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Synthesis of Quaternary-Substituted Thiazolines via Halocyclization of *S*-Allyl Thioimidate Salts

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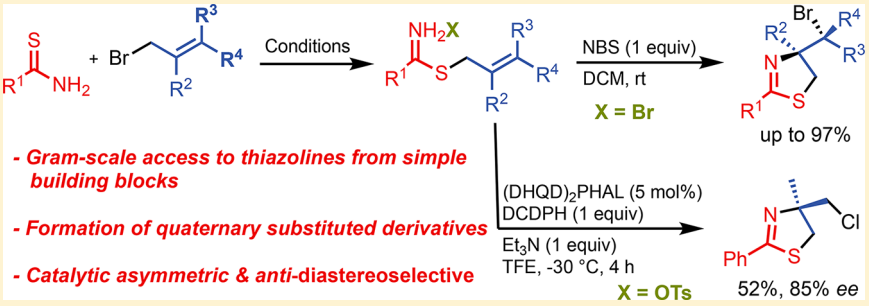
Supporting Information



ABSTRACT: An efficient synthesis of *S*-allyl thioimidate hydrobromide salts via coupling of thioamides with allyl bromide derivatives is described. A range of mono-, di-, and trisubstituted olefins as well as alkyl- and arylthioamides with variations in electronics are tolerated. A rapid *anti*-diastereoselective halocyclization of these salts provides a variety of substituted alkyl- and arylthiazolines. Initial development of an efficient enantioselective synthesis of quaternary-substituted thiazolines through the organo-catalyzed halocyclization of sulfonate thioimidate salts is also described.

INTRODUCTION

Nitrogen-containing heterocyclic motifs are the core structural elements of many natural products[1] and approved pharmaceuticals.[2] Although there has been intense development of synthetic methods for the construction of nitrogen heterocycles since the advent of modern organic chemistry, there remains a need for improved access to these privileged scaffolds.

2-Thiazolines are five-membered heterocycles found in many natural products and biologically relevant compounds showcasing activities such as anticancer,[3] antimicrobial,[1,4] antiviral,[5] and neurological properties.[6] They have also been used as metal ligands in asymmetric catalysis[7] and can be found in a variety of flavors, aromas, and luminescent compounds.[8] As a result, many methods currently exist for their synthesis.[9] The most common of these methods utilizes β-amino alcohols and β-amino thiols (Figure 1a), but with limited commercial availability and difficult synthetic accessibility of starting material, these methods can take multiple steps in cases where unnatural amino acids are required or quaternary substitution is desired.[10] Therefore, the development of efficient and stereoselective methods for the synthesis of thiazolines is still an ongoing challenge.

As part of our program directed toward the development of novel methods to construct nitrogen-containing heterocycles,[11] we previously developed a *syn*-diastereoselective synthesis of thiazolines through a copper-catalyzed cyclization of *S*-allyl thiohydroximic acids (Figure 1b).[12] The reaction is thought to proceed through an oxidative addition of copper bromide to the nitrogen−oxygen bond of the activated substrate, followed by a *cis*-iminocupration across the olefin to form the thiazoline ring.

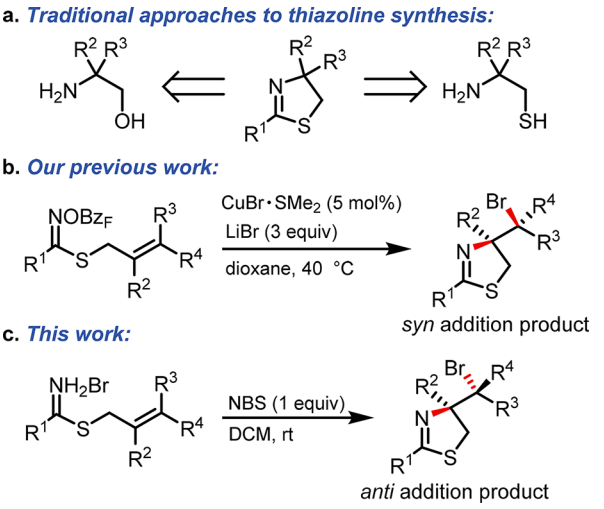


Figure 1. Approaches for thiazoline synthesis.

Finally, the copper is reductively eliminated to provide the bromothiazoline product. Although this reaction was efficient and diastereoselective, a straightforward method for accessing the corresponding quaternary-substituted derivative or *anti*-diastereomer (vs the alternate six-membered ring products) as well as obtaining the thiazolines in enantioenriched form remained elusive.

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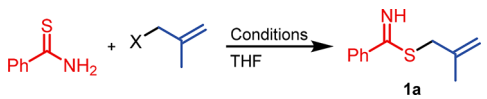
To address these limitations, we envisioned that a halocyclization of *S*-allyl thioimidates would provide access to the *anti*-diastereomer, favor the 5-exo cyclization pathway, and could potentially be rendered asymmetric (Figure 1c). Halocyclization reactions have been described in the literature for well over a century with the first reported bromolactonization by Fittig in 1883.[13] Lactones were the most common heterocycles synthesized during the first century, and it was not until the latter half of the 1900s when halocyclization reactions were applied to the synthesis of other heterocycles. Due to side reactions that plagued asymmetric approaches, such as olefin-to-olefin halogen exchange,[14,15] enantioselective versions of halocyclizations did not appear in the literature until 1981 with the first substrate-controlled iodolactonization reported by Takano and co-workers, where proline was used as a chiral auxiliary to provide 16% ee.[16] The first reagent-controlled halocyclization was reported by Taguchi and co-workers in 1992, which employed stoichiometric amounts of a chiral titanium complex to obtain iodolactones in up to 64% ee,[17] and the first catalytic asymmetric reaction was reported by Wang and co-workers in 2004, which utilized a chiral phase transfer catalyst to provide iodolactones in up to 42% ee.[18] Since 2004, there has been a surge in the number of reported catalytic asymmetric halocyclization reactions, and the potential for this area of synthetic chemistry is still being revealed.[15] Herein, we have developed an efficient *anti*-diastereoselective halocyclization of *S*-allyl thioimidate salts to prepare quaternary 2-thiazolines and have demonstrated the initial utility of these reactions to achieve thiazoline synthesis in an asymmetric fashion.

RESULTS AND DISCUSSION

In order to begin studying the proposed thiazoline synthesis, a straightforward method for preparing *S*-allyl thioimidates was required. Previous methods for accessing these substrates were scarce, and few provided detailed experimental procedures.[19] We began by employing a reported procedure for *S*-alkyl thioimidates for the synthesis of our desired allylic substrates.[20] Reacting thiobenzamide with 3-chloro-2-methylpropene in refluxing tetrahydrofuran with base and catalytic tetrabutylammonium iodide (TBAI) provided no reaction (Table 1, entries 1 and 2). Employing 3-bromo-2-methylpropene as a more reactive electrophile also provided no reaction at room temperature (entry 3) but yielded 16% of the thioimidate under reflux in tetrahydrofuran (entry 4). The addition of triethylamine as a basic additive provided higher yield (entry 5); however, the yield was decreased significantly when mildly acidic workup was employed to remove triethylamine (entry 6). Further, the reaction yields were highly irreproducible and resulted in no isolated thioimidate products in many cases (entry 7).

Table 1. Optimization of *S*-Allyl Thioimidate 1a

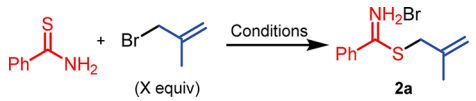


entry	X	conditions	yield of **1a**[a] (%)
1	Cl	LiHMDS, TBAI (10 mol %), 67 °C, 47 h	NR[b]
2	Cl	NaH, TBAI (10 mol %), 67 °C, 47 h	NR[b,c]
3	Br	NaH (1.2 equiv), rt, 96 h	NR[b]
4	Br	KHMDS, 67 °C, 44 h	16[d]
5	Br	Et_3N, TBAI (10 mol %), rt, 47 h	39[d]
6	Br	Et_3N, TBAI (10 mol %), 67 °C, 6 h	2[e]
7	Br	Et_3N, TBAI (10 mol %), 67 °C, 4 h	0–55

[a]Isolated yield. [b]Observed by LC-MS. [c]Decomposition observed. [d]Reactions did not go to completion. [e]Acidic workup.

As a result of the instability of compound **1a**, we re-evaluated our approach. Reacting thiobenzamide with 1 equiv of 3-bromo-2-methylpropene in tetrahydrofuran at room temperature provided compound **2a** as the hydrobromide salt of compound **1a** (Table 2, entry 1). The reaction was significantly faster at reflux in tetrahydrofuran, but it also did not go to completion (entry 2). Increasing the concentration of thioamide and employing 2 equiv of 3-bromo-2-methylpropene provided the highest yield of 92% (entry 3), whereas increasing the equivalents of allyl bromide to 3 decreased the yield to 78% (entry 4). Further studies on the stability of compounds **1a** and **2a** were conducted, and it was found that while compound **1a** shows significant decomposition after a day at room temperature, compound **2a** is stable indefinitely.[21] In addition, the reaction provides high yields of **2a** as a solid, and the purification only requires filtration and trituration in ethyl acetate.

Table 2. Optimization of *S*-Allyl Thioimidate Salt 2a



entry	X	conditions	yield of **2a** (%)
1	1	THF (0.2 M), rt, 142 h	**2a** observed[a]
2	1	THF (0.2 M), 67 °C, 24 h	**2a** observed[a]
3	2	THF (0.5 M), 67 °C, 5 h	92[b]
4	3	THF (0.2 M), 67 °C, 3 h	78[b]

[a]Observed by LC-MS; reactions did not go to completion. [b]Isolated yield.

With the optimized conditions in hand, the substrate scope of *S*-allyl thioimidate formation was evaluated (Figure 2). We began by exploring the olefin substitution on the allylic bromides (R^2–R^4, **2a**–**2k**). The reaction performed well on various types of mono-, di-, and trialkyl-substituted olefins (**2a**–**2d**). Electronically poor alkenes cleanly undergo reaction, albeit with slightly lower isolated yields (**2e** and **2f**). The reaction also works well for vinyl halides (**2g**) and similarly for benzylic- and aromatic-substituted olefins (**2h**–**2k**). We also examined the substrate scope by exploring the nature of the thioamide (R^1, **2l**–**2t**, Figure 2). Simple alkylated thioamides (**2l**) and electron-rich thioamides provide the desired product in good yield (**2m**), whereas electron-poor thioamides give moderate yields (**2n**). The reaction also performs well for various halogenated and heteroaryl thiobenzamides (**2o**–**2q**) as well as heteroaromatic thioamides such as the benzothiophenyl thioimidate **2r**. Finally, we examined the use of alkyl bromides, providing thioimidates with remote alkenes in moderate yields (**2s** and **2t**).

