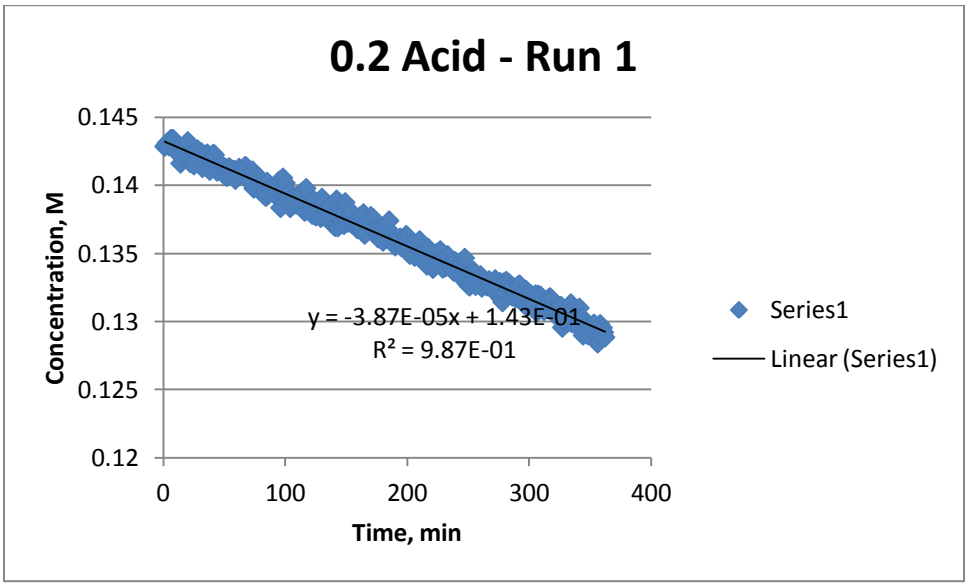
[**56**] = 0.14 M

[**MsOH**] = 0.028 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	18989.4	21949.5	0.142857
16	19132.4	22082.6	0.142649
31	18808.5	21675.7	0.142432
46	19085.5	21813.6	0.141258
61	19028.4	21729.8	0.141137
76	18921.9	21409.9	0.139842
91	19005.1	21428.2	0.139349

106	18973.3	21365.3	0.139173
121	18849.8	21158.5	0.138729
136	18881.7	21148.7	0.13843
151	18941.1	21040.2	0.137288
166	18744.6	20809.6	0.137207
181	18890.7	20833.6	0.136303
196	18873.4	20713	0.135638
211	18833.6	20514.3	0.134621
226	18859.8	20589.6	0.134927
241	18858.7	20464.8	0.134117
256	18896.8	20280.9	0.132644
271	18846.9	20172.2	0.132282
286	18815.5	20075	0.131865
301	18739.4	20014.9	0.132004
316	18649	19874.3	0.131712
331	18821.3	19782.9	0.129906
346	18777.1	19695.5	0.129636
361	18810.3	19664.7	0.129205
376	18765.2	19570.4	0.128895
391	18917.7	19479	0.127259
406	18761.5	19375.2	0.127634
421	18757.2	19292.3	0.127117
436	18803.5	19254.8	0.126558
451	18723.8	19013.8	0.125506
466	18826.1	19096	0.125363
481	18696.5	18860.7	0.124677
496	18685.7	18856.7	0.124723
511	18745.6	18829.2	0.124143
526	18725.6	18615.3	0.122863
541	18764.8	18605.4	0.122542
556	18645.5	18347.8	0.121618
571	18817.6	18363.6	0.12061
586	18813.5	18276.8	0.120066
601	18759.2	18185.6	0.119812
616	18676.5	18187.3	0.120354
631	18735.1	18004.7	0.118773
646	18577	17815.8	0.118527
661	18772.9	17817	0.117298
676	18778.2	17764.8	0.116922
691	18668.2	17522.5	0.116006
706	18731.9	17611.5	0.116199
721	18714.2	17416.3	0.11502
736	18765.2	17369.9	0.114402
751	18685.4	17283.4	0.114318
766	18755.7	17248.7	0.113661
781	18650.1	16925.1	0.11216



Determination of Rate for 0.2 equiv. of acid - Run 2 [DJK-5-56-2]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (1.3 µL, 0.02 mmol, 0.2 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 3.31E-05 M/min

[**101**] = 0.14 M

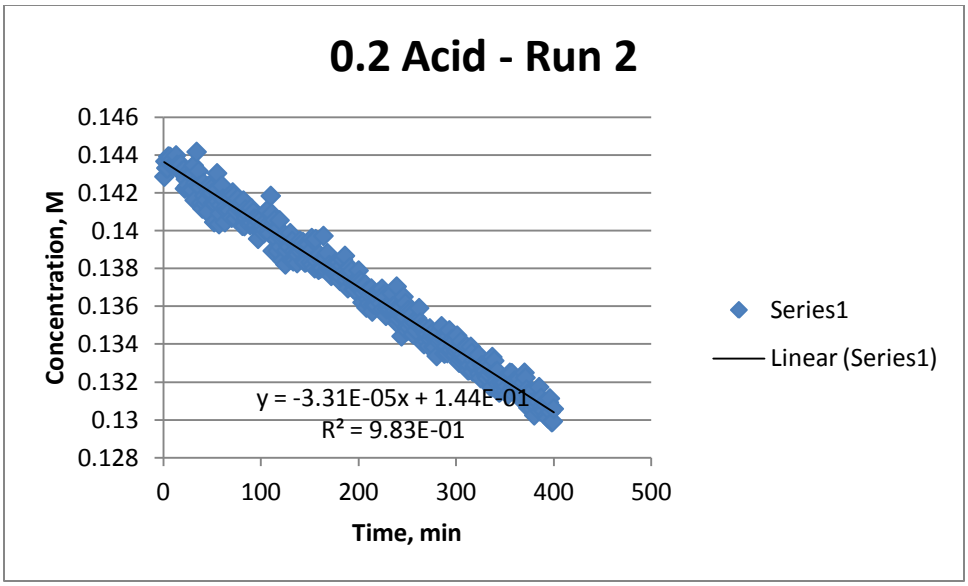
[**56**] = 0.14 M

[**MsOH**] = 0.028 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	18590.2	22080.8	0.142857
16	18453.5	21978.6	0.143249
31	18332	21864.7	0.143451
46	18359.6	21731.2	0.142361

61	18364.9	21634.9	0.141689
76	18306.9	21568.2	0.1417
91	18420.1	21506.3	0.140425
106	18236.8	21389.5	0.141066
121	18362.3	21315.7	0.139619
136	18333.3	21155.3	0.138787
151	18365.2	21122.7	0.138333
166	18282.3	21056	0.138521
181	18429.6	21044.6	0.13734
196	18273.1	20795.1	0.136874
211	18348.7	20768.5	0.136135
226	18282.3	20766.4	0.136616
241	18309.5	20603.7	0.135344
256	18366	20541	0.134517
271	18138.2	20286.9	0.134522
286	18182.5	20308.1	0.134334
301	18249	20400	0.13445
316	18183.2	20187.2	0.133529
331	18299.1	20131.9	0.13232
346	18117.6	19879	0.131967
361	18259.9	19985.3	0.131639
376	18131	19811	0.131418
391	18242.2	19860.3	0.130942
406	18118.9	19664.1	0.130531
421	18221.1	19605.1	0.129409
436	18300.4	19664.9	0.129242
451	18201.3	19461.4	0.128601
466	18242.5	19403.2	0.127926
481	18264.9	19135.8	0.126009
496	18207.2	19198.7	0.126824
511	18213.7	19130.9	0.126331
526	18165.6	19105.7	0.126498
541	18218	19034	0.125661
556	18140.5	18980.2	0.125841
571	18063.2	18832.5	0.125396
586	18155.6	18762.6	0.124295
601	18074.4	18788.7	0.125027
616	18084.7	18543.8	0.123327
631	18125.6	18446.6	0.122404
646	18002.3	18413	0.123018
661	18255.4	18407.6	0.121277
676	18063.5	18291.5	0.121792
691	18133.8	18238.9	0.120971
706	18160.9	18130.2	0.120071



Determination of Rate for 0.2 equiv. of acid - Run 3 [DJK-5-56-3]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (1.3 µL, 0.02 mmol, 0.2 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 3.62E-05 M/min

[**101**] = 0.14 M

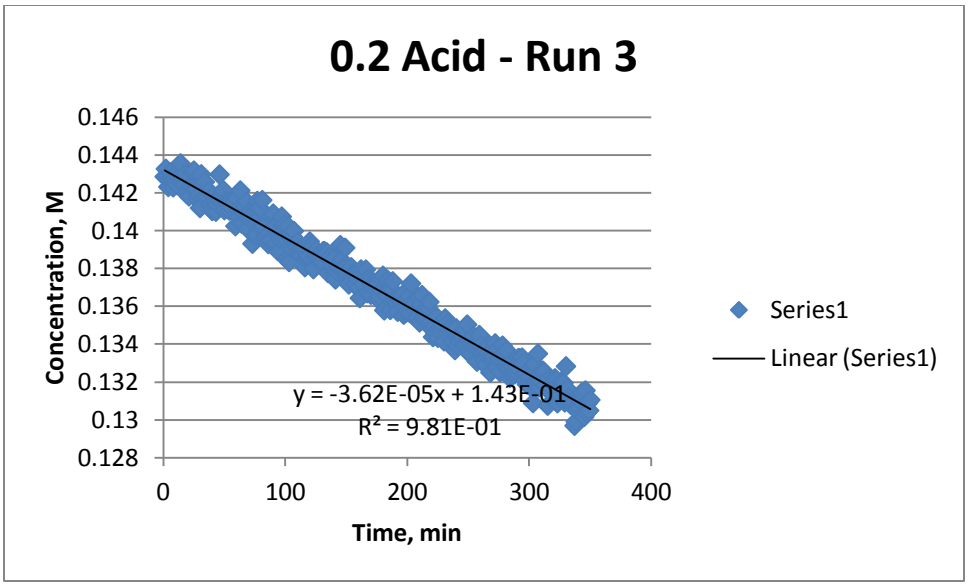
[**56**] = 0.14 M

[**MsOH**] = 0.028 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	16700.8	19326.7	0.142857
16	16585.2	19183.5	0.142787
31	16644.4	19277.8	0.142979
46	16664.8	19300.1	0.142969
61	16618.4	18995.9	0.141108
76	16741.2	18954.4	0.139767
91	16682.3	18944	0.140184

106	16621.9	18806.9	0.139675
121	16763.2	18903.9	0.139212
136	16579.5	18603.6	0.138518
151	16643.9	18573	0.137755
166	16524.5	18465	0.137944
181	16710	18380.6	0.135789
196	16591.8	18360.7	0.136608
211	16447.8	18132.6	0.136092
226	16578.1	18106.1	0.134825
241	16633.8	18047.4	0.133938
256	16547.2	17957.1	0.133966
271	16599.7	17926.9	0.133317
286	16569.7	17827.7	0.13282
301	16614.6	17742.4	0.131827
316	16517.7	17683.4	0.132159
331	16461.9	17553	0.131629
346	16498.5	17581.4	0.13155
361	16481	17534.3	0.131337
376	16458.7	17349.4	0.130128
391	16588	17374.4	0.1293
406	16459.5	17182.7	0.128871
421	16518.9	17161.1	0.128247
436	16520.5	17055.5	0.127445
451	16498.9	16978.8	0.127038
466	16545.7	16802.7	0.125365
481	16612.5	16910.3	0.12566
496	16497.2	16706.3	0.125012
511	16423.3	16708.7	0.125593
526	16500.4	16553.6	0.123845
541	16505.9	16584.5	0.124035
556	16401	16439.5	0.123737
571	16463.6	16406.5	0.123019
586	16543.5	16400.2	0.122378



Determination of Rate for 0.35 equiv. of acid - Run 1 [DJK-5-61-1]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (2.2 µL, 0.035 mmol, 0.35 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 5.87E-05 M/min

[**101**] = 0.14 M

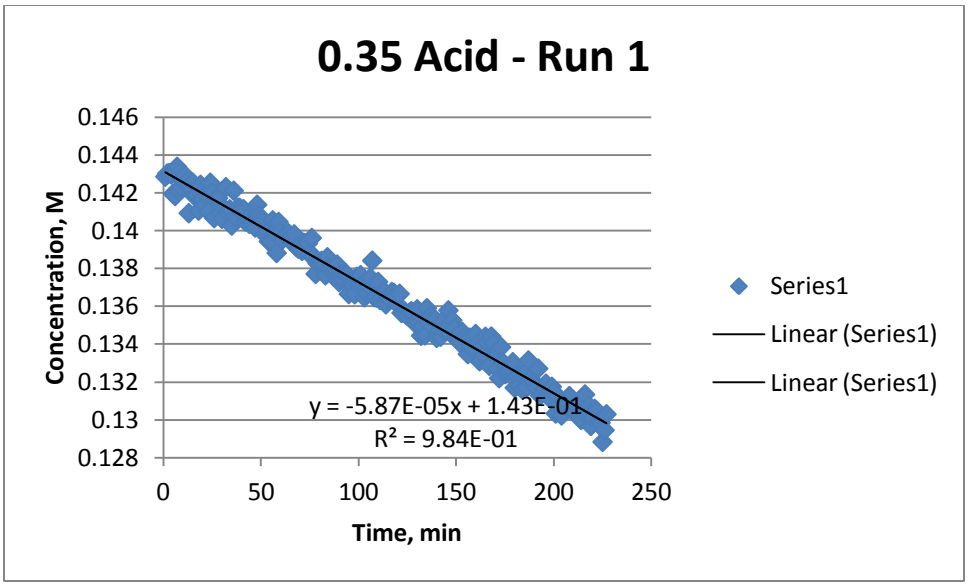
[**56**] = 0.14 M

[**MsOH**] = 0.05 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	17621.8	20620.4	0.142857
16	17504.6	20335.1	0.141824
31	17596.9	20350.1	0.141184
46	17526.4	20171.5	0.140508
61	17526.3	20031.4	0.139533
76	17512.6	20027.4	0.139614
91	17349.8	19570.6	0.13771

106	17390.9	19587.3	0.137502
121	17346.5	19417.6	0.136659
136	17259.6	19101.3	0.13511
151	17419.9	19177.3	0.134399
166	17131.7	18814.9	0.134078
181	17384.4	18842.3	0.132321
196	17274.9	18665.5	0.13191
211	17337.1	18569.7	0.130763
226	17283.4	18326.7	0.129452
241	17251	18245.4	0.12912
256	17177.9	18090.7	0.12857
271	17289.3	18073.6	0.127621
286	17143.6	17757.7	0.126456
301	17454.7	17938.4	0.125466
316	17243.8	17683.7	0.125197
331	17260	17542.9	0.124084
346	17228.5	17325.9	0.122773
361	17252.7	17227.8	0.121907
376	17046.8	16931.9	0.12126
391	17057.7	16869.4	0.120735
406	17243.7	16818.8	0.119075
421	17077.4	16656.6	0.119075
436	17103.8	16431.3	0.117283
451	17088.3	16405.4	0.117204
466	17099.9	16252.8	0.116035
481	17173.3	16260.3	0.115593
496	17220.3	16134.9	0.114388
511	17126.8	15862.5	0.113071
526	17017.8	15823.5	0.113515
541	17155.6	15723.8	0.111894
556	17239	15731.3	0.111406
571	16991.3	15361.8	0.110375
586	17132.7	15328.9	0.10923
601	17280.1	15423.8	0.108968



Determination of Rate for 0.35 equiv. of acid - Run 2 [DJK-5-61-2]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (2.2 µL, 0.035 mmol, 0.35 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 6.18E-05 M/min

[**101**] = 0.14 M

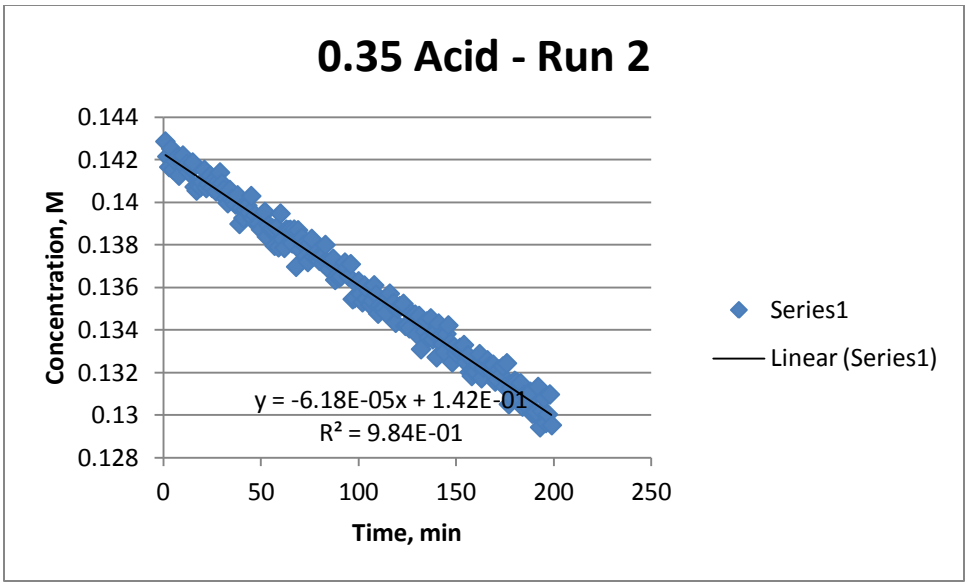
[**56**] = 0.14 M

[**MsOH**] = 0.05 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	19532.9	22364.4	0.142857
16	19865.1	22686.6	0.142492
31	19604.2	22291.3	0.141872
46	19498.9	22224.3	0.14221
61	19505.3	22121	0.141502
76	19793.3	22353.2	0.140907
91	19489.3	22058	0.141215

106	19332.2	21803	0.140717
121	19327.1	21876	0.141225
136	19425.6	21710.7	0.139448
151	19501.3	21825.3	0.139639
166	19519.5	21673	0.138536
181	19373.7	21561.9	0.138863
196	19475.1	21709.3	0.139084
211	19618.7	21913	0.139362
226	19254.9	21401	0.138677
241	19452.1	21465.3	0.137684
256	19571.7	21513.4	0.137149
271	19390.1	21261.5	0.136812
286	19269.3	21199.7	0.13727
301	19442.4	21124	0.135562
316	19314.7	21200.6	0.136953
331	19439.7	21191.5	0.136014
346	19310.6	20906.6	0.135082
361	19546.7	21065.7	0.134466
376	19443.9	21081	0.135276
391	19360.3	20899.7	0.134691
406	19194.6	20687.7	0.134476
421	19249.5	20807.9	0.134872
436	19252.6	20709.2	0.13421
451	19227.5	20699.3	0.134321
466	19153.1	20500	0.133545
481	19289.4	20623.1	0.133397
496	19301.4	20521.3	0.132656
511	19385.9	20642.7	0.132859
526	19249.9	20406.4	0.132266
541	19190.9	20275.9	0.131825
556	19386.6	20447.4	0.131598
571	19214.4	20292.9	0.131774
586	19277.1	20237	0.130983



Determination of Rate for 0.35 equiv. of acid - Run 3 [DJK-5-61-3]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (2.2 µL, 0.035 mmol, 0.35 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 6.23E-05 M/min

[**101**] = 0.14 M

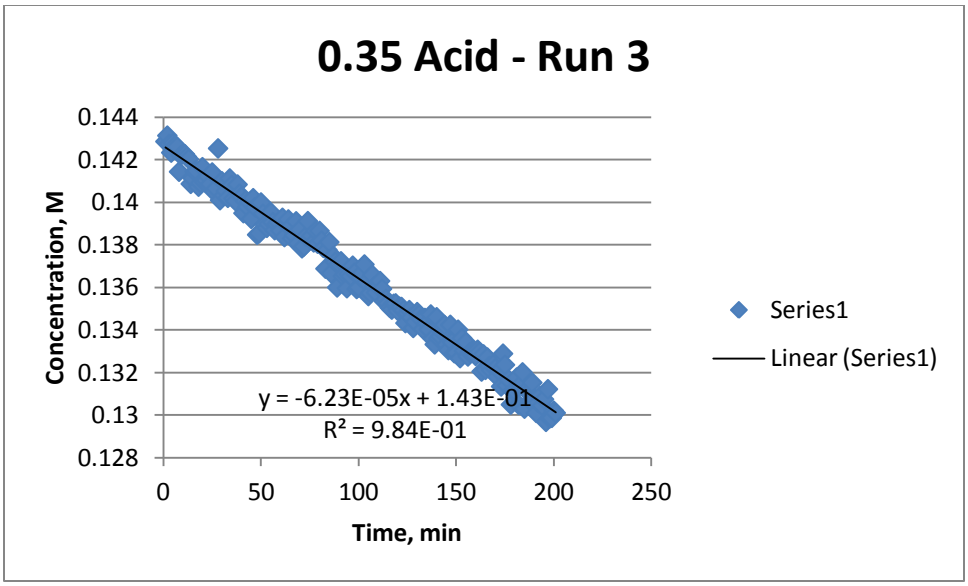
[**56**] = 0.14 M

[**MsOH**] = 0.05 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	19398.7	23024	0.142857
16	19619.6	23054.8	0.141438
31	19541.3	22783.8	0.140335
46	19505.9	22719.6	0.140194
61	19355.2	22395.9	0.139272
76	19682.2	22635.8	0.138425
91	19462.1	22188.9	0.137227

106	19263.5	21723.2	0.135732
121	19322.8	21687.7	0.135094
136	19270.1	21456	0.134017
151	19113.4	21280.9	0.134013
166	19179.9	21146.5	0.132705
181	19430.5	21271.1	0.131765
196	19572.6	21087.7	0.12968
211	19361.9	20821.1	0.129434
226	19376.2	20690.6	0.128528
241	19340.8	20416.1	0.127055
256	19323.7	20246.9	0.126114
271	19214.3	20043.9	0.12556
286	19234.3	19981.8	0.125041
301	19118.9	19587.8	0.123315
316	19292.9	19557.9	0.122016
331	19154.1	19454.1	0.122248
346	19220.1	19474.4	0.121956
361	19190	19104.2	0.119825
376	19158.8	19068.6	0.119797
391	19127.6	18926.7	0.119099
406	19040.9	18625.3	0.117736
421	19306.1	18800.2	0.117209
436	19387.4	18739.2	0.116339
451	19188.5	18342.4	0.115056
466	19143.4	18331.1	0.115256
481	19104.6	18072.4	0.11386
496	19244.2	18061.9	0.112969
511	19108	17783.8	0.112022
526	19219.4	17705.7	0.110884
541	19268.2	17685.9	0.110479
556	19179.1	17437.8	0.109435



Determination of Rate for 0.6 equiv. of acid - Run 1 [DJK-5-68-1]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (3.9 μL, 0.06 mmol, 0.6 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 8.65E-05 M/min

[**101**] = 0.14 M

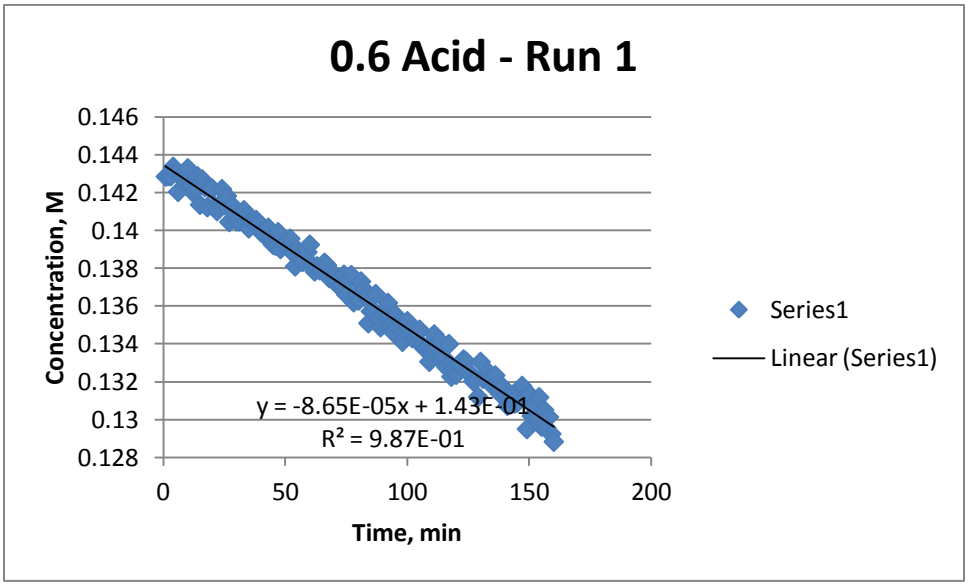
[**56**] = 0.14 M

[**MsOH**] = 0.085 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	18121.2	18480.9	0.142857
16	18084.7	18422.3	0.142692
31	18147.7	18200.3	0.140483
46	18085.7	17973	0.139204
61	18175	17930.1	0.138189
76	18074.2	17721.5	0.137343
91	18051.4	17496.2	0.135768

106	18048	17258.7	0.133951
121	18050	17127.2	0.132915
136	18030.4	17034.8	0.132342
151	17927.2	16663.4	0.130202
166	17958.6	16472.5	0.128485
181	18057.7	16567.3	0.128515
196	18035.6	16304.2	0.126629
211	17919.1	16121.4	0.126024



Determination of Rate for 0.6 equiv. of acid - Run 2 [DJK-5-68-2]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (3.9 µL, 0.06 mmol, 0.6 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 7.79E-05 M/min

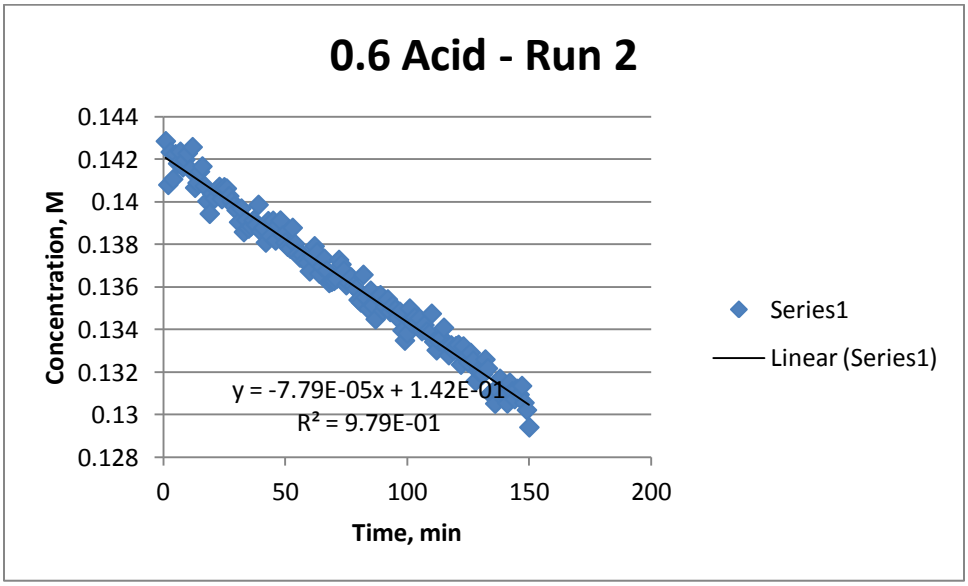
[**101**] = 0.14 M

[**56**] = 0.14 M

[**MsOH**] = 0.085 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	18908.7	21360.4	0.142857
16	18977	21259.7	0.141672
31	19027.3	20921.9	0.139052
46	19021.5	20786.2	0.138193
61	19065.6	20716.1	0.137408
76	18866.5	20319.5	0.1362
91	18865.1	20150.4	0.135076
106	18992.4	20114.5	0.133932
121	18833.9	19850.1	0.133284
136	18953.5	19562.5	0.130524
151	18807.9	19340.1	0.130039
166	18898.3	19319.4	0.129278
181	18826.8	18973	0.127442
196	18769.7	18904.5	0.127369
211	18971.1	18709.3	0.124715
226	18819.4	18540.2	0.124584
241	18710	18424.2	0.124529
256	18830.1	18299	0.122894



Determination of Rate for 0.6 equiv. of acid - Run 3 [DJK-5-68-3]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (3.9 µL, 0.06 mmol, 0.6 equiv)

were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^oC. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 8.11E-05 M/min

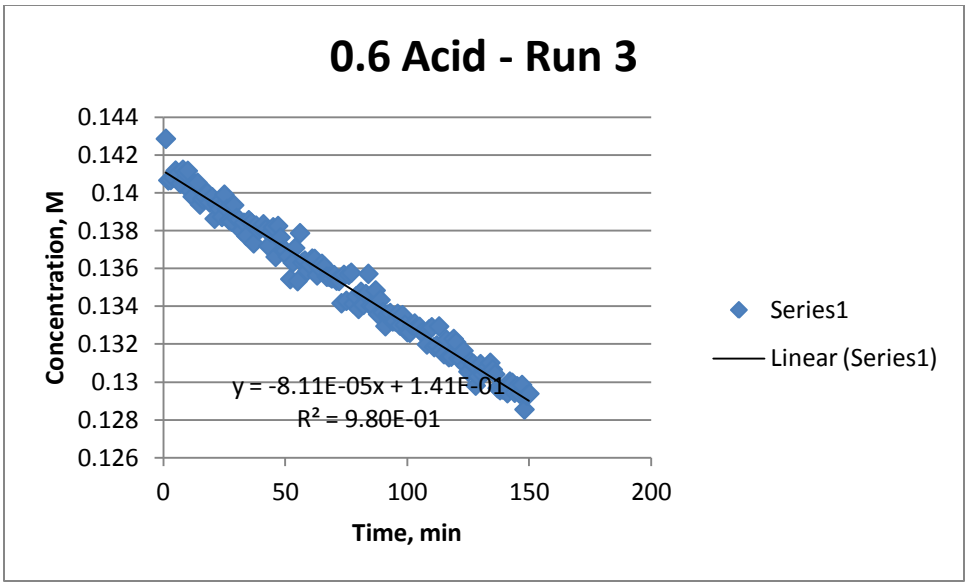
[**101**] = 0.14 M

[**56**] = 0.14 M

[**MsOH**] = 0.085 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	15095.7	18451.9	0.142857
16	15253.6	18229.2	0.139672
31	15253.7	18086.7	0.138579
46	15417.1	18021.2	0.136614
61	15213.1	17770.8	0.136522
76	15144.6	17579.8	0.135666
91	15395.7	17513.4	0.132949
106	15202.6	17250.2	0.132614
121	15100	16957.2	0.131248
136	15194.1	16953.8	0.130409
151	14938.4	16553.4	0.129508
166	15066.2	16533.8	0.128258
181	15053.3	16375.1	0.127135
196	15015.8	16232.8	0.126345
211	14923.1	15912.5	0.124622
226	15005.5	15808.1	0.123124



Determination of Rate for 1.8 equiv. of acid - Run 1 [DJK-5-54-1]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (11.7 µL, 0.18 mmol, 1.8 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 5.80E-05 M/min

[**101**] = 0.14 M

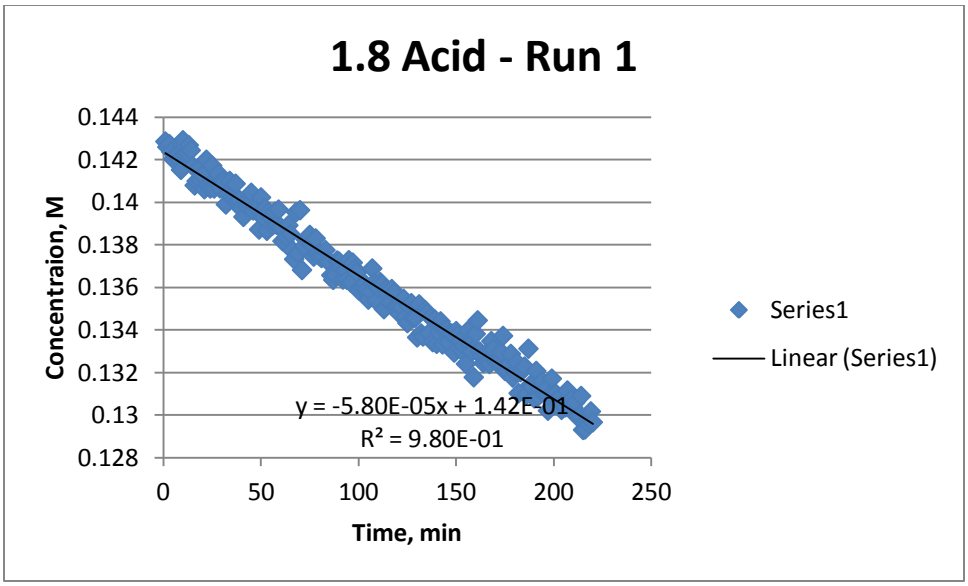
[**56**] = 0.14 M

[**MsOH**] = 0.26 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	19053.2	21171.4	0.142857
16	19263.7	21096.3	0.140795
31	19437.3	21305.6	0.140922
46	19110.6	20753.6	0.139617
61	19247.1	20686.4	0.138178
76	19372.3	20795.3	0.138008
91	19121.6	20365.2	0.136926

106	19211.7	20294.1	0.135808
121	19270.6	20198.7	0.134756
136	18852.8	19627.4	0.133847
151	19284.6	20068.2	0.133788
166	18881.1	19462.8	0.132525
181	18866.7	19440.4	0.132474
196	19128.4	19522.6	0.131214
211	19188.3	19491.5	0.130596
226	19352.4	19710.9	0.130946
241	18965.1	18963.5	0.128553
256	19021	18939.3	0.128012
271	19041.3	18806.3	0.126978
286	19064	18730	0.126312
301	19068.6	18590.8	0.125343
316	19050	18380.4	0.124045
331	19043.5	18351.7	0.123894
346	19088.8	18069.9	0.121702
361	18896.7	17771.2	0.120907
376	18986.7	17971	0.121687
391	19042.3	17783.9	0.120068
406	19034.5	17542.4	0.118486
421	19131.3	17572.4	0.118088
436	18915	17299.9	0.117587
451	18978.3	17207.5	0.116568
466	19009.8	16920.9	0.114437
481	18998.8	16971.3	0.114844
496	18989.5	16621.3	0.112531
511	18968.1	16626.5	0.112693
526	18926.6	16446.6	0.111718
541	18886.5	16179.8	0.110139
556	18788.7	15992.9	0.109434
571	18855.9	15964.9	0.108853
586	18893.8	15852.7	0.107871



Determination of Rate for 1.8 equiv. of acid - Run 2 [DJK-5-54-2]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (11.7 µL, 0.18 mmol, 1.8 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 5.85E-05 M/min

[**101**] = 0.14 M

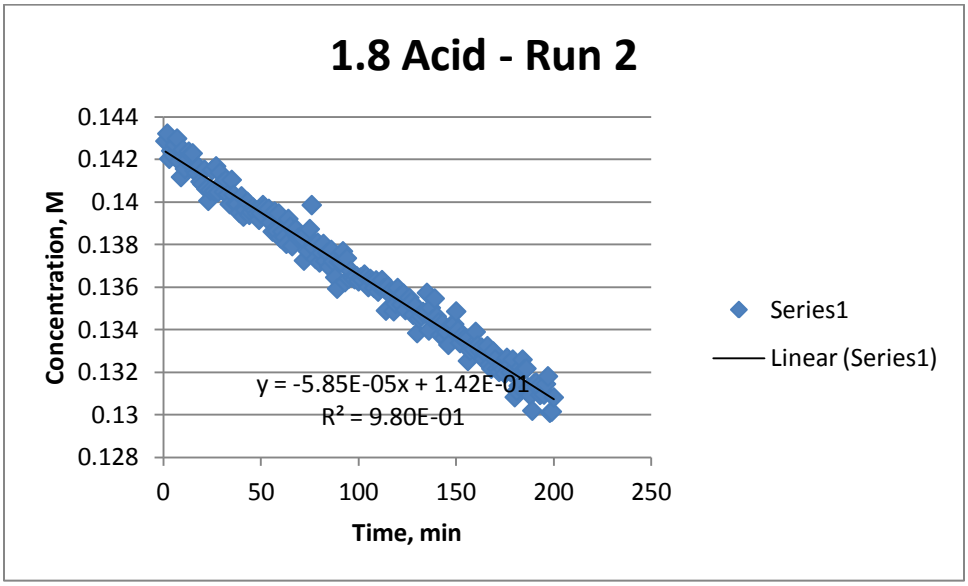
[**56**] = 0.14 M

[**MsOH**] = 0.26 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	18016	20748.4	0.142857
16	17926.9	20445.4	0.141471
31	17834.5	20196.2	0.14047
46	17921.4	20188	0.139732
61	17854.6	19950.6	0.138606
76	18081.8	20386	0.139851
91	17902.1	19793.2	0.137147

106	17798.9	19569.1	0.136381
121	17852.6	19510.4	0.135563
136	17854.6	19281.5	0.133957
151	17658.2	19071.4	0.133971
166	17725.9	19037.4	0.133222
181	17833.3	18851.2	0.131124
196	17794.1	18855.5	0.131443
211	17791.5	18725.8	0.130558
226	17706	18389.2	0.12883
241	17772	18425.8	0.128607
256	17764.8	18250.1	0.127433



Determination of Rate for 1.8 equiv. of acid - Run 3 [DJK-5-54-3]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (11.7 µL, 0.18 mmol, 1.8 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 0 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 5.19E-05 M/min

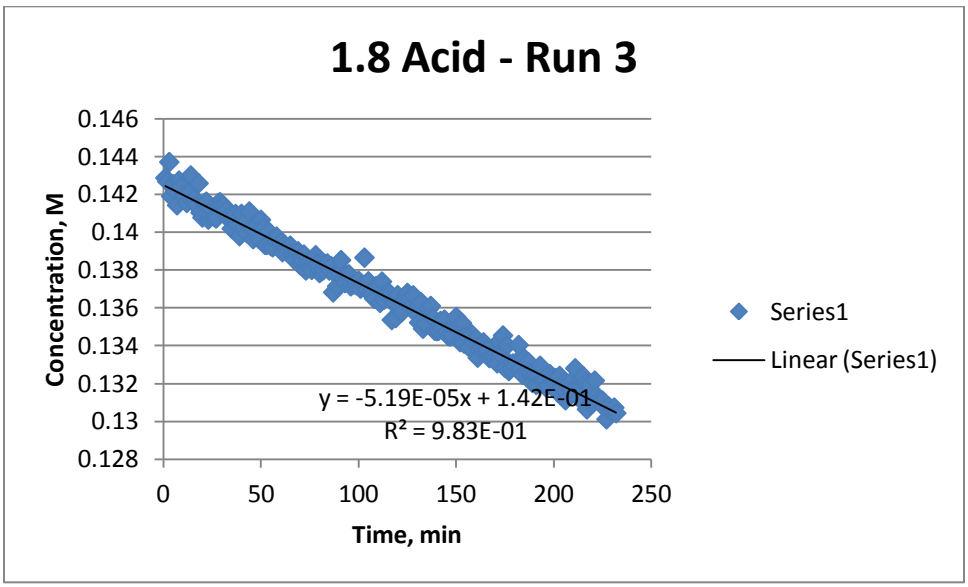
[**101**] = 0.14 M

[**56**] = 0.14 M

[**MsOH**] = 0.26 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	16601.5	17900.1	0.142857
16	16444	17590.9	0.141734
31	16549.9	17659.4	0.141376
46	16543.6	17434.1	0.139625
61	16678.4	17489.2	0.138934
76	16569.1	17257.8	0.138
91	16476	17224.5	0.138512
106	16426.9	16964	0.136825
121	16389.9	16827	0.136027
136	16672.5	17104.7	0.135928
151	16549.7	16861.7	0.134991
166	16436.6	16597.2	0.133788
181	16400.6	16478.9	0.133126
196	16461.4	16374.5	0.131794
211	16404.3	16441.3	0.132792
226	16463.9	16243.6	0.13072



Determination of Rate at 10 °C - Run 1 [DJK-11-56]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 1.0 equiv)

were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 10 ^oC. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.69E-04 M/min

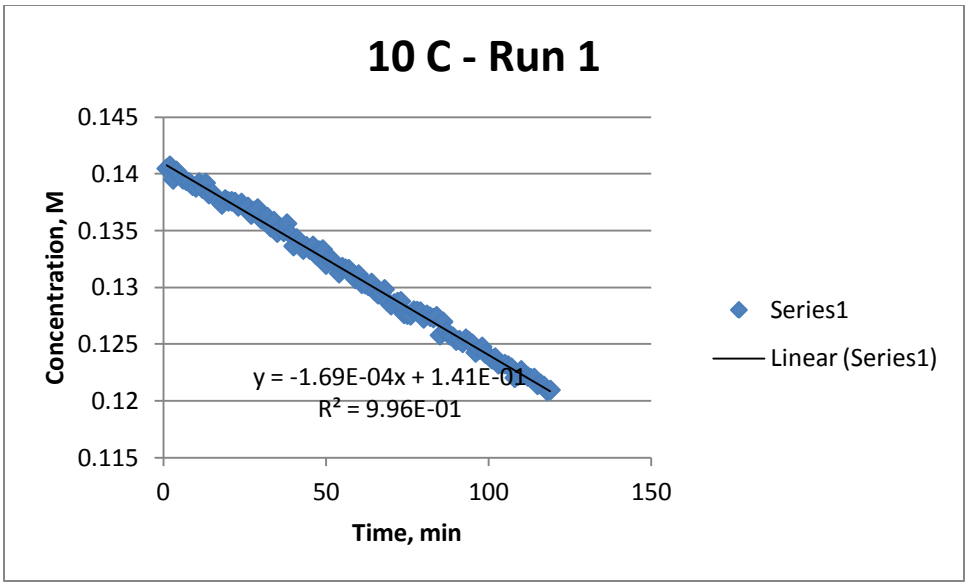
[**101**] = 0.14 M

[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	2559.74	3354.43	0.140476
16	2571.18	3308.79	0.137948
31	2543.22	3232.63	0.136255
46	2529.03	3153.45	0.133663
61	2532.07	3078.15	0.130315
76	2508.46	2984.49	0.127539
91	2492.61	2914.93	0.125358
106	2488.31	2857.75	0.123112
121	2487.11	2795.62	0.120493
136	2474.38	2728.95	0.118225
151	2468.5	2654.88	0.11529
166	2468.76	2604.86	0.113106
181	2472.42	2539.98	0.110126
196	2467.17	2477.84	0.10766
211	2457.99	2422.17	0.105634
226	2499.78	2399.79	0.102909
241	2489.23	2336.73	0.100629
256	2471.02	2284.59	0.099109
271	2482.83	2231.52	0.096346
286	2477.38	2184.11	0.094507



Determination of Rate at 10 ^{o}C - Run 2 [DJK-11-57]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 1.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 10 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.71E-04 M/min

[**101**] = 0.14 M

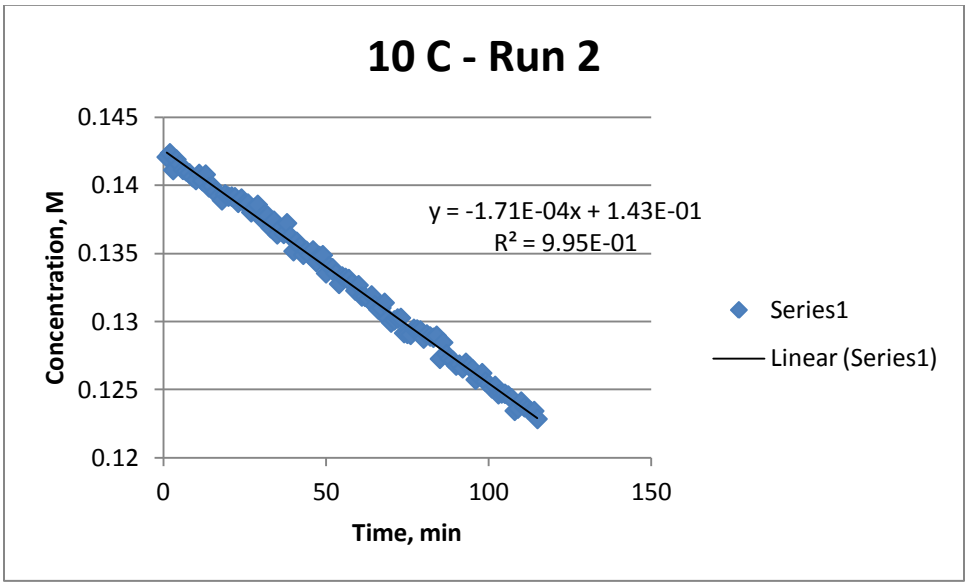
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	2558.85	3354.59	0.142063
16	2569.87	3308.73	0.139521
31	2541.85	3232.96	0.137828
46	2527.21	3153.2	0.135207
61	2530.53	3078.32	0.131823
76	2506.99	2984.56	0.129008
91	2490.83	2915.02	0.126819

106	2485.98	2857.4	0.124555
121	2485.79	2795.54	0.121868
136	2472.38	2728.46	0.119589
151	2466.55	2654.34	0.116615
166	2467.25	2604.34	0.114386
181	2470.3	2539.66	0.111407
196	2465.64	2477.34	0.108879
211	2456.4	2421.76	0.106837
226	2497.99	2399.64	0.104098
241	2487.62	2336.39	0.101777
256	2469	2284.25	0.100256
271	2480.55	2230.93	0.09746
286	2475.34	2183.03	0.095568



Determination of Rate at 10 ^{o}C - Run 3 [DJK-11-58]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (6.5 μL, 0.1 mmol, 1.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 10 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 1.91E-04 M/min

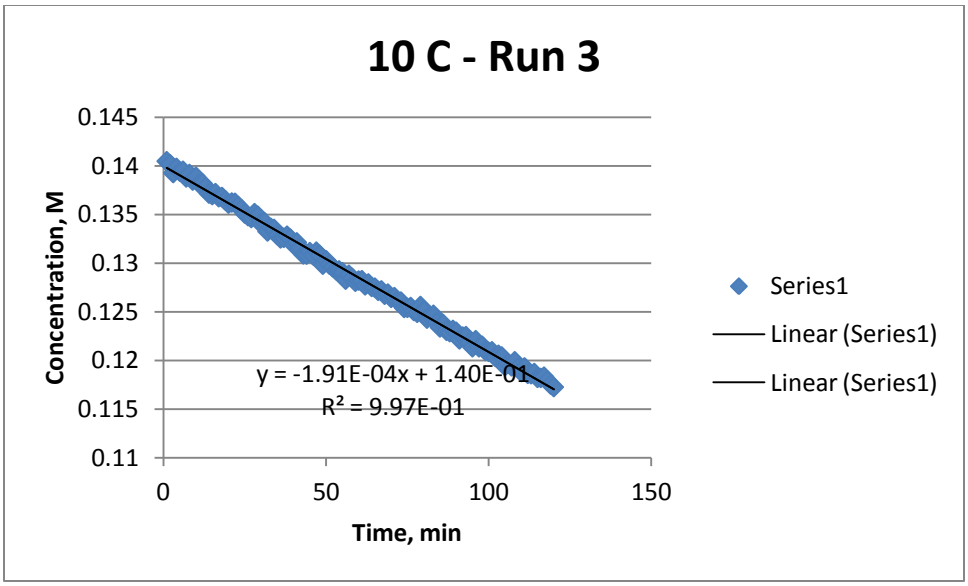
[**101**] = 0.14 M

[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	2632.63	3389.63	0.140476
16	2669.72	3357.12	0.137196
31	2664.27	3277.61	0.134221
46	2667.96	3198.62	0.130805
61	2658.73	3125.25	0.128248
76	2649.64	3047.51	0.125487
91	2660.1	2978.35	0.122157
106	2654.94	2911.53	0.119648
121	2649.79	2840.85	0.116971
136	2656.62	2785.71	0.114405
151	2633.86	2727.25	0.112972
166	2646.5	2658.12	0.109583
181	2629.75	2587.83	0.107365
196	2627.55	2528.64	0.104997
211	2620.84	2480.77	0.103273
226	2631.92	2431.46	0.100794
241	2622.41	2368.77	0.098551
256	2644.87	2327.53	0.096013
271	2628.87	2260.78	0.093827
286	2630.9	2215.19	0.091864
301	2637.68	2157.74	0.089252
316	2635.36	2119.19	0.087734
331	2622.84	2067	0.085982
346	2618.82	2011.07	0.083784
361	2610.2	1967.17	0.082226
376	2590.29	1913.78	0.080609
391	2594.44	1865.7	0.078458
406	2580.81	1823.22	0.077077
421	2575.34	1780.13	0.075415
436	2563.59	1738.65	0.073995
451	2561.28	1685.78	0.07181
466	2562.64	1661.87	0.070754
481	2551.46	1609.84	0.068839



Determination of Rate at 20 ^{o}C - Run 1 [DJK-11-53]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 1.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 20 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 2.45E-04 M/min

[**101**] = 0.14 M

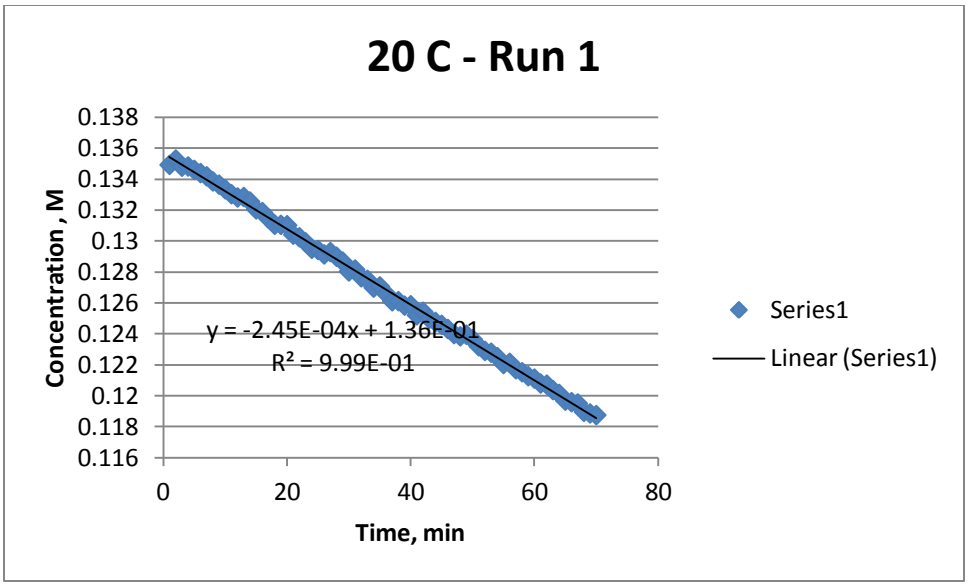
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	14353.4	15176.3	0.134921
16	14328.3	14807.1	0.131869
31	14251.9	14313.2	0.128154
46	14252.9	13885.2	0.124313
61	14138.8	13383.7	0.12079
76	14124.8	12982.9	0.117289
91	14107.4	12570	0.113699

106	14007.3	12178.6	0.110946
121	14013.1	11779.8	0.107268
136	14004	11418.2	0.104043
151	13967.1	11067.5	0.101114
166	13877.9	10705	0.098431
181	13892.8	10435.1	0.095846
196	13941.7	10121.2	0.092637
211	13882.7	9813.19	0.090199
226	13887.1	9526.65	0.087538
241	13864.6	9245.34	0.085091
256	13884.8	8969.75	0.082434
271	13859	8711.64	0.080211
286	13882.3	8462.98	0.077791
301	13813.6	8202.65	0.075773
316	13818.3	8005.72	0.073929
331	13783.3	7743.26	0.071687
346	13775.8	7513.42	0.069597
361	13774.7	7317.23	0.067785
376	13751.1	7091.38	0.065805
391	13769.3	6937.72	0.064294
406	13812.3	6741.33	0.06228
421	13776.9	6554.02	0.060705
436	13682.1	6320.11	0.058944
451	13682.9	6138.33	0.057245
466	13460.8	5870.27	0.055649
481	13429.3	5684.86	0.054017
496	13405.7	5509.02	0.052439
511	13409.6	5385.85	0.051251
526	13370	5204.31	0.049671
541	13378.6	5032.66	0.048001



Determination of Rate at 20 ^{o}C - Run 2 [DJK-11-54]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (6.5 μL, 0.1 mmol, 1.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 20 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 2.67E-04 M/min

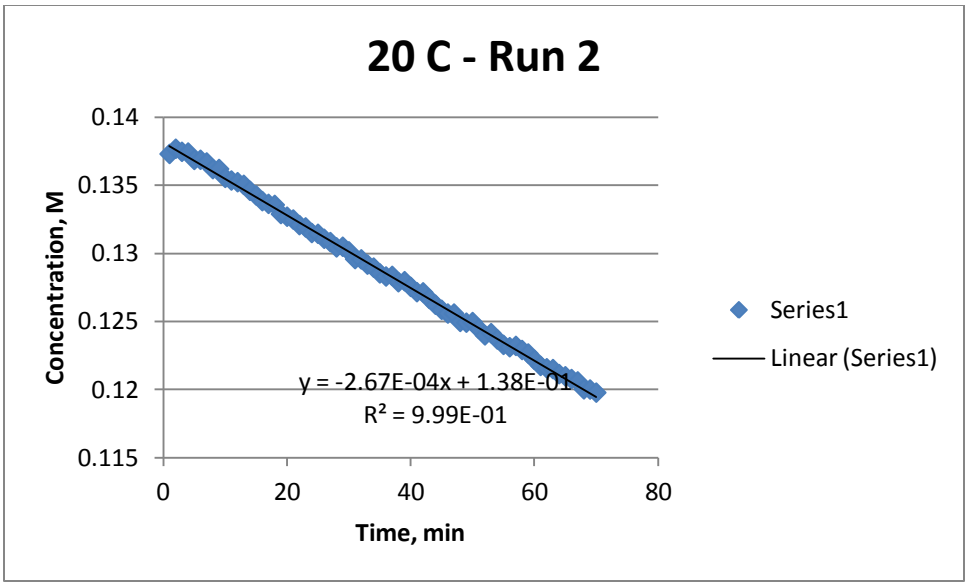
[**101**] = 0.14 M

[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	11378	13502.4	0.137302
16	11276.8	13044.4	0.133835
31	11374.6	12739.4	0.129582
46	11225	12183.7	0.125581
61	11169.1	11751.5	0.121732
76	11184.6	11410.8	0.118039



Determination of Rate at 20 ^{o}C - Run 3 [DJK-11-55]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 1.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at 20 ^{o}C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 2.54E-04 M/min

[**101**] = 0.14 M

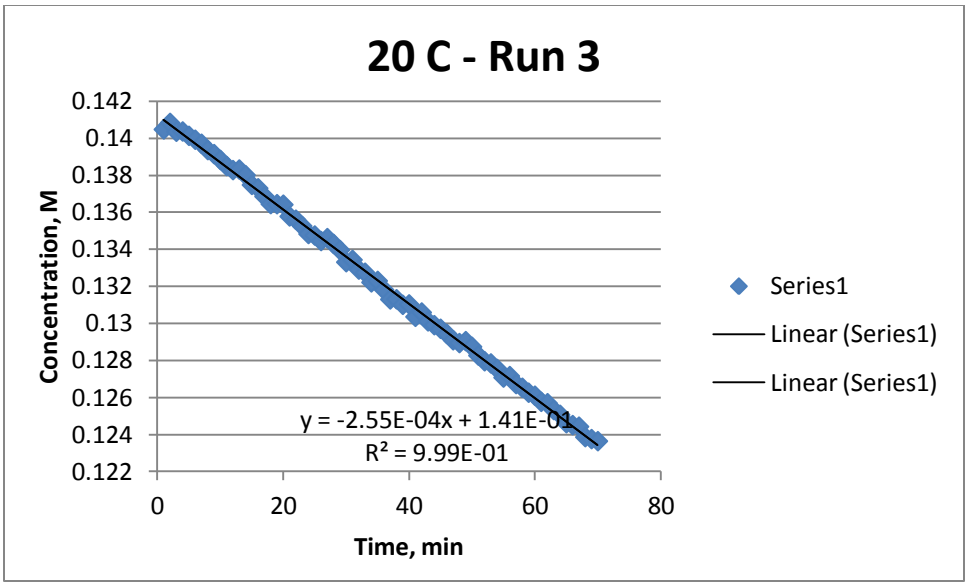
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	14353.4	15176.3	0.140476
16	14328.3	14807.1	0.137299
31	14251.9	14313.2	0.133431
46	14252.9	13885.2	0.129432
61	14138.8	13383.7	0.125764
76	14124.8	12982.9	0.122118
91	14107.4	12570	0.11838

