Synthesis K. D. Safa, M. Alyari Paper

Synthesis of Thioalkyne-Substituted Thiazolidine-2-thiones Using Tris(trimethylsilyl)methyllithium and Carbon Disulfide

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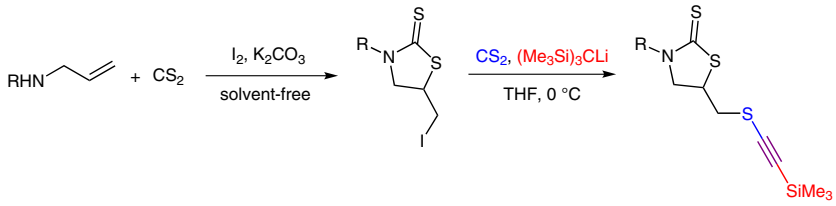

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Abstract An efficient, environmentally benign, and simple one-pot approach to the synthesis of 5-(iodomethyl)thiazolidine-2-thiones via multicomponent reaction of allylamines, carbon disulfide, and iodine under solvent-free conditions is presented. The obtained 5-(iodomethyl)thiazolidine-2-thiones were converted into silyl-protected terminal [(ethynylthio)methyl]-substituted thiazolidine-2-thiones by treatment with lithium 2,2,2-tris(trimethylsilyl)ethanedithioate, produced by the reaction of tris(trimethylsilyl)methyllithium with carbon disulfide.

Key words thioalkyne, thiazolidine-2-thione, organosilicon, organosulfur, tris(trimethylsilyl)methyllithium, carbon disulfide

Thioalkynes are a desirable platform for drug diversification considering the variety of existing acetylene chemistry, in particular the extensively used copper-catalyzed azide-alkyne cycloaddition, and the powerful position of organosulfur compounds among top-selling pharmaceutical drugs. Existing methods to form S–Csp bonds are rare and require harsh conditions. Currently, the most common techniques require functionalization of the thiol.[1] In this paper, we set out to investigate the feasibility of a facile and efficient method to gain access to a thioalkyne substituent on a thiazolidine-2-thione, because of the exceptional reactivity of sulfur and its importance in biology, medicine, and material science. Of particular interest to us are silylacetylenes as a direct gateway to the most versatile terminal alkynes in various biologically important compounds.

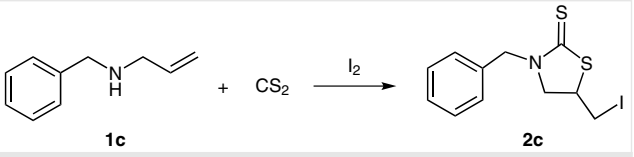
Nitrogen-containing five- or six-membered heterocyclic compounds are of great interest to organic chemists because of their presence in various natural compounds; they have interesting bioactivity.[2] Thiazolidine-2-thione is a five-membered heterocyclic compound, containing sulfur and nitrogen atoms attached to the carbon of a C=S group, that has been extensively studied in recent years.[3–7] Thiazolidine-2-thiones have received considerable attention because of their wide range of applications and the diverse biological activity of many representatives of this class of compounds.[8,9]

In recent years a central purpose in synthetic organic chemistry has been to develop greener and economically competitive processes for the efficient synthesis of biologically active compounds. It reduces the use of organic solvents and minimizes the formation of other waste. Recently, Ziyaei-Halimehjani and co-workers described a one-pot, three-component reaction for the synthesis of thiazolidine-2-thione involving the reaction of allylamines with carbon disulfide in tetrahydrofuran to afford dithiocarbamate salts, then iodocyclization of these new compounds produced 5-(iodomethyl)thiazolidine-2-thiones.[5]

This reported method suffers from several disadvantages such as the use of harmful organic solvents, prolonged reaction times, and unsatisfactory yields. Therefore searching for more facile and practical synthetic routes to thiazolidine-2-thiones remains desirable. To improve the synthesis of thiazolidine-2-thiones, herein we report a novel, efficient, and green synthesis of these compounds under solvent-free conditions by the three-component reaction of an allylamine, carbon disulfide, and iodine.

The reaction of *N*-benzylallylamine (**1c**) (3 mmol), carbon disulfide (5 mmol), and iodine (3.3 mmol) in tetrahydrofuran at room temperature for 24 hours without a catalyst, afforded the desired thiazolidine-2-thione **2c** in 60% yield.[5] In order to improve the reaction efficiency, we varied the molar ratios of the reactions and used potassium carbonate as a catalyst (Scheme 1,Table 1). Potassium dithiocarbamates are obtained by treating allylamines with carbon disulfide in the presence of potassium carbonate. This method has the advantage that only one equivalent of amine is required. When a 1:3:4 ratio of **1c**/carbon disulfide/iodine was used in the presence of potassium carbon-

ate, the product was isolated in the highest yields among those in Table 1 (entries 5, 6 and 11). Lowering the amount of iodine increased the reaction time and decreased the yield (entries 1–3). To our delight, when the reaction was carried out in water for 40 minutes **2c** was obtained in high yield (entry 5). The use of a co-solvent or an organic solvent was not beneficial to the process (entries 7–10). We observed that under solvent-free conditions at room temperature the one-pot reaction proceeded to completion, affording the thiazolidine-2-thione **2c** in good yield; the reaction conditions were then finally established as shown in entry 11.



