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Lewis Base/Brønsted Acid Cocatalysis for Thiocyanation of Amides and Thioamides

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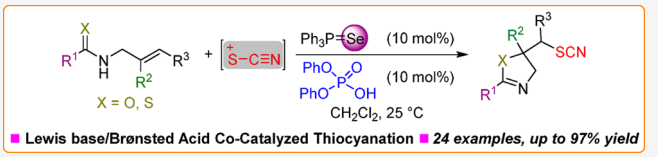
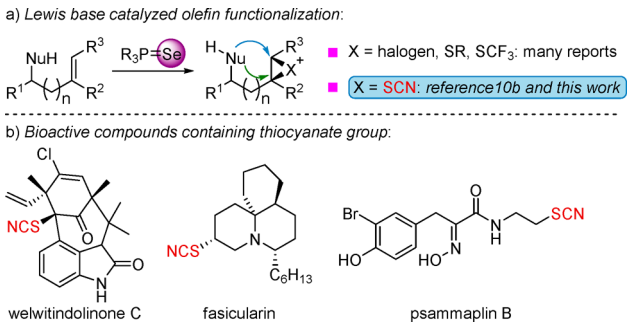
ABSTRACT: Lewis base/Brønsted acid cocatalysis for electrophilic thiocyanation of olefins is reported. Using a combination of triphenylphosphine selenide and diphenyl phosphate as a catalyst, a wide range of unsaturated amides and thioamides underwent thiocyanation to furnish thiocyanated thiazoline and oxazoline derivatives in high yields (up to 97%).



Catalytic olefin functionalization is a proven and widely applicable tool to attain molecular diversity.[1] Amid several modes of olefin functionalizations, the applications of Lewis base catalysis are noteworthy.[2] Denmark et al. elegantly utilized Lewis base catalysis for enantioselective olefin functionalizations.[3] Similarly, Lewis base-catalyzed halofunctionalization[4] and trifluoromethylthiolation of olefins are also reported.[5] Despite these developments, Lewis base-catalyzed thiocyanation reactions remain underexplored. We unveil here a Lewis base/Brønsted acid-cocatalyzed thiocyanation of unsaturated amides and thioamides (Scheme 1a). Thiocyanates are important intermediates for the synthesis of a broad array of sulfur-containing compounds.[6] Natural products containing a thiocyanate group are also known (Scheme 1b). Their utility has prompted the development of several methods for thiocyanation.[7] The reaction of aromatic and heteroaromatic arenes with nucleophilic thiocyanates (MSCN, M = K, NH_4^+, etc.) via a thiocyano radical is broadly studied.[8] Visible-light-mediated thiocyanation of arenes, heteroarenes, and the addition of *N*-thiocyanatosulfoximines to styrene is also reported.[9] More recently, an inclination toward the development of electrophilic thiocyanating reagents has emerged.[10] In 2018, *N*-thiocyanatosaccharin was developed for the thiocyanation of indoles, aromatic ketones, oxindoles, and *β*-ketocarbonyl compounds.[10e] TMSCl-catalyzed electrophilic thiocyano-oxy fuctionalization of olefins was reported by Chen et al.[10d] Very recently, through the same mechanistic concept, they have reported the semipinacol rearrangement of allylic alcohols.[10a] Zhao et al. also revealed an elegant report on selenide-catalyzed thiocyanoaminocyclization of olefins.[10b] Notwithstanding these developments, thiocyanation of unsaturated amides and thioamides remains elusive. Herein we present a Lewis base/Brønsted acid-cocatalyzed thiocyanation of unsaturated thioamides and amides.

Scheme 1. Lewis Base-Catalyzed Olefin Functionalizations and Thiocyanate in Natural Products



At the outset, thioamide **1a** was chosen as a model substrate for the reaction conditions optimization (Table 1). Thioamides are an intrinsically challenging substrate for electrophilic olefin functionalization. The substrate−electrophile interaction poses major resistance to catalysis, and often complex background reactions are observed. We also noticed complete decomposition of the starting material in the absence of any catalyst (entry 1). Contemplating that a Lewis base can catalyze the reaction via activation of a thiocyanating reagent (**2**), different Lewis bases were screened (entries 2−6). The reaction was indeed catalyzed by dibenzyl selenium; however, **3a** was obtained in only 28% yield (entry 2). Screening of diphenyl selenide yielded **3a** in 45% yield (entry 3). Shifting to a stronger Lewis base, triphenylphosphine selenide improved the reaction yield to 54% (entry 4). It is important to note that triphenylphosphine selenide outperformed the corresponding oxide and sulfide derivatives (entries 5 and 6). These results validate the importance of Lewis base activation of a thiocyanating reagent. Attempts to further improve the reaction yield by modulating the thiocyanating reagent,

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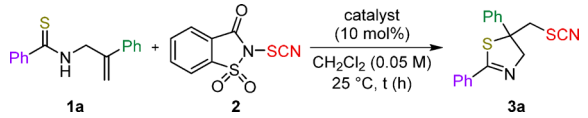
Table 1. Reaction Conditions Optimization for Thiocyanation of β,γ-Unsaturated Thioamide 1a[a]



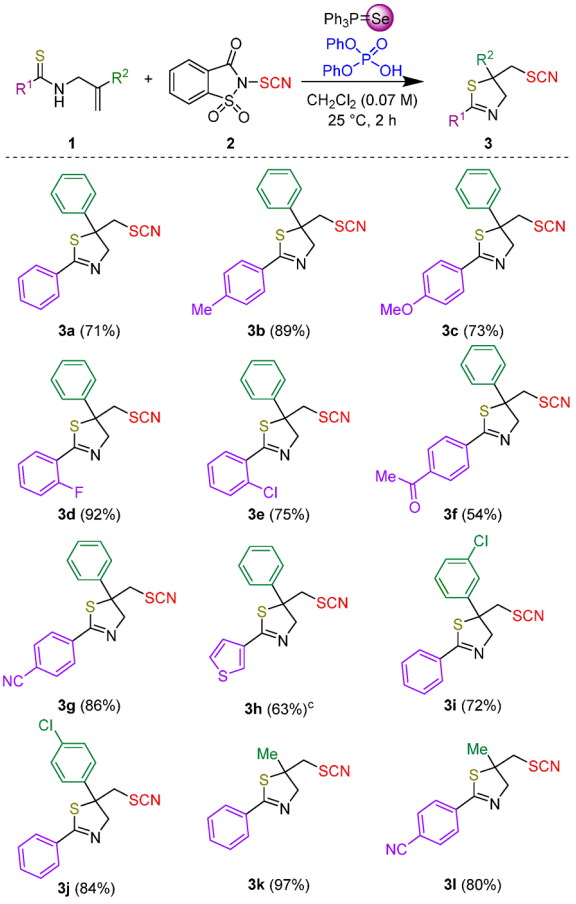
entry	Lewis base	Brønsted acid	t (h)	yield (%)[b]
1			16	<10
2	Bn_2Se		8	28
3	Ph_2Se		8	45
4	Ph_3PSe		8	54
5	Ph_3PO		8	37
6	Ph_3PS		8	42
7		CF_3CO_2H	8	32
8	Ph_3PSe	CF_3CO_2H	8	58
9	Ph_3PSe	CF_3CO_2H	16	64
10[d]	Ph_3PSe	CF_3CO_2H	16	60
11[e]	Ph_3PSe	CF_3CO_2H	16	38
12[f]	Ph_3PSe	CF_3CO_2H	16	30
13[g]	Ph_3PSe	CF_3CO_2H	16	12
14[h]	Ph_3PSe	CF_3CO_2H	16	9
15	Ph_3PSe	CH_3SO_3H	8	47
16	Ph_3PSe	CH_3CO_2H	8	60
17	Ph_3PSe	$(C_6H_5O)_2P(O)OH$	1	73
18	Ph_3PSe	$(C_6H_5O)_2P(O)OH$	2	92 (71)[c]

[a]Reaction conditions: **1a** (0.1 mmol, 1.0 equiv), **2** (0.15 mmol, 1.5 equiv), Lewis base (0.01 mmol, 0.1 equiv), and Brønsted acid (0.01 mmol, 0.1 equiv). [b]^{1}H NMR yield. [c]Isolated yield. [d]Solvent: $CHCl_3$. [e]Solvent: CH_3CN. [f]Solvent: $(CH_3)_2CO$. [g]Solvent: $C_6H_5CH_3$. [h]Solvent: DMF.

concentration, and temperature were futile. Inspired by Denmark's work on cooperative Lewis base/Brønsted acid catalysis for enantioselective bromoetherification,[11] we inferred that the addition of Brønsted acid cocatalyst might be helpful. The catalytic combination of triphenylphosphine selenide and trifluoroacetic acid (TFA) moderately improved the reaction yield to 58% (entry 8). At this point, the effects of different solvents (entries 9−14) such as chloroform, acetonitrile, acetone, toluene, and *N*,*N*-dimethylformamide (DMF) were examined; however, dichloromethane remained the solvent of choice (entry 9). Screening of methanesulfonic acid and acetic acid could not render significant enhancement in the reaction yield (entries 15 and 16). The major influence of Lewis base/Brønsted acid cocatalysis was realized with the combination of triphenylphosphine selenide and diphenyl phosphate (entries 17 and 18). The reaction was adeptly catalyzed, and **3a** was obtained in a 92% ^{1}H NMR yield (71% isolated yield) after 2 h (entry 18).

