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Intramolecular, Reductive Cyclization of β-Ketoisothiocyanates Promoted by Using Samarium Diiodide

Min Seok Cho, In Sang Lee, Sung Ho Kang, and Yong Hae Kim*[a]

This paper is dedicated to Professor Dong Han Kim on the occasion of his retirement from the Pohang Institute of Technology

Abstract: A novel samarium diiodide (SmI_2) promoted intramolecular cyclization of β-ketoisothiocyanate, derived from α,β-unsaturated esters and ammonium thiocyanate led to α-hydroxythiolactams and/or thiolactams in high yields. Treatment of β-ketoisothiocyanate with two equivalents of SmI_2 gave a mixture of α-hydroxythiolactam and thiolactam. Four equivalents of SmI_2 afforded only thiolactam in high yields. The intramolecular cyclization took place with high to complete stereoselectivity. A mechanism to explain this transformation is proposed.

Keywords: cyclization · diastereoselectivity · heterocycles · radical reactions · samarium

Introduction

Thioamides are valuable intermediates in organic synthesis,[1] and in particular, for the preparation of heterocycles of natural products.[2] There have been numerous procedures reported for the synthesis of thiolactams or thioamides by transformation of the corresponding lactams or amides: Various reagents such as Lawesson's reagent,[3] P_2S_5,[4] R_3OBF_4–NaSH,[5] R_2PSX,[6] $(Et_2Al)_2S$,[7] $(TMS)_2S_8$ (TMS = trimethylsilyl),[1a] and tetrathiomolybdate have been reported.[1b] However, direct preparations of thiolactams are not commonly known. To our knowledge, only one direct synthesis of thiolactams has been reported: the reaction of alkenyl isothiocyanates with nBu$_3$SnH and azobis(isobutyronitrile) (AIBN).[8]

The formation of a cyclic system through the intramolecular addition of a ketyl radical to carbon–carbon multiple bonds has been widely exploited in recent years.[9] Since Kagan and his co-workers' pioneering work,[10a] samarium diiodide (SmI_2) has become a highly useful reagent to organic synthesis during the past two decades.[10] The single-electron transfer ability of samarium(II) makes it possible to perform radical or anionic reactions, such as reductive cyclizations initiated by carbonyl radicals,[11,9a–d] deoxygenations of epoxides,[12] Reformatsky reactions,[13] and pinacol-coupling reactions.[14]

We now report on a new approach to the sequential radical cyclization of β-carbonyl isothiocyanates for producing α-hydroxythiolactams which opens up a promising avenue for the successful synthesis of heterocycles. It is the first time that the synthesis of α-hydroxythiolactams occuring by a one-step reaction has been reported.

The cyclization appears to be initiated by formation of a ketyl radical (**I**) and/or a thioimidoyl radical (**II**) which could be subsequently exocyclized to form α-hydroxythiolactam (**2**) with high stereoselectivity. Compound **2** was converted to thiolactam (**3**) with an excess amount of SmI_2, as depicted in Scheme 1.

Results and Discussion

The starting materials were readily prepared by the addition of ammonium thiocyanate to α,β-unsaturated carbonyl compounds.[15] Treatment of **1a** with freshly prepared SmI_2[16] in tetrahydrofuran (THF) in the presence of tBuOH afforded **2a** as the major product in a 78% yield as shown in Scheme 2. The reaction gave cyclized α-hydroxythiolactam (**2a**), and its dehydroxylated product **3a**, in which the major product depends on the amount of SmI_2 used and the reaction temperature. When the reaction was carried out at 25 °C with four equivalents of SmI_2, the deoxygenated product **3a** was obtained in a 90% yield (Scheme 2).

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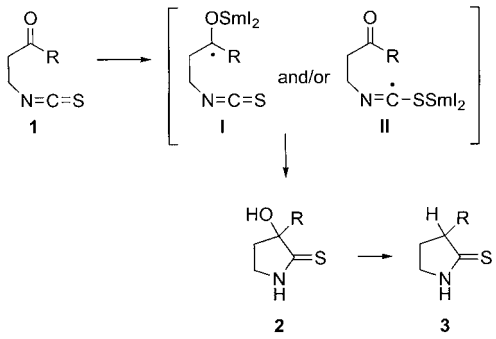
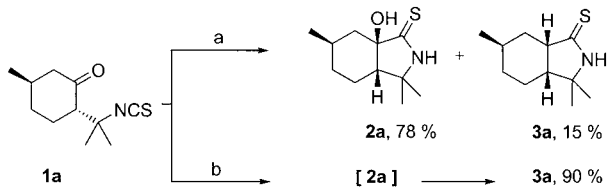
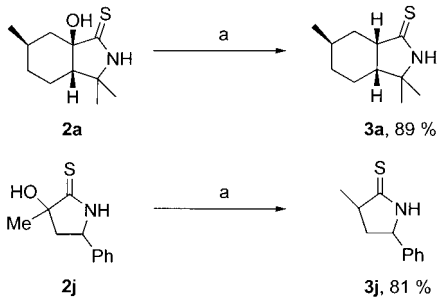


Scheme 1. Cyclization of β-ketoisothiocyanate (**1**) to α-hydroxythiolactam (**2**) and thiolactam (**3**) with an excess amount of SmI_2: this appears to be initiated by formation of a ketyl radical (**I**) and/or a thioimidoyl radical (**II**).



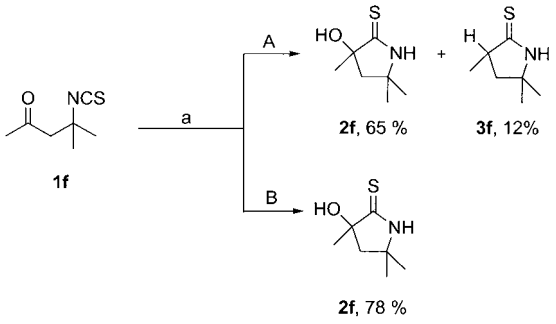
Scheme 2. Reaction of **1a** with SmI_2 under different reaction conditions: a) 2 SmI_2, THF, *t*BuOH, −78 °C, 1 h; b) 4 SmI_2, THF, *t*BuOH, 25 °C, 8 h.

The isolated intermediates **2a** or **2j**, when reacted with 2 equivalents of SmI_2 at 25 °C for 4 hours, afforded **3a** (89 %) or **3j** (81 %), respectively, as shown in Scheme 3. The formation of **3a** is deduced to undergo a sequential radical cyclization of **1a** followed by deoxygenation. Recently, several examples of deoxygenations of tertiary alcohols with SmI_2 have been reported.[17]



Scheme 3. Dehydroxylation of isolated intermediate **2** to thiolactam **3**. a) 2 SmI_2, THF, *t*BuOH (2 equiv), −25 °C, 4 h.

Interestingly, the formation of two different products was observed depending on the order of the reagent addition. For example, in the case of acyclic β-ketoisothiocyanate (**1f**), addition of a solution of **1f** in THF and 2 equivalents of *t*BuOH to a solution of SmI_2 in THF (0.1 M) at −78 °C produced the cyclized product α-hydroxythiolactam **2f** (65 %) as the major product together with dehydroxylated thiolactam **3f** (12 %) as the minor product (method A). Whereas, when the solution of SmI_2 in THF was added to the solution of **1f** in THF under the same conditions, only **2f** was obtained (78 %; method B) as shown in Scheme 4.



