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Versatile Synthesis of Secondary 2-Amino Thiols and/or Their Disulfides via Thiazolinium Salts

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Commercially available β-amino alcohols have been transformed into various secondary β-amino thiols and/or their disulfides by using methyl dithioacetate as a source of sulfur. The transformation involves a thiazolinium salt as a versatile key intermediate, which enables easy modulation of the product structure by varying the substituents on the heterocycle and the *N*-alkylating agent.

Introduction

In comparison with primary 2-amino thiols, which are important compounds in medicinal chemistry, their secondary amino derivatives are less well studied. The most frequently encountered derivatives are *N*-substituted cysteine[1] and cysteamine,[2] which are obtained from the corresponding available primary 2-amino thiols, and (2-pyrrolidinyl)-methanethiol (prolinethiol),[3] obtained from (*S*)-prolinol. Although some secondary 2-amino thiols, as well as their disulfides, have found interesting applications as ligands in transition-metal catalysis[2c,4] and in medicinal chemistry,[5] their application remains limited mainly because of the poor number of available structures, which can be attributed to the lack of general methods for their synthesis. The main routes to secondary 2-amino thiols (or their disulfides) start from α-amino acids (or their 2-amino alcohol derivatives)[3,4a,4b,6] and require a multistep sequence: *N*-alkylation,[7] introduction of a sulfur nucleophile, and protection/deprotection of the amino and thiol groups. A few other methods involving secondary amines and less accessible sulfur substrates, such as thiiranes,[4d,8] α,α′-dithiodiisobutyraldehyde,[9] or mercaptoethyl carbonates,[10] have also been reported. Thus, an efficient and general access to secondary 2-amino thiols would be a welcome addition to the field.

In this paper we report a new method for the synthesis of secondary 2-amino thiols using amino alcohols and methyl dithioacetate as convenient starting materials[11] via thiazolinium salts as versatile precursors.

Results and Discussion

We envisioned two routes for the preparation of the thiazolinium salt intermediates (Routes 1 and 2 in Scheme 1). The first route involves two steps, thioacylation of a secondary 2-amino alcohol with methyl dithioacetate and subsequent intramolecular cyclization of the resulting *N*-(β-hydroxy)thioamide. The second route, described by us previously,[12] requires first the synthesis of a thiazoline[13] from a primary 2-amino alcohol and methyl dithioacetate and then its *N*-alkylation. Acid hydrolysis of the intermediate thiazolinium salts leads to the secondary 2-amino thiols (Scheme 1).[14]

First, we examined the feasibility of the transformation of (*S*)-prolinol into its sulfur counterpart, (*S*)-prolinethiol (Scheme 2), according to the general Route 1. Thioacylation of commercial (*S*)-prolinol with methyl dithioacetate led to thioamide **1a**. During the first series of experiments for the cyclization of **1a** using 1.2 equiv. of MsCl, the expected thiazolinium salt **3a** could neither be detected nor isolated from the reaction mixture, but we identified a new compound, the 2-[(methylsulfonyl)methylidene]thiazolidine **4a**. By using 2 equiv. of mesyl chloride[15] in the presence of triethylamine, **1a** was completely converted into **4a**, which was isolated in 57% yield. Heating of **4a** at reflux in aqueous 5 M HCl resulted in complete conversion into the desired (*S*)-prolinethiol hydrochloride (**5a**), as shown by the ^{1}H NMR spectrum of the crude product. The amino thiol was accompanied by (methylsulfonyl)acetic acid (**8**), which also resulted from the hydrolysis reaction. As it was difficult

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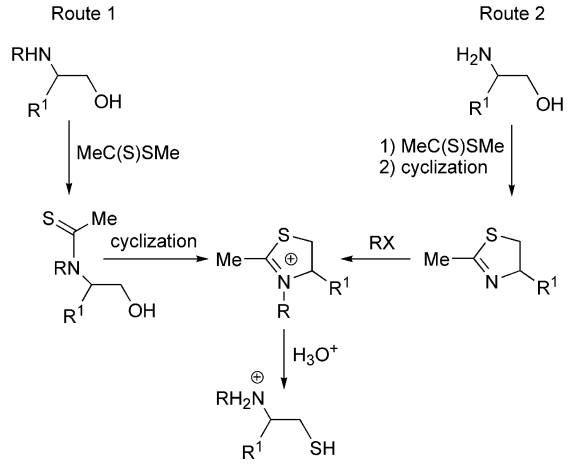
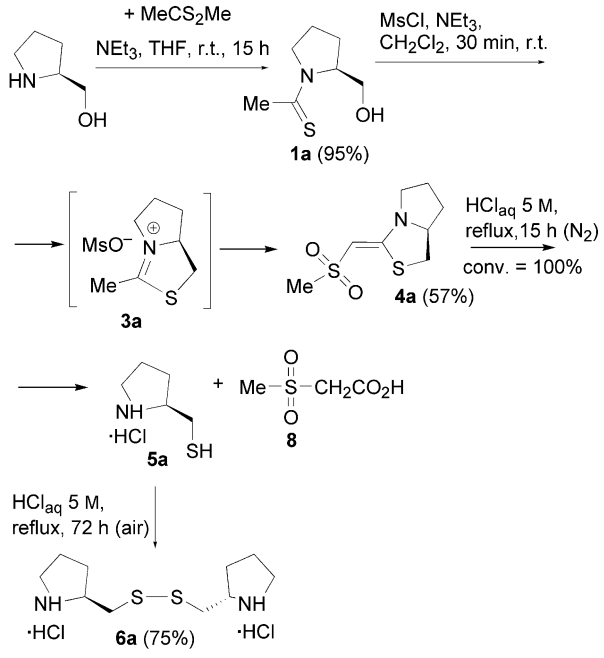


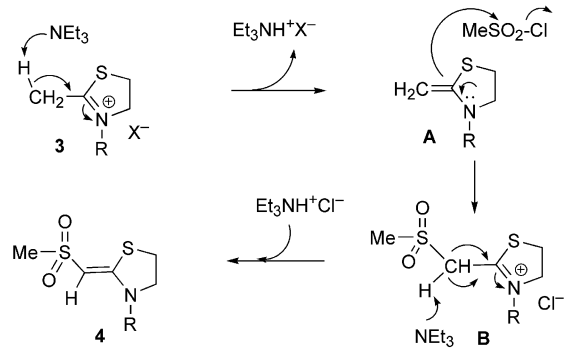
Scheme 1. General synthesis of thiazolinium salts from 2-amino alcohols and methyl dithioacetate and their subsequent hydrolysis to secondary 2-amino thiols.

to isolate the prolinethiol hydrochloride (**5a**) due to partial oxidation to the disulfide during the separation from **8**, the mixture of **5a** and **8** was heated in air in aqueous 5 M HCl. The resulting disulfide **6a** was easily separated from compound **8** and isolated in 75% yield.