With the optimized reaction conditions in hand (Table 1, entry 18), the generality of this thiocyanation reaction was explored. As summarized in Table 2, a broad range of β,γ-unsaturated thioamides underwent thiocyanation by Lewis base/Brønsted acid cocatalysis (Table 2). Both electron-rich and electron-deficient aryl substitutions were well tolerated. With heteroaryl substituted unsaturated thioamides, the reaction took longer than usual, after the reaction time of 4 h, the product **3h** was obtained in 63% yield. It is noteworthy that substrates bearing cyano and keto functional groups were well tolerated (**3f** and **3g**). Besides, aliphatic substitution on olefin worked exceedingly well furnishing **3k** and **3l** in good yields. Thioamide **4**, comprising 1,2-disubstituted olefin, was

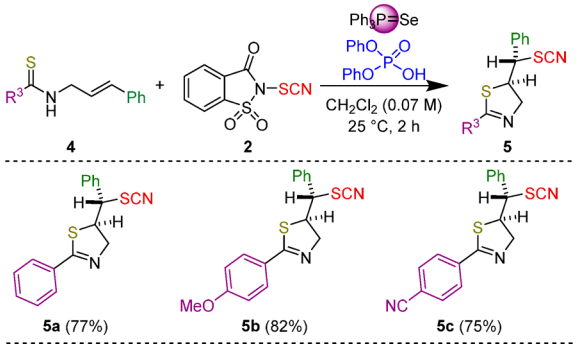
Table 2. Substrate Scope for the Thiocyanation of Unsaturated Thioamides 1[a]



[a]Reaction conditions: **1** (0.1 mmol, 1.0 equiv), **2** (0.15 mmol, 1.5 equiv), Ph_3PSe (0.01 mmol, 0.1 equiv), and $(C_6H_5O)_2P(O)OH$ (0.01 mmol, 0.1 equiv). [b]Isolated yield. [c]The reaction was carried out for 4 h.

also applied to the optimized reaction conditions. The reaction proceeded through 5-*exo*-*trig* cyclization, furnishing **5** as a major product in a good yield (Scheme 2). The structure and relative configuration of **5** was confirmed through an X-ray

Scheme 2. Reaction with 1,2-Disubstituted Olefin



[a]Reaction conditions: **4** (0.1 mmol, 1.0 equiv), **2** (0.15 mmol, 1.5 equiv), Ph_3PSe (0.01 mmol, 0.1 equiv), and $(C_6H_5O)_2P(O)OH$ (0.01 mmol, 0.1 equiv). [b]Isolated yield.

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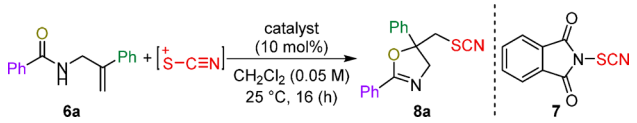
structure analysis of **5a**.[12] The structure and relative configuration of **5b** and **5c** were assigned in analogy to **5a**.

After successfully exploring the substrate scope for thiocyanation of unsaturated thioamides, we attempted the thiocyanation of unsaturated amides. The optimization of reaction conditions was carried out with **6a** as a model substrate (Table 3). The absence of any background reaction

Table 3. Reaction Conditions Optimization for the Thiocyanation of β,γ-Unsaturated Amide 6a[a]



entry	Lewis base	Brønsted acid	[⁺SCN]	yield (%)[b]
1			**2**	<5
2	Ph_3PSe	$(C_6H_5O)_2P(O)OH$	**2**	46
3	Ph_3PSe	$(C_6H_5O)_2P(O)OH$	**7**	71
4[c]	Ph_3PSe	$(C_6H_5O)_2P(O)OH$	**7**	82

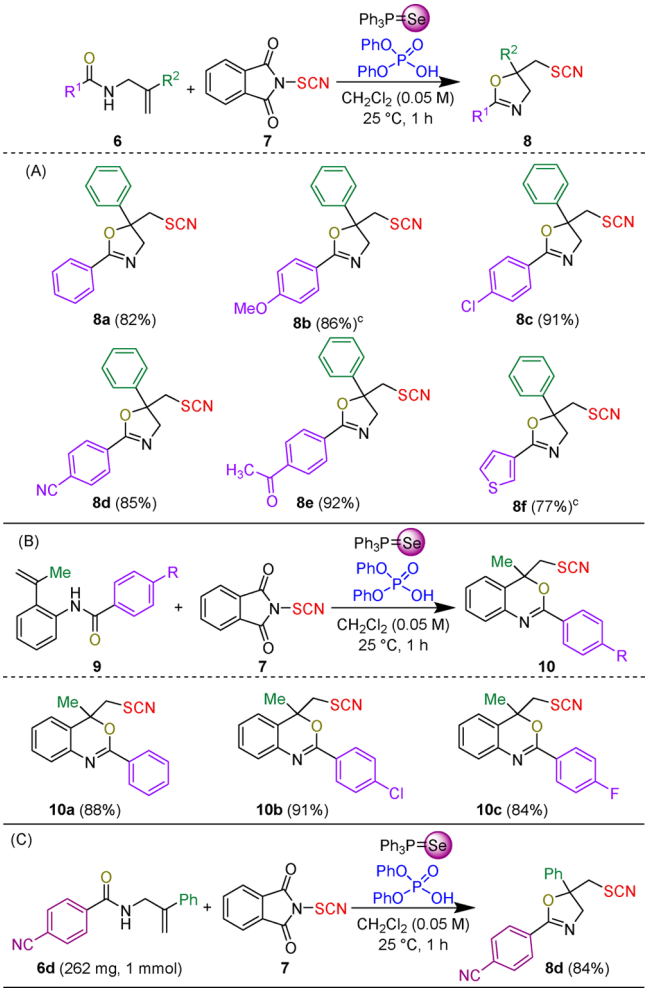
[a]Reaction conditions: **6a** (0.1 mmol, 1.0 equiv), thiocyanating reagent (0.15 mmol, 1.5 equiv), Lewis base (0.01 mmol, 0.1 equiv), and Brønsted acid (0.01 mmol, 0.1 equiv). [b]Isolated yield. [c]Reaction was carried over 1 h with 2.0 equiv of **7**.

paved the way for catalyst screening (entry 1). Even after an extended reaction time of 16 h, the conditions optimized for thiocyanation of **1a** (Table 1, entry 18) yielded **8a** in only 46% yield (Table 3, entry 2). However, tweaking the reaction conditions via altering the thiocyanating reagent from **2** to **7** improved the yield to 71% (entry 3). Finally, by using 2.0 equiv of thiocyanating reagent **7**, the product **8a** was obtained in 82% yield (entry 4). It is worth mentioning that the instability of reagent **7** engendered a serious hurdle, which was surmounted by the in situ generation of **7** from *N*-chlorophthalimide and ammonium thiocyanate.