Scheme 4. Cyclization of **1f** to **2f** and **3f**: a) SmI_2, THF, *t*BuOH, −78 °C, 1 h. Method A: addition of a solution of **1f** in THF to a solution of SmI_2 in THF. Method B: addition of a solution of SmI_2 in THF to a solution of **1f** in THF solution.

Various cyclic and acyclic β-ketothiocyanates were reacted with samarium diiodide in the presence of *t*BuOH to give **2a** or **3a** in good yields depending on the amount of SmI_2 used and reaction temperatures. The results obtained are summarized in Table 1.

The (2*R*,5*S*)-configured **1a** gave the *cis*-α-hydroxybicyclic-thiolactam (**2a**) and *cis*-deoxygenated thiolactam (**3a**) in a stereospecific manner: only one diastereomer was obtained and confirmed by using chiral HPLC analysis. The (2*R*,5*R*)-configured **1b** gave *trans*-fused diastereomers **2b** and **3b**. The structures and stereoconfigurations of **2a** and **3a** were established by using ^1H and ^{13}C NMR spectra,[18] and 2D COSY NMR experiments.

When **1c** was treated with 2 equivalents of SmI_2, *cis*-fused-ring product **2c** was produced in an 84 % yield giving almost a single diastereomer (Table 1, entry 5). Compound **1e** afforded **2e** in a 70 % yield with complete stereoselectivity (*trans*/*cis* = 100:0, Table 1, entry 7). On the other hand, the seven-membered ring isothiocyanate **1d** resulted in a mixture of *cis* and *trans* isomers (entry 4, *cis*/*trans* = 4:1) of **2d** and **3d**. Acyclic β-ketoisothiocyanates **1f–1p** were cyclized to **2f–2p** and/or **3f–3p** in variable diastereoselectivities depending upon their substituents. When R was substituted with Ph or C_6H_4(*p*-OMe), **1j** or **1k** resulted in high selectivity of 1:10.8 (Table 1, entry 13) or 1:8.8 (Table 1, entry 14), respectively. But other isothiocyanates gave lower selectivities.

The SmI_2-mediated intramolecular couplings between aldehydes and isothiocyanates occurred much faster (Table 1, entries 20, 22) than those between other ketones and isothiocyanates.

Although β-ketoisothiocyanates were readily cyclized to α-hydroxythiolactams, γ-ketoisothiocyanates did not undergo the cyclization reaction under the same reaction conditions: starting materials were recovered quantitatively.

Table 1. Cyclization of β-ketoisothiocyanates with SmI_2.[a]

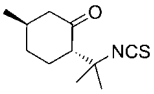
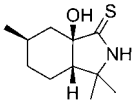
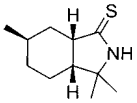
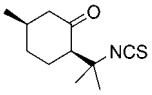
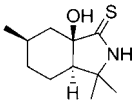
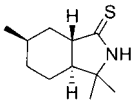
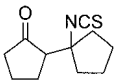
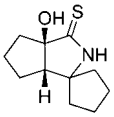
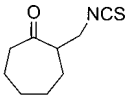
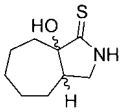
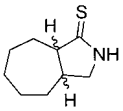
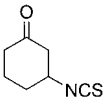
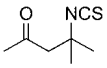
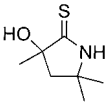
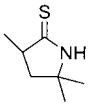
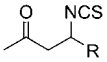
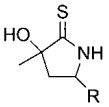
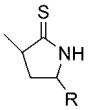
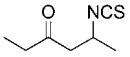
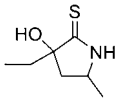
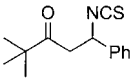
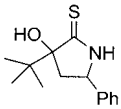
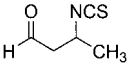
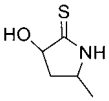
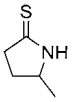
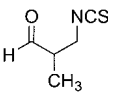
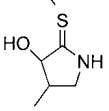
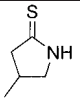
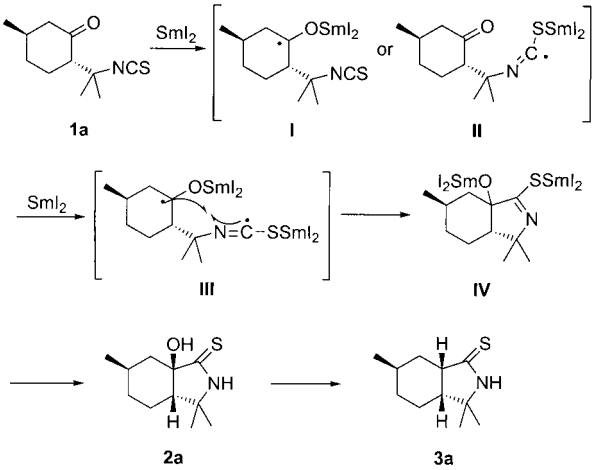
Entry	Substrates		Products		Yield [%][b]	*cis*:*trans*[c]
1		**1a**	 **2a**	 **3a**	78 (**2a**) 15 (**3a**)	100:0
2[d]		**1a**		**3a**	90	100:0
3		**1b**	 **2b**	 **3b**	72 (**2b**) 25 (**3b**)	0:100
4[d]		**1b**		**3b**	81	0:100
5[e]		**1c**		**2c**	84	100:0
6[e]		**1d**	 **2d**	 **3d**	82 (**2d**) 16 (**3d**)	4:1
7		**1e**		**2e**	70	0:100
8		**1f**		**2f**	78	
9[d]		**1f**		**3f**	87	
10		**1g**: R = Me		**2g**	75	1:1.2
11		**1h**: R = *i*Pr		**2h**	77	1:2.3
12		**1i**: R = *t*Bu		**2i**	72	1:2.9
13		**1j**: R = Ph		**2j**	89	1:10.8
14		**1k**: R = *p*-MeOPh		**2k**	81	1:8.8
15		**1l**: R = H		**2l**	76	
16[d]		**1g**: R = Me		**3g**	85	
17[d]		**1l**: R = H		**3l**	83	
18		**1m**		**2m**	81	1:6.7
19		**1n**		**2n**	68	1:2.9
20[f]		**1o**		**2o**	62	1:2.5
21[d]		**1o**		**3o**	78	
22[f]		**1p**		**2p**	72	1:6.7

Table 1. (Continued)

Entry	Substrates	Products	Yield [%][b]	*cis*:*trans*[c]
23[d]	**1p**	 **3p**	80	

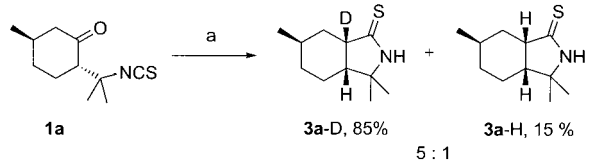
[a] The reactions were carried out in THF with β-ketoisothiocyanate **1** (0.25 mmol), SmI_2 (0.5 mmol), and *t*BuOH (0.5 mmol) at −78 °C for 2 h except where otherwise stated. [b] Isolated yields. [c] The ratio was determined by ^{1}H NMR spectroscopy. [d] β-ketoisothiocyanate **1** (0.25 mmol), SmI_2 (1.0 mmol), and *t*BuOH (1.0 mmol) at 25 °C for 8 h. [e] Reaction time: 0.5 h. [f] Reaction time: 5 min at −78 °C.