Scheme 1

Table 1 Optimization of the Synthesis of 3-Benzyl-5-(iodomethyl)thiazolidine-2-thione (**2c**)

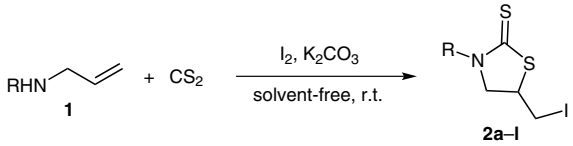
Entry	Ratio **1c**/CS_2/I_2 (equiv)	Catalyst (equiv)	Solvent	Time (min)	Yield[a] (%)
1	1:3:1	none	H_2O	60	72
2	1:3:1.5	none	H_2O	60	75
3	1:3:1.5	K_2CO_3 (0.5)	H_2O	50	81
4	1:3:4	none	H_2O	50	83
5	1:3:4	K_2CO_3 (0.5)	H_2O	40	85
6	1:3:4	K_2CO_3 (0.5)	H_2O (50 °C)	35	87
7	1:3:4	K_2CO_3 (0.5)	THF	120	70
8	1:3:4	K_2CO_3 (0.5)	CH_2Cl_2	120	68
9	1:3:4	K_2CO_3 (0.5)	EtOH	50	78
10	1:3:4	K_2CO_3 (0.5)	EtOH–H_2O (1:1)	50	75
11	1:3:4	K_2CO_3 (0.5)	neat	30	90

[a] Isolated yield.

Encouraged by these results, the synthesis of thiazolidine-2-thiones **2a**–**l** was carried out using four equivalents of iodine under solvent-free conditions (Table 2). It should be noted that in all of these experiments the alternative 6-*endo*-trig cyclization was not detected.

We have recently used bulky tris(trimethylsilyl)methyllithium as a reagent in various reactions such as the preparation of vinylsilanes, epoxysilanes, halovinylsilanes, silyl ethers, etc.[10–13] In addition we have investigated its behavior with carbon disulfide at low temperatures.[14] In the previous publications we reported a new type of chemistry of carbon disulfide proceeding via nucleophilic attack of tris(trimethylsilyl)methyllithium at the carbon of carbon

Table 2 One-Pot Synthesis of Thiazolidine-2-thiones

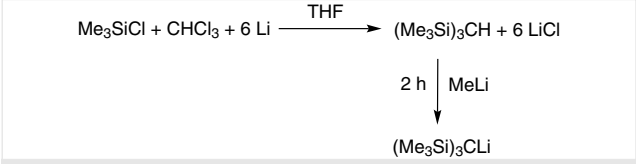


Entry	R	Product	Time/min	Yield[a] (%)
1	H	**2a**	30	93
2	CH_2Cy	**2b**	40	85
3	Bn	**2c**	30	90
4	4-$MeC_6H_4CH_2$	**2d**	25	90
5	4-*i*-$PrC_6H_4CH_2$	**2e**	25	92
6	(*E*)-CH_2CH=CHPh	**2f**	45	80
7	4-$ClC_6H_4CH_2$	**2g**	30	91
8	3-$ClC_6H_4CH_2$	**2h**	40	83
9	1-naphthylmethyl	**2i**	60	80
10	2-furylmethyl	**2j**	60	80
11	5-methyl-2-furylmethyl	**2k**	50	83
12	2-thienylmethyl	**2l**	45	85

[a] Isolated yield.

disulfide at –46 °C. To extend our investigations to organosilicon compounds, we decided to study the reaction of tris(trimethylsilyl)methyllithium with carbon disulfide in the presence of various 5-(iodomethyl)thiazolidine-2-thiones at temperatures ranging from 0 to 25 °C.

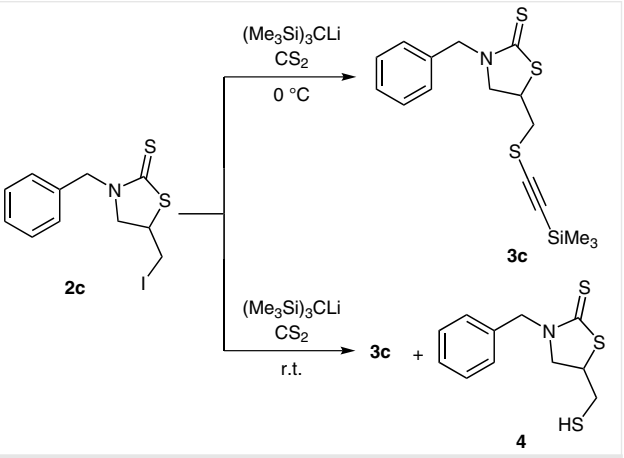
The precursor tris(trimethylsilyl)methane was prepared by the reaction of chloroform, lithium, and chlorotrimethylsilane in tetrahydrofuran. The organolithium reagent tris(trimethylsilyl)methyllithium was obtained by treatment of tris(trimethylsilyl)methane with methyllithium at reflux in tetrahydrofuran (Scheme 2).[15]



Scheme 2 Preparation of tris(trimethylsilyl)methyllithium

We began our study with 3-benzyl-5-(iodomethyl)thiazolidine-2-thione (**2c**) as a model substrate. In our experiments, carbon disulfide was added in one portion to a solution consisting of the tris(trimethylsilyl)methyllithium and tetrahydrofuran and this was stirred for 15 minutes. The color of the solution changed to orange-red immediately, which indicates the formation of new anion. Then, a solution of **2c** in tetrahydrofuran was added slowly and dropwise to the stirred solution. The product **3c**, with a silyl-

protected terminal alkyne, was isolated in 85% yield at 0 °C as the main product and only a trace amount of product **4** was obtained at this temperature (Scheme 3). The yield of **4** increased with increasing temperature and at room temperature both products were obtained approximately in equal yields.