106	14007.3	12178.6	0.115514
121	14013.1	11779.8	0.111685
136	14004	11418.2	0.108327
151	13967.1	11067.5	0.105277
166	13877.9	10705	0.102484
181	13892.8	10435.1	0.099793
196	13941.7	10121.2	0.096451
211	13882.7	9813.19	0.093913
226	13887.1	9526.65	0.091142
241	13864.6	9245.34	0.088595
256	13884.8	8969.75	0.085829
271	13859	8711.64	0.083514
286	13882.3	8462.98	0.080994
301	13813.6	8202.65	0.078893
316	13818.3	8005.72	0.076973
331	13783.3	7743.26	0.074638
346	13775.8	7513.42	0.072462
361	13774.7	7317.23	0.070576
376	13751.1	7091.38	0.068515
391	13769.3	6937.72	0.066942
406	13812.3	6741.33	0.064844
421	13776.9	6554.02	0.063204
436	13682.1	6320.11	0.061371
451	13682.9	6138.33	0.059602
466	13460.8	5870.27	0.05794
481	13429.3	5684.86	0.056242
496	13405.7	5509.02	0.054598
511	13409.6	5385.85	0.053362
526	13370	5204.31	0.051716
541	13378.6	5032.66	0.049978



Determination of Rate at -20 °C - Run 1 [DJK-11-59]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 1.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at -20 °C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 2.66E-05 M/min

[**101**] = 0.14 M

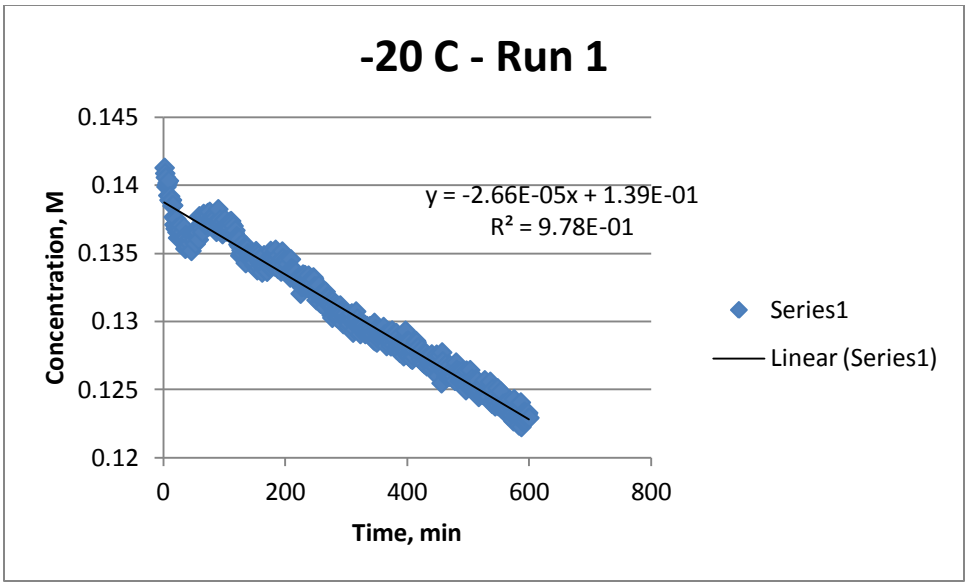
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	3072.85	3278.18	0.140872
16	3201.49	3330.23	0.13852
31	3199.57	3269.13	0.13606
46	3189.11	3237.39	0.135181
61	3144.89	3249.5	0.137595
76	3127.28	3241.89	0.138046
91	3124.69	3210.11	0.136806

106	3123.43	3215.04	0.137071
121	3120.54	3191.67	0.136201
136	3116.21	3172.01	0.13555
151	3120.83	3156.89	0.134704
166	3117.93	3141	0.134151
181	3117.13	3152.31	0.134668
196	3103.8	3137.9	0.134628
211	3110.64	3115.08	0.133355
226	3123.45	3111.12	0.13264
241	3103.81	3096.87	0.132868
256	3118.69	3077.45	0.131404
271	3106.48	3073.1	0.131734
286	3118.99	3050.78	0.130253
301	3116.97	3046.42	0.130151
316	3108.74	3051.92	0.130731
331	3119.85	3024.05	0.129076
346	3106.33	3030.07	0.129896
361	3106.64	3023.3	0.129593
376	3113.74	3010.44	0.128747
391	3113.87	2986.74	0.127729
406	3114.37	2976.37	0.127265
421	3104.63	2973.27	0.127531
436	3110.26	2966.8	0.127023
451	3112.94	2971.07	0.127096
466	3106.91	2941.07	0.126057
481	3104.05	2947.18	0.126435
496	3115.18	2923.1	0.124954
511	3106.99	2926.53	0.125431
526	3111.69	2914.94	0.124745
541	3119.34	2909.71	0.124216
556	3102	2881.13	0.123684
571	3112.39	2891.51	0.123715
586	3092.53	2880.81	0.124049
601	797.858	714.839	0.119309



Determination of Rate at -20 °C - Run 2 [DJK-11-60]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 1.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at -20 °C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 2.16E-05 M/min

[**101**] = 0.14 M

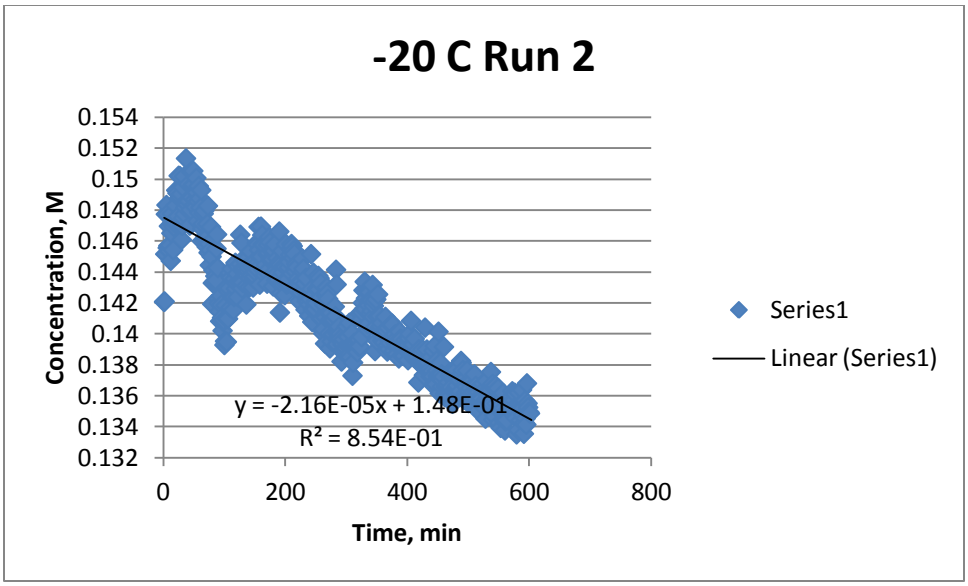
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	3000.29	2245.43	0.142063
16	3074.59	2355.43	0.145422
31	3050.52	2362.15	0.146987
46	3014.57	2389.47	0.15046
61	3009.69	2348.89	0.148145
76	2999.84	2282.54	0.144433
91	3049.22	2280.68	0.141978

106	3062.9	2274.73	0.140975
121	3066.95	2324.77	0.143886
136	3109.79	2324.62	0.141895
151	3091.02	2345.01	0.144009
166	3084.93	2342.46	0.144136
181	3089.54	2342.91	0.143949
196	3084.75	2339.35	0.143953
211	3095.88	2346.75	0.143889
226	3085.61	2319.04	0.142664
241	3073.67	2303.72	0.142272
256	3067.56	2320.48	0.143592
271	3117.28	2321.65	0.141373
286	3111.9	2295.67	0.140033
301	3111.6	2302.73	0.140477
316	3122.38	2290.04	0.139221
331	3072.42	2292.11	0.141612
346	3066.96	2295.82	0.142094
361	3066.97	2257.95	0.13975
376	3059.94	2266.25	0.140586
391	3061.15	2234.84	0.138582
406	3054.38	2266.19	0.140838
421	3056.57	2223.61	0.138093
436	3054.99	2214.08	0.137572
451	3045.6	2248.44	0.140138
466	3066.41	2208.28	0.136701
481	3053.82	2196.73	0.136546
496	3051.94	2189.68	0.136192
511	3057.08	2188.18	0.13587
526	3050.59	2179.59	0.135624
541	3052.08	2161.86	0.134455
556	3052.65	2171.2	0.135011
571	3046.2	2176.3	0.135615
586	3052.43	2161.43	0.134413
601	3051.27	2167.67	0.134852



Determination of Rate at -20 °C - Run 3 [DJK-11-61]

Following the General Procedure, **56** (25.6 mg, 0.1 mmol, 1.0 equiv), **101** (18 mg, 0.1 mmol), catalyst **100** (4.5 mg, 0.1 mmol, 0.1 equiv) and MsOH (6.5 µL, 0.1 mmol, 1.0 equiv) were combined in an NMR tube containing 0.7 mL of $CDCl_3$. The tube was inserted into an NMR spectrometer at -20 °C. The reaction was then followed by ^{19}F NMR spectroscopy. K_{obs} = 2.23E-05 M/min

[**101**] = 0.14 M

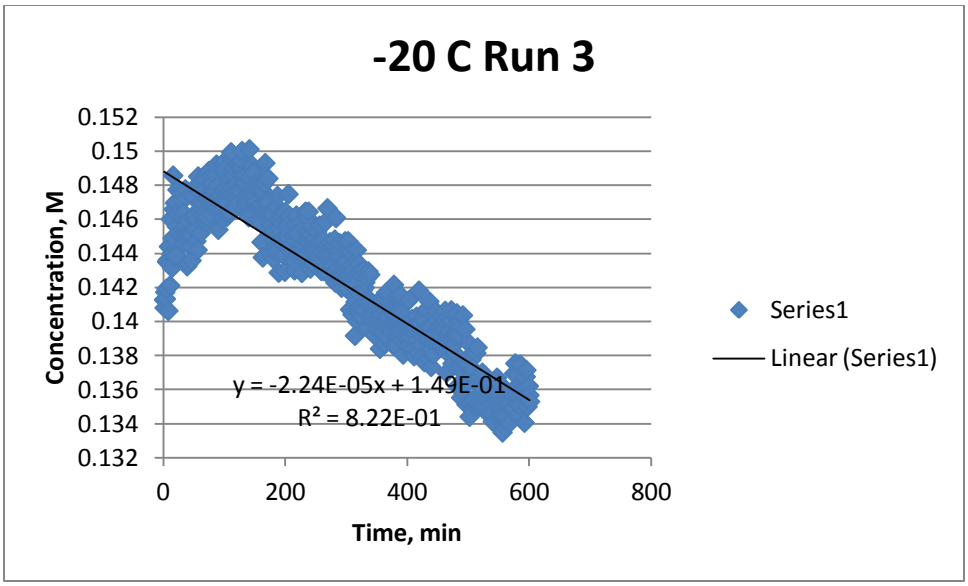
[**56**] = 0.14 M

[**MsOH**] = 0.14 M

Kinetic Data:

time, min	area, IS	area, Substrate	[Substrate]
1	3344.53	2336.24	0.14127
16	3396.27	2494.94	0.148568
31	3384.9	2461.68	0.14708
46	3376.97	2397.4	0.143576
61	3359.76	2411.87	0.145182
76	3329.52	2423.51	0.147208
91	3323.64	2410.83	0.146696

106	3303.49	2410.84	0.147592
121	3286.15	2406.52	0.148105
136	3284.41	2393.13	0.147359
151	3279.11	2381.04	0.146851
166	3282.1	2380.78	0.146702
181	3277.23	2327.96	0.14366
196	3292.09	2351.89	0.144482
211	3279.72	2343.34	0.144499
226	3272.9	2330.61	0.144014
241	3276.72	2318.65	0.143108
256	3256.73	2345.05	0.145626
271	3264.34	2326.84	0.144158
286	3276.35	2319.28	0.143163
301	3260.15	2287.67	0.141913
316	3273.86	2277.21	0.140673
331	3267.62	2299.12	0.142297
346	3268.15	2249.36	0.139195
361	3255.88	2251.15	0.139831
376	3266.07	2239.36	0.138665
391	3259.24	2263.85	0.140475
406	3256.42	2252.5	0.139892
421	3254.38	2251.24	0.139901
436	3254.91	2272	0.141168
451	3263	2239.05	0.138776
466	3246.81	2251.52	0.140245
481	3261.84	2265.61	0.140472
496	3250.91	2208.75	0.137407
511	3266.25	2181.16	0.135053
526	3264.14	2175.69	0.134802
541	3253.59	2179.5	0.135476
556	3261.75	2152.8	0.133481
571	3259.47	2188.94	0.135817
586	3244.85	2178.5	0.135778
601	3260.3	2180.96	0.135287



5.5. Experimental Procedures for Chapter 4.

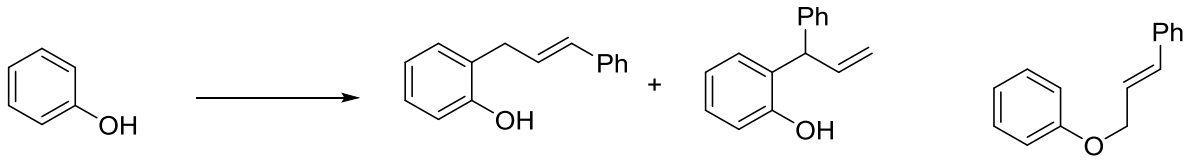
Optimization of Phenol Cinnamylation

General Procedure

To an oven dried Schlenk flask was added washed, dry NaH (1.05 equiv) in a glovebox. For alkali metals, the metal was weighed in hexanes outside the glovebox and dried before addition to the reaction flask. The flask was transferred to a Schlenk line. Solvent (0.5M) was added to afford a cloudy mixture. The mixture was placed in an ice bath and the corresponding phenol (1 equiv) was added portionwise. During this phase, substantial gas evolution was observed. The insoluble material appeared to change in texture from an amorphous, cloudy particulate matter to a finely distributed crystallized solid. The reaction was removed from the ice bath and then allowed to stir at rt for 30 min. Subsequently, cinnamyl chloride (1.1 equiv) was added dropwise via syringe. After the addition was complete, the reaction was placed in an oil bath and then heated to reflux for the specified amount of time. After completion of the reaction as adjudged by TLC, the flask was removed from the heat source and allowed to cool to rt. The mixture was then transferred to a separatory funnel, diluted with water (5 mL) and dichloromethane (10 mL), and then acidified to pH <1 with slow addition of a 6 M HCl solution. The aqueous layer was separated and then back extracted with a further 10 mL of

dichloromethane. The combined organic layers were then washed with brine, dried over $MgSO_4$, and then filtered through glass wool. The filtrate was dried by rotary evaporation (3 mm Hg, 30 ^oC). The residue was then taken up in 10 mL dichloromethane. ^1H NMR of the crude material was taken at this point. Celite was added and the mixture was concentrated to afford a white powder, which was then subjected to flash column chromatography.

Cinnamylation of Phenol with Na in Tetrahydrofuran (Table 14 Entry 1) [DJK-18-46]



114 **115** **116**

Following General Procedure 8, Na (24 mg, 1.05 mmol), THF (2 mL), phenol (94 mg, 1 mmol) and cinnamyl chloride (153 μL, 1.1 mmol) were combined in a 10-mL Schlenk flask. The reaction was stirred at 22 ^oC for 16 h. The reaction was then worked up according to the General Procedure with the following modification: diethyl ether was used as the extraction solvent instead of dichloromethane. Silica gel flash column chromatography (12:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) afforded 25 mg (12%) of a >9:1 mixture of **114** and **115** as a pale oil.

Data for **114**:

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

7.39 – 7.35 (m, 2H), 7.33 – 7.28 (m, 2H), 7.25 – 7.14 (m, 3H), 6.92 (td, *J* = 7.4, 1.2 Hz, 1H), 6.83 (dd, *J* = 7.9, 1.2 Hz, 1H), 6.52 (d, *J* = 15.9 Hz, 1H), 6.40 (dt, *J* = 15.9, 6.5 Hz, 1H), 3.59 (d, *J* = 6.0 Hz, 1H).

Diagnostic for **115**:

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

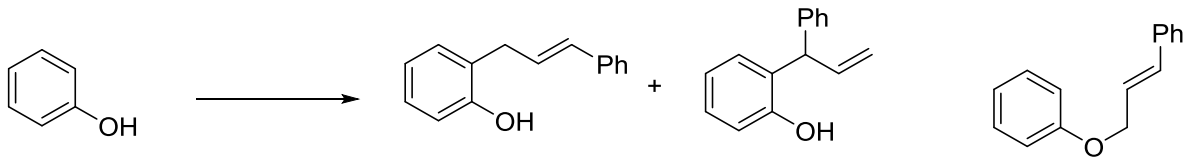
6.29 (ddd, *J* = 17.2, 10.2, 7.3 Hz, 1H), 5.21 (d, *J* = 10.2 Hz, 1H), 5.02 – 4.97 (m, 2H)

Diagnostic for **116**:

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

6.74 (dt, *J* = 15.9, 1.7 Hz, 1H), 6.49 – 6.38 (m, 1H), 4.71 (dd, *J* = 5.8, 1.5 Hz, 1H).

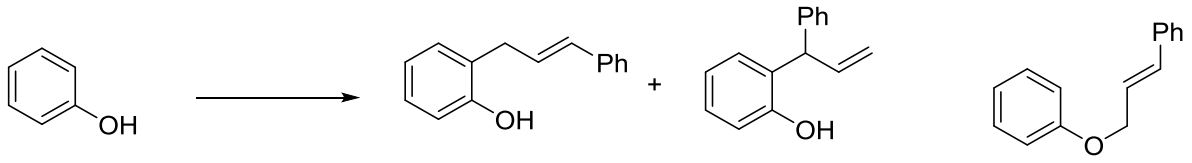
Cinnamylation of Phenol with Na in Et_2O (Table 14 Entry 2) [DJK-18-47]



114 **115** **116**

Following General Procedure 8, Na (24 mg, 1.05 mmol), ether (2 mL), phenol (94 mg, 1 mmol) and cinnamyl chloride (153 μL, 1.1 mmol) were combined in a 10-mL Schlenk flask. The reaction was stirred at 22 ^oC for 16 h. The reaction was then worked up according to the General Procedure with the following modification: diethyl ether was used as the extraction solvent. Silica gel flash column chromatography (12:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) afforded 137 mg (65%) of a 4.5:1 mixture of **114** and **115** as a pale oil.

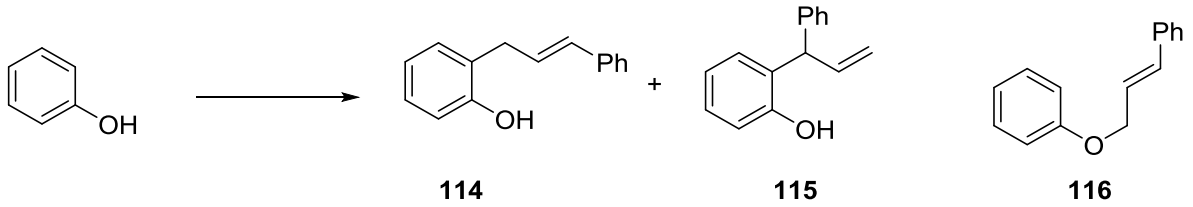
Cinnamylation of Phenol with Na in CH_2Cl_2 (Table 14, Entry 3) [DJK-18-48]



114 **115** **116**

Following General Procedure 8, Na (24 mg, 1.05 mmol), CH_2Cl_2 (2 mL), phenol (94 mg, 1 mmol) and cinnamyl chloride (153 μL, 1.1 mmol) were combined in a 10-mL Schlenk flask. The reaction was stirred at 22 ^oC for 16 h. The reaction was then worked up according to the General Procedure. Silica gel flash column chromatography (12:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) afforded 78 mg (37%) of a 4:1 mixture of **114** and **115** as a pale oil.

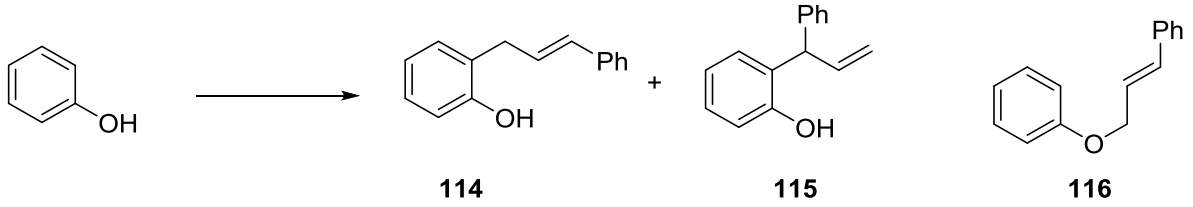
Cinnamylation of Phenol with Li in CH_2Cl_2 (Table 14, Entry 4) [DJK-18-49]



114 **115** **116**

Following General Procedure 8, washed lithium (8 mg, 1.1 mmol), CH_2Cl_2 (2 mL), phenol (94 mg, 1 mmol) and cinnamyl chloride (153 μL, 1.1 mmol) were combined in a 10-mL Schlenk flask. The reaction was stirred at 22 ^oC for 16 h. The reaction was then worked up according to the General Procedure. The crude NMR did not show appreciable amounts of product and the material was not purified further

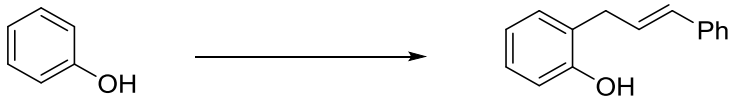
Cinnamylation of Phenol with K in CH_2Cl_2 (Table 14, Entry 5) [DJK-18-50]



114 **115** **116**

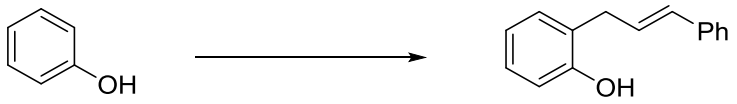
Following General Procedure 8, washed potassium (42 mg, 1.05 mmol), CH_2Cl_2 (2 mL), phenol (94 mg, 1 mmol) and cinnamyl chloride (153 μL, 1.1 mmol) were combined in a 10-mL Schlenk flask. The reaction was stirred at 22 ^oC for 16 h. The reaction was then worked up according to the General Procedure.Silica gel flash column chromatography (12:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) afforded 61 mg (29%) of a 2:1 mixture of **114** and **115** as a pale oil.

Cinnamylation of Phenol with NaH in CH_2Cl_2 (Table 14 Entry 6) [DJK-18-51]



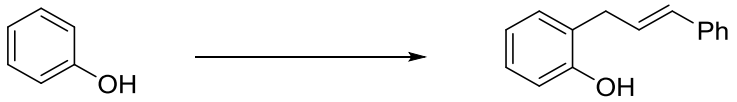
Following General Procedure 8, NaH (25 mg, 1.05 mmol), CH_2Cl_2 (2 mL), phenol (94 mg, 1 mmol) and cinnamyl chloride (153 μL, 1.1 mmol) were combined in a 10-mL Schlenk flask. The reaction was stirred at reflux for 16 h. The reaction was then worked up according to the General Procedure. Silica gel flash column chromatography (12:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) afforded 139 mg (66%) of a 7:1 mixture of **114** and **115** as a pale oil.

Cinnamylation of Phenol with NaH in CCl_4 (Table 14 Entry 7) [DJK-18-52]



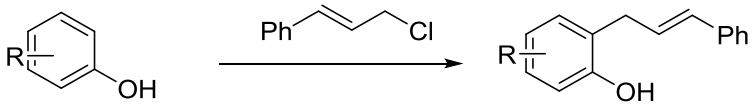
Following General Procedure 8, NaH (25 mg, 1.05 mmol), CCl_4 (2 mL), phenol (94 mg, 1 mmol) and cinnamyl chloride (153 μL, 1.1 mmol) were combined in a 10-mL Schlenk flask. The reaction was stirred at reflux for 16 h. The reaction was then worked up according to the General Procedure. Silica gel flash column chromatography (12:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) afforded 143 mg (68%) of a 9.5:1 mixture of **114** and **115** as a pale oil.

Cinnamylation of Phenol with NaH in Benzene (Table 14 Entry 8) [DJK-18-53]



Following General Procedure 8, NaH (25 mg, 1.05 mmol), benzene (2 mL), phenol (94 mg, 1 mmol) and cinnamyl chloride (153 μL, 1.1 mmol) were combined in a 10-mL Schlenk flask. The reaction was stirred at reflux for 16 h. The reaction was then worked up according to the General Procedure with the following modification: diethyl ether was used as the extraction solvent. Silica gel flash column chromatography (12:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) afforded 155 mg (74%) of a 9:1 mixture of **114** and **115** as a pale oil.

Preparation of cinnamyl-substituted Phenols (Table 15)



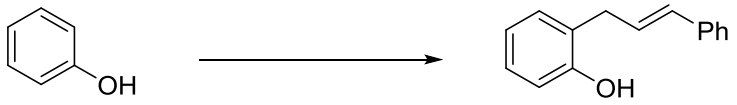
114

General Procedure

To a 50-mL oven dried Schlenk flask was added washed, dry NaH (1.05 equiv) in a glovebox. The flask was transferred to a Schlenk line. Solvent (0.5M) was added to afford a cloudy mixture. The mixture was placed in an ice bath and the corresponding phenol (1 equiv) was added portionwise. During this phase, substantial gas evolution was observed. The insoluble material appeared to change in texture from an amorphous, cloudy particulate matter to a finely

distributed crystallized solid. The reaction was removed from the ice bath and then allowed to stir at rt for 30 min. Subsequently, cinnamyl chloride (1.1 equiv) was added dropwise via syringe. After the addition was complete, the reaction was placed in an oil bath and then heated to reflux for the specified amount of time. After completion of the reaction as adjudged by TLC, the flask was removed from the heat source and allowed to cool to rt. The mixture was then transferred to a separatory funnel, diluted with water (20 mL) and dichloromethane (20 mL), and then acidified to pH <1 with slow addition of a 6M HCl solution. The aqueous layer was separated and then back extracted with a further 30 mL of dichloromethane. The combined organic layers were then washed with brine, dried over $MgSO_4$, and then filtered through glass wool. The filtrate was dried under reduced pressure (~3 mm Hg, rotary evaporator). The residue was then taken up in 10 mL dichloromethane. Celite was added and the mixture was concentrated to afford a white powder, which was then subjected to flash column chromatography. If necessary, a second flash column chromatography operation was performed using silica impregnated with 10% $AgNO_3$ (w/w).

Preparation of (*E*)-2-(3-Phenyl-2-propen-1-yl)phenol (114) [DJK-11-24]



114

Following General Procedure 9, NaH (252 mg, 10.5 mmol), CCl_4 (20 mL), phenol (0.94 g, 10 mmol) and cinnamyl chloride (1.53 mL, 11 mmol) were combined in a 50-mL Schlenk flask. The reaction was worked up according to the General Procedure. Silica gel flash column chromatography (3:1 hexanes/toluene, 30 mm diameter, 14 cm SiO_2) followed by a second silica gel flash column chromatography (9:1, hexanes/ethyl acetate, 30 mm diameter, 50 g SiO_2 (10% $AgNO_3$ w/w)) afforded a pale oil. Distillation afforded 1.49 g of **114** (71%) as a pale oil that solidifed upon standing. The spectroscopic data matched those reported in the literature.[161]

Data for **114**:

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

δ 7.39 – 7.35 (m, 2H), 7.33 – 7.28 (m, 2H), 7.25 – 7.14 (m, 3H), 6.92 (td, *J* = 7.4, 1.2 Hz, 1H), 6.83 (dd, *J* = 7.9, 1.2 Hz, 1H), 6.52 (d, *J* = 15.9 Hz, 1H), 6.40 (dt, *J* = 15.9, 6.5 Hz, 1H), 3.59 (d, *J* = 6.0 Hz, 1H).

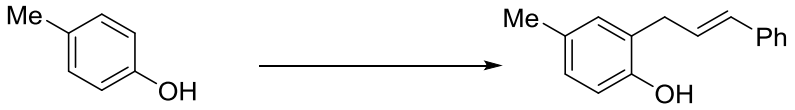
^{13}C NMR: (126 MHz,$CDCl_3$)

δ 154.2, 137.3, 131.8, 130.7, 128.8, 128.2, 128.1, 127.6, 126.5, 125.9, 121.3, 116.0, 34.4.

MS: (EI, 70 eV, m/z)

210 (100, M^+), 119 (33), 115 (38), 104 (66), 91 (82), 69 (45).

Preparation of (*E*)-2-(3-Phenyl-2-propen-1-yl)-4-methylphenol (114b) [DJK-9-67]



114b

Following General Procedure 9, NaH (252 mg, 10.5 mmol), CCl_4 (20 mL), p-cresol (1.08 g, 10 mmol) and cinnamyl chloride (1.53 mL, 11 mmol) were combined in a 50-mL Schlenk flask. The reaction was worked up according to the General Procedure. Silica gel flash column chromatography (3:1 hexanes/toluene, 30 mm diameter, 16 cm SiO_2) followed by a second silica gel flash column chromatography (9:1, hexanes/ethyl acetate, 50 g SiO_2 (10% $AgNO_3$ w/w)) afforded a pale oil. Distillation afforded 1.05 g of **114b** (47%) as a pale oil that solidified upon standing. The spectral data matched those reported in the literature.[162]

Data for **114b**:

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

δ 7.40 – 7.35 (m, 2H), 7.32 (td, *J* = 7.6, 1.1 Hz, 2H), 7.26 – 7.21 (m, 1H), 7.06 (t, *J* = 8.3 Hz, 1H), 6.84 (t, *J* = 7.5 Hz, 1H), 6.56 (d, *J* = 16.0 Hz, 0H), 6.41 (dtd, *J* = 15.8, 6.6, 1.0 Hz, 1H), 4.96 (s, 1H), 3.59 (dd, *J* = 6.7, 1.6 Hz, 2H), 2.28 (s, 3H)

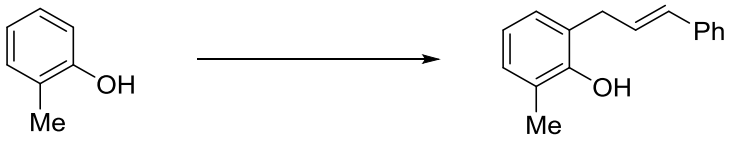
^{13}C NMR: (126 MHz,$CDCl_3$)

δ 149.7, 135.1, 129.3, 128.9, 128.2, 126.5, 126.2, 126.1, 125.2, 124.2, 124.1, 123.4, 113.6, 32.1, 18.5.

MS: (EI, 70 eV, m/z)

224 (100, M^+), 209 (30), 133 (55), 115 (30), 104 (35), 91 (69), 77 (22)

Preparation of (*E*)-2-(3-Phenyl-2-propen-1-yl)-6-methylphenol (114c) [DJK-11-20]



114c

Following General Procedure 9, NaH (252 mg, 10.5 mmol), CCl_4 (20 mL), *o*-cresol (1.08 g, 10 mmol) and cinnamyl chloride (1.53 mL, 11 mmol) were combined in a 50-mL Schlenk flask. The reaction was worked up according to the General Procedure. Silica gel flash column chromatography (3:1 hexanes/toluene, 30 mm diameter, 14 cm SiO_2) followed by a second silica gel flash column chromatography (9:1, hexanes/ethyl acetate, 30 mm diameter 50 g SiO_2 (10% $AgNO_3$ w/w)) afforded a pale oil. Distillation afforded 1.38 g of **114c** (62%) as a pale oil that solidified upon standing. The spectral data matched those reported in the literature.[163]

Data for **114c**:

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

δ 7.41 – 7.35 (m, 2H), 7.34 – 7.30 (m, 2H), 7.23 (ddd, *J* = 12.8, 6.5, 1.7 Hz, 1H), 7.06 (t, *J* = 8.7 Hz, 1H), 6.90 – 6.80 (m, 1H), 6.56 (d, *J* = 16.0 Hz, 0H), 6.41 (ddd, *J* = 15.9, 8.0, 5.6 Hz, 1H), 3.59 (dd, *J* = 6.6, 1.7 Hz, 2H).

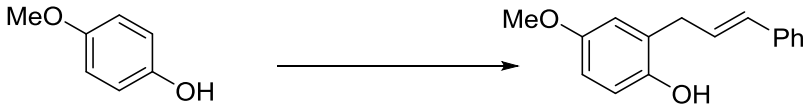
^{13}C NMR: (126 MHz,$CDCl_3$)

δ 152.5, 136.9, 131.6, 129.4, 128.5, 128.1, 127.9, 127.4, 126.2, 124.9, 124.0, 120.4, 34.6, 15.9.

MS: (EI, 70 eV, m/z)

224 (100, M^+), 209 (33), 168 (26), 141 (28), 120 (29), 115 (52), 105 (47), 91 (71), 77 (76), 69 (41).

Preparation of (*E*)-2-(3-Phenyl-2-propen-1-yl)-4-methoxyphenol (114d) [DJK-10-26]



114d

Following General Procedure 9, NaH (252 mg, 10.5 mmol), CCl_4 (20 mL), 4-methoxyphenol (1.24 g, 10 mmol) and cinnamyl chloride (1.53 mL, 11 mmol) were combined in a 50-mL Schlenk flask. The reaction was worked up according to the General Procedure. Silica gel flash column chromatography (3:1, hexanes/toluene, 30 mm diameter, 14 cm SiO_2) followed by a second silica gel flash column chromatography (9:1 hexanes/ethyl acetate, 30 mm diameter, 50 g SiO_2 (10% $AgNO_3$ w/w)) afforded a pale oil. Distillation afforded 1.17 g of **114d** (49%) as a pale oil that solidified upon standing. The spectral data matched those reported in the literature.[164]

Data for **114d**:

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

δ 7.39 – 7.14 (m, 5H), 6.81 – 6.65 (m, 3H), 6.48 (d, 1H, *J* = 15.9 Hz), 6.35 (dt, *J* = 15.9, 6.5 Hz, 1H), 3.74 (s, 3H), 3.52 (d, *J* = 5.7 Hz, 1H).

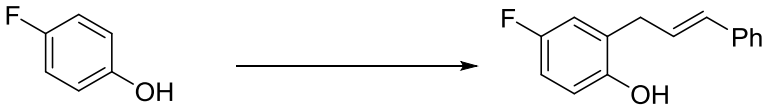
^{13}C NMR: (126 MHz,$CDCl_3$)

δ 153.8, 147.9, 137.0, 131.5, 128.5, 127.7, 127.3, 126.8, 126.2, 116.4, 116.0, 112.6, 55.7, 34.3.

MS: (EI, 70 eV, m/z)

240 (100, M^+), 149 (66), 136 (99), 121 (25), 115 (31), 108 (44), 91 (79), 77 (21).

Preparation of (*E*)- 2-(3-Phenyl-2-propen-1-yl)-4-fluorophenol (114e) [DJK-18-44]



114e

Following General Procedure 9, NaH (252 mg, 10.5 mmol), CCl_4 (20 mL), 4-fluorophenol (1.12 g, 10 mmol) and cinnamyl chloride (1.53 mL, 11 mmol) were combined in a 50-mL Schlenk flask. The reaction was worked up according to the General Procedure. Silica gel flash column chromatography (3:1 hexanes/toluene, 30 mm diameter, 16 cm SiO_2) followed by a

second silica gel flash column chromatography (9:1, hexanes/ethyl acetate, 30 mm diameter, 50 g SiO_2 (10% $AgNO_3$ w/w)) afforded a pale oil. Distillation afforded 1.73 g of **114e** (76%) as a yellow oil that solidified upon standing.[165]

Data for **114e**:

bp: 100 °C (ABT, $3*10^{-5}$ T)

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

δ 7.40 – 7.32 (m, 2H), 7.29 (ddd, *J* = 7.9, 6.2, 1.3 Hz, 2H), 7.24 – 7.18 (m, 1H), 6.88 (dd, *J* = 9.0, 3.0 Hz, 1H), 6.82 (td, *J* = 8.3, 3.1 Hz, 1H), 6.74 (dd, *J* = 8.7, 4.7 Hz, 1H), 6.49 (dt, *J* = 15.7, 1.6 Hz, 1H), 6.33 (dt, *J* = 15.9, 6.6 Hz, 1H), 3.52 (dd, *J* = 6.6, 1.5 Hz, 2H).

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

δ 157.2 (d, *J* = 232 Hz) , 149.8, 136.9, 132.0, 128.6, 127.5, 127.3 (d, *J* = 7 Hz), 126.9, 126.2, 116.6 (d, *J* = 23 Hz), 116.5 (d, *J* = 8.5 Hz), 113.9 (d, *J* = 25 Hz), 34.0.

^{19}F NMR: (476 MHz,$CDCl_3$)

δ -123.9 (m)

IR: (ATR, cm^{-1})

3429 (br), 3027 (w), 1619 (w), 1598 (w), 1494 (s), 1438 (s), 1327 (w), 1254 (w), 1176 (s), 1141 (m), 1090 (w), 1028 (w), 958 (m), 928 (w), 872 (w), 809 (m), 748 (s), 731 (m**),** 716 (w), 692 (s).

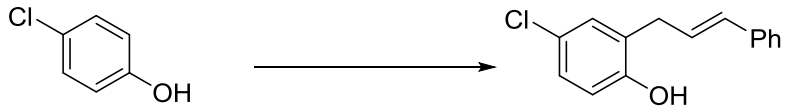
MS: (EI, 70 eV, m/z)

228 (100, M^+), 137 (46), 115 (21), 109 (21), 104 (85), 91 (57)

HRMS: Calcd for $C_{15}H_{13}OF$ 200.0950, found 200.0952, error 0.7

TLC: R_f 0.30 (4:1, hexanes/ethyl acetate) [UV,CAM]

Preparation of (*E*)- 2-(3-Phenyl-2-propen-1-yl)-4-chlorophenol (114f) [DJK-11-32]



114f

Following General Procedure 9, NaH (252 mg, 10.5 mmol), CCl_4 (20 mL), 4-chlorophenol (1.28 g, 10 mmol) and cinnamyl chloride (1.53 mL, 11 mmol) were combined in a

50-mL Schlenk flask. The reaction was worked up according to the General Procedure. Silica gel flash column chromatography (3:1 hexanes/toluene, 30 mm diameter, 16 cm SiO_2) followed by a second silica gel flash column chromatography (9:1, hexanes/ethyl acetate, 50 g SiO_2 (10% $AgNO_3$ w/w)) afforded a pale oil. Distillation afforded 1.49 g of **114f** (61%) as a yellow oil that solidified upon standing. The spectroscopic data matched those reported in the literature.[166]

Data for **114f**:

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

δ 7.43 – 7.07 (m, 5H), 6.77 (d, *J* = 8.5 Hz, 1H), 6.57 – 6.49 (m, 1H), 6.36 (dt, *J* = 15.9, 6.6 Hz, 1H), 4.97 (s, 1H), 3.60 – 3.47 (m, 2H).

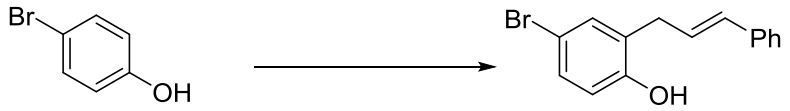
^{13}C NMR: (126 MHz,$CDCl_3$)

δ 159.4, 152.8, 137.1, 132.4, 130.3, 128.8, 127.8, 127.7, 127.1, 126.5, 117.2, 34.1.

MS: (EI, 70 eV, m/z)

246 (33, M^++2), 244 (96, M^+), 209 (75), 165 (19), 153 (42), 115 (42), 105 (60), 104 (100), 91 (87), 81 (40), 77 (59), 69 (81)

Preparation of (*E*)-2-(3-Phenyl-2-propen-1-yl)-4-bromophenol (114g) [DJK-11-31]



114g

Following General Procedure 9, NaH (252 mg, 10.5 mmol), CCl_4 (20 mL), 4-bromophenol (1.73 g, 10 mmol) and cinnamyl chloride (1.53 mL, 11 mmol) were combined in a 50-mL Schlenk flask. The reaction was worked up according to the General Procedure. Silica gel flash column chromatography (3:1 hexanes/toluene, 30 mm diameter, 16 cm SiO_2) followed by a second silica gel flash column chromatography (9:1, hexanes/ethyl acetate, 30 mm diameter 50 g SiO_2 (10% AgNO3 w/w)) afforded a pale oil. Distillation afforded 1.62 g of **114g** (56%) as a pale oil that solidified upon standing. The spectroscopic data matched those reported in the literature.[167]

Data for **114g**:

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

δ 7.42 – 7.19 (m, 5H), 6.74 (ddd, *J* = 9.9, 8.5, 1.3 Hz, 1H), 6.53 (dd, *J* = 15.9, 1.7 Hz, 1H), 6.36 (dt, *J* = 15.9, 6.6 Hz, 0H), 4.99 (d, *J* = 1.3 Hz, 0H), 3.55 (dd, *J* = 6.6, 1.6 Hz, 2H).

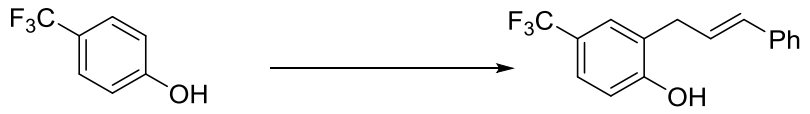
^{13}C NMR: (126 MHz,$CDCl_3$)

δ 153.4, 150.1, 137.1, 133.2, 132.4, 130.8, 128.8, 128.3, 127.8, 127.1, 126.5, 117.7, 113.2, 34.1.

MS: (EI, 70 eV, m/z)

290 (71, M^++2), 288 (76, M^+), 209 (93), 131 (24), 118 (39), 115 (45), 104 (100), 91 (82), 77 (41).

Preparation of (*E*)- 2-(3-Phenyl-2-propen-1-yl)-4-trifluoromethylphenol (114h) [DJK-17-46]



114h

Following General Procedure 9, NaH (126 mg, 5.25 mmol), toluene (10 mL), 4-trifluoromethylphenol (810 mg, 5 mmol) and cinnamyl chloride (715 μL, 5.5 mmol) were combined in a 50-mL Schlenk flask. The reaction was worked up according to the General Procedure. Silica gel flash column chromatography (3:1 hexanes/toluene, 30 mm diameter, 16 cm SiO_2) followed by a second silica gel flash column chromatography (9:1, hexanes/ethyl acetate, 30 mm diameter 50 g SiO_2 (10% $AgNO_3$ w/w)) afforded a pale oil. Distillation afforded 885 mg of **114h** (64%) as a clear oil that solidified upon standing.

Data for **114h**:

bp: 120 ^{o}C (ABT, 3.2 * 10^{-5} T)

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

δ 7.47 – 7.28 (m, 6H), 7.24 (dd, *J* = 8.6, 6.2 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 6.54 (dt, *J* = 15.8, 1.6 Hz, 1H), 6.36 (dt, *J* = 15.9, 6.6 Hz, 1H), 5.26 (s, 1H), 3.64 – 3.57 (m, 2H).

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

δ 156.95, 136.96, 132.57, 129.13, 129.05, 128.91, 128.85, 128.75, 127.93, 127.90, 127.87, 127.85, 126.86, 126.50, 126.46, 126.37, 125.98, 125.69, 125.59, 125.56, 125.53, 125.50, 116.04, 77.51, 77.46, 77.26, 77.01, 34.26.

^{19}F NMR: (500 MHz, $CDCl_3$)

-61.56

IR: (ATR, cm^{-1})

3498 (br), 3027 (w), 2923 (w), 1614 (w), 1496 (w), 1485 (w), 1448 (w), 1355 (s), 1335 (s), 1250 (w), 1201 (s), 1152 (s), 1114 (s), 1028 (w), 967 (m), 928 (w), 889 (w), 805 (w), 743 (m), 692 (s).

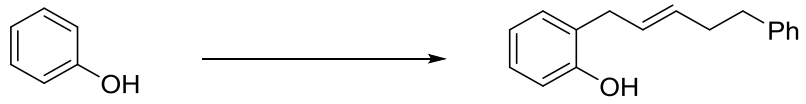
MS: (EI, 70 eV, m/z)

278 (4, M^+), 260 (83), 223 (30), 184 (23), 168 (60), 156 (35), 149 (40), 141 (60), 128 (51), 115 (74), 104 (40), 91 (69), 77 (100)..

HRMS: Calcd for $C_{16}H_{13}OF_3$ 278.0919, found 278.0912, error -2.4

TLC: R_f 0.33 (4:1, hexanes/ethyl acetate) [UV,CAM]

Preparation of (*E*)-2-(5-Phenylpent-2-en-1-yl)phenol (114i) [DJK-9-87]



114i

Following General Procedure 9, NaH (126 mg, 5.25 mmol), toluene (10 mL), 4-trifluoromethylphenol (810 mg, 5 mmol) and phenethyl allyl chloride (990 mg, 5.5 mmol) were combined in a 50-mL Schlenk flask. The reaction was worked up according to the General Procedure. Silica gel flash column chromatography (3:1, hexanes/toluene, 30 mm diameter, 16 cm SiO_2) followed by a second silica gel flash column chromatography (9:1, hexanes/ethyl acetate, 30 mm diameter SiO_2 (10% $AgNO_3$ w/w)) afforded a pale oil. Distillation afforded 940 mg of **114i** (79%) as a clear oil.

Data for **114i**:

bp: 160 °C (ABT, 0.05 T)

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

δ 7.30 – 7.26 (m, 2H), 7.21 – 7.10 (m, 5H), 7.05 (dd, *J* = 7.5, 1.7 Hz, 1H), 6.87 (td, *J* = 7.4, 1.2 Hz, 1H), 6.82 (dd, *J* = 8.0, 1.2 Hz, 1H), 5.64 (ddd, *J* = 5.5, 3.9, 1.7 Hz, 2H), 5.01 (s, 1H), 3.35 (dd, *J* = 4.5, 1.8 Hz, 3H), 2.70 (dd, *J* = 8.8, 6.7 Hz, 3H), 2.42 – 2.32 (m, 3H).

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

δ 154.2, 141.7, 131.9, 130.2, 128.4, 128.3, 128.2, 127.8, 125.8, 120.8, 115.8, 35.7, 34.2, 34.0.

IR: (ATR, cm^{-1})

3498 (br), 3027 (w), 2923 (w), 1614 (w), 1496 (w), 1485 (w), 1448 (w), 1355 (s), 1335 (s), 1250 (w), 1201 (s), 1152 (s), 1114 (s), 1028 (w), 967 (m), 928 (w), 889 (w), 805 (w), 743 (m), 692 (s).

MS: (EI, 70 eV, m/z)

238 (95, M^+), 147 (100), 131 (21), 107 (42), 91 (62)

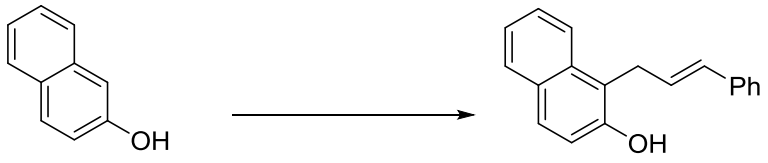
TLC: R_f 0.27 (4:1, hexanes/ethyl acetate) [UV,CAM]

Analysis: $C_{17}H_{18}O$ (238.33)

Calcd: C, 85.67; H, 7.61%

Found: C, 85.31; H, 7.63%

Preparation of (*E*)-1-(3-Phenyl-2-propen-1-yl)naphthalen-2-ol (114j) [DJK-12-54]



114j

Following General Procedure 9, NaH (252 mg, 10.5 mmol), CCl_4 (20 mL), 2-naphthol (1.44g, 10 mmol) and cinnamyl chloride (1.53 mL, 11 mmol) were combined in a 50-mL Schlenk flask. The reaction was worked up according to the General Procedure. Silica gel flash column chromatography (3:1 hexanes/toluene, 30 mm diameter, 16 cm SiO_2) followed by a second silica gel flash column chromatography (9:1, hexanes/ethyl acetate, 30 mm diameter 50 g

SiO_2 (10% $AgNO_3$ w/w)) afforded a pale pink solid. The spectroscopic data matched those reported in the literature.[168]

Data for **114j**:

mp: 62-64 °C (hexanes)

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

8.00 (d, *J* = 8.6 Hz, 1H), 7.82 (d, *J* = 8.1 Hz, 1H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.52 (ddt, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.39 – 7.35 (m, 1H), 7.34 – 7.29 (m, 2H), 7.30 – 7.24 (m, 2H), 7.22 – 7.18 (m, 1H), 7.16 – 7.09 (m, 2H), 6.47 (p, *J* = 1.9 Hz, 2H), 4.01 (dd, *J* = 3.1, 1.4 Hz, 2H).

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

δ 151.1, 137.2, 133.3, 130.9, 129.4, 128.6, 128.4, 128.3, 127.6, 127.1, 126.6, 126.1, 126.0, 123.2, 123.1, 117.9, 117.1, 28.43.

MS: (EI, 70 eV, m/z)

260 (100, M^+), 169 (59), 156 (36), 128 (38), 117 (25), 115 (24), 104 (44), 91 (38).

Preparation of 2-(3-Methylbut-2-en-1-yl)phenol (114k) [DJK-14-83]

114k

Following General Procedure 9, NaH (126 mg, 5.25 mmol), CCl_4 (10 mL), phenol (470 mg, 5 mmol) and prenyl chloride (605 μL, 5.5 mmol) were combined in a 50-mL Schlenk flask. The reaction was worked up according to the General Procedure. Silica gel flash column chromatography (3:1, hexanes/toluene, 30 mm diameter, 16 cm SiO_2) followed by a second silica gel flash column chromatography (9:1, hexanes/ethyl acetate, 30 mm diameter 50 g SiO_2 (10% $AgNO_3$ w/w)) afforded a pale oil. Distillation afforded 525 mg (65%) of **114k** as a clear oil. The spectroscopic data matched those reported in the literature.[169]

Data for **114k**:

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

δ 7.14 (t, *J* = 7.4 Hz, 1H), 6.89 (td, *J* = 7.5, 1.2 Hz, 1H), 6.83 (dt, *J* = 7.6, 1.3 Hz, 1H), 5.35 (dddd, *J* = 7.3, 5.8, 2.9, 1.5 Hz, 1H), 5.09 (s, 1H), 3.38 (d, *J* = 7.2 Hz, 2H), 1.80 (dd, *J* = 5.1, 1.4 Hz, 6H).

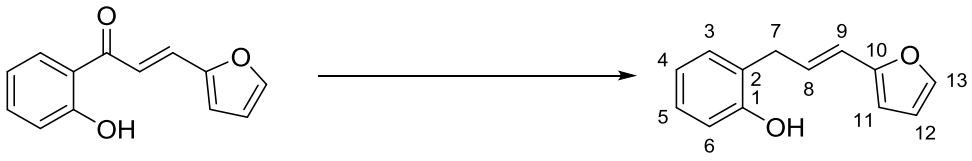
^{13}C NMR: (126 MHz,$CDCl_3$)

δ 154.1, 129.8, 127.3, 121.8, 120.6, 115.5, 29.4, 25.7, 17.7.

MS: (EI, 70 eV, m/z)

162 (21, M^+), 145 (39), 133 (38), 115 (33), 107 (100), 91 (77), 77 (47)

Preparation of (*E*)-2-(3-(Furan-2-yl)allyl)phenol (119b) [DJK-17-70]



118b **119b**

To a 5-mL Schlenk flask equipped with a stir bar was added, under argon, (*E*)-3-(furan-2-yl)-1-(2-hydroxyphenyl)prop-2-en-1-one **118b** (749 mg, 3.5 mmol), THF (3.5 mL) and triethylamine (535 μL, 3.85 mmol, 1.1 equiv). To this solution was added with vigorous stirring ethyl chloroformate (370 μL, 3.85 mmol, 1.1 equiv). The color of the solution changed from dark brown to light gold with concomitant precipitation of solid triethylammonium chloride. The mixture was stirred for a further 30 min and the reaction was assayed for completion by TLC. To a separate 50-mL flask, under argon and equipped with a stir bar, was added ethanol (15 mL) and cerium chloride heptahydrate (1.56 g, 4.2 mmol, 1.2 equiv) and the resulting clear solution was stirred for 20 min. The solution containing the ethyl carbonate of the starting material was then filtered into the second flask through glass wool. THF (2x 5mL) was used to wash the flask and filter cake. To the resulting light yellow solution was added $NaBH_4$ (160 mg, 4.2 mmol, 1.2 equiv) and the solution was stirred for a further 1 h. Water (1 mL) was added to quench the reaction, and the solution was then stirred a further 15 min. The resulting heterogenous mixture was transferred to a 125-mL separatory funnel and diluted with water (15 mL) and CH_2Cl_2 (30 mL). The layers were separated and the aq. layer was extracted with CH_2Cl_2 (2x 30 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated by rotary evaporation (30 ^{o}C,

3 mm Hg). The crude material thus obtained was redissolved in 10 mL of CH_2Cl_2 and adsorbed onto Celite. Purification by silica gel flash column chromatography (12:1, hexanes/ethyl acetate, 20 mm diameter, 18 cm SiO_2) followed by bulb-to-bulb diffusion pump distillation afforded 112 mg (16%) of **119b** as a pale yellow oil .

Data for **119b**:

bp: 70 ^oC, 2 x 10^{-4} mm Hg

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

δ 7.33 (d, *J* = 1.8 Hz, 1H, HC(11)), 7.17 (m, 2H, HC(3), HC(5)), 6.93 (t, *J* = 7.5 Hz, 1H, HC(4)), 6.83 (d, *J* = 7.9 Hz, 1H, HC(6)), 6.41–6.31 (m, 2H, HC(8), HC(12)), 6.28 (d, *J* = 15.9 Hz, 1H, HC(9)), 6.18 (d, *J* = 3.3 Hz, 1H, HC(13)), 4.87 (s, 1H, OH), 3.55 (d, *J* = 6.3 Hz, 2H, HC(7)).

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

δ 154.1 (C1), 141.9 (C2), 130.8 (C3), 128.2 (C5), 127.0 (C8), 121.3 (C9), 120.2 (C4), 115.9 (C6), 111.4, 107.3 (C13), 33.9 (C7).