With the optimization of starting material complete, and a panel of substrates in hand, we began our investigations into thiazoline synthesis. Gratifyingly, treatment of thioimidate **2a** with 2 equiv of *N*-bromosuccinimide (NBS) in dichloromethane at room temperature provided 90% of thiazoline **3a** (Table 3, entry 1). The reaction became dark yellow and was finished upon addition of NBS. Lowering the equivalents of

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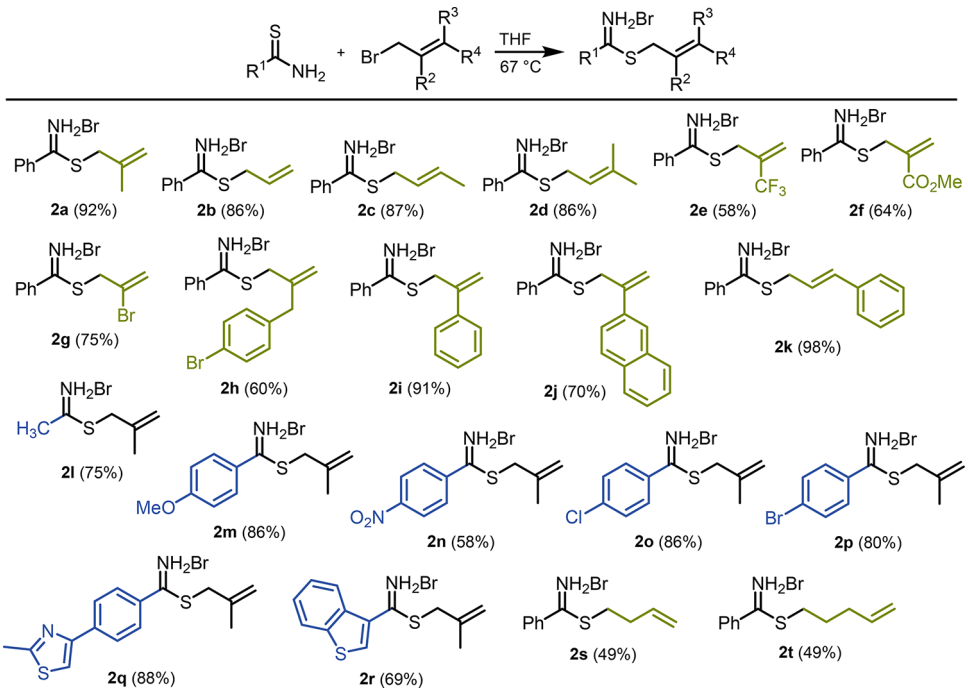
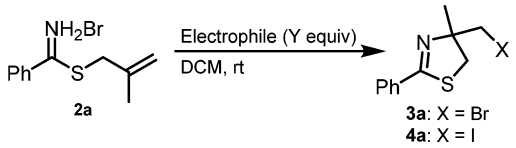


Figure 2. *S*-Allyl thioimidate substrate scope.

Table 3. Optimization of *anti*-Diastereoselective Thiazoline Synthesis



entry[a]	electrophile	Y	yield of **3a**/**4a**[b] (%)
1	NBS	2	90
2	NBS	1.1	90
3	NBS	1	87
4	NIS	1.1	91

[a]Reactions were performed on 0.05 g scale at 0.05 M. [b]Isolated yield.

NBS gave thiazoline **3a** in similar 90 and 87% yields (entries 2 and 3, respectively). The reaction also works well for forming iodinated thiazolines. Reacting **2a** with 1.1 equiv of *N*-iodosuccinimide (NIS) in dichloromethane gave thiazoline **4a** in 91% yield (entry 4). It should be noted, however, that reacting compound **2a** with *N*-chlorosuccinimide (NCS) provided bromothiazoline **3a** as the only observed product. The observation that bromide (vs chloride) is incorporated was surprising and becomes mechanistically important with our investigations into asymmetric synthesis of thiazolines (vide infra).

With the optimal conditions in hand, we investigated the substrate scope of thiazoline formation (Figure 3). We began by examining the substitutions on the olefin of the substrate (R^2–R^4, **3a**–**3k**). Substrates **2a** and **2b** provided thiazolines **3a** and **3b** in 90 and 60% yield, respectively. Substrate **2c** gave a 69% overall yield of a mixture of thiazoline **3c** and thiazine **3c-1**. After a second purification via reverse-phase chromatography, pure thiazoline **3c** and thiazine **3c-1** were obtained in 33 and 34% yield, respectively. As in the case with substrate **2c**, thioimidate **2d** gave an overall yield of 68% of a mixture of thiazoline **3d** and thiazine **3d-1**. After a second purification under reverse-phase chromatography, pure thiazoline **3d** and pure thiazine **3d-1** were obtained in 12 and 45% yield, respectively. The reaction shuts down completely in the presence of electronically poor olefins. Compounds **3e** and **3f** were not observed under the reaction conditions, which gave a complex mixture consisting of mostly starting material after a day.[22] Further attempts to synthesize **3e**, such as performing the reaction at elevated temperatures, gave similar results. The reaction also did not work on the vinyl-bromide-containing substrate **2g**. As in the case with substrates **2e** and **2f**, this reaction gave mostly starting material after a day, and neither thiazoline **3g** nor the corresponding thiazole was observed. The reaction works well for benzylic-substituted compounds such as thiazoline **3h**, which was synthesized in 75% yield. This is significant as it could provide access to certain quaternary-substituted analogues of thiazoline-containing natural products that were previously inaccessible with current methods.[10] The cyclization also works well for other aromatic thiazolines such as **3i** and **3j**, which were synthesized in 66 and 57% yield, respectively. Finally, substrate **2k** provided thiazoline **3k** in 77% yield with no formation of thiazine observed.

We also examined the substitutions on the left-hand side of the starting material (R^1, **3l**–**3r**, Figure 3). The reaction works for simple alkyl substrates such as thiazoline **3l**, which was synthesized in 69% yield. Electronically rich substrates such as the *p*-methoxy compound **2m** provided thiazoline **3m** with an excellent yield of 97%. The reaction also works well on electronically poor substrates such as the nitro-containing compound **2n**, which provided thiazoline **3n** in 81% yield. Various halogen-substituted aromatic rings were tolerated as well with chloro- and bromothiazolines **3o** and **3p** prepared in 81 and 77% yield, respectively. Heteroaryl-containing substrates are also effective substrates. Thiazole-substituted thiazoline **3q** was synthesized in 90% yield, and benzothiophene-containing thiazoline **3r** was synthesized in 88% yield.

Finally, we examined the utility of this reaction on the substrates that contain extended olefins (**2s** and **2t**, Figure 2).

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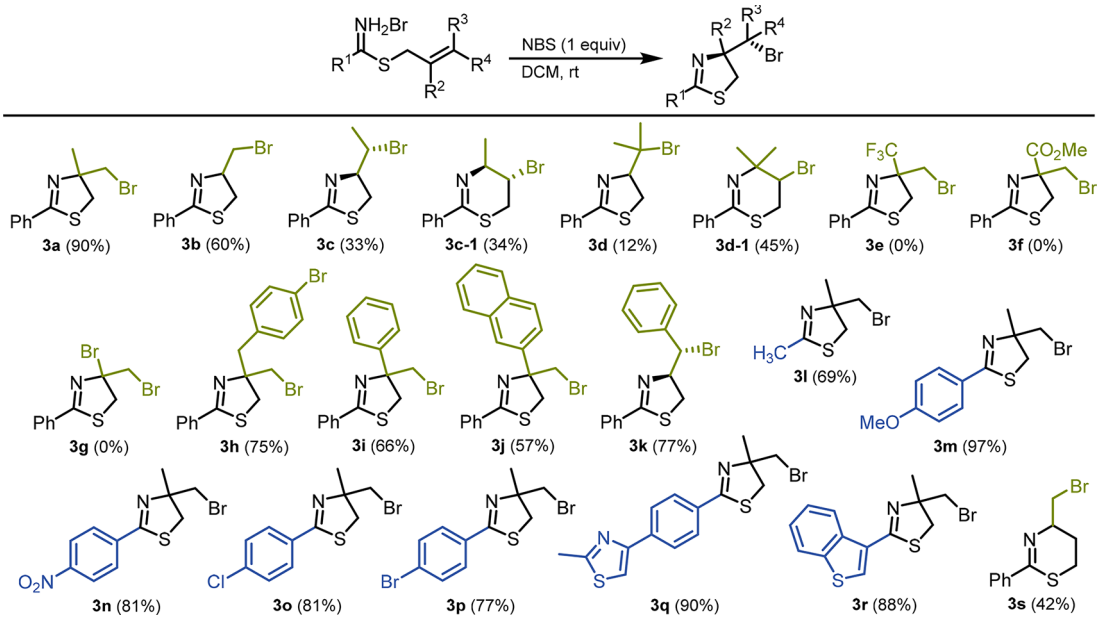
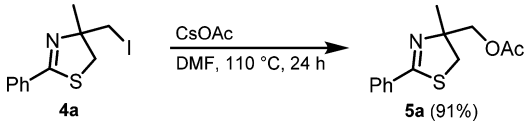


Figure 3. Thiazoline substrate scope.

Homoallyl thioimidate **2s** was converted to thiazine **3s** with a moderate yield of 42% and no observation of the corresponding seven-membered thiazepine (Figure 3); however, there was no observation of either thiazepine or an eight-membered thiazocine in the case of substrate **2t**.

We were previously able to demonstrate the utility of these brominated thiazolines to be displaced with various nucleophiles;[12] however, we were unable to form a hydroxylated thiazoline through this route. Because many thiazoline-containing natural products have an exocyclic oxygen functionality in this position,[3−6,8] we wanted to investigate this further. It had been reported that oxazoline-containing neopentyl iodides could be displaced with cesium acetate.[23] To this end, iodinated thiazoline **4a** was readily displaced for an acetate to form compound **5a** in 91% yield (Scheme 1).