Scheme 3 Reaction of tris(trimethylsilyl)methyllithium and carbon disulfide with **2c**

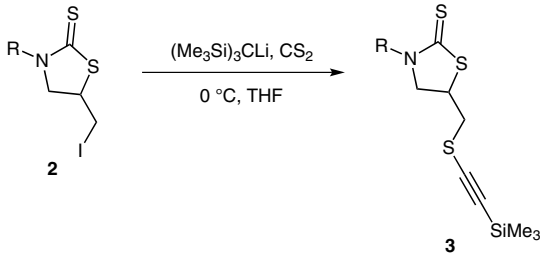
The reaction of various 5-(iodomethyl)thiazolidine-2-thiones **2** was studied and the results are summarized in Table 3; all experiments were carried out at 0 °C.

On the basis of the experimental results and the literature,[6,16–18] a possible mechanism for the formation of thioalkyne derivatives is presented in Scheme 4. According to the literature, the reaction of carbon disulfide with organolithium compounds leads to the formation of two different types of intermediate, 1,1-dithioenolates $RHC{=}C(SLi)_2$ and dithiocarboxylates RC(S)SLi. In the present work, addition of carbon disulfide to tris(trimethylsilyl)methyllithium at 0 °C produced lithium 2,2,2-tris(trimethylsilyl)ethanedithioate $(Me_3Si)_3C(S)SLi$ as an intermediate, which subsequently reacted with 5-(iodomethyl)thiazolidine-2-thiones **2** to give the final products **3**.

In conclusion, we have reported a highly efficient and green protocol for the one-pot synthesis of thiazolidine-2-thione derivatives starting from amines, carbon disulfide, and iodine. Then we have described a novel and efficient preparation of silyl-protected terminal ethynylthio-substituted thiazolidine-2-thiones from the reaction of the lithium 2,2,2-tris(trimethylsilyl)ethanedithioate intermediate with various thiazolidine-2-thiones.

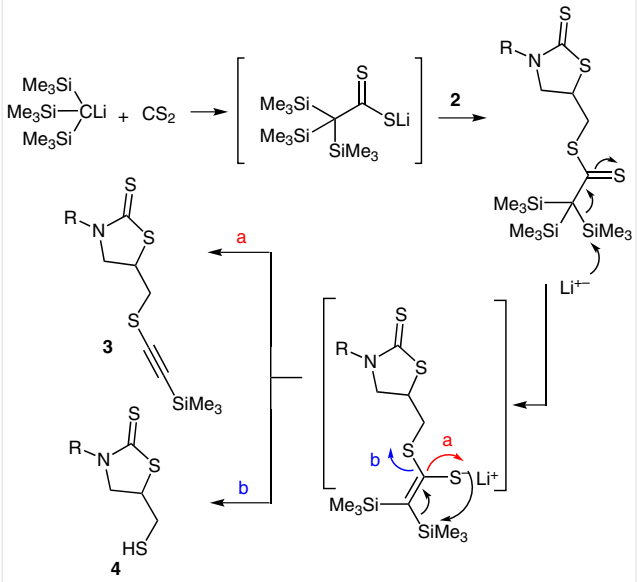
Reactions were carried out under dry argon. Solvents and carbon disulfide were dried by standard methods. Substrates for the preparation of tris(trimethylsilyl)methyllithium, namely chlorotrimethylsilane (Merck), lithium (Merck), chloroform (Merck) and substrates for the preparation of thiazolidine-2-thione, namely allylamines, carbon disulfide (Merck), *n*-hexane (Merk) and ethyl acetate (Merck) for TLC, were used as received.

Table 3 Synthesis of N-Substituted 5-({[(Trimethylsilyl)ethynyl]thio}methyl)thiazolidine-2-thiones



Entry	R	Product	Yield[a] (%)
1	H	**3a**	75
2	CH_2Cy	**3b**	83
3	Bn	**3c**	85
4	4-$MeC_6H_4CH_2$	**3d**	88
5	4-*i*-$PrC_6H_4CH_2$	**3e**	90
6	(*E*)-$CH_2CH{=}CHPh$	**3f**	83
7	4-$ClC_6H_4CH_2$	**3g**	87
8	3-$ClC_6H_4CH_2$	**3h**	80
9	1-naphthylmethyl	**3i**	78
10	2-furylmethyl	**3j**	82
11	5-methyl-2-furylmethyl	**3k**	85
12	2-thienylmethyl	**3l**	85

[a] Isolated yield.



Scheme 4 The mechanism of the reaction of tris(trimethylsilyl)methyllithium, carbon disulfide, and 5-(iodomethyl)thiazolidine-2-thiones

^{1}H and ^{13}C NMR were recorded with a Bruker FT-400MHz spectrometer at room temperature and $CDCl_3$ as a solvent. The mass spectra were obtained with a GC-mass Agilent quadrupole mode 5973N instrument, operating at 70 eV. Fourier transform infrared spectroscopy (FTIR) was performed using a Bruker-Tensor 270 spectrophotometer. Elemental analyses were carried out on a Vario EL III instrument.