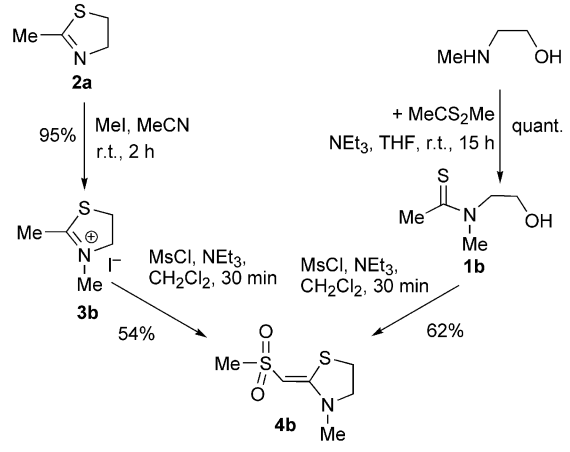
Scheme 2. Synthesis of (*S*)-prolinethiol from (*S*)-prolinol and methyl dithioacetate.

To explain the formation of **4a** we have proposed the mechanism shown in Scheme 3. The thiazolinium mesylate **3**, believed to be formed after intramolecular cyclization of the thioamide precursor, is deprotonated at the position α to the heterocycle by triethylamine to give thiazolidine **A**,[16] which reacts with mesyl chloride to form the α-sulfonylthiazolinium salt **B**. This is subsequently deprotonated at the position α to the heterocycle to afford sulfonylthiazolidine **4**.



Scheme 3. Proposed mechanism for the formation of thiazolidine **4** from thiazolinium salt **3**.

To support this mechanism and to demonstrate that the formation of the thiazolidine occurred via a thiazolinium salt, we prepared thiazolidine **4b** by two methods (Scheme 4). The first method (similar to that leading to **4a**) started with the thioacylation of 2-(methylamino)ethanol with methyl dithioacetate to give thioamide **1b**, which afforded thiazolidine **4b** after treatment with mesyl chloride and triethylamine. In the second method, commercially available 2-methylthiazoline (**2a**) was *N*-alkylated with iodomethane to give thiazolinium iodide **3b**, which was treated with mesyl chloride and triethylamine to afford **4b**. The (*Z*) geometry of the double bond of the thiazolidine **4b** was unambiguously determined by NMR spectroscopy and X-ray diffraction (Figure 1). The formation of the (*Z*) isomer is likely controlled by the steric hindrance arising from the presence of a substituent on the nitrogen atom. These two experiments confirm that thiazolidine **4** is formed via thiazolinium salt **3**, as proposed in the mechanism shown in Scheme 3.



Scheme 4. Synthesis of thiazolidine **4b** from 2-(methylamino)-ethanol or from methylthiazoline **2a**.

To obtain methylamino thiol **5b**, both thiazolinium salt **3b** and thiazolidine **4b** were subjected to acid hydrolysis in aqueous HCl (Scheme 5). At room temperature, thiazolin-

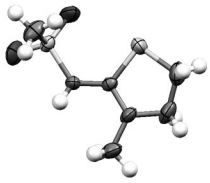
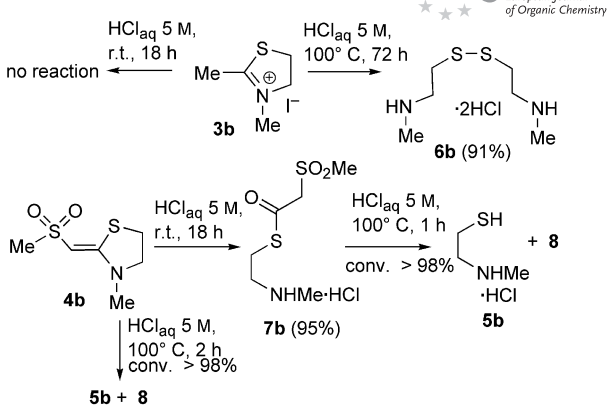


Figure 1. Crystal structure of thiazolidine **4b** (structure of one of the four crystallographically independent molecules of **4b**).

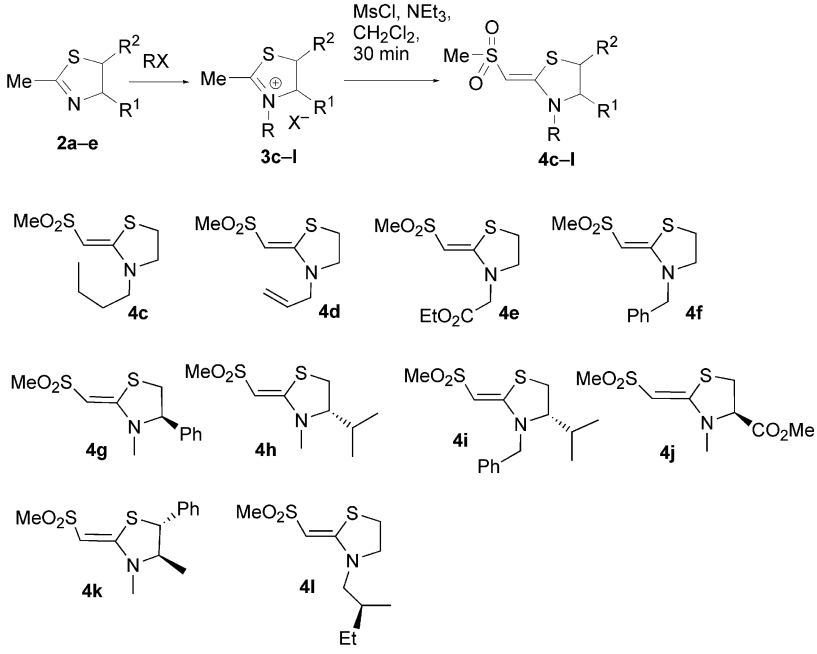


Scheme 5. Acid hydrolysis of thiazolinium salt **3b** and of thiazolidine **4b**.

ium salt **3b** remained unchanged overnight, whereas at 100 °C, **3b** did not afford the expected product after 72 h, but the corresponding disulfide **6b** in 91% yield. Under the same conditions at room temperature, thiazolidine **4b** gave the thioester **7b** after 18 h, whereas at 100 °C it was totally converted into the desired amino thiol hydrochloride **5b** after 2 h. The ^{1}H NMR spectrum of the crude product showed the presence of **5b** together with (methylsulfonyl)-acetic acid (**8**), which indicates that the formation of **8** could be caused by the *S*-deprotection of **7b**. Indeed, the acid hydrolysis at 100 °C of thioester **7b** afforded **5b**.[17] These preliminary results showed that a secondary amino thiol could be efficiently synthesized starting from a primary amino alcohol and methyl dithioacetate via a thiazolinium salt by acid hydrolysis of a thiazolidine intermediate.