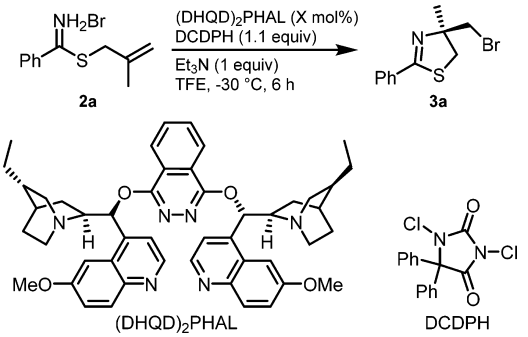
Scheme 1. Synthesis of Alcohol-Containing Thiazoline



Following our successes in racemic thiazoline synthesis, we planned to investigate the potential for this reaction to be rendered asymmetric. There have been numerous reports on enantioselective synthesis of oxazoline rings through organocatalyzed halocyclization of *N*-allyl amides.[24,25] Due to their high analogy to thiazolines, we initially explored these methods.

When applied to the asymmetric synthesis of thiazolines, many of the reports for chiral oxazolines gave either no product or provided racemic thiazolines;[24] however, one report by Borhan and co-workers utilizes the quinine-based catalyst $(DHQD)_2PHAL$ and hydantoin-based halogen electrophiles and provided moderate yields as well as measurable selectivity in the synthesis of thiazolines in our initial studies (Table 4).[25] Under the originally reported conditions, 2 mol % of catalyst provided 53% yield and 26% ee of thiazoline **3a** (entry 1). Gradual increases in catalyst loading provided gradual increases

Table 4. Initial Investigations into Asymmetric Synthesis of 3a



entry[a]	X	yield of 3a[b] (%)	% ee
1	2	53	26
2	10	53	44
3	20	53	52
4	50	44	58

[a]Reactions were performed on 0.10 g scale at 0.05 M. [b]Isolated yield.

in the measured selectivity, with the best results achieved at 50 mol % of catalyst, which gave 58% ee (entries 2−4). Although this is clearly not an optimal catalyst loading, this reaction provided initial promise for further optimization efforts.

One interesting outcome of the results from Table 4 is the formation of brominated thiazoline **3a** considering that the electrophilic halogen source was a chlorinated hydantoin. The chlorinated thiazoline was not observed, and this posed intriguing mechanistic questions. Bromide is unlikely to displace a neopentyl chloride at such low temperatures, and we therefore hypothesized that the bromide of thioimidate **2a** was reacting with the chlorinating agent to form bromine chloride as the active electrophile. Freebasing compound **2a** to compound **1a** and subjecting that to the reaction conditions with 20 mol % of catalyst provided chlorinated thiazoline **6a** with a 31% jump in enantioselectivity (Scheme 2). To further explore this hypothesis, tetrabutylammonium bromide was added to a solution of DCDPH, after which the solution turned

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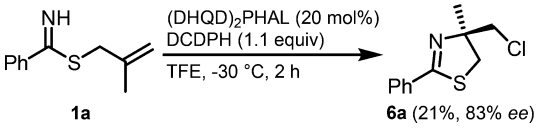
Scheme 2. Enantioselective Synthesis of Thiazoline 6a from Thioimidate 1a

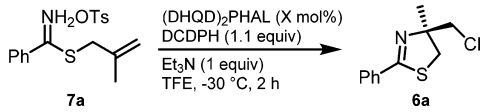


1a **6a** (21%, 83% *ee*)

a deep yellow color, indicating the formation of bromine chloride, and this resulting mixture displayed effective electrophilic bromination reactivity.

With these results in hand, we began investigating the synthesis of thioimidate salts that contained non-nucleophilic counterions. Protonation of thioimidate **1a** with 1 equiv of *p*-toluenesulfonic acid (*p*-TsOH) provided thioimidate **7a**. Subjecting **7a** to the reaction conditions with 20 mol % of catalyst provided 41% yield of thiazoline **6a** in 87% ee (Table 5, entry 1). Lowering the catalyst loading to 10 and 5 mol % gave no change in selectivity (entries 2 and 3). At 2 mol % of catalyst, a slight decrease in selectivity to 83% ee was observed (entry 4).

Table 5. Synthesis of 6a from Thioimidate 7a



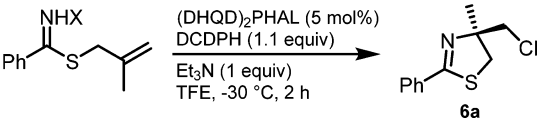
7a **6a**

entry[a]	X	yield of **6a**[b] (%)	% ee
1	20	41	87
2	10	45	87
3	5	37	87
4	2	38	83

[a]Reactions were performed on 0.10 g scale at 0.05 M. [b]Isolated yield.

To ensure that the counterion was no longer having an effect on the reaction selectivity, a few other thioimidates, including chiral sulfonate salts were synthesized. Methanesulfonic acid thioimidate **8a** provided similar results to *p*-TsOH salt **7a**, providing 86% ee (Table 6, entries 1 and 2). Neither enantiomer of camphorsulfonic acid ((+)-CSA and (−)-CSA) salts **9a** and **10a** showed a matched preference for enantioselectivity, providing thiazoline **6a** in 89 and 86% ee, respectively (entries 3 and 4). The absolute stereochemistry of the hydrobromide salt of **6a** was obtained though X-ray analysis (Figure 4).

Table 6. Screening of Sulfonate Thioimidate Salts for the Synthesis of 6a

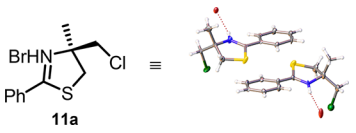


6a

entry[a]	X	compound	yield of **6a**[b] (%)	% ee
1	*p*-TsOH	**7a**	37	87
2	MsOH	**8a**	32	86
3	(+)-CSA	**9a**	36	89
4	(−)-CSA	**10a**	22	86

[a]Reactions were done on 0.05 g scale at 0.05 M. [b]Isolated yield.

With the reaction enantioselectivity addressed, we moved on to investigating possible causes for the modest reaction yields.

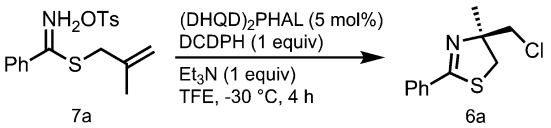


11a

Figure 4. Crystal structure of compound **11a**.

To examine product stability, we subjected thiazoline **6a** to the reaction conditions and only recovered 24% after 23 h. Thiazoline **6a** was stirred with each individual reagent, and decomposition was observed to be caused by the chlorinating agent DCDPH. Furthermore, when compound **7a** is added slowly to the reaction mixture containing DCDPH, only trace amounts of product are observed. This could be due to the product decomposition directly as it is formed, leaving only starting material as DCDPH disappears. Lowering the equivalents of DCDPH to 1 equiv gave a slight increase in yield from 37 to 43% (Table 7, entry 1). Adding DCDPH slowly over time gave another gradual increase in yield to 52% (Table 7, entry 2).

Table 7. Investigations into the Addition Method for DCDPH



7a **6a**

entry[a]	DCDPH addition method	yield (%)[b]	% ee
1	no change	43	83
2	four aliquots at 30 min intervals	52	85

[a]Reactions were performed on 0.05 g scale at 0.05 M. [b]Isolated yield.

Due to the product decomposition, any inhibition of the catalyst by the product would slow the reaction rate and allow for a negative effect on the yield. To probe the interaction of catalyst and product, an NMR of 1 equiv of catalyst to thiazoline **3a** was compared to an NMR of pure **3a** (Figure 5). The chemical shifts for the two ring protons (blue) were shifted upfield, indicating that they are shielded by the catalyst. Also, the splitting of each proton into double doublets is an indication of a diastereomeric pair formed between the enantiopure catalyst and the racemic thiazoline. We are continuing to evaluate the role of product inhibition of the reaction and exploring a variety of approaches to overcome the modest yields in the asymmetric processes.

CONCLUSIONS

We have developed an efficient method for synthesizing *S*-allyl thioimidate salts through the coupling of thioamides with allyl bromide derivatives. The reaction has a broad scope tolerating a variety of substituted olefins as well as alkyl- and arylthioamides. We have demonstrated the use of these salts in the rapid and efficient *anti*-diastereoselective synthesis of quaternary-substituted thiazolines. The reaction works well for various alkyl- and aryl-substituted thioimidates but does not proceed with electron-poor olefins. The initial developments for an efficient enantioselective synthesis of quaternary-substituted thiazolines through the organo-catalyzed halocyclization of sulfonate thioimidate salts has also been demonstrated. Efforts to improve the yield of this reaction are ongoing

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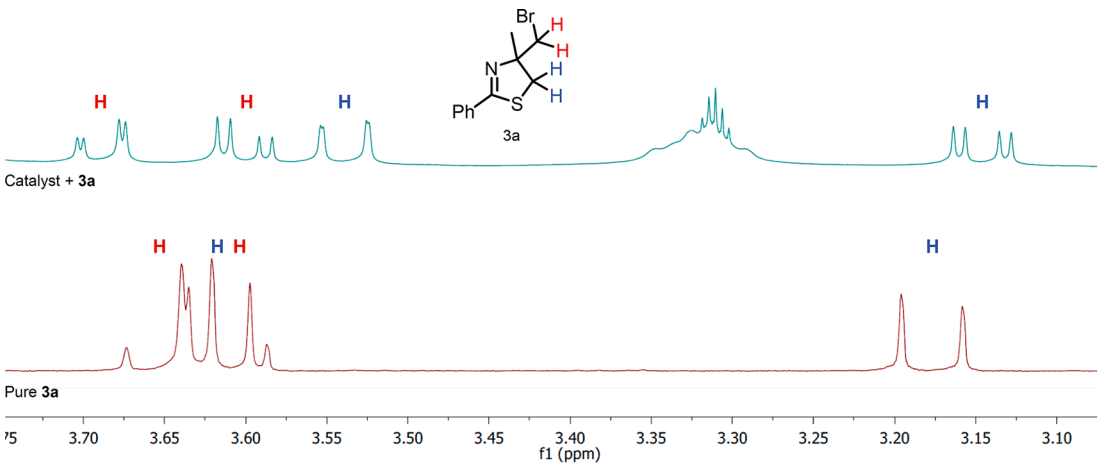

Figure 5. Catalyst complexation with thiazoline **3a**.

in our lab along with the use of these functionalized thiazolines in natural product analogue synthesis.