The optimum reaction conditions for thiocyanation of unsaturated amides (Table 3, entry 4) were applied to different substrates (Table 4). β,γ-Unsaturated amides (**6**) bearing substituents of diverse steric and electronic nature underwent cyclization to afford thiocyanated oxazoline derivatives **8a**−**8f** in good yields (Table 4A). Although the reactivity profile relied upon the electronic nature of the substrates, with electron-donating aryl and heteroaromatic substituents on the amide end, the reaction proceeded slowly, but after 3 h, **8b** and **8f** were obtained in good yield. The electron-deficient substituents on aryl rings such as chloro, cyano, and keto were particularly suitable for this reaction, and thiocyanated oxazoline derivatives **8c**−**8e** were obtained in an excellent yield. The viability of accessing thiocyanated benzo[*d*][1,3]-oxazine derivatives was also probed (Table 4B). With unsaturated benzamides **9a**, **9b**, and **9c**, the reaction proceeded smoothly to provide **10a**, **10b**, and **10c** in 88, 91, and 84% yields , respectively. The scalability of the protocol was tested with β,γ-unsaturated amide **6d** on a 1 mmol scale (Table 4C). No detrimental effect of scale-up was observed, and **8d** was obtained in an 84% yield. Efforts to develop an asymmetric variant of this thiocyanation reaction with chiral phosphoric acids yielded racemic products.[12]

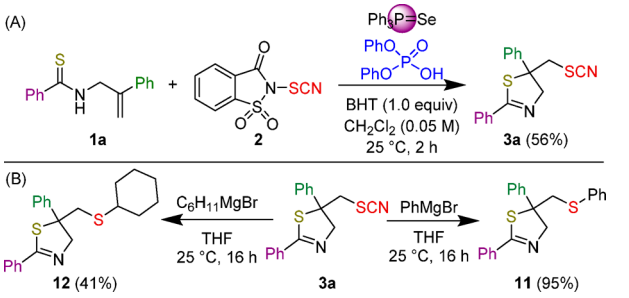
For further understanding, the reaction was carried out in the presence of radical quencher butylated hydroxytoluene (BHT) (Scheme 3A). Even though the reaction proceeded with a diminished yield of **3a** (56%), it disfavors the possibility

Table 4. Substrate Scope for Thiocyanation of Unsaturated Amides 6[a]



[a]Reaction conditions: **6** (0.1 mmol, 1.0 equiv), **7** (0.2 mmol, 2.0 equiv), Ph_3PSe (0.01 mmol, 0.1 equiv), and $(C_6H_5O)_2P(O)OH$ (0.01 mmol, 0.1 equiv). [b]Isolated yield. [c]Reaction was carried for 3 h.

Scheme 3. Synthetic Transformations of 3a and the Influence of the Radical Quencher



of a radical pathway. To demonstrate synthetic utility, the thiocyanated product **3a** was subjected to Grignard addition, which furnished corresponding thiosulfides (Scheme 3B). The thiosulfides are an important class of compounds with several applications in pharmaceutics and biology.[13] Thiocyanated thiazoline **3a** reacted efficiently with phenyl and cyclohexyl Grignard reagents to, respectively, furnish thiosulfides **11** and **12**.

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In summary, a Lewis Base/Brønsted acid-cocatalyzed thiocyanation of unsaturated amides and thioamides is developed. A broad range of substrates reacted with electrophilic thiocyanating reagents to provide thiocyanated thiazoline and oxazoline derivatives in high yields. Given the synthetic and biological relevance of these scaffolds, this method will find broad applications in multiple disciplines.

EXPERIMENTAL SECTION

General Information. Infrared (FT-IR) spectra were recorded on a Bruker-Alpha Spectrometer with ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^1H NMR spectra were recorded on a BRUKER-AV400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26). Data are reported as follows: chemical shift, multiciplity (s = singlet, d = doublet, dd = doublet of doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. $^{13}C\{^1H\}$ NMR spectra were recorded on a BRUKER-AV400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 77.16). Mass spectra were measured with a Q-TOF microspectrometer.

Unless otherwise noted, all reactions have been carried out with dried and distilled solvents under an atmosphere of argon. Oven-dried (120 °C) glassware with standard vacuum line techniques were used. All work up and purification were carried out with reagent grade solvents in air. Thin-layer chromatography was performed using Merck silica gel 60 F_{254} precoated plates (0.25 mm). Column chromatography was performed using silica gel (230−400 mesh) and neutral alumina. The heating reactions were carried out by using a heating stirrer and an oil bath over it. The thiocyanated products are unstable in nature. Thus, quick purification and storage at −20 °C are recommended.

General Procedure for Thiocyanation of Unsaturated Thioamides. In an oven-dried 15 mL Schlenk tube, **2** (36.0 mg, 0.15 mmol, 1.5 equiv) was added. The reaction flask was degassed *in vacuo*, and DCM (0.5 mL) was added. Subsequently, a solution of triphenylphosphine selenide (3.4 mg, 0.01 mmol, 0.1 equiv) and diphenyl phosphate (2.5 mg, 0.01 mmol, 0.1 equiv) in DCM (0.5 mL) was added. To the resulting mixture, a solution of **1** (0.1 mmol, 1.0 equiv) in DCM (0.5 mL) was added. The reaction mixture was stirred at 25 °C for 2 h. The reaction was monitored by TLC and diluted with H_2O (5 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography over neutral alumina to afford **3**.

2,5-Diphenyl-5-(thiocyanatomethyl)-4,5-dihydrothiazole (3a). Light yellow oil (22 mg, 0.071 mmol, 71% yield). Compound **3a** was purified over neutral alumina using 4:96 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3019 (br), 2400 (w), 2163 (w). ^1H NMR (400 MHz, $CDCl_3$): δ 7.89−7.82 (m, 2H), 7.55−7.34 (m, 8H), 4.92 (d, J = 16.2 Hz, 1H), 4.55 (d, J = 16.2 Hz, 1H), 3.70 (d, J = 13.2 Hz, 1H), 3.64 (d, J = 13.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.5, 138.9, 132.8, 131.9, 129.3, 128.8, 128.7, 128.4, 127.3, 111.7, 73.5, 69.4, 47.0. HRMS (ESI+): calcd for $C_{17}H_{15}N_2S_2$ ([M + H]$^+$), 311.0677; found, 311.0670.

5-Phenyl-5-(thiocyanatomethyl)-2-(*p*-tolyl)-4,5-dihydrothiazole (3b). Light yellow oil (29 mg, 0.089 mmol, 89% yield). Compound **3b** was purified over neutral alumina using 6:94 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3019 (w), 2163 (w), 1541 (w). ^1H NMR (400 MHz, $CDCl_3$): δ 7.77−7.70 (m, 2H), 7.47−7.32 (m, 5H), 7.27−7.21 (m, 2H), 4.88 (d, J = 16.3 Hz, 1H), 4.53 (d, J = 16.3 Hz, 1H), 3.69 (d, J = 13.4 Hz, 1H), 3.63 (d, J = 13.4 Hz, 1H), 2.40 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.4, 142.5, 139.0, 130.1, 129.5, 129.3, 128.7, 128.3, 127.3, 111.8, 73.4, 69.2, 47.0, 21.7. HRMS (ESI+): calcd for $C_{18}H_{17}N_2S_2$ ([M + H]$^+$), 325.0833; found, 325.0818.

2-(4-Methoxyphenyl)-5-phenyl-5-(thiocyanatomethyl)-4,5-dihydrothiazole (3c). Light yellow oil (25 mg, 0.073 mmol, 73% yield). Compound **3c** was purified over neutral alumina using 10:90 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2163 (w), 1606 (w), 1509 (w). ^1H NMR (400 MHz, $CDCl_3$): δ 7.84−7.75 (m, 2H), 7.46−7.33 (m, 5H), 6.98−6.90 (m, 2H), 4.87 (d, J = 15.9 Hz, 1H), 4.52 (d, J = 15.9 Hz, 1H), 3.86 (s, 3H), 3.69 (d, J = 13.2 Hz, 1H), 3.63 (d, J = 13.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.8, 162.6, 139.0, 130.1, 129.3, 128.7, 127.3, 125.6, 114.2, 111.8, 73.3, 69.3, 55.6, 47.0. HRMS (ESI+): calcd for $C_{18}H_{17}N_2OS_2$ ([M + H]$^+$), 341.0782; found, 341.0778.

