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Switchable Copper-Catalyzed Cascade Synthesis of Thiazolidine-2-thiones and Thiazole-2(3*H*)-thiones

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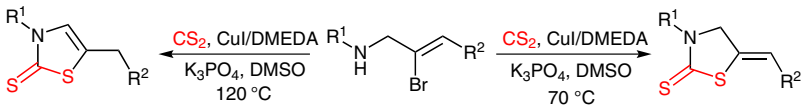

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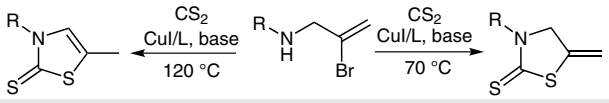
Abstract A novel copper-catalyzed cascade synthesis of thiazolidine-2-thiones from *N*-(2-bromoallyl)amines and carbon disulfide has been developed. The procedure combines carbamodithioic acid formation and copper-catalyzed intramolecular S-vinylation in one sequence. By elevating the temperature, the one-pot reaction efficiently affords thiazole-2(3*H*)-thiones in moderate to good yields.

Key words copper catalyst, carbon disulfide, thiazole synthesis, cascade process

A cascade reaction is one in which a sequence of chemical transformations occurs consecutively in a one-pot procedure and a complex molecule is rapidly built up by the formation of several chemical bonds.[1] The benefits of cascade reactions are well known, such as step-economy and economy of time, labor, and resource management.[2] The development of new cascade reactions is highly desirable.

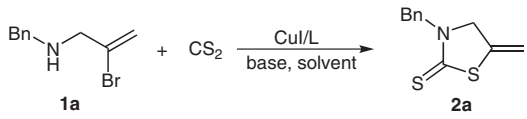
Thiazolidine-2-thiones are a class of important organic intermediates,[3] especially in pharmaceutical chemistry and asymmetric synthesis.[4] Although there are some useful methods for the preparation of thiazolidine-2-thiones from the reaction of vicinal amino alcohols, aziridines, allylamines, and propargylamines with carbon disulfide,[5] no copper-catalyzed intramolecular S-vinylation strategy has been reported.[6] Thiazole-2(3*H*)-thiones are widely used as sulfur-transfer reagents in organic synthesis,[7] as building blocks in biological molecule synthesis, and in material science,[8] but unfortunately few efficient synthetic routes have been reported.[9] In the process of our continued research on the copper-catalyzed synthesis of heterocycles,[10] we recently reported a cascade synthesis of oxazolidin-2-ones from *N*-(2-bromoallyl)amines and potassium carbonate.[11] We were keen to develop an efficient, practical synthesis of thiazolidine-2-thiones via a cascade process of carbamodithioic acid formation and sequential copper-catalyzed intramolecular S-vinylation (Scheme 1). Interestingly, we also constructed thiazole-2(3*H*)-thiones via this cascade process by switching to a higher reaction temperature (Scheme 1). Herein, we wish to report these results in detail.



Scheme 1 Switchable copper-catalyzed cascade synthesis strategy

Our primary investigation was initiated by subjecting *N*-(2-bromoallyl)benzylamine (**1a**) to carbon disulfide in the presence of copper(I) iodide (0.2 equiv), *N*,*N*-dimethylethane-1,2-diamine (DMEDA, 0.4 equiv), and tripotassium phosphate (2.0 equiv), in dimethyl sulfoxide at 60 °C for four hours. To our delight the desired product **2a** was obtained in 41% yield (Table 1, entry 1). When the temperature was increased to 70 °C, the yield sharply increased to 83% (entry 2). Increasing the reaction temperature to 90 °C or 100 °C did not improve the yield (entries 3–5). Varying the S-vinylation coupling ligand to L-proline, *N*,*N*-diethylglycine, *N*-methylglycine, or 1,10-phenanthroline did not improve the yield of **2a** (entries 6–9), and changing the solvent to *N*,*N*-dimethylformamide, tetrahydrofuran, or 1,4-dioxane also did not enhance the yield (entries 10–12).