The possible mechanism for the sequential cyclization is proposed as shown in Scheme 5. Formation of ketyl radicals of carbonyls with SmI_2 has been well documented.[9] The reaction appears to be initiated by generating a requisite ketyl



Scheme 5. Proposed mechanism for the formation of α-hydroxythiolactam/thiolactam by using SmI_2.

radical (**I**) or a thioimidoyl radical (**II**) with one electron transfer from SmI_2. The use of two equivalents of SmI_2 may form both ketyl and imidoyl radicals in **III**. Intramolecular radical–radical coupling will give cyclized **IV**. Dehydroxylation of the tertiary alcohol[17] and deoxygenation of the α-hydroxy carbonyl compound are well known.[19] **2a** is readily converted to dehydroxylated **3a** with an excess amount of SmI_2. In order to see whether the α-hydrogen of **3a** originated from the proton source of the alcohol or from THF, the sequential cyclization was carried out in the presence of CD_3OD. Product **3a** was found to contain 85% deuterium atoms and 15% hydrogen atoms incorporated as shown in Scheme 6. The ratio (5:1) of **3a**-D and **3a**-H was determined by using ^{1}H NMR and mass spectra.



Scheme 6. Cyclization of **1a** in CD_3OD and THF: a) 4 SmI_2, THF, CD_3OD, 25 °C.

Conclusion

In summary, we have demonstrated the intramolecular, reductive cyclization of β-ketoisothiocyanates (**1**) by using SmI_2. The direct preparations of α-hydroxythiolactams and thiolactams are possible with **1** as the starting material. The scope and applications of this method to the synthesis of natural products are under investigation.

Experimental Section

General: THF was distilled from sodium/benzophenone. Yields refer to chromatography and spectroscopically (^{1}H NMR) defined homogeneous materials, unless otherwise stated. The reactions were monitored by using thin-layer chromatography on glass plates (0.25 mm) coated with silica gel 60 F_{254} (Merck). ^{1}H NMR spectra were recorded on Bruker AM-300 (300 MHz) and AM-400 spectrometers (400 MHz) at ambient temperature. ^{13}C NMR spectra were recorded on Bruker AM-300 (75 MHz) and Bruker AM-400 spectrometers (100 MHz) at ambient temperature. Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard (deuterochloroform at 77.00 ppm). IR spectra were recorded on a Bruker EQUINOX55 FT-IR spectrophotometer. High-resolution mass spectra (HRMS) were recorded on a Hewlett–Packard 5980 A GC–MS (at 70 eV) system using the electron impact (EI) method. HPLC spectra were recorded on an Agilent 1100 series with Daicel Chiralcel OD-H column. Melting points were recorded on an Electrothermal® melting point apparatus and are uncorrected. The relative configuration (*cis* or *trans*) of **2** was determined by using ^{1}H NMR spectroscopy. For instance, the chemical shift of the methine proton of **2h** (*trans*) appears at 3.62 ppm, thus shifted more downfield than that of the *cis* form (3.44 ppm). The stereochemistry was also confirmed by using NOE experiments.

General procedure for the preparation of α-hydroxythiolactam from β-ketoisothiocyanate by using SmI_2: **1j** (41 mg, 0.25 mmol) and *t*-butanol (50 μL, 0.5 mmol) were dissolved in THF (1.5 mL) and purged with argon. Freshly prepared SmI_2 from Sm metal (100 mg) and diiodomethane (41 μL) in THF (10 mL) was added to the vigorously stirred solution over a period of 5 minutes at −78 °C. After 2 h, the reaction was quenched with 1 N HCl solution, and the mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The two isomers were readily separated (*trans*-**2j**: 81%; *cis*-**2j**: 8%) by using silica-gel column chromatography (Merck 60, 230–400 mesh, 2 × 25 cm, *n*Hex/EtOAc = 3:1). The stereochemistry of the diastereoisomers was determined by using NOE experiments.

(1*R*,3*R*,6*S*)-1-Hydroxy-3,7,7-trimethyl-8-azabicyclo[4.3.0]nonane-9-thione (2a): R_f = 0.35 (*n*Hex/EtOAc = 3:1); m.p. 152–153 °C; $[\alpha]_D = -65.98$ (c = 0.68, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (br, 1H; -N*H*-), 2.41 (dq, J = 6.4, 2.7 Hz, 1H; -C*H*−C(CH_3)$_2$-), 2.27 (br, 1H; -O*H*), 2.06 (m, 1H; -C*H*(CH_3)-), 1.86–1.80 (m, 1H; -CH(OH)−CH_aH$_b$−CH(CH_3)-), 1.62–1.58 (m, 1H; -CH(OH)−CH_a*H*$_b$−CH(CH_3)-), 1.55 (s, 3H; -C(CH_{3a})(CH_{3b})-), 1.36–1.30 (m, 2H; -CH(CH_3)−CH_2−CH$_2$-), 1.23 (s, 3H; -C(CH_{3a})(CH_{3b})-), 1.12–1.05 (m, 2H; -CH$_2$−CH_2−CH-), 0.97 ppm (d, J =

6.4 Hz, 3H; -CH(CH_3)-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 205.4, 83.4, 65.0, 49.4, 43.1, 31.5, 29.9, 29.2, 25.3, 23.7, 21.8 ppm; IR (KBr): $\tilde{\nu}$ = 3354, 3193, 2950, 1687, 1529, 1459, 1161, 1029, 911, 729, 656 cm^{-1}; t_R = 11.16 min (OD-H, 254 nm, *i*PrOH/*n*Hex = 1:9); HRMS: *m*/*z* (%) calcd for $C_{11}H_{19}NOS$: 213.1187 [M^+]; found: 213.1187.

(1*R*,3*R*,6*R*)-1-Hydroxy-3,7,7-trimethyl-8-azabicyclo[4.3.0]nonane-9-thione (2b): R_f = 0.39 (*n*Hex/EtOAc = 3:1); m.p. 119–121 °C; $[\alpha]_D$ = −10.63 (*c* = 0.16, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.73 (br, 1H; -N*H*-), 2.91 (s, 1H; -O*H*), 2.15 (m, 1H; -C*H*−C(CH_3)$_2$-), 1.87–1.70 (m, 4H; -CH(OH)−CH_2−CH(CH_3)-, -CH(CH_3)−CH_2−CH_2-), 1.60–1.56 (m, 1H; -C*H*(CH_3)-), 1.33 (s, 3H; -C(CH_{3a})(CH_{3b})-), 1.30 (s, 3H; -C(CH_{3a})(CH_{3b})-), 1.11–1.00 (m, 2H; -CH_2−CH_2−CH-), 0.91 ppm (d, *J* = 3.2 Hz, 3H; -CH(CH_3)-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 208.0, 81.9, 64.3, 48.9, 44.6, 30.7, 30.0, 26.6, 24.7, 22.3, 20.6 ppm; IR (KBr): $\tilde{\nu}$ = 3411, 3174, 2929, 1691, 1532, 1455, 1139, 1018, 944, 781 cm^{-1}; t_R = 10.28 min (OD-H, 254 nm, *i*PrOH/*n*Hex = 1:9); HRMS: *m*/*z* (%) calcd for $C_{11}H_{19}NOS$: 213.1187 [M^+]; found: 213.1186.