2-(2-Fluorophenyl)-5-phenyl-5-(thiocyanatomethyl)-4,5-dihydrothiazole (3d). Light yellow oil (30 mg, 0.092 mmol, 92% yield). Compound **3d** was purified over neutral alumina using 4:96 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2157 (w), 1596 (w). ^1H NMR (400 MHz, $CDCl_3$): δ 7.91 (td, J = 7.6, 1.8 Hz, 1H), 7.51−7.33 (m, 6H), 7.25−7.13 (m, 2H), 4.90 (dd, J = 16.6, 1.2 Hz, 1H), 4.52 (d, J = 16.6 Hz, 1H), 3.70 (d, J = 13.3 Hz, 1H), 3.63 (d, J = 13.3 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 162.5, 160.7 (d, J = 254 Hz), 138.9, 133.2 (d, J = 8.7 Hz), 130.4, 129.4, 128.8, 127.3, 124.6, 120.9 (d, J = 10.8 Hz), 116.7 (d, J = 22.2 Hz), 111.7, 72.3, 68.8, 46.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ —110.6. HRMS (ESI+): calcd for $C_{17}H_{14}FN_2S_2$ ([M + H]$^+$), 329.0582; found, 329.0574.

2-(2-Chlorophenyl)-5-phenyl-5-(thiocyanatomethyl)-4,5-dihydrothiazole (3e). Light yellow oil (26 mg, 0.075 mmol, 75% yield). Compound **3e** was purified over neutral alumina using 10:90 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3019 (w), 2157 (w). ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 (dd, J = 7.7, 1.8 Hz, 1H), 7.52−7.29 (m, 8H), 4.92 (d, J = 16.0 Hz, 1H), 4.55 (d, J = 16.0 Hz, 1H), 3.75 (d, J = 13.2 Hz, 1H), 3.67 (d, J = 13.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.8, 138.7, 132.7, 132.4, 131.7, 130.74, 130.70, 129.4, 128.9, 127.3, 127.1, 111.7, 72.7, 70.3, 46.8. HRMS (ESI+): calcd for $C_{17}H_{14}ClN_2S_2$ ([M + H]$^+$), 345.0287; found, 345.0279.

1-(4-(5-Phenyl-5-(thiocyanatomethyl)-4,5-dihydrothiazol-2-yl)phenyl)ethan-1-one (3f). Light yellow oil (19 mg, 0.054 mmol, 54% yield). Compound **3f** was purified over neutral alumina using 10:90 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2163 (w), 1685 (m). ^1H NMR (400 MHz, $CDCl_3$): δ 8.04−7.98 (m, 2H), 7.96−7.90 (m, 2H), 7.48−7.33 (m, 5H), 4.95 (d, J = 16.4 Hz, 1H), 4.59 (d, J = 16.4 Hz, 1H), 3.70 (d, J = 13.3 Hz, 1H), 3.64 (d, J = 13.3 Hz, 1H), 2.64 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 197.4, 166.7, 139.4, 138.8, 136.6, 129.4, 128.9, 128.7, 128.6, 127.2, 111.7, 73.7, 69.9, 47.0, 26.9. HRMS (ESI+): calcd for $C_{19}H_{17}N_2OS_2$ ([M + H]$^+$), 353.0782; found, 353.0772.

4-(5-Phenyl-5-(thiocyanatomethyl)-4,5-dihydrothiazol-2-yl)benzonitrile (3g). Light yellow oil (29 mg, 0.086 mmol, 86% yield). Compound **3g** was purified over neutral alumina using 10:90 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2231 (w), 2156 (w), 1600 (w). ^1H NMR (400 MHz, $CDCl_3$): δ 7.99−7.92 (m, 2H), 7.78−7.71 (m, 2H), 7.48−7.32 (m, 5H), 4.96 (d, J = 16.5 Hz, 1H), 4.60 (d, J = 16.5 Hz, 1H), 3.68 (d, J = 13.4 Hz, 1H), 3.63 (d, J = 13.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.8, 138.5, 136.4, 132.5, 129.3, 128.9, 128.8, 127.0, 118.0, 115.2, 111.5, 73.6, 70.3, 46.8. HRMS (ESI+): calcd for $C_{18}H_{14}N_3S_2$ ([M + H]$^+$), 336.0629; found, 336.0621.

5-Phenyl-5-(thiocyanatomethyl)-2-(thiophen-3-yl)-4,5-dihydrothiazole (3h). White solid (20 mg, 0.063 mmol, 63% yield). Compound **3h** was purified over 230−400 silica gel mesh using 10:90 EtOAc/petroleum ether as an eluent. The reaction was carried over 4 h. The product obtained from column chromatography was recrystallized twice in CH_2Cl_2/hexane mixture. FT-IR (thin film): 2157 (w), 1652 (w). ^1H NMR (400 MHz, $CDCl_3$): δ 7.81 (dd, J = 3.96, 1.8 Hz, 1H), 7.52 (dd, J = 6.3, 3.8 Hz, 1H), 7.45−7.34 (m, 6H), 4.85 (d, J = 16.0 Hz, 1H), 4.49 (d, J = 16.0 Hz, 1H), 3.69 (d, J = 13.3 Hz, 1H), 3.64 (d, J = 13.3 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 161.8, 138.9, 135.6, 129.4, 129.2, 128.8, 127.3, 126.9,

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126.7, 111.7, 73.3, 69.8, 47.0. HRMS (ESI+): calcd for $C_{15}H_{13}N_2S_3$ ([M + H]$^+$), 317.0241; found, 317.0226.

5-(3-Chlorophenyl)-2-phenyl-5-(thiocyanatomethyl)-4,5-dihydrothiazole (3i). Light yellow oil (25 mg, 0.072 mmol, 72% yield). Compound **3i** was purified over 100−200 silica gel mesh using 6:94 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3019 (w), 2157 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87−7.81 (m, 2H), 7.55−7.41 (m, 3H), 7.41−7.34 (m, 3H), 7.27−7.24 (m, 1H), 4.88 (d, J = 16.2 Hz, 1H), 4.54 (d, J = 16.2 Hz, 1H), 3.68 (d, J = 13.4 Hz, 1H), 3.63 (d, J = 13.4 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.3, 141.1, 135.4, 132.6, 132.1, 130.6, 129.0, 128.9, 128.4, 127.6, 125.5, 111.5, 73.7, 69.0, 46.7. HRMS (ESI+): calcd for $C_{17}H_{14}ClN_2S_2$ ([M + H]$^+$), 345.0287; found, 345.0284.

5-(4-Chlorophenyl)-2-phenyl-5-(thiocyanatomethyl)-4,5-dihydrothiazole (3j). Light yellow oil (29 mg, 0.084 mmol, 84% yield). Compound **3j** was purified over 100−200 silica gel mesh using 6:94 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2157 (w), 1492 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86−7.81 (m, 2H), 7.54−7.37 (m, 5H), 7.36−7.28 (m, 2H), 4.87 (d, J = 16.2 Hz, 1H), 4.52 (d, J = 16.2 Hz, 1H), 3.68 (d, J = 13.4 Hz, 1H), 3.63 (d, J = 13.4 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.4, 137.6, 134.9, 132.7, 132.1, 129.5, 128.8, 128.7, 128.4, 111.6, 73.8, 68.9, 46.7. HRMS (ESI+): calcd for $C_{17}H_{14}ClN_2S_2$ ([M + H]$^+$), 345.0287; found, 345.0284.

5-Methyl-2-phenyl-5-(thiocyanatomethyl)-4,5-dihydrothiazole (3k). Colorless oil (24 mg, 0.097 mmol, 97% yield). Compound **3k** was purified over neutral alumina using 6:94 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2158 (w), 1604 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82−7.73 (m, 2H), 7.52−7.36 (m, 3H), 4.45 (d, J = 16.3 Hz, 1H), 4.14 (d, J = 16.3 Hz, 1H), 3.42 (d, J = 13.4 Hz, 1H), 3.35 (d, J = 13.4 Hz, 1H), 1.78 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.6, 133.0, 131.8, 128.8, 128.3, 112.6, 74.6, 62.6, 45.7, 24.8. HRMS (ESI+): calcd for $C_{12}H_{13}N_2S_2$ ([M + H]$^+$), 249.0520; found, 249.0507.