Table 1 Optimization of Reaction Conditions for the Formation of **2a**[a]



1a **2a**

Entry	Ligand	Solvent	Temp (°C)	Yield[b] (%)
1	DMEDA	DMSO	60	41
2	**DMEDA**	**DMSO**	**70**	**83**
3	DMEDA	DMSO	80	75
4	DMEDA	DMSO	90	72
5	DMEDA	DMSO	100	65
6	L-proline	DMSO	70	67
7	*N*,*N*-diethylglycine	DMSO	70	70
8	*N*-methylglycine	DMSO	70	73
9	1,10-phenanthroline	DMSO	70	72
10	DMEDA	DMF	70	58
11	DMEDA	THF	70	70
12	DMEDA	1,4-dioxane	70	69

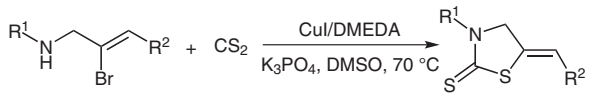
[a] Reaction conditions: *N*-(2-bromoallyl)benzylamine (**1a**, 0.5 mmol), CS_2 (0.75 mmol), CuI (0.1 mmol), ligand (0.2 mmol), K_3PO_4 (1.0 mmol), solvent (2.0 mL), pressurized process vial, 4 h.
[b] Isolated yield of **2a** was based on **1a**.

With the optimal conditions in hand, the use of various *N*-(2-bromoallyl)amines **1a**–**q** was examined (Table 2). Alkylamine substrates **1a**–**k** afforded the corresponding products **2a**–**k** in moderate to good yields (entries 1–11), and it is noteworthy that even strained cyclopropyl-substituted amine **1i** gave the corresponding ring conserved product **2i**. In contrast, the reaction of arylamine **1l** did not give the corresponding product due to the poor nucleophilicity of arylamines (entry 12). More importantly, this process could be extended to the reactions of internal alkenyl bromides **1m**–**q**, and products with retained configuration **2m**–**q** were obtained in good yields under identical reaction conditions (entries 13–17).

According to previous reports,[12] a proposed mechanism for this thiazolidine-2-thione formation process is described in Scheme 2. The substrate **1a** reacts with carbon disulfide in the presence of tripotassium phosphate to form the carbamodithioic acid salt **X**. The oxidative addition of **X** with copper catalyst gives intermediate **Y**. An intramolecular nucleophilic S-vinylation of **Y** generates **Z**. The subsequent reductive elimination in **Z** readily affords the final product **2a** and regenerates a copper species to fulfill the catalytic cycle.

As proof of this mechanism, a controlled experiment was conducted (Scheme 3). When the mixture of **1a** and carbon disulfide was heated for two hours in the presence of tripotassium phosphate, intermediate **X** was observed

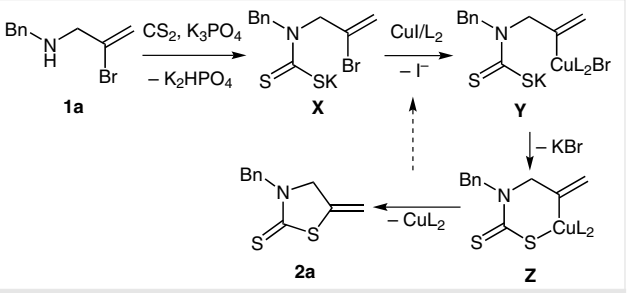
Table 2 Cascade Synthesis of Thiazolidine-2-thiones **2**[a]