EXPERIMENTAL SECTION

General Considerations. All reactions were performed under a nitrogen atmosphere. All reagents were purchased through Acros Organics or Sigma-Aldrich and used as received. However, further purification of some thioamides was required prior to thioimidate formation. Reactions were monitored by LC-MS analysis (Shimadzu LC-MS 2020 with Kinetex 2.6 mm C18 50 × 2.10 mm). Enantiomeric excess was monitored by chiral HPLC analysis (Shimadzu HPLC with Lux 5 μm Amylose-2 LC Column 250 × 4.6 mm). Solvent system for chiral HPLC was as follows: isocratic flow at 40% of a 20 mM solution of NH_4HCO_3 in H_2O, 60% MeCN, and 0.1% diethylamine. Flash chromatography on silica gel was used to purify the thiazoline crude reaction mixtures and performed on a Biotage Isolera utilizing Biotage cartridges and linear gradients. Melting points were determined by using a Thomas-Hoover capillary melting point apparatus. IR spectra were recorded on Jasco FT/IR-4100 spectrometer. ^{1}H (300 or 400 MHz) and ^{13}C NMR (100 MHz) spectra were obtained on a Varian Mercury-VX 300 or a Varian Mercury-VX 400 instrument. Chemical shifts were reported in parts per million with the residual solvent peak used as an internal standard ($CDCl_3$: ^{1}H δ = 7.26 and ^{13}C δ = 77.16). ^{13}C NMR spectra were run at 100 MHz using a proton-decoupling pulse sequence with a d_1 of 0 s unless otherwise noted. High-resolution mass spectra were obtained on a Thermo Fisher Scientific, Exactive Plus mass spectrometer (ion trap) using heated electrospray ionization (HESI).

General Procedure A: Synthesis of *S*-Allyl Thioimidate Hydrobromide Salts. Reactions can be performed on multigram scale (see Supporting Information for experimental details). To a solution of thioamide derivative in THF (0.5 M) was added allyl bromide derivative (2 equiv), and the solution was stirred at reflux until thioamide was consumed. The resulting solid was filtered and washed with hexanes and EtOAc. If no precipitation was observed, the solution was concentrated in vacuo. EtOAc was added to the subsequent oil, and the slurry was sonicated for 5 min. The resulting white solid was filtered and washed with hexanes and EtOAc. The solid was dissolved in $CHCl_3$, filtered to remove impurities, and washed with $CHCl_3$ to obtain pure product.

*2-Methylallyl Benzimidothioate Hydrobromide (**2a**):* Prepared from thiobenzamide (1.0 g, 6.9 mmol) and 3-bromo-2-methylpropene (1.9 g, 14 mmol) according to general procedure A to yield 1.7 g (92%) of **2a** as a white solid; mp 143−144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.42 (s, 1H), 11.62 (s, 1H), 8.09 (d, J = 8.1 Hz, 2H), 7.67 (t, J = 7.4 Hz, 1H), 7.55 (t, J = 7.7 Hz, 2H), 5.26 (s, 1H), 5.07 (s, 1H), 4.40 (s, 2H), 1.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 187.7, 135.9, 135.9, 130.1, 129.5, 129.1, 118.1, 41.5, 21.9; IR (neat) ν_{max} 3172, 2916, 1595, 1449, 1267, 936, 861 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{14}NS$ $[M - Br]^+$ 192.0841, found 192.0842.

*Allyl Benzimidothioate Hydrobromide (**2b**):* Prepared from thiobenzamide (1.0 g, 6.9 mmol) and allyl bromide (1.7 g, 14 mmol) according to general procedure A to yield 1.5 g (86%) of **2b** as a white solid; mp 140−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.41 (s, 1H), 11.63 (s, 1H), 8.07 (d, J = 8.5 Hz, 2H), 7.65 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 5.91 (ddt, J = 17, 10, and 6.8 Hz, 1H), 5.61 (dd, J = 17 and 0.9 Hz, 1H), 5.34 (dq, J = 10 and 0.9 Hz, 2H), 4.41 (dt, J = 6.8 and 1.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.1, 135.8, 130.0, 129.4, 129.1, 127.9, 122.4, 36.9; IR (neat) ν_{max} 3035, 2907, 1594, 1249, 1120, 947, 865, 698 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{10}H_{12}NS$ $[M - Br]^+$ 178.0685, found 178.0683.

*(E)-But-2-en-1-yl Benzimidothioate Hydrobromide (**2c**):* Prepared from thiobenzamide (1.0 g, 6.9 mmol) and crotyl bromide (2.2 g, 14 mmol) according to general procedure A to yield 1.6 g (87%) of **2c** as a white solid; mp 150−152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.64 (s, 1H), 11.91 (s, 1H), 8.05 (d, J = 8.4 Hz, 2H), 7.63 (t, J = 7.5 Hz, 1H), 7.46 (t, J = 7.5 Hz, 2H), 6.03 (dqt, J = 15, 8.5, and 1.3 Hz, 1H), 5.51 (dtq, J = 15, 7.2, and 1.7 Hz, 1H), 4.35 (dd, J = 7.2 and 1.1 Hz, 2H), 1.67 (dd, J = 6.6 and 1.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.3, 135.7, 134.6, 130.0, 129.3, 129.0, 120.3, 36.9, 18.0; IR (neat) ν_{max} 3035, 2899, 1598, 1245, 1120, 974, 865, 698 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{14}NS$ $[M - Br]^+$ 192.0842, found 192.0834.

*3-Methylbut-2-en-1-yl Benzimidothioate Hydrobromide (**2d**):* Prepared from thiobenzamide (1.0 g, 6.9 mmol) and 1-bromo-3-methyl-2-butene (2.1 g, 14 mmol) according to general procedure A to yield 1.7 g (86%) of **2d** as a white solid; mp 147−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.35 (s, 1H), 11.65 (s, 1H), 8.08 (d, J = 7.4 Hz, 2H), 7.66 (t, J = 7.5 Hz, 1H), 7.51 (t, J = 7.9 Hz, 2H), 5.31 (tq, J = 8.5 and 1.1 Hz, 1H), 4.39 (d, J = 8.0 Hz, 2H), 1.76 (s, 3H), 1.75 (d, J = 1.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.3, 143.1, 135.7, 130.2, 129.4, 129.1, 113.0, 34.1, 25.8, 18.5; IR (neat) ν_{max} 3059, 2915, 1602, 1241, 1124, 865, 846, 698 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{12}H_{16}NS$ $[M - Br]^+$ 206.0998, found 206.0991.

*2-(Trifluoromethyl)allyl Benzimidothioate Hydrobromide (**2e**):* Prepared from thiobenzamide (1.0 g, 6.9 mmol) and 2-bromomethyl-3,3,3-trifluoropropene (2.7 g, 14 mmol) according to general procedure A to yield 1.3 g (58%) of **2e** as a white solid; mp 141−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.51 (s, 1H), 11.92 (s, 1H), 8.07 (d, J = 7.3 Hz, 2H), 7.70 (t, J = 7.5 Hz, 1H), 7.53 (t, J = 7.5 Hz, 2H), 6.28 (s, 1H), 6.04 (s, 1H), 4.70 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.9, 136.4, 130.3, 130.0, 129.7, 129.6, 129.4, 127.2, 127.1, 127.1, 127.0, 33.4; IR (neat) ν_{max} 3062, 2907, 1605, 1168, 1113, 857, 842, 698 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{11}F_3NS$ $[M - Br]^+$ 246.0559, found 246.0551.

*2-(Methylcarboxylate)allyl Benzimidothioate Hydrobromide (**2f**):* Prepared from thiobenzamide (0.069 g, 0.48 mmol) and methyl-2-(bromomethyl)acrylate (0.18 g, 0.96 mmol) according to general

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procedure A to yield 0.096 g (64%) of **2f** as a white solid; mp 126−127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.38 (s, 1H), 11.83 (s, 1H), 8.09 (d, J = 7.3 Hz, 2H), 7.70 (t, J = 7.5 Hz, 1H), 7.54 (t, J = 8.2 Hz, 2H), 6.57 (s, 1H), 6.49 (s, 1H), 4.73 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.4, 165.7, 136.1, 132.5, 132.3, 130.1, 129.6, 129.3, 52.7, 35.2; IR (neat) ν_{max} 2950, 1721, 1605, 1442, 1337, 1206, 1144, 761, 702 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{12}H_{14}NO_2S$ [M − Br]$^+$ 236.0740, found 236.0732.

*2-Bromoallyl Benzimidothioate Hydrobromide (**2g**):* Prepared from thiobenzamide (1.0 g, 6.9 mmol) and 2,3-dibromopropene (3.5 g, 14 mmol) according to general procedure A to yield 1.7 g (75%) of **2g** as a white solid; mp 142−143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.49 (s, 1H), 11.79 (s, 1H), 8.13 (d, J = 7.4 Hz, 2H), 7.72 (t, J = 7.5 Hz, 1H), 7.57 (d, J = 7.6 Hz, 2H), 6.51 (t, J = 2.3 Hz, 1H), 5.76 (d, J = 2.3 Hz, 1H), 4.89 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.7, 136.4, 130.0, 129.7, 129.6, 125.2, 122.6, 44.4; IR (neat) ν_{max} 2915, 1598, 1276, 1195, 1124, 865, 698 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{10}H_{11}BrNS$ [M − Br]$^+$ 255.9790, found 255.9783.

*2-(4-Bromobenzyl)allyl Benzimidothioate Hydrobromide (**2h**):* Prepared from thiobenzamide (0.027 g, 0.19 mmol) and 3-bromo-2-(4-bromobenzyl)propene (0.12 g, 0.19 mmol) according to general procedure A to yield 0.048 g (60%) of **2h** as a white solid; mp 105−106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.45 (s, 1H), 11.62 (s, 1H), 8.03 (d, J = 8.5 Hz, 2H), 7.70 (t, J = 7.7 Hz, 1H), 7.53 (t, J = 7.3 Hz, 2H), 7.41 (d, J = 8.3 2H), 7.12 (d, J = 8.5 2H), 5.46 (s, 1H), 5.08 (s, 1H), 4.41 (s, 2H), 3.53 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.5, 139.3, 136.7, 136.0, 131.9, 131.1, 130.1, 129.6, 129.2, 120.8, 119.0, 41.6, 39.2; IR (neat) ν_{max} 3387, 2915, 1598, 1487, 1276, 1070, 1011, 700 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{17}H_{17}BrNS$ [M − Br]$^+$ 346.0260, found 346.0268.

*2-Phenylallyl Benzimidothioate Hydrobromide (**2i**):* Prepared from thiobenzamide (0.58 g, 4.0 mmol) and 2,3-dibromopropene (1.6 g, 8.1 mmol) according to general procedure A to yield 1.2 g (91%) of **2i** as a white solid; mp 154−155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.50 (s, 1H), 11.86 (s, 1H), 8.05 (d, J = 7.7 Hz, 2H), 7.67 (t, J = 7.5 Hz, 1H), 7.52−7.49 (m, 4H), 7.38−7.33 (m, 3H), 5.72 (s, 1H), 5.68 (s, 1H), 4.97 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.8, 139.1, 137.6, 136.0, 130.1, 129.5, 129.3, 128.9, 128.8, 126.4, 120.0, 40.2; IR (neat) ν_{max} 2915, 1598, 1446, 1241, 1128, 869, 780, 698 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{16}H_{16}NS$ [M − Br]$^+$ 254.0998, found 254.0990.