4-(5-Methyl-5-(thiocyanatomethyl)-4,5-dihydrothiazol-2-yl)benzonitrile (3l). Light yellow oil (22 mg, 0.08 mmol, 80% yield). Compound **3l** was purified over neutral alumina using 6:94 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2216 (w), 2158 (w), 1604 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88−7.86 (m, 2H), 7.72−7.70 (m, 2H), 4.50 (d, J = 16.7 Hz, 1H), 4.19 (d, J = 16.7 Hz, 1H), 3.40 (d, J = 13.6 Hz, 1H), 3.35 (d, J = 13.7 Hz, 1H), 1.78 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.0, 136.7, 132.5, 128.9, 118.2, 115.1, 112.3, 74.8, 63.6, 45.5, 24.9. HRMS (ESI+): calcd for $C_{13}H_{12}N_3S_2$ ([M + H]$^+$), 274.0473; found, 274.0472.

(*R)-2-Phenyl-5-((*S**)-phenyl(thiocyanato)methyl)-4,5-dihydrothiazole (5a).** Light yellow oil (24 mg, 0.077 mmol, 77% yield, dr: >20:1). Compound **5a** was purified over 230−400 silica gel mesh using 6:94 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2361 (w), 2157 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75−7.68 (m, 2H), 7.50−7.32 (m, 8H), 4.84 (dd, J = 16.1, 3.4 Hz, 1H), 4.75−4.67 (m, 1H), 4.61 (dd, J = 16.1, 8.0 Hz, 1H), 4.28 (d, J = 10.5 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.0, 137.9, 132.7, 131.7, 129.5, 129.3, 128.7, 128.4, 127.8, 110.3, 68.5, 56.7, 54.7. HRMS (ESI+): calcd for $C_{17}H_{15}N_2S_2$ ([M + H]$^+$), 311.0677; found, 311.0670. Recrystallization from the CH_2Cl_2/hexane mixture yielded diffraction quality crystals.

(*R)-2-(4-Methoxyphenyl)-5-((*S**)-phenyl(thiocyanato)-methyl)-4,5-dihydrothiazole (5b).** Light yellow oil (28 mg, 0.082 mmol, 82% yield, dr: >20:1). Compound **5b** was purified over 230−400 silica gel mesh using 10:90 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2157 (w), 1606 (m), 1509 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70−7.61 (m, 2H), 7.44−7.33 (m, 5H), 6.90−6.84 (m, 2H), 4.83 (dd, J = 15.8, 3.6 Hz, 1H), 4.72−4.65 (m, 1H), 4.57 (dd, J = 16.1, 7.9 Hz, 1H), 4.28 (d, J = 10.5 Hz, 1H), 3.83 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.5, 162.4, 138.0, 130.1, 129.5, 129.3, 127.8, 125.4, 114.0, 110.3, 68.3, 56.6, 55.5, 54.7. HRMS (ESI+): calcd for $C_{18}H_{17}N_2OS_2$ ([M + H]$^+$), 341.0782; found, 341.0780.

4-((*R)-5-((*S**)-Phenyl(thiocyanato)methyl)-4,5-dihydrothiazol-2-yl)benzonitrile (5c).** Light yellow oil (25 mg, 0.075 mmol, 75% yield, dr: >20:1). Compound **5c** was purified over 230−400 silica gel mesh using 10:90 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2230 (m), 2153 (m), 1716 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83−7.78 (m, 2H), 7.68−7.64 (m, 2H), 7.43−7.32 (m, 5H), 4.86 (dd, J = 16.4, 3.9 Hz, 1H), 4.82−4.76 (m, 1H), 4.65 (dd, J = 16.4, 7.9 Hz, 1H), 4.29 (d, J = 10.3 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 165.4, 137.5, 136.4, 132.5, 129.7, 129.4, 128.9, 127.7, 118.1, 115.0, 110.1, 68.7, 56.5, 55.5. HRMS (ESI+): calcd for $C_{18}H_{14}N_3S_2$ ([M + H]$^+$), 336.0629; found, 336.0629.

General Procedure for Thiocyanation of Unsaturated Amides. In an oven-dried 15 mL Schlenk tube, *N*-chlorophthalimide (36.0 mg, 0.2 mmol, 2.0 equiv) and ammonium thiocyanate (15.0 mg, 0.2 mmol, 2.0 equiv) were taken. The reaction flask was degassed *in vacuo*, and DCM (1.0 mL) was added. The resulting mixture was stirred at 25 °C for 0.5 h. Subsequently, a solution of triphenylphosphine selenide (3.4 mg, 0.01 mmol, 0.1 equiv) and diphenyl phosphate (2.5 mg, 0.01 mmol, 0.1 equiv) in DCM (0.5 mL) was added. To the resulting mixture, a solution of **6** (0.1 mmol, 1.0 equiv) in DCM (0.5 mL) was added. The reaction mixture was stirred at 25 °C for 1 h. The reaction was monitored by TLC, and H_2O (5 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography over 100−200 silica gel mesh to afford **8**.

2,5-Diphenyl-5-(thiocyanatomethyl)-4,5-dihydrooxazole (8a). Yellow oil (24 mg, 0.082 mmol, 82% yield). Compound **8a** was purified over 230−400 silica gel mesh using 15:85 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2158 (w), 1653 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13−8.05 (m, 2H), 7.54−7.34 (m, 8H), 4.42 (d, J = 15.1 Hz, 1H), 4.31 (d, J = 15.1 Hz, 1H), 3.57 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.1, 141.2, 132.1, 129.2, 128.9, 128.8, 128.7, 128.6, 124.8, 111.9, 87.4, 66.9, 44.8. HRMS (ESI+): calcd for $C_{17}H_{15}N_2OS$ ([M + H]$^+$), 295.0905; found, 295.0893.

2-(4-Methoxyphenyl)-5-phenyl-5-(thiocyanatomethyl)-4,5-dihydrooxazole (8b). Light yellow oil (28 mg, 0.086 mmol, 86% yield). Compound **8b** was purified over 100−200 silica gel mesh using 14:86 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2157 (w), 1651 (m), 1609 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05−7.98 (m, 2H), 7.48−7.32 (m, 5H), 7.01−6.93 (m, 2H), 4.38 (d, J = 14.8 Hz, 1H), 4.28 (d, J = 14.8 Hz, 1H), 3.87 (s, 3H), 3.56 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.9, 162.7, 141.3, 130.4, 129.2, 128.7, 124.8, 119.4, 114.1, 112.0, 87.1, 66.9, 55.5, 44.8. HRMS (ESI+): calcd for $C_{18}H_{17}N_2O_2S$ ([M + H]$^+$), 325.1011; found, 325.1007.

2-(4-Chlorophenyl)-5-phenyl-5-(thiocyanatomethyl)-4,5-dihydrooxazole (8c). Light yellow oil (30 mg, 0.091 mmol, 91% yield). Compound **8c** was purified over 100−200 silica gel mesh using 8:92 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2157 (w), 1655 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04−8.00 (m, 2H), 7.88−7.85 (m, 1H), 7.77−7.73 (m, 1H), 7.46−7.41 (m, 4H), 7.39−7.27 (m, 2H), 4.42 (d, J = 15.2 Hz, 1H), 4.32 (d, J = 15.2 Hz, 1H), 3.55 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.2, 162.2, 141.0, 138.4, 134.4, 132.8, 129.9, 129.2, 129.0, 128.9, 125.4, 124.8, 124.6, 123.7, 111.9, 87.7, 66.8, 44.8. HRMS (ESI+): calcd for $C_{17}H_{14}ClN_2OS$ ([M + H]$^+$), 329.0515; found, 329.0508.