1 **2**

Entry	Substrate	R^1	R^2	Product	Yield[b] (%)
1	**1a**	Bn	H	**2a**	83
2	**1b**	Pr	H	**2b**	81
3	**1c**	*i*-Pr	H	**2c**	50
4	**1d**	Bu	H	**2d**	79
5	**1e**	*i*-Bu	H	**2e**	73
6	**1f**	*s*-Bu	H	**2f**	56
7	**1g**	octyl	H	**2g**	74
8	**1h**	$(CH_2)_2Ph$	H	**2h**	82
9	**1i**	*c*-Pr	H	**2i**	69
10	**1j**	*c*-Pent	H	**2j**	75
11	**1k**	Cy	H	**2k**	79
12	**1l**	Ph	H	**2l**	–
13	**1m**	Bn	Ph	**2m**	65
14	**1n**	Pr	Ph	**2n**	78
15	**1o**	*i*-Pr	Ph	**2o**	75
16	**1p**	octyl	Ph	**2p**	68
17	**1q**	Bn	Me	**2q**	62

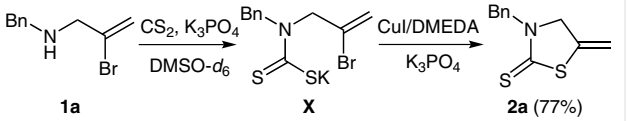
[a] Reaction conditions: **1** (0.5 mmol), CS_2 (0.75 mmol), CuI (0.1 mmol), DMEDA (0.2 mmol), K_3PO_4 (1.0 mmol), DMSO (2.0 mL), pressurized process vial, 70 °C, 4 h.
[b] The isolated yield for **2** was based on the amine **1**.



1a **X** **Y** **2a** **Z**

Scheme 2 Proposed mechanism for the formation of **2a**

and confirmed by NMR spectrum; subsequent copper-catalyzed intramolecular S-vinylation successfully gave the final product.

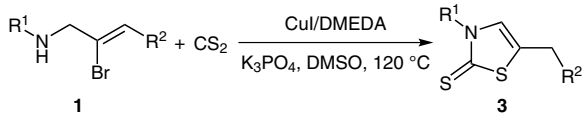


1a **X** **2a** (77%)

Scheme 3 Investigation of the mechanism

In the process of our research, we noticed that the yields of thiazolidine-2-thione (**2a**) decreased when the reaction temperature increased (Table 1, entries 2–5). However, we were surprised to find that the thiazole-2(3*H*)-thione **3a** was obtained in 77% yield when the temperature was 120 °C. Although the yield of **3a** could not be enhanced after painstaking investigation, this result remained a cause for optimism. The cascade process could be switched by the temperature, which encouraged us to extend the scope of the synthesis to thiazole-2(3*H*)-thiones **3a**–**g**,**i**,**k**, which were constructed via the cascade process in moderate to good yields (Table 3). The switching failed to give corresponding thiazole-2(3*H*)-thiones when internal alkenyl bromides such as **1m** and **1q** were used as substrates. This might be due to the stability of the thiazolidine-2-thione products (entries 10 and 11).

Table 3 Cascade Synthesis of Thiazole-2(3*H*)-thiones **3**[a]

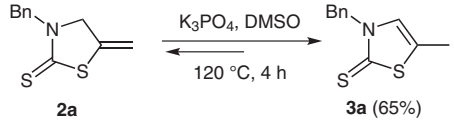


1 **3**

Entry	Substrate	R^1	R^2	Product	Yield[b] (%)
1	**1a**	Bn	H	**3a**	77
2	**1b**	Pr	H	**3b**	74
3	**1c**	*i*-Pr	H	**3c**	66
4	**1d**	Bu	H	**3d**	75
5	**1e**	*i*-Bu	H	**3e**	79
6	**1f**	*s*-Bu	H	**3f**	56
7	**1g**	octyl	H	**3g**	79
8	**1i**	*c*-Pr	H	**3i**	69
9	**1k**	Cy	H	**3k**	76
10[c]	**1m**	Bn	Ph	**3m**	trace
11[c]	**1q**	Bn	Me	**3q**	trace

[a] Reaction conditions: **1** (0.5 mmol), CS_2 (0.75 mmol), CuI (0.1 mmol), DMEDA (0.2 mmol), K_3PO_4 (1.0 mmol), DMSO (2 mL), pressurized process vial, 120 °C, 4 h.
[b] The isolated yield for **3** was based on the amine **1**.
[c] The reaction temperature: 135 °C.