3′*H*-Spiro[cyclopentane-1,4′-[1*R,5*S**][1]hydroxy[3]azabicyclo[3.3.0]octane[2]thione] (2c)**: R_f = 0.26 (*n*Hex/EtOAc = 3:1); m.p. 167–168 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.37 (br, 1H; -N*H*-), 2.52 (dd, *J* = 4.3, 3.3 Hz, 1H; -C*H*-C(spirocyclopentyl)-), 2.25 (s, 1H; -O*H*), 2.19–2.13 (m, 1H; -CH(OH)−CH_aH$_b$-), 2.02–1.96 (m, 1H; -CH(OH)−CH$_a$H$_b$-), 1.92–1.88 (m, 2H; -CH_2−CH_2−CH_2-), 1.82–1.67 (m, 8H; spirocyclopentyl), 1.65–1.55 ppm (m, 2H; -CH_2−CH_2−CH-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 206.3, 93.9, 75.1, 54.6, 41.4, 40.7, 33.4, 29.4, 25.4, 23.0, 22.7 ppm; IR (KBr): $\tilde{\nu}$ = 3261, 2946, 1699, 1507, 1286, 1138, 1079, 1065 cm^{-1}; HRMS: *m*/*z* (%) calcd for $C_{11}H_{17}NOS$: 211.1031 [M^+]; found: 211.1034.

1-Hydroxy-9-azabicyclo[5.3.0]decane-10-thione (2d): Inseparable white powder; R_f = 0.37 (*n*Hex/EtOAc = 2:1); ^{1}H NMR (300 MHz, $CDCl_3$): major isomer: δ = 7.98 (br, 1H; -N*H*-), 3.71–3.64 (m, 1H; -CH_aH$_b$−NH-), 2.97–2.92 (m, 1H; -CH$_a$$H_b$−NH-), 2.27–2.15 (m, 1H; -CH$_2$−C*H*−CH$_2$-), 1.95–1.23 ppm (m, 10H; -C(OH)−(CH_2)$_5$−CH-); minor isomer: δ = 8.09 (br, 1H; -N*H*-), 3.16–3.10 (m, 1H; -CH_aH$_b$−NH-), 2.82–2.70 (m, 1H; -CH$_a$$H_b$−NH-), 2.61–2.52 (m, 1H; -CH$_2$−C*H*−CH$_2$-), 1.95–1.23 ppm (m, 10H; -C(OH)−(CH_2)$_5$−CH-); ^{13}C NMR (75 MHz, $CDCl_3$): major isomer: δ = 210.5, 57.7, 54.6, 40.6, 31.5, 31.3, 30.1, 28.9, 28.2 ppm; minor isomer: δ = 207.8, 56.7, 52.5, 46.6, 43.6, 31.8, 28.8, 27.3, 25.8 ppm; IR (KBr) as mixture: $\tilde{\nu}$ = 3367, 2919, 2850, 1695, 1549, 1455, 1306, 1166, 1040, 1015 cm^{-1}; HRMS: *m*/*z* (%) calcd for $C_9H_{15}NOS$: 185.0874 [M^+]; found: 185.0875.

1-Hydroxy-6-azabicyclo[3.2.1]octane-7-thione (2e): Pale yellow oil; R_f = 0.38 (*n*Hex/EtOAc = 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.35 (br, 1H; -N*H*-), 3.98 (q, *J* = 6.7 Hz, 1H; -C*H*−NH-), 3.17 (s, 1H; -O*H*), 2.31–2.28 (m, 1H; -CH−CH_aH$_b$−CH(OH)-), 1.94 (d, *J* = 5.2 Hz, 1H; -CH−CH$_a$$H_b$−CH(OH)-), 1.79–1.41 ppm (m, 6H; -C(OH)−CH_2−CH_2−CH_2−CH-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 208.7, 81.3, 56.0, 45.4, 41.3, 35.1, 25.4, 18.9 ppm; IR (neat): $\tilde{\nu}$ = 3261, 2946, 1699, 1507, 1286, 1138, 1079, 1065 cm^{-1}; HRMS: *m*/*z* (%) calcd for $C_7H_{11}NOS$: 157.0561 [M^+]; found: 157.0562.

3-Hydroxy-3,5,5-trimethylpyrrolidine-2-thione (2f): R_f = 0.62 (*n*Hex/EtOAc = 1:1); m.p. 123–125 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.85 (br, 1H; -N*H*-), 2.92 (br, 1H; -O*H*), 2.17 (dd, *J* = 18.0, 6.8 Hz, 2H; -CH_2−C(CH_3)$_2$-), 1.50 (s, 3H; -C(CH_3)(OH)), 1.40 (s, 3H; -C(CH_{3a})(CH$_{3b}$)), 1.34 ppm (s, 3H; -C(CH$_{3a}$)(CH_{3b})); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.9, 81.8, 61.9, 49.4, 29.7, 29.3, 28.6 ppm; IR (KBr): $\tilde{\nu}$ = 3351, 3167, 2967, 1659, 1514, 1376, 1194, 946, 779, 514 cm^{-1}; HRMS: *m*/*z* (%) calcd for $C_7H_{13}NOS$: 159.0718 [M^+]; found: 159.0718.

***cis*-3,5-Dimethyl-3-hydroxypyrrolidine-2-thione (*cis*-2g)**: Yellow oil; R_f = 0.49 (*n*Hex/EtOAc = 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (br, 1H; -N*H*-), 3.89–3.80 (m, 1H; -C*H*(CH)$_3$−NH-), 2.45 (dd, *J* = 6.2, 3.0 Hz, 1H; -C(OH)(CH$_3$)−CH_aH$_b$-), 2.41 (br, 1H; -O*H*), 1.84 (dd, *J* = 6.2, 4.6 Hz, 1H; -C(OH)(CH$_3$)−CH$_a$$H_b$-), 1.38 (s, 3H; -C(OH)(CH_3)), 1.32 ppm (d, *J* = 3.2 Hz, 3H; -CH(CH_3)−NH-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 210.2, 81.3, 53.5, 44.9, 26.9, 20.4 ppm; IR (neat): $\tilde{\nu}$ = 3385, 2974, 1653, 1540, 1448, 1383, 1278, 1173, 1049 cm^{-1}.

***trans*-3,5-Dimethyl-3-hydroxypyrrolidine-2-thione (*trans*-2g)**: Yellow oil; R_f = 0.41 (*n*Hex/EtOAc = 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22 (br, 1H; -N*H*-), 4.09–4.02 (m, 1H; -C*H*(CH)$_3$−NH-), 2.53 (dd, *J* = 6.7, 3.8 Hz, 1H; -C(OH)(CH$_3$)−CH_aH$_b$-), 2.23 (br, 1H; -O*H*), 1.78 (dd, *J* = 6.2, 4.6 Hz, 1H; -C(OH)(CH$_3$)−CH$_a$$H_b$-), 1.52 (s, 3H; -C(OH)(CH_3)), 1.29 ppm (d, *J* = 3.3 Hz, 3H; -CH(CH_3)−NH-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 208.6, 81.3, 53.9, 43.6, 28.4, 20.8 ppm; IR (neat): $\tilde{\nu}$ = 3418, 2978, 1653, 1540, 1448, 1301, 1165, 1044 cm^{-1}; HRMS: *m*/*z* (%) calcd for C_5H_9NOS: 131.0405 [M^+]; found: 131.0405.

***cis*-3-Hydroxy-5-isopropyl-3-methylpyrrolidine-2-thione (*cis*-2h)**: R_f = 0.31 (*n*Hex/EtOAc = 3:1); m.p. 89–90 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.17 (br, 1H; -N*H*-), 3.44 (m, 1H; -C*H*(CH)−NH-), 2.80 (br, 1H; -O*H*), 2.34 (dd, *J* = 6.2, 3.0 Hz, 1H; -C(OH)(CH$_3$)−CH_aH$_b$-), 1.89 (dd, *J* = 6.2, 4.7 Hz, 1H; -C(OH)(CH$_3$)−CH$_a$$H_b$-), 1.76 (dt, *J* = 13.8, 6.9 Hz, 1H; -C*H*(CH$_3$)$_2$), 1.38 (s, 3H; -C(OH)(CH_3)), 0.99 (d, *J* = 1.3 Hz, 3H; -CH(CH_{3a})(CH$_{3b}$)), 0.91 ppm (d, *J* = 1.3 Hz, 3H; -CH(CH$_{3a}$)(CH_{3b})); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 210.5, 81.0, 64.0, 40.7, 32.2, 27.2, 19.2, 18.1 ppm; IR (KBr): $\tilde{\nu}$ = 3164, 2970, 1691, 1532, 1271, 1096, 780 cm^{-1}.