*2-(Naphthalen-2-yl)allyl Benzimidothioate Hydrobromide (**2j**):* Prepared from thiobenzamide (0.19 g, 1.3 mmol) and 3-bromo-2-(naphthalen-2-yl)propene (0.34 g, 1.3 mmol) according to general procedure A to yield 0.36 g (70%) of **2j** as a white solid; mp 168−169 °C; ^{1}H NMR (400 MHz, DMSO) δ 12.01 (s, 1H), 8.20 (s, 1H), 7.96−7.94 (m, 3H), 7.85−7.79 (m, 4H), 7.76−7.53 (m, 4H), 5.96 (s, 1H), 5.77 (s, 1H), 4.88 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ 186.9, 138.9, 135.3, 134.4, 132.9, 132.7, 131.0, 129.5, 128.4, 128.3, 128.3, 127.5, 126.7, 126.6, 125.2, 124.0, 119.1, 37.0; IR (neat) ν_{max} 3047, 2861, 1613, 1591, 1445, 1276, 1231, 1126, 920, 870, 826 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{20}H_{18}NS$ [M − Br]$^+$ 304.1155, found 304.1156.

*3-Phenylallyl Benzimidothioate Hydrobromide (**2k**).* Prepared from thiobenzamide (0.50 g, 3.5 mmol) and cinnamyl bromide (1.4 g, 6.9 mmol) according to general procedure A to yield 1.1 g (98%) of **2k** as a white solid; mp 178−179 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.37 (s, 1H), 11.84 (s, 1H), 8.12 (d, J = 7.9 Hz, 2H), 7.67 (t, J = 7.5 Hz, 1H), 7.52 (t, J = 8.0 Hz, 2H), 7.37 (d, J = 8.3 Hz, 2H), 7.30−7.24 (m, 3H), 6.94 (d, J = 16 Hz, 1H), 6.26 (dt, J = 16 and 7.4 Hz, 1H) 4.64 (d, J = 7.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.3, 137.5, 135.9, 135.6, 130.0, 129.5, 129.2, 128.7, 128.5, 126.7, 118.5, 37.5; IR (neat) ν_{max} 3055, 3028, 2915, 1598, 1446, 1272, 1233, 1124, 698 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{16}H_{16}NS$ [M − Br]$^+$ 254.0998, found 254.0992.

*2-Methylallyl Ethanimidothioate Hydrobromide (**2l**):* Prepared from thioacetamide (0.50 g, 6.5 mmol) and 3-bromo-2-methylpropene (1.8 g, 13 mmol) according to general procedure A to yield 1.0 g (75%) of **2l** as a white solid; mp 114−116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.28 (s, 1H), 11.23 (s, 1H), 5.11 (s, 1H), 4.94 (s, 1H), 4.05 (s, 2H), 2.64 (s, 3H), 1.75 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.4, 135.5, 117.5, 40.2, 24.0, 21.5; IR (neat) ν_{max} 2923, 2652, 2574, 1656, 1602, 1423, 1377, 1287, 857 cm^{-1}; HRMS (ESI, m/z) calcd for $C_6H_{12}NS$ [M − Br]$^+$ 130.0685, found 130.0683.

*2-Methylallyl 4-Methoxybenzimidothioate Hydrobromide (**2m**):* Prepared from 4-methoxythiobenzamide (0.75 g, 4.4 mmol) and 3-bromo-2-methylpropene (1.2 g, 8.7 mmol) according to general procedure A to yield 1.1 g (86%) of **2m** as a white solid; mp 170−173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 9.0 Hz, 2H), 7.19 (d, J = 9.0 Hz, 2H), 5.25 (s, 1H), 5.15 (s, 1H), 4.87 (s, 2H), 4.15 (s, 2H), 3.94 (s, 3H), 1.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.4, 167.7, 138.2, 132.1, 123.9, 117.7, 116.3, 56.7, 40.6, 21.7; IR (neat) ν_{max} 3182, 2965, 1671, 1604, 1501, 1278, 1185, 1013, 836 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{12}H_{16}NOS$ [M − Br]$^+$ 222.0947, found 222.0946.

*2-Methylallyl 4-Nitrobenzimidothioate Hydrobromide (**2n**):* Prepared from 4-nitrothiobenzamide (0.60 g, 3.2 mmol) and 3-bromo-2-methylpropene (0.89 g, 6.4 mmol) according to general procedure A to yield 0.59 g (58%) of **2n** as a white solid; mp 152−155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 8.7 Hz, 2H), 8.24 (d, J = 8.7 Hz, 2H), 5.30 (s, 1H), 5.14 (s, 1H), 4.44 (s, 2H), 1.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.7, 151.6, 135.3, 135.1, 130.5, 124.4, 118.8, 42.2, 21.9; IR (neat) ν_{max} 3055, 2815, 1619, 1526, 1347, 848, 726, 691 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{13}N_2O_2S$ [M − Br]$^+$ 237.0692, found 237.0690.

*2-Methylallyl 4-Chlorobenzimidothioate Hydrobromide (**2o**):* Prepared from 4-chlorothiobenzamide (0.50 g, 2.8 mmol) and 3-bromo-2-methylpropene (0.79 g, 5.7 mmol) according to general procedure A to yield 0.75 g (86%) of **2o** as a white solid; mp 165−166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.47 (s, 1H), 11.67 (s, 1H), 8.06 (d, J = 8.9 Hz, 2H), 7.50 (d, J = 8.9 Hz, 2H), 5.27 (s, 1H), 5.09 (s, 1H), 4.40 (s, 2H), 1.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.7, 142.8, 135.8, 130.5, 129.9, 128.4, 118.4, 41.7, 21.9; IR (neat) ν_{max} 3082, 2973, 1590, 1485, 1404, 1233, 1128, 1093, 876, 838 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{13}ClNS$ [M − Br]$^+$ 226.0452, found 226.0446.

*2-Methylallyl 4-Bromobenzimidothioate Hydrobromide (**2p**):* Prepared from 4-bromothiobenzamide (0.50 g, 2.2 mmol) and 3-bromo-2-methylpropene (0.62 g, 4.5 mmol) according to general procedure A to yield 0.63 g (80%) of **2p** as a white solid; mp 162−164 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.46 (s, 1H), 11.68 (s, 1H), 7.97 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 8.3 Hz, 2H), 5.26 (s, 1H), 5.09 (s, 1H), 4.39 (s, 2H), 1.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.9, 135.7, 132.9, 131.6, 130.5, 128.8, 118.4, 41.7, 21.9; IR (neat) ν_{max} 3031, 2973, 1602, 1586, 1481, 1396, 1117, 1070, 1009, 729 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{13}BrNS$ [M − Br]$^+$ 269.9947, found 269.9941.

*2-Methylallyl 4-(2-Methylthiazol-4-yl)benzimidothioate Hydrobromide (**2q**):* Prepared from 4-(2-methyl-4-thiazolyl)thiobenzamide (0.50 g, 2.1 mmol) and 3-bromo-2-methylpropene (0.59 g, 4.3 mmol) according to general procedure A to yield 0.69 g (88%) of **2q** as a white solid; mp 165−166 °C; ^{1}H NMR (400 MHz, DMSO) δ 11.85 (s, 1H), 8.35 (s, 1H), 8.34 (d, J = 8.3 Hz, 2H), 8.01 (d, J = 8.4 Hz, 2H), 5.23 (s, 1H), 5.07 (s, 1H), 4.24 (s, 2H), 2.73 (s, 3H), 1.87 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 186.7, 166.9, 152.1, 140.8, 137.6, 130.0, 129.8, 126.9, 118.7, 117.0, 39.4, 21.8, 19.4; IR (neat) ν_{max} 3066, 2915, 1412, 1268, 1172, 846, 714 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{15}H_{17}N_2S_2$ [M − Br]$^+$ 289.0828, found 289.0823.

*2-Methylallyl Benzo[b]thiophene-3-carbimidothioate Hydrobromide (**2r**):* Prepared from 1-benzothiophene-3-carbothioamide (0.51 g, 2.6 mmol) and 3-bromo-2-methylpropene (0.74 g, 5.3 mmol) according to general procedure A to yield 0.60 g (69%) of **2r** as a white solid; mp 143−144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.34 (s, 1H), 11.59 (s, 1H), 8.92 (s, 1H), 8.31 (d, J = 8.2 Hz, 1H), 7.89 (d, J = 8.2 Hz, 1H), 7.52 (t, J = 7.7 Hz, 1H), 7.45 (t, J = 7.9 Hz, 1H), 5.32 (s, 1H), 5.13 (s, 1H), 4.46 (s, 2H), 1.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.9, 140.8, 139.5, 136.0, 134.6, 126.5, 126.2, 126.2, 123.6, 123.3, 118.4, 41.9, 22.0; IR (neat) ν_{max} 3086, 2899, 1586, 1480, 1420, 1254, 1235, 1070, 815, 764 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{13}H_{14}NS_2$ [M − Br]$^+$ 248.0562, found 248.0561.

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*But-3-en-1-yl Benzimidothioate Hydrobromide (**2s**):* Prepared from thiobenzamide (0.75 g, 5.2 mmol) and 4-bromo-1-butene (1.4 g, 10 mmol) according to general procedure A to yield 0.69 g (49%) of **2s** as a white solid; mp 143−145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.35 (s, 1H), 11.67 (s, 1H), 8.04 (d, J = 7.4 Hz, 2H), 7.64 (t, J = 7.5 Hz, 1H), 7.48 (t, J = 8.0 Hz, 2H), 5.83 (ddt, J = 17, 10, and 6.7 Hz, 1H), 5.17 (dd, J = 17 and 1.4 Hz, 1H), 5.11 (dd, J = 10 and 1.2 Hz, 1H), 3.78 (t, J = 6.8 Hz, 2H), 2.58 (dt, J = 6.7 and 6.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.9, 135.7, 133.9, 130.2, 129.3, 128.9, 118.5, 33.8, 31.3; IR (neat) ν_{max} 3051, 2853, 1594, 1446, 1405, 1273,1231, 1123, 866, 703 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{14}NS$ [M − Br]$^+$ 192.0842, found 192.0839.