By varying the alkylating agent, the second route (Route 2, Scheme 1), more general than Route 1, allows a large variety of structures to be synthesized. To examine the scope and limitation of the process, we selected various 2-amino alcohols and *N*-alkylating agents. A series of thiazolinium salts were first prepared by *N*-alkylation[12] of the achiral 2-methylthiazoline (**2a**) or of the chiral enantiopure thiazolines **2b**–**e**[11] (Scheme 6, Table 1). The *N*-alkylation was performed with simple alkyl, allyl, and benzyl halides, as well as with functionalized alkylating reagents (iodoacetate). Thiazolinium salts **3** were obtained in good yields (54–88%), except in the case of **3l** (22%), for which the alkylating agent was the chiral enantiopure (*S*)-2-methyl-1-iodobutane. Thiazolinium salts **3** were then treated with mesyl chloride and triethylamine to afford thiazolidines **4** in moderate to good yields (47–81%).

In the final step, thiazolidines **4** were subjected to acid hydrolysis conditions, free of oxygen to avoid the oxidation of amino thiols to the corresponding disulfides (Scheme 7, Table 2). Thiazolidines **4c**–**g** were totally converted into the corresponding secondary 2-amino thiols and (methylsulfonyl)acetic acid (**8**). The expected 2-amino thiols **5c**–**e** were isolated as their hydrochloride salts in good yields and in pure analytical form after separation from byproduct **8** by



Scheme 6. Synthesis of thiazolinium salts **3** and thiazolidines **4**.

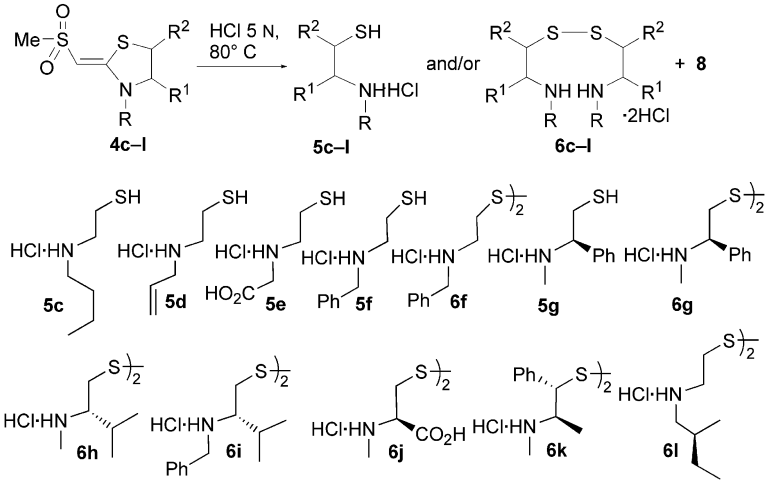
Table 1. Synthesis of thiazolinium salts **3** and thiazolidines **4**.

Starting material (config.)	R^1,R^2	RX	**3** (yield [%])	**4** (yield [%])
2a	H,H	BuI	**3c** (88)	**4c** (58)
2a	H,H	CH_2=$CHCH_2Br$	**3d** (88)	**4d** (64)
2a	H,H	$EtOC(O)CH_2I$	**3e** (75)	**4e** (49)
2a	H,H	BnBr	**3f** (60)	**4f** (72)
2c (*R*)	Ph,H	MeI	**3g** (88)	**4g** (68)
2b (*S*)	*i*Pr,H	MeI	**3h** (83)	**4h** (57)
2b (*S*)	*i*Pr,H	BnBr	**3i** (65)	**4i** (81)
2d (*R*)	CO_2Me,H	MeI	**3j** (54)	**4j** (51)
2e (*R*,*R*)	Me,Ph	MeI	**3k** (63)	**4k** (75)
2a	H,H	$EtMeCHCH_2Br$[a]	**3l** (22)	**4l** (47)

[a] Enantiopure alkyl bromide with an (*S*) configuration.

simple washing with acetone (Table 1, Entries 1–3). In the case of amino thiols **5f** and **5g** (Table 1, Entries 4 and 5), it was not possible to avoid their partial oxidation to the corresponding disulfides during their separation from **8**. However, amino thiols **5f** and **5g** could be characterized by NMR spectroscopy and HRMS in the crude mixture (in the presence of **8**). To remove **8**, the amino thiols **5f** and **5g** were totally oxidized to their disulfides by heating the mixture in a 5 M aqueous solution of HCl in air. The disulfides **6f** and **6g** obtained were easily isolated as their hydrochloride salts in 85 and 79% yields, respectively (Table 1, Entries 4 and 5). In the case of thiazolidines **4h**–**l**, despite the exclusion of oxygen during the hydrolysis, we did not observe the expected amino thiols in the crude reaction mixture, and only amino disulfides **6h**–**l** were isolated from compound **8** and characterized (Table 1, Entries 6–10).

Note that partial hydrolysis should allow isolation of the *S*-protected product, that is, an amino thioester of type **7** (such as **7b** in Scheme 5). As an example, thiazolidine **4f** was partially hydrolyzed at 60 °C to afford selectively amino



Scheme 7. Hydrolysis of thiazolidines **4** into 2-amino thiols **5** and/or disulfides **6**.

Table 2. Synthesis of 2-amino thiols **5** and/or disulfides **6**.

Entry	Starting thiazolidine	Amino thiol **5** (yield [%])	Disulfide **6** (yield [%])
1	**4c**	**5c** (91)	–
2	**4d**	**5d** (60)	–
3	**4e**	**5e** (71)[a]	–
4	**4f**	**5f** (–)[b]	**6f** (85)
5	(*R*)-**4g**	(*R*)-**5g** (–)[b]	(*R*,*R*)-**6g** (79)
6	(*S*)-**4h**	–	(*S*,*S*)-**6h** (83)
7	(*S*)-**4i**	–	(*S*,*S*)-**6i** (84)
8	(*R*)-**4j**	–	(*R*,*R*)-**6j** (62)[c]
9	(4*R*,5*R*)-**4k**	–	(4,4′*R*, 5,5′*R*)-**6k** (23)
10	(*S*)-**4l**	–	(*S*,*S*)-**6l** (66)

[a] Amino thiol **5e** possesses R^1 = CO_2H as a result of acid hydrolysis of R^1 = CO_2Et. [b] The amino thiol was obtained as a mixture with compound **8** and not isolated. [c] Disulfide **6j** possesses R^1 = CO_2H as a result of acid hydrolysis of R^1 = CO_2Me.

thioester **7f** in 78% yield after 1 h. A single crystal of **7f** was isolated and analyzed by X-ray diffraction (Figure 2). Also, when amino disulfides are obtained, it should be possible to reduce them into the corresponding 2-amino thiols by known procedures.[5b,9b]

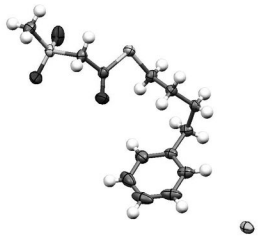


Figure 2. Crystal structure of amino thioester **7f**.