IR: (ATR, cm^{-1})

3409 (br), 1593 (w), 1489 (m), 1455 (s), 1232 (m), 1095 (w), 1012 (m), 964 (m), 753 (s)

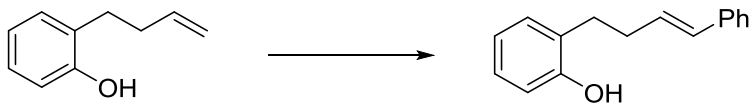
MS: (EI, 70 eV, m/z)

200 (100, M^+), 171 (16), 131 (19), 107 (16), 94 (54), 81 (24)

HRMS: Calcd for $C_{13}H_{12}O_2$ 200.0837, found 200.0842, error 2.3

TLC: R_f 0.36 (4:1, hexanes/ethyl acetate) [UV, CAM]

Preparation of (*E*)-2-(4-Phenylbut-3-en-1-yl)phenol 120 [DJK-12-69]



120

To a 5 mL oven-dried Schlenk flask was added Grubbs-I-indenylidene (92 mg, 0.1 mmol, 0.05 equiv.) in a glovebox. The flask was transferred to a Schlenk line and CH_2Cl_2 (4 mL) was added. To this stirring solution was added styrene (1.15 mL, 10.0 mmol, 5 equiv) and 2-(but-3-en-1-yl)phenol (296 mg, 2.0 mmol). The solution was stirred at rt for 24 h. The volatiles were then removed by rotary evaporation (30 ^oC, 3 mm Hg). Purification by silica gel flash column

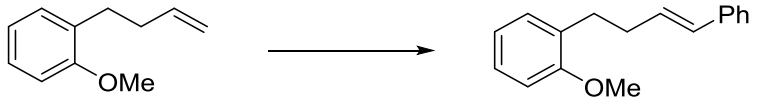
chromatography (12:1, hexanes/ethyl acetate, 20 mm diameter, 18 cm SiO_2) afforded 274 mg (62%) of **120** as a pale oil. The spectral data matched those reported in the literature.[170]

Data for **120**:

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

δ 7.38 (d, *J* = 6.9 Hz, 2H, HC(12)), 7.33 (t, *J* = 7.7 Hz, 2H, HC(13)), 7.24 (t, *J* = 7.2 Hz, 1H, HC(14)), 7.20 (dd, *J* = 7.5, 1.6 Hz, 1H, HC(3)), 7.14 (td, *J* = 7.7, 1.7 Hz, 1H, HC(5)), 6.93 (td, *J* = 7.4, 1.1 Hz, 1H, HC(4)), 6.81 (dd, *J* = 8.0, 1.2 Hz, 1H, HC(6)), 6.48 (dt, *J* = 15.9, 1.4 Hz, 1H, HC(10)), 6.33 (dt, *J* = 15.8, 6.9 Hz, 1H, HC(9)), 4.69 (s, 1H, OH), 2.84 (dd, *J* = 8.8, 6.6 Hz, 2H, HC(7)), 2.62–2.54 (app q, *J* = 7.5 Hz, 2H, HC(8)).

Preparation of (*E*)-2-(4-Phenylbut-3-en-1-yl)phenol methyl ether 130a [DJK-17-14]



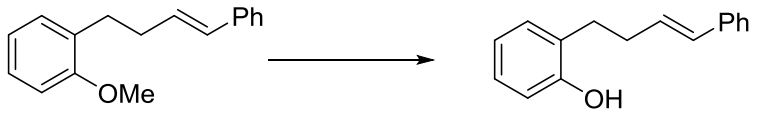
To a 5 mL oven-dried Schlenk flask was added Grubbs-I-indenylidene (24 mg, 0.026 mmol, 0.03 equiv.) in a glovebox. The flask was transferred to a Schlenk line and CH_2Cl_2 (3 mL) was added. To this stirring solution was added styrene (745 μL, 6.5 mmol, 5 equiv) and 2-(but-3-en-1-yl)phenol methyl ether (211 mg, 1.3 mmol). The solution was stirred at rt for 24 h. After 24 h, 8 mg of indeylidene catalyst (0.008 mmol, 0.01 equiv) was added and the reaction was stirred a further 12 h. The volatiles were then removed by rotary evaporation (30 ^{o}C, 3 mm Hg). Purification by silica gel flash column chromatography (40:1, hexanes/ethyl acetate, 20 mm diameter, 18 cm SiO_2) afforded 213 mg (69%) of **130a** as a pale oil.

Data for **130a**:

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

δ 7.38 (d, *J* = 6.9 Hz, 2H, HC(12)), 7.33 (t, *J* = 7.7 Hz, 2H, HC(13)), 7.24 (t, *J* = 7.2 Hz, 1H, HC(14)), 7.20 (dd, *J* = 7.5, 1.6 Hz, 1H, HC(3)), 7.14 (td, *J* = 7.7, 1.7 Hz, 1H, HC(5)), 6.93 (td, *J* = 7.4, 1.1 Hz, 1H, HC(4)), 6.81 (dd, *J* = 8.0, 1.2 Hz, 1H, HC(6)), 6.48 (dt, *J* = 15.9, 1.4 Hz, 1H, HC(10)), 6.33 (dt, *J* = 15.8, 6.9 Hz, 1H, HC(9)), 4.69 (s, 1H, OH), 2.84 (dd, *J* = 8.8, 6.6 Hz, 2H, HC(7)), 2.62–2.54 (app q, *J* = 7.5 Hz, 2H, HC(8)).

Preparation of (*E*)-2-(4-Phenylbut-3-en-1-yl)phenol (120) [DJK-17-16]



131a **120**

Following the procedure of Ammann and White[96b], to a 50-mL oven-dried Schlenk flask was added NaH (48 mg, 2.0 mmol, 2.2 equiv). The flask was transferred to a Schlenk line and DMF (1.5 mL) was added. The flask was placed in an ice bath and ethanethiol (155 μL) was added dropwise. In the process of addition the solution turned homogenous. Methyl ether **131b** (238 mg, 1 mmol) was dissolved in DMF (1.5 mL) and added to the mixture. The solution was then heated to reflux for 3 h. After this time, the solution was cooled down to rt, and then transferred to a 60-mL separatory funnel. The mixture was diluted with water (5 mL) and ethyl acetate (10 mL), and then acidified to pH 1 with 1 M HCl. The biphasic solution was shaken well, and the layers were separated. The aq. layer was further extracted with a portion of ethyl acetate (10 mL). The organic layers were combined and then washed with water (2x 10 mL) followed by brine (10 mL). The organic layers were then dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^oC , 3 mm Hg). Purification by silica gel flash column chromatography (12:1, hexanes/ethyl acetate, 20 mm diameter, 15 cm SiO_2) afforded 169 mg (84%) of **120** as a pale oil. The spectral data matched those reported in the literature.[170]

Data for **120**:

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

δ 7.38 (d, *J* = 6.9 Hz, 2H, HC(12)), 7.33 (t, *J* = 7.7 Hz, 2H, HC(13)), 7.24 (t, *J* = 7.2 Hz, 1H, HC(14)), 7.20 (dd, *J* = 7.5, 1.6 Hz, 1H, HC(3)), 7.14 (td, *J* = 7.7, 1.7 Hz, 1H, HC(5)), 6.93 (td, *J* = 7.4, 1.1 Hz, 1H, HC(4)), 6.81 (dd, *J* = 8.0, 1.2 Hz, 1H, HC(6)), 6.48 (dt, *J* = 15.9, 1.4 Hz, 1H, HC(10)), 6.33 (dt, *J* = 15.8, 6.9 Hz, 1H, HC(9)), 4.69 (s, 1H, OH), 2.84 (dd, *J* = 8.8, 6.6 Hz, 2H, HC(7)), 2.62–2.54 (app q, *J* = 7.5 Hz, 2H, HC(8)).

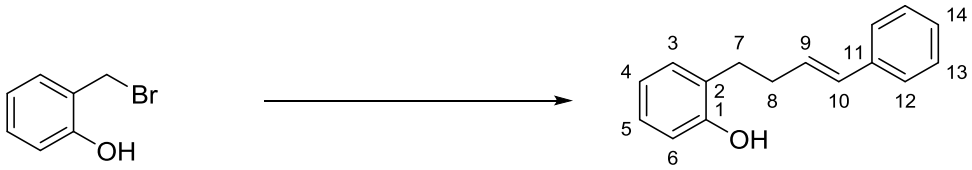
^{13}C NMR: (126 MHz, $CDCl_3$)

δ 153.7, 137.9, 130.7, 130.6, 130.4, 128.7, 127.5, 127.2, 126.2, 121.1, 115.5, 115.1, 33.5, 30.4.

MS: (EI, 70 eV, m/z)

224 (59, M^+), 117 (100), 115 (26), 107 (97), 91 (20), 77 (20)

Preparation of (*E*)-2-(4-Phenylbut-3-en-1-yl)phenol (120) [DJK-15-15]



120

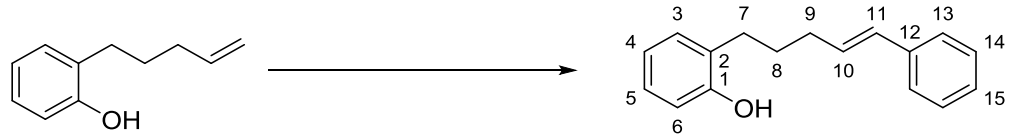
To a 50-mL Schlenk flask under argon was added BuLi (2.23 M in hexanes, 9.5 mL, 21 mmol, 2.1 equiv) followed by a further 4 mL of hexanes. Tetramethylethylenediamine (TMEDA, 2.44 g, 21 mmol, 2.1 equiv) was added via syringe and the flask was placed in a -78 ^oC bath (dry ice/*i*-PrOH). The internal temperature was monitored until it dropped below -40 ^oC. Cresol (1.08 g, 10 mmol) was dissolved in hexanes (6 mL) and added to the cold mixture as a solution. To this cold mixture was then added solid KO*t*-Bu (2.36 g, 21 mmol, 2.1 equiv). The formation of a yellow suspension was observed. The flask was then removed from the -78 ^oC bath and placed in a -20 ^oC bath (*i*-PrOH, IBC-4A cryocool) and the solution within allowed to stir for 30 min. The flask was then removed and allowed to warm to rt over 15 min. THF (10 mL) was added. The flask was then returned to the aforementioned -78 ^oC bath and the internal temperature was monitored until it was below -60 ^oC and then allowed to equilibrate for a further 20 min. Cinnamyl chloride (1.98 g, 13 mmol, 1.3 equiv) was dissolved in THF (2 mL) and added to the mixture. The solution was then allowed to warm to rt and stirred for 1 h. The reaction was quenched by the addition of aq. sat. NH_4Cl (10 mL). The mixture was transferred to a 250-mL separatory funnel and the pH adjusted to <1 with 6 M HCl. The layers were separated and the aq. layer was extracted with ether (2x 30 mL). The organic layers were combined, dried over $MgSO_4$, filtered and concentrated (30 ^oC, 3 mm Hg). The product was purified by two successive silica gel flash column chromatography operations (1, 9:1 hexanes/ethyl acetate, 30 mm diameter, 15 cm SiO_2; 2, 50:1 toluene/ethyl acetate, 30 mm diameter, 14 cm SiO_2) and then distilled under vacuum to afford 330 mg (15%) of **120** a clear oil. The spectroscopic data match those reported in the literature.[170]

Data for **120**:

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

δ 7.38 (d, *J* = 6.9 Hz, 2H, HC(12)), 7.33 (t, *J* = 7.7 Hz, 2H, HC(13)), 7.24 (t, *J* = 7.2 Hz, 1H, HC(14)), 7.20 (dd, *J* = 7.5, 1.6 Hz, 1H, HC(3)), 7.14 (td, *J* = 7.7, 1.7 Hz, 1H, HC(5)), 6.93 (td, *J* = 7.4, 1.1 Hz, 1H, HC(4)), 6.81 (dd, *J* = 8.0, 1.2 Hz, 1H, HC(6)), 6.48 (dt, *J* = 15.9, 1.4 Hz, 1H, HC(10)), 6.33 (dt, *J* = 15.8, 6.9 Hz, 1H, HC(9)), 4.69 (s, 1H, OH), 2.84 (dd, *J* = 8.8, 6.6 Hz, 2H, HC(7)), 2.62–2.54 (app q, *J* = 7.5 Hz, 2H, HC(8)).

Preparation of (*E*)-2-(5-Phenylpent-4-en-1-yl)phenol (130b) [DJK-DR-9004]



142q **130b**

Dichloromethane was degassed by purging with argon for 30 min. To a 10-mL flask was added Grubbs-I-indenylidene catalyst (46 mg, 0.05 mmol, 0.033 equiv) in a glovebox. The flask was transferred to a Schlenk line and degassed dichloromethane (3 mL), **142q** (241 mg, 1.5 mmol) and styrene (890 μL, 7.5 mmol, 5 equiv) were added in order. The solution was stirred for 24 h, whereupon a second portion of catalyst (23 mg, 0.025 mmol, 0.016 equiv) was added. The solution was then stirred for a further 24 h. The solution was then transferred to a 100 mL RB-flask, and the volatiles were removed by rotary evaporation (30 ^{o}C. 3 mm Hg). The material was redissolved in 10 mL of CH_2Cl_2 and adsorbed onto Celite. Purification by silica gel flash column chromatography (12:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) followed by distillation afforded 150 mg (42%) of **130b** as a clear oil.

Data for **130b**:

bp: 150 ^{o}C, (ABT), 0.05 mm Hg

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

δ 7.35 (d, *J* = 8.1 Hz, 2H, HC(13)), 7.30 (t, *J* = 7.6 Hz, 2H, HC(14)), 7.20 (t, *J* = 7.2 Hz, 1H, HC(15)), 7.14 (d, *J* = 7.4 Hz, 1H, HC(3), 7.09 (t, *J* = 7.7 Hz, 1H, HC(5)), 6.88 (t, *J* = 7.4 Hz, 1H, HC(4)), 6.76 (d, *J* = 8.0 Hz, 1H, HC(6)), 6.42 (d, *J* = 16.1 Hz, 1H, HC(11), 6.26 (dt, *J* = 15.9, 6.7 Hz, 1H, HC(10), 4.65 (s, 1H, OH), 2.68 (t, *J* = 7.7 Hz, 1H, HC(7), 2.29 (q, *J* = 6.9 Hz, 1H, HC(9)), 1.82 (p, *J* = 7.4 Hz, 1H, HC(8)).

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

δ 153.8 (C1), 138.1 (C12), 130.9 (C3), 130.6 (C11), 130.5 (C10), 128.8 (C14), 128.6 (C2), 127.4 (C5), 127.2 (C15), 126.3 (C13), 121.1 (C4), 115.6 (C6), 33.0 (C9), 29.7 (C7), 29.6 (C8).

IR: (ATR, cm^{-1})

3401 (br), 3059 (w), 3025 (w), 2926 (w), 2857 (w), 1650 (w), 1592.1 (w), 1490 (m), 1454 (s), 1327 (m), 1234 (m), 1169 (w), 1104 (w), 1068 (w), 1042 (w), 1028 (w), 963 (s), 933 (w), 911 (w), 842 (w), 747 (s), 691 (s).

MS: (EI, 70 eV, m/z)

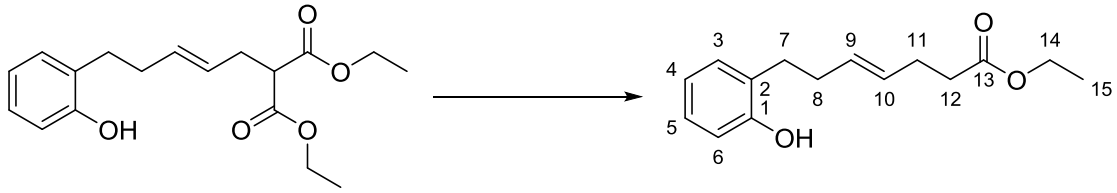
238 (100, M^{+}), 147 (45), 131 (34), 117 (42), 107 (74), 91 (43), 77 (25)

TLC: R_f 0.44 (4:1 hexanes/ethyl acetate) [UV, CAM]

Analysis: $C_{16}H_{16}O$ (224.34)

Calcd:	C, 85.67;	H, 7.61%
Found:	C, 85.27;	H, 7.43%

Preparation of Ethyl (*E*)-7-(2-Hydroxyphenyl)hept-4-enoate (138) [DJK-15-83]



137 **138**

To a 50-mL round bottom flask equipped with a stir bar was added, under argon, LiI (1.87 g, 14 mmol, 4.0 equiv) and NaCN (189 mg, 3.85 mmol, 1.1 equiv). To this was added DMSO (10 mL) and the solution was stirred for 15 min. The diester **137**[160] (1.12 g, 3.5 mmol) was then dissolved in DMSO (10 mL) and added to the stirring solution. The solution was heated to 160 ^{o}C (internal temperature, oil bath) for 3 h. Consumption of starting material was followed by TLC. The flask was then removed from the heat source and allowed to cool to rt. The solution was transferred to a 125-mL separatory funnel and diluted with water (50 mL) and ethyl acetate (50 mL). Use of other solvent ratios occasionally resulted in persistent emulsions. The layers were separated and the aq. layer was extracted with ethyl acetate (50 mL). The organic layers were washed thoroughly (5x 30 mL water) then was washed with brine (15 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation (30 ^{o}C, 3 mm Hg). The material was then redissolved in 10 mL of diethyl ether and adsorbed onto Celite. Purification by silica gel flash chromatography (7:1, hexanes/ethyl acetate, 20 mm diameter, 18 cm SiO_2) followed by bulb-to-bulb vacuum distillation afforded 476 mg (57%) of **138** as a clear oil.

Data for **138**:

bp: 130 ^{o}C, (ABT), 0.05 mm Hg

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

7.15–7.05 (m, 2H, HC(3), HC(5)), 6.87 (t, *J* = 7.4 Hz, 1H, HC(4)), 6.78 (d, *J* = 7.9 Hz, 1H, HC(6)), 5.57 (dt, *J* = 15.3, 6.7 Hz, 1H, HC(9)), 5.47 (dt, *J* = 15.3, 6.0 Hz, 1H, HC(10)), 5.24 (s, 1H, OH), 4.16 (q, *J* = 7.1 Hz, 2H, HC(14)), 2.68 (dd, *J* = 8.7, 6.7 Hz, 2H, HC(11)), 2.42–2.26 (m, 6H, HC(7), HC(8), HC(10)), 1.28 (t, *J* = 7.1 Hz, 3H, HC(15)).

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

173.8 (C13), 153.9 (C1), 131.2 (C9), 130.5 (C3), 129.1 (C10), 128.2 (C2), 127.4 (C5), 120.9 (C4), 115.6 (C6), 60.7 (C14), 34.5 (C7/C8/C10), 32.9 (C7/C8/C10), 30.4(C11), 28.1 (C7/C8/C10), 14.5 (C15).

IR: (ATR, cm^{-1})

3416 (br), 2981 (w), 2926 (w), 2854 (w), 1706 (s), 1608 (w), 1593 (w), 1504 (w), 1490 (w), 1455 (s), 1372 (m), 1344 (w), 1299 (w), 1232 (s), 1176 (s), 1150 (s), 1101 (m), 1033 (m), 968 (m), 850 (m), 751 (s).

MS: (EI, 70 eV, m/z)

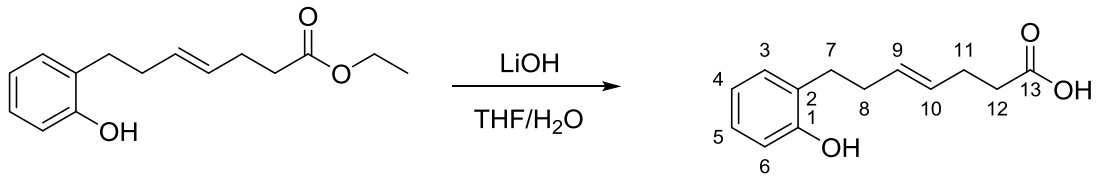
248 (29, M^+), 107 (100)

TLC: R_f 0.31 (4:1, hexanes/ethyl acetate) [UV, CAM]

Analysis: $C_{15}H_{20}O_3$ (248.32)

Calcd:	C, 72.55;	H, 8.12%
Found:	C, 72.43;	H, 8.14%

Preparation of (*E*)-7-(2-Hydroxyphenyl)hept-4-enoic acid (139) [DJK-15-34]



138 **139**

To a 10-mL Schlenk flask under argon was added ester **138** (447 mg, 1.8 mmol), and THF (10 mL). Water was added via syringe (2.5 mL) followed by solid $LiOH{\bullet}H_2O$ (272 mg, 6.48 mmol, 3.6 equiv). The solution was allowed to stir 16 h at rt. The mixture was transferred to a 60-mL separatory funnel, diluted with ether (30 mL) and water (20 mL). The biphasic mixture was acidified with 1 M HCl to pH <2, whereupon a white precipitate formed, which disappeared upon thorough shaking. The layers were separated and the aq. layer was extracted with ether (2x 15 mL). The organic layers were combined, washed with brine (15 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). The material was redissolved in 10 mL of diethyl ether and then was adsorbed onto Celite. Purification by silica gel flash column chromatography (4:1, hexanes/ethyl acetate, 30 mm diameter, 16 cm SiO_2) followed by recrystallization from hexanes (5 mL) afforded 326 mg (83%) of **139** as white spindles.

Data for **139**:

mp: 108-110 °C (hexanes)

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

δ 7.17–7.08 (m, 2H, HC(3), HC(5)), 6.91 (t, *J* = 7.4 Hz, 1H, HC(4)), 6.80 (d, *J* = 7.9 Hz, 1H, HC(2)), 5.60 (dt, *J* = 15.6, 6.5 Hz, 1H, HC(9)), 5.50 (dt, *J* = 15.4, 6.3 Hz, 1H, HC(10)), 2.70 (dd, *J* = 8.5, 6.6 Hz, 2H, HC(8)), 2.45 (t, *J* = 7.1 Hz, 2H, HC(11)), 2.35 (app p, *J* = 6.8 Hz, 4H, HC(7), HC(12)).

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

δ 179.0 (C13), 153.6 (C1), 131.4 (C10), 130.6 (C5), 128.8 (C9), 128.0 (C2) , 127.4 (C3), 121.1 (C4), 115.6 (C6), 34.1 (C11), 32.9 (C7), 30.3 (C8), 27.8 (C12)

IR: (ATR, cm^{-1})

3184 (br), 3042 (w), 2934 (w), 2908 (w), 1703 (s), 1613 (w), 1591 (m), 1503 (w), 1455 (s), 1441 (m), 1425 (m), 1409 (m), 1373 (m), 1280 (m), 1262 (w), 1236 (s), 1192 (s), 1109 (w), 1041 (w), 990 (w), 974 (s), 930 (w), 909 (w), 845 (w), 821 (m), 747 (s), 688 (w).

MS: (EI, 70 eV, m/z)

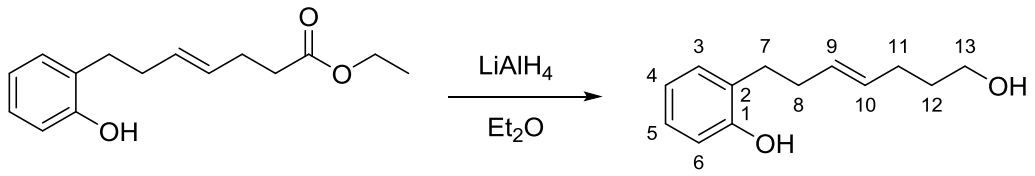
220 (16, M^+), 137 (16), 107 (100)

TLC: R_f 0.06 (4:1 hexanes/ethyl acetate) [UV, CAM]

Analysis: $C_{13}H_{16}O_3$ (220.27)

Calcd:	C, 70.89;	H, 7.32%
Found:	C, 71.12;	H, 7.24%

Preparation of (*E*)-2-(7-Hydroxyhept-3-en-1-yl)phenol (140) [DJK-15-84]



138 **140**

To a 50-mL Schlenk flask under argon was added lithium aluminium hydride (126 mg, 3.3 mmol, 1.5 equiv) and THF (4 mL). The flask was placed in an ice bath for 10 min. Ester **138**

(520 mg, 2.2 mmol) was dissolved in THF (4 mL) and added dropwise to the cold solution. The solution was then allowed to stir at 0 ^{o}C for 2 h. The flask was then once again placed in an ice bath for 15 min. The reaction was quenched by the addition of water (2 mL, dropwise) with substantial gas evolution and the formation of copious amounts of solids. After addition of water was complete, a further 5 mL of water were added, followed by dropwise addition of 6 M HCl to pH <2. The resulting biphasic mixture was transferred to a 125-mL separatory funnel and then was shaken well. The layers were separated and the aq. layer was extracted with diethyl ether (3x 20mL). The organic layers were combined, washed with brine (15 mL), dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^{o}C, 3 mm Hg). The resulting material was dissolved in 10 mL of ether and adsorbed onto Celite. Purification by silica gel flash column chromatography (3:1 hexanes/ethyl acetate, 20 mm diameter, 17 cm SiO_2) followed by bulb-to-bulb distillation afforded 416 mg (91%) of **140** as a clear oil.

Data for **140**:

bp: 140 ^{o}C, (ABT), 0.05 mm Hg

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

δ 7.17–7.07 (m, 2H, HC(3), HC(5)), 6.90 (t, *J* = 8.0 Hz, 1H, HC(4)), 6.79 (d, *J* = 8.2 Hz, 1H, HC(6)), 5.56 (dt, *J* = 15.1, 6.5 Hz, 1H, HC(9)), 5.48 (dt, *J* = 15.6, 6.5 Hz, 1H, HC(10)), 3.65 (t, *J* = 6.5 Hz, 2H, HC(13)), 2.71 (dd, *J* = 8.3, 6.8 Hz, 2H, HC(7)), 2.35 (q, *J* = 7.4 Hz, 2H, HC(8)), 2.12 (q, *J* = 6.8 Hz, 2H, HC(11)), 1.65 (p, *J* = 6.8 Hz, 2H, HC(12)).

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

δ 154.2 (C1), 130.8 (C10), 130.5 (C5), 130.3 (C9), 128.5 (C2), 127.3 (C3), 120.7 (C4), 115.7 (C6), 62.6 (C13), 33.1 (C8), 32.2 (C12), 30.3 (C7), 29.0 (C11).

IR: (ATR, cm^{-1})

3307 (br), 3033 (w), 2932 (w), 2851 (w), 1607 (w), 1592 (w), 1504 (w), 1489 (w), 1455 (m), 1354 (w), 1238 (m), 1178 (w), 1153 (w), 1094 (w), 1042 (m), 1015 (w), 968 (w) , 929 (w), 847 (w), 750 (s).

MS: (EI, 70 eV, m/z)

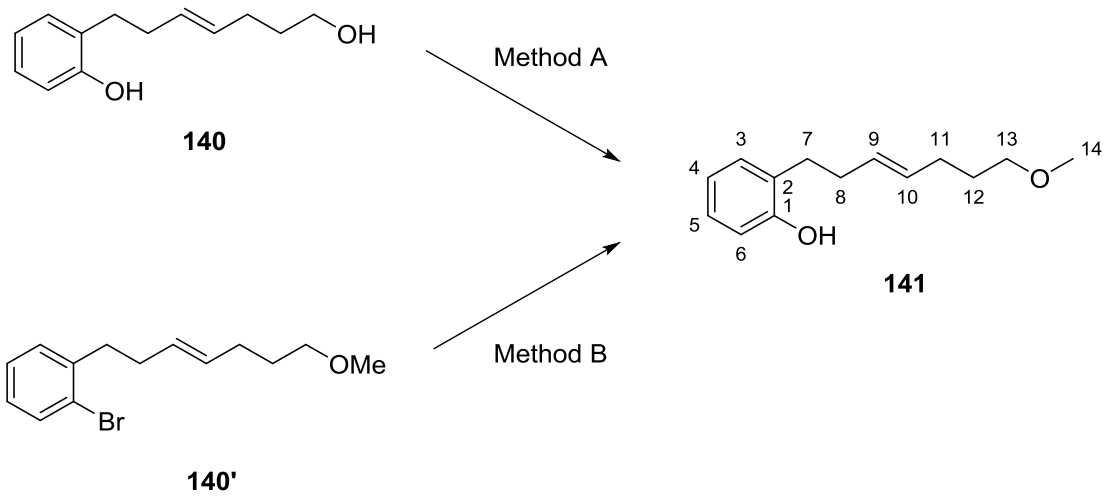
206 (20, M^{+}), 120 (14), 107 (100)

TLC: R_f 0.1 (4:1 hexanes/ethyl acetate) [UV, CAM]

Analysis: $C_{13}H_{18}O_2$ (206.29)

Calcd:	C, 75.69;	H, 8.80%
Found:	C, 75.48;	H, 8.56%

Preparation of (*E*)-2-(7-Methoxyhept-3-en-1-yl)phenol (141) [A, DJK-EK9014], [B, DJK-16-22]



This compound was prepared in two ways:

Method A:

To a 10-mL Schlenk flask in a glovebox was added NaH (27 mg, 1.1 mmol, 2.1 equiv). The flask was transferred to the Schlenk line and THF (1.5 mL) was added. To this was added the alcohol **140** (103 mg, 0.5 mmol) in THF (0.5 mL). The solution was stirred for 15 min at rt and MeI (34 μL, 0.55 mmol, 1.1 equiv) was added dropwise. The solution was then allowed to stir at rt for 16 h. The reaction was quenched by the addition of water (1 mL) and 1 M HCl (0.5 mL). The mixture was transferred to a 60-mL separatory funnel, diluted with ether (10 mL) and water (10 mL) and the pH adjusted to <2 with 3 M HCl. The layers were separated and the aq. layer was extracted with ether (2x 10 mL). The organic layers were combined, washed with brine (15 mL), dried over $MgSO_4$ and concentrated by rotary evaporation (30 ^oC, 3 mm Hg) . Purification by silica gel flash column chromatography (12:1 hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) afforded 63 mg (57%) of **141** as a clear oil.

Method B:

To a 10-mL Schlenk flask was added **140'**, (368 mg, 1.3 mmol) and THF (15 mL). The flask was cooled to -76 ^{o}C (internal temperature, dry ice/*i*-PrOH). BuLi (2.3 M, 620 μL, 1.43 mmol, 1.1 equiv) was added via syringe and the solution was allowed to stir for for 1 h. Triisopropyl borate (489 mg, 2.6 mmol, 2.0 equiv) was added via syringe and the solution was allowed to warm to rt. After stirring for 6 h at rt, the flask was placed in an ice bath. In a separate 25-mL RB-flask, a basic hydrogen peroxide solution was prepared by combining 20 mL of 30% H_2O_2 with 2 g of NaOH. A portion of this solution (2 mL) was then added dropwise to the flask containing the borate (strong exotherm) followed by the remaining 8 mL of basic peroxide and the solution allowed to stir for 5 h at rt. The excess peroxide solution was quenched with sat. aq. $Na_2S_2O_3$. After the allotted time had passed, the mixture was transferred to a 125-mL separatory funnel and sat. aq. $Na_2S_2O_3$ was added until no more peroxide was evident (Quantifix test strip). The mixture was then diluted with ether (15 mL) and water (15 mL) and acidified with 1 M HCl to pH <2. The layers were separated and the aq. layer was extracted with ether (3x 10 mL). The organic layers were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^{o}C, 3 mm Hg). Purification by silica gel flash column chromatography (12:1 hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) followed by bulb-to-bulb vacuum distillation afforded 213 mg of **141** as a clear oil (76%).

Data for **141**:

bp: 100 ^{o}C (ABT), 0.05 mm Hg

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

δ 7.15–7.05 (m, 2H, HC(3), HC(5)), 6.88 (t, *J* = 7.6 Hz, 1H, HC(4)), 6.77 (d, *J* = 8.0 Hz, 1H, HC(6)), 5.62–5.38 (m, 2H, HC(9), HC(10)), 3.45–3.32 (m, 5H, HC(13), HC(14)), 2.68 (dd, *J* = 8.6, 6.7 Hz, 2H, HC(7)), 2.32 (app q, *J* = 7.8 Hz, 2H, HC(8)), 2.11–2.01 (app q, *J* = 7.7 Hz, 2H, HC(11)), 1.64 (app p, *J* = 7.2, 6.8 Hz, 2H, HC(12)).

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

δ 153.8 (C1), 130.7 (C9), 130.5 (C5), 130.3 (C10), 128.2 (C2), 127.4 (C3), 120.9 (C4), 115.6 (C6), 72.4 (C13), 58.7 (C14), 33.0 (C8), 30.5 (C7), 29.5 (C11), 29.3 (C12).

IR: (ATR, cm^{-1})

3308 (br), 2930 (w), 2852 (w), 1607 (w), 1593 (w), 1504 (w), 1489 (w), 1455 (s), 1353 (w), 1234 (m), 1179 (m), 1099 (m), 1042 (w), 968 (m), 931 (w), 847 (w), 750 (s).

MS: (EI, 70 eV, m/z)

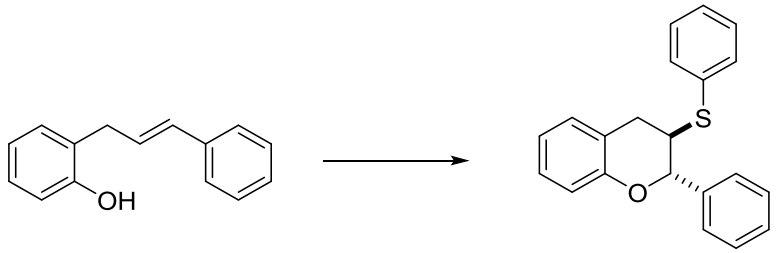
220 (17, M^+), 149 (15), 107 (100), 81 (35)

TLC: R_f 0.33 (4:1 hexanes/ethyl acetate) [UV, CAM]

Analysis: $C_{14}H_{20}O_2$ (220.31)

Calcd:	C, 76.33;	H, 9.15%
Found:	C, 76.10;	H, 8.91%

Optimization of the Phenoxysulfenylation Reaction (Table 17)

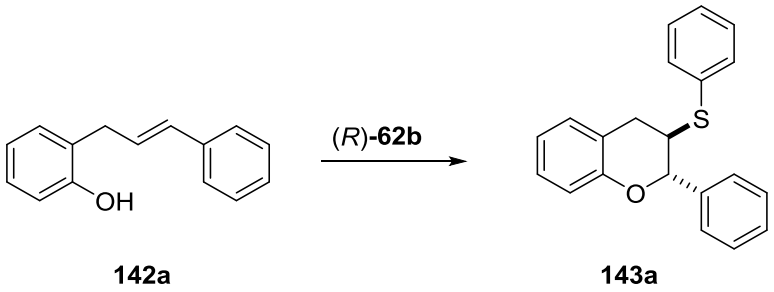


142a **143a**

General Procedure

To a 1-dram vial flushed with nitrogen and equipped with a stir bar was added the substrate followed by CH_2Cl_2. The electrophile and the catalyst were then added as solids and the solution was placed in an *i*-PrOH bath maintained at -20 ^oC by a Neslab IBC-4A cryocool for temperature control. The solution was allowed to equilibrate for 20 min and MsOH was added neat via syringe. The solution was stirred for the specified time, and then was quenched with Et_3N (50 μL).

Phenoxysulfenylation in the presence of catalyst 62b (Table 17 Entry 1) [DJK-7-26]

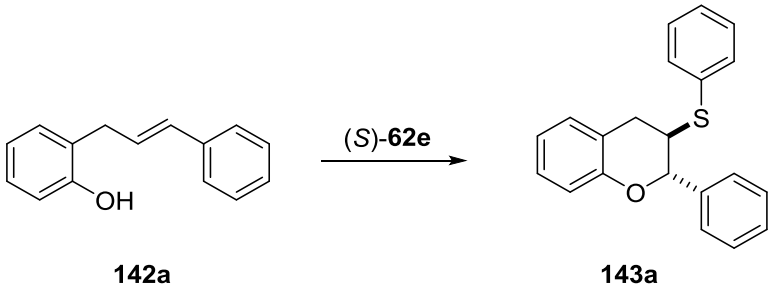


142a **143a**

Following General Procedure 10, **142a** (21 mg, 0.1 mmol), **56** (25.6 mg, 0.1 mmol, 1.0 equiv) and (*R*)-**62b** (5.2 mg, 0.01 mmol, 0.1 equiv) and CH_2Cl_2 (0.25 mL) were combined in a 1-dram vial. The vial was cooled to -20 ^oC in an *i*-PrOH bath and MsOH (5 μL, 0.077 mmol, 0.77 equiv) was added directly. The solution was stirred for 24 h, then was quenched with Et_3N (50 μL). The volatiles were removed under rotary evaporation (30 ^oC, 3 mm Hg) and the residue was then directly subjected to silica gel flash column chromatography (40:1 hexanes/ethyl acetate, 10 mm diameter, 16 cm SiO_2) to afford 11 mg (35%) of **143a** as a white solid.

CSP-SFC: (2*R*,3*S*)-**143a** t_{maj} 13.6 min, (65.6%), (2*S*,3*R*)-**143a** t_{min} 18.8 min, (34.4%) (Chiralpak AD, 220 nm, 200 bar, 40 ^oC, 95:5, sCO_2/MeOH, 2 mL/min)

Phenoxysulfenylation in the presence of catalyst 62e (Table 17 Entry 2) [DJK-7-30]

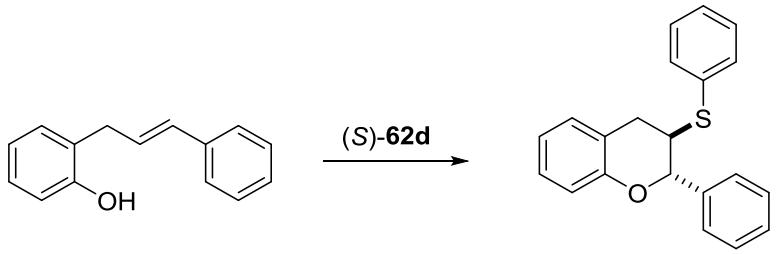


142a **143a**

Following General Procedure 10, **142a** (21 mg, 0.1 mmol), **56** (25.6 mg, 0.1 mmol, 1.0 equiv) and (*S*)-**62e** (5.2 mg, 0.01 mmol, 0.1 equiv) and CH_2Cl_2 (0.25 mL) were combined in a 1-dram v ial. The solution was cooled to -20 ^oC in an *i*-PrOH bath and MsOH (5 μL, 0.077 mmol, 0.77 equiv) was added directly. The solution was stirred for 24 h, then was quenched with Et_3N (50 μL). The volatiles were removed under rotary evaporation (30 ^oC, 3 mm Hg) and the residue was then directly subjected to silica gel flash column chromatography (40:1 hexanes/ethyl acetate, 10 mm diameter, 16 cm SiO_2) to afford 14 mg (46%) of **143a** as a white solid.

CSP-SFC: (2*R*,3*S*)-**143a** t_{min} 13.7 min, (5.1%), (2*S*,3*R*)-**143a** t_{maj} 18.9 min, (94.9%) (Chiralpak AD, 220 nm, 200 bar, 40 ^{o}C, 95:5, sCO_2/MeOH, 2 mL/min)

Phenoxysulfenylation in the presence of catalyst 62d (Table 17 Entry 3) [DJK-7-29]

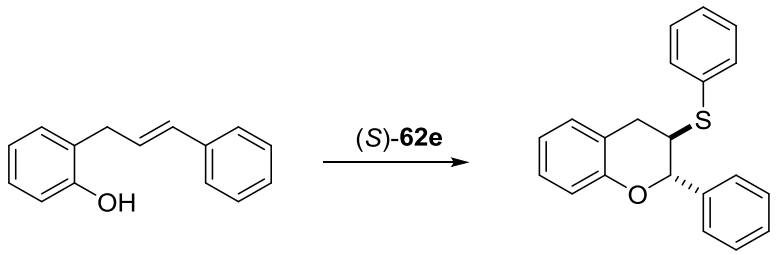


142a **143a**

Following General Procedure 10, **142a** (21 mg, 0.1 mmol), **56** (25.6 mg, 0.1 mmol, 1.0 equiv) and (*S*)-**62d** (5.5 mg, 0.01 mmol, 0.1 equiv) and CH_2Cl_2 (0.25 mL) were combined in a 1-dram vial. The solution was cooled to -20 ^{o}C in an *i*-PrOH bath and MsOH (5 μL, 0.077 mmol, 0.77 equiv) was added directly. The solution was stirred for 24 h, then was quenched with Et_3N (50 μL). The volatiles were removed under rotary evaporation (30 ^{o}C, 3 mm Hg) and the residue was then directly subjected to silica gel flash column chromatography (40:1 hexanes/ethyl acetate, 10 mm diameter, 16 cm SiO_2) to afford 9 mg (27%) of **143a** as a white solid.

CSP-SFC: (2*R*,3*S*)-**143a** t_{min} 13.6 min, (6.9%), (2*S*,3*R*)-**143a** t_{maj} 18.8 min, (93.1%) (Chiralpak AD, 220 nm, 200 bar, 40 ^{o}C, 95:5, sCO_2/MeOH, 2 mL/min)

Phenoxysulfenylation at 0.15M concentration (Table 17 Entry 4) [DJK-10-90]



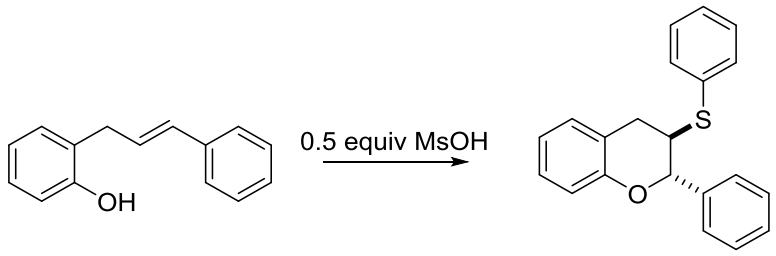
142a **143a**

Following General Procedure 10, **142a** (21 mg, 0.1 mmol), **56** (25.6 mg, 0.1 mmol, 1.0 equiv) and (*S*)-**62e** (5.2 mg, 0.01 mmol, 0.1 equiv) and CH_2Cl_2 (0.63 mL) were combined in a 1-dram vial. The solution was cooled to -20 ^{o}C in an *i*-PrOH bath and MsOH (5 μL, 0.077 mmol, 0.77 equiv) was added directly. The solution was stirred for 24 h, then was quenched with Et_3N (50 μL). The volatiles were removed under rotary evaporation (30 ^{o}C, 3 mm Hg) and the residue

was then directly subjected to silica gel flash column chromatography (5:1 hexanes/dichloromethane, 10 mm diameter, 16 cm SiO_2) to afford 29 mg (92%) of **143a** as a white solid.

CSP-SFC: (2*R*,3*S*)-**4a** t_{min} 13.6 min, (5.4%), (2*S*,3*R*)-**4a** t_{maj} 18.8 min, (94.6%), (Chiralpak AD, 220 nm, 200 bar, 40 ^{o}C, 95:5 sCO_2/MeOH, 2 mL/min)

Phenoxysulfenylation with 0.5 equiv MsOH (Table 17 Entry 5) [DJK-18-54]

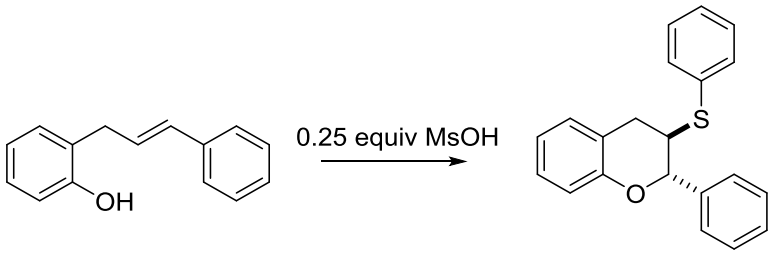


142a **143a**

Following General Procedure 10, **142a** (21 mg, 0.1 mmol), **56** (25.6 mg, 0.1 mmol, 1.0 equiv) and (*S*)-**62e** (5.2 mg, 0.01 mmol, 0.1 equiv) and CH_2Cl_2 (0.63 mL) were combined in a 1-dram vial. The solution was cooled to -20 ^{o}C in an *i*-PrOH bath and MsOH (3.3 μL, 0.051 mmol, 0.51 equiv) was added directly. The solution was stirred for 24 h, then was quenched with Et_3N (50 μL). The volatiles were removed under rotary evaporation (30 ^{o}C, 3 mm Hg) and the residue was then directly subjected to silica gel flash column chromatography (5:1 hexanes/dichloromethane, 10 mm diameter, 16 cm SiO_2) to afford 30.2 mg (95%) of **143a** as a white solid.

CSP-SFC: (2*R*,3*S*)-**143a**, t_{min} 13.7 min, (4.7%), (2*S*,3*R*)-**143a** t_{maj} 18.9 min, (95.3%) (Chiralpak AD, 220 nm, 200 bar, 40 ^{o}C, 95:5, sCO_2/MeOH, 2 mL/min)

Phenoxysulfenylation with 0.25 equiv MsOH (Table 17 Entry 6) [DJK-18-55]

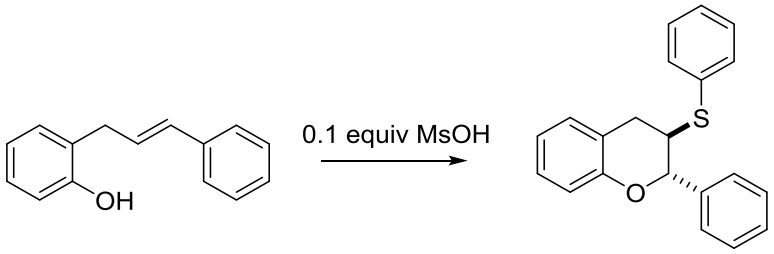


142a **143a**

Following General Procedure 10, **142a** (21 mg, 0.1 mmol), **56** (25.6 mg, 0.1 mmol, 1.0 equiv) and (*S*)-**62e** (5.2 mg, 0.01 mmol, 0.1 equiv) and CH_2Cl_2 (0.63 mL) were combined in a 1-dram vial. The solution was cooled to -20 ^oC in an *i*-PrOH bath and MsOH (1.7 μL, 0.026 mmol, 0.26 equiv) was added directly. The solution was stirred for 24 h, then was quenched with Et_3N (50 μL). The volatiles were removed under rotary evaporation (30 ^oC, 3 mm Hg) and the residue was then directly subjected to silica gel flash column chromatography (5:1 hexanes/dichloromethane, 10 mm diameter, 16 cm SiO_2) to afford 29.8 mg (94%) of **143a** as a white solid.

CSP-SFC: (2*R*,3*S*)-**143a** t_{min} 13.4 min, (4.3%), (2*S*,3*R*)-**143a** t_{maj} 16.0 min, (95.7%) (Chiralpak AD, 220 nm, 200 bar, 40 ^oC, 95:5 sCO_2/MeOH, 2 mL/min)

Phenoxysulfenylation with 0.1 equiv MsOH (Table 17 Entry 7) [DJK-18-56]



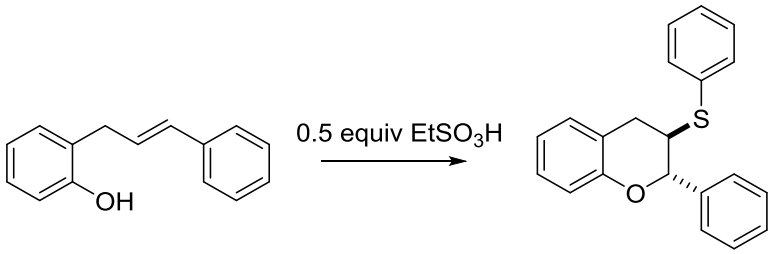
142a **143a**

Following General Procedure 10, **142a** (21 mg, 0.1 mmol), **56** (25.6 mg, 0.1 mmol, 1.0 equiv) and (*S*)-**62e** (5.2 mg, 0.01 mmol, 0.1 equiv) and CH_2Cl_2 (0.63 mL) were combined in a 1-dram vial. The solution was cooled to -20 ^oC in an *i*-PrOH bath and MsOH (0.65 μL, 0.010 mmol, 0.10 equiv) was added directly. The solution was stirred for 24 h, then was quenched with Et_3N (50 μL). The volatiles were removed under rotary evaporation (30 ^oC, 3 mm Hg) and the residue was then directly subjected to silica gel flash column chromatography (5:1

hexanes/dichloromethane, 10 mm diameter, 16 cm SiO_2) to afford 10.3 mg (32%) of **143a** as a white solid (32%). 10.7 mg (51%) of **142a** was recovered as well.

CSP-SFC: (2*R*,3*S*)-**143a** t_{min} 13.4 min, (5.1%), (2*S*,3*R*)-**143a** t_{maj} 16.0 min, (94.9%) (Chiralpak AD, 220 nm, 200 bar, 40 ^{o}C, 95:5, sCO_2/MeOH, 2 mL/min)

Phenoxysulfenylation with 0.5 equiv $EtSO_3H$ (Table 17 Entry 8) [DJK-18-57]



142a **143a**

Following General Procedure 10, **142a** (21 mg, 0.1 mmol), **56** (25.6 mg, 0.1 mmol, 1.0 equiv) and (*S*)-**62e** (5.2 mg, 0.01 mmol, 0.1 equiv) and CH_2Cl_2 (0.63 mL) were combined in a 1-dram vial. The solution was cooled to -20 ^{o}C in an *i*-PrOH bath and $EtSO_3H$ (4 μL, 0.049 mmol, 0.49 equiv) was added directly. The solution was stirred for 24 h, then was quenched with Et_3N (50 μL). The volatiles were removed under rotary evaporation (30 ^{o}C, 3 mm Hg) and the residue was then directly subjected to silica gel flash column chromatography (5:1 hexanes/dichloromethane, 10 mm diameter, 16 cm SiO_2) to afford 30.6 mg (96%) of **143a** as a white solid.

CSP-SFC: (2*R*,3*S*)-**143a** t_{min} 13.4 min, (5.7%), (2*S*,3*R*)-**143a** t_{maj} 16.0 min, (94.3%) (Chiralpak AD, 220 nm, 200 bar, 40 ^{o}C, 95:5 sCO_2/MeOH, 2 mL/min)

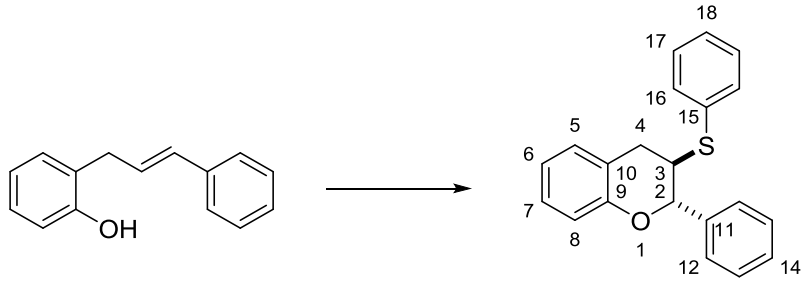
Descriptive Phenoxysulfenylation of Alkenes (Table 18)

General Procedure

To a 10-mL, oven-dried flask equipped with a magnetic stir bar under an argon atmosphere was added substrate and CH_2Cl_2. The catalyst and the electrophile were added as solids and allowed to dissolve to obtain a clear or pale yellow solution. The reaction vessel was placed in an *i*-PrOH bath kept at constant temperature by means of a Neslab IBC-4A cryocool with probe. The reaction mixture was cooled to the appropriate reaction temperature and the

internal temperature was checked. After the temperature stabilized to +/- 2 ^{o}C, MsOH was added to the stirring reaction mixture via syringe. (Note: It is important to not let the acid touch the walls of the reaction vessel as it may immediately freeze.) After addition of the acid, rapid formation of a yellow color can be observed. The reaction mixture was then stirred for the appropriate time. Over the course of the reaction, white crystals of phthalimide precipitate out of the mixture. After the reaction is complete as judged by TLC and ^{1}H NMR spectroscopy, Et_3N was added directly to the cold reaction mixture. The flask was then allowed to warm to rt, whereupon the white crystals slowly dissolve to afford a homogenous solution. This solution was then either: (1) poured into a separatory funnel containing 1 M NaOH solution, shaken well, extracted with dichloromethane, dried and concentrated or (2) directly concentrated. Subsequently ^{1}H NMR spectra of the crude residue was recorded. Products were purified by silica flash chromatography and analytically pure samples were obtained by recrystallization or distillation as specified.

Preparation of (2*S*,3*R*)-2-Phenyl-3-(phenylthio)chromane (143a) (Table 18 Entry 1) [DJK-13-98]



142a **143a**

Following General Procedure 11, **142a** (210 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to -20 ^oC (probe). After equilibration (ca. 20 min), MsOH (17 μL, 0.25 mmol, 0.25 equiv) was added directly via syringe. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^1H NMR), the reaction was quenched with triethylamine (300 μL) and allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, then was diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). Purification by silica gel flash column chromatography (40:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) followed by recrystallization from hexanes (3 mL) afforded, in two crops, 268 mg (84%) of **143a** as white needles.

Data for **143a**:

mp: 121-122 ^oC (hexanes)

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

δ 7.41–7.32 (m, 5 H, HC(aryl)), 7.30 (m, 2H, HC(aryl)), 7.26 (m, 3 H, HC(aryl)), 7.20 (t, *J* = 7.8 Hz, 1H, HC(7)), 7.08 (d, *J* = 7.5 Hz, 1H, HC(5)), 6.97 (d, *J* = 8 Hz, 1H, HC(8)), 6.94 (t, *J* = 8 Hz, 1H, HC(6)), 5.09 (d, *J* = 7.8 Hz, 1H, HC(2)), 3.81 (ddd, *J* = 9.5, 7.7, 5.2 Hz, 1H, HC(3)), 3.15 (dd, *J* = 16.6, 5.1 Hz, 1H, HC(4)), 2.99 (dd, *J* = 16.6, 9.1 Hz, 1H, HC(4))

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

δ 154.3 (C9), 139.4 (C15), 133.7 (C11), 133.3 (C17), 129.5 (C5), 129.1 (C13), 128.6 (C12), 128.6 (C14), 128.1 (C7), 127.7 (C18), 127.3 (C16), 121.0 (C6), 120.7 (C10), 116.8 (C8), 81.2 (C2), 47.2 (C3), 31.8 (C4).

IR: (ATR, cm^{-1})

2912 (w), 1583 (w), 1487 (m), 1449 (w), 1439 (w), 1427 (w), 1306 (w), 1277 (w), 1222 (m), 1205 (w), 1193 (w), 1150 (w), 1111 (w), 1086 (w), 1069 (w), 1024 (w), 1000 (m), 969 (w), 904 (w), 851 (w), 831 (w), 797 (w), 757 (s), 750 (s), 727 (w), 716 (m), 700 (s).

MS: (EI, 70 eV, m/z)

318 (36, M^+), 208 (40), 200 (100), 199 (98), 119 (19)

TLC: R_f 0.48 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

Opt. Rot.: $[\alpha]_D^{23}$ = -40.0 (c = 0.87, $CHCl_3$)

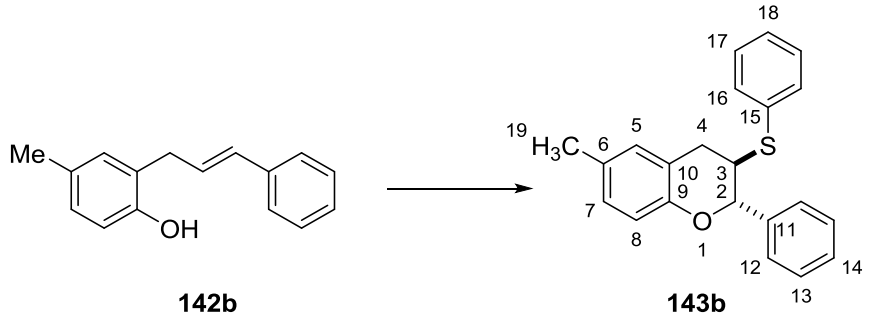
CD: (-), Cotton sign, 230-280 nm

CSP-SFC: (2*R*,3*S*)-**143a** t_{min} 13.4 min, (5.1%), (2*S*,3*R*)-**143a** t_{maj} 18.5 min, (94.9%) (Chiralpak AD, 220 nm, 200 bar, 40 °C, 95:5, sCO_2/MeOH, 2 mL/min)

Analysis: $C_{21}H_{18}OS$ (318.43)

Calcd:	C, 79.21;	H, 5.70%
Found:	C, 78.91;	H, 5.62%

Preparation of (2*S*,3*R*)-6-Methyl-2-phenyl-3-(phenylthio)chromane (143b) (Table 18 Entry 2) [DJK-CV-1410]



142b **143b**

Following General Procedure 11, **142b** (224 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-

PrOH bath and cooled to -20 °C (probe). After equilibration (ca. 20 min), MsOH (17 μL, 0.25 mmol, 0.25 equiv) was added directly via syringe. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^{1}H NMR), the reaction was quenched with triethylamine (300 μL) and the mixture was then allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, then was diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 °C, 3 mm Hg). Purification by silica gel flash column chromatography (4:1, hexanes/$CHCl_3$ to 3:1, hexanes/$CHCl_3$, 20 mm diameter, 20 cm SiO_2) followed by recrystallization from hexanes (3 mL) afforded, in two crops, 272 mg (82%) of **143b** as white needles.