4-(5-Phenyl-5-(thiocyanatomethyl)-4,5-dihydrooxazol-2-yl)benzonitrile (8d). Light yellow oil (27 mg, 0.085 mmol, 85% yield). Compound **8d** was purified over 100−200 silica gel mesh using 12:88 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2231 (w), 2157 (w), 1656 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22−8.17 (m, 2H), 7.80−7.73 (m, 2H), 7.48−7.35 (m, 5H), 4.46 (d, J = 15.8 Hz, 1H), 4.36 (d, J = 15.8 Hz, 1H), 3.57 (d, J = 14.1 Hz, 1H), 3.52 (d, J = 14.1 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.7, 140.8, 132.5, 130.9, 129.3, 129.2, 129.0, 124.7, 118.2, 115.5, 111.8, 88.3, 66.9, 44.7. HRMS (ESI+): calcd for $C_{18}H_{14}N_3OS$ ([M + H]$^+$, 320.0858; found, 320.0853. On a 1 mmol scale, **8d** was obtained in 84% yield (270 mg, 0.84 mmol)

1-(4-(5-Phenyl-5-(thiocyanatomethyl)-4,5-dihydrooxazol-2-yl)phenyl)ethan-1-one (8e). Light yellow oil (31 mg, 0.092 mmol,

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92% yield). Compound **8e** was purified over 100−200 silica gel mesh using 12:88 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2157 (w), 1686 (w), 1654 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22−8.15 (m, 2H), 8.08−7.99 (m, 2H), 7.50−7.32 (m, 5H), 4.46 (d, J = 15.4 Hz, 1H), 4.36 (d, J = 15.4 Hz, 1H), 3.59 (d, J = 14.1 Hz, 1H), 3.55 (d, J = 14.1 Hz, 1H), 2.65 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 197.6, 162.3, 140.9, 139.6, 130.9, 130.4, 129.3, 128.9, 128.6, 128.3, 124.7, 111.9, 84.9, 66.9, 44.7, 26.9. HRMS (ESI+): calcd for $C_{19}H_{17}N_2O_2S$ ([M + H]$^+$), 337.1011; found, 337.1010.

5-Phenyl-5-(thiocyanatomethyl)-2-(thiophen-3-yl)-4,5-dihydrooxazole (8f). Light yellow oil (23 mg, 0.077 mmol, 77% yield). Compound **8f** was purified over 100−200 silica gel mesh using 12:88 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2163 (w), 1657 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (dd, J = 2.8, 1.1 Hz, 1H), 7.59 (dd, J = 5.1, 1.1 Hz, 1H), 7.47−7.33 (m, 6H), 4.37 (d, J = 15.0 Hz, 1H), 4.28 (d, J = 15.0 Hz, 1H), 3.57 (d, J = 13.9 Hz, 1H), 3.52 (d, J = 13.9 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 159.9, 141.1, 130.0, 129.2, 129.1, 128.8, 127.3, 126.7, 124.8, 112.0, 87.3, 66.9, 44.7. HRMS (ESI+): calcd for $C_{15}H_{13}N_2OS_2$ ([M + H]$^+$), 301.0469; found, 301.0465.

4-Methyl-2-phenyl-4-(thiocyanatomethyl)-4*H*-benzo[*d*][1,3]oxazine (10a). Light yellow oil (26 mg, 0.088 mmol, 88% yield). Compound **10a** was purified over 100−200 silica gel mesh using 3:97 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2163 (w), 1626 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19−8.13 (m, 2H), 7.55−7.33 (m, 5H), 7.28−7.23 (m, 1H), 7.14 (dd, J = 7.5, 1.1 Hz, 1H), 3.59 (d, J = 13.9 Hz, 1H), 3.45 (d, J = 13.9 Hz, 1H), 1.92 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.5, 138.8, 132.0, 131.9, 130.1, 128.5, 128.1, 127.4, 126.5, 126.1, 123.0, 112.3, 79.0, 44.6, 25.9. HRMS (ESI+): calcd for $C_{17}H_{15}N_2OS$ ([M + H]$^+$), 295.0905; found, 295.0897.

2-(4-Chlorophenyl)-4-methyl-4-(thiocyanatomethyl)-4*H*-benzo[*d*][1,3]oxazine (10b). Light yellow oil (30 mg, 0.091 mmol, 91% yield). Compound **10b** was purified over 230−400 silica gel mesh using 4:96 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3019 (w), 2407 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14−8.06 (m, 2H), 7.46−7.25 (m, 5H), 7.13 (dd, J = 7.7, 1.2 Hz, 1H), 3.58 (d, J = 13.9 Hz, 1H), 3.44 (d, J = 13.9 Hz, 1H), 1.91 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.3, 138.6, 138.2, 130.5, 130.2, 129.4, 128.8, 127.6, 126.4, 126.2, 123.0, 112.2, 79.3, 44.6, 26.0. HRMS (ESI+): calcd for $C_{17}H_{14}ClN_2OS$ ([M + H]$^+$), 329.0515; found, 329.0506.

2-(4-Fluorophenyl)-4-methyl-4-(thiocyanatomethyl)-4*H*-benzo[*d*][1,3]oxazine (10c). Light yellow oil (25 mg, 0.080 mmol, 80% yield). Compound **10c** was purified over 230−400 silica gel mesh using 1.5:98.5 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2163 (w), 1508 (w), 1214 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20−8.15 (m, 2H), 7.44−7.31 (m, 2H), 7.28−7.24 (m, 1H), 7.17−7.09 (m, 3H), 3.58 (d, J = 13.9 Hz, 1H), 3.44 (d, J = 13.9 Hz, 1H), 1.91 (s, 3H).^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 165.3 (d, J = 251.2 Hz), 154.6, 138.7, 130.4 (d, J = 8.9 Hz), 130.1, 128.2 (d, J = 3.1 Hz) 127.4, 126.3, 126.0, 123.0, 115.7, 115.5, 112.2, 79.2, 44.6, 26.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ −107.6. HRMS (ESI+): calcd for $C_{17}H_{14}FN_2OS$ ([M + H]$^+$), 313.0811; found, 313.0806.

General Procedure for Thiocyanation of Unsaturated Amide 6d at 1 mmol Scale. In an oven-dried 50 mL round-bottom flask, *N*-chlorophthalimide(363.0 mg, 2.0 mmol, 2.0 equiv) and ammonium thiocyanate (150.0 mg, 2.0 mmol, 2.0 equiv) were taken. The reaction flask was degassed *in vacuo*, and DCM (8.0 mL) was added. The resulting mixture was stirred at 25 °C for 0.5 h. Subsequently, a solution of triphenylphosphine selenide (34.0 mg, 0.1 mmol, 0.1 equiv) and diphenyl phosphate (25.0 mg, 0.1 mmol, 0.1 equiv) in DCM (2.0 mL) was added. To the resulting mixture, a solution of **6d** (1.0 mmol, 1.0 equiv) in DCM (5.0 mL) was added. The reaction mixture was stirred at 25 °C for 1 h. The reaction was monitored by TLC, and H_2O (15 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography over 100−200 silica gel mesh using 8:92 EtOAc/petroleum ether as an eluent to yield **8d** (270 mg, 0.84 mmol, 84% yield).

General Procedure for Grignard Addition to 3a. In an oven-dried 15 mL Schlenk tube, **3a** (1.0 equiv) was taken. The reaction flask was degassed *in vacuo*, and THF (2.0 mL) was added. Subsequently, the corresponding Grignard reagent (2.0 equiv) was added. The reaction mixture was stirred at 25 °C for 16 h. The reaction was monitored by TLC, and NH_4Cl (5 mL) was added. The aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography over 230−400 silica gel mesh to afford corresponding thiosulfides.

2,5-Diphenyl-5-((phenylthio)methyl)-4,5-dihydrothiazole (11). The reaction was done with 0.07 mmol of **3a**. Colorless oil (24 mg, 0.066 mmol, 95% yield). Compound **12** was purified over 230−400 silica gel mesh using 2:98 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3019 (m), 2407 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87−7.80 (m, 2H), 7.52−7.09 (m, 13H), 4.93 (d, J = 16.0 Hz, 1H), 4.56 (d, J = 16.0 Hz, 1H), 3.73 (d, J = 13.0 Hz, 1H), 3.67 (d, J = 13.0 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.0, 141.4, 136.7, 133.4, 131.5, 130.3, 128.9, 128.7, 128.3, 127.8, 127.3, 126.6, 73.8, 69.9, 47.8. HRMS (ESI+): calcd for $C_{22}H_{20}NS_2$ ([M + H]$^+$), 362.1037; found, 362.1026.