*Pent-4-en-1-yl Benzimidothioate Hydrobromide (**2t**):* Prepared from thiobenzamide (0.75 g, 5.2 mmol) and 5-bromo-1-pentene (1.6 g, 10 mmol) according to general procedure A to yield 0.73 g (49%) of **2t** as a white solid; mp 131−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.37 (s, 1H), 11.64 (s, 1H), 8.05 (d, J = 8.4 Hz, 2H), 7.64 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 8.0 Hz, 2H), 5.75 (ddt, J = 17, 10, and 6.7 Hz, 1H), 5.05 (dd, J = 17 and 1.5 Hz, 1H), 4.99 (dt, J = 10 and 1.2 Hz, 2H), 3.69 (t, J = 7.2 Hz, 2H), 2.27 (dt, J = 7.3 and 7.3 Hz, 2H), 1.91 (p, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.9, 136.3, 135.6, 130.2, 129.3, 128.9, 116.5, 33.6, 32.1, 26.6; IR (neat) ν_{max} 3442, 3055, 2919, 1594, 1265, 845, 699 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{12}H_{16}NS$ [M − Br]$^+$ 206.0998, found 206.0994.

General Procedure B: *anti*-Diastereoselective Synthesis of 2-Thiazolines. *S*-Allyl thioimidate hydrobromide salt was dissolved in CH_2Cl_2 (0.05 M). NBS (1.1 equiv) was added, and the solution turned orange. The reaction was complete upon addition of NBS, quenched with $Na_2S_2O_3$, and extracted with CH_2Cl_2 (×3). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The crude residue was purified by flash chromatography on silica gel.

*4-(Bromomethyl)-4-methyl-2-phenyl-4,5-dihydrothiazole (**3a**):*[12] Prepared from **2a** (0.05 g, 0.18 mmol) and NBS (0.036 g, 0.20 mmol) according to general procedure B and purified (hexanes/EtOAc: 98/2) to yield 0.045 g (90%) of **3a** as a clear oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 6.8 Hz, 2H), 7.50−7.37 (m, 3H), 3.66 (d, J = 10 Hz, 1H), 3.62 (d, J = 11 Hz, 1H), 3.60 (d, J = 10 Hz, 1H), 3.18 (d, J = 11 Hz, 1H), 1.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 133.2, 131.6, 128.6, 128.5, 81.9, 41.7, 40.5, 24.9.

*4-(Bromomethyl)-2-phenyl-4,5-dihydrothiazole (**3b**):* Prepared from **2b** (0.10 g, 0.39 mmol) and NBS (0.077 g, 0.43 mmol) according to general procedure B and purified (hexanes/EtOAc: 95/5) to yield 0.059 g (60%) of **3b** as a clear oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 7.0 Hz, 2H), 7.48 (t, J = 7.6 Hz, 1H), 7.42 (t, J = 7.7 Hz, 2H), 5.00 (tdd, J = 8.4, 7.1, and 3.9 Hz, 1H), 3.76 (dd, J = 10 and 3.9 Hz, 1H), 3.58 (dd, J = 11 and 8.5 Hz, 1H), 3.57 (dd, J = 10 and 8.3 Hz, 1H), 3.44 (dd, J = 11 and 7.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.9, 131.8, 128.7, 128.6, 77.9, 36.8, 34.3; IR (neat) ν_{max} 3060, 2958, 1604, 1576, 1490, 1446, 1244, 1014, 942, 767, 690, 607 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{10}H_{11}BrNS$ [M + H]$^+$ 255.9790, found 255.9788.

*4-(1-Bromoethyl)-2-phenyl-4,5-dihydrothiazole (**3c**):* Prepared from **2c** (0.10 g, 0.37 mmol) and NBS (0.073 g, 0.40 mmol) according to general procedure B and purified (hexanes/EtOAc: 97/3) to yield 0.068 g (69%) of a mixture of **3c** and **3c-1**. Further purification was accomplished by reverse-phase chromatography (gradient of 10% to 90% MeCN in H_2O) to yield 0.033 g (33%) of **3c** as a clear oil and 0.034 g (34%) of **3c-1** as a clear oil. In this reaction, the starting material contains a small amount of the *cis*-alkene, which leads to a small amount of the corresponding minor diastereomer and these compounds are not readily separable. For compound **3c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.4 Hz, 2H), 7.50 (t, J = 7.6 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 4.83 (td, J = 8.6 and 6.5 Hz, 1H), 4.51 (p, J = 6.8 Hz, 1H), 3.60 (dd, J = 11 and 8.9 Hz, 1H), 3.50 (dd, J = 11 and 8.3 Hz, 1H), 1.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.1, 131.9, 128.8, 128.7, 82.6, 52.7, 36.1, 24.0; IR (neat) ν_{max} 3028, 2926, 1670, 1604, 1577, 1491, 1445, 1190, 1000, 768, 690 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{13}BrNS$ [M + H]$^+$ 269.9947, found 269.9942. For compound **3c-1**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.4 Hz, 2H), 7.60 (t, J = 7.5 Hz, 1H), 7.48 (t, J = 8.4 Hz, 2H), 4.47−4.37 (m, 2H), 3.70 (dd, J = 13 and 3.3 Hz, 1H), 3.54 (ddd, J = 13, 7.1, and 1.3 Hz, 1H), 1.60 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.7, 129.3, 128.9, 127.6, 57.3, 43.1, 32.7, 20.9; IR (neat) ν_{max} 3060, 2927, 1673, 1605, 1425, 1202, 1130, 765, 687 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{13}BrNS$ [M + H]$^+$ 269.9947, found 269.9942.

*4-(2-Bromopropan-2-yl)-2-phenyl-4,5-dihydrothiazole (**3d**):*[12] Prepared from **2d** (0.10 g, 0.35 mmol) and NBS (0.069 g, 0.38 mmol) according to general procedure B and purified (hexanes/EtOAc: 98/2) to yield 0.068 g (68%) of a mixture of **3d** and **3d-1**. Further purification was accomplished by reverse-phase chromatography (gradient of 10% to 65% MeCN in H_2O) to yield 0.012 g (12%) of **3d** as a clear oil and 0.045 g (45%) of **3d-1** as a white solid. For compound **3d**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 7.3 Hz, 2H), 7.49 (t, J = 6.9 Hz, 1H), 7.42 (t, J = 7.8 Hz, 2H), 4.79 (t, J = 9.1 Hz, 1H), 3.63 (dd, J = 9.7 and 7.4 Hz, 1H), 3.58 (dd, J = 8.1 and 5.9 Hz, 1H), 1.98 (s, 3H), 1.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.0, 129.1, 128.7, 126.7, 68.9, 35.9, 33.1, 30.4, 25.8; IR (neat) ν_{max} 3028, 2925, 1606, 1578, 1490, 1447, 1106, 992, 942, 766, 689 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{12}H_{15}BrNS$ [M + H]$^+$ 284.0103, found 284.0097. For compound **3d-1**: mp 44−47 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.2 Hz, 2H), 7.44−7.35 (m, 3H), 4.35 (dd, J = 10 and 4.2 Hz, 1H), 3.61 (dd, J = 13 and 10 Hz, 1H), 3.50 (dd, J = 13 and 4.2 Hz, 1H), 1.53 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 138.8, 130.6, 128.5, 126.6, 56.4, 54.2, 31.5, 30.2, 24.4; IR (neat) ν_{max} 3028, 2980, 1596, 1577, 1443, 1422, 1306, 1235, 1209, 947, 921, 766, 691 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{12}H_{15}BrNS$ [M + H]$^+$ 284.0103, found 284.0099.

*4-(4-Bromobenzyl)-4-(bromomethyl)-2-phenyl-4,5-dihydrothiazole (**3h**):* Prepared from **2h** (0.043 g, 0.099 mmol) and NBS (0.020 g, 0.11 mmol) according to general procedure B and purified (hexanes/EtOAc: 96/4) to yield 0.032 g (75%) of **3h** as a clear oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 7.2 Hz, 2H), 7.49 (t, J = 7.3 Hz, 1H), 7.44−7.41 (m, 4H), 7.23 (d, J = 8.3 Hz, 2H), 3.59 (d, J = 11 Hz, 1H), 3.54 (s, 2H), 3.26 (d, J = 11 Hz, 1H), 3.20 (d, J = 14 Hz, 1H), 3.12 (d, J = 14 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.4, 133.8, 132.6, 131.8, 131.3, 128.7, 128.5, 121.0, 84.7, 42.7, 40.2, 38.4; IR (neat) ν_{max} 3062, 2923, 1594, 1488, 1445, 1258, 1072, 1012, 942, 766, 689 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{17}H_{16}Br_2NS$ [M + H]$^+$ 423.9365, found 423.9374.

*4-(Bromomethyl)-2,4-diphenyl-4,5-dihydrothiazole (**3i**):* Prepared from **2i** (0.10 g, 0.30 mmol) and NBS (0.059 g, 0.33 mmol) according to general procedure B and purified (hexanes/EtOAc: 96/4) to yield 0.065 g (66%) of **3i** as a clear oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.1 Hz, 2H), 7.57 (d, J = 7.2 Hz, 1H), 7.51−7.45 (m, 3H), 7.39 (t, J = 7.4 Hz, 2H), 7.32 (t, J = 7.3 Hz, 2H), 4.03 (d, J = 11 Hz, 1H), 3.95 (d, J = 10 Hz, 1H), 3.83 (d, J = 10 Hz, 1H), 3.71 (d, J = 11 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 133.1, 131.7, 128.7, 128.7, 128.6, 128.1, 126.3, 86.6, 41.9, 41.9; IR (neat) ν_{max} 3060, 2956, 1606, 1575, 1492, 1447, 1031, 942, 767, 690 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{16}H_{15}BrNS$ [M + H]$^+$ 332.0103, found 332.0099.

*4-(Bromomethyl)-4-(naphthalen-2-yl)-2-phenyl-4,5-dihydrothiazole (**3j**):* Prepared from **2j** (0.10 g, 0.26 mmol) and NBS (0.051 g, 0.29 mmol) according to general procedure B and purified (hexanes/EtOAc: 96/4) to yield 0.057 g (57%) of **3j** as a clear oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03−7.99 (m, 3H), 7.89−7.83 (m, 3H), 7.67 (dd, J = 8.6 and 1.8 Hz, 1H), 7.55−7.45 (m, 5H), 4.10 (d, J = 11 Hz, 1H), 4.03 (d, J = 10 Hz, 1H), 3.94 (d, J = 10 Hz, 1H), 3.83 (d, J = 11 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 133.2, 133.1, 133.0, 131.8, 128.8, 128.7, 128.5, 128.5, 127.7, 126.5, 126.4, 125.4, 124.3, 86.8, 41.9, 41.7; IR (neat) ν_{max} 3057, 1601, 1490, 1446, 1257, 1243, 1036, 942, 768, 750, 690 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{20}H_{17}BrNS$ [M + H]$^+$ 382.0260, found 382.0258.