Conclusions

We have succeeded in preparing various secondary 2-amino thiols and/or their disulfide derivatives (achiral or chiral, acyclic or cyclic) via thiazolinium salts starting from easily accessible 2-amino alcohols and methyl dithioacetate. The introduction of a substituent onto the nitrogen atom, otherwise difficult, was achieved simply by *N*-alkylation. Therefore, easy modulation is possible by varying the substituents on the heterocycle and the *N*-alkylating agent. The procedure involves the acid hydrolysis of a thiazolidine intermediate. Although the method has a rather low atom economy compared with other methods, it enables access to a large number of amino thiols and amino disulfides, which could find new synthetic or biological applications.

Experimental Section

General: All reagents were purchased from Acros Organics or Sigma Aldrich and were used without further purification. The reactions were carried out under nitrogen unless stated otherwise and monitored by TLC on silica plates (Merck 60 F254). RPE grade solvents were used without further purification. Anhydrous solvents were obtained by using a PURESOLV SPS400 apparatus developed by Innovative Technology Inc. Flash chromatography was performed on a silica gel column (Merck silica gel, 40–63 μm). ^{1}H and ^{13}C NMR spectra were recorded with a Bruker DPX 250, DRX 400, or Avance III 500 spectrometer. Samples were dissolved in an appropriate deuteriated solvent ($CDCl_3$, [D_6]DMSO, D_2O). Chemical shifts are reported in ppm downfield from tetramethylsilane with the residual solvent signal used as an internal standard; coupling constants are indicated in Hz. High-resolution mass spectrometry (HRMS) was performed with a Waters Q-TOF micro spectrometer. Optical rotation values $[\alpha]_D^{20}$ were measured with a Perkin–Elmer 241 polarimeter and are given in 10^{-1} degree cm^2 g^{-1} with *c* in g/100 mL. The preparation and characterization of thioamides **1a** and **1b**, thiazolinium salts **3**, thioesters **7b** and **7f**, and (methylsulfonyl)acetic acid (**8**) are given in the Supporting Information.

Synthesis of Thiazolidines 4a–l

(*Z*)-2-[(Methylsulfonyl)methylidene]pyrrolidino[2,1-*c*]thiazolidine (4a): Mesyl chloride (195 μL, 2.5 mmol, 2 equiv.) was added to a solution of (*S*)-thioacetylprolinol (**1a**; 200 mg, 1.3 mmol) in dichloromethane (1 mL) under nitrogen. The mixture was cooled to 0 °C, and triethylamine (0.53 mL, 3.8 mmol, 3 equiv.) was added dropwise. After stirring at room temperature for 30 min, acetone was added to the reaction mixture, and the precipitate formed was filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (eluent: AcOEt) to afford product **4a** as a yellow solid (158 mg, 0.72 mmol, 57%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.47–1.54 (m, 1 H), 2.02–2.09 (m, 1 H), 2.18–2.38 (m, 2 H), 2.82 (t, J = 10.8 Hz, 1 H), 2.91 (s, 3 H, CH_3S), 3.03–3.11 (m, 3 H), 4.14–4.21 (m, 1 H, CHN), 4.77 (br. s, 1 H, CH=C) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 29.2, 30.9, 34.5, 45.2, 45.3, 68.5, 87.8, 157.9 ppm. HRMS: calcd. for $C_8H_{14}NO_2S_2$ 220.0466; found 220.0459.

General Procedure for the Synthesis of Thiazolidines 4 from Thiazolinium Salts 3: Mesyl chloride (78 μL, 1 mmol, 1 equiv.) was added to a solution of thiazolinium salt **3** (1 mmol) in dichloromethane (1 mL) under nitrogen. The mixture was cooled to 0 °C, and triethylamine (0.42 mL, 3 mmol, 3 equiv.) was added dropwise. After stirring at room temperature for 30 min, acetone was added to the reaction mixture, and the precipitate formed was filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (eluent: AcOEt) to afford product **4**.

***N*-Methyl-2-[(*Z*)-(methylsulfonyl)methylidene]thiazolidine (4b):** According to the General Procedure described above for the synthesis of **4a**, mesyl chloride (343 μL, 4.4 mmol, 2 equiv.) was added to a solution of thioamide **1b** (352 mg, 2.2 mmol) in dichloromethane (1 mL) under nitrogen. The mixture was cooled to 0 °C, and triethylamine (0.93 mL, 6.6 mmol, 3 equiv.) was added dropwise. After stirring at room temperature for 30 min, acetone was added to the reaction mixture, and the precipitate formed was filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (eluent: AcOEt) to afford product **4b** as a white solid (263 mg, 1.36 mmol, 62%). In a second approach, prepared according to the general procedure from thiazolinium salt **3b** and obtained as a white solid (104 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.91 (s, 3 H, CH_3), 3.01 (s, 3 H, CH_3), 3.12 (t, J = 7.0 Hz, 2 H, CH_2S), 3.69 (t, J = 7.2 Hz, 2 H, CH_2N), 5.05 (s, 1 H, CH=C) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 27.5, 35.0, 44.4, 56.4, 87.3, 162.0 ppm. $C_6H_{11}NO_2S_2$ (193.29): calcd. C 37.28, H 5.74, N 7.25; found C 37.24, H 5.91, N 7.30.

***N*-Butyl-2-[(*Z*)-(methylsulfonyl)methylidene]thiazolidine (4c):** Prepared according to the General Procedure from thiazolinium salt **3c** and obtained as a light-brown solid (136 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, J = 7.6 Hz, 3 H, CH_3CH_2), 1.34 (sext, J = 7.6 Hz, 2 H, $CH_3CH_2CH_2$), 1.59 (q, J = 7.6 Hz, 2 H, CH_3CH_2), 3.00 (s, 3 H, CH_3SO_2), 3.09 (t, J = 6.8 Hz, 2 H, CH_2N), 3.21 (t, J = 7.6 Hz, 2 H, CH_2S), 3.70 (t, J = 6.8 Hz, 2 H, CH_2N), 5.05 (s, 1 H, CH=C) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 20.7, 28.0, 28.4, 44.8, 48.6, 55.1, 87.2, 161.5 ppm. HRMS: calcd. for $C_9H_{17}NO_2S_2$ 236.0779; found 236.0780.

***N*-Allyl-2-[(*Z*)-(methylsulfonyl)methylidene]thiazolidine (4d):** Prepared according to the General Procedure from thiazolinium salt **3d** and obtained as a yellow solid (140 mg, 64%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.92 (s, 3 H, CH_3SO_2), 3.04 (t, J = 7.0 Hz, 2 H, CH_2S), 3.62 (t, J = 7.0 Hz, 2 H, CH_2N), 3.77 (dt, J = 1.3, 5.5 Hz, 2 H, $CHCH_2N$), 5.04 (s, 1 H, CH=C), 5.16 [dq, J = 1.3, 17.1 Hz, 1 H, CH=C*H*H(*E*)], 5.20 [dq, J = 1.3, 10.3 Hz, 1 H,

CH=CH*H*(*Z*)], 5.69 (ddt, *J* = 5.5, 10.3, 17.1 Hz, 1 H, C*H*=CH_2) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 27.5, 44.3, 50.7, 54.4, 88.0, 118.8, 129.9, 161.1 ppm. HRMS: calcd. for $C_8H_{14}NO_2S_2$ 220.0466; found 220.0462. $C_8H_{14}NO_2S_2$ (219.32 + 0.4H_2O): calcd. C 42.41, H 6.14, N 6.18, S 28.31; found C 42.65, H 6.07, N 6.17, S 28.43.