5-((Cyclohexylthio)methyl)-2,5-diphenyl-4,5-dihydrothiazole (12). The reaction was done with 0.1 mmol of **3a**. White solid (16 mg, 0.041 mmol, 41% yield). Compound **12** was purified over 230−400 silica gel mesh using 1:99 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3019 (m), 2361 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88−7.82 (m, 2H), 7.51−7.27 (m, 8H), 4.95 (d, J = 15.8 Hz, 1H), 4.51 (d, J = 15.8 Hz, 1H), 3.29 (d, J = 13.1 Hz, 1H), 3.20 (d, J = 13.1 Hz, 1H), 2.19−2.09 (m, 1H), 1.86−1.58 (m, 6H), 1.19−1.06 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.2, 142.0, 133.4, 131.4, 128.6, 128.5, 128.2, 127.6, 127.3, 73.4, 70.1, 45.3, 43.0, 33.7, 33.6, 26.2, 26.1, 25.7. HRMS (ESI+): calcd for $C_{22}H_{26}NS_2$ ([M + H]$^+$), 368.1507; found, 368.1500.

Thiocyanation of 6a with Chiral Phosphoric Acid Derivatives. *General Procedure.* In an oven-dried 15 mL Schlenk tube, *N*-chlorophthalimide (27.0 mg, 0.15 mmol, 1.5 equiv) and ammonium thiocyanate (11.4 mg, 0.15 mmol, 1.5 equiv) were taken. The reaction flask was degassed *in vacuo*, and DCM (1.0 mL) was added. The resulting mixture was stirred at 25 °C for 0.5 h. The resultant mixture was cooled to −78 °C. Subsequently, a solution of chiral phosphoric acid (8.6 mg, 0.01 mmol, 0.1 equiv) in DCM (0.2 mL) was added. To the resulting mixture, a solution of **6a** (23.7 mg, 0.1 mmol, 1.0 equiv) in DCM (0.8 mL) was added. The reaction mixture was stirred at −78 °C for 48 h. The reaction was monitored by TLC, and H_2O (5 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The conversion and er of product **8a** were determined. The enantiomeric ratio was determined by HPLC analysis using a Daicel Chiralpak AD-H column (IPA/*n*-hexane 10:90, 1.0 mL/min, 20 °C, 254 nm, τ = 14.9 and 15.1 min).[12]

Synthesis of Unsaturated Amides and Thioamides. *Unsaturated Amides.* The unsaturated amides **6** and **9** were prepared by following the reported procedure, and the spectral data are in accordance with the literature.[14] The spectral data for previously unreported unsaturated amides **6e** and **6f** are given below.

*1-(4-Acetylphenyl)-2-((1-phenylvinyl)amino)ethan-1-one (**6e**).* White solid (472 mg, 1.69 mmol, 45% yield). Compound **6e** was purified over 100−200 silica gel mesh using 4:96 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2919 (w), 1683 (s), 1664 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J = 8.4 Hz, 2H), 7.78 (d, J = 8.4 Hz, 2H), 7.47−7.45 (m, 2H), 7.36−7.29 (m, 3H), 6.46 (br s, 1H), 5.52 (s, 1H), 5.31 (s, 1H), 4.53 (d, J = 5.4 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 197.5, 166.6, 144.1, 139.3, 138.4, 138.3, 128.7, 128.6, 128.3, 127.4, 126.2, 114.3, 44.0, 26.9. HRMS (ESI+): calcd for $C_{18}H_{18}NO_2$ ([M + H]$^+$), 280.1338; found, 280.1328.

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*2-((1-Phenylvinyl)amino)-1-(thiophen-3-yl)ethan-1-one (**6f**).* White solid (600 mg, 2.47 mmol, 65% yield). Compound **6f** was purified over 230−400 silica gel mesh using 7:93 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 1629 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81−7.80 (m, 1H), 7.48−7.45 (m, 2H), 7.37−7.28 (m, 5H), 6.07 (br s, 1H), 5.51 (s, 1H), 5.31 (s, 1H), 4.5 (d, J = 5.68 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.0, 144.3, 138.4, 137.5, 128.8, 128.3, 128.2, 126.7, 126.2, 126.1, 114.2, 43.6. HRMS (ESI+): calcd for $C_{14}H_{14}NOS$ ([M + H]$^+$), 244.0796; found, 244.0788.

Unsaturated Thioamides. In an oven-dried flask, **4** (1.0 equiv), THF (2.0 mL/mmol), and Lawesson reagent (1.5 equiv) were taken. The mixture was heated at 60 °C for 4 h. The reaction was concentrated *in vacuo*, and the oil was purified by column chromatography on neutral alumina to obtain unsaturated thioamides.

*N-(2-Phenylallyl)benzothioamide (**1a**).* Yellow oil (120 mg, 0.45 mmol, 45% yield). Compound **1a** was purified over neutral alumina using 2:98 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3020 (w), 1511 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64−7.59 (m, 2H), 7.51−7.47 (m, 2H), 7.45−7.31 (m, 6H), 5.63 (s, 1H), 5.40 (s, 1H), 4.90 (dd, J = 5.1, 0.7 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 199.4, 142.7, 141.9, 137.7, 131.2, 129.2, 128.9, 128.6, 126.7, 126.2, 116.0, 50.9. HRMS (ESI+): calcd for $C_{16}H_{16}NS$ ([M + H]$^+$), 254.1003; found, 254.0996.

*4-Methyl-N-(2-phenylallyl)benzothioamide (**1b**).* Yellow oil (105 mg, 0.34 mmol, 39% yield). Compound **1b** was purified over neutral alumina using 4:96 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3021 (w), 1497 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56−7.47 (m, 4H), 7.41−7.30 (m, 3H), 7.13 (d, J = 8.1 Hz, 2H), 5.62 (s, 1H), 5.39 (s, 1H), 4.89 (d, J = 5.1 Hz, 2H), 2.34 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 199.1, 142.7, 141.8, 139.0, 137.8, 129.2, 128.9, 128.6, 126.7, 126.2, 115.8, 50.8, 21.4. HRMS (ESI+): calcd for $C_{17}H_{18}NS$ ([M + H]$^+$), 268.1160; found, 268.1153.

*4-Methoxy-N-(2-phenylallyl)benzothioamide (**1c**).* Yellow oil (66 mg, 0.23 mmol, 25% yield). Compound **1c** was purified over neutral alumina using 3:97 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 1623 (m), 1489 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66−7.60 (m, 2H), 7.51−7.46 (m, 2H), 7.41−7.30 (m, 3H), 6.85−6.79 (m, 2H), 5.62 (s, 1H), 5.39 (s, 1H), 4.89 (dd, J = 5.1, 0.7 Hz, 2H), 3.81 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 198.2, 162.3, 142.8, 137.8, 134.1, 128.9, 128.6, 126.2, 115.8, 113.8, 55.6, 50.8. HRMS (ESI+): calcd for $C_{17}H_{18}NOS$ ([M + H]$^+$), 284.1109; found, 284.1101.

*2-Fluoro-N-(2-phenylallyl)benzothioamide (**1d**).* Yellow oil (125 mg, 0.46 mmol, 59% yield). Compound **1d** was purified over neutral alumina using 2:98 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3049 (m), 1541 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (td, J = 16.0, 1.8 Hz, 1H), 7.94 (br s, 1H), 7.51−7.45 (m, 2H), 7.41−7.30 (m, 4H), 7.21−7.15 (m, 1H), 7.01 (m, 1H), 5.61 (s, 1H), 5.41 (s, 1H), 4.92 (d, J = 5.1 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 193.6, 157.8 (d, J = 246.8 Hz), 142.4, 137.9, 133.5, 132.5 (d, J = 9.0 Hz), 128.8, 128.5, 126.2, 124.7, 116.0 (d, J = 23.6 Hz), 115.7, 51.0. HRMS (ESI+): calcd for $C_{16}H_{15}FNS$ ([M + H]$^+$), 272.0909; found, 272.0902.

*2-Chloro-N-(2-phenylallyl)benzothioamide (**1e**).* Yellow oil (35 mg, 0.12 mmol, 33% yield). Compound **1e** was purified over neutral alumina using 1.5:98.5 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3019 (m), 1516 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43−7.38 (m, 3H), 7.33−7.12 (m, 7H), 5.54 (s, 1H), 5.35 (s, 1H), 4.80 (dd, J = 5.2, 0.7 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 197.4, 142.3, 141.9, 137.7, 130.5, 130.1, 130.0, 128.8, 128.6, 127.0, 126.3, 116.3, 50.6. HRMS (ESI+): calcd for $C_{16}H_{15}ClNS$ ([M + H]$^+$), 288.0614; found, 288.0601.