*4-(Bromo(phenyl)methyl)-2-phenyl-4,5-dihydrothiazole (**3k**):* Prepared from **2k** (0.10 g, 0.30 mmol) and NBS (0.059 g, 0.33 mmol) according to general procedure B; the reaction was filtered and washed with hexanes and EtOAc to yield 0.077 g (77%) of **3k** as a white solid; mp 203−205 °C; ^{1}H NMR (400 MHz, DMSO) δ 7.84 (d, J = 7.0 Hz, 2H), 7.69 (t, J = 6.8 Hz, 1H), 7.59 (t, J = 7.5 Hz, 2H), 7.47−7.40 (m,

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5H), 5.50 (d, J = 5.6 Hz, 1H), 5.08−5.03 (m, 1H), 3.75 (dd, J = 14 and 6.9 Hz, 1H), 3.56 (dd, J = 14 and 3.1 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 138.7, 133.3, 129.2, 128.9, 128.6, 127.5, 127.0, 126.2, 64.1, 44.3, 32.0; IR (neat) ν_{max} 1591, 1568, 1409, 1225, 1017, 795, 761, 743, 701 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{16}H_{15}BrNS$ $[M + H]^+$ 332.0103, found 332.0110.

*4-(Bromomethyl)-2,4-dimethyl-4,5-dihydrothiazole (**3l**):* Prepared from **2l** (0.10 g, 0.48 mmol) and NBS (0.094 g, 0.52 mmol) according to general procedure B and purified (hexanes/EtOAc: 88/12) to yield 0.068 g (69%) of **3l** as a clear oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 (d, J = 10 Hz, 1H), 3.51 (d, J = 12 Hz, 1H), 3.48 (d, J = 10 Hz, 1H), 3.06 (d, J = 11 Hz, 1H), 2.19 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 81.5, 42.8, 40.6, 24.9, 20.5; IR (neat) ν_{max} 3229, 2929, 1623, 1434, 1371, 1150, 785, 671 cm^{-1}; HRMS (ESI, m/z) calcd for $C_6H_{11}BrNS$ $[M + H]^+$ 207.9790, found 207.9790.

*4-(Bromomethyl)-2-(4-methoxyphenyl)-4-methyl-4,5-dihydrothiazole (**3m**):* Prepared from **2m** (0.10 g, 0.33 mmol) and NBS (0.065 g, 0.36 mmol) according to general procedure B and purified (hexanes/EtOAc: 92/8) to yield 0.057 g (97%) of **3m** as a clear oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 9.0 Hz, 2H), 6.90 (d, J = 9.0 Hz, 2H), 3.84 (s, 3H), 3.63 (d, J = 10 Hz, 1H), 3.59 (d, J = 11 Hz, 1H), 3.58 (d, J = 10 Hz, 1H), 3.15 (d, J = 11 Hz, 1H), 1.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 130.2, 125.9, 113.9, 81.7, 55.6, 41.7, 40.4, 24.9; IR (neat) ν_{max} 2969, 2838, 1606, 1509, 1308, 1254, 1172, 1033, 962, 836 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{12}H_{15}BrNOS$ $[M + H]^+$ 300.0052, found 300.0059.

*4-(Bromomethyl)-4-methyl-2-(4-nitrophenyl)-4,5-dihydrothiazole (**3n**):* Prepared from **2n** (0.10 g, 0.32 mmol) and NBS (0.062 g, 0.35 mmol) according to general procedure B and purified (hexanes/EtOAc: 92/8) to yield 0.080 g (81%) of **3n** as a white solid; mp 65−66 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, J = 9.0 Hz, 2H), 7.96 (d, J = 9.0 Hz, 2H), 3.68 (d, J = 11 Hz, 3H), 3.68 (d, J = 10 Hz, 1H), 3.60 (d, J = 10 Hz, 1H), 3.25 (d, J = 11 Hz, 1H), 1.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 149.5, 138.6, 129.4, 123.7, 82.4, 42.2, 40.3, 24.8; IR (neat) ν_{max} 3066, 2929, 1585, 1521, 1346, 966, 855, 688 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{12}BrN_2O_2S$ $[M + H]^+$ 314.9797, found 314.9795.

*4-(Bromomethyl)-2-(4-chlorophenyl)-4-methyl-4,5-dihydrothiazole (**3o**):* Prepared from **2o** (0.10 g, 0.33 mmol) and NBS (0.065 g, 0.36 mmol) according to general procedure B and purified (hexanes/EtOAc: 95/5) to yield 0.081 g (81%) of **3o** as a clear oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.7 Hz, 2H), 7.37 (d, J = 8.8 Hz, 2H), 3.64 (d, J = 10 Hz, 1H), 3.63 (d, J = 11 Hz, 1H), 3.59 (d, J = 10 Hz, 1H), 3.19 (d, J = 11 Hz, 1H), 1.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 131.6, 129.8, 128.9, 82.0, 41.9, 40.4, 24.8; IR (neat) ν_{max} 3055, 2973, 1598, 1488, 1399, 1271, 1090, 961, 833, 608 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{12}BrClNS$ $[M + H]^+$ 303.9557, found 303.9557.

*4-(Bromomethyl)-2-(4-bromophenyl)-4-methyl-4,5-dihydrothiazole (**3p**):* Prepared from **2p** (0.10 g, 0.28 mmol) and NBS (0.056 g, 0.31 mmol) according to general procedure B and purified (hexanes/EtOAc: 90/10) to yield 0.076 g (77%) of **3p** as a clear oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.5 Hz, 2H), 7.53 (d, J = 8.4 Hz, 2H), 3.64 (d, J = 10 Hz, 1H), 3.62 (d, J = 11 Hz, 1H), 3.59 (d, J = 10 Hz, 1H), 3.19 (d, J = 11 Hz, 1H), 1.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.0, 131.8, 130.0, 126.2, 82.0, 41.9, 40.3, 24.8; IR (neat) ν_{max} 3052, 2974, 1595, 1486, 1396, 1269, 1068, 1011, 961, 831, 608 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{12}Br_2NS$ $[M + H]^+$ 347.9052, found 347.9053.

*4-(4-(4-(Bromomethyl)-4-methyl-4,5-dihydrothiazol-2-yl)phenyl)-2-methylthiazole (**3q**):* Prepared from **2q** (0.10 g, 0.27 mmol) and NBS (0.054 g, 0.30 mmol) according to general procedure B and purified (hexanes/EtOAc: 89/11) to yield 0.089 g (90%) of **3q** as a white solid; mp 104−107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.3 Hz, 2H), 7.84 (d, J = 8.3 Hz, 2H), 7.38 (s, 1H), 3.66−3.59 (m, 3H), 3.17 (d, J = 11 Hz, 1H), 2.76 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 166.2, 154.1, 137.4, 132.4, 129.0, 126.3, 113.9, 81.9, 41.7, 40.4, 24.8, 19.5; IR (neat) ν_{max} 3112, 2972, 2927, 1593, 1410, 1273, 1171, 961, 851, 757 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{15}H_{16}BrN_2S_2$ $[M + H]^+$ 366.9933, found 366.9932.

*2-(Benzo[b]thiophen-3-yl)-4-(bromomethyl)-4-methyl-4,5-dihydrothiazole (**3r**):* Prepared from **2r** (0.10 g, 0.30 mmol) and NBS (0.060 g, 0.34 mmol) according to general procedure B and purified (hexanes/EtOAc: 96/4) to yield 0.087 g (88%) of **3r** as a clear oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (ddd, J = 8.1, 1.3, and 0.64 Hz, 1H), 7.94 (s, 1H), 7.85 (ddt, J = 7.8, 1.2, and 0.62 Hz, 1H), 7.47 (td, J = 8.0 and 1.2 Hz, 1H), 7.41 (td, J = 7.8 and 1.4 Hz, 1H), 3.72 (d, J = 10 Hz, 1H), 3.68 (d, J = 10 Hz, 1H), 3.59 (d, J = 11 Hz, 1H), 3.16 (d, J = 11 Hz, 1H), 1.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.3, 136.5, 133.1, 125.5, 125.4, 122.5, 41.0, 40.5, 25.0; IR (neat) ν_{max} 3064, 2928, 1594, 1497, 1459, 1424, 1117, 880, 759 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{13}H_{13}BrNS_2$ $[M + H]^+$ 325.9667, found 325.9665.

*4-(Bromomethyl)-2-phenyl-5,6-dihydro-4H-1,3-thiazine (**3s**):* Prepared from **2s** (0.10 g, 0.37 mmol) and NBS (0.073 g, 0.40 mmol) according to general procedure B and purified (hexanes/EtOAc: 96/4) to yield 0.042 g (42%) of **3s** as a clear oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, J = 8.2 and 1.4 Hz, 2H), 7.45−7.36 (m, 3H), 3.84−3.79 (m, 2H), 3.57 (dd, J = 11 and 8.6 Hz, 1H), 3.25 (td, J = 12 and 4.3 Hz, 1H), 3.12 (dt, J = 12 and 4.5 Hz, 1H), 2.32 (ddd, J = 14, 7.6, and 4.5 Hz, 1H), 1.68 (dddd, J = 14, 12, 9.3, and 4.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 139.1, 130.7, 128.4, 126.6, 57.8, 38.0, 25.6, 23.0; IR (neat) ν_{max} 3449, 3059, 2956, 2848, 1603, 1576, 1444, 1309, 1287, 1229, 936 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{13}BrNS$ $[M + H]^+$ 269.9947, found 269.9951.

*4-(Iodomethyl)-4-methyl-2-phenyl-4,5-dihydrothiazole (**4a**):* Thioimidate **2a** (0.050 g, 0.18 mmol) was dissolved in CH_2Cl_2 (3.6 mL). NIS (0.046 g, 0.20 mmol)) was added, and the solution turned orange. The reaction was complete upon addition of NIS, quenched with $Na_2S_2O_3$, and extracted with CH_2Cl_2 (×3). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The crude residue was purified by flash chromatography over silica gel (hexanes/EtOAc: 97/3) to yield 0.053 g (91%) of **4a** as a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, J = 6.7 Hz, 2H), 7.50−7.37 (m, 3H), 3.55 (d, J = 10 Hz, 1H), 3.54 (d, J = 11 Hz, 1H), 3.48 (d, J = 10 Hz, 1H), 3.20 (d, J = 11 Hz, 1H), 1.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 133.2, 131.5, 128.6, 128.5, 81.1, 43.1, 26.0, 16.9; IR (neat) ν_{max} 3060, 2926, 1593, 1576, 1446, 689 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{13}INS$ $[M + H]^+$ 317.9808, found 317.9805.