We converted thiazolidine-2-thione **2a** into **3a** by treating it with tripotassium phosphate at 120 °C for four hours. The result showed that about 65% of **2a** was isomerized into the thermodynamically stable product **3a**, but the conversion was not complete (Scheme 4).



2a **3a** (65%)

Scheme 4 The conversion of **2a** into **3a**

In conclusion, we have established the switchable cascade synthesis of thiazolidine-2-thiones and thiazole-2(3*H*)-thiones, via tripotassium phosphate mediated carbamodithioic acid formation/copper-catalyzed intramolecular S-vinylation of *N*-(2-bromoallyl)amines to carbon disulfide. This protocol uses readily available starting materials and mild reaction conditions, and it has high efficiency. Further synthetic applications for this method are under investigation in our laboratory and will be reported in due time.

All solvents were dried by standard procedures. Reactions were followed by TLC using SILG/UV 254 silica gel plates which were visualized via a UV fluorescent lamp or iodine vapor. Melting points were obtained using micro-melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were obtained on a Bruker 500 MHz instrument. LR-MS and HRMS were obtained using EI ionization. All starting materials were of commercial grade, (*Z*)-(2,3-dibromoprop-1-enyl)benzene was synthesized from cinnamaldehyde[13]and (*Z*)-1,2-dibromobut-2-ene was synthesized from *trans*-crotonaldehyde.[14]

3-Benzyl-5-methylenethiazolidine-2-thione (2a); Typical Procedure

N-Benzyl-2-bromoprop-2-en-1-amine (**1a**; 0.5 mmol), CS_2 (0.75 mmol), CuI (0.1 mmol), DMEDA (0.2 mmol), K_3PO_4 (1.0 mmol), anhyd DMSO (2.0 mL), and a stirrer bar were sealed in a pressurized process vial. The vial was heated to 70 °C and the mixture was stirred in an oil bath for 4 h. After cooling to r.t., the mixture was partitioned between EtOAc and H_2O. The organic layer was dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography (silica gel, petroleum ether–EtOAc, 8:1) to afford **2a**[15] as a white solid; yield: 92 mg (83%); mp 44–45 °C.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.32 (m, 5 H), 5.14 (q, *J* = 2.3 Hz, 1 H), 5.09 (dd, *J* = 4.9, 2.7 Hz, 1 H), 5.03 (s, 2 H), 4.58 (t, *J* = 2.6 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 194.5, 136.2, 134.6, 129.0, 128.4, 128.3, 104.8, 61.2, 51.9.

MS (EI): *m*/*z* calcd for $C_{11}H_{11}NS_2$: 221.34; found: 220.5.

5-Methylene-3-propylthiazolidine-2-thione (2b)

Pale yellow liquid; yield: 70 mg (81%).

^1H NMR (500 MHz, $CDCl_3$): δ = 5.21 (q, *J* = 2.3 Hz, 1 H), 5.10 (dd, *J* = 4.9, 2.7 Hz, 1 H), 4.72 (t, *J* = 2.6 Hz, 2 H), 3.76 (dd, *J* = 8.3, 6.9 Hz, 2 H), 1.78–1.69 (m, 2 H), 0.98 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.7, 136.7, 104.5, 62.1, 50.2, 20.0, 11.2.

HRMS (EI^+): *m*/*z* $[M]^+$ calcd for $C_7H_{11}NS_2$: 173.0333; found: 173.0330.

3-Isopropyl-5-methylenethiazolidine-2-thione (2c)

Pale yellow liquid; yield: 43 mg (50%).