Data for **143b**:

mp: 114-115 °C (hexanes)

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

δ 7.40–7.29 (m, 7H, HC(aryl)), 7.27–7.23 (m, 3H, HC(aryl))), 7.00 (d, *J* = 8.5 Hz, 1H, HC(7)), 6.88, (s, 1H, HC(5)), 6.87 (d, *J* = 8.5 Hz, 1H, HC(8)), 5.06 (d, *J* = 7.7 Hz, 1H, HC(2)), 3.80 (ddd, *J* = 8.8, 7.6, 5.2 Hz, 1H, HC(3)), 3.09 (dd, *J* = 16.6, 5.2 Hz, 1H, HC(4)), 2.95 (dd, *J* = 16.6, 8.9 Hz, 1H, HC(4)), 2.31 (s, 3H, HC(19)).

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

δ 152.1 (C9), 139.6 (C15), 133.8 (C11), 133.2 (C17), 130.2 (C6), 129.9 (C5), 129.1 (C13), 128.7 (C7), 128.6 (C12), 128.5 (C14), 127.7 (C18), 127.3 (C16), 120.3 (C10), 116.5 (C8), 81.1 (C2), 47.3 (C3), 31.7 (C4), 20.8 (C19).

IR: (ATR, cm^{-1})

2923 (w), 1588 (w), 1497 (m), 1474 (w), 1457 (w), 1436 (w), 1301 (w), 1239 (m), 1227 (s), 1148 (w), 1127 (w), 1027 (w), 988 (m), 937 (w), 909 (w), 880 (w), 852 (w), 831 (m), 818 (w), 798 (w), 745 (s), 729 (w), 691 (s).

MS: (EI, 70 eV, m/z)

332 (60, M^+), 200 (88), 199 (80), 133 (60), 91 (100)

TLC: R_f 0.67 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

Opt. Rot.: $[\alpha]_D^{23}$ = -32.9 (c = 0.88 in $CHCl_3$)

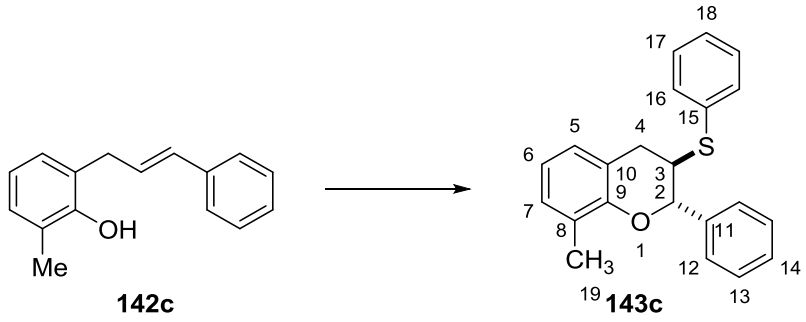
CD: (-), Cotton sign, 230-280 nm

CSP-SFC: (2*R*,3*S*)-**143b** t_{min} 10.2 min (5.0%), (2*S*,3*R*)-**143b** t_{maj} 14.3 min (95.0%) (Chiralpak AD, 220 nm, 200 bar, 40 °C, 85:15 sCO_2/MeOH, 2 mL/min)

Analysis: $C_{22}H_{20}OS$ (332.46)

Calcd:	C, 79.48;	H, 6.06%
Found:	C, 79.15;	H, 5.97%

Preparation of (2*S*,3*R*)-8-Methyl-2-phenyl-3-(phenylthio)chromane (143c) (Table 18 Entry 3) [DJK-CV-1411]



Following General Procedure 11, **142c** (224 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to -20 °C (probe). After equilibration (ca. 20 min), MsOH (17 μL, 0.25 mmol, 0.25 equiv) was added directly via syringe. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^{1}H NMR), the reaction was quenched with triethylamine (300 μL) and the mixture was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 °C, 3 mm Hg). Purification by silica gel flash column chromatography (60:1, hexanes/ethyl acetate then 40:1, hexanes/ethyl acetate, 30 mm diameter, 16 cm SiO_2) afforded a white solid. Recrystallization from hexanes (3 mL) afforded, in two crops, 259 mg (78%) of **143c** as white needles (78%).

Data for **143c**:

mp: 89-90 °C (hexanes)

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

δ 7.38–7.30 (m, 5H, HC(aryl)), 7.28 (d, *J* = 2.1 Hz, 2H, HC(aryl)), 7.25–7.19 (m, 3H, HC(aryl)), 7.05 (d, *J* = 7.5 Hz, 1H, HC(5)), 6.88 (dd, *J* = 7.7, 1.9 Hz, 1H, HC(7)), 6.81 (t, *J* = 7.4 Hz, 1H, HC(6)), 5.11 (d, *J* = 7.6 Hz, 1H, HC(2)), 3.75 (ddd, *J* = 8.9, 7.5, 5.0 Hz, 1H, HC(3)), 3.08 (dd, *J* = 16.6, 5.1 Hz, 1H, HC(4)), 2.95 (dd, *J* = 16.5, 8.8 Hz, 1H, HC(4)), 2.23 (s, 3H, HC(19)).

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

δ 152.4 (C9), 139.9 (C15), 133.9 (C11), 133.0 (C17), 129.2 (C5), 129.2 (C16), 128.6 (C13), 128.4 (C18), 127.6 (C14), 127.1 (C7, C16), 126.0 (C10), 120.4 (C6), 120.1 (C8), 81.0 (C2), 47.3 (C3), 31.8 (C4), 16.4 (C19).

IR: (ATR, cm^{-1})

1594 (w), 1467 (m), 1432 (w), 1379 (w), 1304 (w), 1259 (w), 1239 (w), 1204 (s), 1101 (w), 1072 (w), 1026 (w), 985 (m), 959 (w), 924 (w), 910 (w), 828 (w), 798 (w), 757 (s), 744 (s), 728 (m), 699 (s).

MS: (EI, 70 eV, m/z)

332 (43, M^+), 222 (48), 200 (100), 199 (60), 149 (20), 133 (41)

TLC: R_f 0.77 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

Opt. Rot.: $[\alpha]_D^{23}$ = -4.5 (c = 0.88 in $CHCl_3$)

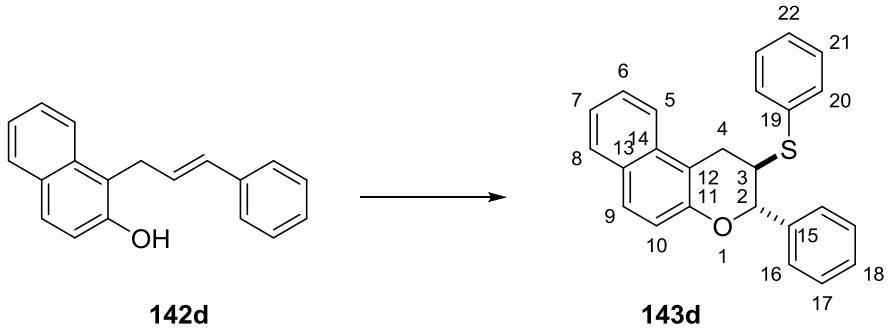
CD: (-), Cotton sign, 230-280 nm

CSP-SFC: (2*R*,3*S*)-**143c** t_{min} 10.5 (4.0%), (2*S*,3*R*)-**143c** t_{maj} 11.8 (96.0%) (Chiralpak AD, 220 nm, 200 bar, 40 °C, 95:5, sCO_2/MeOH, 2 mL/min)

Analysis: $C_{22}H_{20}OS$ (332.46)

Calcd:	C, 79.48;	H, 6.06%
Found:	C, 79.54;	H, 6.19%

Preparation of (2*R*,3*S*)-3-Phenyl-2-(phenylthio)-2,3-dihydro-1H-benzo[f]chromene (4d) (Table 18 Entry 4) [DJK-12-57]



142d **143d**

Following General Procedure 11, **143d** (260 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to -20 ^oC (probe). After equilibration (ca. 20 min), MsOH (17 μL, 0.25 mmol, 0.25 equiv) was added directly via syringe. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^1H NMR), the reaction was quenched with triethylamine (300 μL) and then was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). Purification by silica gel flash column chromatography (60:1, hexanes/ethyl acetate then 40:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) followed by recrystallization (hexanes, 3 mL, ether, 0.2 mL) afforded, in two crops, 290 mg (79%) of **143d** as pale pink prisms.

Data for **143d**:

mp: 136-138 ^{o}C (hexanes/ether)

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

δ 7.83 (d, *J* = 7.8 Hz, 1H, HC(5)), 7.77 (d, *J* = 8.5, 1H, HC(8)), 7.72 (d, *J* = 8.9 Hz, 1H, HC(9)), 7.53 (dd, *J* = 8.3, 7.0 Hz, 1H, HC(7)), 7.46–7.38 (m, 4H, HC(aryl), HC(6)), 7.38–7.27 (m, 4H, HC(aryl)), 7.27–7.22 (m, 3H HC(aryl)), 7.19 (d, 1H, 8.9 Hz, HC(10)), 5.15 (d, *J* = 8.0 Hz, 1H, HC(2)), 3.95 (ddd, *J* = 8.9, 8.0, 5.6, 1H, HC(3)), 3.49 (dd, *J* = 16.8, 5.6 Hz, 1H, HC(4)), 3.26 (dd, *J* = 16.8, 8.9 Hz, 1H, HC(4)).

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

δ 152.0 (C11), 139.1 (C19), 133.9 (C14), 133.3 (C21), 132.9 (C12), 129.4 (C13), 129.2 (C17), 128.8 (C18), 128.7 (C5), 128.7 (C16), 128.6 (C9), 127.8 (C22), 127.5 (C20), 126.9 (C7), 123.8 (C6), 122.0 (C8), 118.9 (C10), 112.7 (C12), 81.2 (C2), 47.4 (C3), 28.9 (C4).

IR: (ATR, cm^{-1})

3054 (w), 1621 (w), 1596 (m), 1508 (w), 1466 (m), 1456 (w), 1433 (m), 1397 (m), 1259 (w), 1227 (s), 1166 (m), 1140 (w), 1080 (w), 1066 (m), 1024 (w), 991 (s), 971 (s), 913 (w), 862 (w), 847 (w), 818 (s), 801 (m), 767 (s), 746 (s), 736 (s), 703 (s).

MS: (EI, 70 eV, m/z)

368 (65, M^+), 318 (25), 258 (44), 208 (32), 200 (97), 199 (100), 169 (49), 168 (46)

TLC: R_f 0.74 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

Opt. Rot.: $[\alpha]_D^{23}$ = -89.4 (c = 0.86 in $CHCl_3$)

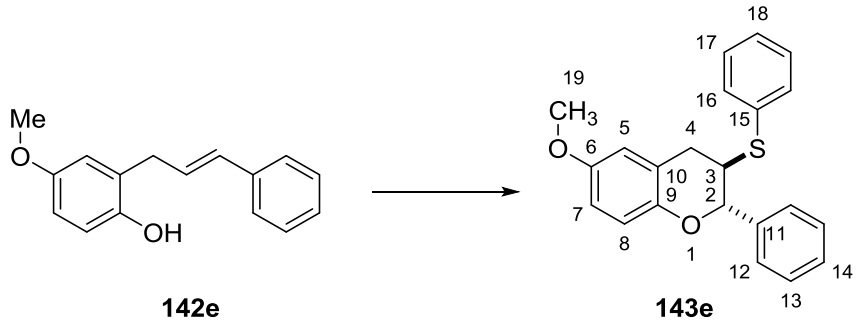
CD: (-), Cotton sign, 230-280 nm

CSP-HPLC: (2*S*,3*R*)-**143d** t_{min} 11.3 (6.8%), (2*R*,3*S*)-**143d** t_{maj} 17.6 (93.2%) (Chiralpak AD, 220 nm, 95:5, hexanes/*i*-PrOH, 0.8 mL/min)

Analysis: $C_{25}H_{20}OS$ (368.49)

Calcd:	C, 81.49;	H, 5.47%
Found:	C, 81.32;	H, 5.50%

Preparation of (2*S*,3*R*)-6-Methoxy-2-phenyl-3-(phenylthio)chromane (4e) (Table 18 Entry 5) [DJK-CV-1412]



142e **143e**

Following General Procedure 11, **142e** (240 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to -20 ^oC (probe). After equilibration (ca. 20 min), MsOH (17 μL, 0.25 mmol, 0.25 equiv) was added directly via syringe. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^1H NMR), the reaction was quenched with triethylamine (300 μL) and the mixture was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, then was diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). Purification by silica gel flash column chromatography (60:1, hexanes/ethyl acetate to 40:1, hexanes/ethyl acetate, 30 mm diameter, 18 cm SiO_2) followed by recrystallization from hexanes (3 mL) afforded, in two crops, 293 mg (84%) of **143e** white needles.

Data for **143e**:

mp: 128-129 ^oC (hexanes)

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

δ 7.42–7.26 (m, 7H, HC(aryl)), 7.25–7.19 (m, 3H, HC(aryl)), 6.87 (d, *J* = 8.9 Hz, 1H, HC(8)), 6.75 (dd, *J* = 8.9, 2.8 Hz, 1H, HC(7)), 6.58 (d, *J* = 3.1, 1H, HC(5)), 5.02 (dd, *J* = 7.7, 1.2 Hz, 1H, HC(2)), 3.83–3.72 (m, 4H, HC(3), HC(19)), 3.09 (dd, *J* = 16.7, 5.2 Hz, 1H, HC(4)), 2.95 (dd, *J* = 16.7, 8.9 Hz, 1H, HC(4)).

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

δ 153.9 (C9), 148.3 (C6), 139.5 (C15), 133.7 (C11), 133.2 (C17), 129.1 (C13), 128.6 (C12), 128.6 (C14), 127.7 (C18), 127.3 (C16), 121.3 (C10), 117.5 (C8), 114.2 (C7), 113.9 (C5), 81.1 (C2), 56.0 (C19), 47.2 (C3), 32.1 (C4).

IR: (ATR, cm^{-1})

2835 (w), 1583 (w), 1496 (m), 1457 (w), 1429 (m), 1293 (w), 1245 (w), 1224 (s), 1209 (s), 1151 (m), 1122 (w), 1086 (w), 1040 (s), 994 (s), 934 (w), 909 (w), 875 (w), 851 (w), 820 (m), 787 (w), 742 (s), 727 (s).

MS: (EI, 70 eV, m/z)

348 (69, M^+), 199 (42), 149 (56), 91 (100)

TLC: R_f 0.44 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

Opt. Rot.: $[\alpha]_D^{23}$ = -36.2 (c = 0.96 in $CHCl_3$)

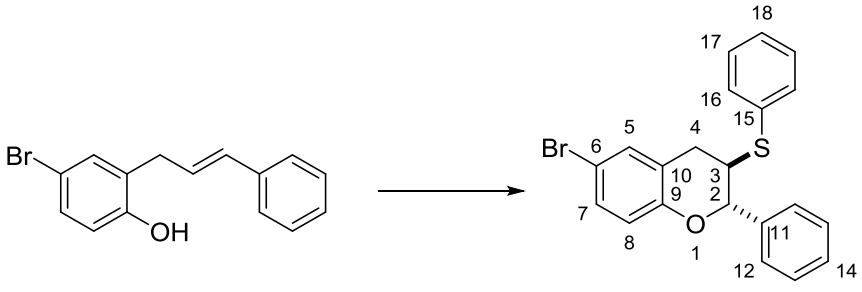
CD: (-), Cotton sign, 230-280 nm

CSP-SFC: (2*R*,3*S*)-**143e** t_{min} 13.9 min (5.6%), (2*S*,3*R*)-**143e** t_{maj} 16.0 min (94.4%) (Chiralpak AD, 220 nm, 200 bar, 40 °C, 85:15, sCO_2/MeOH, 2mL/min)

Analysis: $C_{22}H_{20}O_2S$ (348.46)

Calcd:	C, 75.83;	H, 5.79%
Found:	C, 76.04;	H, 5.57%

Preparation of (2*S*,3*R*)-6-Bromo-2-phenyl-3-(phenylthio)chromane (4f) (Table 18 Entry 6) [DJK-12-58]



142f **143f**

Following General Procedure 11, **142f** (289 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to -20 °C (probe). After equilibration (ca. 20 min), MsOH (17 μL, 0.25

mmol, 0.25 equiv) was added directly via syringe. The solution was allowed to stir for 36 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^{1}H NMR), the reaction was quenched with triethylamine (300 μL) and the mixture was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, then was diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^{o}C, 3 mm Hg). Purification by silica gel flash column chromatography (60:1, hexanes/ethyl acetate, then 40:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) followed by recrystallization (hexanes, 3 mL, ether, 0.2 mL), afforded, in two crops, 320 mg (81%) of **143f** a white solid.

Data for **143f**:

mp: 138-139 ^{o}C (hexanes/ether)

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

δ 7.40–7.24 (m, 11H, HC(aryl), HC(7)), 7.19 (d, *J* = 2.4 Hz, 1H, HC(5)), 6.85 (d, *J* = 8.7 Hz, 1H, HC(8)), 5.10 (d, *J* = 7.3 Hz, 1H, HC(2)), 3.77 (ddd, *J* = 8.7, 7.3, 5.1 Hz, 1H, HC(3)), 3.07 (dd, *J* = 16.8, 5.1 Hz, 1H, HC(4)), 2.92 (dd, *J* = 16.7, 8.5 Hz, 1H, HC(4)).

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

δ 153.4 (C9), 139.1 (C15), 133.4 (C17), 133.3 (C11), 132.1 (C5), 131.0 (C7), 129.2 (C13), 128.7 (C12, C14), 128.0 (C18), 127.0 (C16), 122.8 (C6), 118.6 (C8), 113.0 (C10), 81.0 (C2), 46.7 (C3), 31.0 (C4).

IR: (ATR, cm^{-1})

3037 (w), 1573 (w), 1473 (m), 1432 (w), 1405 (w), 1288 (w), 1232 (s), 1182 (m), 1121 (m), 1088 (w), 1067 (w), 1027 (w), 977 (m), 935 (w), 911 (w), 890 (m), 866 (m), 844 (w), 830 (w), 815 (w), 799 (w), 776 (w), 743 (s), 699 (s).

MS: (EI, 70 eV, m/z)

397 (18, M^+), 395 (18, M^+), 199 (100), 91 (88)

TLC: R_f 0.44 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

Opt. Rot.: $[\alpha]_D^{23}$ = -49.2 (c = 0.84 in $CHCl_3$)

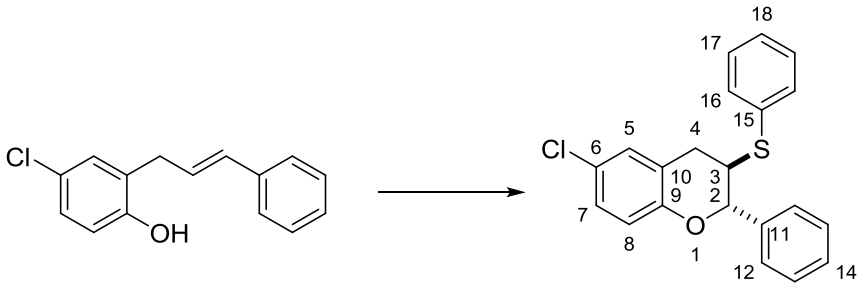
CD: (-), Cotton sign, 230-280 nm

CSP-HPLC: (2*R*,3*S*)-**143f**, t_{min} 9.3 (6.2%), (2*S*,3*R*)-**143f**, t_{maj} 10.4 (93.8%) (Chiralpak AD, 220 nm, 95:5, hexanes/*i*-PrOH, 0.8 mL/min)

Analysis: $C_{21}H_{17}BrOS$ (397.33)

Calcd:	C, 63.48;	H, 4.31%
Found:	C, 63.38;	H, 4.30%

Preparation of (2*S*,3*R*)-6-Chloro-2-phenyl-3-(phenylthio)chromane (4g) (Table 18 Entry 7) [DJK-17-19]



Following General Procedure 11, **142g** (245 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to -20 ^oC (probe). After equilibration (ca. 20 min), MsOH (17 μL, 0.25 mmol, 0.25 equiv) was added directly via syringe. The solution was allowed to stir for 36 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^1H NMR), the reaction was quenched with triethylamine (300 μL) and the mixture was allowed to warm to rt, whereupon the white solid dissolved. The material was transferred to a 250-mL RB-flask using 20 mL CH_2Cl_2 and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). The material was then redissolved in 10 mL of CH_2Cl_2 and then adsorbed onto Celite. Purification by silica gel flash column chromatography (5:1, hexanes/CH_2Cl_2, 20 mm diameter, 16 cm SiO_2) followed by recrystallization from hexanes (3 mL) afforded, in two crops, 248 mg (70%) of **143g** as white needles.

Data for **143g**:

mp: 144-145 ^{o}C (hexanes)

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

δ 7.38–7.29 (m, 7H, HC(aryl)), 7.29–7.25 (m, 3H, HC(aryl)), 7.15 (dd, *J* = 8.7, 2.5 Hz, 1H, HC(7)), 7.04 (d, *J* = 2.6 Hz, 1H, HC(5)), 6.90 (d, *J* = 8.7, 1H, HC(8)), 5.09 (d, *J* = 7.3 Hz, 1H, HC(2)), 3.77 (ddd, *J* = 8.5, 7.3, 5.1 Hz, 1H, HC(3)), 3.07 (dd, *J* = 16.8, 5.1 Hz, 1H, HC(4)), 2.92 (dd, *J* = 16.8, 8.5 Hz, 1H, HC(4)).

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

δ 152.9 (C9), 148.7 (C6) 139.1 (C15), 133.4 (C17), 133.3 (C11), 129.2 (C13), 129.1 (C5), 128.7 (C12), 128.1 (C7), 128.0 (C14/C18), 127.0 (C16), 125.7 (C14/C18), 122.2 (C10), 118.1 (C8), 81.0 (C2), 46.7 (C3), 31.2 (C4).

IR: (ATR, cm^{-1})

3059 (w), 1578 (w), 1476 (m), 1432 (w), 1411 (w), 1290 (w), 1235 (s), 1187 (m), 1123 (m), 1068 (w), 1027 (w), 981 (m), 935 (m), 898 (m), 875 (s), 849 (w), 831 (m), 794 (w), 781 (w), 743 (s), 699 (s).

MS: (EI, 70 eV, m/z)

354 (12, M^+), 352 (20, M^+), 247 (44), 199 (89), 149 (36), 133 (41), 107 (23), 91 (80)

TLC: R_f 0.45 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

Opt. Rot.: $[\alpha]_D^{23}$ = -42.6 (c =1.12 in $CHCl_3$)

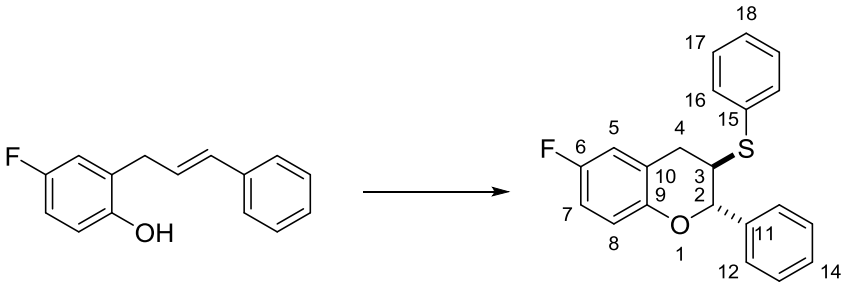
CD: (-), Cotton sign, 230-280 nm

CSP-HPLC: (2*R*,3*S*)-**143g** t_{min} 9.2 (6.2%), (2*S*,3*R*)-**143g** t_{min} 12.4 (93.8%) (Chiralpak AD, 220 nm, 95:5, hexanes/*i*-PrOH, 0.8 mL/min)

Analysis: $C_{21}H_{17}ClOS$ (352.88)

Calcd:	C, 71.48;	H, 4.86%
Found:	C, 71.73;	H, 5.11%

Preparation of (2*S*,3*R*)-6-Fluoro-2-phenyl-3-(phenylthio)chromane (143h) (Table 18 Entry 8) [DJK-CV-1409]



142h **143h**

Following General Procedure 11, **142h** (228 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to -20 ^oC (probe). After equilibration (ca. 20 min), MsOH (17 μL, 0.25 mmol, 0.25 equiv) was added directly via syringe. The solution was allowed to stir for 36 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^1H NMR), the reaction was quenched with triethylamine (300 μL) and the mixture was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). Purification by silica gel flash column chromatography (6:1, hexanes/$CHCl_3$ then 4:1, then 3:1, hexanes/$CHCl_3$, 20 mm diameter, 17 cm SiO_2) followed by recystallization from hexanes (3 mL) afforded, in two crops, 289 mg (86%) of **143h** as white needles.

Data for **143h**:

mp: 111-112 ^oC (hexanes)

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

δ 7.38–7.32 (m, 5H, HC(aryl)), 7.30 (m, 2H, HC(aryl)), 7.28–7.24 (m, 3H, HC(aryl)), 6.93–6.88 (m, 2H, HC(8), HC(5)), 6.81–6.74 (d, *J* = 8.4 Hz, 1H, HC(7)), 5.07 (d, *J* = 7.6 Hz, 1H, HC(2)), 3.78 (ddd, *J* = 8.6, 7.5, 5.2 Hz, 1H, (HC(3)), 3.10 (dd, *J* = 16.9, 5.2 Hz, 1H, HC(4)), 2.95 (dd, *J* = 16.8, 8.8 Hz, 1H, HC(4)).

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

δ 157.2 (d, *J* = 238.9 Hz, C6), 150.3 (C9), 139.2 (C15), 133.4 (C11), 133.4 (C17), 129.2 (C13), 128.7 (C12,C14), 127.9 (C18), 127.2 (C16), 121.8 (d, *J* = 7.4 Hz, C10), 117.7 (d, *J* = 8.1 Hz, C8), 115.4 (d, *J* = 22.8 Hz, C7), 114.9 (d, *J* = 23.2 Hz, C5), 81.1 (C2), 46.8 (C3), 31.7 (C4).

^{19}F NMR: (470 MHz, $CDCl_3$)

δ -124.03 (app q, *J* = 7.3 Hz).

IR: (ATR, cm^{-1})

3072 (w), 1580 (w), 1491 (s), 1473 (m), 1458 (w), 1438 (w), 1429 (m), 1374 (w), 1332 (w), 1283 (w), 1240 (m), 1222(s), 1203 (s), 1140 (m), 1103 (w), 1087 (w), 1067 (w), 1036 (w), 984 (s), 948 (m), 933 (m), 911 (w), 873 (m), 850 (m), 827 (m), 792 (m), 744 (s), 730 (s).

MS: (EI, 70 eV, m/z)

336 (33, M^+), 226 (27), 199 (100), 91 (93)

TLC: R_f 0.49 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

Opt. Rot.: $[\alpha]_D^{23}$ = -23.4 (c = 0.94 in $CHCl_3$)

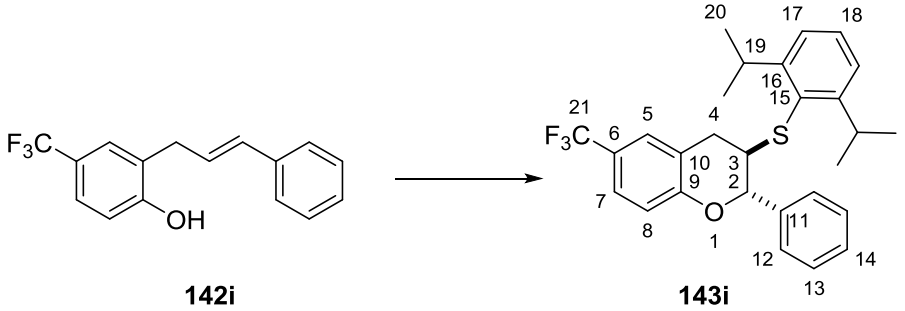
CD: (-), Cotton sign, 230-280 nm

CSP-SFC: (2*R*,3*S*)-**143h** t_{min} 9.0 min (6.8%), (2*S*,3*R*)-**143h** t_{maj} 11.6 min (93.2%) (Chiralpak AD, 220 nm, 95:5, hexanes/*i*-PrOH, 0.8 mL/min)

Analysis: $C_{21}H_{17}FOS$ (336.42)

Calcd:	C, 74.97;	H, 5.09%
Found:	C, 74.73;	H, 5.02%

Preparation of (2*S*,3*R*)-3-((2,6-Diisopropylphenyl)thio)-2-phenyl-6-(trifluoromethyl)chromane (143i) (Table 18 Entry 9) [DJK-17-47]



Following General Procedure 11, **143i** (276 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **103** (339 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and stirred at rt. MsOH (17 μL, 0.25 mmol, 0.25 equiv) was added directly via syringe. The solution was allowed to stir for 12 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^{1}H NMR), the reaction was quenched with triethylamine (300 μL) and the mixture was allowed to warm to rt, whereupon the white solid dissolved. The material was transferred to a 250 mL RB-flask using 20 mL of CH_2Cl_2 and concentrated by rotary evaporation (30 ^{o}C, 3 mm Hg) to afford a pale yellow residue. The material was then redissolved in 10 mL CH_2Cl_2 and adsorbed onto Celite. Purification by silica gel flash column chromatography of the adsorbed material (5:1, hexanes/CH_2Cl_2, 20 mm diameter, 16 cm SiO_2) followed by recrystallization from hexanes (3 mL) afforded, in two crops, 416 mg (89%) of **143i** as white prisms.

Data for **143i**:

mp: 137-140 ^{o}C (hexanes)

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

δ 7.44 (dd, *J* = 8.5 Hz, 2.2 Hz, 1H, HC(7)), 7.34 (m, 4H, HC(aryl)), 7.25 (m, 2H, HC(aryl)), 7.22–7.20 (br s, 1H, HC(5)), 7.18 (d, *J* = 7.7 Hz, 2H, HC(17)), 7.04 (d, *J* = 8.6 Hz, 1H, HC(8)), 5.19 (d, *J* = 5.5 Hz, 1H, HC(2)), 3.75 (p, *J* = 6.9 Hz, 2H, HC(19)), 3.50 (q, *J* = 5.6 Hz, 1H, HC(3)), 2.77 (d, *J* = 5.5 Hz, 2H, HC(4)), 1.18 (d, *J* = 6.9 Hz, 12H, HC(20)).

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

δ 156.6 (C15), 154.2 (C9), 139.6 (C11), 130.0 (C14), 128.8 (C13), 128.7 (C16), 128.6 (C18), 127.1 (C5), 126.2 (C12), 125.5 (C7), 124.1 (C17), 120.6 (C4), 117.0 (C8), 79.8 (C2) , 47.2 (C3), 31.8 (C19), 29.1 (C4), 24.7 (m, C20).

^{19}F NMR: (376 MHz, $CDCl_3$)

δ -61.87 (s)

IR: (ATR, cm^{-1})

2961 (w), 2926 (w), 1738(w), 1620 (w), 1594 (w), 1507 (w), 1455 (w), 1380 (w), 1361 (w), 1330 (s), 1292 (m), 1241 (s), 1188 (w), 1159 (s), 1115 (s), 1070 (w), 1050 (w), 1032 (w), 990 (m), 971(m), 936 (w), 905 (m), 889 (m), 846 (m), 799 (m), 781 (w), 748 (m), 740 (m), 696 (s).

MS: (EI, 70 eV, m/z)

470 (25, M^+), 283 (100), 276 (21), 194 (22), 149 (51)

TLC: R_f 0.65 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

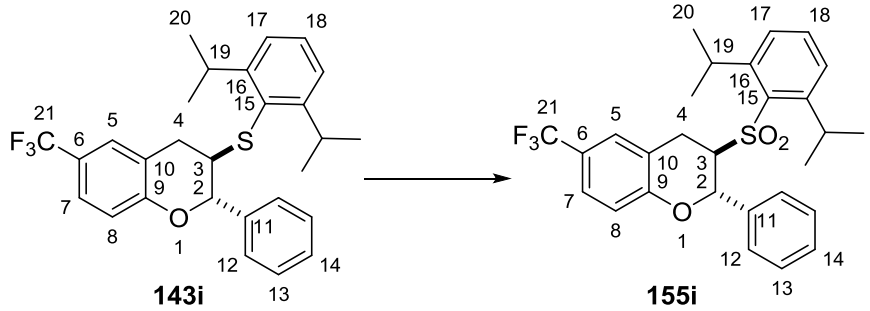
Opt. Rot.: $[\alpha]_D^{23}$ = -7.0 (c = 0.9 in $CHCl_3$)

CD: (-), Cotton sign, 230-280 nm

Analysis: $C_{28}H_{29}F_3OS$ (470.59)

Calcd:	C, 71.46;	H, 6.21%
Found:	C, 71.38;	H, 6.22%

Preparation of (2*S*,3*R*)-3-((2,6-Diisopropylphenyl)sulfonyl)-2-phenyl-6-(trifluoromethyl)-chromane (155i) [DJK-17-48]



To determine enantiomeric composition, **143i** was oxidized to the sulfone **155i**. To a 4-dram vial under nitrogen was added solid **143i** (20 mg, 0.04 mmol, 1 equiv), followed by CH_2Cl_2 (1mL) and solid mCPBA (18 mg, 0.11 mmol, 2.5 equiv). The resulting solution was stirred at rt for 3 h. The solution was then diluted with hexanes (3 mL) and directly purified by silica gel flash column chromatography (9:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) to afford 22 mg of **155i** as a white solid. The product sulfone was then analyzed by chiral stationary phase HPLC.

Data for **155i**:

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

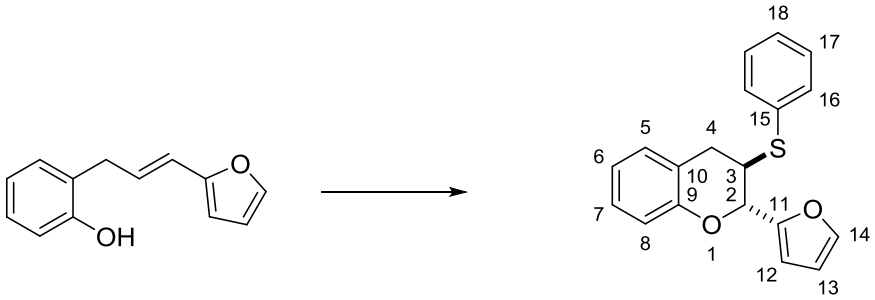
δ 7.56–7.44 (m, 2H, HC(7), HC(5)), 7.35 (d, *J* = 7.7 Hz, 3H, HC(aryl)), 7.31–7.27 (m, 5H, HC(aryl)), 7.19 (dd, *J* = 6.7, 2.9 Hz, 2H, HC(aryl)), 7.08 (d, *J* = 8.5 Hz, 1H, HC(8)), 5.82 (d, *J* = 4.4 Hz, 1H, HC(2)), 4.04 (p, *J* = 6.7 Hz, 2H, HC(19)), 3.86 (app q, *J* = 5.8 Hz, 1H, HC(3)), 3.30 (dd, *J* = 17.5, 5.5 Hz, 1H, HC(4)), 3.03 (dd, *J* = 17.5, 6.4 Hz, 1H, HC(4)), 1.30 (d, *J* = 6.7 Hz, 6H, HC(20)), 1.25 (d, *J* = 6.7 Hz, 6H, HC(21)).

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

δ 151.2, 138.2, 133.6, 129.1, 128.9, 126.6, 126.4, 126.2, 119.1, 117.4, 74.9, 62.5, 30.0, 25.3, 25.2, 22.6.

CSP-HPLC: (2*S*,3*R*)-**155i** t_{maj} 6.9 min (95.2%) (2*R*,3*S*)-**155i** t_{min} 7.7 min (4.8%) (Chiralpak AD, 220 nm, 95:5, hexanes/*i*-PrOH, 0.8 mL/min)

Preparation of (2*S*,3*R*)-2-(Furan-2-yl)-3-(phenylthio)chromane (143j) (Table 19 Entry 1) [DJK-DR-9009]



142j **143j**

For compound **143j**, General Procedure 11 was modified as following: To a dried 10-mL Schlenk flask was added CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to -20 ^oC (probe). After equilibration (ca. 20 min), MsOH (17 μL, 0.25 mmol, 0.25 equiv) was added directly via syringe, and allowed to stir for 5 min. Substrate **142j** (200 mg, 1.0 mmol) was then added directly to the cold solution. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^1H NMR), the reaction was quenched with triethylamine (300 μL) and then was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). The material was dissolved in CH_2Cl_2 (10 mL) and adsorbed onto Celite. Purification by silica gel flash column chromatography (5:1, hexanes/CH_2Cl_2, 20 mm diameter, 16 cm SiO_2), followed by recrystallization from hexanes (3 mL) afforded, in two crops, 271 mg (88%) of **143j** as white needles.

Data for **143j**:

mp: 72-73 ^{o}C (hexanes)

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

δ 7.44–7.38 (m, 2H, HC(17)), 7.36–7.26 (m, 4H, HC(14), HC(16), HC(18)), 7.16 (dd, *J* = 8.4, 7.4, 1H, HC(7)), 7.06 (d, *J* = 7.2 Hz, 1H, HC(5)), 6.96–6.88 (m, 2H, HC(8), HC(6)), 6.45–6.39 (m, 1H, HC(12), 6.35 (ddd, *J* = 3.2, 1.8, 1.0 Hz, 1H, HC(13), 5.09 (dd, *J* = 8.1, 1.1 Hz, 1H, HC(2)), 3.98 (ddd, *J* = 9.2, 8.1, 5.4, 1H, HC(3)), 3.21 (dd, *J* = 16.6, 5.4 Hz, 1H, HC(4)), 3.03–2.89 (dd, *J* = 16.6, 9.2 Hz, 1H HC(4)).

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

δ 153.7 (C9), 151.5 (C11), 142.9 (C14), 133.6 (C117), 132.9 (C15), 129.5 (C5), 129.1 (C16), 128.0 (C7), 127.9 (C18), 121.2 (C6), 120.5 (C10), 116.9 (C8), 110.6 (C13), 109.9 (C12), 74.6 (C2), 44.3 (C3), 31.7 (C4).

IR: (ATR, cm^{-1})

3058 (w), 1733 (w), 1583 (m), 1504 (w), 1487 (m), 1476 (m), 1453 (m), 1439 (w), 1349 (w), 1331 (w), 1301 (w), 1279 (w), 1234 (s), 1217 (m), 1190 (w), 1170 (w), 1150 (m), 1111 (m), 1079 (w), 1033 (m), 1013 (m), 978 (s), 931 (m), 902 (m), 885 (m), 876 (m), 846 (w), 820 (m), 778 (w), 747 (s), 728 (s), 703 (m).

MS: (EI, 70eV, m/z)

308 (31, M^+), 199 (29), 190 (46), 81 (100).

TLC: R_f 0.42 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

Opt. Rot.: $[\alpha]_D^{23}$ = -55.5 (c = 0.96 in $CHCl_3$)

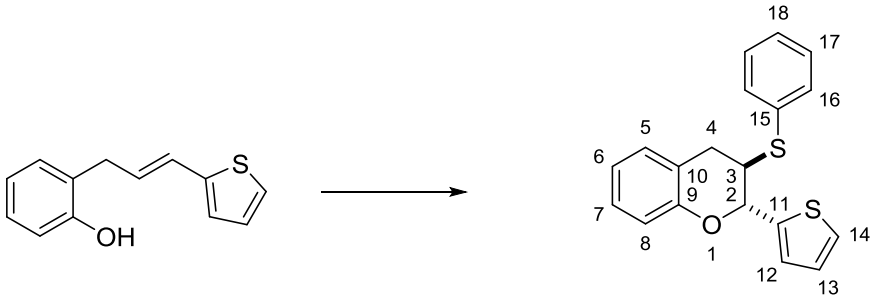
CD: (-), Cotton sign, 230-280 nm

CSP-HPLC: (2*R*,3*S*)-**143j** t_{min} 8.7 min (7.5%), (2*S*,3*R*)-**143j** t_{maj} 9.7 min (92.5%) (Chiralpak AD, 220 nm, 95:5, hexanes/*i*-PrOH, 0.8 mL/min)

Analysis: $C_{19}H_{16}O_2S$ (308.40)

Calcd:	C, 74.00;	H, 5.23%
Found:	C, 73.83;	H, 5.16%

Preparation of (2*R*,3*R*)-3-(Phenylthio)-2-(thiophen-2-yl)chromane (143k) (Table 19 Entry 2) [DJK-DR-9008]



142k **143k**

Following General Procedure 11, **142k** (216 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) was added. The flask was placed in an *i*-PrOH bath and cooled to -20 ^oC (probe). After equilibration (ca. 20 min), MsOH (17 μL, 0.25 mmol, 0.25 equiv) was added directly via syringe. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^1H NMR), the reaction was quenched with triethylamine (300 μL) and then was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). Purification by silica gel flash column chromatography (60:1, hexanes/ethyl acetate then 40:1, hexanes/ethyl acetate, 30 mm diameter, 15 cm SiO_2) afforded 278 mg (86%) of **143k** as white prisms.

Data for **143k**:

mp: 98-99 ^oC (hexanes/ethyl acetate)

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

δ 7.39 (m, 2H, HC(17)), 7.30 (m, 4H, HC(16), HC(18), HC(7)), 7.19 (t, *J* = 8.3 Hz, 1H, HC(6)), 7.13 (d, *J* = 3.5 Hz, 1H, HC(12)), 7.06 (d, *J* = 7.5 Hz, 1H, HC(5), 6.99 (t, *J* = 4.0 Hz, 1H, HC(13)), 6.94 (m, 2H, HC(14), HC(8)), 5.36 (d, *J* = 7.6 Hz, 1H, HC(2)), 3.80 (td, *J* = 8.1, 5.4 Hz, 1H, HC(3)), 3.21 (dd, *J* = 16.7, 5.3 Hz, 1H, HC(4)), 2.99 (dd, *J* = 16.7, 8.7 Hz, 1H, HC(4)).

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

δ 153.6 (C9), 142.6 (C15), 133.4 (C17), 133.3 (C11), 129.5 (C13), 129.2 (C16), 128.1 (C12), 127.9 (C18) , 126.8 (C6), 126.5 (C5), 126.0 (C7), 121.3 (C14), 120.4 (C10), 117.0 (C8), 77.0 (C2), 47.7 (C3), 31.6 (C4).

IR: (ATR, cm^{-1})

2923 (w), 1582 (w), 1485 (m), 1456 (w), 1437 (w), 1345 (w), 1305 (w), 1275 (w), 1233 (w), 1219 (s), 1191 (m), 1149 (w), 1120 (w), 1104 (w), 1078 (m), 1042 (w), 1026 (w), 991 (m), 965 (m), 900 (w), 846 (m), 839 (m), 757 (s), 747 (s), 710 (s).

MS: (EI, 70 eV, m/z)

324 (15, M^+), 215 (30), 205 (26), 97 (100)

TLC: R_f 0.42 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

Opt. Rot.: $[\alpha]_D^{23}$ = -49.8 (c = 0.95 in $CHCl_3$)

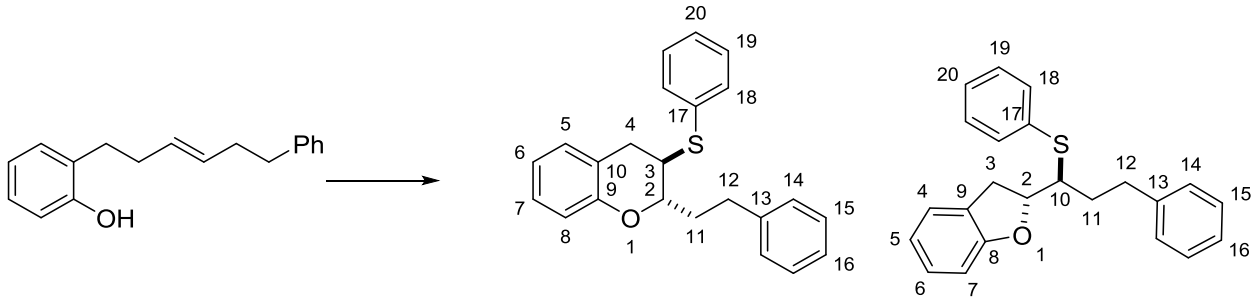
CD: (-), Cotton sign, 230-280 nm

CSP-HPLC: (2*R*,3*R*)-**143k** t_{maj} 26.6 min (93.9%), (2*S*,3*S*)-**143k** t_{maj} 34.2 min (6.1%) (Reverse-Phase Chiralpak OJ-RH, 220 nm, 65:35, MeCN/H_2O, 0.5 mL/min)

Analysis: $C_{19}H_{16}OS_2$ (324.46)

Calcd:	C, 70.33;	H, 4.97%
Found:	C, 69.93;	H, 4.83%

Preparation of (2*S*,3*R*)-2-Phenethyl-3-(phenylthio)chromane (143l) and (*R*)-2-((*S*)-3-Phenyl-1-(phenylthio)propyl)-2,3-dihydrobenzofuran (144l) (Table 19 Entry 3) [DJK-DR-9054]



142l **143l** **144l**

Following General Procedure 11, **142l** (238 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-

PrOH bath and cooled to -20 °C (probe). After equilibration (ca. 20 min), MsOH (17 μL, 0.25 mmol, 0.25 equiv) was added directly via syringe. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^{1}H NMR), the reaction was quenched with triethylamine (300 μL) and then was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, then was diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated (30 °C, 3 mm Hg). The crude **143l**/**144l** ratio (1.5:1) was established by ^{1}H NMR spectroscopy. The material was dissolved in 10 mL of CH_2Cl_2 and adsorbed onto Celite. Purification by silica gel flash column chromatography of this material (60:1, hexanes/ethyl acetate then 40:1, hexanes/ethyl acetate, 30 mm diameter, 14 cm SiO_2) followed by bulb-to-bulb distillation afforded 258 mg (74%) of a 1.5:1 mixture of **143l/144l** as a clear oil.

Data for mixture:

bp: 120°C (ABT), 0.05 mm Hg

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

δ 7.51–7.40 (m, 5H, HC(aryl)), 7.32 (m, 13H, HC(aryl)), 7.25 (m, 7H, HC(aryl)), 7.21–7.09 (m, 4H, HC(aryl)), 7.02 (d, *J* = 7.6 Hz, 1H, HC(aryl)), 6.97–6.81 (m, 4H), 6.74 (d, *J* = 8.0 Hz, 1H)

IR: (ATR, cm^{-1})

3025 (w), 2923 (w), 1599 (w), 1584 (m), 1488 (m), 1479 (m), 1455 (m), 1437 (m), 1303 (w), 1231 (s), 1174 (w), 1111 (w), 1088 (w), 1066 (w), 1024 (w), 964 (w), 942 (w), 872 (w), 796 (w), 744 (s).

MS: (EI, 70 eV, m/z)

346 (73, M^+), 145 (30), 131 (41), 117 (65), 91 (100), 69 (29)

TLC: R_f 0.49 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

CSP-SFC: (2*R*,3*S*)-**143l**, t_{min} 16.2 (3.4%), (2*S*,3*R*)-**143l** t_{maj} 17.7 (96.6%), (2*S*,10*R*)-**144l**, t_{min} 13.3 (3.7%), (2*S*,10*R*)-**144l** t_{maj} 14.7 (96.3%) (Chiralpak AD, 220 nm, 95:5 sCO_2/MeOH, 2 mL/min)

Analysis: $C_{23}H_{22}OS$ (346.49)

Calcd: C, 79.73; H, 6.40%

Found: C, 79.87; H, 6.51%

Diagnostic for **144l**:

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

δ 4.86 (dt, *J* = 9.1, 7.4 Hz, 1H, HC(2)), 3.35 (dd, *J* = 15.9, 9.2 Hz, 1H, HC(3)), 3.29 (ddd, *J* = 10.2, 7.0, 3.6 Hz, 1H, HC(10)), 3.22–3.15 (m, 2H, HC(3), HC(12)), 2.88 (m, HC(12)), 2.26 (dddd, *J* = 14.3, 9.6, 7.1, 3.6 Hz, 1H, HC(11)), 1.95 (dtd, *J* = 14.4, 9.6, 4.9 Hz, 1H, HC(11)).

^{13}C NMR: (126 MHz, CDCl3)

δ 85.1 (C2), 53.9 (C10), 34.2 (C3), 33.1 (C12), 32.7 (C11)

Diagnostic for **143l**:

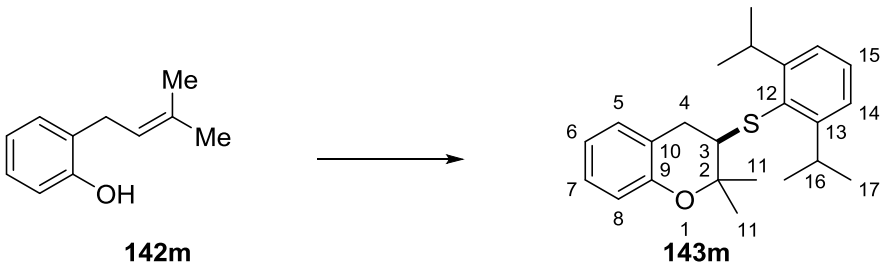
^{1}H NMR: (500 MHz, $CDCl_3$)

δ 4.06 (td, *J* = 8.4, 2.9 Hz, 1H, HC(2)), 3.45 (ddd, *J* = 9.0, 7.9, 5.3 Hz, 1H, HC(3)), 3.15–3.08 (m, 1H, HC(4)), 3.00–2.91 (m, 1H, HC(4)), 2.91–2.82 (m, 2H, HC(12)), 2.36 (dddd, *J* = 14.0, 10.0, 7.3, 3.0 Hz, 1H, HC(11)), 2.10 (dtd, *J* = 14.0, 9.0, 5.0 Hz, 1H, HC(11))

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

δ 77.4 (C2), 45.0 (C3), 35.0 (C11), 31.7 (C4), 31.4 (C12)

Preparation of (*S*)-3-((2,6-Diisopropylphenyl)thio)-2,2-dimethylchromane (143m) (Table 19 Entry 4) [DJK-DR-9079]



142m **143m**

Following General Procedure 11, **142m** (162 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **103 (**339 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an

i-PrOH bath and cooled to 0 °C (probe). MsOH (17 μL, 0.25 mmol, 0.25 equiv) was added directly via syringe. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^{1}H NMR), the reaction was quenched with triethylamine (300 μL) and then was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated (30 °C, 3 mm Hg). The material was then dissolved in 10 mL of CH_2Cl_2 and adsorbed onto Celite. Purification by silica gel flash column chromatography of this material (5:1, hexanes/CH_2Cl_2, 20 mm diameter, 16 cm SiO_2) followed by recrystallization (EtOH, 5 mL), afforded, in two crops, 330 mg (93%) of **143m** as white needles.

Data for **143m**:

mp: 74-75 °C (EtOH)

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

δ 7.35 (t, *J* = 7.8 Hz, 1H, HC(15)), 7.18 (d, *J* = 7.7 Hz, 2H, HC(14)), 7.08 (t, *J* = 8.1 Hz, 1H, HC(7)), 6.89 (d, *J* = 7.3 Hz, 1H, HC(5)), 6.83–6.75 (m, 2H, HC(6), HC(8)), 3.89 (p, *J* = 6.8 Hz, 2H, HC(16)), 3.16 (dd, *J* = 8.1, 6.9 Hz, 1H, HC(3)), 2.72 (d, *J* = 7.2 Hz, 2H, HC(4)), 1.55 (s, 3H, HC(11)), 1.49 (s, 3H, HC(11)), 1.24 (d, *J* = 6.8 Hz, 6H, HC(17)), 1.18 (d, *J* = 6.8 Hz, 6H, HC(17)).

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

δ 154.2 (C12), 153.2 (C9), 129.7 (C15), 129.5 (C13), 129.4 (C7), 127.9 (C5), 124.1 (C14), 120.6 (C13), 120.4 (C6), 117.4 (C8), 77.5 (C2), 52.1 (C3), 31.8 (C16), 31.7 (C16), 29.8 (C4), 27.9 (C11), 25.0 (C17), 24.5 (C17), 22.2 (C11).

IR: (ATR, cm^{-1})

3058 (w), 2962 (m), 2928 (m), 2867 (w), 1609 (w), 1583 (m), 1489 (s), 1455 (s), 1420 (w), 1382 (m), 1368 (m), 1360 (w), 1315 (w), 1301 (m), 1265 (s), 1252 (m), 1236 (s), 1178 (m), 1150 (s), 1127 (s), 1099 (s), 1052 (m), 1033 (m), 974 (w), 944 (s), 927 (m), 896 (w), 858 (s), 847 (w), 825 (w), 804 (m), 748 (s), 741 (s), 713 (m).

MS: (EI, 70 eV, m/z)

354 (69, M^+), 235 (98), 194 (28), 161 (100), 149 (33), 145 (60), 119 (71), 91 (41)

TLC: R_f 0.60 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

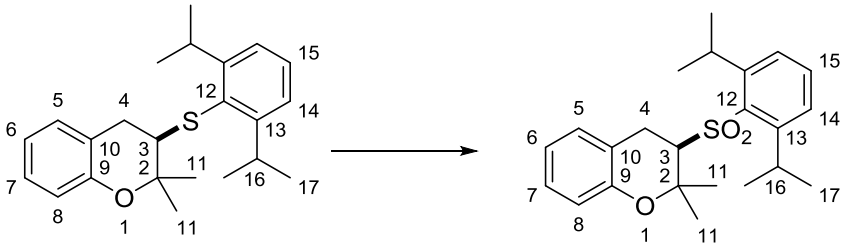
Opt. Rot.: $[\alpha]_D^{23}$ = -104.8 (c = 0.79 in $CHCl_3$)

CD: (+), Cotton sign, 230-280 nm

Analysis: $C_{23}H_{30}OS$ (354.55)

Calcd:	C, 77.92;	H, 8.53%
Found:	C, 77.71;	H, 8.31%

Preparation of (*S*)-3-((2,6-Diisopropylphenyl)sulfonyl)-2,2-dimethylchromane (155m) [DJK-14-97]



To determine enantiomeric composition, **143m** was oxidized to the sulfone. To a 4-dram vial was added solid **143m** (20 mg, 0.055 mmol, 1 equiv), followed by CH_2Cl_2 (1 mL) and mCPBA (25 mg, 0.15 mmol, 2.5 equiv) The solution was stirred at rt for 3 h. The solution was diluted with hexanes (3 mL) and then directly purified by silica gel flash column chromatography (9:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) to afford 21 mg of **155m** as a white solid. The product was analyzed by chiral stationary phase HPLC.