***N*-[(Ethoxycarbonyl)methyl]-2-[(*Z*)-(methylsulfonyl)methylidene]thiazolidine (4e):** Prepared according to the General Procedure from thiazolinium salt **3e**, except for the purification by chromatography on silica gel, for which the eluent was dichloromethane/acetone (85:15), and obtained as a yellow solid (129 mg, 49%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, *J* = 7.2 Hz, 3 H, CH_3CH$_2$), 2.96 (s, 3 H, CH_3SO_2), 3.15 (t, *J* = 7.2 Hz, 2 H, CH_2S), 3.82 (t, *J* = 7.2 Hz, 2 H, CH_2N), 3.98 (s, 2 H), 4.21 (q, *J* = 7.2 Hz, 2 H, CH_3CH_2), 4.98 (s, 1 H, CH=C) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.6, 28.2, 44.7, 49.5, 55.8, 62.2, 88.9, 162.2, 167.7 ppm.

***N*-Benzyl-2-[(*Z*)-(methylsulfonyl)methylidene]thiazolidine (4f):** Prepared according to the General Procedure from thiazolinium salt **3f**, except for the purification by chromatography on silica gel, for which the eluent was dichloromethane/acetone (75:25), and obtained as a yellow solid (193 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.00 (s, 3 H, CH_3SO_2), 3.13 (t, *J* = 7.1 Hz, 2 H, CH_2S), 3.68 (t, *J* = 7.1 Hz, 2 H, CH_2N), 4.43 (s, 2 H, CH_2Ph), 5.22 (s, 1 H, CH=C), 7.19–7.40 (m, 5 H, C_6H_5) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.0, 44.7, 52.3, 55.0, 88.6, 126.6, 127.6, 128.5, 129.6, 162.0 ppm. HRMS: calcd. for $C_{12}H_{14}NO_2S_2$ 270.0622; found 270.0632.

(*R*)-*N*-Methyl-2-[(*Z*)-(methylsulfonyl)methylidene]-4-phenylthiazolidine (4g): Prepared according to the General Procedure from thiazolinium salt **3g** and obtained as a yellow solid (183 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.70 (s, 3 H, CH_3N), 3.04 (dd, J_{AX} = 7.1, J_{AB} = 11.4 Hz, 1 H, C*H*HS), 3.06 (s, 3 H, CH_3SO_2), 3.50 (dd, J_{BX} = 7.1, J_{AB} = 11.4 Hz, 1 H, CH*H*S), 4.78 (dd, J_{AX} = J_{BX} = 7.1 Hz, 1 H, CHN), 5.15 (s, 1 H, CH=C), 7.26–7.29 (m, 2 H, C_6H_5), 7.37–7.44 (m, 3 H, C_6H_5) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.3, 35.9, 44.6, 71.0, 88.3, 126.8, 129.0, 129.3, 138.2, 162.3 ppm. HRMS: calcd. for $C_{12}H_{16}NO_2S_2$ 270.0622; found 270.0623.

(*S*)-4-Isopropyl-*N*-methyl-2-[(*Z*)-(methylsulfonyl)methylidene]thiazolidine (4h): Prepared according to the General Procedure from thiazolinium salt **3h** and obtained as a yellow solid (134 mg, 57%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (d, *J* = 6.9 Hz, 3 H, CH_3CH), 0.96 (d, *J* = 6.9 Hz, 3 H, CH_3CH), 2.17 (dsept, *J* = 4.9, 6.9 Hz, 1 H, C*H*Me$_2$), 2.85 (s, 3 H, CH_3), 2.90 (dd, J_{AX} = 4.9, J_{AB} = 11.4 Hz, 1 H, C*H*HS), 2.97 (s, 3 H, CH_3), 3.13 (dd, J_{BX} = 8.0, J_{AB} = 11.4 Hz, 1 H, CH*H*S), 3.73 (dt, *J* = 4.9, 8.0 Hz, 1 H, CHN), 4.96 (s, 1 H, CH=C) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.8, 19.2, 27.8, 29.8, 34.3, 44.6, 71.9, 86.1, 162.2 ppm. HRMS: calcd. for $C_9H_{18}NO_2S_2$ 236.0779; found 236.0789.

(*S*)-*N*-Benzyl-4-isopropyl-2-[(*Z*)-(methylsulfonyl)methylidene]thiazolidine (4i): Prepared according to the General Procedure from thiazolinium salt **3i**, except for the purification by chromatography on silica gel, for which the eluent was pentane/AcOEt (50:50), and obtained as a yellow solid (252 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (d, *J* = 5.1 Hz, 3 H, CH_3CH), 0.97 (d, *J* = 5.1 Hz, 3 H, CH_3CH), 2.16–2.24 (m, 1 H, C*H*Me$_2$), 2.94 (s, 3 H, CH_3), 3.00 (dd, J_{AB} = 11.2, J_{AX} = 4.8 Hz, 1 H, C*H*HS), 3.19 (dd, J_{AB} = 11.2, J_{BX} = 8.0 Hz, 1 H, CH*H*S), 3.84 (dt, *J* = 4.8, 8.0 Hz, 1 H, CHN), 4.39 (d, *J* = 16.6 Hz, 1 H, C*H*HPh), 4.56 (d, *J* = 16.6 Hz, 1 H, CH*H*Ph), 5.12 (s, 1 H, CH=C), 7.15–7.20 (m, 2 H, C_6H_5), 7.30–7.37 (m, 1 H, C_6H_5), 7.32–7.39 (m, 2 H, C_6H_5) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.9, 19.5, 27.8, 29.5, 44.3, 50.3, 70.2, 88.1, 126.7, 127.9, 129.0, 134.9, 162.0 ppm. HRMS: calcd. for $C_{15}H_{22}NO_2S_2$ 312.1092; found 312.1086.

(*R*)-*N*-Methyl-4-(methoxycarbonyl)-2-[(*Z*)-(methylsulfonyl)methylidene]thiazolidine (4j): Prepared according to the General Procedure from thiazolinium salt **3j** and obtained as a yellow oil (128 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.89 (s, 3 H, CH_3), 2.92 (s, 3 H, CH_3), 3.25 (dd, J_{BX} = 2.2, J_{AB} = 11.2 Hz, 1 H, C*H*HS), 3.31 (dd, J_{AX} = 7.5, J_{AB} = 11.2 Hz, 1 H, CH*H*S), 3.73 (s, 3 H, CH_3O), 4.35 (dd, J_{BX} = 2.2, J_{AX} = 7.5 Hz, 1 H, CHN), 5.07 (s, 1 H, CH=C) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.9, 35.3, 44.6, 53.0, 67.9, 89.5, 160.9, 170.0 ppm. HRMS: calcd. for $C_8H_{14}NO_4S_2$ 252.0364; found 252.0374.