^1H NMR (500 MHz, $CDCl_3$): δ = 5.25–5.24 (m, 1 H), 5.21 (dd, *J* = 14.0, 7.2 Hz, 1 H), 5.11 (dd, *J* = 4.8, 2.7 Hz, 1 H), 4.64 (t, *J* = 2.6 Hz, 2 H), 1.27 (d, *J* = 6.8 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.8, 137.0, 104.6, 56.3, 49.3, 19.3.

HRMS (EI^+): *m*/*z* $[M]^+$ calcd for $C_7H_{11}NS_2$: 173.0333; found: 173.0337.

3-Butyl-5-methylenethiazolidine-2-thione (2d)

Pale yellow liquid; yield: 74 mg (79%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.20 (q, *J* = 2.3 Hz, 1 H), 5.10 (dd, *J* = 4.8, 2.7 Hz, 1 H), 4.71 (t, *J* = 2.6 Hz, 2 H), 3.83–3.76 (m, 2 H), 1.72–1.63 (m, 2 H), 1.44–1.35 (m, 2 H), 0.97 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.5, 136.7, 104.5, 62.0, 48.5, 28.7, 20.0, 13.7.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_8H_{13}NS_2$: 187.0489; found: 187.0494.

3-Isobutyl-5-methylenethiazolidine-2-thione (2e)

Pale yellow liquid; yield: 68 mg (73%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.22–5.19 (m, 1 H), 5.10 (dd, *J* = 4.7, 2.3 Hz, 1 H), 4.71 (t, *J* = 2.5 Hz, 2 H), 3.63 (d, *J* = 7.7 Hz, 2 H), 2.17 (dp, *J* = 13.8, 6.9 Hz, 1 H), 0.98 (d, *J* = 6.7 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 194.3, 136.7, 104.5, 62.7, 55.8, 27.1, 20.0.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_8H_{13}NS_2$: 187.0489; found: 187.0490.

3-*sec*-Butyl-5-methylenethiazolidine-2-thione (2f)

Pale yellow liquid; yield: 52 mg (56%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.24 (dd, *J* = 4.5, 2.4 Hz, 1 H), 5.11 (dd, *J* = 4.8, 2.7 Hz, 1 H), 5.09–5.01 (m, 1 H), 4.59 (qt, *J* = 16.3, 2.6 Hz, 2 H), 1.69–1.55 (m, 2 H), 1.24 (d, *J* = 6.8 Hz, 3 H), 0.94 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.5, 137.0, 104.5, 77.3, 77.0, 76.8, 56.3, 54.7, 27.2, 17.1, 10.8.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_8H_{13}NS_2$: 187.0489; found: 187.0492.

5-Methylene-3-octylthiazolidine-2-thione (2g)

Pale yellow liquid; yield: 90 mg (74%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.20 (q, *J* = 2.3 Hz, 1 H), 5.10 (dd, *J* = 4.8, 2.7 Hz, 1 H), 4.71 (t, *J* = 2.6 Hz, 2 H), 3.80–3.75 (t, 2 H), 1.72–1.63 (m, 2 H), 1.41–1.20 (m, 10 H), 0.88 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.5, 136.7, 104.5, 62.0, 48.8, 31.8, 29.2, 29.1, 26.7, 26.6, 22.6, 14.1.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_{12}H_{21}NS_2$: 243.1115; found: 243.1118.

5-Methylene-3-phenethylthiazolidine-2-thione (2h)[16]

White solid; yield: 96 mg (82%); mp 92–93 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 (dd, *J* = 10.4, 4.4 Hz, 2 H), 7.29–7.25 (m, 3 H), 5.10 (q, *J* = 2.3 Hz, 1 H), 5.06 (dd, *J* = 4.9, 2.7 Hz, 1 H), 4.49 (t, *J* = 2.6 Hz, 2 H), 4.05–3.94 (m, 2 H), 3.08–3.03 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.7, 138.0, 136.6, 128.9, 128.8, 126.9, 104.5, 63.0, 50.4, 32.7.