3-Substituted 5-(Iodomethyl)thiazolidine-2-thiones 2; General Procedure

N-Substituted allylamine **1** (1 mmol), K_2CO_3 (0.5 mmol), and CS_2 (3 mmol) were added to a test tube equipped with a magnetic stir bar. The mixture was stirred for 5 min, I_2 (4 mmol) was added and stirring was maintained until the reaction was complete (TLC). Then the mixture was treated with 2 M aq $NaHSO_3$ solution (5 mL) and extracted with CH_2Cl_2 (2 × 10 mL). The organic layer was dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification was achieved by recrystallization (EtOH). Compounds **2a**,**c**,**d**,**g**,**i** have been described previously.[5]

3-(Cyclohexylmethyl)-5-(iodomethyl)thiazolidine-2-thione (2b)

Yellow solid; yield: 0.30 g (85%); mp 82–84 °C; R_f = 0.66 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 1488, 1442, 1272, 1144, 951, 830 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.00–1.29 (m, 5 H, CH_2CHCH_2), 1.65–1.87 (m, 6 H, $CH_2CH_2CH_2$), 3.35 (t, *J* = 10.85 Hz, 1 H, CHI), 3.42–3.50 (m, 2 H), 3.73 (dd, *J* = 7.63, 13.43 Hz, 1 H, H4), 3.81–3.88 (m, 1 H, H5), 4.03–4.14 (m, 2 H, CH_2N).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 6.66, 24.61, 25.10, 29.64, 29.74, 35.53, 42.69, 54.18, 61.33, 193.29 (C=S).

Anal. Calcd for $C_{11}H_{18}INS_2$: C, 37.18; H, 5.11; N, 3.94. Found: C, 37.36; H, 5.30; N, 3.73.

5-(Iodomethyl)-3-(4-isopropylbenzyl)thiazolidine-2-thione (2e)

Yellow solid; yield: 0.36 g (92%); mp 74–76 °C; R_f = 0.38 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 1494, 1414, 1254, 1176, 818, 548 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (d, *J* = 6.92 Hz, 6 H, 2 CH_3), 2.92–2.95 (m, 1 H, CH), 3.24 (dd, *J* = 10.30, 10.12 Hz, 1 H, CHI), 3.38 (dd, *J* = 4.33, 10.12 Hz, 1 H, CHI), 3.81–3.84 (m, 1 H, H5), 3.90 (dd, *J* = 2.99, 12.17 Hz, 1 H, H4), 4.04 (dd, *J* = 7.40, 12.17 Hz, 1 H, H4), 4.89 (d, *J* = 14.41 Hz, 1 H, CHN), 5.04 (d, *J* = 14.41 Hz, 1 H, CHN), 7.25 (d, *J* = 8.24 Hz, 2 H, Ar), 7.29 (d, *J* = 8.24 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 6.42, 22.85, 32.70, 42.51, 51.28, 59.59, 126.19, 127.09, 129.65, 130.75, 193.20 (C=S).

Anal. Calcd for $C_{14}H_{18}INS_2$: C, 42.97; H, 4.64; N, 3.58. Found: C, 43.12; H, 4.78; N, 3.34.

3-Cinnamyl-5-(iodomethyl)thiazolidine-2-thione (2f)

Yellow sticky solid; yield: 0.30 g (80%); R_f = 0.20 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 1487, 1438, 1249, 1168, 827 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.94 (dd, *J* = 3.98, 10.19 Hz, 1 H, CHI), 3.29 (dd, *J* = 4.67, 10.19 Hz, 1 H, CHI), 4.16–4.20 (m, 1 H, H5), 4.45 (dd, *J* = 3.52, 12.04 Hz, 1 H, H4), 4.46 (dd, *J* = 5.13, 12.04 Hz, 1 H, H4), 4.78 (dd, *J* = 5.54, 13.91 Hz, 1 H, CHN), 4.94 (dd, *J* = 5.62, 13.91 Hz, 1 H, CHN), 6.12–6.21 (m, 1 H, =CH), 6.64 (d, *J* = 15.64 Hz, 1 H, =CH), 7.28–7.40 (m, 5 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.68, 41.22, 45.96, 52.43, 121.67, 125.52, 125.61, 127.32, 127.44, 133.41, 133.61, 194.10 (C=S).

Anal. Calcd for $C_{13}H_{14}INS_2$: C, 41.60; H, 3.76; N, 3.73. Found: C, 41.81; H, 3.99; N, 3.52.

3-(3-Chlorobenzyl)-5-(iodomethyl)thiazolidine-2-thione (2h)

Yellow sticky solid; yield: 0.32 g (83%); R_f = 0.45 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 1486, 1416, 1257, 1168, 821, 557 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.22 (t, *J* = 10.61 Hz, 1 H, CHI), 3.35 (dd, *J* = 4.28, 10.10 Hz, 1 H, CHI), 3.77–3.83 (m, 1 H, H5), 3.87 (dd, *J* = 2.10, 12.21 Hz, 1 H, H4), 4.00 (dd, *J* = 12.21, 14.42 Hz, 1 H, CH4), 4.87 (d, *J* = 14.49 Hz, 1 H, CHN), 5.06 (d, *J* = 14.49 Hz, 1 H, CHN), 7.20 (s, 1 H, Ar), 7.25–7.33 (m, 3 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.64, 39.98, 46.01, 59.65, 125.51, 128.17, 128.67, 130.36, 133.06, 133.12, 194.34 (C=S).

Anal. Calcd for $C_{11}H_{11}ClINS_2$: C, 34.43; H, 2.89; N, 3.65. Found: C, 34.68; H, 3.10; N, 3.44.