(*R*,*R*)-3,4-Dimethyl-5-phenyl-2-[(*Z*)-(methylsulfonyl)methylidene]thiazolidine (4k): Prepared according to the General Procedure from thiazolinium salt **3k** and obtained as a light-brown solid (212 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (d, *J* = 6.2 Hz, 3 H, CH_3CH), 2.86 (s, 3 H, CH_3), 3.02 (s, 3 H, CH_3), 3.81 (dq, *J* = 6.2, *J* = 6.2 Hz, 1 H, CH_3C*H*), 4.16 (d, *J* = 6.2 Hz, 1 H, CHN), 5.08 (s, 1 H, CH=C), 7.30–7.37 (m, 5 H, C_6H_5) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.2, 33.4, 44.5, 54.4, 69.6, 87.5, 127.7, 128.5, 129.0, 138.3, 161.2 ppm. HRMS: calcd. for $C_{13}H_{18}NO_2S_2$ 284.0779; found 284.0781.

(*S*)-*N*-(2-Methylbutyl)-2-[(*Z*)-(methylsulfonyl)methylidene]thiazolidine (4l): Prepared according to the General Procedure from thiazolinium salt **3l** and obtained as a yellow oil (117 mg, 47%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83 (d, *J* = 6.7 Hz, 3 H, CHCH_3), 0.85 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3), 1.06 (m, 1 H, C*H*HCH$_3$), 1.34 (m, 1 H, CH*H*CH$_3$), 1.75 (m, 1 H, C*H*CH$_3$), 2.90 (dd, *J* = 8.1, 14.3 Hz, 1 H, CHCH*H*N), 2.92 (s, 3 H, SO_2CH_3), 3.01 (t, *J* = 7.1 Hz, 2 H, CH_2S), 3.04 (dd, *J* = 7.0, 14.3 Hz, 1 H, CHC*H*HN), 3.63 (t, *J* = 7.1 Hz, 2 H, CH_2N), 4.97 (s, 1 H, CH=C). HRMS: calcd. for $C_{10}H_{20}NO_2S_2$ 250.0935; found 250.0947.

Synthesis of Amino Thiols 5 and Disulfides 6

Method A. General Procedure for the Synthesis of Amino Thiols 5 from Thiazolidines 4: (i) A 5 M aqueous solution of HCl (2 mL) was added to thiazolidine **4** (0.33 mmol), and the mixture was stirred at 80 °C under nitrogen until the reaction was complete (see reaction time for each case). The reaction was monitored by ^{1}H NMR spectroscopy. The aqueous solution was washed with diethyl ether (2 × 5 mL), and then water was removed under reduced pressure, and the residue obtained was characterized by NMR spectroscopy as an equimolecular mixture of amino thiol **5** and (methylsulfonyl)-acetic acid (**8**). (ii) The residue was washed with acetone and the precipitate formed was filtered and dried to afford pure amino thiol hydrochloride **5**. The filtrate contained compound **8**. *Note*: Amino thiol **5** can be easily oxidized to the corresponding disulfide **6** on exposure to air. This is because in some cases we did not succeed in isolating the pure amino thiol hydrochloride.

Method B. General Procedure for the Synthesis of Disulfides 6 from Crude Amino Thiols 5 [in the Presence of (Methylsulfonyl)acetic Acid (8)]: A 5 M aqueous solution of HCl (2 mL) was added to the crude mixture of **5** and **8** obtained according to the General Procedure A (i), and the mixture was stirred at 80 °C, under air, until the reaction was complete (see reaction time for each case). The reaction was monitored by ^{1}H NMR spectroscopy. The aqueous solution was concentrated under reduced pressure, and the residue obtained was washed with acetone. The precipitate formed was filtered and dried to afford pure disulfide hydrochloride **6** (the isolated yields were calculated starting from thiazolidine **4**). The filtrate contained compound **8**.

(*S*)-Prolinethiol Hydrochloride (5a): Prepared according to the General Procedure A (i) from thiazolidine **4a**; quantitative crude yield

after 15 h, characterized in the presence of compound **8**. ^{1}H NMR (500 MHz, D_2O): δ = 1.64 (dq, J = 8.6, 13.2 Hz, 1 H), 1.86–2.01 (m, 2 H), 2.10–2.19 (m, 1 H), 2.65 (dd, J_{AX} = 8.4, J_{AB} = 14.5 Hz, 1 H, CH*H*S), 2.87 (dd, J_{BX} = 5.1, J_{AB} = 14.5 Hz, 1 H, C*H*HS), 3.18–3.27 (m, 2 H, CH_2N), 3.58–3.54 (m, 1 H, CHN) ppm. ^{13}C NMR (125 MHz, D_2O): δ = 23.2, 25.0, 28.9, 45.3, 62.6 ppm. HRMS: calcd. for $C_5H_{12}NS$ 118.0690; found 118.0696.

Bis{[(*S*,*S*)-2-pyrrolidinyl]methyl} Disulfide Hydrochloride (6a): Prepared according to the General Procedure B from amino thiol **5a**; quantitative crude yield after 72 h, isolated as a white powder in (76 mg, 75%). $[\alpha]_D^{20}$ = +289.2 (c = 0.5, MeOH). ^{1}H NMR (400 MHz, D_2O): δ = 1.67–1.74 (m, 2 H), 1.93–2.03 (m, 4 H), 2.17–2.23 (m, 2 H), 2.85 (dd, J_{AX} = 9.6, J_{AB} = 14.4 Hz, 2 H, CH*H*S), 3.11 (dd, J_{BX} = 4.4, J_{AB} = 14.4 Hz, 2 H, C*H*HS), 3.23–3.29 (m, 4 H, CH_2N), 3.89–3.97 (m, 2 H, CHN) ppm. ^{13}C NMR (63 MHz, D_2O): δ = 23.6, 29.7, 37.5, 45.8, 59.3 ppm. HRMS: calcd. for $C_{10}H_{21}N_2S_2$ 233.1146; found 233.1154. $C_{10}H_{22}Cl_2N_2S_2$ (305.33 + 0.4HCl): calcd. C 37.54, H 8.76, N 7.06, S 20.04; found C 37.42, H 8.70, N 7.25, S 19.77.

2-(Methylamino)ethanethiol Hydrochloride (5b): Prepared according to the General Procedure A (i) from thiazolidine **4b**; quantitative crude yield after 2 h, characterized in the presence of compound **8**. ^{1}H NMR (500 MHz, D_2O): δ = 2.69 (s, 3 H, CH_3), 2.80 (t, J = 6.0 Hz, 2 H, CH_2S), 3.19 (t, J = 6.0 Hz, 2 H, CH_2N) ppm.