MS (EI): *m*/*z* calcd for $C_{12}H_{13}NS_2$: 235.37, found: 235.9.

3-Cyclopropyl-5-methylenethiazolidine-2-thione (2i)

Pale yellow liquid; yield: 59 mg (69%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.19 (q, *J* = 2.3 Hz, 1 H), 5.06 (dd, *J* = 4.8, 2.7 Hz, 1 H), 4.61 (t, *J* = 2.6 Hz, 2 H), 3.14–3.08 (m, 1 H), 1.01–0.85 (m, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 195.6, 137.3, 104.7, 62.2, 31.4, 6.9.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_7H_9NS_2$: 171.0176; found: 171.0176.

3-Cyclopentyl-5-methylenethiazolidine-2-thione (2j)

Pale yellow liquid; yield: 75 mg (75%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.27–5.17 (m, 2 H), 5.07 (dd, *J* = 4.8, 2.7 Hz, 1 H), 4.65 (t, *J* = 2.6 Hz, 2 H), 2.07–1.96 (m, 2 H), 1.81–1.48 (m, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.1, 136.7, 104.5, 58.6, 57.3, 28.4, 23.7.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_8H_{13}NS_2$: 199.0489; found: 199.0486.

3-Cyclohexyl-5-methylenethiazolidine-2-thione (2k)

White solid; yield: 84 mg (79%); mp 106–108 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.22 (q, *J* = 2.3 Hz, 1 H), 5.09 (dd, *J* = 4.8, 2.7 Hz, 1 H), 4.79 (m, *J* = 11.5, 3.7 Hz, 1 H), 4.65 (t, *J* = 2.6 Hz, 2 H), 1.97–1.83 (m, 4 H), 1.76–1.70 (m, 1 H), 1.50–1.33 (m, 4 H), 1.20–1.09 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.6, 137.3, 104.4, 57.6, 57.3, 29.8, 25.4, 25.3.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_{10}H_{15}NS_2$: 213.0646; found: 213.0648.

(*Z*)-3-Benzyl-5-benzylidenethiazolidine-2-thione (2m)

Yellow solid; yield: 96 mg (65%); mp 139–141 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.44–7.34 (m, 7 H), 7.27 (d, *J* = 8.4 Hz, 1 H), 7.22 (d, *J* = 7.4 Hz, 2 H), 6.42 (t, *J* = 2.2 Hz, 1 H), 5.08 (s, 2 H), 4.77 (d, *J* = 2.3 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.7, 135.2, 134.6, 129.1, 128.7, 128.4, 128.3, 127.8, 127.5, 127.3, 119.4, 62.7, 51.8.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_{17}H_{15}NS_2$: 297.0646; found: 297.0650.

(*Z*)-5-Benzylidene-3-propylthiazolidine-2-thione (2n)

Pale yellow liquid; yield: 97 mg (78%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38 (t, *J* = 7.7 Hz, 2 H), 7.26 (dd, *J* = 12.1, 8.2 Hz, 3 H), 6.49 (t, *J* = 2.1 Hz, 1 H), 4.91 (d, *J* = 2.0 Hz, 2 H), 3.88–3.73 (m, 2 H), 1.77 (dd, *J* = 15.0, 7.5 Hz, 2 H), 1.00 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.8, 135.3, 128.7, 127.8, 127.8, 127.4, 119.1, 63.6, 50.1, 20.1, 11.2.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_{13}H_{15}NS_2$: 249.0646; found: 249.0642.

(*Z*)-5-Benzylidene-3-isopropylthiazolidine-2-thione (2o)

Yellow solid; yield: 93 mg (75%); mp 96–98 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37 (t, *J* = 7.7 Hz, 2 H), 7.25 (t, *J* = 8.9 Hz, 3 H), 6.53 (t, *J* = 2.2 Hz, 1 H), 5.24 (dt, *J* = 13.6, 6.8 Hz, 1 H), 4.82 (d, *J* = 2.3 Hz, 2 H), 1.30 (d, *J* = 6.8 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 191.9, 135.4, 128.7, 128.1, 127.8, 127.4, 119.3, 58.0, 49.3, 19.4.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_{13}H_{15}NS_2$: 249.0646; found: 249.0649.