***trans*-3-Hydroxy-5-isopropyl-3-methylpyrrolidine-2-thione (*trans*-2h)**: R_f = 0.18 (*n*Hex/EtOAc = 3:1); m.p. 107–108 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.47 (br, 1H; -N*H*-), 3.62 (q, *J* = 11.1 Hz, 1H; -C*H*(CH)−NH-), 2.51 (br, 1H; -O*H*), 2.41 (dd, *J* = 6.8, 3.7 Hz, 1H; -C(OH)(CH$_3$)−CH_aH$_b$-), 1.83 (dd, *J* = 6.8, 3.3 Hz, 1H; -C(OH)(CH$_3$)−CH$_a$$H_b$-), 1.69 (dt, *J* = 17.3, 10.5 Hz, 1H; -C*H*(CH$_3$)$_2$), 1.50 (s, 3H; -C(OH)(CH_3)), 0.98 (d, *J* = 3.3 Hz, 3H; -CH(CH_{3a})(CH$_{3b}$)), 0.91 ppm (d, *J* = 3.3 Hz, 3H; -CH(CH$_{3a}$)(CH_{3b})); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 208.7, 81.1, 64.7, 39.7, 32.3, 27.9, 19.3, 18.5 ppm; IR (KBr): $\tilde{\nu}$ = 3417, 3178, 2963, 1686, 1538, 1372, 1287, 1155, 1050, 942, 779 cm^{-1}; HRMS: *m*/*z* (%) calcd for $C_8H_{15}NOS$: 173.0874 [M^+]; found: 173.0873.

***cis*-5-*tert*-Butyl-3-hydroxy-3-methylpyrrolidine-2-thione (*cis*-2i)**: R_f = 0.47 (*n*Hex/EtOAc = 2:1); m.p. 130–132 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10 (br, 1H; -N*H*-), 3.51–3.46 (m, 1H; -C*H*(CMe$_3$)-), 2.65 (br, 1H; -O*H*), 2.22 (dd, *J* = 6.3, 3.1 Hz, 1H; -C(OH)(CH$_3$)−CH_aH$_b$-), 2.02–1.91 (m, 1H; -C(OH)(CH$_3$)−CH$_a$$H_b$-), 1.40 (s, 3H; -C(OH)(CH_3)), 0.93 ppm (s, 9H; -C(CH_3)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 210.8, 81.0, 67.2, 38.4, 32.7, 27.4, 25.7 ppm (×3).

***trans*-5-*tert*-Butyl-3-hydroxy-3-methylpyrrolidine-2-thione (*trans*-2i)**: R_f = 0.32 (*n*Hex/EtOAc = 2:1); m.p. 143–144 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.51 (br, 1H; -N*H*-), 3.73 (t, *J* = 7.6 Hz, 1H; -C*H*(CMe$_3$)-), 2.61 (br, 1H; -O*H*), 2.28 (dd, *J* = 6.9, 3.6 Hz, 1H; -C(OH)(CH$_3$)−CH_aH$_b$-), 1.81 (dd, *J* = 6.9, 4.0 Hz, 1H; -C(OH)(CH$_3$)−CH$_a$$H_b$-), 1.50 (s, 3H; -C(OH)(CH_3)), 0.90 ppm (s, 9H; -C(CH_3)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 208.4, 81.3, 68.1, 37.3, 32.7, 27.2, 25.7 ppm (×3); IR (KBr): $\tilde{\nu}$ = 3412, 3170, 2967, 1673, 1537, 1372, 1264, 1128, 1076, 939, 774, 559 cm^{-1}; HRMS: *m*/*z* (%) calcd for $C_9H_{17}NOS$: 187.1031 [M^+]; found: 187.1033.

***cis*-3-Hydroxy-3-methyl-5-phenylpyrrolidine-2-thione (*cis*-2j)**: R_f = 0.46 (*n*Hex/EtOAc = 2:1); m.p. 107–109 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.29 (m, 5H; -*Ph*), 4.75 (dd, *J* = 4.8, 3.1 Hz, 1H; -C*H*Ph-), 2.71 (dd, *J* = 6.4, 3.1 Hz, 1H; -CH_aH$_b$-CHPh-), 2.21 (dd, *J* = 6.3, 4.8 Hz, 1H; -CH$_a$$H_b$−CHPh-), 1.51 ppm (s, 3H; -C(OH)(CH_3)); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 210.9, 138.8, 129.2 (×2), 128.9, 126.6 (×2), 81.2, 61.5, 46.8, 27.0 ppm; IR (KBr): $\tilde{\nu}$ = 3357, 3215, 2965, 1634, 1521, 1262, 1134, 1060, 955, 750, 700 cm^{-1}.

***trans*-3-Hydroxy-3-methyl-5-phenylpyrrolidine-2-thione (*trans*-2j)**: R_f = 0.32 (*n*Hex/EtOAc = 2:1); m.p. 126–128 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.33 (br, 1H; -N*H*-), 7.40–7.23 (m, 5H; -*Ph*), 5.03 (t, *J* = 7.0 Hz, 1H; -C*H*Ph-), 2.81 (dd, *J* = 6.8, 3.8 Hz, 1H; -CH_aH$_b$−CHPh-), 2.62 (br, 1H; -O*H*), 2.09 (dd, *J* = 6.7, 3.3 Hz, 1H; -CH$_a$$H_b$−CHPh-), 1.49 ppm (s, 3H; -C(OH)(CH_3)); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 209.7, 139.5, 129.1 (×2), 128.4, 125.8 (×2), 81.1, 61.5, 45.8, 27.6 ppm; IR (KBr): 3351, 3208, 2971, 1667, 1527, 1260, 1135, 1059, 954, 765, 700, 522 cm^{-1}; HRMS: *m*/*z* (%) calcd for $C_{11}H_{13}NOS$: 207.0718 [M^+]; found: 207.0718.

***cis*-3-Hydroxy-5-(4-methoxyphenyl)-3-methylpyrrolidine-2-thione (*cis*-2k)**: R_f = 0.44 (*n*Hex/EtOAc = 2:1); m.p. 105–106 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (br, 1H; -N*H*-), 7.24–7.21 (m, 2H; -*Ar*-), 6.91–6.87 (m, 2H; -*Ar*-), 4.71 (dd, *J* = 4.8, 3.1 Hz, 1H; -C*H*Ar-), 3.79 (s, 3H; -ArOCH_3), 2.68 (dd, *J* = 6.4, 3.1 Hz, 1H; - CH_aH$_b$−CHAr-), 2.20 (dd, *J* = 6.4, 4.8 Hz, 1H; -CH$_a$$H_b$−CHAr-), 2.15 (br, 1H; -O*H*), 1.47 ppm (s, 3H; -C(OH)(CH_3)); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 210.7, 160.1, 130.6, 128.0 (×2), 114.5 (×2), 81.1, 61.0, 55.3, 46.8, 26.9 ppm; IR (KBr): $\tilde{\nu}$ = 3383, 3187, 2962, 1611, 1515, 1248, 819 cm^{-1}.