*(4-Methyl-2-phenyl-4,5-dihydrothiazol-4-yl)methyl Acetate (**5a**):* Thiazoline **4a** (0.027 g, 0.085 mmol) was dissolved in DMF (0.23 mL). Cesium acetate (0.082 g, 0.43 mmol) was added, and the solution was stirred at room temperature for 24 h. The reaction was brought to room temperature, quenched with H_2O, and extracted with EtOAc (×3). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The crude residue was purified by flash chromatography over silica gel (hexanes/EtOAc: 90/10) to yield 0.019 g (91%) of **5a** as a clear oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.0 Hz, 2H), 7.46 (t, J = 6.4 Hz, 1H), 7.39 (t, J = 7.0 Hz, 1H), 4.27 (d, J = 11 Hz, 1H), 4.23 (d, J = 11 Hz, 1H), 3.44 (d, J = 11 Hz, 1H), 3.14 (d, J = 11 Hz, 1H), 2.08 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 167.2, 133.2, 131.5, 128.6, 128.5, 81.2, 68.9, 40.6, 23.3, 21.1; IR (neat) ν_{max} 3062, 2973, 1742, 1604, 1447, 1370, 1236, 1043, 948, 768, 690 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{13}H_{16}NO_2S$ $[M + H]^+$ 250.0896, found 250.0895.

General Procedure C: Synthesis of *S*-Allyl Thioimidate Sulfonate Salts. Thioimidate **1a** was dissolved in THF (0.5 M). Sulfonic acid derivative (1 equiv) was added, and the solution was stirred at room temperature for 30 min. The solvent was removed, and the crude residue was triturated in EtOAc. The resulting white precipitate was filtered, washed with EtOAc, dissolved in $CHCl_3$, and filtered to remove insoluble impurities.

*2-Methylallyl Benzimidothioate p-Toluenesulfonate (**7a**):* Prepared from **1a** (3.0 g, 16 mmol) and *p*-TsOH (3.0 g, 16 mmol) according to general procedure C to yield 5.1 g (89%) of **7a** as a white solid; mp 135−136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.39 (s, 1H), 11.57 (s, 1H), 7.87 (d, J = 7.8 Hz, 2H), 7.70 (d, J = 6.6 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.44−7.39 (m, 2H), 7.09 (d, J = 7.7 Hz, 2H), 5.13 (s, 1H), 5.02 (s, 1H), 4.13 (s, 2H), 2.31 (s, 3H), 1.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.4, 142.1, 140.0, 136.2, 135.2, 131.0,

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129.4, 128.8, 128.8, 126.1, 117.9, 40.1, 21.7, 21.4; IR (neat) ν_{max} 3460, 3125, 2939, 1638, 1236, 1181, 1169, 680 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{18}H_{21}NO_3S_2Na$ $[M + Na]^+$ 386.0855, found 386.0846.

*2-Methylallyl Benzimidothioate Methanesulfonate (**8a**):* Prepared from **1a** (0.14 g, 0.73 mmol) and MsOH (0.071 g, 0.73 mmol) according to general procedure C to yield 0.25 g (quant.) of **8a** as a clear oil; ^1H NMR (400 MHz, $CDCl_3$) δ 12.12 (s, 1H), 11.31 (s, 1H), 7.93 (d, J = 7.2 Hz, 2H), 7.66 (t, J = 7.1 Hz, 1H), 7.52 (t, J = 7.6 Hz, 2H), 5.21 (s, 1H), 5.07 (s, 1H), 4.14 (s, 2H), 2.74 (s, 3H), 1.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6, 136.1, 135.5, 130.9, 129.5, 128.6, 118.0, 39.9, 39.4, 21.8; IR (neat) ν_{max} 3437, 2975, 1650, 1449, 1280, 1204, 1046, 917 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{12}H_{17}NO_3S_2Na$ $[M + Na]^+$ 310.0542, found 310.0539.

*2-Methylallyl Benzimidothioate (S)-Camphorsulfonate (**9a**):* Prepared from **1a** (0.30 g, 1.1 mmol) and (+)-CSA (0.26 g, 1.1 mmol) according to general procedure C to yield 0.27 g (59%) of **9a** as a white solid; mp 138−139 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 11.98 (s, 1H), 7.95 (d, J = 8.2 Hz, 2H), 7.64 (t, J = 8.4 Hz, 1H), 7.51 (t, J = 7.9 Hz, 2H), 5.20 (s, 1H), 5.05 (s, 1H), 4.23 (s, 2H), 3.24 (d, J = 15 Hz, 1H), 2.68 (d, J = 15 Hz, 1H), 2.55 (ddd, J = 15, 12, and 4.0 Hz, 1H), 2.24 (dt, J = 18 and 3.7 Hz, 1H), 1.95 (t, J = 4.5 Hz, 1H), 1.89 (s, 3H), 1.80 (d, J = 18 Hz, 2H), 1.58 (ddd, J = 13, 9.3, and 4.7 Hz, 1H), 1.27 (ddd, J = 13, 9.4, and 4.0 Hz, 1H), 0.97 (s, 3H), 0.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.8, 188.0, 136.5, 135.1, 131.2, 129.4, 128.8, 117.9, 58.4, 47.9, 47.3, 42.9, 42.6, 40.1, 27.1, 24.4, 21.8, 20.0, 19.8; IR (neat) ν_{max} 3448, 2959, 1740, 1642, 1189, 1042, 704, 617 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{21}H_{29}NO_4S_2Na$ $[M + Na]^+$ 446.1430, found 446.1419.

*2-Methylallyl Benzimidothioate (R)-Camphorsulfonate (**10a**):* Prepared from **1a** (0.3 g, 1.1 mmol) and (−)-CSA (0.26 g, 1.1 mmol) according to general procedure C to yield 0.38 g (81%) of **10a** as a white solid; mp 139−140 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 12.29 (s, 1H), 11.60 (s, 1H), 7.96 (d, J = 8.5 Hz, 2H), 7.67 (t, J = 8.1 Hz, 1H), 7.51 (t, J = 7.5 Hz, 2H), 5.23 (s, 1H), 5.08 (s, 1H), 4.24 (s, 2H), 3.28 (d, J = 15 Hz, 1H), 2.74 (d, J = 15 Hz, 1H), 2.57 (ddd, J = 15, 12, and 4.1 Hz, 1H), 2.27 (dt, J = 18 and 4.0 Hz, 1H), 1.92 (t, J = 4.6 Hz, 1H), 1.92 (s, 3H), 1.83 (d, J = 18 Hz, 2H), 1.62 (ddd, J = 13, 9.9, and 4.8 Hz, 1H), 1.31 (ddd, J = 13, 9.4, and 4.0 Hz, 1H), 1.00 (s, 3H), 0.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.9, 188.1, 136.5, 135.2, 131.3, 129.5, 128.8, 118.1, 58.5, 48.0, 47.4, 42.7, 42.7, 40.2, 27.1, 24.6, 21.9, 20.0, 19.9; IR (neat) ν_{max} 3491, 3168, 2919, 1737, 1610, 1189, 1042, 621 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{21}H_{29}NO_4S_2Na$ $[M + Na]^+$ 446.1430, found 446.1422.

*(R)-4-(Chloromethyl)-4-methyl-2-phenyl-4,5-dihydrothiazole (**6a**):* Thioimidate **2a** (0.10 g, 0.28 mmol), $(DHQD)_2PHAL$ (0.011 g, 0.014 mmol), and Et_3N (0.028 g, 0.28 mmol) were dissolved in TFE (5.5 mL) in a screw cap vial. The vial was capped and placed in a chiller set to −30 °C for 10 min. DCDPH (0.022 g, 0.069 mmol) was added as one aliquot. An aliquot of DCDPH was added every 30 min until a total of 0.28 mmol was reached (4 aliquots total). The reaction stirred at −30 °C for 4 h. The reaction was quenched with $Na_2S_2O_3$ and extracted with CH_2Cl_2 (×3). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The crude residue was purified by flash chromatography over silica gel (hexanes/EtOAc: 98/2) to yield 0.040 g (52%) of **6a** as a clear oil: 85% ee (*S* enantiomer R_t = 7.6 min; *R* enantiomer R_t = 9.0 min); ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.0 Hz, 2H), 7.47 (t, J = 7.1 Hz, 1H), 7.40 (t, J = 8.0 Hz, 2H), 3.75 (d, J = 11 Hz, 1H), 3.70 (d, J = 11 Hz, 1H), 3.61 (d, J = 11 Hz, 1H), 3.16 (d, J = 11 Hz, 1H), 1.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 133.1, 131.6, 128.6, 128.5, 82.5, 50.6, 40.8, 24.1; IR (neat) ν_{max} 3061, 2975, 1599, 1449, 1267, 964, 940, 687 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{13}ClNS$ $[M + H]^+$ 226.0451, found 226.0451.

*(R)-4-(Chloromethyl)-4-methyl-2-phenyl-4,5-dihydrothiazole Hydrobromide (**11a**):* To a round-bottom flask were added thiazoline **6a** (0.18 g, 0.80 mmol) and THF (1.6 mL). Hydrobromic acid (0.13 g, 0.80 mmol) was added, and the reaction stirred for 30 min. The solvent was removed, and the crude residue was triturated in EtOAc. The resulting white precipitate was filtered, washed with EtOAc, dissolved in $CHCl_3$, and filtered to remove insoluble impurities to yield 0.21 g (85%) of **11a** as a white solid: mp 188−189 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 7.5 Hz, 2H), 7.71 (t, J = 7.5 Hz, 1H), 7.54 (t, J = 7.8 Hz, 2H), 4.46 (d, J = 12 Hz, 1H), 4.02 (d, J = 12 Hz, 1H), 3.95 (d, J = 12 Hz, 1H), 3.60 (d, J = 12 Hz, 1H), 1.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.3, 137.1, 130.7, 129.8, 124.8, 76.1, 49.2, 39.7, 24.3; IR (neat) ν_{max} 3050, 2984, 1589, 1572, 1449, 1387, 1376, 996, 954, 771, 711 cm^{-1}; HRMS (ESI, m/z) calcd for $C_{11}H_{13}ClNS$ $[M - Br]^+$ 226.0451, found 226.0450.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b02299.

Gram-scale synthesis of thioimidate salt **2a**, thermal ellipsoid plot diagram of the X-ray crystal structure of compound **11a**, ^1H and ^{13}C NMR spectra for all new compounds (PDF)

X-ray data (CIF)

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Notes

The authors declare no competing financial interest.

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