(*Z*)-5-Benzylidene-3-octylthiazolidine-2-thione (2p)

Pale yellow liquid; yield: 108 mg (68%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38 (t, *J* = 7.7 Hz, 2 H), 7.31– 7.20 (m, 3 H), 6.48 (s, 1 H), 4.90 (d, *J* = 2.0 Hz, 2 H), 3.86–3.74 (m, 2 H), 1.78–1.68 (m, 2 H), 1.37–1.27 (m, 10 H), 0.90 (t, *J* = 6.9 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.5, 135.3, 128.7, 127.8, 127.7, 127.3, 119.1, 63.6, 48.6, 31.7, 29.2, 29.1, 26.7, 26.6, 22.6, 14.0.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_{18}H_{25}NS_2$: 319.1428; found: 319.1432.

(*Z*)-3-Benzyl-5-ethylidenethiazolidine-2-thione (2q)

Pale yellow liquid; yield: 73 mg (62%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38–7.32 (m, 5 H), 5.46 (qt, *J* = 6.8, 2.3 Hz, 1 H), 5.01 (s, 2 H), 4.54–4.51 (m, 2 H), 1.63 (dt, *J* = 6.8, 2.3 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.8, 134.6, 128.8, 128.1, 127.4, 115.0, 77.3, 77.0, 76.8, 60.4, 51.8, 16.0.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_{11}H_{13}NS_2$: 235.0489; found: 235.0481.

3-Benzyl-5-methylthiazole-2(3*H*)-thione (3a); Typical Procedure

N-Benzyl-2-bromoprop-2-en-1-amine (**1a**; 0.5 mmol), CS_2 (0.75 mmol), CuI (0.1 mmol), DMEDA (0.2 mmol), K_3PO_4 (1.0 mmol), anhyd DMSO (2.0 mL) and a stirrer bar were sealed in a pressurized process vial. The vial was heated to 120 °C and the mixture was stirred in an oil bath for 4 h. After cooling to r.t., the mixture was partitioned between EtOAc and H_2O. The organic layer was dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography (silica gel, petroleum ether–EtOAc, 5:1) to afford **3a** as a pale yellow liquid; yield: 85 mg (77%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.29 (m, 5 H), 6.69–6.60 (m, 1 H), 5.32 (s, 2 H), 2.15 (d, *J* = 1.3 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 187.4, 135.2, 129.0, 128.3, 128.2, 127.1, 124.4, 52.5, 12.6.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_7H_9NS_2$: 221.0333; found: 221.0332.

5-Methyl-3-propylthiazole-2(3*H*)-thione (3b)

Pale yellow liquid; yield: 64 mg (74%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.73 (q, *J* = 1.3 Hz, 1 H), 4.09–4.03 (m, 2 H), 2.20 (d, *J* = 1.3 Hz, 3 H), 1.88–1.75 (m, 2 H), 0.96 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 186.7, 127.6, 124.2, 51.1, 21.8, 12.6, 11.0.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_7H_{11}NS_2$: 173.0333; found: 173.0330.

3-Isopropyl-5-methylthiazole-2(3*H*)-thione (3c)

Pale yellow liquid; yield: 57 mg (66%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.81 (q, *J* = 1.3 Hz, 1 H), 5.34 (dt, *J* = 13.6, 6.8 Hz, 1 H), 2.21 (d, *J* = 1.3 Hz, 3 H), 1.36 (d, *J* = 6.8 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 185.9, 124.8, 123.4, 50.2, 21.6, 12.7.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_7H_{11}NS_2$: 173.0333; found: 173.0339.