***trans*-3-Hydroxy-5-(4-methoxyphenyl)-3-methylpyrrolidine-2-thione (*trans*-2k)**: R_f=0.33 (*n*Hex/EtOAc=2:1); m.p. 115–117 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.20 (br, 1H; -N*H*-), 7.18–7.14 (m, 2H; -*Ar*-), 6.90–6.86 (m, 2H; -*Ar*-), 4.98 (t, J=7.1 Hz, 1H; -C*H*Ar-), 3.78 (s, 3H; -ArOCH_3), 2.76 (dd, J=6.8, 3.7 Hz, 1H; -CH_aH$_b$–CHAr-), 2.40 (br, 1H; -O*H*), 2.05 (dd, J=6.8, 3.4 Hz, 1H; -CH$_a$$H_b$–CHAr-), 1.50 ppm (s, 3H; -C(OH)(CH_3)); ^{13}C NMR (100 MHz, $CDCl_3$): δ=209.2, 159.7, 131.3, 127.2 (×2), 114.4 (×2), 81.2, 61.2, 55.3, 45.8, 27.5 ppm; IR (KBr): $\tilde{\nu}$= 3394, 3175, 2969, 1614, 1515, 1249, 832 cm^{-1}; HRMS: *m*/*z* (%) calcd for $C_{12}H_{15}NO_2S$: 237.0823 [M^+]: found; 237.0828.

3-Hydroxy-3-methylpyrrolidine-2-thione (2l): R_f=0.42 (*n*Hex/EtOAc= 1:2); m.p. 121–123 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.18 (br, 1H; -N*H*-), 3.66–3.55 (m, 1H; -CH_aH$_b$–NH-), 3.51–3.44 (m, 1H; -CH$_a$$H_b$–NH-), 2.58 (br, 1H; -O*H*), 2.32–2.26 (m, 2H; -C(OH)(CH$_3$)-CH_2-), 1.41 ppm (s, 3H; -C(OH)(CH_3)); ^{13}C NMR (100 MHz, $CDCl_3$): δ=210.8, 80.8, 45.2, 36.3, 26.5 ppm; IR (KBr): $\tilde{\nu}$=3358, 1642, 1546, 1308, 1208, 1134, 1008, 792 cm^{-1}; HRMS: *m*/*z* (%) calcd for C_5H_9NOS: 131.0405 [M^+]; found: 131.0404.

***cis*-3-Ethyl-3-hydroxy-5-methylpyrrolidine-2-thione (*cis*-2m)**: Yellow oil; R_f=0.53 (*n*Hex/EtOAc=1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.90 (br, 1H; -N*H*-), 3.86–3.81 (m, 1H; -C*H*(CH$_3$)–NH-), 2.56 (dd, J=6.4, 3.2 Hz, 1H; -C(OH)(C$_2$H$_5$)–CH_aH$_b$-), 2.02 (br, 1H; -O*H*), 1.79–1.72 (m, 2H; -C(OH)(C$_2$H$_5$)–CH$_a$$H_b$-, -C(OH)–C$H_aH_b$–CH$_3$), 1.63–1.56 (m, 1H; -C(OH)–CH$_a$$H_b$–CH$_3$), 1.32 (d, J=3.2 Hz, 3H; -CH(CH_3)–NH-), 0.98 ppm (t, J=7.4 Hz, 3H; -CH$_2$–CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=209.4, 84.1, 53.8, 41.7, 32.6, 21.0, 7.9 ppm; IR (neat): $\tilde{\nu}$=3386, 1646, 1539, 1276, 913, 748 cm^{-1}.

***trans*-3-Ethyl-3-hydroxy-5-methylpyrrolidine-2-thione (*trans*-2m)**: R_f= 0.45 (*n*Hex/EtOAc=1:1); m.p. 104–106 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.26 (br, 1H; -N*H*-), 4.10–4.04 (m, 1H; -C*H*(CH$_3$)–NH-), 2.38 (dd, J=6.8, 3.7 Hz, 1H; -C(OH)(C$_2$H$_5$)–CH_aH$_b$-), 2.02 (br, 1H; -O*H*), 1.95–1.91 (m, 1H; -C(OH)–CH_aH$_b$–CH$_3$), 1.79–1.72 (dd, J=6.8, 3.2 Hz, 1H; -C(OH)(C$_2$H$_5$)–CH$_a$$H_b$-), 1.68–1.63 (m, 1H; -C(OH)–CH$_a$$H_b$–CH$_3$), 1.28 (d, J=3.2 Hz, 3H; -CH(CH_3)–NH-), 0.96 ppm (t, J=7.4 Hz, 3H; -CH$_2$–CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=208.2, 84.4, 54.1, 40.5, 33.0, 20.8, 8.1 ppm; IR (neat): $\tilde{\nu}$=3430, 3163, 1795, 1542, 1280, 1255, 986, 798 cm^{-1}; HRMS: *m*/*z* (%) calcd for $C_7H_{13}NOS$: 159.0718 [M^+]; found: 159.0719.

***cis*-3-*tert*-Butyl-3-hydroxy-5-phenylpyrrolidine-2-thione (*cis*-2n)**: Pale yellow oil; R_f=0.69 (*n*Hex/EtOAc=1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.93 (br, 1H; -N*H*-), 7.38–7.26 (m, 5H; -*Ph*), 4.71 (dd, J=4.3, 3.7 Hz, 1H; -C*H*Ph-), 3.10 (dd, J=7.0, 3.6 Hz, 1H; -CH_aH$_b$–CHPh-), 2.13 (dd, J=7.0, 4.3 Hz, 1H; -CH$_a$$H_b$–CHPh-), 1.14 ppm (s, 9H; -C(CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=208.8, 140.4, 129.1 (×2), 128.8, 126.6 (× 2), 87.4, 61.0, 43.9, 38.8, 25.5 ppm (×3); IR (neat): $\tilde{\nu}$=3419, 2964, 1645, 1520, 1266, 1148, 762 cm^{-1}.

***trans*-3-*tert*-Butyl-3-hydroxy-5-phenylpyrrolidine-2-thione (*trans*-2n)**: R_f=0.52 (*n*Hex/EtOAc=1:1); m.p. 128–129 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.10 (br, 1H; -N*H*-), 7.39–7.24 (m, 5H; -*Ph*), 4.92 (t, J= 7.8 Hz, 1H; -C*H*Ph-), 2.64 (br, 1H; -O*H*), 2.57 (dd, J=7.0, 3.6 Hz, 1H; -CH_aH$_b$–CHPh-), 2.19 (dd, J=7.0, 4.2 Hz, 1H; -CH$_a$$H_b$–CHPh-), 1.19 ppm (s, 9H; -C(CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=208.6, 139.8, 129.1 (×2), 128.4, 125.9 (×2), 87.7, 61.0, 42.4, 37.2, 25.1 ppm (×3); IR (KBr): $\tilde{\nu}$=3550, 3273, 2960, 1697, 1510, 1232, 1148, 758 cm^{-1}; HRMS: *m*/*z* (%) calcd for $C_{14}H_{19}NOS$: 249.1187 [M^+]; found: 249.1184.