Data for **155m**:

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

δ 7.55 (t, *J* = 7.8 Hz, 1H, HC(15)), 7.41(d, *J* =7.8 Hz, 2H, HC(14)), 7.14 (t, *J* = 7.7 Hz, 1H, HC(7), 6.97 (d, *J* = 7.6 Hz, 1H, HC(6)), 6.91–6.79 (m, 2H, HC(5), HC(8)), 4.26 (q, *J* = 7.0 Hz, 2H, HC(16)), 3.54 (ddd, *J* = 13.0, 5.3, 2.0 Hz, 1H, HC(3)), 3.36 (dd, *J* = 16.2, 12.7 Hz, 1H, HC(4)), 2.73 (dd, *J* = 16.2, 5.2 Hz, 1H,

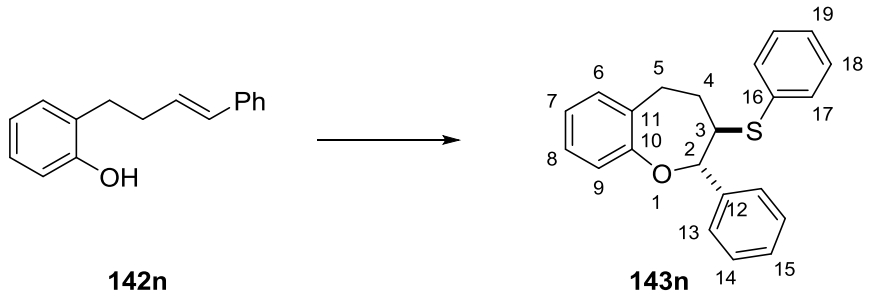
HC(4)), 1.84 (s, 3H, HC(11)), 1.56 (s, 3H, HC(11)), 1.36 (d, J = 6.9, 6H, HC(17)), 1.29 (d, J = 6.7 Hz, 6H, HC(17)).

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

δ 151.6, 133.5, 129.2, 128.3, 126.6, 121.0, 118.9, 117.6, 76.5, 66.6, 30.0, 29.3, 25.2, 21.8.

CSP-HPLC: (*R*)-**155m** t_{min} 55.9 min (4.6%), (*S*)-**155m** t_{maj} 60.0 (95.4%) (Reverse-phase Chiralpak AD-RH, 220 nm, 45:55, MeCN/H_2O, 0.15 mL/min)

Preparation of (2*S*,3*R*)-2-Phenyl-3-(phenylthio)-2,3,4,5-tetrahydrobenzo[b]oxepine (143n) (Table 19 Entry 5) [DJK-DY-7309]



142n **143n**

Following General Procedure 11, **142n** (224mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to -20 ^{o}C (probe). After equilibration (ca. 20 min), MsOH (33 μL, 0.5 mmol, 0.5 equiv) was added directly via syringe. The solution was allowed to stir for 18 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^{1}H NMR), the reaction was quenched with triethylamine (300 μL) and then was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, then was diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^{o}C, 3 mm Hg). The residue was taken up in 10 mL of CH_2Cl_2 and then adsorbed onto Celite. Purification by silica gel flash column chromatography of this material (5:1, hexanes/CH_2Cl_2, 20 mm diameter, 16 cm SiO_2) followed by bulb-to-bulb distillation afforded 304 mg (92%) of **143n** as a clear oil.

Data for **143n**:

bp: 150 °C (ABT), 0.05 mm Hg

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

δ 7.49 (m, 2H, HC(aryl)), 7.43–7.34 (m, 3H, HC(aryl)), 7.25–7.12 (m, 7H), 7.05 (t, *J* = 7.4, 1H, HC(7)), 6.97 (d, *J* = 7.9, 1H, HC(9)), 4.61 (dd, *J* = 10.6, 1H, HC(2)), 3.85 (ddd, *J* = 10.6, 8.6, 4.2, 1H, HC(3)), 3.05 (dt, *J* = 6.9, 2.8 Hz, 2H, HC(5)), 2.63 (ddd, *J* = 12.1, 10.4, 4.2 Hz, 1H, HC(4)), 1.91 (dt, *J* = 14.5, 8.7 Hz, 1H, HC(4)).

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

δ 159.25 (C10), 140.66 (C16), 134.32 (C12), 134.25 (C11), 132.92 (C18), 130.22 (C15), 128.96 (C14), 128.49 (C13), 128.44 (C8), 127.68 (C17), 127.64 (C6), 127.36 (C19), 123.99 (C7), 121.62 (C9), 88.36 (C2), 55.46 (C3), 33.38 (C4), 30.88 (C5)

IR: (ATR, cm^{-1})

3060 (w), 3031 (w), 2930 (w), 1603 (w), 1581 (w), 1487 (s), 1453 (m), 1438 (m), 1350 (w), 1303 (w), 1260 (w), 1232 (s), 1187 (m), 1155 (w), 1106 (w), 1090 (w), 1042 (m), 1024 (w), 978 (m), 939 (w), 914 (m), 887 (w), 754 (s), 738 (s).

MS: (EI, 70 eV, m/z)

340 (25, M^+), 199 (56), 133 (100), 115 (26), 107 (24)

TLC: R_f 0.50 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

Opt. Rot.: $[\alpha]_D^{23}$ = +39.6 (0.96 in $CHCl_3$)

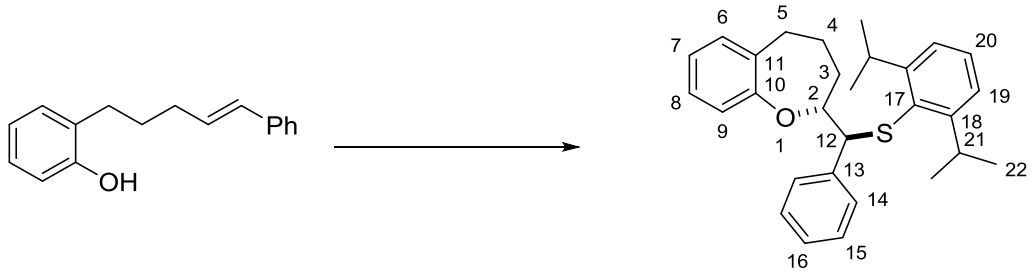
CD: (-), Cotton sign, 230-280 nm

CSP-SFC: (2*R*,3*S*)-**143n** t_{min} 7.6 (5.6%), (2*S*,3*R*)-**143n** t_{maj} 8.1 min (94.4%) (Chiralpak AD, 220 nm, 97:3, hexanes/*i*-PrOH, 0.8 mL/min)

Analysis: $C_{22}H_{20}OS$ (332.46)

Calcd:	C, 79.48;	H, 6.06%
Found:	C, 79.53;	H, 6.09%

Preparation of (*R*)-2-((*S*)-((2,6-Diisopropylphenyl)thio)(phenyl)methyl)-2,3,4,5-tetrahydrobenzo[b]oxepine (144o) (Table 19 Entry 6) [DJK-17-24]



142o **144o**

Following General Procedure 11, **142o** (238 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **103** (339 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to 0 ^oC (probe). After equilibration (ca. 20 min), MsOH (33 μL, 0.5 mmol, 0.5 equiv) was added directly via syringe. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^1H NMR), the reaction was quenched with triethylamine (300 μL) and then was allowed to warm to rt, whereupon the white solid dissolved. The material was transferred to a 250-mL RB flask using CH_2Cl_2 (20 mL) and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). Purification by silica gel flash column chromatography (5:1 hexanes/CH_2Cl_2, 20 mm diameter, 17 cm SiO_2) followed by recrystallization (MeOH, 3 mL) afforded, in two crops, 327 mg (76%) of **144o** as white needles.

Data for **144o**:

mp: 52-55 ^oC (MeOH)

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

δ 7.31–7.29 (m, 1H, HC(20)), 7.28–7.24 (m, 5H, H-aryl), 7.14 (ddd, *J* = 7.0, 4.2 Hz, 2H, H-aryl, HC(6), HC(8)), 7.11 (d, *J* = 7.7 Hz, 2H, HC(19)), 7.01 (t, *J* = 7.4 Hz, 1H, HC(7)), 6.86 (d, *J* = 8.2Hz, 1H, HC(9)), 4.15 (ddd, *J* = 11.0, 6.2, 1.5 Hz, 1H, HC(2)), 3.81–3.67 (m, 3H, HC(12), HC(21)), 2.89 (dd, *J* = 14.4, 12.1, 1H, HC(5)), 2.78–2.67 (m, 1H, HC(5)), 2.31–2.19 (m, 1H, HC(3)), 2.12–1.98 (m, 1H, HC(4)), 1.76 (dddd, *J* = 14.2, 12.0, 10.9, 3.6 Hz, 1H, HC(3)), 1.66–1.47 (m, 1H, HC(4)), 1.16 (d, *J* = 6.9 Hz, 6H, HC(22)), 0.97 (d, *J* = 6.8 Hz, 6H, HC(22)).

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

δ 159.62 (C17), 153.91 (C10), 140.17 (C18), 136.01 (C18), 131.07 (C13), 130.25 (C8), 129.37 (C20), 129.27 (C15), 128.06 (C14), 127.53 (C6), 127.26 (C16), 123.84 (C7), 123.77 (C19), 121.83 (C9), 85.71 (C2), 62.24 (C12), 36.19 (C3), 33.96 (C5), 31.70 (C21), 26.28 (C4), 24.77 (C22), 24.16 (C22).

IR: (ATR, cm^{-1})

3057 (w), 3026 (w), 2960 (m), 2924 (m), 2865 (w), 1602 (w), 1580 (w), 1487 (s), 1453 (m), 1382 (w), 1360 (m), 1305 (w), 1231 (s), 1209 (m), 1178 (w), 1107 (w), 1075 (w), 1052 (m), 953 (m), 924 (w), 861 (w), 801 (m), 755 (s), 743 (s), 733 (s), 720 (m).

MS: (EI, 70 eV, m/z)

430 (39, M^+), 283 (72), 237 (61), 147 (41), 107 (62), 91 (100)

TLC: R_f 0.8 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

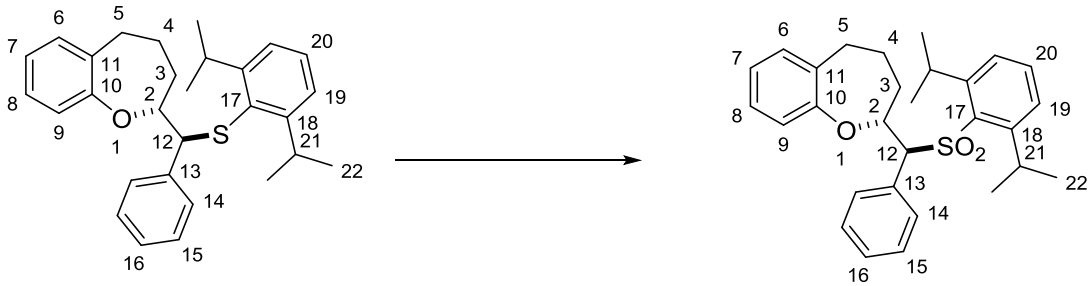
Opt. Rot.: $[\alpha]_D^{23}$ = -144.2 (c = 0.74 in $CHCl_3$)

CD: (-), Cotton sign, 230-280 nm

Analysis: $C_{29}H_{34}OS$ (430.65)

Calcd:	C, 80.88;	H, 7.96%
Found:	C, 80.79;	H, 7.91%

Preparation of (*R*)-2-((*S*)-((2,6-Diisopropylphenyl)sulfonyl)(phenyl)methyl)-2,3,4,5-tetrahydrobenzo[b]oxepine (155o) [DJK-17-50]



144o **155o**

To determine enantiomeric composition, **5o** was oxidized to the sulfone **155o**. To a 4-dram vial was added solid **144o** (20 mg, 0.05 mmol 1 equiv), followed by CH_2Cl_2 (1 mL) and mCPBA (22 mg, 0.13 mmol, 2.7 equiv) The solution was stirred at rt for 3 h. The solution was

diluted with hexanes (3 mL) and then directly purified by silica gel flash column chromatography (9:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) to afford 21 mg (99%) of **155o** as a white solid which was analyzed by chiral stationary phase HPLC.

Data for **155o**:

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

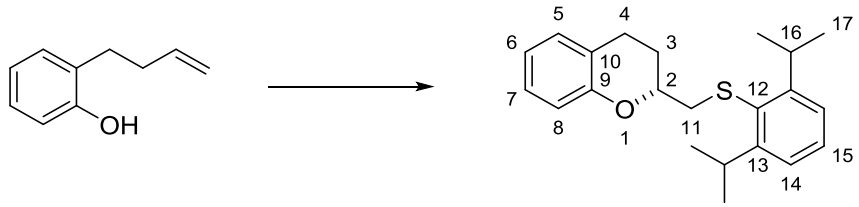
δ 7.40 (t, *J* = 7.9 Hz, 2H, HC(aryl)), 7.34–7.04 (m, 10H, HC(aryl)), 7.04–6.90 (m, 1H, HC(aryl)), 4.86 (ddd, *J* = 11.0, 4.3, 1.5 Hz, 1H, HC(2)), 4.19 (d, *J* = 4.3 Hz, 1H, HC(12)), 2.91–2.78 (m, 1H, HC(5)), 2.68 (dd, *J* = 14.3, 5.9 Hz, 1H, HC(5)), 1.99 (tdd, *J* = 10.6, 7.9, 4.3 Hz, 2H, HC(4)), 1.82–1.46 (m, 2H, HC(3)), 1.43–1.00 (m, 12H, HC(22)).

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

δ 159.3, 135.8, 134.1, 133.0, 132.3, 130.7, 130.3, 130.1, 129.2, 128.5, 127.9, 126.0, 124.2, 122.5, 80.5, 79.7, 76.6, 36.6, 33.8, 30.0, 26.3.

CSP-HPLC: (2*S*,12*R*)-**155o** t_{min} 6.7 min (7.4 %), (2*R*,12*S*)-**155o** t_{maj} 7.2 min (92.6%) (BG, 220 nm, 95:5, hexanes/*i*-PrOH, 0.8 mL/min)

Preparation of (*R*)-2-(((2,6-Diisopropylphenyl)thio)methyl)chromane (144p) (Table 19 Entry 7) [DJK-14-51]



142p **144p**

Following General Procedure 11, **142p** (148 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **103** (339 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) was added. The flask was placed in an *i*-PrOH bath and cooled to 0 ^oC (probe). After equilibration (ca. 20 min), MsOH (33 μL, 0.5 mmol, 0.5 equiv) was added directly via syringe. The solution was allowed to stir for 12 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^{1}H NMR), the reaction was quenched with triethylamine (300 μL) and then was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-

mL separatory funnel, diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with CH_2Cl_2 (15 mL). The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). The residue was dissolved in 10 mL of CH_2Cl_2 and adsorbed onto Celite. Purification by silica gel flash column chromatography (5:1, hexanes/CH_2Cl_2, 20 mm diameter, 16 cm SiO_2) followed by bulb-to-bulb distillation afforded 308 mg (91%) of **144p** as a clear oil.

Data for **144p**:

bp: 160 ^oC (ABT), 0.05 mm Hg

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

δ 7.37 (t, *J* = 7.7 Hz, 1H, HC(15)), 7.23 (d, *J* = 7.7 Hz, 2H, HC(14)), 7.17–7.11 (t, *J* = 7.6 Hz, 1H, HC(7)), 7.09 (d, *J* = 7.7, 1H, HC(5)), 6.89 (t, *J* = 7.4, 1H, HC(6)), 6.85 (d, *J* = 8.3, 1H, HC(8)), 4.16–3.99 (m, 3H, HC(2), HC(16)), 3.06 (dd, *J* = 12.9, 6.2 Hz, 1H, HC(11)), 2.92 (dd, *J* = 12.9, 6.6 Hz, 1H, HC(11)), 2.90–2.80 (m, 2H, HC(4)), 2.24 (ddd, *J* = 13.4, 6.0, 3.7 Hz, 1H, HC(3)), 1.88 (dddd, *J* = 13.4, 10.7, 9.7, 5.7 Hz, 1H, HC(3)), 1.30 (dd, *J* = 6.9, 3.9 Hz, 12H, HC(17)).

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

δ 154.8 (C12), 153.6 (C9), 131.6 (C4), 129.7 (C7), 129.5 (C14), 127.5 (C5), 124.0 (C10), 122.0 (C13), 120.5 (C6), 117.1 (C8), 74.8 (C2), 42.6 (C11), 31.8 (C3), 27.1 (C4), 24.8 (C17), 24.7 C(17).

IR: (ATR, cm^{-1})

3054 (w), 2960 (m), 2924 (m), 2866 (w), 1610 (w), 1582 (m), 1487 (s), 1456 (s), 1420 (w), 1382 (w), 1361 (w), 1339 (w), 1301 (m), 1274 (w), 1232 (s), 1113 (m), 1075 (w), 1050 (s), 1029 (w), 996 (m), 930 (w), 886 (w), 842 (w), 800 (m), 750(s), 710 (w).

MS: (EI, 70 eV, m/z)

340 (88, M^+), 194 (29), 161 (49), 147 (47), 133 (100)

TLC: R_f 0.61 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

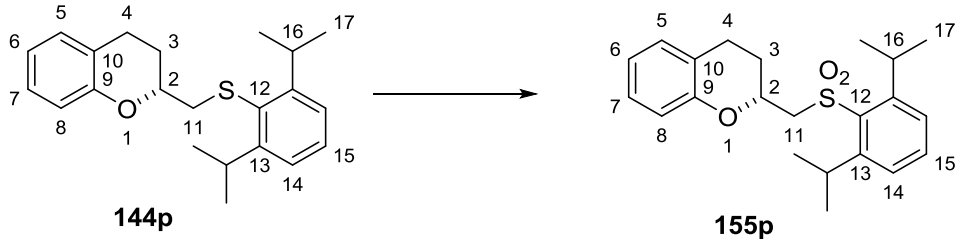
Opt. Rot.: $[\alpha]_D^{23}$ = +69.7 (c = 1.01 in $CHCl_3$)

CD: (-), Cotton sign, 230-280 nm

Analysis: $C_{22}H_{28}OS$ (340.53)

Calcd:	C, 77.60;	H, 8.29%
Found:	C, 77.54;	H, 7.93%

Preparation of of (*R*)-2-(((2,6-Diisopropylphenyl)sulfonyl)methyl)chromane (155p) [DJK-14-94]



To determine enantiomeric composition, **144p** was oxidized to the sulfone. To a 4-dram vial was added solid **144p** (20 mg, 0.06 mmol 1 equiv), followed by CH_2Cl_2 (1 mL) and mCPBA (26 mg, 0.15 mmol, 2.5 equiv) The solution was stirred at rt for 3 h. The material was then diluted with hexanes (3 mL) and directly purified by silica gel flash column chromatography (9:1 hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) to afford 22 mg (99%) of **155p** as a white solid. The product was analyzed by chiral stationary phase HPLC.

Data for **155p**:

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

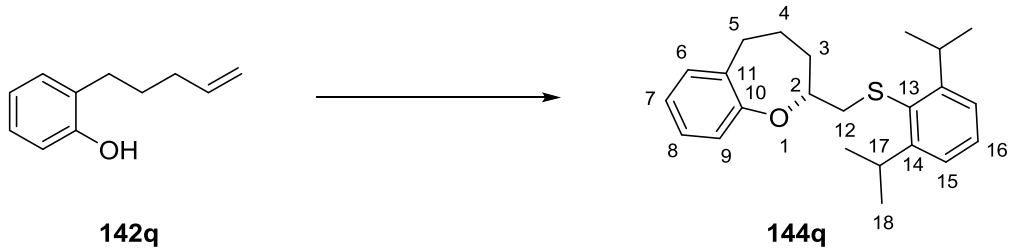
δ 7.53 (t, *J* = 7.8 Hz, 1H, HC(15)), 7.37 (d, *J* = 7.8 Hz, 2H, HC(14)), 7.01 (d, *J* = 7.5, 1H, HC(5)), 6.95 (t, *J* = 7.8 Hz, 1H, HC(7)), 6.81 (t, *J* = 7.4, 1H, HC(7)), 6.20 (d, *J* = 8.2, 1H, HC(8)), 4.77 (dddd, *J* = 8.8, 7.3, 4.4, 2.7 Hz, 1H, HC(2)), 4.21 (p, *J* = 6.7 Hz, 2H, HC(16)), 3.74 (dd, *J* = 14.3, 7.4 Hz, 1H, HC(11)), 3.37 (dd, *J* = 14.4, 4.4 Hz, 1H, HC(11)), 2.88 (ddd, *J* = 16.0, 9.5, 6.1 Hz, 1H, HC(4)), 2.77 (dt, *J* = 16.7, 5.4 Hz, 1H, HC(4)), 2.25 (dddd, *J* = 13.8, 6.2, 5.1, 2.7 Hz, 1H, HC(3)), 1.90 (dddd, *J* = 13.5, 9.5, 8.8, 5.7 Hz, 1H, HC(3)), 1.28 (d, *J* = 6.7 Hz, 6H, HC(17)), 1.23 (d, *J* = 6.8 Hz, 6H, HC(17)).

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

δ 153.3, 151.3, 136.2, 133.1, 129.6, 127.6, 126.2, 121.2, 121.0, 117.0, 70.3, 62.4, 29.9, 27.4, 25.2, 25.0, 23.7.

CSP-HPLC: (*R*)-**155p** t_{min} 8.4 (97.2%), (*S*)-**155p** t_{maj} 9.0 min (2.8%) (Chiralpak AD, 220 nm, 95:5, hexanes/*i*-PrOH, 0.8 mL/min)

Preparation of (*R*)-2-(((2,6-Diisopropylphenyl)thio)methyl)-2,3,4,5-tetrahydrobenzo-[b]oxepine (144q) (Table 19 Entry 8) [DJK-14-54]



142q **144q**

Following General Procedure 11, **142q** (162 mg, 1.0 mmol) was weighed into a dried 10 mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to 0 ^oC (probe). After equilibration (ca. 20 min), MsOH (33 μL, 0.5 mmol, 0.5 equiv) was added directly via syringe. The solution was allowed to stir for 48 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^1H NMR), the reaction was quenched with triethylamine (300 μL) and then was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). Purification by silica gel flash column chromatography (5:1, hexanes/CH_2Cl_2, 20 mm diameter, 20 cm SiO_2) followed by bulb-to-bulb distillation afforded 296 mg (84%) of **144q** as a clear viscous oil (84%).

Data for **144q**:

bp: 180 ^oC (ABT), 0.05 mm Hg

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

δ 7.34 (t, *J* = 7.7 Hz, 1H, HC(16)), 7.21–7.17 (m, 3H, HC(8), HC(15)), 7.17–7.12 (m, 2H, HC(6), HC(9)), 7.03 (ddt, *J* = 8.9, 7.2 Hz, 1H, HC(7)), 4.02 (p, *J* = 6.8 Hz, 2H, HC(17)), 3.79 (ddd, *J* = 10.2, 8.0, 4.0 Hz, 1H, HC(2)), 3.15 (dd, *J* = 12.0 Hz, 8.0 Hz, 1H, HC(12)), 2.93 (dd, *J* = 14.4, 12.0 Hz, 1H, HC(5)), 2.74 (ddd, *J* =

14.9, 12.6, 5.3 Hz, 2H, HC(12), HC(5)), 2.12–1.97 (m, 2H, HC(4), HC(3)), 1.91–1.79 (m, 1H, HC(3)), 1.60–1.48 (m, 1H, HC(4)) 1.28 (d, *J* = 6.8 Hz, 6H, HC(18)), 1.23 (d, *J* = 6.8 Hz, 6H, HC(18)).

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

δ 159.1 (C13), 153.5 (C10), 135.8 (C14), 132.3 (C14), 130.3 (C6), 129.3 (C16), 127.6 (C8) , 123.9 (C15), 123.8 (C7), 121.9 (C9), 110.0 (C11), 82.6 (C2) , 44.7 (C12), 37.0 (C3), 33.9 (C5), 31.8 (C17), 25.9 (C4), 24.7 (C18), 24.6 (C18).

IR: (ATR, cm^{-1})

3055 (w), 2960 (m), 2924 (m), 2865 (w), 1602 (w), 1579 (w), 1487 (s), 1454 (m), 1382 (w), 1360 (m), 1306 (w), 1231(s), 1194 (w), 1178 (w), 1105 (w), 1065 (m), 1052 (m), 1035 (m), 1019 (m), 955 (s), 926 (m), 864 (w), 830 (w), 799 (s), 762 (s), 736 (s), 718 (w).

MS: (EI, 70 eV, m/z)

354 (82, M^+), 194 (100), 160 (81), 153 (51), 151 (51), 107 (98)

TLC: R_f 0.56 (1:1 hexanes:CH_2Cl_2) [UV, CAM]

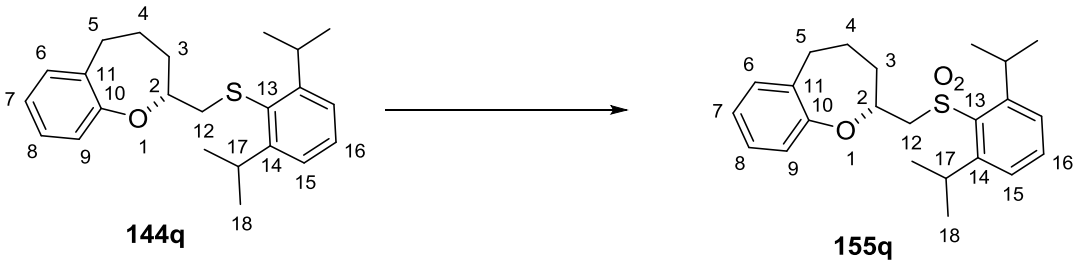
Opt. Rot.: $[\alpha]_D^{23}$ = +36.9 (c = 1.1 in $CHCl_3$)

CD: (+), Cotton sign, 230-280 nm

Analysis: $C_{23}H_{30}OS$ (354.55)

Calcd:	C, 77.92;	H, 8.53%
Found:	C, 77.75;	H, 8.25%

Preparation of (*R*)-2-(((2,6-Diisopropylphenyl)sulfonyl)methyl)-2,3,4,5-tetrahydrobenzo-[b]oxepine (155q) [DJK-14-95]



To determine enantiomeric composition, **144q** was oxidized to the sulfone. To a 4-dram vial was added neat **144q** (20 mg, 0.06 mmol 1 equiv), followed by CH_2Cl_2 (1 mL) and mCPBA (26 mg, 0.15 mmol, 2.5 equiv) The solution was stirred at rt for 3 h. The material was diluted

with hexanes (3 mL) and then directly purified by silica gel flash column chromatography (9:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) to afford 20 mg of a white solid which was analyzed by chiral stationary phase HPLC.

Data for **155q**:

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

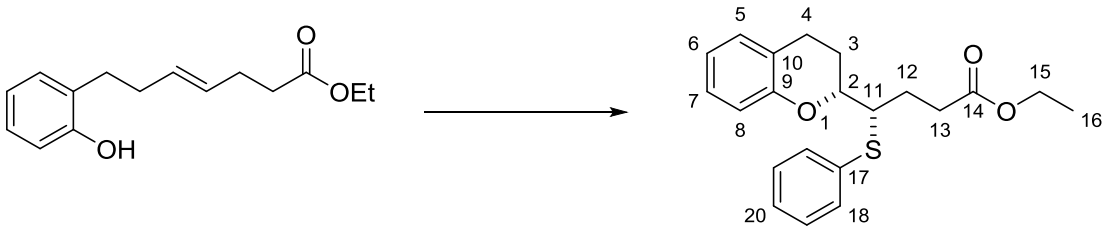
δ 7.54 (t, *J* = 7.8 Hz, 1H, HC(16)), 7.39 (d, *J* = 7.7 Hz, 2H, HC(15)), 7.08 (d, *J* = 7.3 Hz, 1H, HC(6)), 7.02 (t, *J* = 7.6, 1H, HC(8)), 6.96 (t, *J* = 7.3, 1H, HC(7)), 6.51 (d, *J* = 7.8 Hz, 1H, HC(9)), 4.32 (dt, *J* = 9.0, 3.6, 1H, HC(2)), 4.22 (p, *J* = 6.7 Hz, 2H, HC(17)), 3.85 (dd, *J* = 14.4, 7.1 Hz, 1H, HC(12)), 3.32 (dd, *J* = 14.3, 3.5 Hz, 1H, HC(12)), 2.94–2.80 (m, 1H, HC(5)), 2.80–2.68 (m, 1H, HC(5)), 2.15–1.90 (m, 3H, HC(3), HC(4)), 1.72–1.46 (m, 1H, HC(3), HC(4)), 1.30 (d, *J* = 6.7 Hz, 6H, HC(18), 1.24 (d, *J* = 6.7 Hz, 6H, HC(18)).

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

δ 158.4, 151.4, 136.0, 135.4, 133.2, 130.2, 127.6, 126.4, 126.4, 124.2, 121.9, 76.8, 64.6, 38.2, 33.6, 29.9, 25.9, 25.3, 24.9.

CSP-HPLC: (*S*)-**155q** t_{maj} 10.5 min (2.3%), (*R*)-**155q** t_{min} 11.1 min (97.7%) (Chiralpak AD, 220 nm, 95:5, hexanes/*i*-PrOH, 0.8 mL/min)

Preparation of Ethyl (*S*)-1-((*R*)-chroman-2-yl)-1-(phenylthio)butanoate (144r) (Table 19 Entry 9) [DJK-DY-7308]



142r **144r**

Following General Procedure 11, **142r** (248 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56 (**255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to -20 ^oC (probe). After equilibration (ca. 20 min), MsOH (33 μL, 0.5 mmol, 0.5 equiv) was added directly via syringe. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the

starting material (TLC, ^{1}H NMR), the reaction was quenched with triethylamine (300 μL) and then was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, then was diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with CH_2Cl_2 (15 mL). The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). The material was dissolved in ethyl acetate (10 mL) and adsorbed onto Celite. Purification by silica gel flash column chromatography (20:1, hexanes/ethyl acetate, 20 mm diameter, 16 cm SiO_2) followed by bulb-to-bulb distillation afforded 286 mg (80%) of **144r** as a clear viscous oil.

Data for **144r**:

bp: 180 ^oC (ABT), 0.05 mm Hg

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

δ 7.52 (d, *J* = 7.3 Hz, 2H, HC(19)), 7.37–7.31 (m, 2H, HC(16)), 7.30–7.28 (m, 1H, HC(20)), 7.11 (dd, *J* = 8.2, 7.4, 1H, HC(7)), 7.07 (d, *J* = 7.5 Hz, 1H, HC(5)), 6.87 (t, *J* = 7.3 Hz, 1H, HC(6)), 6.81 (d, *J* = 8.2 Hz, 1H, HC(8)), 4.22–4.07 (m, 3H, HC(2), HC(15)), 3.38–3.28 (m, 1H, HC(11)), 2.91–2.73 (m, 3H, HC(13), HC(4)), 2.71–2.63 (m, 1H, HC(13)), 2.42–2.32 (m, 2H, HC(3), HC(12)), 2.06–1.90 (m, 2H, HC(12), HC(3)), 1.28 (t, *J* = 7.2 Hz, 3H, HC(16)).

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

δ 173.7 (C14), 154.8 (C9), 135.4 (C17), 132.7 (C19), 129.7 (C5), 129.3 (C18), 127.5 (C7,C20), 122.2 (C10), 120.6 (C6), 117.1 (C8), 78.4 (C2), 60.7 (C15), 53.5 (C11), 32.0 (C13), 26.4 (C3), 25.1 (C4), 24.9 (C12), 14.5 (C16).

IR: (ATR, cm^{-1})

2930 (w), 1729 (s), 1609 (w), 1582 (m), 1487 (s), 1457 (m), 1438 (m), 1373 (m), 1302 (m), 1273 (m), 1231 (s), 1183 (s), 1150 (m), 1103 (m), 1067 (m), 1024 (m), 995 (m), 935 (w), 883 (w), 852 (w), 832 (w), 749 (s).

MS: (EI, 70 eV, m/z)

356 (36, M^+), 311 (22), 247 (100), 201 (58), 177 (43), 159 (65), 149 (81), 133 (100), 107 (62) .

TLC: R_f 0.22 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

Opt. Rot.: $[\alpha]_D^{23}$ = +92.0 (c = 0.70 in $CHCl_3$)

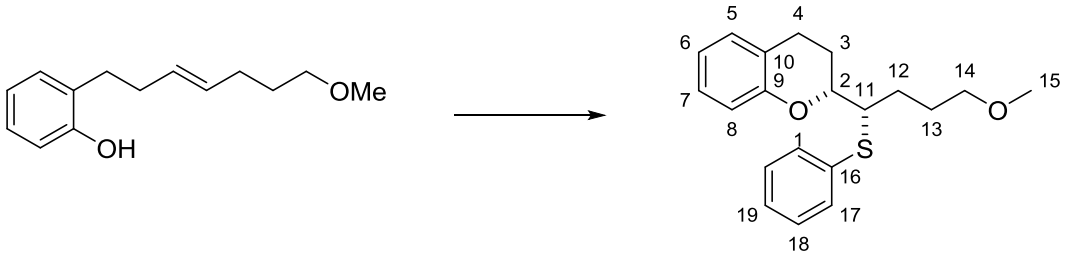
CD: (+), Cotton sign, 230-280 nm

CSP-HPLC: (2*S*,11*R*)-**144r** t_{min} 16.5 min (6.8%),(2*R*,11*S*)-**144r** t_{maj} 24.7 min (93.2%) (Chiralcel OJ, 220 nm, 95:5 hexanes/*i*-PrOH, 0.8 mL/min)

Analysis: $C_{21}H_{24}O_3S$ (356.48)

Calcd:	C, 70.76;	H, 6.79%
Found:	C, 70.82;	H, 6.67%

Preparation of (*R*)-2-((*S*)-4-Methoxy-1-(phenylthio)butyl)chromane (144s) (Table 19 Entry 10) [DJK-EK-9062]



142s **144s**

Following General Procedure 11, **142s** (220 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to -20 ^oC (probe). After equilibration (ca. 20 min), MsOH (33 μL, 0.5 mmol, 0.5 equiv) was added directly via syringe. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^1H NMR), the reaction was quenched with triethylamine (300 μL) and then was allowed to warm to rt, whereupon the white solid dissolved. The material was transferred to a 250-mL RB-flask using 20 mL of CH_2Cl_2 and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). The material was dissolved in 10 mL of CH_2Cl_2 and adsorbed onto Celite. Purification by silica gel flash column chromatography (5:1, hexanes/CH_2Cl_2, 20 mm diameter, 18 cm SiO_2) followed by bulb-to-bulb distillation afforded 287 mg (88%) of **144s** as a clear viscous oil.

Data for **144s**:

bp: 150 ^{o}C (ABT), 0.05 mm Hg

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

δ 7.56–7.48 (m, 2H, HC(18)), 7.32 (t, *J* = 6.8, 2H, HC(17)), 7.29–7.25 (m, 1H, HC(19)), 7.11 (t *J* = 7.3 Hz, 1H, HC(7)), 7.06 (d, *J* = 7.3 Hz, 1H, HC(5)), 6.86 (t, *J* = 7.4 Hz, 1H, HC(6)), 6.79 (d, *J* = 8.1 Hz, 1H, HC(8)), 4.12 (ddd, *J* = 9.9, 6.5, 2.2 Hz, 1H, HC(2)), 3.52–3.41 (m, 2H, HC(14)), 3.37 (s, 3H, HC(15)), 3.33 (ddd, *J* = 8.9, 6.5, 3.3 Hz, 1H, HC(11)), 2.90–2.81 (m, 1H, HC(4)), 2.80–2.72 (m, 1H, HC(4)), 2.26 (dddd, *J* = 13.4, 5.8, 3.5, 2.3 Hz, 1H, HC(3)), 2.13–1.92 (m, 3H, HC(3), HC(12), HC(13)), 1.88–1.76 (m, 1H, HC(13)), 1.76–1.67 (m, 1H, HC(12)).

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

δ 154.9 (C9), 136.1 (C16), 132.4 (C18), 129.7 (C5), 129.2 (C17), 127.5 (C7), 127.2 (C19), 122.3 (C10), 120.4 (C6), 117.0 (C8), 78.5 (C2), 72.9 (C14), 58.9 (C15), 54.1 (C11), 28.0 (C3), 27.5 (C12), 25.0 (C4), 24.9 (C11).

IR: (ATR, cm^{-1})

2924 (w), 2855 (w), 1736 (w), 1609 (w), 1582 (m), 1487 (s), 1456 (m), 1438 (m), 1374 (w) 1302 (m), 1273 (w), 1232 (s), 1194(m), 1114 (s), 1051 (m), 1024 (m), 995 (m), 886 (m), 850 (w), 830 (w), 748 (s).

MS: (EI, 70 eV, m/z)

328 (58, M^{+}), 219 (69), 195 (52), 187 (36), 163 (84), 133 (97), 107 (100), 85 (50), 69 (66).

TLC: R_f 0.15 (1:1, hexanes/CH_2Cl_2) [UV, CAM]

Opt. Rot.: $[\alpha]_D^{23}$ = +81.4 (c = 0.68 in $CHCl_3$)

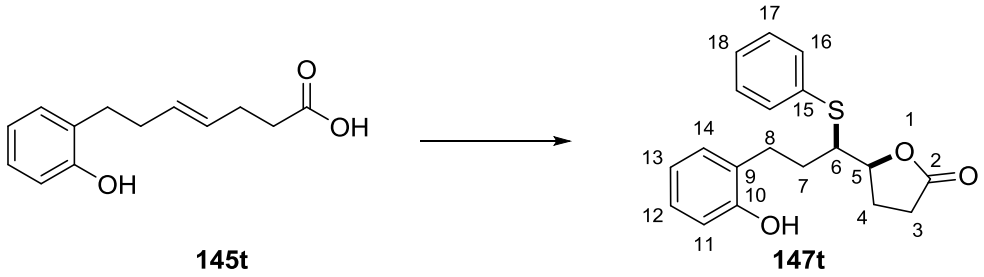
CD: (+), Cotton sign, 230-280 nm

CSP-HPLC: (2*S*,11*R*)-**144s** t_{min} 10.4 (3.3%), (2*R*,11*S*)-**144s** t_{maj} 13.4 min (96.7%) (Chiralcel OJ, 220 nm, 95:5, hexanes/*i*-PrOH, 0.8 mL/min)

Analysis: $C_{20}H_{24}O_2S$ (328.47)

Calcd:	C, 73.13;	H, 7.37%
Found:	C, 73.41;	H, 7.28%

Preparation of (*S*)-5-((*R*)-3-(2-Hydroxyphenyl)-1-(phenylthio)propyl)-dihydrofuran-2(3H)-one (147t) (Table 19 Entry 11) [DJK-15-44]



145t **147t**

Following General Procedure 11, **145t** (220 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to -20 ^oC (probe). After equilibration (ca. 20 min), MsOH (33 μL, 0.5 mmol, 0.5 equiv) was added directly via syringe. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^1H NMR), the reaction was quenched with triethylamine (300 μL) and then was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, then was diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). Purification by silica gel flash column chromatography (6:1, hexanes/ethyl acetate, then 3:1, hexanes/ethyl acetate then 2:1, hexanes/ethyl acetate, 30 mm diameter, 16 cm SiO_2) followed by bulb-to-bulb distillation afforded 300 mg (92%) of **147t** as a clear viscous oil.

Data for **147t**:

bp: 120 ^oC (ABT), 2.4x 10^{-5} mm Hg

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

δ 7.53–7.48 (m, 2H, HC(17)), 7.37–7.31 (m, 3H, HC(16), HC(18)), 7.17–7.11 (m, 2H, HC(12), HC(14)), 6.90 (t, *J* = 7.5 Hz, 1H, HC(13)), 6.82 (d, *J* = 8.2, 1H, HC(11)), 5.09 (s, 1H, OH)), 4.59 (q, *J* = 7.3 Hz, 1H, HC(5)), 3.26–3.15 (m, 1H, HC(6)), 3.08 (ddd, *J* = 13.9, 9.2, 4.9 Hz, 1H, HC(8)), 2.88 (ddd, *J* = 14.1, 9.1, 7.1 Hz, 1H, HC(8)), 2.68–2.49 (m, 2H, HC(3)), 2.41 (dddd, *J* = 13.1, 9.6, 7.1, 4.9 Hz,

1H, HC(4)), 2.28–2.18 (m, 1H, HC(7)), 2.14–2.01 (m, 1H, HC(4)), 1.87 (dtd, *J* = 14.2, 9.5, 4.9 Hz, 1H, HC(7)).

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

δ 176.9 (C2), 153.9 (C10), 133.9 (C15), 133.0 (C17), 130.7 (C12), 129.4 (C16), 128.1 (C18), 127.9 (C14), 127.1 (C9), 121.2 (C13), 115.8 (C11), 82.6 (C5), 54.2 (C6), 31.8 (C8), 29.0 (C3), 27.4 (C4), 26.1 (C7).

IR: (ATR, cm^{-1})

3360 (br), 2924 (w), 1749 (s), 1582 (w), 1504 (w), 1488 (w), 1455 (s), 1438 (w), 1345 (w), 1303 (w), 1230 (s), 1180 (s), 1100 (w), 1068 (w), 1023 (w), 913 (w), 846 (w), 748 (s).

MS: (EI, 70eV, m/z)

328 (9), 249 (21), 247 (83), 201 (38), 177 (27), 159 (44), 149 (60), 133 (100), 107 (68)

TLC: R_f 0.05 (4:1, hexanes/ethyl acetate) [UV, CAM]

Opt. Rot.: $[\alpha]_D^{23}$ = +35.4 (c = 0.68 in $CHCl_3$)

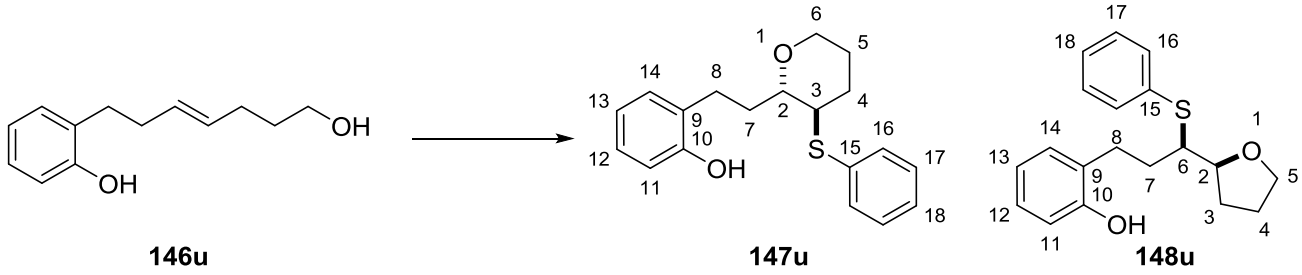
CD: (-), Cotton sign, 230-280 nm

CSP-HPLC: (5*R*,6*S*)-**147t** t_{min} 20.2 min (7.8%), (5*S*,6*R*)-**147t** t_{min} 23.5 min (92.2%) (Reverse Phase Chiralpak AD-RH, 220 nm, 48:52, H_2O/MeCN, 0.3 mL/min)

Analysis: $C_{19}H_{20}O_3S$ (328.43)

Calcd:	C, 69.49;	H, 6.14%
Found:	C, 69.56;	H, 6.08%

Preparation of ((*R*)-3-(Phenylthio)-3-((*S*)-tetrahydrofuran-2-yl)propyl)phenol (147u) and 2-((*R*)-3-(phenylthio)-3-((*S*)-tetrahydrofuran-2-yl)propyl)phenol (148u) (Table 19 Entry 12) [DJK-EK-9063]



146u **147u** **148u**

Following General Procedure 11, **146u** (206 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to -20 ^oC (probe). After equilibration (ca. 20 min), MsOH (33 μL, 0.5 mmol, 0.5 equiv) was added directly via syringe. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^1H NMR), the reaction was quenched with triethylamine (300 μL) and then was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, then was diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). The crude ratio of **147u:148u** (1.1:1) was established by ^1H NMR spectroscopy. Purification by silica gel flash column chromatography (12:1, hexanes/ethyl acetate, 30 mm diameter, 16 cm SiO_2) followed by bulb-to-bulb distillation afforded 276 mg (88%) of a 1:1 mixture of **147u**:**148u** as a clear oil.

Data for **147u**:

bp: 180 ^{o}C (ABT), 0.05 mm Hg

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

δ 7.41–7.37 (m, 2H, HC(17)), 7.34–7.22 (m, 3H, HC(16), HC(18)), 7.16 (dd, *J* = 7.9, 7.3 Hz, 1H, HC(12)), 7.07 (dd, *J* = 7.5 Hz, 1H, HC(14)), 6.89 (d, *J* = 8.1 Hz, 1H, HC(11)), 6.85 (t, 7.8 Hz, 1H, HC(13)), 6.82 (br s, 1H, OH), 4.06 (ddd, *J* = 8.7, 7.7, 6.4 Hz, 1H, HC(2)), 4.01 (dt, *J* = 8.0, 6.9 Hz, 1H, HC(5)), 3.90 (td, *J* = 7.9, 6.2 Hz, 1H, HC(5)), 3.12 (dt, *J* = 8.9, 5.5 Hz, 1H, HC(6)), 2.93 (ddd, *J* = 13.9, 9.0, 6.8 Hz, 1H, HC(8)), 2.79 (ddd, *J* = 14.4, 9.1, 6.1 Hz, 1H, HC(8)), 2.21 (dddd, *J* = 12.6, 7.9, 6.4, 5.0 Hz, 1H, HC(3)), 2.16–1.89 (m, 4H, HC(4), HC(8)), 1.77 (ddt, *J* = 12.5, 8.4, 7.6 Hz, 1H, HC(7)).

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

δ 154.8 (C10), 134.7 (C15), 132.0 (C17), 130.5 (C14), 129.2 (C16), 127.9 (C12), 127.3 (C18), 127.1 (C9), 120.4 (C13), 116.3 (C11), 82.7 (C2), 68.8 (C5), 52.3 (C6), 34.1 (C7), 31.4 (C3), 27.6 (C8), 25.9 (C4).

IR: (ATR, cm^{-1})

3306 (br), 2927 (w), 2866 (w), 1737 (w), 1582 (m), 1488 (m), 1455 (s), 1438 (m), 1359 (m), 1232 (s), 1177 (m), 1088 (m), 1041 (s), 921 (m), 843 (w), 746 (s).

MS: (EI, 70 eV, m/z)

314 (47, M^+), 133 (67), 107 (100), 71 (62)

TLC: R_f 0.25 (4:1, hexanes/ethyl acetate) [UV, CAM]

Opt. Rot.: $[\alpha]_D^{23}$ = -17.3 (c = 0.52 in $CHCl_3$)

CD: (-), Cotton sign, 230-280 nm

Data for **148u**:

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

δ 7.31 (m, 3H, HC(aryl)), 7.24 (m, 3H, HC(aryl)), 7.17–7.05 (m, 2H, HC(12), H(C14)), 6.86 (m, 2H, HC(11), HC(13)), 4.04 (dd, *J* = 11.4, 4.0, 1H, HC(2)), 3.41 (td, *J* = 11.7, 2.7 Hz, 1H, HC(5)), 3.16 (td, *J* = 9.9, 2.8 Hz, 1H, HC(5)), 2.91–2.67 (m, 2H, HC(3), HC(8)), 2.62 (ddd, *J* = 14.3, 6.1, 4.2 Hz, 1H, HC(8)), 2.45 (dddd, *J* = 13.9, 10.9, 6.1, 2.8 Hz, 1H, HC(3)), 2.17–2.01 (m, 1H, HC(4)), 2.01–1.57 (m, 3H, HC(3), HC(4), HC(7)), 1.53–1.34 (m, 1H, HC(7)).

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

δ 155.0 (C10), 135.0 (C15), 133.7 (C17), 130.7 (C14), 129.2 (C16), 128.0 (C12), 124.4 (C9), 120.7 (C13), 116.4 (C11), 79.7 (C2), 68.3 (C5), 49.3 (9), 34.6 (C8), 31.7 (C4), 27.0 (C3), 25.2 (C7).

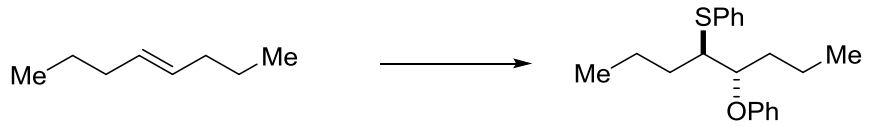
CSP-HPLC: (2*R*,6*S*)-**148u** t_{maj} 19.2 min (97.1%), (2*S*,6*R*)-**148u** t_{min} 20.83 min (2.9%) (Chiralpak AD, 220 nm, 90:10, hexanes/*i*-PrOH, 0.6 mL/min)

(2*R*,3*S*)-**147u**, t_{maj} 14.6 min (96.9%), **(**2*S*,3*R*)-**147u**, t_{min} 18.1 min (3.1%) (Chiralpak AD 220 nm, 90:10 hexanes/*i*-PrOH, 0.6 mL/min)

Analysis: $C_{19}H_{22}O_2S$ (314.44)

Calcd:	C, 72.58;	H, 7.05%
Found:	C, 72.64;	H, 6.95%

Preparation of ((4*R*,5*S*)-5-Phenoxyoctan-4-yl)(phenyl)sulfide (149) (Table 20 Entry 1) [DJK-16-40]



149

Following General Procedure 11, 4-octene (112 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to -20 ^{o}C (probe). After equilibration (ca. 20 min), MsOH (33 μL, 0.5 mmol, 0.5 equiv) was added directly via syringe. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^{1}H NMR), the reaction was quenched with triethylamine (300 μL) and then was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, then was diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^{o}C, 3 mm Hg). Purification by silica gel flash column chromatography (5:1

hexanes/dichloromethane, 30 mm diameter, 16 cm SiO_2) followed by bulb-to-bulb distillation afforded 229 mg (73%) of **149** as a clear viscous oil. This compound was not further characterized

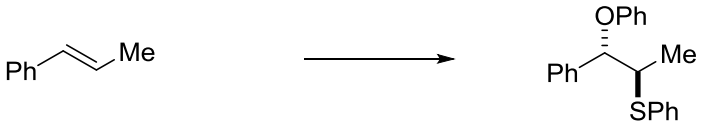
Data for **149**:

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

δ 7.55 – 7.45 (m, 1H), 7.38 – 7.10 (m, 6H), 6.91 (t, *J* = 7.4 Hz, 1H), 6.84 – 6.77 (m, 2H), 4.39 (dt, *J* = 8.1, 4.3 Hz, 1H), 3.34 (dt, *J* = 8.7, 4.2 Hz, 1H), 1.55 (s, 8H), 0.90 (dt, *J* = 13.4, 7.2 Hz, 6H).

CSP-HPLC: (4*R*,5*S*)-**149** t_{maj} 4.8 min (93.0%), (4*S*,5*R*)-**149** t_{min} 5.2 min (7.0%) (Chiralpak OJ-H, 220 nm, 97:3, hexanes/*i*-PrOH, 0.8 mL/min)

Preparation of ((1*S*,2*R*)-1-Phenoxy-1-phenylpropan-2-yl)(phenyl)sulfide (150) (Table 20 Entry 2) [DJK-16-41]



150

Following General Procedure 11, 4-octene (112 mg, 1.0 mmol) was weighed into a dried 10-mL Schlenk flask. Subsequently, CH_2Cl_2 (7 mL), electrophile **56** (255 mg, 1.0 mmol, 1.0 equiv) and catalyst (*S*)-**62e** (52 mg, 0.1 mmol, 0.1 equiv) were added. The flask was placed in an *i*-PrOH bath and cooled to -20 ^oC (probe). After equilibration (ca. 20 min), MsOH (33 μL, 0.5 mmol, 0.5 equiv) was added directly via syringe. The solution was allowed to stir for 24 h at constant temperature during which time phthalimide precipitated. Upon consumption of the starting material (TLC, ^{1}H NMR), the reaction was quenched with triethylamine (300 μL) and then was allowed to warm to rt, whereupon the white solid dissolved. The solution was transferred to a 60-mL separatory funnel, then was diluted with CH_2Cl_2 (10 mL) and 1 M NaOH (15 mL). The phases were separated and the aq. layer was extracted with 15 mL of CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered and concentrated by rotary evaporation (30 ^oC, 3 mm Hg). Purification by silica gel flash column chromatography (5:1 hexanes/dichloromethane, 30 mm diameter, 16 cm SiO_2) followed by bulb-to-bulb distillation afforded 140 mg (44%) of **150** as a clear viscous oil.

Data for **150**:

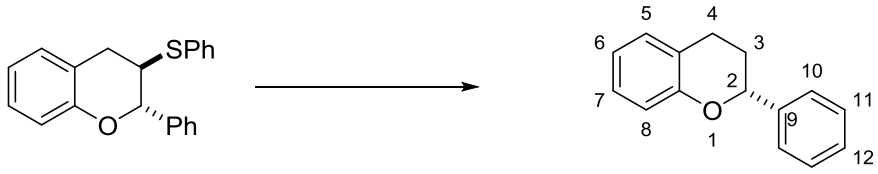
^{1}H NMR: (500 MHz, $CDCl_3$)

δ 7.41 – 7.15 (m, 13H), 6.80 – 6.74 (m, 2H), 4.04 – 3.94 (m, 1H), 3.91 (d, *J* = 10.2 Hz, 1H), 1.26 (d, *J* = 6.5 Hz, 3H).

CSP-HPLC: Reverse-Phase, (1*R*,2*S*)-**150** t_{min} 16.0 min (82.1%), (1*S*,2*R*)-**150** t_{min} 16.0 min (17.9%) (Chiralpak AD-RH, 220 nm, 65:35, H_2O/MeCN, 0.6 mL/min)

Manipulations of 143a

Preparation of (*R*)-2-Phenylchromane (154a) [DJK-19-16]



143a **154a**

To a 50-mL Schlenk flask under argon was added *i*-PrOH (20 mL), followed by solid **143a** (238 mg, 0.75 mmol). The solid was dissolved by heating, and the flask was then cooled in an ice bath (internal temperature <5 ^oC). Solid $NiCl_2$•$6H_2O$ (600 mg, 2.5 mmol, 3.3 equiv) to form a green solution. In a seperate flask, $NaBH_4$ (300 mg, 7.9 mmol, 10.5 equiv) was dissolved in EtOH (20 mL) with stirring. This flask was then also cooled in an ice bath (internal temperature 3 ^oC). The cold borohydride solution in ethanol was cannulated into the flask containing the substrate and the nickel chloride. The solution turned black, and gas evolution was observed. The flask was maintained in the ice bath for a further 4 h. The resulting black suspension was filtered through Celite while cold and the filter cake was washed with CH_2Cl_2 (2x25 mL). The filtrate was then concentrated by rotary evaporation (30 ^oC, 3 mm Hg). Purification of the residue by silica gel flash column chromatography (9:1, hexanes/CH_2Cl_2, 20 mm diameter, 15 cm SiO_2) afforded 111 mg (71%) of **154** as a white solid. The spectroscopic data match those reported in the literature.[171] Absolute configuration was established by correlation with the known optical rotation.[103]

Data for **154**:

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

δ 7.47 (d, *J* = 7.5 Hz, 2H, HC((11)), 7.43 (t, *J* = 7.4 Hz, 2H, HC(10)), 7.36 (t, *J* = 7.2 Hz, 1H, HC(12)), 7.17 (t, *J* = 7.7 Hz, 1H, HC(7)), 7.13 (d, *J* = 7.1 Hz, 1H, HC(5)), 6.95 (d, *J* = 7.5 Hz, 1H, HC(8)), 6.92 (t, *J* = 7.4 Hz, 1H, HC(6)), 5.11 (dd, *J* = 10.2, 2.5 Hz, 1H, HC(2)), 3.05 (ddd, *J* = 17.0, 11.4, 5.9 Hz, 1H, HC(4)), 2.85 (ddd, *J* = 16.5, 5.3, 3.3 Hz, 1H, HC(4)), 2.26 (dddd, *J* = 13.7, 5.9, 3.3, 2.4 Hz, 1H, HC(3)), 2.14 (dddd, *J* = 13.7, 11.2, 10.2, 5.3 Hz, 1H, HC(3)).