3-(Furan-2-ylmethyl)-5-(iodomethyl)thiazolidine-2-thione (2j)

Yellow sticky solid; yield: 0.27 g (80%); R_f = 0.33 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 1492, 1421, 1261, 1163, 820, 552 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.29 (t, *J* = 10.71 Hz, 1 H, CHI), 3.36–3.40 (dd, *J* = 4.26, 10.11 Hz, 1 H, CHI), 3.79–3.85 (m, 1 H, H5), 4.02–4.12 (m, 2 H, H4), 4.83 (d, *J* = 15.26 Hz, 1 H, CHN), 5.08 (d, *J* = 15.26 Hz, 1 H, CHN), 6.38 (s, 1 H, furyl), 6.41 (d, *J* = 3.03 Hz, 1 H), 7.42 (s, 1 H, furyl).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 6.09, 42.81, 44.30, 60.00, 109.06, 109.69, 142.10, 147.02, 193.52 (C=S).

Anal. Calcd for $C_9H_{10}INOS_2$: C, 31.87; H, 2.97; N, 4.13. Found: C, 32.01; H, 3.16; N, 3.95.

5-(Iodomethyl)-3-[(5-methylfuran-2-yl)methyl]thiazolidine-2-thione (2k)

White solid; yield: 0.29 g (83%); mp 101–103 °C; R_f = 0.34 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 1480, 1430, 1146, 1073, 794, 558 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.30 (s, 3 H, CH_3), 3.30 (dd, *J* = 10.23, 11.31 Hz, 1 H, CHI), 3.38 (dd, *J* = 4.28, 10.14 Hz, 1 H, CHI), 3.78–3.84 (m, 1 H, H5), 4.08 (d, *J* = 4.70 Hz, 2 H, H4), 4.96 (d, *J* = 15.26 Hz, 1 H, CHN), 5.08 (d, *J* = 15.26 Hz, 1 H, CHN), 5.95 (d, *J* = 2.24 Hz, 1 H, furyl), 6.28 (d, *J* = 3.06 Hz, 1 H, furyl).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 6.23, 12.75, 42.84, 44.49, 59.82, 105.57, 109.99, 145.08, 152.03, 193.13 (C=S).

Anal. Calcd for $C_{10}H_{12}INOS_2$: C, 34.00; H, 3.42; N, 3.97. Found: C, 34.21; H, 3.61; N, 3.80.

5-(Iodomethyl)-3-(thiophen-2-ylmethyl)thiazolidine-2-thione (2l)

Yellow solid; yield: 0.30 g (85%); mp 60–62 °C; R_f = 0.35 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 1478, 1424, 1261, 1144, 1071, 563 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.24 (t, *J* = 10.45 Hz, 1 H, CH_2I), 3.36 (dd, *J* = 4.35, 10.45 Hz, 1 H, CH_2I), 3.78–3.84 (m, 1 H, H5), 3.98 (dd, *J* = 2.87, 12.02 Hz, 1 H, H4), 4.07 (dd, *J* = 7.25, 12.02 Hz, 1 H, H4), 5.00 (d,

J = 14.99 Hz, 1 H, CHN), 5.23 (d, *J* = 14.99 Hz, 1 H, CHN), 6.99 (dd, *J* = 3.50, 5.11 Hz, 1 H, thienyl), 7.10 (d, *J* = 2.91 Hz, 1 H, thienyl), 7.29 (dd, *J* = 1.08, 5.11 Hz, 1 H, thienyl).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 6.44, 42.57, 46.02, 59.35, 125.51, 125.85, 126.97, 135.07, 193.20 (C=S).

Anal. Calcd for $C_9H_{10}INS_3$: C, 30.43; H, 2.84; N, 3.94. Found: C, 30.65; H, 3.02; N, 3.76.

3-Substituted 5-({[(Trimethylsilyl)ethynyl]thio}methyl)thiazolidine-2-thiones 3; General Procedure

To a stirred solution of tris(trimethylsilyl)methyllithium (1 mmol) in THF, CS_2 (1.2 mmol) was added in one portion at 0 °C under an argon atmosphere. The mixture was stirred for 15 min and then 3-substituted 5-(iodomethyl)thiazolidine-2-thione **2** (1 mmol) was added at this temperature and stirring was maintained until the reaction was complete (TLC). The mixture was poured into water and extracted with CH_2Cl_2. The organic layer was washed with water, dried (Na_2SO_4), and filtered. The solvent was removed in vacuo and the product was purified by preparative TLC (silica gel, *n*-hexane–EtOAc, 3:1).

5-({[(Trimethylsilyl)ethynyl]thio}methyl)thiazolidine-2-thione (3a)

Yellow solid; yield: 0.20 g (75%); mp 100–102 °C; R_f = 0.32 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 2093, 1505, 1459, 1244, 1169, 1026, 878, 840, 644 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.18 (s, 9 H, $SiMe_3$), 2.94 (dd, *J* = 9.90, 13.42 Hz, 1 H, CHS), 3.09 (dd, *J* = 5.16, 13.42 Hz, 1 H, CHS), 4.03–4.06 (dd, *J* = 3.41, 11.66 Hz, 1 H, H4), 4.09–4.14 (dd, *J* = 6.95, 11.66 Hz, 1 H, H4), 4.19–4.22 (m, 1 H, H5), 7.64 (br s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –1.15 ($SiMe_3$), 37.65, 48.05, 53.27, 90.59, 101.95, 194.01 (C=S).