Bis[2-(methylamino)ethyl] Disulfide Hydrochloride (6b): Prepared according to the General Procedure B from amino thiol **5b**; quantitative crude yield after 5 d, isolated as a white powder (76 mg, 91%). ^{1}H NMR (400 MHz, D_2O): δ = 2.64 (s, 6 H, 2 NCH_3), 2.92 (t, J = 6.5 Hz, 4 H, 2 SCH_2), 3.32 (t, J = 6.5 Hz, 4 H, 2 NCH_2) ppm. ^{13}C NMR (63 MHz, D_2O): δ = 31.9, 32.8, 47.0 ppm. HRMS: calcd. for $C_6H_{17}N_2S_2$ 181.0833; found 181.0836. $C_6H_{18}Cl_2N_2S_2$ (253.26 + 0.4HCl): calcd. C 26.91, H 6.92, N 10.46, S 23.94; found C 27.12, H 7.13, N 10.26, S 23.69.

2-(Butylamino)ethanethiol Hydrochloride (5c): Prepared according to the General Procedure A (i, ii) from thiazolidine **4c**; quantitative crude yield after 15 h, isolated as a white powder (51 mg, 91%). ^{1}H NMR (400 MHz, D_2O): δ = 0.82 (t, J = 7.6 Hz, 3 H, C*H*$_3$CH$_2$), 1.28 (sext, J = 7.6 Hz, 2 H, CH$_3$C*H*$_2$), 1.52–1.60 (m, 2 H, CH_2), 2.73 (t, J = 6.8 Hz, 2 H, CH_2S), 2.96 (t, J = 7.6 Hz, 2 H, NC*H*$_2$), 3.14 (t, J = 6.8 Hz, 2 H, CH_2N) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 12.7, 19.1, 19.8, 27.3, 47.2, 49.6 ppm. HRMS: calcd. for $C_6H_{16}NS$ 134.1003; found 134.1009. $C_6H_{16}ClNS$ (169.72 + 0.1HCl): calcd. C 41.57, H 9.36, N 8.08; found C 41.77, H 9.57, N 8.03.

2-(Allylamino)ethanethiol Hydrochloride (5d): Prepared according to the General Procedure A (i, ii) from thiazolidine **4d**; quantitative crude yield after 15 h, isolated as a white powder (30 mg, 60%). ^{1}H NMR (400 MHz, D_2O): δ = 2.88 (t, J = 7.3 Hz, 2 H, CH_2S), 3.20 (t, J = 7.3 Hz, 2 H, CH_2N), 3.60 (d, J = 6.9 Hz, 2 H, $CHCH_2N$), 5.38–5.44 (m, 2 H, C*H*$_2$=CH), 5.75–5.85 (m, 1 H, C*H*=CH$_2$) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 29.9, 46.3, 49.4, 124.0, 127.1 ppm. HRMS: calcd. for $C_5H_{12}NS$ 118.0690; found 118.0679.

2-[(2-Mercaptoethyl)amino]ethanoic Acid Hydrochloride (5e): Prepared according to the General Procedure A (i, ii) from thiazolidine **4e**; quantitative crude yield after 15 h, isolated as a light-brown powder (40 mg, 71%). ^{1}H NMR (400 MHz, D_2O): δ = 2.98 (t, J = 6.8 Hz, 2 H, CH_2S), 3.42 (t, J = 6.8 Hz, 2 H, CH_2N), 3.79 (s, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 32.5, 46.2, 48.1, 169.6 ppm. $C_4H_{10}ClNO_2S$ (171.65 + 0.1HCl): calcd. C 27.41, H 5.81, N 7.99; found C 27.50, H 5.68, N 7.84.

2-(Benzylamino)ethanethiol Hydrochloride (5f): Prepared according to the General Procedure A (i) from thiazolidine **4f**; quantitative crude yield after 6 h, characterized in the presence of compound **8**. ^{1}H NMR (500 MHz, D_2O): δ = 2.82 (t, J = 6.9 Hz, 2 H, CH_2S), 3.25 (t, J = 6.9 Hz, 2 H, CH_2N), 4.25 (s, 2 H, CH_2Ph), 7.47 (s, 5 H, C_6H_5) ppm. HRMS: calcd. for $C_9H_{14}NS$ 168.0847; found 168.0844.

Bis[2-(benzylamino)ethyl] Disulfide Hydrochloride (6f): Prepared according to the General Procedure B from amino thiol **5f**; quantitative crude yield after 15 h, isolated as a white powder (113 mg, 85%). ^{1}H NMR (500 MHz, D_2O): δ = 2.89 (t, J = 7.3 Hz, 4 H, 2 CH_2S), 3.33 (t, J = 7.3 Hz, 4 H, 2 CH_2N), 4.20 (s, 2 H, 4 CH_2Ph), 7.38–7.43 (m, 10 H, 2 C_6H_5) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 38.4, 44.8, 50.9, 129.3, 129.8, 129.9, 130.3 ppm. HRMS: calcd. for $C_{18}H_{25}N_2S_2$ 333.1459; found 333.1462. $C_{18}H_{26}Cl_2N_2S_2$ (405.45 + 1.6HCl): calcd. C 46.61, H 6.00, N 6.04; found C 46.47, H 5.88, N 6.42.

(*R*)-2-(Methylamino)-2-phenylethanethiol Hydrochloride (5g): Prepared according to the General Procedure A (i) from thiazolidine **4g**; quantitative crude yield after 2 h, characterized in the presence of compound **8**. ^{1}H NMR (400 MHz, D_2O): δ = 2.55 (s, 3 H, NCH_3), 3.12–3.17 (m, 2 H, CH_2S), 4.32 (t, J = 7.2 Hz, 1 H, CHN), 7.41–7.45 (m, 2 H, C_6H_5), 7.49–7.52 (m, 3 H, C_6H_5) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 25.9, 30.9, 65.0, 128.2, 129.5, 130.1, 132.5 ppm. HRMS: calcd. for $C_9H_{14}NS$ 168.0847; found 168.0852.

Bis[(*R*,*R*)-2-(methylamino)-2-phenylethyl] Disulfide Hydrochloride (6g): Prepared according to the General Procedure B from amino thiol **5g**; quantitative crude yield after 72 h, isolated as a white powder (105 mg, 79%). $[\alpha]_D^{20}$ = +93.1 (c = 0.8, MeOH). ^{1}H NMR (400 MHz, D_2O): δ = 2.55 (s, 6 H, 2 NCH_3), 3.28 (dd, J_{AX} = 8.2, J_{AB} = 14.3 Hz, 2 H, 2 CH*H*S), 3.39 (dd, J_{BX} = 6.4, J_{AB} = 14.3 Hz, 2 H, 2 C*H*HS), 4.46 (dd, J_{AX} = 8.2, J_{BX} = 6.4 Hz, 2 H, 2 CHN), 7.38–7.43 (m, 4 H, C_6H_5), 7.50–7.55 (m, 6 H, C_6H_5) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 30.8, 39.4, 62.1, 128.6, 129.6, 130.3, 132.0 ppm. HRMS: calcd. for $C_{18}H_{25}N_2S_2$ 333.1459; found 333.1448. $C_{18}H_{26}Cl_2N_2S_2$ (405.45 + 0.2HCl): calcd. C 52.37, H 6.40, N 6.79; found C 52.35, H 6.41, N 6.73.