*4-Acetyl-N-(2-phenylallyl)benzothioamide (**1f**).* Yellow oil (60 mg, 0.20 mmol, 30% yield). Compound **1f** was purified over neutral alumina using 2:98 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3019 (w), 1684 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J = 8.4 Hz, 2H), 7.69 (br s, 1H), 7.64 (d, J = 8.4 Hz, 2H), 7.50−7.44 (m, 2H), 7.41−7.30 (m, 3H), 5.62 (s, 1H), 5.39 (s, 1H), 4.89 (d, J = 4.8 Hz, 2H), 2.54 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 198.0, 197.4, 145.4, 142.4, 138.6, 137.6, 128.9, 128.7, 128.5, 126.9, 126.1, 116.1, 50.8, 26.8. HRMS (ESI+): calcd for $C_{18}H_{18}NOS$ ([M + H]$^+$), 296.1109; found, 296.1103.

*4-Cyano-N-(2-phenylallyl)benzothioamide (**1g**).* Yellow oil (60 mg, 0.21 mmol, 43% yield). Compound **1g** was purified over neutral alumina using 10:90 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3019 (w), 2232 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68−7.63 (m, 3H), 7.60−7.56 (m, 2H), 7.49−7.44 (m, 2H), 7.39−7.35 (m, 2H), 5.63 (s, 1H), 5.39 (s, 1H), 4.87 (dd, J = 5.3, 0.7 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 197.0, 145.3, 142.2, 137.5, 132.4, 128.9, 128.7, 127.4, 126.1, 118.1, 116.3, 114.4, 50.9. HRMS (ESI+): calcd for $C_{17}H_{15}N_2S$ ([M + H]$^+$), 279.0956; found, 279.0951.

*N-(2-Phenylallyl)thiophene-3-carbothioamide (**1h**).* Yellow oil (49 mg, 0.19 mmol, 23% yield). Compound **1h** was purified over neutral alumina using 2:98 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3019 (w), 1670 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (dd, J = 3.0, 1.3 Hz, 1H), 7.52 (br s, 1H), 7.49−7.43 (m, 1H), 7.39−7.30 (m, 4H), 7.25−7.19 (m, 1H), 5.59 (s, 1H), 5.34 (s, 1H), 4.85 (dd, J = 5.1, 0.6 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 191.7, 143.5, 142.5, 137.7, 128.8, 128.5, 126.6, 126.4, 126.3, 126.1, 115.6, 50.1. HRMS (ESI+): calcd for $C_{14}H_{14}NS_2$ ([M + H]$^+$), 260.0568; found, 260.0557.

*N-(2-(3-Chlorophenyl)allyl)benzothioamide (**1i**).* Yellow oil (75 mg, 0.26 mmol, 32% yield). Compound **1i** was purified over neutral alumina using 2:98 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3019 (w), 1507 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68−7.61 (m, 2H), 7.55 (br s, 1H), 7.50−7.28 (m, 7H), 5.61 (s, 1H), 5.42, (s, 1H), 4.87 (d, J = 5.1 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 199.7, 141.8, 141.7, 139.8, 134.9, 131.3, 130.1, 128.7, 128.6, 126.7, 126.4, 124.3, 116.8, 50.4. HRMS (ESI+): calcd for $C_{16}H_{15}ClNS$ ([M + H]$^+$), 288.0614; found, 288.0605.

*N-2-(4-Chlorophenyl)allyl)benzothioamide (**1j**).* Yellow oil (40 mg, 0.14 mmol, 16% yield). Compound **1j** was purified over neutral alumina using 2:98 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3018 (w), 1493 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64−7.59 (m, 2H), 7.59 (br s, 1H), 7.44−7.38 (m, 3H), 7.35−7.29 (m, 4H), 5.59 (s, 1H), 5.38 (s, 1H), 4.86 (d, J = 5.0 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 199.5, 141.7, 136.2, 134.5, 131.3, 129.0, 128.8, 128.6, 127.5, 126.7, 116.2, 50.5. HRMS (ESI+): calcd for $C_{16}H_{15}ClNS$ ([M + H]$^+$), 288.0614; found, 288.0607.

*N-(2-Methylallyl)benzothioamide (**1k**).* Yellow oil (35 mg, 0.18 mmol, 15% yield). Compound **1k** was purified over neutral alumina using 2:98 EtOAc/petroleum ether as an eluent. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78−7.70 (m, 3H), 7.51−7.41 (m, 1H), 7.40−7.33 (m, 2H), 4.96 (s, 1H), 4.93 (s, 1H), 4.40 (d, J = 5.8 Hz, 2H), 1.83 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 199.7, 141.9, 140.1, 131.2, 128.6, 126.7, 112.6, 52.0, 20.9. HRMS (ESI+): calcd for $C_{11}H_{14}NS$ ([M + H]$^+$), 192.0847; found, 192.0839.

*4-Cyano-N-(2-methylallyl)benzothioamide (**1l**).* Yellow oil (35 mg, 0.18 mmol, 15% yield). Compound **1l** was purified over neutral alumina using 4:96 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3020 (w), 2233 (w), 1519(w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84−7.73 (m, 3H), 7.66 (d, J = 7.8 Hz, 2H), 4.99 (s, 1H), 4.95 (s, 1H), 4.40 (d, J = 4.4 Hz, 2H), 1.84 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 197.4, 145.4, 139.7, 132.3, 127.3, 118.0, 114.3, 113.0, 52.1, 20.8. HRMS (ESI+): calcd for $C_{12}H_{13}N_2S$ ([M + H]$^+$), 217.0799; found, 217.0788.

*N-Cinnamylbenzothioamide (**4a**).* Yellow oil (150 mg, 0.59 mmol, 56% yield). Compound **4a** was purified over neutral alumina using 4:96 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3273 (s), 1651 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81−7.74 (m, 2H), 7.68 (br s, 1H), 7.49−7.44 (m, 1H), 7.42−7.26 (m, 7H), 6.70 (d, J = 15.7 Hz, 1H), 6.37 (dt, J = 15.7, 6.4 Hz, 1H), 4.63 (t, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 199.3, 141.8, 136.2, 134.7, 131.3, 128.8, 128.7, 128.3, 126.8, 126.6, 123.0, 48.98. HRMS (ESI+): calcd for $C_{16}H_{16}NS$ ([M + H]$^+$), 254.1003; found, 254.0994.

*N-Cinnamyl-4-methoxybenzothioamide (**4b**).* Yellow oil (78 mg, 0.275 mmol, 28% yield). Compound **4b** was purified over neutral alumina using 2:98 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 3021 (w), 1605 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 8.3 Hz, 2H), 7.29−7.13 (m, 5H), 6.73 (d, J = 8.2 Hz, 2H), 6.52 (d,

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J = 15.7 Hz, 1H), 6.26−6.17 (m, 1H), 4.46 (m, 3H), 3.69 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 197.8, 162.2, 136.3, 134.1, 133.8, 128.7, 128.0, 126.5, 123.2, 113.6, 55.5, 48.8. HRMS (ESI+): calcd for $C_{17}H_{18}NOS$ ($[M + H]^+$), 284.1109; found, 284.1095.

N-Cinnamyl-4-cyanobenzothioamide (4c). Yellow oil (88 mg, 0.32 mmol, 32% yield). Compound **4c** was purified over neutral alumina using 5:95 EtOAc/petroleum ether as an eluent. FT-IR (thin film): 2232 (w), 1652 (m). ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (br s, 1H) 7.68 (d, J = 7.4 Hz, 2H), 7.45 (d, J = 7.0 Hz, 2H), 7.29−7.13 (m, 5H), 6.55 (d, J = 15.8 Hz, 1H), 6.27−6.17 (m, 1H), 4.45 (s, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 196.6, 145.0, 136.0, 134.7, 132.2, 128.7, 128.2, 127.5, 126.5, 122.3, 118.1, 113.9, 49.0. HRMS (ESI+): calcd for $C_{17}H_{15}N_2S$ ($[M + H]^+$), 279.0956; found, 279.0952.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.9b03275.

Spectral data of new compounds and X-ray analysis (PDF)

X-ray crystallography data for compound **5a** (CIF)

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Notes

The authors declare no competing financial interest.

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