MS (EI, 70 eV): *m*/*z* (%) = 73 (100), 261 (71) [M]$^+$.

3-(Cyclohexylmethyl)-5-({[(trimethylsilyl)ethynyl]thio}methyl)thiazolidine-2-thione (3b)

Yellow solid; yield: 0.30 g (83%); mp 102–104 °C; R_f = 0.75 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 2097, 1444, 1406, 1248, 1135, 1030, 879, 838, 756 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.17 (s, 9 H, $SiMe_3$), 1.00–1.08 (m, 2 H, CH_2), 1.15–1.27 (m, 3 H, $CHCH_2$), 1.64–1.85 (m, 6 H, $CH_2CH_2CH_2$), 2.83 (dd, *J* = 10.38, 13.48 Hz, 1 H, CHS), 3.08 (dd, *J* = 4.85, 13.48 Hz, 1 H, CHS), 3.56–3.68 (m, 2 H, H4), 3.87–3.91 (m, 1 H, H5), 4.13–4.22 (m, 2 H, CHN).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –1.15 ($SiMe_3$), 24.61, 25.11, 29.63, 29.79, 35.52, 37.95, 41.10, 54.28, 59.55, 90.66, 101.77, 193.88 (C=S).

MS (EI, 70 eV): *m*/*z* (%) = 73 (91), 97 (54), 357 (100) [M]$^+$.

3-Benzyl-5-({[(trimethylsilyl)ethynyl]thio}methyl)thiazolidine-2-thione (3c)

Yellow solid; yield: 0.30 g (85%); mp 55–57 °C; R_f = 0.52 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 2092, 1423, 1264, 1177, 1038, 878, 842, 705 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.15 (s, 9 H, $SiMe_3$), 2.71 (dd, *J* = 9.83, 13.40 Hz, 1 H, CHS), 3.00 (dd, *J* = 5.20, 13.40 Hz, 1 H, CHS), 3.82–3.88 (m, 1 H, H5), 3.97 (dd, *J* = 3.20, 12.05 Hz, 1 H, H4), 4.06 (dd, *J* = 7.40, 12.05 Hz, 1 H, H4), 4.96 (d, *J* = 14.50 Hz, 1 H, CHN), 5.01 (d, *J* = 14.50 Hz, 1 H, CHN), 7.32–7.36 (m, 5 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –1.21 ($SiMe_3$), 37.94, 40.76, 51.53, 57.88, 90.55, 101.60, 127.09, 127.30, 127.94, 133.67, 194.17 (C=S).

MS (EI, 70 eV): *m*/*z* (%) = 73 (24), 91 (100), 351 (51) [M]$^+$.

3-(4-Methylbenzyl)-5-({[(trimethylsilyl)ethynyl]thio}methyl)thiazolidine-2-thione (3d)

Yellow solid; yield: 0.32 g (88%); mp 60–62 °C; R_f = 0.42 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 2087, 1433, 1241, 1157, 1037, 880, 837, 688 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.15 (s, 9 H, $SiMe_3$), 2.35 (s, 3 H, CH_3), 2.69 (dd, *J* = 10.12, 13.27 Hz, 1 H, CHS), 3.01 (dd, *J* = 5.00, 13.27 Hz, 1 H, CHS), 3.78–3.87 (m, 1 H, H5), 3.96 (dd, *J* = 2.72, 11.96 Hz, 1 H, H4), 4.05 (dd, *J* = 7.35, 11.96 Hz, 1 H, H4), 4.91 (d, *J* = 14.38 Hz, 1 H, CHN), 4.98 (d, *J* = 14.38 Hz, 1 H, CHN), 7.16 (d, *J* = 7.66 Hz, 2 H, Ar), 7.22 (d, *J* = 7.66 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –1.17 ($SiMe_3$), 20.18, 37.93, 40.73, 51.39, 57.86, 90.55, 101.65, 127.18, 128.65, 130.64, 137.22, 194.04 (C=S).

MS (EI, 70 eV): *m*/*z* (%) = 73 (15), 105 (100), 365 (36) [M]$^+$.

3-(4-Isopropylbenzyl)-5-({[(trimethylsilyl)ethynyl]thio}methyl)thiazolidine-2-thione (3e)

Pale brown solid; yield: 0.35 g (90%); mp 94–96 °C; R_f = 0.38 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 2094, 14.92, 1423, 1240, 1153, 1029, 880, 845, 695 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.15 (s, 9 H, $SiMe_3$), 1.24 (d, *J* = 6.92 Hz, 6 H, 2 CH_3), 2.70 (dd, *J* = 9.96, 13.43 Hz, 1 H, CHS), 2.87–2.93 (m, 1 H, CH), 3.01 (dd, *J* = 5.13, 13.43 Hz, 1 H, CHS), 3.81–3.87 (m, 1 H, H5), 3.97 (dd, *J* = 3.18, 11.62 Hz, 1 H, H4), 4.07 (dd, *J* = 7.33, 11.62 Hz, 1 H, H4), 4.95 (s, 2 H, CHN), 7.21 (d, *J* = 7.72 Hz, 2 H, Ar), 7.25 (d, *J* = 7.72 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –1.17 ($SiMe_3$), 22.90, 32.81, 37.98, 40.80, 51.38, 57.92, 90.65, 101.61, 126.01, 127.20, 131.02, 148.15, 194.01 (C=S).

MS (EI, 70 eV): *m*/*z* (%) = 73 (64), 133 (100), 393 (31) [M]$^+$.