3-Hydroxy-5-methylpyrrolidine-2-thione (2o): Yellow oil; inseparable diastereomers; R_f=0.50 (*n*Hex/EtOAc=1:2); ^{1}H NMR (400 MHz, $CDCl_3$): *trans* isomer: δ=8.53 (br, 1H; -N*H*-), 4.52 (t, J=7.4 Hz, 1H; -C*H*(OH)-), 4.08–4.02 (m, 1H; -C*H*(CH$_3$)-), 2.30–2.23 (m, 1H; -CH(OH)–CH_aH$_b$-), 2.21–2.16 (m, 1H; -CH(OH)–CH$_a$$H_b$-), 1.28 ppm (d, J=3.3 Hz, 3H; -CH(CH_3)-); *cis* isomer: δ=8.38 (-N*H*-), 4.37 (dd, J=5.0, 3.8 Hz, 1H; -C*H*(OH)-), 3.93–3.84 (m, 1H; -C*H*(CH$_3$)-), 2.77–2.70 (m, 1H; -CH(OH)–CH_aH$_b$-), 1.88 (dd, J=3.4, 0.9 Hz, 1H; -CH(OH)–CH$_a$$H_b$-), 1.32 ppm (d, J=3.2 Hz, 3H; -CH(CH_3)-); ^{13}C NMR (100 MHz, $CDCl_3$): *trans* isomer: δ=205.6, 76.9, 55.0, 38.0, 21.2 ppm; *cis* isomer: δ=206.1, 77.6, 53.7, 39.6, 20.5 ppm; HRMS: *m*/*z* (%) calcd for C_5H_9NOS: 131.0405 [M^+]; found: 131.0405.

3-Hydroxy-4-methylpyrrolidine-2-thione (2p): White powder; inseparable diastereomers; R_f=0.45 (*n*Hex/EtOAc=1:1); ^{1}H NMR (400 MHz, $CDCl_3$): *trans* isomer: δ=8.09 (br, 1H; -N*H*-), 3.89 (d, J=4.8 Hz, 1H; -C*H*(OH)-), 3.65–3.60 (m, 1H; -CH_aH$_b$–NH-), 3.18 (t, J=10.7 Hz, 1H; -CH$_a$$H_b$–NH-), 2.41–2.31 (m, 1H; -C*H*(CH$_3$)-), 1.27 ppm (d, J=3.3 Hz, 3H; -CH(CH_3)-); *cis* isomer: δ=8.09 (br, 1H; -N*H*-), 4.31 (d, J=3.4 Hz, 1H; -C*H*(OH)-), 3.70 (dd, J=5.5, 2.9 Hz, 1H; -CH_aH$_b$–NH-), 3.22 (dt, J=6.2, 1.8 Hz, 1H; -CH$_a$$H_b$–NH-), 2.83–2.79 (m, 1H; -C*H*(CH$_3$)-), 0.99 ppm (d, J=3.5 Hz, 3H; -CH(CH_3)-); ^{13}C NMR (100 MHz, $CDCl_3$): *trans* isomer: δ=207.5, 82.8, 51.7, 40.3, 15.4 ppm; *cis* isomer: δ=206.6, 78.8, 52.6, 35.8, 12.1 ppm; HRMS: *m*/*z* (%) calcd for C_5H_9NOS: 131.0405 [M^+]; found: 131.0405.

General procedure for the preparation of thiolactam from β-ketoisothiocyanate by using SmI_2: 1a (52 mg, 0.25 mmol) and *tert*-butyl alcohol (100 μL, 1.0 mmol) were dissolved in THF (1.5 mL) and purged with argon. Freshly prepared SmI_2 from Sm metal (200 mg) and diiodomethane (81 μL) in THF (20 mL) was added to the vigorously stirred solution over a period of 5 minutes at room temperature. After 8 h, the reaction was quenched with 1 N HCl solution, and the mixture was extracted with ethyl acetate (3×10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The product was readily separated by using silica-gel column chromatography (Merck 60, 230–400 mesh, 2×25 cm, *n*Hex/EtOAc=3:1).

(1*S*,3*R*,6*R*)-3,7,7-Trimethyl-8-azabicyclo[4.3.0]nonane-9-thione (3a): R_f= 0.56 (*n*Hex/EtOAc=3:1); m.p. 135–136 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.49 (br, 1H; -N*H*-), 3.03 (t, J=6.0 Hz, 1H; -C*H*-(C=S)-), 2.53 (dq, J=6.9, 1.7 Hz, 1H; -C*H*–C(CH$_3$)$_2$-), 1.99–1.96 (m, 1H; -C*H*(CH$_3$)-), 1.61–1.57 (m, 2H; -CH(CH$_3$)–CH_2–CH$_2$-), 1.27 (s, 3H; -C(CH_3)$_a$(CH$_3$)$_b$), 1.22 (s, 3H; -C(CH$_3$)$_a$(CH_3)$_b$), 1.19–1.12 (m, 3H; -CH_2–CH_aH$_b$–CH-), 0.88 (d, J=3.2 Hz, 3H; -CH(CH_3)-), 0.78 ppm (m, 1H; -CH$_2$–CH$_a$$H_b$–CH-); ^{13}C NMR (100 MHz, $CDCl_3$): δ=205.9, 63.8, 50.5, 45.9, 33.6, 32.7, 28.4, 26.1, 25.0, 22.4, 22.2 ppm; IR (KBr): $\tilde{\nu}$=3159, 2947, 1691, 1515, 1454, 1237, 1114, 759 cm^{-1}; t_R=9.81 min (OD-H, 254 nm, *i*PrOH/*n*Hex= 1:9); HRMS: *m*/*z* (%) calcd for $C_{11}H_{19}NS$: 197.1238 [M^+]; found: 197.1238.

(1*S*,3*R*,6*S*)-3,7,7-Trimethyl-8-azabicyclo[4.3.0]nonane-9-thione (3b): R_f= 0.54 (*n*Hex/EtOAc=3:1); m.p. 150–151 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.95 (br, 1H; -N*H*-), 3.04 (t, J=6.0 Hz, 1H; -C*H*-(C=S)-), 2.54 (d, J= 6.9 Hz, 1H; -C*H*–C(CH$_3$)$_2$-), 2.02–1.98 (m, 1H; -C*H*(CH$_3$)-), 1.63–1.58 (m, 2H; -CH(CH$_3$)–CH_2–CH$_2$-), 1.29 (s, 3H; -C(CH_3)$_a$(CH$_3$)$_b$), 1.23 (s, 3H; -C(CH$_3$)$_a$(CH_3)$_b$), 1.20–1.10 (m, 3H; -CH_2–CH_aH$_b$–CH-), 0.89 (d, J=3.2 Hz, 3H; -CH(CH_3)-), 0.79–0.76 ppm (m, 1H; -CH$_2$–CH$_a$$H_b$–CH-); ^{13}C NMR (100 MHz, $CDCl_3$): δ=206.3, 63.7, 50.5, 45.9, 33.6, 32.7, 28.4, 26.2, 25.0, 22.4, 22.3 ppm; IR (KBr): $\tilde{\nu}$=3167, 2859, 1672, 1574, 1398, 1371, 1238, 1112, 955, 761 cm^{-1}; t_R=9.88 min (OD-H, 254 nm, *i*PrOH/ *n*Hex=1:9); HRMS: *m*/*z* (%) calcd for $C_{11}H_{19}NS$: 197.1238 [M^+]; found: 197.1239.