3-Butyl-5-methylthiazole-2(3*H*)-thione (3d)

Pale yellow liquid; yield: 70 mg (75%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.73 (q, *J* = 1.3 Hz, 1 H), 4.09–4.03 (m, 2 H), 2.21 (d, *J* = 1.3 Hz, 3 H), 1.82–1.73 (m, 2 H), 1.39 (m, *J* = 14.8, 7.4 Hz, 2 H), 0.97 (m, *J* = 7.4, 3.2 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 186.7, 127.5, 124.3, 49.5, 30.6, 19.9, 13.6, 12.6.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_8H_{13}NS_2$: 187.0489; found: 187.0485.

3-Isobutyl-5-methylthiazole-2(3*H*)-thione (3e)

Pale yellow liquid; yield: 74 mg (79%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.70 (q, *J* = 1.3 Hz, 1 H), 3.91 (d, *J* = 7.5 Hz, 2 H), 2.35–2.25 (m, 1 H), 2.20 (d, *J* = 1.3 Hz, 3 H), 0.96 (d, *J* = 6.7 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 186.5, 124.7, 123.6, 55.5, 29.3, 19.5, 12.7, 10.5.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_8H_{13}NS_2$: 187.0489; found: 187.0493.

3-*sec*-Butyl-5-methylthiazole-2(3*H*)-thione (3f)

Pale yellow liquid; yield: 52 mg (56%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.75 (q, *J* = 1.3 Hz, 1 H), 5.22–5.09 (m, 1 H), 2.21 (d, *J* = 1.3 Hz, 3 H), 1.75–1.64 (m, 2 H), 1.30 (d, *J* = 6.8 Hz, 3 H), 0.87 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 186.5, 124.7, 123.6, 55.5, 29.3, 19.5, 12.7, 10.5.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_8H_{13}NS_2$: 187.0489; found: 187.0496.

5-Methyl-3-octylthiazole-2(3*H*)-thione (3g)

Pale yellow liquid; yield: 96 mg (79%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.73 (q, *J* = 1.2 Hz, 1 H), 4.14–4.05 (m, 2 H), 2.20 (d, *J* = 1.2 Hz, 3 H), 1.83–1.72 (m, 2 H), 1.39–1.20 (m, 10 H), 0.88 (t, *J* = 6.9 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 186.6, 127.5, 124.2, 49.7, 31.7, 29.1, 28.5, 26.5, 22.5, 14.0, 12.6.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_{15}H_{21}NS_2$: 243.1115; found: 243.1113.

3-Cyclopropyl-5-methylthiazole-2(3*H*)-thione (3i)

Pale yellow liquid; yield: 59 mg (69%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.62 (q, *J* = 1.4 Hz, 1 H), 3.40 (td, *J* = 7.4, 3.7 Hz, 1 H), 2.18 (d, *J* = 1.4 Hz, 3 H), 1.19–1.13 (m, 2 H), 0.99–0.93 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 188.7, 127.2, 123.8, 32.2, 12.7, 7.7.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_7H_9NS_2$: 171.0176; found: 171.0175.

3-Cyclohexyl-5-methylthiazole-2(3*H*)-thione (3k)

Pale yellow liquid; yield: 81 mg (76%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.81 (q, *J* = 1.2 Hz, 1 H), 4.92 (tt, *J* =11.8, 3.7 Hz, 1 H), 2.20 (d, *J* = 1.2 Hz, 3 H), 2.05–1.97 (m, 2 H), 1.86 (m, *J* = 13.6 Hz, 2 H), 1.72 (s, 1 H), 1.53–1.32 (m, 4 H), 1.26–1.12 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 185.8, 124.4, 124.2, 57.8, 32.1, 25.4, 25.2, 12.6.

HRMS (EI$^+$): *m*/*z* [M]$^+$ calcd for $C_{10}H_{15}NS_2$: 213.0646; found: 213.0644.

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Supporting Information

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