3-Cinnamyl-5-({[(trimethylsilyl)ethynyl]thio}methyl)thiazolidine-2-thione (3f)

Pale brown sticky solid; yield: 0.31 g (83%); R_f = 0.19 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 2092, 1482, 1444, 1248, 1177, 1031, 878, 842, 694 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.16 (s, 9 H, $SiMe_3$), 2.86 (dd, *J* = 3.45, 9.98 Hz, 1 H, CHS), 3.06 (dd, *J* = 5.11, 9.98 Hz, 1 H, CHS), 3.92–3.95 (m, 1 H, H5), 4.12 (dd, *J* = 3.46, 12.08 Hz, 1 H, H4), 4.23 (dd, *J* = 7.46, 12.08 Hz, 1 H, H4), 4.49 (dd, *J* = 6.90, 14.66 Hz, 1 H, CHN), 4.63 (dd, *J* = 6.55, 14.66 Hz, 1 H, CHN), 6.16–6.23 (m, 1 H, =CH), 6.64 (d, *J* = 15.81 Hz, 1 H, =CH), 7.26–7.40 (m, 5 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –1.15 ($SiMe_3$), 37.98, 40.96, 50.41, 58.36, 90.61, 101.82, 120.14, 125.58, 125.72, 127.32, 127.70, 134.40, 134.72, 193.98 (C=S).

MS (EI, 70 eV): *m*/*z* (%) = 73 (100), 117 (17), 377 (25) [M]$^+$.

3-(4-Chlorobenzyl)-5-({[(trimethylsilyl)ethynyl]thio}methyl)thiazolidine-2-thione (3g)

Yellow solid; yield: 0.34 g (87%); mp 74–76 °C; R_f = 0.50 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 2094, 1484, 1430, 1254, 1179, 1023, 877, 840, 694 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.13 (s, 9 H, $SiMe_3$), 2.68 (dd, *J* = 10.22, 13.17 Hz, 1 H, CHS), 2.98 (dd, *J* = 4.85, 13.17 Hz, 1 H, CHS), 3.79–3.87 (m, 1 H, H5), 3.93 (dd, *J* = 3.40, 11.78 Hz, 1 H, H4), 4.03 (dd, *J* = 7.62, 11.78 Hz, 1 H, H4), 4.89 (d, *J* = 14.67 Hz, 1 H, CHN), 4.94 (d, *J* = 14.67 Hz, 1 H, CHN), 7.24 (d, *J* = 8.02 Hz, 2 H, Ph), 7.29 (d, J = 8.02 Hz, 2 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –1.21 ($SiMe_3$), 37.92, 40.79, 50.82, 57.93, 90.44, 101.77, 128.13, 128.52, 132.18, 133.22, 194.54 (C=S).

MS (EI, 70 eV): *m*/*z* (%) = 73 (48), 125 (100), 385 (48) $[M]^+$.

3-(3-Chlorobenzyl)-5-({[(trimethylsilyl)ethynyl]thio}methyl)thiazolidine-2-thione (3h)

Pale brown solid; yield: 0.31 g (80%); mp 56–58 °C; R_f = 0.51 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 2091, 1483, 1419, 1256, 1028, 876, 842, 692 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.10 (s, 9 H, $SiMe_3$), 2.69 (dd, *J* = 9.97, 13.36 Hz, 1 H, CHS), 2.98 (dd, *J* = 5.12, 13.36 Hz, 1 H, CHS), 3.83–3.87 (m, 1 H, H5), 3.93 (dd, *J* = 2.92, 11.94 Hz, 1 H, H4), 4.02 (dd, *J* = 7.50, 11.94 Hz, 1 H, H4), 4.87 (d, *J* = 14.64 Hz, 1 H, CHN), 4.95 (d, *J* = 14.64 Hz, 1 H, CHN), 7.17–7.18 (m, 1 H, Ph), 7.25–7.26 (m, 3 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –1.21 ($SiMe_3$), 37.92, 40.82, 50.90, 57.94, 90.45, 101.77, 125.20, 127.13, 127.53, 129.29, 133.74, 135.66, 194.68 (C=S).

MS (EI, 70 eV): *m*/*z* (%) = 73 (48), 125 (100), 385 (53) $[M]^+$.

3-(Naphthalen-1-ylmethyl)-5-({[(trimethylsilyl)ethynyl]thio}methyl)thiazolidine-2-thione (3i)

Pale brown solid; yield: 0.31 g (78%); mp 101–103 °C; R_f = 0.63 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 2087, 1649, 1424, 1233, 1151, 1019, 879, 838, 688 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.12 (s, 9 H, $SiMe_3$), 2.04 (dd, *J* = 9.84, 13.39 Hz, 1 H, CHS), 2.76 (dd, *J* = 5.22, 13.39 Hz, 1 H, CHS), 3.85–3.86 (m, 1 H, H5), 4.00 (dd, *J* = 3.25, 12.07 Hz, 1 H, H4), 4.08 (dd, *J* = 7.40, 12.07 Hz, 1 H, H4), 5.16 (s, 2 H, CHN), 7.45 (d, *J* = 8.43 Hz, 1 H, naphthyl), 7.51 (t, *J* = 4.47 Hz, 2 H, naphthyl), 7.77 (s, 1 H, naphthyl), 7.82–7.86 (m, 3 H, naphthyl).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –1.19 ($SiMe_3$), 38.05, 40.87, 51.87, 58.04, 90.68, 101.93, 124.62, 125.45, 125.60, 126.44, 126.79, 128.10, 131.29, 132.11, 132.25, 194.08 (C=S).