9-Azabicyclo[5.3.0]decane-10-thione (3d): R_f=0.45 (*n*Hex/EtOAc=2:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.22 (br, 1H; -N*H*-), 3.56–3.50 (m, 1H; -CH_aH$_b$–NH-), 3.11 (t, J=10.2 Hz, 1H; -CH$_a$$H_b$–NH-), 2.53–2.44 (m, 1H; -C*H*–(C=S)-), 1.98–1.90 (m, 1H; -CH$_2$–C*H*–CH$_2$-), 1.70–1.19 ppm (m, 10H; -CH–(CH_2)$_5$–CH-); ^{13}C NMR (75 MHz, $CDCl_3$): δ=209.5, 54.4, 52.3, 40.8, 36.0, 31.1, 29.7, 27.9, 22.2 ppm; IR (KBr): $\tilde{\nu}$=3173, 2923, 1655, 1541, 1452, 1240 cm^{-1}; HRMS: *m*/*z* (%) calcd for $C_9H_{15}NS$: 169.0925 [M^+]; found: 169.0926.

3,5,5-Trimethylpyrrolidine-2-thione (3f): R_f=0.50 (*n*Hex/EtOAc=2:1); m.p. 85–87 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.24 (br, 1H; -N*H*-), 2.98–2.90 (m, 1H; -C*H*(CH$_3$)-), 2.25 (dd, J=6.3, 4.1 Hz, 1H; -CH_aH$_b$–C(CH$_3$)$_2$-), 1.62 (dd, J=6.3, 4.8 Hz, 1H; -CH$_a$$H_b$–C(CH$_3$)$_2$-), 1.34 (s, 3H; -C(C$H_{3a}$)(CH$_{3b}$)-), 1.33 (d, J=2.7 Hz, 3H; -CH(CH_3)-), 1.29 ppm (s, 3H; -C(CH$_{3a}$)(CH_{3b})-); ^{13}C NMR (100 MHz, $CDCl_3$): δ=208.0, 62.2, 46.7, 45.4, 28.9, 27.5, 19.1 ppm; IR (KBr): $\tilde{\nu}$=3181, 2968, 2918, 1633, 1528, 1455, 1237, 750 cm^{-1}; HRMS: *m*/*z* (%) calcd for $C_7H_{13}NS$: 143.0769 [M^+]; found: 143.0768.

3,5-Dimethylpyrrolidine-2-thione (3g): Pale yellow oil; inseparable diastereomers; R_f=0.70 (*n*Hex/EtOAc=1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.82 (br, 1H; -N*H*-), 3.90–3.87 (m, 1H; -C*H*(CH$_3$)–NH-), 2.82–2.78 (m, 1H; -C*H*(CH$_3$)–CH$_2$-), 2.58–2.52 (m, 1H; -CH_aH$_b$–CH(CH$_3$)-), 2.02–1.98 (m, 1H; -CH$_a$$H_b$–CH(CH$_3$)-), 1.36 (d, J=2.4 Hz, 3H; -CH(CH_3)–

NH-), 1.29 ppm (d, $J=3.0$ Hz, 3H; -CH(CH_3)–CH_2-); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=210.1$, 55.1 (55.0), 47.7 (46.8), 40.1 (38.7), 20.9 (21.0), 18.9 ppm (19.1); IR (KBr): $\tilde{\nu}=3220$, 2967, 2919, 1633, 1525, 1293, 913, 744 cm^{-1}; HRMS: *m/z* (%) calcd for $C_6H_{11}NS$: 129.0612 [M^+]; found: 129.0614.

3-Methylpyrrolidine-2-thione (3l): $R_f=0.45$ (*n*Hex/EtOAc=1:1); m.p. 81–82 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.40$ (br, 1H; -N*H*-), 3.56–3.51 (m, 2H; -CH_2–NH-), 2.84–2.78 (m, 1H; -C*H*(CH_3)-), 2.43–2.38 (m, 1H; -CH(CH_3)–CH_aH$_b$-), 1.84–1.74 (m, 1H; -CH(CH_3)–CH_aH$_b$-), 1.32 ppm (dd, $J=3.5$, 1.2 Hz, 3H; -CH(CH_3)-); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$ 210.6, 47.2, 47.0, 31.0, 18.7 ppm; IR (KBr): $\tilde{\nu}=3189$, 2973, 1538, 1449, 1299, 1095, 1037, 748 cm^{-1}; HRMS: *m/z* (%) calcd for C_5H_9NS: 115.0456 [M^+]; found: 115.0455.

5-Methylpyrrolidine-2-thione (3o): $R_f=0.64$ (*n*Hex/EtOAc=1:2); m.p. 79–81 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.14$ (br, 1H; -N*H*-), 4.04 (dq, $J=6.7$, 3.3 Hz, 1H; -C*H*(CH_3)-), 3.00–2.92 (m, 1H; -(C=S)–CH_aH$_b$-), 2.90–2.81 (m, 1H; -(C=S)–CH$_a$H$_b$-), 2.40–2.31 (m, 1H; -CH_aH$_b$–CH(CH_3)-), 1.78–1.72 (m, 1H; -CH$_a$H$_b$–CH(CH_3)-), 1.28 ppm (d, $J=$ 3.2 Hz, 3H; -CH(CH_3)); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=205.1$, 58.0, 43.1, 31.3, 20.9; IR (KBr, cm^{-1}): 3163, 2963, 1655, 1541, 1292, 1141, 1039, 779 ppm; HRMS: *m/z* (%) calcd for C_5H_9NS: 115.0456 [M^+]; found: 115.0456.

4-Methylpyrrolidine-2-thione (3p): $R_f=0.53$ (*n*Hex/EtOAc=1:1); m.p. 81–83 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.79$ (br, 1H; -N*H*-), 3.76–3.72 (m, 1H; -CH_aH$_b$–NH-), 3.22 (dd, $J=5.4$, 2.9 Hz, 1H; -CH$_a$H$_b$–NH-), 3.03 (dd, $J=8.8$, 4.1 Hz, 1H; -(C=S)–CH_aH$_b$-), 2.69–2.64 (m, 1H; -C*H*(CH_3)-), 2.51 (dd, $J=8.8$, 3.4 Hz, 1H; -(C=S)–CH$_a$H$_b$-), 1.13 ppm (d, $J=3.3$, 3H; -CH(CH_3)-); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=206.1$, 56.4, 51.0, 32.0, 19.0 ppm; IR (KBr): 3199, 1635, 1276, 1262, 750 cm^{-1}; HRMS: *m/z* (%) calcd for C_5H_9NS: 115.0456 [M^+]; found: 115.0457.

General procedure for cyclization of γ-ketoisothiocyanates: 5-Isothiocyanato-5-phenylpentan-2-one (54 mg, 0.25 mmol) and *tert*-butyl alcohol (50 μL, 0.5 mmol) were dissolved in THF (1.5 mL) and purged with argon. Freshly prepared SmI_2 from Sm metal (100 mg) and diiodomethane (41 μL) in THF (10 mL) was added to the vigorously stirred solution over a period of 5 minutes at room temperature. The reaction was monitored with thin-layer chromatography (TLC). As there was no change in the TLC analysis, the reaction was quenched after 12 h with a 1 N HCl solution, and the mixture was extracted with ethyl acetate (3× 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The starting material was readily recovered by using silica-gel column chromatography (Merck 60, 230–400 mesh, 2×25 cm, CH_2Cl_2/Hex=3:1). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.38$–7.29 (m, 5H; *Ph*), 4.43–4.38 (m, 1H; -C*H*(NCS)-), 2.53–2.35 (m, 4H; -CH(NCS)–CH_2–CH_2-), 2.09 ppm (s, 3H; -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=206.6$, 137.8, 129.2 (×2), 129.1, 127.4 (×2), 111.3, 52.4, 40.5, 30.0, 29.4 ppm.

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