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

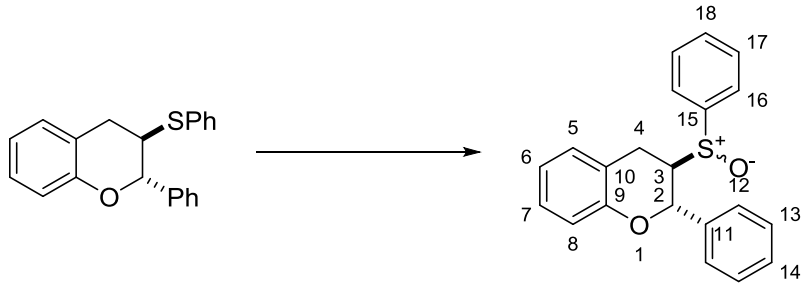
δ 155.1, 141.7, 129.5, 128.5, 128.4, 127.8, 127.3, 125.9, 121.8, 120.3, 116.9, 77.7, 29.9, 25.0.

MS: (EI, 70 eV, m/z)

210 (100, M^+), 129 (32), 171 (14), 119 (14), 104 (27), 77 (12)

Opt. Rot: $[\alpha]_D^{23}$ = +16.6 (c = 1.05 in $CHCl_3$)

Preparation of (2*S*,3*R*)-2-Phenyl-3-((*R*,*S*)-phenylsulfinyl)chromane (151a/b) [DJK-17-62]



143a **151a/b**

To a 250-mL RB-flask under argon was added MeOH (100 mL) and **143a** (2.23 g, 7.0 mmol). Sodium periodate (1.65 mg, 7.7 mmol, 1.1 equiv) was added as a solid resulting in a heterogenous solution. The mixture was then heated to 50 ^{o}C for 16 h. TLC analysis showed trace amounts of remaining starting material, however, formation of the corresponding sulfone was also observed and the flask therefore removed from heat. After the solution cooled to rt, water (100 mL) and CH_2Cl_2 (100 mL) was added to afford a clear, biphasic mixture. The mixture was transferred to a 500-mL separatory funnel, was shaken thoroughly, and the layers were separated. The aq. layer was extracted with further CH_2Cl_2 (2x 50 mL). The organic layers were combined, washed with water (25 mL), brine (25 mL), dried over $MgSO_4$, filtered and

concentrated by rotary evaporation (30 ^{o}C, 3 mm Hg). Analysis of the crude material by ^{1}H NMR spectroscopy revealed a 2:1 diastereomeric mixture. Purification by silica gel flash column chromatography (9:1, hexanes/ethyl acetate, then 4:1, hexanes/ethyl acetate, 30 mm diameter, 16 cm SiO_2) separated the diastereomers. Recombination of the diastereomers **151a** and **151b**, followed by recrystallization (EtOH, 2 mL) afforded, in two crops, 284 mg (85% combined yield) of a 2:1 mixture of **151a**/**151b** as white to pale yellow prisms.

Data for **151a**:

mp: 138-140 ^{o}C (EtOH)

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

δ 7.59–7.39 (m, 10H, HC(aryl)), 7.12 (t, *J* =8.4 Hz, 1H, HC(7)), 7.03 (d, *J* = 8.4 Hz, 1H, HC(5)), 6.95–6.84 (m, 2H, HC(6), HC(8)), 5.12 (d, *J* = 9.1 Hz, 1H, HC(2)), 3.50 (dd, *J* = 16.9, 10.2 Hz, 1H, HC(4)), 3.12 (ddd, *J* = 10.3, 9.1, 5.4 Hz, 1H, HC(3)), 2.31 (dd, *J* = 16.8, 5.4 Hz, 1H, HC(4)).

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

δ 154.2 (C9), 141.4 (C15), 138.2 (C11), 131.3 (C18), 130.2 (C7), 129.5 (C17), 129.4 (C14), 129.3 (C13), 127.9 (C5), 127.6 (C16), 124.6 (C12), 121.5 (C6), 120.2 (C10), 117.0 (C8), 77.7 (C2), 63.5 (C3), 20.4 (C4).

IR: (ATR, cm^{-1})

3050 (w), 1609 (w), 1583 (w), 1487 (m), 1455 (m), 1443 (m), 1369 (w), 1298 (w), 1232 (s), 1194 (w), 1177 (w), 1110(w), 1085 (m), 1034 (s), 999 (m), 931 (m), 910 (m), 873 (w), 840 (w), 830 (w), 788 (m), 747 (s), 698 (s), 686 (s)

MS: (EI, 70 eV, m/z)

335 ($M+H^+$, 100), 209 (66)

TLC: R_f 0.2 (4:1 hexanes/ethyl acetate) [UV, CAM]

Analysis: $C_{21}H_{18}O_2S$ (334.43)

Calcd: C, 75.42; H, 5.43%

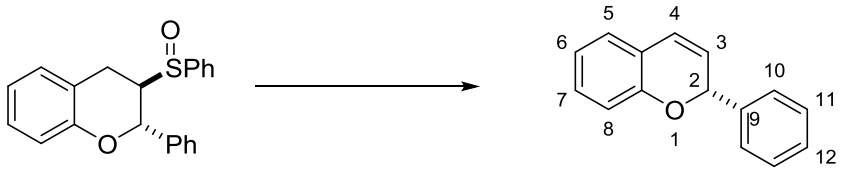
Found: C, 75.06; H, 5.23%

Data for 151b:

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

δ 7.72–7.65 (m, 2H, HC(aryl)), 7.61–7.53 (m, 3H, HC(aryl)), 7.37–7.33 (m, 4H, HC(aryl)), 7.27 (m, 2H, HC(aryl)), 7.10 (d, *J* = 8.4 Hz, 1H, HC(5)), 6.97–6.92 (m, 2H, HC(6), HC(8)), 6.09 (dd, *J* = 3.1, 1.5 Hz, 1H, HC(2)), 3.42 (dt, *J* = 5.2, 3.2 Hz, 1H, HC(3)), 2.82 (dd, *J* = 17.7, 5.2 Hz, 1H, HC(4)), 2.38 (ddd, *J* = 17.7, 2.9, 1.2 Hz, 2H, HC(4)).

Preparation of (*S*)-2-Phenyl-2H-chromene (154b) [DJK-17-64]



151a,b **154b**

To a 10-mL Schlenk flask under argon was added a 1:1 diastereomeric mixture of sulfoxides **151a,b** (334 mg, 1.0 mmol) and toluene (10 mL). Trimethylphosphite (236 μL, 2.0 mmol, 2 equiv) was added via syringe. The solution was then heated to reflux in an oil bath for 4 h. After the reaction was complete (TLC), the flask was removed from the oil bath and allowed to cool to rt. The solution was concentrated by rotary evaporation (30 ^{o}C, 3 mm Hg). Purification by silica gel flash column chromatography (9:1 hexanes/CH_2Cl_2 then 5:1 hexanes/CH_2Cl_2, 20 mm diameter, 16 cm SiO_2) afforded 193 mg (92%)of **154b** a clear oil. The spectroscopic data match those reported in the literature.[103] The rotation is in agreement with the absolute configuration shown.[163]

Data for **154b**:

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

δ 7.53–7.46 (m, 2H, HC(aryl)), 7.47–7.33 (m, 3H, HC(aryl)), 7.16 (t, *J* = 7.8 Hz, 1H, HC(7)), 7.06 (d, *J* = 7.5 Hz, 1H, HC(5)), 6.91 (t, *J* = 7.4 Hz, 1H, HC(6)), 6.84 (d, *J* = 8.0 Hz, 1H, HC(8)), 6.58 (d, *J* = 9.8 Hz, 1H, HC(4)), 5.97 (d, *J* = 2.1 Hz, 1H, HC(2)), 5.85 (dd, *J* = 9.9, 3.3 Hz, 1H, HC(3))

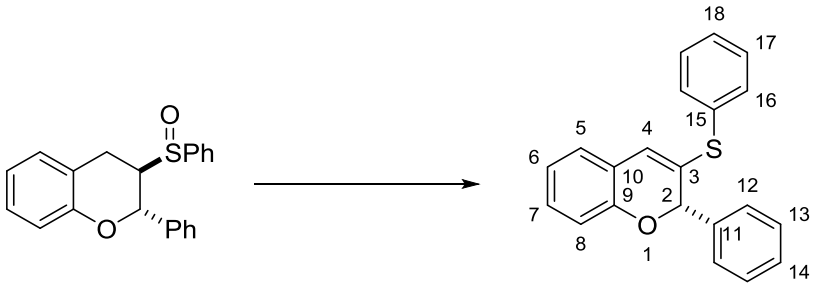
^{13}C NMR: 153.2, 140.9, 129.5, 128.6, 128.3, 127.0, 126.6, 124.8, 124.0, 121.3, 121.2, 116.0, 77.2

MS: (EI, 70 eV, m/z)

208 (90, M^+), 207 (100), 178 (15), 131 (41)

Opt. Rot: $[\alpha]_D^{23}$ = +97.6 (c = 1.1 in $CHCl_3$)

Preparation of (*S*)-2-Phenyl-3-(phenylthio)-2H-chromene (152) [DJK-17-63]



151a,b **152**

To a 50-mL Schlenk flask under argon was added a 1:1 mixture of **151a,b** (334 mg, 1 mmol) and toluene (8 mL). To this was added pyridine (805 μL, 10 mmol, 10 equiv) via syringe followed by trifluoroacetic anhydride (278 μL, 2.0 mmol, 2.0 equiv). The solution was then heated to 80 °C (internal temperature, oil bath) for 4 h. The flask was then removed from the heat source and allowed to cool to rt. The mixture was transferred to a 60-mL separatory funnel and diluted with water (10 mL) and ether (15 mL). The layers were separated and the aq. layer extracted with ether (2x 10 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated by rotary evaporation (30 °C, 3 mm Hg). Purification by silica gel flash column chromatography (9:1, hexanes/CH_2Cl_2 then 5:1, hexanes/CH_2Cl_2, 20 mm diameter, 16 cm SiO_2) followed by recrystallization (hexanes, 2 mL) afforded 292 mg (92%) of **152** as white prisms.

Data for **152**:

mp: 86-88 °C (hexanes)

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

δ 7.49 (d, *J* = 6.6 Hz, 2H, HC(aryl)), 7.43–7.32 (m, 8H, HC(aryl)), 7.12 (t, *J* = 7.7 Hz, 1H, HC(7)), 7.00 (d, *J* = 7.6, Hz, 1H, HC(5)), 6.90 (t, *J* = 7.5 Hz, 1H, HC(6)), 6.78 (d, *J* = 8.0 Hz, 1H, HC(8)), 6.66 (s, 1H, HC(4)), 5.75 (s, 1H, HC(2)).

^{13}C NMR: (126 MHz, CDCl3)

δ 151.8 (C9), 138.5 (C15), 132.5 (C17), 132.3 (C11), 131.4 (C13), 129.7 (C9), 129.6 (C16), 129.1 (C18), 128.7 (C13), 128.3 (C14), 128.0 (C12), 126.3 (C7), 125.4 (C4), 122.4 (C10), 121.8 (C6), 116.5 (C8), 79.6 (C2)

IR: (ATR, cm^{-1})

3047 (w), 3028 (w), 2942 (w), 1902 (w), 1736 (w), 1704 (w), 1625 (w), 1600 (w), 1581 (w), 1570 (w), 1483 (m), 1473 (m), 1450 (m), 1437 (m), 1348 (w), 1326 (m), 1301 (w), 1258 (m), 1223 (m), 1206 (m), 1194 (m), 1160 (w), 1148 (w), 1115 (m), 1078 (w), 1065 (m), 1045 (m),1022 (m), 1000 (w), 962 (m), 937 (m), 924 (m), 905 (m), 889 (m), 854 (m), 832 (w), 776 (m), 764 (m), 747 (s), 737 (s), 697 (s), 688 (s)

MS: (EI, 70 eV, m/z)

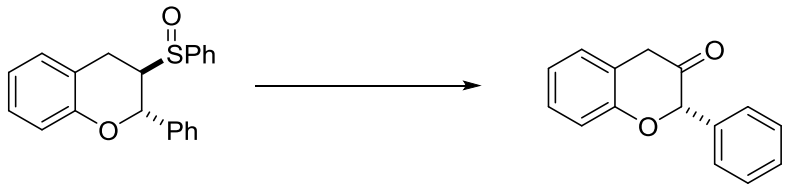
316 (40, M^+), 207 (100), 178 (23)

TLC: R_f 0.57 (4:1 hexanes/ethyl acetate) [UV, CAM]

Analysis: $C_{21}H_{16}OS$ (316.42)

Calcd:	C, 79.71;	H, 5.10%
Found:	C, 79.31;	H, 4.97%

Attempted Conditions for the Pummerer Rearrangement of 151

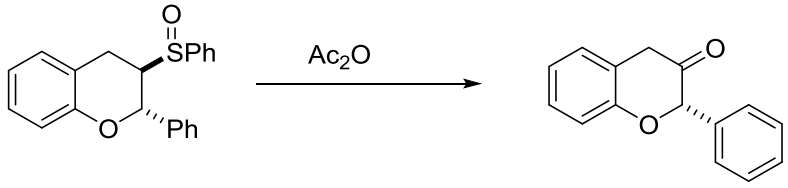


151a,b **152**

General Procedure

To a 5-mL oven- or flame-dried Schlenk flask was added a **151a**, **151b** or a mixture thereof , followed by solvent and additives. The solution was then heated to the specified temperature and then stirred. Aliquots for NMR were obtained by adding ~5 μL of solution to an NMR tube containing 0.7 mL of $CDCl_3$. Ratios were determined by integration of peaks at 5.97 (**154b**), 5.7 ppm (**152**) and 3.8 ppm (**143a**).

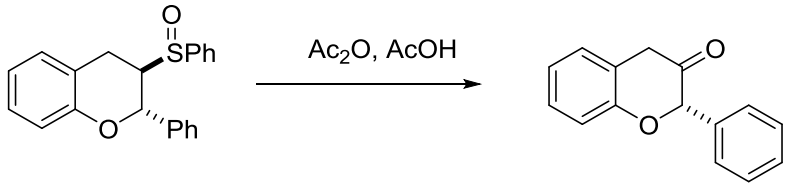
Attempted Preparation of (*S*)-2-phenylchroman-3-one with Ac_2O [DJK-17-75]



151a,b **152**

Sulfoxide **151** (33.4 mg, 0.1 mmol) was added to a Schlenk flask. Acetic anhydride (1 mL) was added and the reaction heated to 110 ^{o}C for 2 h. Analysis by ^{1}H NMR of the reaction showed primarily formation of elimination product **152**. No further manipulations were performed.

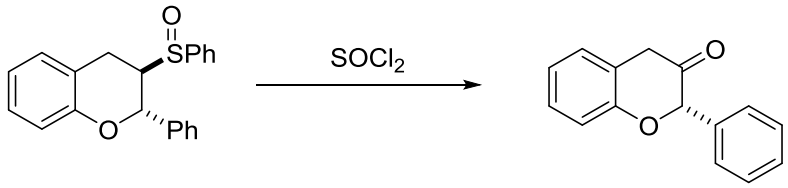
Attempted Preparation of (*S*)-2-phenylchroman-3-one with Ac_2O and AcOH [DJK-17-76]



151a,b **152**

Sulfoxide **151** (33.4 mg, 0.1 mmol) was added to a Schlenk flask. Acetic anhydride (0.75 mL) and acetic acid (0.25 mL) were added and the reaction heated to 110 ^{o}C for 2 h. Analysis by ^{1}H NMR of the reaction showed primarily formation of **154b**. No further manipulations were performed.

Attempted Preparation of (*S*)-2-phenylchroman-3-one with $SOCl_2$ [DJK-17-82]

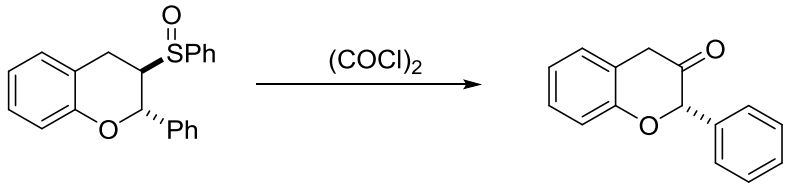


151a,b **152**

Sulfoxide **151** (33.4 mg, 0.1 mmol) was added to a Schlenk flask, followed by CH_2Cl_2. Thionyl chloride (47.6 mg, 0.4 mmol, 4.0 equiv) was added dropwise. The solution was stirred

for 1 h at rt. Analysis of the reaction by ^{1}H NMR spectroscopy showed a 0.75:1:0.1 mixture of **143a**:**151**:**152**. No further manipulations were performed.

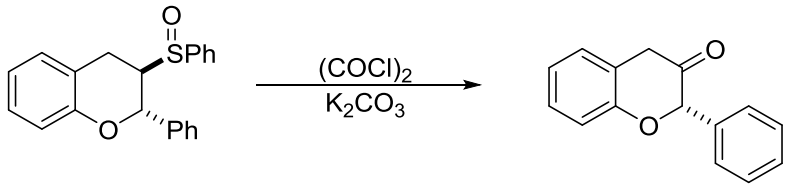
Attempted Preparation of (*S*)-2-phenylchroman-3-one with $(COCl)_2$ [DJK-17-81]



151a,b **152**

Sulfoxide **151** (33.4 mg, 0.1 mmol) was added to a Schlenk flask, followed by CH_2Cl_2 (1 mL). Oxalyl chloride (50.8 mg, 0.4 mmol, 4.0 equiv) was added dropwise. The solution was stirred for 1 h at rt. Analysis of the reaction by ^{1}H NMR spectroscopy showed a 1:1 mixture of **152** and **143a**. No further manipulations were performed.

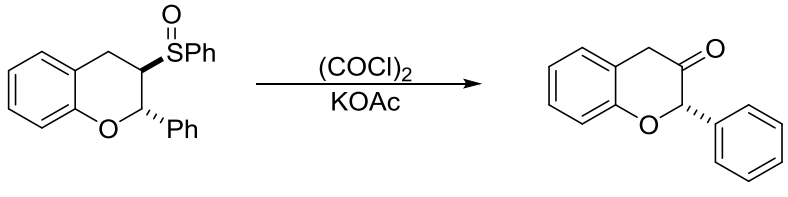
Attempted Preparation of (*S*)-2-phenylchroman-3-one with $(COCl)_2$ and K_2CO_3 [DJK-17-83]



151a,b **152**

Sulfoxide **151** (33.4 mg, 0.1 mmol) was added to a Schlenk flask, followed by CH_2Cl_2 (1 mL) and K_2CO_3 (55.3 mg, 0.4 mmol, 4.0 equiv). Oxalyl chloride (50.8 mg, 0.4 mmol, 4.0 equiv) was added dropwise. The solution was stirred for 2 h at rt. Analysis of the reaction by ^{1}H NMR spectroscopy showed a 3.5:1 mixture of **143a** and **152** and leftover starting material. No further manipulations were performed.

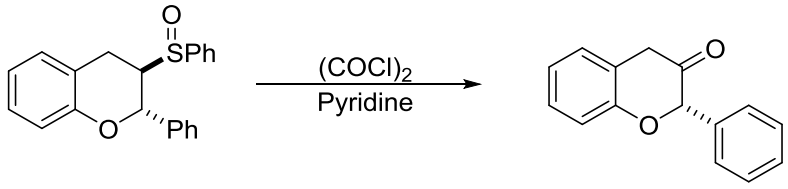
Attempted Preparation of (*S*)-2-phenylchroman-3-one with $(COCl)_2$ and KOAc [DJK-17-84]



151a,b **152**

Sulfoxide **151** (33.4 mg, 0.1 mmol) was added to a Schlenk flask, followed by CH_2Cl_2 (1 mL) and KOAc (39.3 mg, 0.4 mmol, 4.0 equiv). Oxalyl chloride (50.8 mg, 0.4 mmol, 4.0 equiv) was added dropwise. The solution was stirred for 2 h at rt. Analysis of the reaction by ^{1}H NMR spectroscopy showed a 4.8:1 mixture of **143a** and **152** and leftover starting material. No further manipulations were performed.

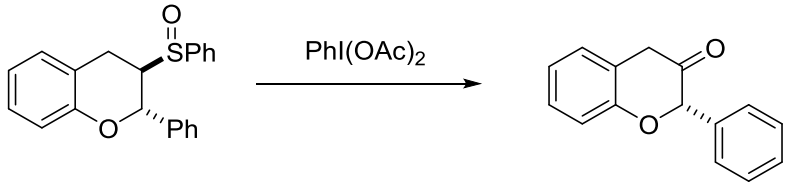
Attempted Preparation of (*S*)-2-phenylchroman-3-one with $(COCl)_2$ and Pyridine [DJK-17-85]



151a,b **152**

Sulfoxide **151** (33.4 mg, 0.1 mmol) was added to a Schlenk flask, followed by CH_2Cl_2 (1 mL) and pyridine (31.6 mg, 0.4 mmol, 4.0 equiv). Oxalyl chloride (50.8 mg, 0.4 mmol, 4.0 equiv) was added dropwise. The solution was stirred for 2 h at rt. Analysis of the reaction by ^{1}H NMR spectroscopy showed a 1:1.25 mixture of **152** and **143a**. No further manipulations were performed.

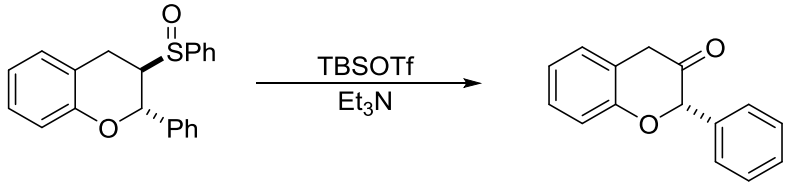
Attempted Preparation of (*S*)-2-phenylchroman-3-one with $PhI(OAc)_2$ [DJK-17-86]



151a,b **152**

Sulfoxide **151** (33.4 mg, 0.1 mmol) was added to a Schlenk flask, followed by dichloroethane (1 mL). Diacetoxyiodobenzene (64.4 mg, 0.2 mmol, 2.0 equiv) was added dropwise. The solution was stirred for 12 h at rt. Analysis of the reaction by ^{1}H NMR spectroscopy showed only starting material. No further manipulations were performed.

Attempted Preparation of (*S*)-2-phenylchroman-3-one with TBSOTf and Et_3N [DJK-17-88]

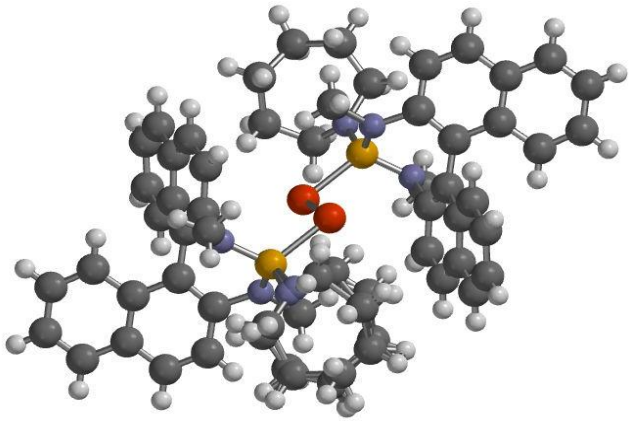


151a,b **152**

Sulfoxide **151** (33.4 mg, 0.1 mmol) was added to a Schlenk flask, followed by dichloromethane (1 mL) and Et_3N (20.2 mg, 0.2 mmol, 2 equiv). TBSOTf (52.9 mg, 0.2 mmol, 2 equiv) was added dropwise. The solution was stirred for 1 h at rt. Analysis of the reaction by ^{1}H NMR spectroscopy showed an 8:1 mixture of **151**:**152**. No further manipulations were performed.

5.6. Crystal Structures.

Crystallographic Data for **102**



Crystal data and structure refinement for bc11tasq.

Identification code	bc11tasq	
Empirical formula	C66 H76 Cl12 N6 O2 P2 Sb2 Se2	
Formula weight	1874.09	
Temperature	193(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 12.0050(6) Å	a= 67.081(2)°.
	b = 12.2783(6) Å	b= 73.258(2)°.
	c = 14.5779(7) Å	g = 88.706(2)°.
Volume	1885.47(16) $Å^3$	
Z	1	
Density (calculated)	1.651 Mg/m^3	
Absorption coefficient	11.470 mm^{-1}	
F(000)	934	
Crystal size	0.374 x 0.215 x 0.172 mm^3	
Theta range for data collection	3.45 to 67.82°.	
Index ranges	-14<=h<=14, -14<=k<=14, -16<=l<=17	
Reflections collected	23671	

Independent reflections	6453 [R(int) = 0.0376]
Completeness to theta = 67.82°	94.4 %
Absorption correction	Integration
Max. and min. transmission	0.3726 and 0.1241
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6453 / 499 / 556
Goodness-of-fit on F^2	1.047
Final R indices [I>2sigma(I)]	R1 = 0.0300, wR2 = 0.0805
R indices (all data)	R1 = 0.0315, wR2 = 0.0816
Largest diff. peak and hole	0.511 and -0.432 e.$Å^{-3}$

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for bc11tasq. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Sb(1)	-127(5)	4413(4)	2512(3)	38(1)
Cl(1)	1698(7)	3617(9)	2293(6)	101(2)
Cl(2)	-476(8)	3773(6)	1285(4)	56(2)
Cl(3)	-1950(6)	5195(6)	2703(6)	69(1)
Cl(4)	221(7)	5042(8)	3744(5)	74(2)
Cl(5)	-1008(8)	2579(4)	3876(4)	57(2)
Cl(6)	771(8)	6246(6)	1151(5)	66(1)
Sb(1B)	56(8)	4348(7)	2492(7)	42(2)
Cl(1B)	1247(10)	2788(10)	2581(8)	82(3)
Cl(2B)	-635(15)	4023(14)	1258(11)	64(5)
Cl(3B)	-1114(14)	5917(11)	2404(10)	104(4)
Cl(4B)	701(14)	4684(13)	3747(11)	85(5)

Cl(5B)	-1467(9)	2969(11)	3835(8)	80(3)
Cl(6B)	1589(11)	5721(12)	1136(9)	115(4)
Sb(1C)	158(5)	4446(4)	2521(3)	37(1)
Cl(1C)	2013(5)	3720(6)	2244(6)	70(1)
Cl(2C)	-203(6)	3843(7)	1287(5)	53(1)
Cl(3C)	-1657(7)	5240(9)	2754(7)	82(2)
Cl(4C)	545(8)	5059(7)	3742(5)	69(2)
Cl(5C)	-684(6)	2591(5)	3866(5)	62(2)
Cl(6C)	1016(9)	6304(6)	1156(6)	78(2)
Se(1)	137(1)	9337(1)	797(1)	41(1)
P(1)	2029(1)	9990(1)	333(1)	33(1)
N(2)	2168(2)	11434(2)	-286(2)	37(1)
N(3)	2920(2)	9529(2)	-496(2)	34(1)
N(1)	2366(6)	9525(7)	1411(3)	40(1)
C(1)	1801(5)	8404(5)	2307(3)	47(1)
C(2)	926(5)	8600(5)	3210(4)	59(1)
C(3)	1201(5)	9687(6)	3379(5)	65(2)
C(4)	2446(6)	9969(7)	3293(4)	69(2)
C(5)	3234(8)	10677(7)	2164(5)	59(1)
C(6)	3449(5)	10026(6)	1444(5)	49(1)
N(1B)	2160(20)	9400(20)	1498(9)	40(3)
C(1B)	1409(18)	8415(16)	2428(12)	47(3)
C(2B)	1381(17)	8417(12)	3474(10)	57(3)
C(3B)	1474(18)	9579(15)	3562(15)	63(3)
C(4B)	2600(20)	10350(20)	3123(16)	64(3)
C(5B)	3220(30)	10740(20)	1950(16)	59(4)
C(6B)	3290(18)	9770(20)	1544(17)	50(3)
C(7)	1380(2)	12156(3)	179(2)	46(1)
C(8)	3238(2)	12050(2)	-1095(2)	37(1)
C(9)	3883(3)	12852(2)	-916(2)	46(1)
C(10)	4881(3)	13476(2)	-1644(2)	49(1)

C(11)	5311(2)	13330(2)	-2599(2)	45(1)
C(12)	6366(3)	13967(3)	-3357(3)	57(1)
C(13)	6795(3)	13801(3)	-4257(3)	64(1)
C(14)	6197(3)	12964(3)	-4425(3)	58(1)
C(15)	5182(2)	12320(3)	-3708(2)	48(1)
C(16)	4681(2)	12501(2)	-2773(2)	40(1)
C(17)	3595(2)	11872(2)	-2011(2)	36(1)
C(18)	2926(2)	11009(2)	-2191(2)	33(1)
C(19)	2558(2)	11330(2)	-3104(2)	35(1)
C(20)	2624(3)	12522(2)	-3821(2)	45(1)
C(21)	2298(3)	12791(3)	-4697(2)	55(1)
C(22)	1900(3)	11872(3)	-4921(2)	56(1)
C(23)	1797(3)	10730(3)	-4245(2)	50(1)
C(24)	2092(2)	10422(2)	-3307(2)	40(1)
C(25)	1916(2)	9237(2)	-2565(2)	42(1)
C(26)	2173(2)	8948(2)	-1655(2)	39(1)
C(27)	2680(2)	9845(2)	-1476(2)	33(1)
C(28)	3479(2)	8429(2)	-109(2)	42(1)

Bond lengths [Å] and angles [°] for bc11tasq.

Sb(1)-Cl(4)	2.350(4)
Sb(1)-Cl(2)	2.352(4)
Sb(1)-Cl(5)	2.356(4)
Sb(1)-Cl(3)	2.357(4)
Sb(1)-Cl(6)	2.358(4)
Sb(1)-Cl(1)	2.366(5)
Sb(1B)-Cl(3B)	2.342(7)
Sb(1B)-Cl(2B)	2.348(7)
Sb(1B)-Cl(1B)	2.350(7)

Sb(1B)-Cl(4B)	2.353(7)
Sb(1B)-Cl(5B)	2.354(7)
Sb(1B)-Cl(6B)	2.363(7)
Sb(1C)-Cl(2C)	2.340(5)
Sb(1C)-Cl(4C)	2.341(5)
Sb(1C)-Cl(5C)	2.354(5)
Sb(1C)-Cl(3C)	2.356(5)
Sb(1C)-Cl(1C)	2.364(4)
Sb(1C)-Cl(6C)	2.369(5)
Se(1)-P(1)	2.2441(6)
Se(1)-Se(1)#1	2.3728(5)
P(1)-N(1)	1.619(3)
P(1)-N(1B)	1.621(8)
P(1)-N(2)	1.633(2)
P(1)-N(3)	1.638(2)
N(2)-C(8)	1.445(3)
N(2)-C(7)	1.483(3)
N(3)-C(27)	1.440(3)
N(3)-C(28)	1.475(3)
N(1)-C(6)	1.472(5)
N(1)-C(1)	1.480(5)
C(1)-C(2)	1.527(6)
C(1)-H(1A)	0.9900
C(1)-H(1B)	0.9900
C(2)-C(3)	1.507(7)
C(2)-H(2A)	0.9900
C(2)-H(2B)	0.9900
C(3)-C(4)	1.500(8)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-C(5)	1.544(6)

C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
C(5)-C(6)	1.515(6)
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
N(1B)-C(6B)	1.466(10)
N(1B)-C(1B)	1.477(9)
C(1B)-C(2B)	1.517(10)
C(1B)-H(1C)	0.9900
C(1B)-H(1D)	0.9900
C(2B)-C(3B)	1.491(10)
C(2B)-H(2C)	0.9900
C(2B)-H(2D)	0.9900
C(3B)-C(4B)	1.487(11)
C(3B)-H(3C)	0.9900
C(3B)-H(3D)	0.9900
C(4B)-C(5B)	1.535(10)
C(4B)-H(4C)	0.9900
C(4B)-H(4D)	0.9900
C(5B)-C(6B)	1.517(10)
C(5B)-H(5C)	0.9900
C(5B)-H(5D)	0.9900
C(6B)-H(6C)	0.9900
C(6B)-H(6D)	0.9900
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(8)-C(17)	1.381(4)
C(8)-C(9)	1.411(4)

C(9)-C(10)	1.350(4)
C(9)-H(9A)	0.9500
C(10)-C(11)	1.419(4)
C(10)-H(10A)	0.9500
C(11)-C(12)	1.415(4)
C(11)-C(16)	1.421(4)
C(12)-C(13)	1.358(5)
C(12)-H(12A)	0.9500
C(13)-C(14)	1.400(5)
C(13)-H(13A)	0.9500
C(14)-C(15)	1.367(4)
C(14)-H(14A)	0.9500
C(15)-C(16)	1.423(4)
C(15)-H(15A)	0.9500
C(16)-C(17)	1.439(4)
C(17)-C(18)	1.488(3)
C(18)-C(27)	1.377(3)
C(18)-C(19)	1.431(4)
C(19)-C(20)	1.417(4)
C(19)-C(24)	1.423(4)
C(20)-C(21)	1.360(4)
C(20)-H(20A)	0.9500
C(21)-C(22)	1.417(5)
C(21)-H(21A)	0.9500
C(22)-C(23)	1.347(5)
C(22)-H(22A)	0.9500
C(23)-C(24)	1.417(4)
C(23)-H(23A)	0.9500
C(24)-C(25)	1.409(4)
C(25)-C(26)	1.358(4)
C(25)-H(25A)	0.9500

C(26)-C(27)	1.414(4)
C(26)-H(26A)	0.9500
C(28)-H(28A)	0.9800
C(28)-H(28B)	0.9800
C(28)-H(28C)	0.9800

Cl(4)-Sb(1)-Cl(2)	179.7(3)
Cl(4)-Sb(1)-Cl(5)	89.3(2)
Cl(2)-Sb(1)-Cl(5)	90.4(2)
Cl(4)-Sb(1)-Cl(3)	90.4(2)
Cl(2)-Sb(1)-Cl(3)	89.7(2)
Cl(5)-Sb(1)-Cl(3)	90.4(2)
Cl(4)-Sb(1)-Cl(6)	90.4(3)
Cl(2)-Sb(1)-Cl(6)	89.8(2)
Cl(5)-Sb(1)-Cl(6)	179.5(3)
Cl(3)-Sb(1)-Cl(6)	90.0(3)
Cl(4)-Sb(1)-Cl(1)	90.7(3)
Cl(2)-Sb(1)-Cl(1)	89.2(3)
Cl(5)-Sb(1)-Cl(1)	89.6(3)
Cl(3)-Sb(1)-Cl(1)	178.8(3)
Cl(6)-Sb(1)-Cl(1)	89.9(3)
Cl(3B)-Sb(1B)-Cl(2B)	89.7(5)
Cl(3B)-Sb(1B)-Cl(1B)	179.3(5)
Cl(2B)-Sb(1B)-Cl(1B)	90.8(5)
Cl(3B)-Sb(1B)-Cl(4B)	89.2(5)
Cl(2B)-Sb(1B)-Cl(4B)	178.6(6)
Cl(1B)-Sb(1B)-Cl(4B)	90.3(4)
Cl(3B)-Sb(1B)-Cl(5B)	91.5(5)
Cl(2B)-Sb(1B)-Cl(5B)	89.2(5)
Cl(1B)-Sb(1B)-Cl(5B)	89.0(4)
Cl(4B)-Sb(1B)-Cl(5B)	89.9(5)

Cl(3B)-Sb(1B)-Cl(6B)	88.9(5)
Cl(2B)-Sb(1B)-Cl(6B)	90.5(5)
Cl(1B)-Sb(1B)-Cl(6B)	90.7(5)
Cl(4B)-Sb(1B)-Cl(6B)	90.4(5)
Cl(5B)-Sb(1B)-Cl(6B)	179.5(5)
Cl(2C)-Sb(1C)-Cl(4C)	179.3(3)
Cl(2C)-Sb(1C)-Cl(5C)	90.5(3)
Cl(4C)-Sb(1C)-Cl(5C)	89.9(3)
Cl(2C)-Sb(1C)-Cl(3C)	90.6(2)
Cl(4C)-Sb(1C)-Cl(3C)	90.0(3)
Cl(5C)-Sb(1C)-Cl(3C)	91.5(3)
Cl(2C)-Sb(1C)-Cl(1C)	89.7(2)
Cl(4C)-Sb(1C)-Cl(1C)	89.8(2)
Cl(5C)-Sb(1C)-Cl(1C)	90.6(2)
Cl(3C)-Sb(1C)-Cl(1C)	177.9(3)
Cl(2C)-Sb(1C)-Cl(6C)	89.1(3)
Cl(4C)-Sb(1C)-Cl(6C)	90.5(3)
Cl(5C)-Sb(1C)-Cl(6C)	179.4(3)
Cl(3C)-Sb(1C)-Cl(6C)	88.9(3)
Cl(1C)-Sb(1C)-Cl(6C)	89.1(3)
P(1)-Se(1)-Se(1)#1	94.31(2)
N(1)-P(1)-N(2)	114.4(3)
N(1B)-P(1)-N(2)	119.9(10)
N(1)-P(1)-N(3)	109.8(3)
N(1B)-P(1)-N(3)	113.4(12)
N(2)-P(1)-N(3)	104.41(10)
N(1)-P(1)-Se(1)	105.4(2)
N(1B)-P(1)-Se(1)	96.3(8)
N(2)-P(1)-Se(1)	108.04(8)
N(3)-P(1)-Se(1)	115.08(8)
C(8)-N(2)-C(7)	116.9(2)

C(8)-N(2)-P(1)	120.66(17)
C(7)-N(2)-P(1)	119.75(18)
C(27)-N(3)-C(28)	117.9(2)
C(27)-N(3)-P(1)	115.13(16)
C(28)-N(3)-P(1)	120.11(17)
C(6)-N(1)-C(1)	115.8(4)
C(6)-N(1)-P(1)	120.2(4)
C(1)-N(1)-P(1)	122.1(4)
N(1)-C(1)-C(2)	113.3(5)
N(1)-C(1)-H(1A)	108.9
C(2)-C(1)-H(1A)	108.9
N(1)-C(1)-H(1B)	108.9
C(2)-C(1)-H(1B)	108.9
H(1A)-C(1)-H(1B)	107.7
C(3)-C(2)-C(1)	116.4(4)
C(3)-C(2)-H(2A)	108.2
C(1)-C(2)-H(2A)	108.2
C(3)-C(2)-H(2B)	108.2
C(1)-C(2)-H(2B)	108.2
H(2A)-C(2)-H(2B)	107.3
C(4)-C(3)-C(2)	117.3(5)
C(4)-C(3)-H(3A)	108.0
C(2)-C(3)-H(3A)	108.0
C(4)-C(3)-H(3B)	108.0
C(2)-C(3)-H(3B)	108.0
H(3A)-C(3)-H(3B)	107.2
C(3)-C(4)-C(5)	114.2(5)
C(3)-C(4)-H(4A)	108.7
C(5)-C(4)-H(4A)	108.7
C(3)-C(4)-H(4B)	108.7
C(5)-C(4)-H(4B)	108.7

H(4A)-C(4)-H(4B)	107.6
C(6)-C(5)-C(4)	115.7(5)
C(6)-C(5)-H(5A)	108.4
C(4)-C(5)-H(5A)	108.4
C(6)-C(5)-H(5B)	108.4
C(4)-C(5)-H(5B)	108.4
H(5A)-C(5)-H(5B)	107.4
N(1)-C(6)-C(5)	113.3(4)
N(1)-C(6)-H(6A)	108.9
C(5)-C(6)-H(6A)	108.9
N(1)-C(6)-H(6B)	108.9
C(5)-C(6)-H(6B)	108.9
H(6A)-C(6)-H(6B)	107.7
C(6B)-N(1B)-C(1B)	117.8(10)
C(6B)-N(1B)-P(1)	113.0(15)
C(1B)-N(1B)-P(1)	128.2(13)
N(1B)-C(1B)-C(2B)	115.6(10)
N(1B)-C(1B)-H(1C)	108.4
C(2B)-C(1B)-H(1C)	108.4
N(1B)-C(1B)-H(1D)	108.4
C(2B)-C(1B)-H(1D)	108.4
H(1C)-C(1B)-H(1D)	107.4
C(3B)-C(2B)-C(1B)	118.8(11)
C(3B)-C(2B)-H(2C)	107.6
C(1B)-C(2B)-H(2C)	107.6
C(3B)-C(2B)-H(2D)	107.6
C(1B)-C(2B)-H(2D)	107.6
H(2C)-C(2B)-H(2D)	107.0
C(4B)-C(3B)-C(2B)	122.3(13)
C(4B)-C(3B)-H(3C)	106.8
C(2B)-C(3B)-H(3C)	106.8

C(4B)-C(3B)-H(3D)	106.8
C(2B)-C(3B)-H(3D)	106.8
H(3C)-C(3B)-H(3D)	106.6
C(3B)-C(4B)-C(5B)	117.2(12)
C(3B)-C(4B)-H(4C)	108.0
C(5B)-C(4B)-H(4C)	108.0
C(3B)-C(4B)-H(4D)	108.0
C(5B)-C(4B)-H(4D)	108.0
H(4C)-C(4B)-H(4D)	107.2
C(6B)-C(5B)-C(4B)	115.2(13)
C(6B)-C(5B)-H(5C)	108.5
C(4B)-C(5B)-H(5C)	108.5
C(6B)-C(5B)-H(5D)	108.5
C(4B)-C(5B)-H(5D)	108.5
H(5C)-C(5B)-H(5D)	107.5
N(1B)-C(6B)-C(5B)	113.3(13)
N(1B)-C(6B)-H(6C)	108.9
C(5B)-C(6B)-H(6C)	108.9
N(1B)-C(6B)-H(6D)	108.9
C(5B)-C(6B)-H(6D)	108.9
H(6C)-C(6B)-H(6D)	107.7
N(2)-C(7)-H(7A)	109.5
N(2)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
N(2)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(17)-C(8)-C(9)	121.7(2)
C(17)-C(8)-N(2)	121.0(2)
C(9)-C(8)-N(2)	117.2(2)
C(10)-C(9)-C(8)	120.6(3)

C(10)-C(9)-H(9A)	119.7
C(8)-C(9)-H(9A)	119.7
C(9)-C(10)-C(11)	120.8(3)
C(9)-C(10)-H(10A)	119.6
C(11)-C(10)-H(10A)	119.6
C(12)-C(11)-C(10)	121.0(3)
C(12)-C(11)-C(16)	120.1(3)
C(10)-C(11)-C(16)	118.9(2)
C(13)-C(12)-C(11)	121.1(3)
C(13)-C(12)-H(12A)	119.5
C(11)-C(12)-H(12A)	119.5
C(12)-C(13)-C(14)	119.4(3)
C(12)-C(13)-H(13A)	120.3
C(14)-C(13)-H(13A)	120.3
C(15)-C(14)-C(13)	121.4(3)
C(15)-C(14)-H(14A)	119.3
C(13)-C(14)-H(14A)	119.3
C(14)-C(15)-C(16)	120.9(3)
C(14)-C(15)-H(15A)	119.6
C(16)-C(15)-H(15A)	119.6
C(11)-C(16)-C(15)	117.1(2)
C(11)-C(16)-C(17)	119.9(2)
C(15)-C(16)-C(17)	123.0(2)
C(8)-C(17)-C(16)	117.9(2)
C(8)-C(17)-C(18)	121.7(2)
C(16)-C(17)-C(18)	120.2(2)
C(27)-C(18)-C(19)	118.1(2)
C(27)-C(18)-C(17)	119.5(2)
C(19)-C(18)-C(17)	122.4(2)
C(20)-C(19)-C(24)	117.9(2)
C(20)-C(19)-C(18)	123.0(2)

C(24)-C(19)-C(18)	119.1(2)
C(21)-C(20)-C(19)	121.3(3)
C(21)-C(20)-H(20A)	119.4
C(19)-C(20)-H(20A)	119.4
C(20)-C(21)-C(22)	120.2(3)
C(20)-C(21)-H(21A)	119.9
C(22)-C(21)-H(21A)	119.9
C(23)-C(22)-C(21)	120.1(3)
C(23)-C(22)-H(22A)	119.9
C(21)-C(22)-H(22A)	119.9
C(22)-C(23)-C(24)	121.1(3)
C(22)-C(23)-H(23A)	119.5
C(24)-C(23)-H(23A)	119.5
C(25)-C(24)-C(23)	121.3(2)
C(25)-C(24)-C(19)	119.5(2)
C(23)-C(24)-C(19)	119.2(3)
C(26)-C(25)-C(24)	121.3(2)
C(26)-C(25)-H(25A)	119.4
C(24)-C(25)-H(25A)	119.4
C(25)-C(26)-C(27)	119.1(2)
C(25)-C(26)-H(26A)	120.4
C(27)-C(26)-H(26A)	120.4
C(18)-C(27)-C(26)	122.5(2)
C(18)-C(27)-N(3)	119.1(2)
C(26)-C(27)-N(3)	118.4(2)
N(3)-C(28)-H(28A)	109.5
N(3)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	109.5
N(3)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28C)	109.5
H(28B)-C(28)-H(28C)	109.5

Symmetry transformations used to generate equivalent atoms:

#1 -x,-y+2,-z

Anisotropic displacement parameters ($Å^2 x\ 10^3$) for bc11tasq. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Sb(1)	48(1)	36(1)	27(1)	-13(1)	-9(1)	7(1)
Cl(1)	65(3)	137(5)	66(2)	-15(3)	-7(2)	49(3)
Cl(2)	99(4)	33(2)	32(2)	-14(1)	-13(2)	-2(2)
Cl(3)	65(2)	87(2)	72(2)	-47(2)	-24(2)	36(2)
Cl(4)	85(3)	99(3)	52(2)	-41(1)	-24(2)	-16(2)
Cl(5)	80(4)	48(2)	29(1)	-12(1)	-1(2)	-13(2)
Cl(6)	95(3)	40(2)	49(2)	1(1)	-29(2)	-21(1)
Sb(1B)	46(4)	33(2)	38(3)	-14(2)	3(2)	-20(2)
Cl(1B)	94(5)	98(6)	73(5)	-58(4)	-22(4)	38(5)
Cl(2B)	98(8)	59(8)	43(5)	-20(4)	-30(5)	-3(6)
Cl(3B)	122(7)	95(6)	102(6)	-36(5)	-50(5)	57(5)
Cl(4B)	90(7)	87(8)	104(7)	-56(5)	-43(5)	3(5)
Cl(5B)	72(5)	97(7)	55(4)	-28(5)	1(4)	-2(5)
Cl(6B)	123(7)	81(6)	101(6)	-26(5)	11(5)	-27(5)
Sb(1C)	45(1)	34(1)	31(1)	-13(1)	-10(1)	3(1)
Cl(1C)	45(2)	82(2)	62(2)	-16(1)	-5(2)	12(2)
Cl(2C)	61(2)	67(3)	41(2)	-36(2)	-11(1)	13(2)
Cl(3C)	74(3)	129(4)	73(2)	-65(2)	-33(2)	59(3)
Cl(4C)	82(4)	76(3)	63(2)	-33(1)	-36(2)	-6(2)
Cl(5C)	67(3)	58(2)	39(1)	0(1)	-10(1)	-21(1)
Cl(6C)	109(4)	46(2)	61(2)	-10(2)	-12(2)	-19(2)
Se(1)	38(1)	44(1)	33(1)	-7(1)	-8(1)	-1(1)

P(1)	36(1)	35(1)	30(1)	-15(1)	-9(1)	4(1)
N(2)	41(1)	36(1)	36(1)	-20(1)	-8(1)	6(1)
N(3)	39(1)	31(1)	33(1)	-13(1)	-9(1)	5(1)
N(1)	40(3)	47(2)	32(2)	-15(2)	-12(1)	2(2)
C(1)	49(3)	53(2)	35(2)	-12(2)	-15(2)	4(2)
C(2)	57(2)	77(3)	34(2)	-17(2)	-6(2)	-7(2)
C(3)	57(3)	89(3)	47(3)	-34(2)	-3(2)	-1(2)
C(4)	72(3)	92(4)	50(3)	-38(3)	-15(2)	-5(3)
C(5)	65(2)	74(3)	45(3)	-31(2)	-15(2)	-14(2)
C(6)	41(2)	65(3)	47(2)	-23(2)	-18(2)	-1(2)
N(1B)	39(5)	49(5)	38(4)	-22(4)	-18(4)	0(4)
C(1B)	51(6)	54(5)	35(4)	-12(4)	-21(4)	-4(5)
C(2B)	56(5)	70(4)	40(4)	-17(4)	-14(4)	-2(4)
C(3B)	66(5)	84(5)	42(4)	-31(4)	-10(4)	-9(4)
C(4B)	64(5)	79(5)	52(5)	-36(5)	-9(4)	-13(5)
C(5B)	56(5)	75(5)	46(5)	-26(5)	-12(5)	-11(4)
C(6B)	50(5)	59(5)	42(4)	-23(4)	-11(4)	0(4)
C(7)	52(1)	46(2)	47(2)	-30(1)	-10(1)	12(1)
C(8)	42(1)	30(1)	38(1)	-15(1)	-11(1)	4(1)
C(9)	58(2)	38(1)	47(2)	-24(1)	-16(1)	3(1)
C(10)	57(2)	37(1)	58(2)	-25(1)	-18(1)	-4(1)
C(11)	50(1)	34(1)	50(2)	-16(1)	-12(1)	-1(1)
C(12)	56(2)	42(2)	60(2)	-15(1)	-7(1)	-13(1)
C(13)	58(2)	55(2)	59(2)	-17(2)	2(1)	-16(1)
C(14)	56(2)	59(2)	49(2)	-22(1)	2(1)	-9(1)
C(15)	51(1)	45(2)	43(2)	-21(1)	-5(1)	-3(1)
C(16)	44(1)	32(1)	41(1)	-14(1)	-10(1)	1(1)
C(17)	42(1)	30(1)	37(1)	-16(1)	-12(1)	4(1)
C(18)	35(1)	32(1)	31(1)	-17(1)	-4(1)	2(1)
C(19)	38(1)	35(1)	32(1)	-16(1)	-6(1)	4(1)
C(20)	58(2)	37(1)	40(1)	-15(1)	-13(1)	4(1)

C(21)	71(2)	46(2)	43(2)	-9(1)	-21(1)	6(1)
C(22)	71(2)	61(2)	35(1)	-17(1)	-19(1)	5(2)
C(23)	58(2)	56(2)	39(1)	-25(1)	-13(1)	-2(1)
C(24)	42(1)	43(1)	35(1)	-20(1)	-5(1)	0(1)
C(25)	52(1)	38(1)	39(1)	-22(1)	-9(1)	-4(1)
C(26)	46(1)	31(1)	37(1)	-14(1)	-7(1)	-1(1)
C(27)	35(1)	32(1)	32(1)	-16(1)	-6(1)	5(1)
C(28)	42(1)	36(1)	45(1)	-14(1)	-10(1)	10(1)

Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3)
for bc11tasq.

	x	y	z	U(eq)
H(1A)	2413	7939	2565	56
H(1B)	1393	7929	2065	56
H(2A)	151	8648	3091	71
H(2B)	858	7892	3862	71
H(3A)	967	10381	2865	78
H(3B)	706	9592	4083	78
H(4A)	2781	9215	3596	83
H(4B)	2455	10432	3715	83
H(5A)	2875	11410	1854	71
H(5B)	3999	10920	2194	71
H(6A)	3893	10583	729	59
H(6B)	3937	9375	1678	59
H(1C)	1678	7655	2406	56
H(1D)	601	8442	2383	56
H(2C)	642	7962	3993	68
H(2D)	2027	7974	3684	68
H(3C)	910	10065	3242	76
H(3D)	1190	9414	4317	76
H(4C)	3140	9921	3508	76
H(4D)	2447	11072	3268	76
H(5C)	2816	11387	1559	71
H(5D)	4029	11082	1798	71
H(6C)	3859	10060	835	60

H(6D)	3583	9075	2002	60
H(7A)	1248	12863	-381	69
H(7B)	1740	12399	602	69
H(7C)	631	11682	621	69
H(9A)	3614	12955	-278	55
H(10A)	5301	14019	-1515	58
H(12A)	6781	14519	-3233	68
H(13A)	7493	14249	-4769	76
H(14A)	6503	12842	-5052	70
H(15A)	4807	11744	-3835	57
H(20A)	2902	13146	-3687	55
H(21A)	2336	13598	-5161	66
H(22A)	1706	12062	-5550	67
H(23A)	1522	10122	-4399	60
H(25A)	1612	8630	-2704	50
H(26A)	2015	8153	-1146	47
H(28A)	4019	8311	-703	63
H(28B)	2877	7751	285	63
H(28C)	3912	8493	347	63

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Torsion angles [°] for bc11tasq.