Bis[(*S*,*S*)-2-isopropyl-2-(methylamino)ethyl] Disulfide Hydrochloride (6h): Prepared according to the General Procedure B from amino thiol **5h**; quantitative crude yield after 48 h, isolated as a light-brown powder (92 mg, 83%). $[\alpha]_D^{20}$ = +247.1 (c = 0.35, MeOH). ^{1}H NMR (500 MHz, D_2O): δ = 0.99 (d, J = 7.0 Hz, 6 H, 2 CHC*H*$_3$), 1.04 (d, J = 7.0 Hz, 6 H, 2 CHC*H*$_3$), 2.21–2.29 (m, 2 H, 2 C*H*CH$_3$), 2.78 (s, 6 H, 2 NCH_3), 2.98 (dd, J_{AX} = 8.2, J_{AB} = 15.0 Hz, 2 H, 2 CH*H*S), 3.16 (dd, J_{BX} = 4.1, J_{AB} = 15.0 Hz, 2 H, 2 C*H*HS), 3.40–3.45 (m, 2 H, 2 CHN) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 16.2, 17.8, 27.7, 31.2, 34.2, 63.2 ppm. HRMS: calcd. for $C_{12}H_{29}N_2S_2$ 265.1772; found 265.1764. $C_{12}H_{30}Cl_2N_2S_2$ (337.42 + 0.6HCl): calcd. C 40.50, H 8.58, N 7.80; found C 39.92, H 8.48, N 8.29.

Bis[(*S*,*S*)-2-(benzylamino)-2-isopropylethyl] Disulfide Hydrochloride (6i): Prepared according to the General Procedure B from amino thiol **5i**; quantitative crude yield after 48 h, isolated as a white powder (135 mg, 84%). $[\alpha]_D^{20}$ = +208.2 (c = 0.5, MeOH). ^{1}H NMR (500 MHz, D_2O): δ = 0.93 (d, J = 7.5 Hz, 6 H, 2 CHC*H*$_3$), 0.96 (d, J = 7.5 Hz, 6 H, 2 CHC*H*$_3$), 2.20–2.27 (m, 2 H, 2 C*H*CH$_3$), 2.85 (dd, J_{AX} = 8.2, J_{AB} = 15.0 Hz, 2 H, 2 C*H*HS), 2.95 (dd, J_{BX} = 4.1, J_{AB} = 15.0 Hz, 2 H, 2 CH*H*S), 3.26–3.30 (m, 2 H, 2 CHN), 4.32–4.39 (m, 4 H, 2 CH_2Ph), 7.50 (s, 10 H, 2 C_6H_5) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 16.1, 17.6, 27.9, 34.4, 49.6, 60.6, 129.5, 129.9, 130.1 ppm. HRMS: calcd. for $C_{24}H_{37}N_2S_2$ 417.2398; found 417.2386. $C_{24}H_{38}Cl_2N_2S_2$ (489.61 + 1.4HCl): calcd. C 53.32, H 7.35; found C 53.55, H 7.38.

(*R*,*R*)-*N*,*N*′-Dimethylcysteine Hydrochloride (6j): Prepared according to the General Procedure B from amino thiol **5j**; quantitative

crude yield after 72 h, isolated as a light-brown solid (69 mg, 62%). $[\alpha]_D^{20}$ = +52 [*c* = 0.1, HCl (5 M)]. ^{1}H NMR (400 MHz, D_2O): δ = 2.79 (s, 6 H, 2 CH_3), 3.38 (d, *J* = 5.1 Hz, 4 H, 2 CH_2S), 3.99 (t, *J* = 5.1 Hz, 2 H, 2 CHN) ppm. ^{13}C NMR (125 MHz, D_2O): δ = 31.9, 36.8, 61.5, 171.8 ppm. HRMS: calcd. for $C_8H_{17}N_2O_4S_2$ 269.0638; found 269.0630.

Bis[(1*R*,2*R*,1′*R*,2′*R*)-2-methyl-2-(methylamino)-1-phenylethyl] Disulfide Hydrochloride (6k): Prepared according to the General Procedure B from amino thiol **5k**; isolated as a white powder (33 mg, 23%). $[\alpha]_D^{20}$ = –32 (*c* = 0.05, MeOH). ^{1}H NMR (400 MHz, D_2O): δ = 1.25 (d, *J* = 6.6 Hz, 6 H, 2 CHCH_3), 2.68 (s, 6 H, 2 CH_3N), 3.76 (m, 2 H, 2 C*H*CH_3), 3.83 (d, *J* = 8.3 Hz, 2 H, 2 CHN), 7.21–7.26 (m, 4 H, C_6H_5), 7.47–7.52 (m, 6 H, C_6H_5) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 12.6, 30.1, 57.0, 57.2, 128.9, 129.2, 129.3, 135.4 ppm. HRMS: calcd. for $C_{20}H_{29}N_2S_2$ 361.1772; found 361.1778.

Bis{(*S*,*S*)-2-[(2-methylbutyl)amino]ethyl} Disulfide Hydrochloride (6l): Prepared according to the General Procedure B from amino thiol **5l**; quantitative crude yield after 1 h, isolated as a white powder (79 mg, 66%). ^{1}H NMR (400 MHz, D_2O): δ = 0.83 (t, *J* = 7.3 Hz, 6 H, C$H_3$$CH_2$), 0.92 (d, *J* = 7.0 Hz, 6 H, CH_3CH), 1.12–1.24 (m, 2 H), 1.31–1.40 (m, 2 H, C$H_2$$CH_3$), 1.71–1.80 (m, 2 H, C*H*CH_3), 2.84 (dd, J_{AX} = 8.0, J_{AB} = 12.3 Hz, 2 H, 2 NCH_2), 2.98 (t, *J* = 6.0 Hz, 4 H, 2 CH_2S), 2.95–3.00 (m, 2 H, NCH_2), 3.37 (t, *J* = 6.0 Hz, 4 H, 2 CH_2N) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 10.0, 15.9, 26.2, 31.6, 31.8, 46.1, 53.2 ppm. HRMS: calcd. for $C_{14}H_{33}N_2S_2$ 293.2085; found 293.2072. $C_{14}H_{34}Cl_2N_2S_2$ (365.47 + 1.1HCl): calcd. C 41.46, H 8.72, N 6.91; found C 41.35, H 8.87, N 6.93.

X-ray Crystallographic Study: CCDC-718259 (**4b**) and -718260 (**7f**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): (1) Experimental procedures and characterization data for compounds **1a**, **1b**, **3b**–**l**, **7b**, **7f**, and **8**; (2) crystallographic data for **4b** and **7f**; (3) ^{1}H and ^{13}C NMR spectra for compounds **1a**, **3b**–**k**, **4a**–**k**, **5a**–**g**, **6a**, **6b**, **6f**–**l**, **7b**, **7f**, and **8**.

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