MS (EI, 70 eV): *m*/*z* (%) = 73 (63), 141 (100), 401 (27) $[M]^+$.

3-(Furan-2-ylmethyl)-5-({[(trimethylsilyl)ethynyl]thio}methyl)thiazolidine-2-thione (3j)

Brown sticky solid; yield: 0.28 g (82%); R_f = 0.48 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 2092, 1511, 1457, 1421, 1263, 1168, 1027, 878, 842, 703 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.16 (s, 9 H, $SiMe_3$), 2.76 (dd, *J* = 10.00, 13.43 Hz, 1 H, CHS), 3.03 (dd, *J* = 5.08, 13.43 Hz, 1 H, CHS), 3.83–3.89 (m, 1 H, H5), 4.10–4.18 (m, 2 H, H4), 4.91 (d, *J* = 15.24 Hz, 1 H, CHN), 5.01 (d, *J* = 15.24 Hz, 1 H, CHN), 6.35–6.36 (t, *J* = 2.52 Hz, 1 H, furyl), 6.39 (d, *J* = 3.11 Hz, 1 H, furyl), 7.39 (d, *J* = 1.00 Hz, 1 H, furyl).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –1.17 ($SiMe_3$), 37.85, 41.05, 44.25, 58.25, 90.69, 101.68, 108.97, 109.68, 141.92, 147.15, 194.16 (C=S).

MS (EI, 70 eV): *m*/*z* (%) = 73 (41), 81 (100), 341 (24) $[M]^+$.

3-[(5-Methylfuran-2-yl)methyl]-5-({[(trimethylsilyl)ethynyl]thio}methyl)thiazolidine-2-thione (3k)

Brown sticky solid; yield: 0.30 g (85%); R_f = 0.60 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 2092, 1649, 1479, 1417, 1252, 1179, 1020, 878, 843, 701 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.17 (s, 9 H, $SiMe_3$), 2.27 (s, 3 H, CH_3), 2.77 (dd, *J* = 10.36, 13.06 Hz, 1 H, CHS), 3.04 (dd, *J* = 4.66, 13.06 Hz, 1 H, CHS), 3.84–3.86 (m, 1 H, H5), 4.13–4.15 (m, 2 H, H4), 4.81 (d, *J* = 15.19 Hz, 1 H, CHN), 4.98 (d, *J* = 15.19 Hz, 1 H, CHN), 5.93 (s, 1 H, furyl), 6.26 (s, 1 H, furyl).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –1.14 ($SiMe_3$), 12.62, 37.89, 41.07, 44.50, 58.17, 90.75, 101.70, 105.60, 109.91, 145.29, 151.83, 193.88 (C=S).

MS (EI, 70 eV): *m*/*z* (%) = 73 (100), 95 (31), 355 (14) $[M]^+$.

3-(Thiophen-2-ylmethyl)-5-({[(trimethylsilyl)ethynyl]thio}methyl)thiazolidine-2-thione (3l)

Brown sticky solid; yield: 0.30 g (85%); R_f = 0.58 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 2090, 1536, 1479, 1438, 1254, 1136, 1043, 878, 841, 706 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.16 (s, 9 H, $SiMe_3$), 2.72 (dd, *J* = 10.16, 13.43 Hz, 1 H, CHS), 3.03 (dd, *J* = 5.03, 13.43 Hz, 1 H, CHS), 3.84–3.87 (m, 1 H, H5), 4.05–4.15 (m, 2 H, H4), 5.08 (d, *J* = 15.00 Hz, 1 H, CHN), 5.20 (d, *J* = 15.00 Hz, 1 H, CHN), 6.98 (dd, *J* = 3.58, 4.89 Hz, 1 H, thienyl), 7.09 (d, *J* = 2.78 Hz, 1 H, thienyl), 7.28 (d, *J* = 4.76 Hz, 1 H, thienyl).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –1.14 ($SiMe_3$), 37.88, 40.86, 46.11, 57.66, 90.65, 101.73, 125.44, 125.92, 126.93, 135.40, 194.08 (C=S).

MS (EI, 70 eV): *m*/*z* (%) = 73 (89), 97 (43), 357 (100) $[M]^+$.

3-Benzyl-5-(mercaptomethyl)thiazolidine-2-thione (4)

Yellow sticky solid; R_f = 0.26 (*n*-hexane–EtOAc, 3:1).

IR (KBr): 2090, 1536, 1479, 1438, 1254, 1136, 1043, 878, 841, 706 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.51 (t, *J* = 8.80 Hz, 1 H, SH), 2.58–2.65 (m, 1 H, CHSH), 2.74–2.81 (m, 1 H, CHSH), 3.58–3.64 (m, 1 H, H5), 3.84–3.88 (dd, *J* = 3.36, 11.97 Hz, 1 H, H4), 4.00–4.05 (dd, *J* = 7.67, 11.97 Hz, 1 H, H4), 4.84 (d, *J* = 14.50 Hz, 1 H, CHN), 5.11 (d, *J* = 14.50 Hz, 1 H, CHN), 7.32–7.40 (m, 5 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.22, 44.62, 51.55, 58.06, 127.18, 127.36, 128.00, 133.85, 194.34 (C=S).

MS (EI, 70 eV): *m*/*z* (%) = 91 (86), 148 (100), 255 (81) $[M]^+$.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-1379253.

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