Se(1)#1-Se(1)-P(1)-N(1)	162.8(3)
Se(1)#1-Se(1)-P(1)-N(1B)	164.4(12)
Se(1)#1-Se(1)-P(1)-N(2)	40.12(8)
Se(1)#1-Se(1)-P(1)-N(3)	-76.06(8)
N(1)-P(1)-N(2)-C(8)	93.6(3)
N(1B)-P(1)-N(2)-C(8)	102.0(12)
N(3)-P(1)-N(2)-C(8)	-26.4(2)
Se(1)-P(1)-N(2)-C(8)	-149.36(17)
N(1)-P(1)-N(2)-C(7)	-67.3(4)
N(1B)-P(1)-N(2)-C(7)	-58.9(12)
N(3)-P(1)-N(2)-C(7)	172.7(2)
Se(1)-P(1)-N(2)-C(7)	49.7(2)
N(1)-P(1)-N(3)-C(27)	177.5(3)
N(1B)-P(1)-N(3)-C(27)	168.4(8)
N(2)-P(1)-N(3)-C(27)	-59.39(18)
Se(1)-P(1)-N(3)-C(27)	58.85(17)
N(1)-P(1)-N(3)-C(28)	27.2(3)
N(1B)-P(1)-N(3)-C(28)	18.1(8)
N(2)-P(1)-N(3)-C(28)	150.26(18)
Se(1)-P(1)-N(3)-C(28)	-91.49(18)
N(1B)-P(1)-N(1)-C(6)	-175(10)
N(2)-P(1)-N(1)-C(6)	-46.5(7)
N(3)-P(1)-N(1)-C(6)	70.4(7)
Se(1)-P(1)-N(1)-C(6)	-165.1(5)
N(1B)-P(1)-N(1)-C(1)	21(9)
N(2)-P(1)-N(1)-C(1)	149.6(5)
N(3)-P(1)-N(1)-C(1)	-93.4(6)
Se(1)-P(1)-N(1)-C(1)	31.1(7)
C(6)-N(1)-C(1)-C(2)	89.3(7)

P(1)-N(1)-C(1)-C(2)	-106.2(8)
N(1)-C(1)-C(2)-C(3)	-33.0(8)
C(1)-C(2)-C(3)-C(4)	-42.3(7)
C(2)-C(3)-C(4)-C(5)	84.0(8)
C(3)-C(4)-C(5)-C(6)	-66.2(9)
C(1)-N(1)-C(6)-C(5)	-78.5(7)
P(1)-N(1)-C(6)-C(5)	116.7(8)
C(4)-C(5)-C(6)-N(1)	52.9(8)
N(1)-P(1)-N(1B)-C(6B)	-2(8)
N(2)-P(1)-N(1B)-C(6B)	-57(2)
N(3)-P(1)-N(1B)-C(6B)	66.9(19)
Se(1)-P(1)-N(1B)-C(6B)	-172.2(17)
N(1)-P(1)-N(1B)-C(1B)	-170(12)
N(2)-P(1)-N(1B)-C(1B)	135(2)
N(3)-P(1)-N(1B)-C(1B)	-101(3)
Se(1)-P(1)-N(1B)-C(1B)	20(3)
C(6B)-N(1B)-C(1B)-C(2B)	39(3)
P(1)-N(1B)-C(1B)-C(2B)	-153(2)
N(1B)-C(1B)-C(2B)-C(3B)	34(3)
C(1B)-C(2B)-C(3B)-C(4B)	-75(2)
C(2B)-C(3B)-C(4B)-C(5B)	57(3)
C(3B)-C(4B)-C(5B)-C(6B)	-45(3)
C(1B)-N(1B)-C(6B)-C(5B)	-90(2)
P(1)-N(1B)-C(6B)-C(5B)	100(3)
C(4B)-C(5B)-C(6B)-N(1B)	72(3)
C(7)-N(2)-C(8)-C(17)	-133.8(3)
P(1)-N(2)-C(8)-C(17)	64.8(3)
C(7)-N(2)-C(8)-C(9)	45.0(3)
P(1)-N(2)-C(8)-C(9)	-116.4(2)
C(17)-C(8)-C(9)-C(10)	0.0(4)
N(2)-C(8)-C(9)-C(10)	-178.8(3)

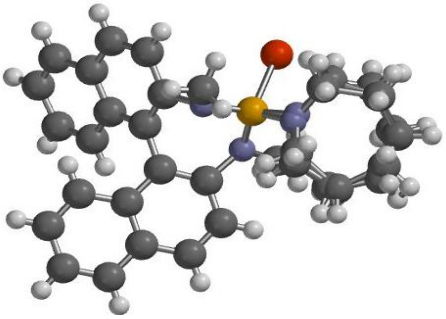
C(8)-C(9)-C(10)-C(11)	-0.7(5)
C(9)-C(10)-C(11)-C(12)	-178.9(3)
C(9)-C(10)-C(11)-C(16)	-0.9(4)
C(10)-C(11)-C(12)-C(13)	178.1(3)
C(16)-C(11)-C(12)-C(13)	0.0(5)
C(11)-C(12)-C(13)-C(14)	-1.6(6)
C(12)-C(13)-C(14)-C(15)	0.8(6)
C(13)-C(14)-C(15)-C(16)	1.6(5)
C(12)-C(11)-C(16)-C(15)	2.3(4)
C(10)-C(11)-C(16)-C(15)	-175.8(3)
C(12)-C(11)-C(16)-C(17)	-178.7(3)
C(10)-C(11)-C(16)-C(17)	3.2(4)
C(14)-C(15)-C(16)-C(11)	-3.1(4)
C(14)-C(15)-C(16)-C(17)	177.9(3)
C(9)-C(8)-C(17)-C(16)	2.3(4)
N(2)-C(8)-C(17)-C(16)	-178.9(2)
C(9)-C(8)-C(17)-C(18)	178.8(2)
N(2)-C(8)-C(17)-C(18)	-2.4(4)
C(11)-C(16)-C(17)-C(8)	-3.9(4)
C(15)-C(16)-C(17)-C(8)	175.0(3)
C(11)-C(16)-C(17)-C(18)	179.6(2)
C(15)-C(16)-C(17)-C(18)	-1.5(4)
C(8)-C(17)-C(18)-C(27)	-54.7(3)
C(16)-C(17)-C(18)-C(27)	121.7(3)
C(8)-C(17)-C(18)-C(19)	127.5(3)
C(16)-C(17)-C(18)-C(19)	-56.1(3)
C(27)-C(18)-C(19)-C(20)	171.4(2)
C(17)-C(18)-C(19)-C(20)	-10.7(4)
C(27)-C(18)-C(19)-C(24)	-8.0(3)
C(17)-C(18)-C(19)-C(24)	169.8(2)
C(24)-C(19)-C(20)-C(21)	-2.6(4)

C(18)-C(19)-C(20)-C(21)	178.0(3)
C(19)-C(20)-C(21)-C(22)	-1.1(5)
C(20)-C(21)-C(22)-C(23)	2.8(5)
C(21)-C(22)-C(23)-C(24)	-0.6(5)
C(22)-C(23)-C(24)-C(25)	175.9(3)
C(22)-C(23)-C(24)-C(19)	-3.1(4)
C(20)-C(19)-C(24)-C(25)	-174.4(2)
C(18)-C(19)-C(24)-C(25)	5.1(3)
C(20)-C(19)-C(24)-C(23)	4.6(4)
C(18)-C(19)-C(24)-C(23)	-176.0(2)
C(23)-C(24)-C(25)-C(26)	-178.4(3)
C(19)-C(24)-C(25)-C(26)	0.6(4)
C(24)-C(25)-C(26)-C(27)	-3.1(4)
C(19)-C(18)-C(27)-C(26)	5.6(3)
C(17)-C(18)-C(27)-C(26)	-172.3(2)
C(19)-C(18)-C(27)-N(3)	-172.90(19)
C(17)-C(18)-C(27)-N(3)	9.2(3)
C(25)-C(26)-C(27)-C(18)	-0.1(4)
C(25)-C(26)-C(27)-N(3)	178.5(2)
C(28)-N(3)-C(27)-C(18)	-136.4(2)
P(1)-N(3)-C(27)-C(18)	72.6(2)
C(28)-N(3)-C(27)-C(26)	45.0(3)
P(1)-N(3)-C(27)-C(26)	-106.0(2)

Symmetry transformations used to generate equivalent atoms:

#1 -x,-y+2,-z

Crystal Structure of (*R*)-62b



Crystal data and structure refinement for bc56ras.

Identification code	bc56ras	
Empirical formula	C28 H30 N3 P Se	
Formula weight	518.48	
Temperature	193(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 16.6637(6) Å	□= 90°.
	b = 9.1966(5) Å	□= 109.839(3)°.
	c = 16.8975(7) Å	□ = 90°.
Volume	2435.84(19) $Å^3$	
Z	4	
Density (calculated)	1.414 Mg/m^3	
Absorption coefficient	2.863 mm^{-1}	
F(000)	1072	
Crystal size	0.344 x 0.177 x 0.04 mm^3	
Theta range for data collection	2.78 to 67.27°.	
Index ranges	-19<=h<=19, -10<=k<=9, -19<=l<=20	
Reflections collected	17531	
Independent reflections	6815 [R(int) = 0.0730]	
Completeness to theta = 67.27°	97.5 %	
Absorption correction	Integration	

Max. and min. transmission	0.9023 and 0.6321
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6815 / 2368 / 1165
Goodness-of-fit on F^2	1.027
Final R indices [I>2sigma(I)]	R1 = 0.0520, wR2 = 0.1265
R indices (all data)	R1 = 0.0618, wR2 = 0.1359
Absolute structure parameter	0.01(2)
Largest diff. peak and hole	0.782 and -0.425 e.Å^{-3}

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for bc56ras. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
P(1)	2068(1)	5405(2)	8330(1)	38(1)
Se(1)	829(1)	4595(1)	8072(1)	61(1)
N(1)	2671(8)	5656(13)	9356(4)	37(2)
C(1)	2259(11)	6609(13)	9759(11)	37(2)
C(2)	2266(9)	8094(12)	9593(10)	36(2)
C(3)	1732(10)	9060(13)	9871(10)	34(2)
C(4)	1593(11)	10507(15)	9627(11)	37(2)
C(5)	1058(9)	11374(15)	9878(10)	37(2)
C(6)	663(8)	10851(17)	10429(8)	36(2)
C(7)	779(8)	9437(17)	10692(9)	38(2)
C(8)	1318(8)	8484(15)	10428(8)	37(2)
C(9)	1408(8)	7010(15)	10639(8)	37(2)
C(10)	1834(9)	6086(15)	10303(9)	39(2)
C(21)	3101(15)	4361(19)	9836(13)	39(3)

N(2)	2137(10)	7050(10)	7945(7)	44(2)
C(11)	2770(10)	8118(18)	8357(8)	40(2)
C(12)	2836(9)	8646(15)	9138(8)	35(2)
C(13)	3528(9)	9641(18)	9554(8)	37(2)
C(14)	3699(8)	10115(16)	10399(8)	39(2)
C(15)	4324(9)	11092(17)	10749(8)	43(2)
C(16)	4858(9)	11589(17)	10326(9)	44(2)
C(17)	4746(8)	11123(17)	9533(9)	40(2)
C(18)	4076(9)	10133(18)	9130(8)	38(2)
C(19)	3968(8)	9578(16)	8325(8)	39(2)
C(20)	3348(8)	8595(15)	7953(7)	40(2)
C(22)	1526(15)	7430(20)	7108(10)	59(4)
N(1B)	2587(10)	5782(16)	9360(5)	39(2)
C(1B)	2179(14)	6831(15)	9715(14)	37(2)
C(2B)	2223(11)	8293(14)	9513(12)	37(2)
C(3B)	1718(12)	9356(16)	9762(12)	35(2)
C(4B)	1637(13)	10795(16)	9493(14)	35(2)
C(5B)	1151(11)	11762(17)	9746(12)	38(2)
C(6B)	706(10)	11321(19)	10271(11)	38(3)
C(7B)	746(9)	9910(20)	10538(10)	36(2)
C(8B)	1238(9)	8864(16)	10275(10)	36(2)
C(9B)	1259(10)	7397(17)	10501(10)	37(2)
C(10B)	1691(11)	6398(16)	10220(12)	39(2)
C(21B)	2923(17)	4470(20)	9873(16)	40(4)
N(2B)	2012(12)	7050(11)	7903(8)	41(2)
C(11B)	2669(12)	8110(20)	8249(10)	41(2)
C(12B)	2788(11)	8713(19)	9026(10)	37(2)
C(13B)	3488(11)	9720(20)	9382(9)	38(2)
C(14B)	3662(10)	10368(19)	10191(9)	39(2)
C(15B)	4339(12)	11260(20)	10515(10)	44(3)
C(16B)	4855(11)	11633(19)	10050(11)	42(3)

C(17B)	4701(10)	11080(20)	9266(11)	43(2)
C(18B)	4017(10)	10100(20)	8915(10)	39(2)
C(19B)	3807(10)	9570(20)	8089(9)	41(2)
C(20B)	3155(11)	8627(19)	7758(9)	43(2)
C(22B)	1541(18)	7080(30)	6988(10)	60(5)
N(3)	2682(10)	4292(18)	8023(15)	45(2)
C(23)	3587(10)	4700(20)	8269(10)	48(2)
C(24)	3911(10)	4850(20)	7535(10)	55(2)
C(25)	3198(13)	4730(20)	6669(11)	72(3)
C(26)	2878(14)	3290(30)	6390(11)	67(3)
C(27)	2249(13)	2660(30)	6770(11)	61(3)
C(28)	2511(16)	2800(20)	7713(11)	53(2)
N(3B)	2648(6)	4320(11)	7969(8)	44(2)
C(23B)	3472(6)	4741(13)	7912(7)	53(2)
C(24B)	3483(8)	5112(12)	7044(7)	64(2)
C(25B)	2857(8)	4184(14)	6327(7)	62(2)
C(26B)	2805(7)	2649(15)	6501(6)	60(2)
C(27B)	2205(7)	2244(13)	6967(6)	53(2)
C(28B)	2452(8)	2770(12)	7861(6)	46(2)
P(2)	6428(1)	8824(2)	6809(1)	42(1)
Se(2)	5340(1)	7860(1)	6945(1)	45(1)
N(4)	7271(5)	7811(14)	7389(7)	43(2)
C(31)	8104(6)	8176(14)	7340(6)	38(2)
C(32)	8230(7)	7954(15)	6587(7)	36(2)
C(33)	8934(9)	8650(19)	6438(7)	39(2)
C(34)	9041(11)	8620(20)	5646(8)	44(2)
C(35)	9697(9)	9394(17)	5503(9)	47(2)
C(36)	10263(8)	10200(16)	6157(10)	49(2)
C(37)	10197(7)	10226(15)	6929(10)	50(2)
C(38)	9555(6)	9412(14)	7107(8)	43(2)
C(39)	9441(6)	9399(15)	7921(7)	47(2)

C(40)	8760(6)	8814(15)	8033(7)	42(2)
C(51)	7297(9)	6951(18)	8136(7)	47(3)
N(5)	6561(7)	8891(12)	5875(4)	37(2)
C(41)	6779(7)	7557(14)	5580(11)	34(2)
C(42)	7608(6)	7057(14)	5926(11)	32(2)
C(43)	7835(9)	5669(18)	5674(17)	33(2)
C(44)	8664(9)	5051(18)	6039(14)	38(2)
C(45)	8836(8)	3675(15)	5851(11)	41(2)
C(46)	8201(9)	2874(15)	5220(8)	42(2)
C(47)	7423(9)	3443(14)	4859(9)	39(2)
C(48)	7198(8)	4834(15)	5068(12)	36(2)
C(49)	6357(8)	5406(15)	4721(11)	38(2)
C(50)	6149(7)	6703(15)	4993(11)	34(2)
C(52)	5907(9)	9807(16)	5277(10)	48(3)
N(4B)	7352(4)	8011(14)	7346(6)	42(2)
C(31B)	8093(6)	8544(14)	7175(7)	41(2)
C(32B)	8213(7)	8097(14)	6449(7)	36(2)
C(33B)	8908(8)	8685(18)	6234(8)	39(2)
C(34B)	9007(10)	8410(20)	5450(8)	41(2)
C(35B)	9646(8)	9105(16)	5231(8)	44(2)
C(36B)	10209(8)	10050(15)	5805(10)	45(2)
C(37B)	10125(7)	10371(13)	6549(10)	45(2)
C(38B)	9472(6)	9705(13)	6786(8)	43(2)
C(39B)	9351(6)	10012(14)	7580(8)	46(2)
C(40B)	8692(6)	9479(16)	7759(7)	46(2)
C(51B)	7429(9)	7620(20)	8203(6)	52(3)
N(5B)	6428(7)	8615(12)	5814(4)	36(2)
C(41B)	6751(6)	7296(14)	5593(11)	32(2)
C(42B)	7617(6)	7011(14)	5901(10)	33(2)
C(43B)	7933(9)	5622(19)	5746(16)	33(2)
C(44B)	8788(8)	5162(17)	6172(13)	37(2)

C(45B)	9069(8)	3862(15)	5991(10)	43(2)
C(46B)	8509(8)	2914(15)	5390(9)	43(2)
C(47B)	7696(8)	3300(13)	4996(9)	40(2)
C(48B)	7377(8)	4654(14)	5153(11)	36(2)
C(49B)	6505(8)	5055(15)	4790(10)	37(2)
C(50B)	6201(7)	6325(16)	5002(11)	35(2)
C(52B)	5729(9)	9312(17)	5126(10)	50(3)
N(6)	6363(8)	10630(8)	6777(9)	48(2)
C(53)	6921(8)	11583(13)	6459(8)	45(2)
C(54)	7474(9)	12659(17)	7067(10)	53(2)
C(55)	7009(10)	14028(14)	7223(10)	57(2)
C(56)	6514(10)	13807(15)	7802(10)	61(2)
C(57)	6162(10)	12343(15)	7849(8)	59(2)
C(58)	5769(8)	11468(16)	7088(9)	54(2)
N(6B)	6558(5)	10530(7)	7138(5)	44(2)
C(53B)	7268(6)	11436(10)	7043(7)	53(2)
C(54B)	7183(8)	13048(12)	7113(7)	58(2)
C(55B)	6294(7)	13690(12)	6645(6)	59(2)
C(56B)	5692(7)	13616(12)	7130(7)	60(2)
C(57B)	5471(6)	12158(11)	7363(6)	52(2)
C(58B)	6170(6)	11112(11)	7741(5)	47(2)

—

Bond lengths [Å] and angles [°] for bc56ras.

P(1)-N(3B)	1.644(5)
P(1)-N(3)	1.651(7)
P(1)-N(2B)	1.664(7)
P(1)-N(2)	1.665(6)
P(1)-N(1B)	1.696(6)
P(1)-N(1)	1.699(6)
P(1)-Se(1)	2.0977(14)
N(1)-C(1)	1.422(9)
N(1)-C(21)	1.482(10)
C(1)-C(2)	1.396(10)
C(1)-C(10)	1.421(9)
C(2)-C(3)	1.445(9)
C(2)-C(12)	1.498(8)
C(3)-C(4)	1.389(11)
C(3)-C(8)	1.443(10)
C(4)-C(5)	1.366(10)
C(4)-H(4A)	0.9500
C(5)-C(6)	1.396(13)
C(5)-H(5A)	0.9500
C(6)-C(7)	1.367(15)
C(6)-H(6A)	0.9500
C(7)-C(8)	1.431(11)
C(7)-H(7A)	0.9500
C(8)-C(9)	1.397(12)
C(9)-C(10)	1.350(11)
C(9)-H(9A)	0.9500
C(10)-H(10A)	0.9500
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800

C(21)-H(21C)	0.9800
N(2)-C(11)	1.437(9)
N(2)-C(22)	1.477(10)
C(11)-C(12)	1.375(8)
C(11)-C(20)	1.427(9)
C(12)-C(13)	1.453(9)
C(13)-C(18)	1.414(9)
C(13)-C(14)	1.426(10)
C(14)-C(15)	1.351(11)
C(14)-H(14A)	0.9500
C(15)-C(16)	1.394(12)
C(15)-H(15A)	0.9500
C(16)-C(17)	1.358(12)
C(16)-H(16A)	0.9500
C(17)-C(18)	1.422(11)
C(17)-H(17A)	0.9500
C(18)-C(19)	1.406(11)
C(19)-C(20)	1.356(11)
C(19)-H(19A)	0.9500
C(20)-H(20A)	0.9500
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800
N(1B)-C(1B)	1.426(9)
N(1B)-C(21B)	1.484(10)
C(1B)-C(2B)	1.395(11)
C(1B)-C(10B)	1.421(9)
C(2B)-C(3B)	1.443(9)
C(2B)-C(12B)	1.496(8)
C(3B)-C(4B)	1.390(12)
C(3B)-C(8B)	1.437(10)

C(4B)-C(5B)	1.365(10)
C(4B)-H(4B)	0.9500
C(5B)-C(6B)	1.397(14)
C(5B)-H(5B)	0.9500
C(6B)-C(7B)	1.364(15)
C(6B)-H(6B)	0.9500
C(7B)-C(8B)	1.432(11)
C(7B)-H(7B)	0.9500
C(8B)-C(9B)	1.399(13)
C(9B)-C(10B)	1.349(12)
C(9B)-H(9B)	0.9500
C(10B)-H(10B)	0.9500
C(21B)-H(21D)	0.9800
C(21B)-H(21E)	0.9800
C(21B)-H(21F)	0.9800
N(2B)-C(11B)	1.434(9)
N(2B)-C(22B)	1.477(11)
C(11B)-C(12B)	1.376(9)
C(11B)-C(20B)	1.424(10)
C(12B)-C(13B)	1.451(9)
C(13B)-C(18B)	1.413(10)
C(13B)-C(14B)	1.427(10)
C(14B)-C(15B)	1.352(12)
C(14B)-H(14B)	0.9500
C(15B)-C(16B)	1.390(13)
C(15B)-H(15B)	0.9500
C(16B)-C(17B)	1.359(13)
C(16B)-H(16B)	0.9500
C(17B)-C(18B)	1.419(11)
C(17B)-H(17B)	0.9500
C(18B)-C(19B)	1.404(11)

C(19B)-C(20B)	1.355(12)
C(19B)-H(19B)	0.9500
C(20B)-H(20B)	0.9500
C(22B)-H(22D)	0.9800
C(22B)-H(22E)	0.9800
C(22B)-H(22F)	0.9800
N(3)-C(28)	1.464(12)
N(3)-C(23)	1.470(11)
C(23)-C(24)	1.518(15)
C(23)-H(23A)	0.9900
C(23)-H(23B)	0.9900
C(24)-C(25)	1.545(15)
C(24)-H(24A)	0.9900
C(24)-H(24B)	0.9900
C(25)-C(26)	1.452(18)
C(25)-H(25A)	0.9900
C(25)-H(25B)	0.9900
C(26)-C(27)	1.516(15)
C(26)-H(26A)	0.9900
C(26)-H(26B)	0.9900
C(27)-C(28)	1.508(12)
C(27)-H(27A)	0.9900
C(27)-H(27B)	0.9900
C(28)-H(28A)	0.9900
C(28)-H(28B)	0.9900
N(3B)-C(23B)	1.460(9)
N(3B)-C(28B)	1.460(10)
C(23B)-C(24B)	1.512(14)
C(23B)-H(23C)	0.9900
C(23B)-H(23D)	0.9900
C(24B)-C(25B)	1.558(14)

C(24B)-H(24C)	0.9900
C(24B)-H(24D)	0.9900
C(25B)-C(26B)	1.450(17)
C(25B)-H(25C)	0.9900
C(25B)-H(25D)	0.9900
C(26B)-C(27B)	1.516(14)
C(26B)-H(26C)	0.9900
C(26B)-H(26D)	0.9900
C(27B)-C(28B)	1.503(10)
C(27B)-H(27C)	0.9900
C(27B)-H(27D)	0.9900
C(28B)-H(28C)	0.9900
C(28B)-H(28D)	0.9900
P(2)-N(6B)	1.654(6)
P(2)-N(6)	1.665(7)
P(2)-N(5)	1.666(6)
P(2)-N(4B)	1.674(6)
P(2)-N(5B)	1.692(6)
P(2)-N(4)	1.693(6)
P(2)-Se(2)	2.1013(13)
N(4)-C(31)	1.457(10)
N(4)-C(51)	1.478(10)
C(31)-C(32)	1.373(9)
C(31)-C(40)	1.429(10)
C(32)-C(33)	1.432(9)
C(32)-C(42)	1.489(8)
C(33)-C(34)	1.410(11)
C(33)-C(38)	1.430(10)
C(34)-C(35)	1.391(11)
C(34)-H(34A)	0.9500
C(35)-C(36)	1.397(15)

C(35)-H(35A)	0.9500
C(36)-C(37)	1.346(15)
C(36)-H(36A)	0.9500
C(37)-C(38)	1.419(14)
C(37)-H(37A)	0.9500
C(38)-C(39)	1.452(14)
C(39)-C(40)	1.325(14)
C(39)-H(39A)	0.9500
C(40)-H(40A)	0.9500
C(51)-H(51A)	0.9800
C(51)-H(51B)	0.9800
C(51)-H(51C)	0.9800
N(5)-C(41)	1.417(9)
N(5)-C(52)	1.474(9)
C(41)-C(42)	1.383(8)
C(41)-C(50)	1.413(10)
C(42)-C(43)	1.436(9)
C(43)-C(48)	1.424(9)
C(43)-C(44)	1.426(9)
C(44)-C(45)	1.359(11)
C(44)-H(44A)	0.9500
C(45)-C(46)	1.425(13)
C(45)-H(45A)	0.9500
C(46)-C(47)	1.338(13)
C(46)-H(46A)	0.9500
C(47)-C(48)	1.412(12)
C(47)-H(47A)	0.9500
C(48)-C(49)	1.423(11)
C(49)-C(50)	1.364(12)
C(49)-H(49A)	0.9500
C(50)-H(50A)	0.9500

C(52)-H(52A)	0.9800
C(52)-H(52B)	0.9800
C(52)-H(52C)	0.9800
N(4B)-C(31B)	1.445(10)
N(4B)-C(51B)	1.455(11)
C(31B)-C(32B)	1.372(9)
C(31B)-C(40B)	1.428(10)
C(32B)-C(33B)	1.432(9)
C(32B)-C(42B)	1.490(8)
C(33B)-C(34B)	1.412(11)
C(33B)-C(38B)	1.428(10)
C(34B)-C(35B)	1.392(11)
C(34B)-H(34B)	0.9500
C(35B)-C(36B)	1.400(14)
C(35B)-H(35B)	0.9500
C(36B)-C(37B)	1.343(15)
C(36B)-H(36B)	0.9500
C(37B)-C(38B)	1.419(14)
C(37B)-H(37B)	0.9500
C(38B)-C(39B)	1.451(14)
C(39B)-C(40B)	1.328(14)
C(39B)-H(39B)	0.9500
C(40B)-H(40B)	0.9500
C(51B)-H(51D)	0.9800
C(51B)-H(51E)	0.9800
C(51B)-H(51F)	0.9800
N(5B)-C(41B)	1.427(9)
N(5B)-C(52B)	1.483(9)
C(41B)-C(42B)	1.382(8)
C(41B)-C(50B)	1.418(10)
C(42B)-C(43B)	1.440(9)

C(43B)-C(48B)	1.423(9)
C(43B)-C(44B)	1.424(9)
C(44B)-C(45B)	1.357(11)
C(44B)-H(44B)	0.9500
C(45B)-C(46B)	1.420(13)
C(45B)-H(45B)	0.9500
C(46B)-C(47B)	1.340(13)
C(46B)-H(46B)	0.9500
C(47B)-C(48B)	1.413(12)
C(47B)-H(47B)	0.9500
C(48B)-C(49B)	1.421(11)
C(49B)-C(50B)	1.369(12)
C(49B)-H(49B)	0.9500
C(50B)-H(50B)	0.9500
C(52B)-H(52D)	0.9800
C(52B)-H(52E)	0.9800
C(52B)-H(52F)	0.9800
N(6)-C(58)	1.483(11)
N(6)-C(53)	1.504(11)
C(53)-C(54)	1.497(15)
C(53)-H(53A)	0.9900
C(53)-H(53B)	0.9900
C(54)-C(55)	1.548(16)
C(54)-H(54A)	0.9900
C(54)-H(54B)	0.9900
C(55)-C(56)	1.492(14)
C(55)-H(55A)	0.9900
C(55)-H(55B)	0.9900
C(56)-C(57)	1.481(15)
C(56)-H(56A)	0.9900
C(56)-H(56B)	0.9900

C(57)-C(58)	1.470(13)
C(57)-H(57A)	0.9900
C(57)-H(57B)	0.9900
C(58)-H(58A)	0.9900
C(58)-H(58B)	0.9900
N(6B)-C(58B)	1.480(10)
N(6B)-C(53B)	1.499(10)
C(53B)-C(54B)	1.498(14)
C(53B)-H(53C)	0.9900
C(53B)-H(53D)	0.9900
C(54B)-C(55B)	1.540(15)
C(54B)-H(54C)	0.9900
C(54B)-H(54D)	0.9900
C(55B)-C(56B)	1.497(13)
C(55B)-H(55C)	0.9900
C(55B)-H(55D)	0.9900
C(56B)-C(57B)	1.479(14)
C(56B)-H(56C)	0.9900
C(56B)-H(56D)	0.9900
C(57B)-C(58B)	1.478(12)
C(57B)-H(57C)	0.9900
C(57B)-H(57D)	0.9900
C(58B)-H(58C)	0.9900
C(58B)-H(58D)	0.9900

N(3B)-P(1)-N(2B)	110.2(9)
N(3)-P(1)-N(2B)	112.2(11)
N(3B)-P(1)-N(2)	106.3(8)
N(3)-P(1)-N(2)	108.0(10)
N(3B)-P(1)-N(1B)	110.2(7)
N(3)-P(1)-N(1B)	107.1(10)

N(2B)-P(1)-N(1B)	101.1(6)
N(2)-P(1)-N(1B)	97.8(8)
N(3B)-P(1)-N(1)	104.0(6)
N(3)-P(1)-N(1)	100.9(9)
N(2B)-P(1)-N(1)	104.2(7)
N(2)-P(1)-N(1)	100.4(5)
N(3B)-P(1)-Se(1)	111.6(3)
N(3)-P(1)-Se(1)	112.7(6)
N(2B)-P(1)-Se(1)	109.0(6)
N(2)-P(1)-Se(1)	115.8(5)
N(1B)-P(1)-Se(1)	114.1(7)
N(1)-P(1)-Se(1)	117.4(5)
C(1)-N(1)-C(21)	117.1(8)
C(1)-N(1)-P(1)	111.0(10)
C(21)-N(1)-P(1)	117.3(11)
C(2)-C(1)-C(10)	120.1(7)
C(2)-C(1)-N(1)	117.9(7)
C(10)-C(1)-N(1)	122.0(8)
C(1)-C(2)-C(3)	119.2(6)
C(1)-C(2)-C(12)	119.1(7)
C(3)-C(2)-C(12)	121.7(8)
C(4)-C(3)-C(8)	118.5(7)
C(4)-C(3)-C(2)	123.5(7)
C(8)-C(3)-C(2)	118.0(7)
C(5)-C(4)-C(3)	121.9(9)
C(5)-C(4)-H(4A)	119.1
C(3)-C(4)-H(4A)	119.1
C(4)-C(5)-C(6)	120.7(10)
C(4)-C(5)-H(5A)	119.6
C(6)-C(5)-H(5A)	119.6
C(7)-C(6)-C(5)	119.9(8)

C(7)-C(6)-H(6A)	120.1
C(5)-C(6)-H(6A)	120.1
C(6)-C(7)-C(8)	121.0(9)
C(6)-C(7)-H(7A)	119.5
C(8)-C(7)-H(7A)	119.5
C(9)-C(8)-C(7)	122.5(8)
C(9)-C(8)-C(3)	119.3(7)
C(7)-C(8)-C(3)	118.0(9)
C(10)-C(9)-C(8)	121.9(8)
C(10)-C(9)-H(9A)	119.0
C(8)-C(9)-H(9A)	119.0
C(9)-C(10)-C(1)	120.5(9)
C(9)-C(10)-H(10A)	119.7
C(1)-C(10)-H(10A)	119.7
C(11)-N(2)-C(22)	117.3(9)
C(11)-N(2)-P(1)	124.6(9)
C(22)-N(2)-P(1)	118.1(10)
C(12)-C(11)-C(20)	120.3(7)
C(12)-C(11)-N(2)	120.8(7)
C(20)-C(11)-N(2)	118.9(8)
C(11)-C(12)-C(13)	118.6(6)
C(11)-C(12)-C(2)	120.9(7)
C(13)-C(12)-C(2)	120.1(7)
C(18)-C(13)-C(14)	117.8(7)
C(18)-C(13)-C(12)	120.0(7)
C(14)-C(13)-C(12)	122.3(7)
C(15)-C(14)-C(13)	120.3(8)
C(15)-C(14)-H(14A)	119.8
C(13)-C(14)-H(14A)	119.8
C(14)-C(15)-C(16)	121.6(9)
C(14)-C(15)-H(15A)	119.2

C(16)-C(15)-H(15A)	119.2
C(17)-C(16)-C(15)	120.3(8)
C(17)-C(16)-H(16A)	119.8
C(15)-C(16)-H(16A)	119.8
C(16)-C(17)-C(18)	119.8(8)
C(16)-C(17)-H(17A)	120.1
C(18)-C(17)-H(17A)	120.1
C(19)-C(18)-C(13)	118.8(7)
C(19)-C(18)-C(17)	121.2(8)
C(13)-C(18)-C(17)	120.0(8)
C(20)-C(19)-C(18)	121.2(7)
C(20)-C(19)-H(19A)	119.4
C(18)-C(19)-H(19A)	119.4
C(19)-C(20)-C(11)	121.0(7)
C(19)-C(20)-H(20A)	119.5
C(11)-C(20)-H(20A)	119.5
C(1B)-N(1B)-C(21B)	116.4(9)
C(1B)-N(1B)-P(1)	114.9(13)
C(21B)-N(1B)-P(1)	113.2(14)
C(2B)-C(1B)-C(10B)	120.4(8)
C(2B)-C(1B)-N(1B)	118.4(8)
C(10B)-C(1B)-N(1B)	121.0(9)
C(1B)-C(2B)-C(3B)	119.8(7)
C(1B)-C(2B)-C(12B)	118.6(8)
C(3B)-C(2B)-C(12B)	121.6(8)
C(4B)-C(3B)-C(8B)	119.0(8)
C(4B)-C(3B)-C(2B)	123.4(8)
C(8B)-C(3B)-C(2B)	117.4(8)
C(5B)-C(4B)-C(3B)	121.3(10)
C(5B)-C(4B)-H(4B)	119.3
C(3B)-C(4B)-H(4B)	119.3

C(4B)-C(5B)-C(6B)	120.6(11)
C(4B)-C(5B)-H(5B)	119.7
C(6B)-C(5B)-H(5B)	119.7
C(7B)-C(6B)-C(5B)	120.6(9)
C(7B)-C(6B)-H(6B)	119.7
C(5B)-C(6B)-H(6B)	119.7
C(6B)-C(7B)-C(8B)	120.4(10)
C(6B)-C(7B)-H(7B)	119.8
C(8B)-C(7B)-H(7B)	119.8
C(9B)-C(8B)-C(7B)	122.0(9)
C(9B)-C(8B)-C(3B)	120.1(8)
C(7B)-C(8B)-C(3B)	117.9(10)
C(10B)-C(9B)-C(8B)	121.8(9)
C(10B)-C(9B)-H(9B)	119.1
C(8B)-C(9B)-H(9B)	119.1
C(9B)-C(10B)-C(1B)	120.2(9)
C(9B)-C(10B)-H(10B)	119.9
C(1B)-C(10B)-H(10B)	119.9
N(1B)-C(21B)-H(21D)	109.5
N(1B)-C(21B)-H(21E)	109.5
H(21D)-C(21B)-H(21E)	109.5
N(1B)-C(21B)-H(21F)	109.5
H(21D)-C(21B)-H(21F)	109.5
H(21E)-C(21B)-H(21F)	109.5
C(11B)-N(2B)-C(22B)	118.3(10)
C(11B)-N(2B)-P(1)	121.2(12)
C(22B)-N(2B)-P(1)	113.7(12)
C(12B)-C(11B)-C(20B)	119.6(8)
C(12B)-C(11B)-N(2B)	120.4(8)
C(20B)-C(11B)-N(2B)	119.8(8)
C(11B)-C(12B)-C(13B)	119.3(7)

C(11B)-C(12B)-C(2B)	120.4(8)
C(13B)-C(12B)-C(2B)	120.3(8)
C(18B)-C(13B)-C(14B)	118.0(8)
C(18B)-C(13B)-C(12B)	119.5(7)
C(14B)-C(13B)-C(12B)	122.5(8)
C(15B)-C(14B)-C(13B)	120.9(9)
C(15B)-C(14B)-H(14B)	119.6
C(13B)-C(14B)-H(14B)	119.6
C(14B)-C(15B)-C(16B)	120.7(10)
C(14B)-C(15B)-H(15B)	119.7
C(16B)-C(15B)-H(15B)	119.7
C(17B)-C(16B)-C(15B)	120.8(9)
C(17B)-C(16B)-H(16B)	119.6
C(15B)-C(16B)-H(16B)	119.6
C(16B)-C(17B)-C(18B)	120.2(9)
C(16B)-C(17B)-H(17B)	119.9
C(18B)-C(17B)-H(17B)	119.9
C(19B)-C(18B)-C(13B)	118.5(8)
C(19B)-C(18B)-C(17B)	122.0(9)
C(13B)-C(18B)-C(17B)	119.3(9)
C(20B)-C(19B)-C(18B)	121.8(8)
C(20B)-C(19B)-H(19B)	119.1
C(18B)-C(19B)-H(19B)	119.1
C(19B)-C(20B)-C(11B)	120.6(9)
C(19B)-C(20B)-H(20B)	119.7
C(11B)-C(20B)-H(20B)	119.7
N(2B)-C(22B)-H(22D)	109.5
N(2B)-C(22B)-H(22E)	109.5
H(22D)-C(22B)-H(22E)	109.5
N(2B)-C(22B)-H(22F)	109.5
H(22D)-C(22B)-H(22F)	109.5

H(22E)-C(22B)-H(22F)	109.5
C(28)-N(3)-C(23)	113.5(10)
C(28)-N(3)-P(1)	128.9(14)
C(23)-N(3)-P(1)	115.9(11)
N(3)-C(23)-C(24)	114.0(12)
N(3)-C(23)-H(23A)	108.8
C(24)-C(23)-H(23A)	108.8
N(3)-C(23)-H(23B)	108.8
C(24)-C(23)-H(23B)	108.8
H(23A)-C(23)-H(23B)	107.7
C(23)-C(24)-C(25)	113.3(11)
C(23)-C(24)-H(24A)	108.9
C(25)-C(24)-H(24A)	108.9
C(23)-C(24)-H(24B)	108.9
C(25)-C(24)-H(24B)	108.9
H(24A)-C(24)-H(24B)	107.7
C(26)-C(25)-C(24)	116.6(14)
C(26)-C(25)-H(25A)	108.1
C(24)-C(25)-H(25A)	108.1
C(26)-C(25)-H(25B)	108.1
C(24)-C(25)-H(25B)	108.1
H(25A)-C(25)-H(25B)	107.3
C(25)-C(26)-C(27)	116.2(13)
C(25)-C(26)-H(26A)	108.2
C(27)-C(26)-H(26A)	108.2
C(25)-C(26)-H(26B)	108.2
C(27)-C(26)-H(26B)	108.2
H(26A)-C(26)-H(26B)	107.4
C(28)-C(27)-C(26)	114.9(11)
C(28)-C(27)-H(27A)	108.5
C(26)-C(27)-H(27A)	108.5

C(28)-C(27)-H(27B)	108.5
C(26)-C(27)-H(27B)	108.5
H(27A)-C(27)-H(27B)	107.5
N(3)-C(28)-C(27)	114.0(12)
N(3)-C(28)-H(28A)	108.7
C(27)-C(28)-H(28A)	108.7
N(3)-C(28)-H(28B)	108.7
C(27)-C(28)-H(28B)	108.7
H(28A)-C(28)-H(28B)	107.6
C(23B)-N(3B)-C(28B)	115.2(6)
C(23B)-N(3B)-P(1)	123.2(7)
C(28B)-N(3B)-P(1)	120.3(8)
N(3B)-C(23B)-C(24B)	116.5(10)
N(3B)-C(23B)-H(23C)	108.2
C(24B)-C(23B)-H(23C)	108.2
N(3B)-C(23B)-H(23D)	108.2
C(24B)-C(23B)-H(23D)	108.2
H(23C)-C(23B)-H(23D)	107.3
C(23B)-C(24B)-C(25B)	113.9(8)
C(23B)-C(24B)-H(24C)	108.8
C(25B)-C(24B)-H(24C)	108.8
C(23B)-C(24B)-H(24D)	108.8
C(25B)-C(24B)-H(24D)	108.8
H(24C)-C(24B)-H(24D)	107.7
C(26B)-C(25B)-C(24B)	116.5(10)
C(26B)-C(25B)-H(25C)	108.2
C(24B)-C(25B)-H(25C)	108.2
C(26B)-C(25B)-H(25D)	108.2
C(24B)-C(25B)-H(25D)	108.2
H(25C)-C(25B)-H(25D)	107.3
C(25B)-C(26B)-C(27B)	116.2(9)

C(25B)-C(26B)-H(26C)	108.2
C(27B)-C(26B)-H(26C)	108.2
C(25B)-C(26B)-H(26D)	108.2
C(27B)-C(26B)-H(26D)	108.2
H(26C)-C(26B)-H(26D)	107.4
C(28B)-C(27B)-C(26B)	116.0(8)
C(28B)-C(27B)-H(27C)	108.3
C(26B)-C(27B)-H(27C)	108.3
C(28B)-C(27B)-H(27D)	108.3
C(26B)-C(27B)-H(27D)	108.3
H(27C)-C(27B)-H(27D)	107.4
N(3B)-C(28B)-C(27B)	114.4(8)
N(3B)-C(28B)-H(28C)	108.7
C(27B)-C(28B)-H(28C)	108.7
N(3B)-C(28B)-H(28D)	108.7
C(27B)-C(28B)-H(28D)	108.7
H(28C)-C(28B)-H(28D)	107.6
N(6B)-P(2)-N(5)	103.8(5)
N(6)-P(2)-N(5)	87.8(6)
N(6B)-P(2)-N(4B)	104.5(6)
N(6)-P(2)-N(4B)	120.1(7)
N(5)-P(2)-N(4B)	97.9(5)
N(6B)-P(2)-N(5B)	113.4(5)
N(6)-P(2)-N(5B)	95.9(6)
N(4B)-P(2)-N(5B)	100.3(5)
N(6B)-P(2)-N(4)	109.8(6)
N(6)-P(2)-N(4)	126.9(7)
N(5)-P(2)-N(4)	102.6(5)
N(5B)-P(2)-N(4)	103.5(6)
N(6B)-P(2)-Se(2)	112.5(2)
N(6)-P(2)-Se(2)	112.0(4)

N(5)-P(2)-Se(2)	121.1(4)
N(4B)-P(2)-Se(2)	114.9(4)
N(5B)-P(2)-Se(2)	110.6(4)
N(4)-P(2)-Se(2)	106.3(4)
C(31)-N(4)-C(51)	114.8(7)
C(31)-N(4)-P(2)	117.3(8)
C(51)-N(4)-P(2)	124.6(8)
C(32)-C(31)-C(40)	120.3(8)
C(32)-C(31)-N(4)	117.8(7)
C(40)-C(31)-N(4)	121.8(8)
C(31)-C(32)-C(33)	119.2(7)
C(31)-C(32)-C(42)	119.4(8)
C(33)-C(32)-C(42)	121.3(8)
C(34)-C(33)-C(38)	117.9(8)
C(34)-C(33)-C(32)	122.3(7)
C(38)-C(33)-C(32)	119.8(8)
C(35)-C(34)-C(33)	121.0(9)
C(35)-C(34)-H(34A)	119.5
C(33)-C(34)-H(34A)	119.5
C(34)-C(35)-C(36)	119.5(11)
C(34)-C(35)-H(35A)	120.3
C(36)-C(35)-H(35A)	120.3
C(37)-C(36)-C(35)	121.4(9)
C(37)-C(36)-H(36A)	119.3
C(35)-C(36)-H(36A)	119.3
C(36)-C(37)-C(38)	120.7(10)
C(36)-C(37)-H(37A)	119.6
C(38)-C(37)-H(37A)	119.6
C(37)-C(38)-C(33)	119.1(10)
C(37)-C(38)-C(39)	123.8(9)
C(33)-C(38)-C(39)	116.9(8)

C(40)-C(39)-C(38)	122.2(8)
C(40)-C(39)-H(39A)	118.9
C(38)-C(39)-H(39A)	118.9
C(39)-C(40)-C(31)	120.3(9)
C(39)-C(40)-H(40A)	119.9
C(31)-C(40)-H(40A)	119.9
C(41)-N(5)-C(52)	118.2(9)
C(41)-N(5)-P(2)	115.7(11)
C(52)-N(5)-P(2)	111.5(9)
C(42)-C(41)-C(50)	120.6(7)
C(42)-C(41)-N(5)	118.6(7)
C(50)-C(41)-N(5)	120.7(7)
C(41)-C(42)-C(43)	119.7(6)
C(41)-C(42)-C(32)	118.3(7)
C(43)-C(42)-C(32)	121.9(7)
C(48)-C(43)-C(44)	118.2(7)
C(48)-C(43)-C(42)	119.0(7)
C(44)-C(43)-C(42)	122.7(7)
C(45)-C(44)-C(43)	121.3(9)
C(45)-C(44)-H(44A)	119.3
C(43)-C(44)-H(44A)	119.3
C(44)-C(45)-C(46)	119.6(9)
C(44)-C(45)-H(45A)	120.2
C(46)-C(45)-H(45A)	120.2
C(47)-C(46)-C(45)	119.8(9)
C(47)-C(46)-H(46A)	120.1
C(45)-C(46)-H(46A)	120.1
C(46)-C(47)-C(48)	122.7(9)
C(46)-C(47)-H(47A)	118.7
C(48)-C(47)-H(47A)	118.7
C(47)-C(48)-C(49)	122.7(8)

C(47)-C(48)-C(43)	118.1(8)
C(49)-C(48)-C(43)	119.1(8)
C(50)-C(49)-C(48)	120.7(7)
C(50)-C(49)-H(49A)	119.6
C(48)-C(49)-H(49A)	119.6
C(49)-C(50)-C(41)	120.6(8)
C(49)-C(50)-H(50A)	119.7
C(41)-C(50)-H(50A)	119.7
C(31B)-N(4B)-C(51B)	119.3(8)
C(31B)-N(4B)-P(2)	115.5(8)
C(51B)-N(4B)-P(2)	113.8(8)
C(32B)-C(31B)-C(40B)	121.2(8)
C(32B)-C(31B)-N(4B)	118.1(7)
C(40B)-C(31B)-N(4B)	120.7(8)
C(31B)-C(32B)-C(33B)	119.4(7)
C(31B)-C(32B)-C(42B)	119.2(8)
C(33B)-C(32B)-C(42B)	121.5(8)
C(34B)-C(33B)-C(38B)	117.9(8)
C(34B)-C(33B)-C(32B)	122.3(7)
C(38B)-C(33B)-C(32B)	119.5(8)
C(35B)-C(34B)-C(33B)	120.8(9)
C(35B)-C(34B)-H(34B)	119.6
C(33B)-C(34B)-H(34B)	119.6
C(34B)-C(35B)-C(36B)	119.5(10)
C(34B)-C(35B)-H(35B)	120.3
C(36B)-C(35B)-H(35B)	120.3
C(37B)-C(36B)-C(35B)	121.8(9)
C(37B)-C(36B)-H(36B)	119.1
C(35B)-C(36B)-H(36B)	119.1
C(36B)-C(37B)-C(38B)	120.1(10)
C(36B)-C(37B)-H(37B)	119.9

C(38B)-C(37B)-H(37B)	119.9
C(37B)-C(38B)-C(33B)	119.8(10)
C(37B)-C(38B)-C(39B)	122.5(9)
C(33B)-C(38B)-C(39B)	117.7(8)
C(40B)-C(39B)-C(38B)	121.6(8)
C(40B)-C(39B)-H(39B)	119.2
C(38B)-C(39B)-H(39B)	119.2
C(39B)-C(40B)-C(31B)	120.2(9)
C(39B)-C(40B)-H(40B)	119.9
C(31B)-C(40B)-H(40B)	119.9
N(4B)-C(51B)-H(51D)	109.5
N(4B)-C(51B)-H(51E)	109.5
H(51D)-C(51B)-H(51E)	109.5
N(4B)-C(51B)-H(51F)	109.5
H(51D)-C(51B)-H(51F)	109.5
H(51E)-C(51B)-H(51F)	109.5
C(41B)-N(5B)-C(52B)	115.4(9)
C(41B)-N(5B)-P(2)	118.9(10)
C(52B)-N(5B)-P(2)	117.7(9)
C(42B)-C(41B)-C(50B)	119.2(7)
C(42B)-C(41B)-N(5B)	120.1(7)
C(50B)-C(41B)-N(5B)	120.5(7)
C(41B)-C(42B)-C(43B)	120.0(7)
C(41B)-C(42B)-C(32B)	119.9(7)
C(43B)-C(42B)-C(32B)	119.9(7)
C(48B)-C(43B)-C(44B)	118.1(7)
C(48B)-C(43B)-C(42B)	119.4(7)
C(44B)-C(43B)-C(42B)	122.5(7)
C(45B)-C(44B)-C(43B)	120.7(8)
C(45B)-C(44B)-H(44B)	119.6
C(43B)-C(44B)-H(44B)	119.6

C(44B)-C(45B)-C(46B)	120.6(9)
C(44B)-C(45B)-H(45B)	119.7
C(46B)-C(45B)-H(45B)	119.7
C(47B)-C(46B)-C(45B)	120.1(9)
C(47B)-C(46B)-H(46B)	120.0
C(45B)-C(46B)-H(46B)	120.0
C(46B)-C(47B)-C(48B)	121.4(8)
C(46B)-C(47B)-H(47B)	119.3
C(48B)-C(47B)-H(47B)	119.3
C(47B)-C(48B)-C(49B)	122.8(8)
C(47B)-C(48B)-C(43B)	119.1(8)
C(49B)-C(48B)-C(43B)	117.9(8)
C(50B)-C(49B)-C(48B)	121.6(7)
C(50B)-C(49B)-H(49B)	119.2
C(48B)-C(49B)-H(49B)	119.2
C(49B)-C(50B)-C(41B)	120.9(8)
C(49B)-C(50B)-H(50B)	119.5
C(41B)-C(50B)-H(50B)	119.5
N(5B)-C(52B)-H(52D)	109.5
N(5B)-C(52B)-H(52E)	109.5
H(52D)-C(52B)-H(52E)	109.5
N(5B)-C(52B)-H(52F)	109.5
H(52D)-C(52B)-H(52F)	109.5
H(52E)-C(52B)-H(52F)	109.5
C(58)-N(6)-C(53)	113.1(8)
C(58)-N(6)-P(2)	123.5(8)
C(53)-N(6)-P(2)	123.4(7)
C(54)-C(53)-N(6)	116.9(10)
C(54)-C(53)-H(53A)	108.1
N(6)-C(53)-H(53A)	108.1
C(54)-C(53)-H(53B)	108.1

N(6)-C(53)-H(53B)	108.1
H(53A)-C(53)-H(53B)	107.3
C(53)-C(54)-C(55)	115.3(11)
C(53)-C(54)-H(54A)	108.4
C(55)-C(54)-H(54A)	108.4
C(53)-C(54)-H(54B)	108.4
C(55)-C(54)-H(54B)	108.4
H(54A)-C(54)-H(54B)	107.5
C(56)-C(55)-C(54)	114.9(11)
C(56)-C(55)-H(55A)	108.5
C(54)-C(55)-H(55A)	108.5
C(56)-C(55)-H(55B)	108.5
C(54)-C(55)-H(55B)	108.5
H(55A)-C(55)-H(55B)	107.5
C(57)-C(56)-C(55)	118.4(10)
C(57)-C(56)-H(56A)	107.7
C(55)-C(56)-H(56A)	107.7
C(57)-C(56)-H(56B)	107.7
C(55)-C(56)-H(56B)	107.7
H(56A)-C(56)-H(56B)	107.1
C(58)-C(57)-C(56)	121.2(11)
C(58)-C(57)-H(57A)	107.0
C(56)-C(57)-H(57A)	107.0
C(58)-C(57)-H(57B)	107.0
C(56)-C(57)-H(57B)	107.0
H(57A)-C(57)-H(57B)	106.8
C(57)-C(58)-N(6)	116.2(10)
C(57)-C(58)-H(58A)	108.2
N(6)-C(58)-H(58A)	108.2
C(57)-C(58)-H(58B)	108.2
N(6)-C(58)-H(58B)	108.2

H(58A)-C(58)-H(58B)	107.4
C(58B)-N(6B)-C(53B)	114.7(7)
C(58B)-N(6B)-P(2)	122.4(6)
C(53B)-N(6B)-P(2)	120.6(6)
C(54B)-C(53B)-N(6B)	116.3(8)
C(54B)-C(53B)-H(53C)	108.2
N(6B)-C(53B)-H(53C)	108.2
C(54B)-C(53B)-H(53D)	108.2
N(6B)-C(53B)-H(53D)	108.2
H(53C)-C(53B)-H(53D)	107.4
C(53B)-C(54B)-C(55B)	116.1(9)
C(53B)-C(54B)-H(54C)	108.3
C(55B)-C(54B)-H(54C)	108.3
C(53B)-C(54B)-H(54D)	108.3
C(55B)-C(54B)-H(54D)	108.3
H(54C)-C(54B)-H(54D)	107.4
C(56B)-C(55B)-C(54B)	114.1(8)
C(56B)-C(55B)-H(55C)	108.7
C(54B)-C(55B)-H(55C)	108.7
C(56B)-C(55B)-H(55D)	108.7
C(54B)-C(55B)-H(55D)	108.7
H(55C)-C(55B)-H(55D)	107.6
C(57B)-C(56B)-C(55B)	117.4(8)
C(57B)-C(56B)-H(56C)	108.0
C(55B)-C(56B)-H(56C)	108.0
C(57B)-C(56B)-H(56D)	108.0
C(55B)-C(56B)-H(56D)	108.0
H(56C)-C(56B)-H(56D)	107.2
C(58B)-C(57B)-C(56B)	118.3(9)
C(58B)-C(57B)-H(57C)	107.7
C(56B)-C(57B)-H(57C)	107.7

C(58B)-C(57B)-H(57D)	107.7
C(56B)-C(57B)-H(57D)	107.7
H(57C)-C(57B)-H(57D)	107.1
C(57B)-C(58B)-N(6B)	113.7(7)
C(57B)-C(58B)-H(58C)	108.8
N(6B)-C(58B)-H(58C)	108.8
C(57B)-C(58B)-H(58D)	108.8
N(6B)-C(58B)-H(58D)	108.8
H(58C)-C(58B)-H(58D)	107.7

Symmetry transformations used to generate equivalent atoms:

Anisotropic displacement parameters ($Å^2 x\ 10^3$) for bc56ras. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
P(1)	39(1)	45(1)	29(1)	-4(1)	9(1)	4(1)
Se(1)	43(1)	84(1)	52(1)	-7(1)	10(1)	-7(1)
N(1)	40(4)	42(4)	30(3)	-8(3)	12(3)	4(3)
C(1)	36(3)	46(3)	28(3)	-3(3)	10(3)	0(3)
C(2)	35(3)	45(3)	27(3)	-5(3)	11(2)	-1(3)
C(3)	34(3)	41(4)	24(4)	-8(3)	9(3)	-4(3)
C(4)	35(3)	48(5)	30(5)	-6(4)	12(3)	-1(4)
C(5)	34(4)	43(5)	34(5)	-2(4)	11(3)	1(4)
C(6)	32(3)	43(6)	34(5)	-2(5)	14(3)	2(4)
C(7)	34(3)	47(5)	35(4)	-5(4)	13(3)	-1(4)
C(8)	35(3)	44(5)	33(4)	-7(3)	12(3)	-2(3)
C(9)	35(4)	45(5)	33(4)	-5(4)	14(3)	-5(4)
C(10)	37(4)	47(4)	31(4)	-4(3)	9(3)	0(3)
C(21)	38(9)	43(5)	35(5)	-2(4)	12(5)	-1(4)

N(2)	51(4)	45(4)	31(3)	-3(3)	8(3)	9(3)
C(11)	47(4)	42(3)	31(3)	0(3)	11(3)	13(3)
C(12)	38(3)	42(3)	28(3)	3(3)	13(3)	8(3)
C(13)	38(3)	46(3)	31(4)	4(3)	17(3)	5(3)
C(14)	41(3)	54(4)	25(4)	5(4)	13(3)	0(3)
C(15)	45(3)	61(5)	25(5)	8(4)	15(4)	-3(3)
C(16)	47(3)	59(4)	31(5)	7(4)	20(4)	-4(3)
C(17)	46(3)	53(4)	27(5)	8(4)	23(4)	2(3)
C(18)	44(3)	45(3)	29(4)	5(4)	19(3)	9(3)
C(19)	50(4)	46(3)	25(5)	12(4)	18(4)	10(3)
C(20)	53(4)	45(3)	22(4)	4(3)	11(3)	13(3)
C(22)	75(6)	44(8)	45(6)	-10(5)	4(5)	13(6)
N(1B)	37(4)	42(4)	35(4)	-5(3)	9(3)	5(4)
C(1B)	37(3)	44(4)	28(3)	-5(3)	11(3)	0(3)
C(2B)	36(3)	45(3)	28(3)	-4(3)	10(3)	0(3)
C(3B)	34(3)	46(4)	26(4)	-7(4)	12(3)	-3(3)
C(4B)	32(4)	45(5)	30(5)	-2(4)	12(3)	-1(4)
C(5B)	35(4)	45(5)	34(5)	0(4)	11(3)	-2(4)
C(6B)	38(4)	44(6)	35(5)	-1(5)	14(3)	1(5)
C(7B)	34(3)	44(6)	34(4)	0(5)	17(3)	-1(4)
C(8B)	32(3)	44(5)	30(4)	-7(4)	8(3)	-1(4)
C(9B)	34(4)	43(5)	33(4)	-5(4)	11(3)	-4(4)
C(10B)	36(4)	42(5)	36(4)	-5(4)	9(3)	-4(4)
C(21B)	28(8)	51(6)	36(6)	-4(5)	3(5)	9(5)
N(2B)	48(5)	44(4)	31(4)	-5(3)	12(3)	10(3)
C(11B)	47(4)	42(3)	32(4)	0(3)	11(3)	13(3)
C(12B)	38(3)	42(3)	32(4)	0(3)	15(3)	8(3)
C(13B)	40(3)	44(3)	29(4)	5(3)	13(3)	8(3)
C(14B)	39(3)	53(4)	28(5)	8(4)	14(4)	0(3)
C(15B)	47(4)	60(4)	29(5)	8(4)	16(4)	-4(3)
C(16B)	44(4)	56(4)	31(6)	9(5)	20(5)	-3(3)

C(17B)	46(4)	51(4)	36(6)	8(5)	21(4)	8(3)
C(18B)	44(3)	46(3)	30(5)	7(4)	17(4)	11(3)
C(19B)	55(5)	43(4)	27(5)	10(4)	16(4)	12(4)
C(20B)	54(5)	44(4)	30(4)	7(4)	12(4)	13(4)
C(22B)	79(7)	44(9)	39(6)	3(7)	-2(6)	23(7)
N(3)	54(4)	49(4)	37(4)	-5(4)	22(3)	3(4)
C(23)	57(4)	53(4)	41(4)	-9(5)	26(4)	1(4)
C(24)	66(5)	60(5)	48(5)	-13(5)	30(4)	-10(4)
C(25)	88(5)	72(6)	57(5)	-14(5)	25(5)	-12(5)
C(26)	85(5)	63(6)	55(5)	-14(5)	28(4)	-7(5)
C(27)	74(5)	56(5)	53(5)	-12(5)	23(4)	1(5)
C(28)	65(4)	47(4)	46(4)	-5(4)	19(4)	3(4)
N(3B)	50(3)	47(3)	37(3)	-4(3)	18(2)	3(3)
C(23B)	57(3)	56(4)	53(4)	-12(4)	27(3)	1(3)
C(24B)	80(5)	64(4)	59(4)	-24(4)	35(4)	-13(4)
C(25B)	87(4)	60(5)	49(4)	-22(4)	34(3)	-15(4)
C(26B)	79(4)	56(5)	52(4)	-12(4)	34(3)	-4(4)
C(27B)	69(4)	46(4)	49(4)	-2(3)	26(3)	0(3)
C(28B)	62(3)	45(3)	37(3)	0(3)	22(3)	4(3)
P(2)	38(1)	36(1)	58(1)	-3(1)	25(1)	3(1)
Se(2)	40(1)	48(1)	51(1)	12(1)	20(1)	3(1)
N(4)	37(3)	54(4)	41(3)	-6(3)	15(3)	1(3)
C(31)	36(3)	40(4)	37(3)	-7(3)	13(2)	5(3)
C(32)	34(3)	33(3)	39(3)	-4(3)	10(2)	4(3)
C(33)	35(3)	38(3)	44(4)	-4(4)	13(3)	1(3)
C(34)	44(3)	39(4)	48(4)	-4(4)	14(4)	-3(3)
C(35)	46(3)	42(5)	54(5)	-4(4)	18(4)	-3(3)
C(36)	46(4)	42(4)	56(6)	-7(5)	14(4)	-8(3)
C(37)	41(4)	44(4)	57(5)	-8(4)	7(4)	-3(3)
C(38)	36(3)	39(4)	50(4)	-10(4)	10(3)	3(3)
C(39)	43(3)	42(5)	44(4)	-10(4)	-2(3)	5(3)

C(40)	42(3)	41(5)	39(4)	-6(4)	7(3)	12(3)
C(51)	44(5)	59(8)	30(5)	-3(5)	1(4)	-10(5)
N(5)	33(3)	28(4)	53(3)	7(3)	18(3)	-1(3)
C(41)	36(3)	32(4)	33(3)	6(3)	12(2)	0(3)
C(42)	35(3)	34(3)	30(3)	2(3)	13(3)	0(2)
C(43)	34(3)	36(3)	31(4)	-1(3)	13(3)	0(3)
C(44)	34(4)	41(4)	34(5)	-5(3)	6(3)	3(3)
C(45)	32(5)	44(4)	39(5)	-5(4)	1(4)	6(4)
C(46)	38(6)	44(4)	37(5)	-9(4)	5(5)	6(4)
C(47)	38(5)	40(4)	31(4)	-5(3)	3(4)	1(4)
C(48)	36(4)	39(3)	31(4)	-2(3)	9(3)	-2(3)
C(49)	39(4)	38(5)	31(4)	1(4)	3(3)	-2(3)
C(50)	36(3)	35(5)	28(3)	9(4)	8(3)	3(3)
C(52)	39(6)	36(7)	66(6)	8(6)	13(5)	-2(5)
N(4B)	37(3)	54(4)	39(3)	-8(3)	17(3)	5(3)
C(31B)	39(3)	44(4)	40(3)	-10(3)	14(3)	2(3)
C(32B)	33(3)	36(3)	36(3)	-3(3)	10(2)	6(3)
C(33B)	34(3)	38(3)	45(4)	-8(3)	13(3)	3(3)
C(34B)	44(3)	36(5)	46(4)	-7(4)	19(4)	2(3)
C(35B)	47(4)	38(5)	48(5)	-10(4)	17(4)	-5(3)
C(36B)	44(4)	41(4)	50(5)	-10(5)	14(4)	-3(3)
C(37B)	44(4)	38(4)	48(5)	-8(5)	11(4)	-2(3)
C(38B)	39(3)	39(4)	50(4)	-8(4)	11(3)	3(3)
C(39B)	46(3)	41(5)	47(4)	-12(4)	9(3)	-4(3)
C(40B)	46(3)	45(4)	46(4)	-12(4)	14(3)	3(3)
C(51B)	47(5)	73(8)	31(4)	-23(5)	9(4)	-6(6)
N(5B)	30(3)	31(4)	53(3)	8(3)	19(3)	1(3)
C(41B)	34(3)	33(4)	33(3)	7(3)	14(2)	1(3)
C(42B)	34(3)	34(3)	31(3)	3(3)	12(3)	1(2)
C(43B)	35(3)	37(3)	27(4)	-2(3)	11(3)	0(3)
C(44B)	33(4)	39(4)	33(5)	-4(3)	4(3)	2(3)

C(45B)	35(5)	43(4)	39(5)	-9(4)	-4(4)	5(4)
C(46B)	34(5)	43(4)	38(5)	-8(4)	-4(4)	6(4)
C(47B)	36(5)	42(4)	33(4)	-10(3)	0(4)	-2(4)
C(48B)	34(4)	42(3)	28(4)	0(3)	7(3)	0(3)
C(49B)	38(4)	42(5)	28(4)	1(4)	7(3)	-4(3)
C(50B)	32(3)	39(5)	32(3)	5(4)	9(3)	1(3)
C(52B)	47(6)	39(7)	69(6)	26(6)	25(5)	10(5)
N(6)	57(4)	48(4)	52(5)	3(4)	35(4)	4(4)
C(53)	63(5)	39(5)	46(5)	4(4)	36(4)	5(4)
C(54)	70(5)	39(5)	58(4)	0(4)	32(4)	4(4)
C(55)	79(5)	41(4)	58(4)	-1(4)	31(4)	8(4)
C(56)	83(5)	48(5)	59(5)	-8(4)	36(4)	8(4)
C(57)	74(4)	54(4)	56(4)	-2(4)	32(3)	10(4)
C(58)	64(4)	50(4)	54(4)	-2(4)	29(3)	9(4)
N(6B)	51(3)	41(3)	47(4)	2(3)	25(3)	2(3)
C(53B)	59(4)	42(3)	62(4)	0(4)	27(3)	-1(3)
C(54B)	71(4)	45(4)	63(4)	1(4)	28(4)	0(4)
C(55B)	82(4)	47(4)	56(4)	8(4)	32(3)	10(4)
C(56B)	78(4)	52(4)	58(4)	-1(4)	32(3)	13(4)
C(57B)	67(4)	49(4)	46(4)	-2(3)	26(3)	18(3)
C(58B)	59(4)	43(4)	46(3)	0(3)	27(3)	5(3)

Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for bc56ras.

	x	y	z	U(eq)

H(4A)	1878	10905	9276	45
H(5A)	954	12344	9675	45
H(6A)	315	11478	10622	43
H(7A)	496	9080	11055	46
H(9A)	1162	6647	11031	45
H(10A)	1849	5078	10430	47
H(21A)	3323	4595	10437	58
H(21B)	3574	4071	9648	58
H(21C)	2691	3560	9740	58
H(14A)	3371	9743	10717	47
H(15A)	4401	11450	11298	52
H(16A)	5302	12257	10594	52
H(17A)	5114	11457	9249	48
H(19A)	4336	9898	8037	47
H(20A)	3299	8218	7414	49
H(22A)	1839	7755	6743	88
H(22B)	1148	8205	7165	88
H(22C)	1185	6567	6859	88
H(4B)	1926	11111	9127	42
H(5B)	1115	12744	9562	46
H(6B)	372	12006	10444	46
H(7B)	445	9629	10900	43
H(9B)	960	7096	10862	44
H(10B)	1669	5402	10360	46
H(21D)	3347	4753	10412	60
H(21E)	3191	3826	9571	60
H(21F)	2454	3950	9977	60
H(14B)	3298	10168	10505	47
H(15B)	4463	11641	11067	53
H(16B)	5322	12277	10284	50
H(17B)	5054	11361	8951	51

H(19B)	4130	9886	7754	50
H(20B)	3021	8307	7193	51
H(22D)	1546	8070	6776	90
H(22E)	951	6770	6879	90
H(22F)	1815	6419	6702	90
H(23A)	3933	3960	8663	57
H(23B)	3672	5639	8574	57
H(24A)	4339	4076	7578	66
H(24B)	4202	5797	7575	66
H(25A)	2712	5341	6683	87
H(25B)	3413	5161	6241	87
H(26A)	3371	2617	6519	80
H(26B)	2601	3307	5771	80
H(27A)	1693	3157	6513	73
H(27B)	2163	1619	6619	73
H(28A)	2054	2389	7896	63
H(28B)	3031	2206	7974	63
H(23C)	3879	3934	8139	64
H(23D)	3685	5594	8281	64
H(24C)	4070	4974	7036	77
H(24D)	3336	6152	6931	77
H(25C)	2280	4608	6185	75
H(25D)	3028	4275	5822	75
H(26C)	3384	2305	6835	72
H(26D)	2626	2118	5960	72
H(27C)	1632	2634	6649	63
H(27D)	2157	1171	6969	63
H(28C)	1979	2557	8073	56
H(28D)	2957	2214	8209	56
H(34A)	8659	8068	5203	53
H(35A)	9760	9373	4965	57

H(36A)	10703	10742	6054	59
H(37A)	10585	10795	7360	60
H(39A)	9868	9823	8390	57
H(40A)	8708	8820	8576	51
H(51A)	7715	6166	8222	70
H(51B)	6732	6536	8050	70
H(51C)	7461	7583	8633	70
H(44A)	9105	5613	6421	46
H(45A)	9376	3249	6139	50
H(46A)	8331	1939	5056	51
H(47A)	7005	2888	4446	46
H(49A)	5935	4879	4295	46
H(50A)	5575	7035	4785	40
H(52A)	5951	9716	4716	72
H(52B)	5995	10824	5459	72
H(52C)	5339	9491	5259	72
H(34B)	8634	7754	5066	50
H(35B)	9699	8936	4696	53
H(36B)	10663	10476	5665	54
H(37B)	10503	11045	6916	54
H(39B)	9753	10609	7981	55
H(40B)	8618	9720	8276	55
H(51D)	7888	6907	8421	77
H(51E)	6890	7202	8208	77
H(51F)	7561	8493	8558	77
H(44B)	9165	5773	6586	44
H(45B)	9645	3582	6269	52
H(46B)	8712	2006	5268	51
H(47B)	7325	2650	4602	48
H(49B)	6124	4426	4390	45
H(50B)	5614	6560	4751	42

H(52D)	5916	9476	4642	76
H(52E)	5583	10245	5322	76
H(52F)	5228	8677	4959	76
H(53A)	7295	10946	6263	54
H(53B)	6550	12124	5964	54
H(54A)	7932	12974	6855	63
H(54B)	7749	12163	7612	63
H(55A)	7437	14801	7458	69
H(55B)	6614	14379	6675	69
H(56A)	6887	14078	8376	73
H(56B)	6031	14503	7637	73
H(57A)	6632	11755	8233	70
H(57B)	5730	12458	8126	70
H(58A)	5432	12125	6632	65
H(58B)	5366	10776	7201	65
H(53C)	7808	11127	7477	63
H(53D)	7318	11221	6488	63
H(54C)	7600	13526	6897	70
H(54D)	7342	13301	7716	70
H(55C)	6362	14720	6508	71
H(55D)	6039	13161	6108	71
H(56C)	5942	14185	7654	72
H(56D)	5156	14107	6795	72
H(57C)	5160	12292	7763	63
H(57D)	5069	11705	6850	63
H(58C)	5946	10291	7982	56
H(58D)	6619	11597	8207	56

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Torsion angles [°] for bc56ras.

N(3B)-P(1)-N(1)-C(1)	178.8(8)
N(3)-P(1)-N(1)-C(1)	179.8(10)
N(2B)-P(1)-N(1)-C(1)	63.4(11)
N(2)-P(1)-N(1)-C(1)	69.0(11)
N(1B)-P(1)-N(1)-C(1)	3(9)
Se(1)-P(1)-N(1)-C(1)	-57.3(9)
N(3B)-P(1)-N(1)-C(21)	-42.9(13)
N(3)-P(1)-N(1)-C(21)	-41.9(14)
N(2B)-P(1)-N(1)-C(21)	-158.4(15)
N(2)-P(1)-N(1)-C(21)	-152.7(12)
N(1B)-P(1)-N(1)-C(21)	141(11)
Se(1)-P(1)-N(1)-C(21)	81.0(12)
C(21)-N(1)-C(1)-C(2)	145.5(17)
P(1)-N(1)-C(1)-C(2)	-76.1(17)
C(21)-N(1)-C(1)-C(10)	-36(2)
P(1)-N(1)-C(1)-C(10)	102.5(14)
C(10)-C(1)-C(2)-C(3)	-9(2)
N(1)-C(1)-C(2)-C(3)	169.3(14)
C(10)-C(1)-C(2)-C(12)	169.9(12)
N(1)-C(1)-C(2)-C(12)	-11(2)
C(1)-C(2)-C(3)-C(4)	-169.7(15)
C(12)-C(2)-C(3)-C(4)	11(2)
C(1)-C(2)-C(3)-C(8)	10(2)
C(12)-C(2)-C(3)-C(8)	-169.4(11)
C(8)-C(3)-C(4)-C(5)	-2(2)
C(2)-C(3)-C(4)-C(5)	177.5(14)
C(3)-C(4)-C(5)-C(6)	3(2)
C(4)-C(5)-C(6)-C(7)	-3.1(18)
C(5)-C(6)-C(7)-C(8)	1.7(17)
C(6)-C(7)-C(8)-C(9)	-175.8(11)

C(6)-C(7)-C(8)-C(3)	-0.5(17)
C(4)-C(3)-C(8)-C(9)	176.1(13)
C(2)-C(3)-C(8)-C(9)	-3.5(18)
C(4)-C(3)-C(8)-C(7)	0.6(18)
C(2)-C(3)-C(8)-C(7)	-179.0(12)
C(7)-C(8)-C(9)-C(10)	171.7(11)
C(3)-C(8)-C(9)-C(10)	-3.6(17)
C(8)-C(9)-C(10)-C(1)	4.3(18)
C(2)-C(1)-C(10)-C(9)	2(2)
N(1)-C(1)-C(10)-C(9)	-176.3(14)
N(3B)-P(1)-N(2)-C(11)	-90.6(14)
N(3)-P(1)-N(2)-C(11)	-87.7(15)
N(2B)-P(1)-N(2)-C(11)	143(11)
N(1B)-P(1)-N(2)-C(11)	23.2(14)
N(1)-P(1)-N(2)-C(11)	17.5(16)
Se(1)-P(1)-N(2)-C(11)	144.9(11)
N(3B)-P(1)-N(2)-C(22)	87.0(19)
N(3)-P(1)-N(2)-C(22)	90(2)
N(2B)-P(1)-N(2)-C(22)	-39(9)
N(1B)-P(1)-N(2)-C(22)	-159.2(19)
N(1)-P(1)-N(2)-C(22)	-164.9(17)
Se(1)-P(1)-N(2)-C(22)	-38(2)
C(22)-N(2)-C(11)-C(12)	122(2)
P(1)-N(2)-C(11)-C(12)	-60(2)
C(22)-N(2)-C(11)-C(20)	-60(3)
P(1)-N(2)-C(11)-C(20)	118.0(15)
C(20)-C(11)-C(12)-C(13)	-3(2)
N(2)-C(11)-C(12)-C(13)	175.4(15)
C(20)-C(11)-C(12)-C(2)	-176.5(13)
N(2)-C(11)-C(12)-C(2)	2(2)
C(1)-C(2)-C(12)-C(11)	57.3(19)

C(3)-C(2)-C(12)-C(11)	-123.4(17)
C(1)-C(2)-C(12)-C(13)	-116.3(17)
C(3)-C(2)-C(12)-C(13)	63.0(18)
C(11)-C(12)-C(13)-C(18)	5(2)
C(2)-C(12)-C(13)-C(18)	178.5(13)
C(11)-C(12)-C(13)-C(14)	-173.0(15)
C(2)-C(12)-C(13)-C(14)	1(2)
C(18)-C(13)-C(14)-C(15)	5(2)
C(12)-C(13)-C(14)-C(15)	-177.0(14)
C(13)-C(14)-C(15)-C(16)	-5(2)
C(14)-C(15)-C(16)-C(17)	2(2)
C(15)-C(16)-C(17)-C(18)	1(2)
C(14)-C(13)-C(18)-C(19)	174.3(14)
C(12)-C(13)-C(18)-C(19)	-4(2)
C(14)-C(13)-C(18)-C(17)	-3(2)
C(12)-C(13)-C(18)-C(17)	179.1(14)
C(16)-C(17)-C(18)-C(19)	-177.0(14)
C(16)-C(17)-C(18)-C(13)	0(2)
C(13)-C(18)-C(19)-C(20)	0(2)
C(17)-C(18)-C(19)-C(20)	177.6(12)
C(18)-C(19)-C(20)-C(11)	1.6(19)
C(12)-C(11)-C(20)-C(19)	0(2)
N(2)-C(11)-C(20)-C(19)	-178.6(13)
N(3B)-P(1)-N(1B)-C(1B)	174.0(9)
N(3)-P(1)-N(1B)-C(1B)	175.1(11)
N(2B)-P(1)-N(1B)-C(1B)	57.5(14)
N(2)-P(1)-N(1B)-C(1B)	63.4(12)
N(1)-P(1)-N(1B)-C(1B)	178(11)
Se(1)-P(1)-N(1B)-C(1B)	-59.4(11)
N(3B)-P(1)-N(1B)-C(21B)	-48.9(15)
N(3)-P(1)-N(1B)-C(21B)	-47.9(16)

N(2B)-P(1)-N(1B)-C(21B)	-165.5(14)
N(2)-P(1)-N(1B)-C(21B)	-159.5(16)
N(1)-P(1)-N(1B)-C(21B)	-45(10)
Se(1)-P(1)-N(1B)-C(21B)	77.6(14)
C(21B)-N(1B)-C(1B)-C(2B)	149(2)
P(1)-N(1B)-C(1B)-C(2B)	-75(2)
C(21B)-N(1B)-C(1B)-C(10B)	-35(3)
P(1)-N(1B)-C(1B)-C(10B)	100.8(18)
C(10B)-C(1B)-C(2B)-C(3B)	-5(3)
N(1B)-C(1B)-C(2B)-C(3B)	171.2(18)
C(10B)-C(1B)-C(2B)-C(12B)	176.2(16)
N(1B)-C(1B)-C(2B)-C(12B)	-8(3)
C(1B)-C(2B)-C(3B)-C(4B)	-171(2)
C(12B)-C(2B)-C(3B)-C(4B)	8(3)
C(1B)-C(2B)-C(3B)-C(8B)	5(3)
C(12B)-C(2B)-C(3B)-C(8B)	-176.0(14)
C(8B)-C(3B)-C(4B)-C(5B)	4(3)
C(2B)-C(3B)-C(4B)-C(5B)	179.9(18)
C(3B)-C(4B)-C(5B)-C(6B)	-1(2)
C(4B)-C(5B)-C(6B)-C(7B)	0(2)
C(5B)-C(6B)-C(7B)-C(8B)	-1(2)
C(6B)-C(7B)-C(8B)-C(9B)	-176.6(14)
C(6B)-C(7B)-C(8B)-C(3B)	3(2)
C(4B)-C(3B)-C(8B)-C(9B)	175.2(16)
C(2B)-C(3B)-C(8B)-C(9B)	-1(2)
C(4B)-C(3B)-C(8B)-C(7B)	-5(2)
C(2B)-C(3B)-C(8B)-C(7B)	179.0(15)
C(7B)-C(8B)-C(9B)-C(10B)	176.8(14)
C(3B)-C(8B)-C(9B)-C(10B)	-3(2)
C(8B)-C(9B)-C(10B)-C(1B)	3(2)
C(2B)-C(1B)-C(10B)-C(9B)	1(3)

N(1B)-C(1B)-C(10B)-C(9B)	-175.2(17)
N(3B)-P(1)-N(2B)-C(11B)	-84.4(14)
N(3)-P(1)-N(2B)-C(11B)	-81.7(15)
N(2)-P(1)-N(2B)-C(11B)	-29(9)
N(1B)-P(1)-N(2B)-C(11B)	32.2(17)
N(1)-P(1)-N(2B)-C(11B)	26.7(15)
Se(1)-P(1)-N(2B)-C(11B)	152.8(12)
N(3B)-P(1)-N(2B)-C(22B)	66(2)
N(3)-P(1)-N(2B)-C(22B)	69(2)
N(2)-P(1)-N(2B)-C(22B)	122(11)
N(1B)-P(1)-N(2B)-C(22B)	-177.1(18)
N(1)-P(1)-N(2B)-C(22B)	177(2)
Se(1)-P(1)-N(2B)-C(22B)	-57(2)
C(22B)-N(2B)-C(11B)-C(12B)	143(2)
P(1)-N(2B)-C(11B)-C(12B)	-68(3)
C(22B)-N(2B)-C(11B)-C(20B)	-32(3)
P(1)-N(2B)-C(11B)-C(20B)	117.2(18)
C(20B)-C(11B)-C(12B)-C(13B)	-9(3)
N(2B)-C(11B)-C(12B)-C(13B)	176.6(19)
C(20B)-C(11B)-C(12B)-C(2B)	173.7(16)
N(2B)-C(11B)-C(12B)-C(2B)	-1(3)
C(1B)-C(2B)-C(12B)-C(11B)	58(2)
C(3B)-C(2B)-C(12B)-C(11B)	-121(2)
C(1B)-C(2B)-C(12B)-C(13B)	-120(2)
C(3B)-C(2B)-C(12B)-C(13B)	61(2)
C(11B)-C(12B)-C(13B)-C(18B)	2(3)
C(2B)-C(12B)-C(13B)-C(18B)	179.7(15)
C(11B)-C(12B)-C(13B)-C(14B)	-178.7(19)
C(2B)-C(12B)-C(13B)-C(14B)	-1(3)
C(18B)-C(13B)-C(14B)-C(15B)	-3(2)
C(12B)-C(13B)-C(14B)-C(15B)	177.6(18)

C(13B)-C(14B)-C(15B)-C(16B)	3(2)
C(14B)-C(15B)-C(16B)-C(17B)	-1(3)
C(15B)-C(16B)-C(17B)-C(18B)	-1(2)
C(14B)-C(13B)-C(18B)-C(19B)	-174.5(17)
C(12B)-C(13B)-C(18B)-C(19B)	5(3)
C(14B)-C(13B)-C(18B)-C(17B)	1(2)
C(12B)-C(13B)-C(18B)-C(17B)	-179.9(17)
C(16B)-C(17B)-C(18B)-C(19B)	176.4(17)
C(16B)-C(17B)-C(18B)-C(13B)	1(2)
C(13B)-C(18B)-C(19B)-C(20B)	-5(2)
C(17B)-C(18B)-C(19B)-C(20B)	179.7(16)
C(18B)-C(19B)-C(20B)-C(11B)	-1(2)
C(12B)-C(11B)-C(20B)-C(19B)	8(3)
N(2B)-C(11B)-C(20B)-C(19B)	-176.7(17)
N(3B)-P(1)-N(3)-C(28)	-80(15)
N(2B)-P(1)-N(3)-C(28)	-132.4(17)
N(2)-P(1)-N(3)-C(28)	-138.0(17)
N(1B)-P(1)-N(3)-C(28)	117.5(19)
N(1)-P(1)-N(3)-C(28)	117.2(19)
Se(1)-P(1)-N(3)-C(28)	-9(2)
N(3B)-P(1)-N(3)-C(23)	116(17)
N(2B)-P(1)-N(3)-C(23)	63.4(18)
N(2)-P(1)-N(3)-C(23)	57.8(18)
N(1B)-P(1)-N(3)-C(23)	-46.7(19)
N(1)-P(1)-N(3)-C(23)	-47.1(18)
Se(1)-P(1)-N(3)-C(23)	-173.1(13)
C(28)-N(3)-C(23)-C(24)	70(2)
P(1)-N(3)-C(23)-C(24)	-123.6(19)
N(3)-C(23)-C(24)-C(25)	8(2)
C(23)-C(24)-C(25)-C(26)	-77(2)
C(24)-C(25)-C(26)-C(27)	79(2)

C(25)-C(26)-C(27)-C(28)	-48(3)
C(23)-N(3)-C(28)-C(27)	-94.2(19)
P(1)-N(3)-C(28)-C(27)	101(3)
C(26)-C(27)-C(28)-N(3)	57(2)
N(3)-P(1)-N(3B)-C(23B)	-82(15)
N(2B)-P(1)-N(3B)-C(23B)	46.3(13)
N(2)-P(1)-N(3B)-C(23B)	40.6(13)
N(1B)-P(1)-N(3B)-C(23B)	-64.4(14)
N(1)-P(1)-N(3B)-C(23B)	-64.9(13)
Se(1)-P(1)-N(3B)-C(23B)	167.7(9)
N(3)-P(1)-N(3B)-C(28B)	84(16)
N(2B)-P(1)-N(3B)-C(28B)	-147.2(9)
N(2)-P(1)-N(3B)-C(28B)	-153.0(9)
N(1B)-P(1)-N(3B)-C(28B)	102.0(11)
N(1)-P(1)-N(3B)-C(28B)	101.6(10)
Se(1)-P(1)-N(3B)-C(28B)	-25.9(11)
C(28B)-N(3B)-C(23B)-C(24B)	88.9(12)
P(1)-N(3B)-C(23B)-C(24B)	-104.0(13)
N(3B)-C(23B)-C(24B)-C(25B)	-35.0(15)
C(23B)-C(24B)-C(25B)-C(26B)	-40.9(14)
C(24B)-C(25B)-C(26B)-C(27B)	84.3(12)
C(25B)-C(26B)-C(27B)-C(28B)	-66.8(13)
C(23B)-N(3B)-C(28B)-C(27B)	-74.9(12)
P(1)-N(3B)-C(28B)-C(27B)	117.6(12)
C(26B)-C(27B)-C(28B)-N(3B)	50.9(13)
N(6B)-P(2)-N(4)-C(31)	-63.5(10)
N(6)-P(2)-N(4)-C(31)	-50.4(12)
N(5)-P(2)-N(4)-C(31)	46.4(11)
N(4B)-P(2)-N(4)-C(31)	-11(5)
N(5B)-P(2)-N(4)-C(31)	57.9(10)
Se(2)-P(2)-N(4)-C(31)	174.5(8)

N(6B)-P(2)-N(4)-C(51)	94.9(13)
N(6)-P(2)-N(4)-C(51)	108.0(13)
N(5)-P(2)-N(4)-C(51)	-155.2(12)
N(4B)-P(2)-N(4)-C(51)	148(7)
N(5B)-P(2)-N(4)-C(51)	-143.7(13)
Se(2)-P(2)-N(4)-C(51)	-27.1(14)
C(51)-N(4)-C(31)-C(32)	132.9(14)
P(2)-N(4)-C(31)-C(32)	-66.6(15)
C(51)-N(4)-C(31)-C(40)	-50.3(18)
P(2)-N(4)-C(31)-C(40)	110.2(12)
C(40)-C(31)-C(32)-C(33)	-14(2)
N(4)-C(31)-C(32)-C(33)	163.0(13)
C(40)-C(31)-C(32)-C(42)	169.2(12)
N(4)-C(31)-C(32)-C(42)	-13.9(17)
C(31)-C(32)-C(33)-C(34)	-171.8(17)
C(42)-C(32)-C(33)-C(34)	5(2)
C(31)-C(32)-C(33)-C(38)	8(2)
C(42)-C(32)-C(33)-C(38)	-175.3(14)
C(38)-C(33)-C(34)-C(35)	-4(3)
C(32)-C(33)-C(34)-C(35)	175.4(17)
C(33)-C(34)-C(35)-C(36)	0(3)
C(34)-C(35)-C(36)-C(37)	1(2)
C(35)-C(36)-C(37)-C(38)	1(2)
C(36)-C(37)-C(38)-C(33)	-5(2)
C(36)-C(37)-C(38)-C(39)	-179.3(13)
C(34)-C(33)-C(38)-C(37)	6(2)
C(32)-C(33)-C(38)-C(37)	-173.3(14)
C(34)-C(33)-C(38)-C(39)	-178.7(16)
C(32)-C(33)-C(38)-C(39)	2(2)
C(37)-C(38)-C(39)-C(40)	169.3(13)
C(33)-C(38)-C(39)-C(40)	-5(2)

C(38)-C(39)-C(40)-C(31)	0(2)
C(32)-C(31)-C(40)-C(39)	10.3(19)
N(4)-C(31)-C(40)-C(39)	-166.4(12)
N(6B)-P(2)-N(5)-C(41)	158.8(7)
N(6)-P(2)-N(5)-C(41)	171.8(9)
N(4B)-P(2)-N(5)-C(41)	51.7(9)
N(5B)-P(2)-N(5)-C(41)	-52(3)
N(4)-P(2)-N(5)-C(41)	44.4(9)
Se(2)-P(2)-N(5)-C(41)	-73.8(8)
N(6B)-P(2)-N(5)-C(52)	-62.5(10)
N(6)-P(2)-N(5)-C(52)	-49.5(10)
N(4B)-P(2)-N(5)-C(52)	-169.6(10)
N(5B)-P(2)-N(5)-C(52)	87(3)
N(4)-P(2)-N(5)-C(52)	-176.9(9)
Se(2)-P(2)-N(5)-C(52)	65.0(10)
C(52)-N(5)-C(41)-C(42)	147.7(18)
P(2)-N(5)-C(41)-C(42)	-76(2)
C(52)-N(5)-C(41)-C(50)	-37(2)
P(2)-N(5)-C(41)-C(50)	98.7(16)
C(50)-C(41)-C(42)-C(43)	1(3)
N(5)-C(41)-C(42)-C(43)	176(2)
C(50)-C(41)-C(42)-C(32)	-175.6(15)
N(5)-C(41)-C(42)-C(32)	0(3)
C(31)-C(32)-C(42)-C(41)	64(2)
C(33)-C(32)-C(42)-C(41)	-113(2)
C(31)-C(32)-C(42)-C(43)	-113(2)
C(33)-C(32)-C(42)-C(43)	70(3)
C(41)-C(42)-C(43)-C(48)	0(4)
C(32)-C(42)-C(43)-C(48)	176.9(18)
C(41)-C(42)-C(43)-C(44)	-176(2)
C(32)-C(42)-C(43)-C(44)	0(4)

C(48)-C(43)-C(44)-C(45)	-3(4)
C(42)-C(43)-C(44)-C(45)	173(3)
C(43)-C(44)-C(45)-C(46)	6(3)
C(44)-C(45)-C(46)-C(47)	-5(2)
C(45)-C(46)-C(47)-C(48)	1(2)
C(46)-C(47)-C(48)-C(49)	-176.2(17)
C(46)-C(47)-C(48)-C(43)	1(3)
C(44)-C(43)-C(48)-C(47)	0(3)
C(42)-C(43)-C(48)-C(47)	-177(2)
C(44)-C(43)-C(48)-C(49)	177(2)
C(42)-C(43)-C(48)-C(49)	1(4)
C(47)-C(48)-C(49)-C(50)	174.4(17)
C(43)-C(48)-C(49)-C(50)	-3(3)
C(48)-C(49)-C(50)-C(41)	5(3)
C(42)-C(41)-C(50)-C(49)	-4(3)
N(5)-C(41)-C(50)-C(49)	-178.7(17)
N(6B)-P(2)-N(4B)-C(31B)	-63.8(9)
N(6)-P(2)-N(4B)-C(31B)	-49.2(10)
N(5)-P(2)-N(4B)-C(31B)	42.8(9)
N(5B)-P(2)-N(4B)-C(31B)	53.9(9)
N(4)-P(2)-N(4B)-C(31B)	167(6)
Se(2)-P(2)-N(4B)-C(31B)	172.4(6)
N(6B)-P(2)-N(4B)-C(51B)	79.6(11)
N(6)-P(2)-N(4B)-C(51B)	94.2(11)
N(5)-P(2)-N(4B)-C(51B)	-173.8(11)
N(5B)-P(2)-N(4B)-C(51B)	-162.7(11)
N(4)-P(2)-N(4B)-C(51B)	-50(5)
Se(2)-P(2)-N(4B)-C(51B)	-44.1(12)
C(51B)-N(4B)-C(31B)-C(32B)	140.8(14)
P(2)-N(4B)-C(31B)-C(32B)	-77.9(14)
C(51B)-N(4B)-C(31B)-C(40B)	-37.6(19)

P(2)-N(4B)-C(31B)-C(40B)	103.7(13)
C(40B)-C(31B)-C(32B)-C(33B)	-6(2)
N(4B)-C(31B)-C(32B)-C(33B)	175.7(13)
C(40B)-C(31B)-C(32B)-C(42B)	174.2(13)
N(4B)-C(31B)-C(32B)-C(42B)	-4.2(18)
C(31B)-C(32B)-C(33B)-C(34B)	-171.9(16)
C(42B)-C(32B)-C(33B)-C(34B)	8(2)
C(31B)-C(32B)-C(33B)-C(38B)	1(2)
C(42B)-C(32B)-C(33B)-C(38B)	-178.9(13)
C(38B)-C(33B)-C(34B)-C(35B)	1(2)
C(32B)-C(33B)-C(34B)-C(35B)	174.3(16)
C(33B)-C(34B)-C(35B)-C(36B)	2(2)
C(34B)-C(35B)-C(36B)-C(37B)	-3(2)
C(35B)-C(36B)-C(37B)-C(38B)	2(2)
C(36B)-C(37B)-C(38B)-C(33B)	0(2)
C(36B)-C(37B)-C(38B)-C(39B)	-179.9(13)
C(34B)-C(33B)-C(38B)-C(37B)	-2(2)
C(32B)-C(33B)-C(38B)-C(37B)	-175.5(14)
C(34B)-C(33B)-C(38B)-C(39B)	178.2(15)
C(32B)-C(33B)-C(38B)-C(39B)	5(2)
C(37B)-C(38B)-C(39B)-C(40B)	173.9(13)
C(33B)-C(38B)-C(39B)-C(40B)	-6(2)
C(38B)-C(39B)-C(40B)-C(31B)	2(2)
C(32B)-C(31B)-C(40B)-C(39B)	5(2)
N(4B)-C(31B)-C(40B)-C(39B)	-177.2(12)
N(6B)-P(2)-N(5B)-C(41B)	148.4(8)
N(6)-P(2)-N(5B)-C(41B)	159.6(9)
N(5)-P(2)-N(5B)-C(41B)	116(3)
N(4B)-P(2)-N(5B)-C(41B)	37.5(10)
N(4)-P(2)-N(5B)-C(41B)	29.4(10)
Se(2)-P(2)-N(5B)-C(41B)	-84.2(8)

N(6B)-P(2)-N(5B)-C(52B)	-64.2(11)
N(6)-P(2)-N(5B)-C(52B)	-52.9(11)
N(5)-P(2)-N(5B)-C(52B)	-96(3)
N(4B)-P(2)-N(5B)-C(52B)	-175.0(10)
N(4)-P(2)-N(5B)-C(52B)	176.9(10)
Se(2)-P(2)-N(5B)-C(52B)	63.3(11)
C(52B)-N(5B)-C(41B)-C(42B)	140.5(18)
P(2)-N(5B)-C(41B)-C(42B)	-71(2)
C(52B)-N(5B)-C(41B)-C(50B)	-34(2)
P(2)-N(5B)-C(41B)-C(50B)	114.1(15)
C(50B)-C(41B)-C(42B)-C(43B)	-11(3)
N(5B)-C(41B)-C(42B)-C(43B)	174(2)
C(50B)-C(41B)-C(42B)-C(32B)	173.4(15)
N(5B)-C(41B)-C(42B)-C(32B)	-1(3)
C(31B)-C(32B)-C(42B)-C(41B)	57(2)
C(33B)-C(32B)-C(42B)-C(41B)	-123.0(19)
C(31B)-C(32B)-C(42B)-C(43B)	-118(2)
C(33B)-C(32B)-C(42B)-C(43B)	62(3)
C(41B)-C(42B)-C(43B)-C(48B)	11(4)
C(32B)-C(42B)-C(43B)-C(48B)	-173.4(18)
C(41B)-C(42B)-C(43B)-C(44B)	-168(2)
C(32B)-C(42B)-C(43B)-C(44B)	7(4)
C(48B)-C(43B)-C(44B)-C(45B)	2(3)
C(42B)-C(43B)-C(44B)-C(45B)	-178(3)
C(43B)-C(44B)-C(45B)-C(46B)	-2(3)
C(44B)-C(45B)-C(46B)-C(47B)	0(2)
C(45B)-C(46B)-C(47B)-C(48B)	1(2)
C(46B)-C(47B)-C(48B)-C(49B)	-175.5(17)
C(46B)-C(47B)-C(48B)-C(43B)	0(3)
C(44B)-C(43B)-C(48B)-C(47B)	-1(3)
C(42B)-C(43B)-C(48B)-C(47B)	179(2)

C(44B)-C(43B)-C(48B)-C(49B)	174(2)
C(42B)-C(43B)-C(48B)-C(49B)	-5(3)
C(47B)-C(48B)-C(49B)-C(50B)	175.0(17)
C(43B)-C(48B)-C(49B)-C(50B)	0(3)
C(48B)-C(49B)-C(50B)-C(41B)	0(3)
C(42B)-C(41B)-C(50B)-C(49B)	6(3)
N(5B)-C(41B)-C(50B)-C(49B)	-179.7(17)
N(6B)-P(2)-N(6)-C(58)	-76.5(14)
N(5)-P(2)-N(6)-C(58)	141.9(12)
N(4B)-P(2)-N(6)-C(58)	-120.3(11)
N(5B)-P(2)-N(6)-C(58)	134.2(12)
N(4)-P(2)-N(6)-C(58)	-114.0(11)
Se(2)-P(2)-N(6)-C(58)	19.1(13)
N(6B)-P(2)-N(6)-C(53)	101.2(18)
N(5)-P(2)-N(6)-C(53)	-40.4(12)
N(4B)-P(2)-N(6)-C(53)	57.4(14)
N(5B)-P(2)-N(6)-C(53)	-48.2(12)
N(4)-P(2)-N(6)-C(53)	63.7(14)
Se(2)-P(2)-N(6)-C(53)	-163.2(10)
C(58)-N(6)-C(53)-C(54)	58.1(16)
P(2)-N(6)-C(53)-C(54)	-119.8(13)
N(6)-C(53)-C(54)-C(55)	-76.6(15)
C(53)-C(54)-C(55)-C(56)	78.1(17)
C(54)-C(55)-C(56)-C(57)	-29(2)
C(55)-C(56)-C(57)-C(58)	-41(2)
C(56)-C(57)-C(58)-N(6)	82.6(17)
C(53)-N(6)-C(58)-C(57)	-66.8(16)
P(2)-N(6)-C(58)-C(57)	111.2(14)
N(6)-P(2)-N(6B)-C(58B)	114.8(15)
N(5)-P(2)-N(6B)-C(58B)	154.5(8)
N(4B)-P(2)-N(6B)-C(58B)	-103.5(8)

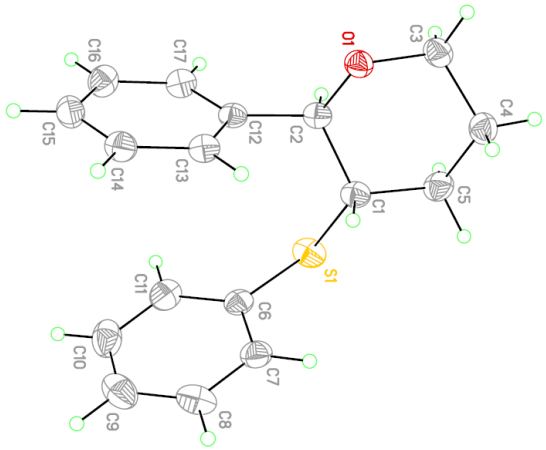
N(5B)-P(2)-N(6B)-C(58B)	148.3(7)
N(4)-P(2)-N(6B)-C(58B)	-96.4(8)
Se(2)-P(2)-N(6B)-C(58B)	21.8(8)
N(6)-P(2)-N(6B)-C(53B)	-83.2(14)
N(5)-P(2)-N(6B)-C(53B)	-43.6(9)
N(4B)-P(2)-N(6B)-C(53B)	58.5(9)
N(5B)-P(2)-N(6B)-C(53B)	-49.7(9)
N(4)-P(2)-N(6B)-C(53B)	65.6(9)
Se(2)-P(2)-N(6B)-C(53B)	-176.2(7)
C(58B)-N(6B)-C(53B)-C(54B)	-34.5(13)
P(2)-N(6B)-C(53B)-C(54B)	162.2(8)
N(6B)-C(53B)-C(54B)-C(55B)	-43.6(14)
C(53B)-C(54B)-C(55B)-C(56B)	84.2(12)
C(54B)-C(55B)-C(56B)-C(57B)	-61.3(13)
C(55B)-C(56B)-C(57B)-C(58B)	47.4(13)
C(56B)-C(57B)-C(58B)-N(6B)	-71.8(11)
C(53B)-N(6B)-C(58B)-C(57B)	87.2(10)
P(2)-N(6B)-C(58B)-C(57B)	-109.9(9)

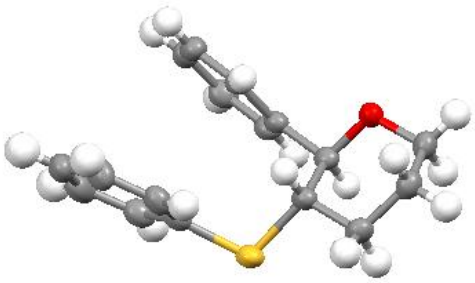
Symmetry transformations used to generate equivalent atoms:

Crystal Structure of 58a

X-Ray Crystal Structure of 58a

ORTEP image of X-ray crystal structure of **58a**.





Distillation of **58a** resulted in a viscous yellow oil. Slow cooling to room temperature followed by storage at -20 ^{o}C resulted in clear crystals, which were harvested directly from the mother liquor.

Identification code	bm34oas	
Empirical formula	C17 H18 O S	
Formula weight	270.37	
Temperature	193(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 6.1559(8) Å	a= 90°.
	b = 8.6293(11) Å	b= 90°.
	c = 27.248(3) Å	g = 90°.
Volume	1447.4(3) Å^3	
Z	4	
Density (calculated)	1.241 Mg/m^3	
Absorption coefficient	0.213 mm^{-1}	
F(000)	576	
Crystal size	0.457 x 0.43 x 0.246 mm^3	
Theta range for data collection	1.49 to 25.68°.	
Index ranges	-7<=h<=7, -10<=k<=10, -33<=l<=33	

Reflections collected	18385
Independent reflections	2748 [R(int) = 0.0223]
Completeness to theta = 25.68°	100.0 %
Absorption correction	Integration
Max. and min. transmission	0.9693 and 0.9372
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2748 / 0 / 172
Goodness-of-fit on F^2	1.022
Final R indices [I>2sigma(I)]	R1 = 0.0248, wR2 = 0.0652
R indices (all data)	R1 = 0.0255, wR2 = 0.0656
Absolute structure parameter	-0.01(6)
Largest diff. peak and hole	0.121 and -0.186 e.Å^{-3}

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for bm34oas. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	3082(1)	7171(1)	1017(1)	45(1)
O(1)	-168(2)	9224(1)	2140(1)	36(1)
C(1)	827(2)	7773(2)	1410(1)	35(1)
C(2)	1630(2)	8827(2)	1828(1)	32(1)
C(3)	-1081(2)	7871(2)	2369(1)	40(1)
C(4)	-2003(3)	6767(2)	1991(1)	41(1)
C(5)	-251(3)	6321(2)	1621(1)	43(1)
C(6)	3137(2)	8625(2)	554(1)	35(1)
C(7)	1369(2)	8852(2)	248(1)	42(1)
C(8)	1466(3)	9944(2)	-123(1)	52(1)
C(9)	3345(3)	10786(2)	-200(1)	55(1)
C(10)	5123(3)	10550(2)	98(1)	56(1)

C(11)	5021(2)	9480(2)	481(1)	46(1)
C(12)	2668(2)	10326(2)	1662(1)	31(1)
C(13)	1573(2)	11355(2)	1354(1)	34(1)
C(14)	2533(2)	12741(2)	1214(1)	39(1)
C(15)	4599(2)	13119(2)	1375(1)	42(1)
C(16)	5698(2)	12106(2)	1681(1)	43(1)
C(17)	4739(2)	10717(2)	1821(1)	38(1)

Bond lengths [Å] and angles [°] for bm34oas.

S(1)-C(6)	1.7783(14)
S(1)-C(1)	1.8290(13)
O(1)-C(2)	1.4371(16)
O(1)-C(3)	1.4387(17)
C(1)-C(5)	1.530(2)
C(1)-C(2)	1.5382(18)
C(1)-H(1)	1.0000
C(2)-C(12)	1.5120(19)
C(2)-H(2)	1.0000
C(3)-C(4)	1.514(2)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-C(5)	1.526(2)
C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(6)-C(7)	1.385(2)
C(6)-C(11)	1.389(2)
C(7)-C(8)	1.383(2)

C(7)-H(7)	0.9500
C(8)-C(9)	1.382(3)
C(8)-H(8)	0.9500
C(9)-C(10)	1.379(3)
C(9)-H(9)	0.9500
C(10)-C(11)	1.394(2)
C(10)-H(10)	0.9500
C(11)-H(11)	0.9500
C(12)-C(17)	1.3884(19)
C(12)-C(13)	1.3969(18)
C(13)-C(14)	1.387(2)
C(13)-H(13)	0.9500
C(14)-C(15)	1.384(2)
C(14)-H(14)	0.9500
C(15)-C(16)	1.384(2)
C(15)-H(15)	0.9500
C(16)-C(17)	1.390(2)
C(16)-H(16)	0.9500
C(17)-H(17)	0.9500
C(6)-S(1)-C(1)	103.25(6)
C(2)-O(1)-C(3)	111.34(10)
C(5)-C(1)-C(2)	110.21(11)
C(5)-C(1)-S(1)	108.44(9)
C(2)-C(1)-S(1)	110.98(9)
C(5)-C(1)-H(1)	109.1
C(2)-C(1)-H(1)	109.1
S(1)-C(1)-H(1)	109.1
O(1)-C(2)-C(12)	107.33(10)
O(1)-C(2)-C(1)	109.35(11)
C(12)-C(2)-C(1)	114.87(10)
O(1)-C(2)-H(2)	108.4

C(12)-C(2)-H(2)	108.4
C(1)-C(2)-H(2)	108.4
O(1)-C(3)-C(4)	111.20(10)
O(1)-C(3)-H(3A)	109.4
C(4)-C(3)-H(3A)	109.4
O(1)-C(3)-H(3B)	109.4
C(4)-C(3)-H(3B)	109.4
H(3A)-C(3)-H(3B)	108.0
C(3)-C(4)-C(5)	110.09(12)
C(3)-C(4)-H(4A)	109.6
C(5)-C(4)-H(4A)	109.6
C(3)-C(4)-H(4B)	109.6
C(5)-C(4)-H(4B)	109.6
H(4A)-C(4)-H(4B)	108.2
C(4)-C(5)-C(1)	110.37(11)
C(4)-C(5)-H(5A)	109.6
C(1)-C(5)-H(5A)	109.6
C(4)-C(5)-H(5B)	109.6
C(1)-C(5)-H(5B)	109.6
H(5A)-C(5)-H(5B)	108.1
C(7)-C(6)-C(11)	119.62(13)
C(7)-C(6)-S(1)	120.73(11)
C(11)-C(6)-S(1)	119.53(11)
C(8)-C(7)-C(6)	120.14(14)
C(8)-C(7)-H(7)	119.9
C(6)-C(7)-H(7)	119.9
C(9)-C(8)-C(7)	120.40(15)
C(9)-C(8)-H(8)	119.8
C(7)-C(8)-H(8)	119.8
C(10)-C(9)-C(8)	119.77(15)
C(10)-C(9)-H(9)	120.1

C(8)-C(9)-H(9)	120.1
C(9)-C(10)-C(11)	120.20(16)
C(9)-C(10)-H(10)	119.9
C(11)-C(10)-H(10)	119.9
C(6)-C(11)-C(10)	119.84(15)
C(6)-C(11)-H(11)	120.1
C(10)-C(11)-H(11)	120.1
C(17)-C(12)-C(13)	118.49(13)
C(17)-C(12)-C(2)	120.20(12)
C(13)-C(12)-C(2)	121.31(12)
C(14)-C(13)-C(12)	120.50(13)
C(14)-C(13)-H(13)	119.8
C(12)-C(13)-H(13)	119.8
C(15)-C(14)-C(13)	120.50(14)
C(15)-C(14)-H(14)	119.8
C(13)-C(14)-H(14)	119.8
C(16)-C(15)-C(14)	119.43(14)
C(16)-C(15)-H(15)	120.3
C(14)-C(15)-H(15)	120.3
C(15)-C(16)-C(17)	120.21(13)
C(15)-C(16)-H(16)	119.9
C(17)-C(16)-H(16)	119.9
C(12)-C(17)-C(16)	120.88(13)
C(12)-C(17)-H(17)	119.6
C(16)-C(17)-H(17)	119.6

Anisotropic displacement parameters ($Å^2 x\ 10^3$) for bm34oas. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}

S(1)	55(1)	36(1)	42(1)	-1(1)	7(1)	14(1)
O(1)	41(1)	32(1)	33(1)	-1(1)	4(1)	1(1)
C(1)	41(1)	31(1)	33(1)	-2(1)	1(1)	6(1)
C(2)	35(1)	31(1)	31(1)	1(1)	-2(1)	6(1)
C(3)	47(1)	39(1)	34(1)	6(1)	2(1)	-1(1)
C(4)	44(1)	37(1)	42(1)	5(1)	0(1)	-4(1)
C(5)	53(1)	31(1)	43(1)	-2(1)	-2(1)	-1(1)
C(6)	38(1)	33(1)	34(1)	-9(1)	3(1)	4(1)
C(7)	42(1)	48(1)	35(1)	-9(1)	1(1)	-3(1)
C(8)	56(1)	66(1)	35(1)	2(1)	-1(1)	10(1)
C(9)	71(1)	48(1)	46(1)	5(1)	17(1)	9(1)
C(10)	52(1)	48(1)	68(1)	-8(1)	21(1)	-8(1)
C(11)	37(1)	51(1)	51(1)	-10(1)	3(1)	1(1)
C(12)	35(1)	30(1)	29(1)	-3(1)	1(1)	6(1)
C(13)	34(1)	34(1)	34(1)	-2(1)	-2(1)	6(1)
C(14)	48(1)	32(1)	36(1)	2(1)	0(1)	7(1)
C(15)	46(1)	36(1)	45(1)	1(1)	10(1)	-2(1)
C(16)	32(1)	47(1)	51(1)	-4(1)	0(1)	-2(1)
C(17)	35(1)	37(1)	40(1)	0(1)	-4(1)	7(1)

Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for bm34oas.

	x	y	z	U(eq)
H(1)	-258	8353	1208	42
H(2)	2715	8236	2027	39
H(3A)	-2247	8189	2598	48
H(3B)	58	7335	2561	48
H(4A)	-3232	7267	1818	50

H(4B)	-2556	5825	2156	50
H(5A)	-908	5710	1351	51
H(5B)	858	5668	1784	51
H(7)	87	8256	293	50
H(8)	234	10116	-326	63
H(9)	3411	11525	-458	66
H(10)	6422	11118	43	67
H(11)	6237	9334	690	56
H(13)	159	11104	1238	41
H(14)	1768	13436	1006	47
H(15)	5256	14066	1277	51
H(16)	7113	12360	1794	52
H(17)	5512	10026	2029	45

Torsion angles [°] for bm34oas.

C(6)-S(1)-C(1)-C(5)	147.61(10)
C(6)-S(1)-C(1)-C(2)	-91.19(10)
C(3)-O(1)-C(2)-C(12)	-172.18(10)
C(3)-O(1)-C(2)-C(1)	62.61(13)
C(5)-C(1)-C(2)-O(1)	-57.56(14)
S(1)-C(1)-C(2)-O(1)	-177.71(8)
C(5)-C(1)-C(2)-C(12)	-178.27(11)
S(1)-C(1)-C(2)-C(12)	61.58(13)
C(2)-O(1)-C(3)-C(4)	-62.90(14)
O(1)-C(3)-C(4)-C(5)	56.56(15)
C(3)-C(4)-C(5)-C(1)	-52.00(15)
C(2)-C(1)-C(5)-C(4)	52.86(15)
S(1)-C(1)-C(5)-C(4)	174.52(10)
C(1)-S(1)-C(6)-C(7)	-61.41(12)
C(1)-S(1)-C(6)-C(11)	122.47(11)
C(11)-C(6)-C(7)-C(8)	-1.2(2)
S(1)-C(6)-C(7)-C(8)	-177.36(11)
C(6)-C(7)-C(8)-C(9)	1.9(2)
C(7)-C(8)-C(9)-C(10)	-0.8(2)
C(8)-C(9)-C(10)-C(11)	-0.8(2)
C(7)-C(6)-C(11)-C(10)	-0.4(2)
S(1)-C(6)-C(11)-C(10)	175.81(11)
C(9)-C(10)-C(11)-C(6)	1.4(2)
O(1)-C(2)-C(12)-C(17)	112.43(13)
C(1)-C(2)-C(12)-C(17)	-125.76(13)
O(1)-C(2)-C(12)-C(13)	-66.72(14)
C(1)-C(2)-C(12)-C(13)	55.10(16)
C(17)-C(12)-C(13)-C(14)	-0.55(19)
C(2)-C(12)-C(13)-C(14)	178.61(12)

C(12)-C(13)-C(14)-C(15)	0.5(2)
C(13)-C(14)-C(15)-C(16)	-0.4(2)
C(14)-C(15)-C(16)-C(17)	0.4(2)
C(13)-C(12)-C(17)-C(16)	0.51(19)
C(2)-C(12)-C(17)-C(16)	-178.66(12)
C(15)-C(16)-C(17)-C(12)	-0.4(2)

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