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1-(Methyldithiocarbonyl)imidazole: a Useful Thiocarbonyl Transfer Reagent for Synthesis of Substituted Thioureas

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Abstract—1-(Methyldithiocarbonyl)imidazole **1** and its *N*-methyl quaternary salt **2** have been shown to be efficient methyldithiocarbonyl and thiocarbonyl transfer reagents for the synthesis of dithiocarbamates, symmetrical and unsymmetrical mono-, di- and tri-substituted thioureas in high yields under mild and simple non-hazardous reaction conditions.

Condensation of primary and secondary amines with thiophosgene[1] or isothiocyanates[2] to give symmetrical and unsymmetrical thioureas constitute the most widely used general methods for the synthesis of this class of compounds. However these methods are hazardous due to the toxic properties of both thiophosgene and isothiocyanates. Despite their toxicity, the application of these reagents remains inevitable due to the importance of symmetrical and unsymmetrical thioureas in biological screening as well as for other commercial purposes. Thus a number of thioureas have found application in agriculture as fungicides, herbicides and rodenticides.[3] They are also active against bacterial and microbial infection such as RVS-37 as potential antitubercular agents.[3,4] Some of them are phenoloxidase enzymatic inhibitors[5] besides their application as biomimetic models.[6] Some thioureas are found to be accelerators in rubber vulcanization.[5,7] They are also useful building blocks for the synthesis of both five and six membered heterocycles.[8]

Several alternative methods have been developed for the synthesis of both symmetrical and unsymmetrical thioureas involving: (a) reaction of carbon disulfide and amines, either direct,[9] catalytic[10] or in the presence of triaryl phosphite or hexaalkyl phosphoroustriamide;[11] (b) reaction of secondary amines with triphenylphosphine–thiocyanogen (TPPT);[12,13] (c) activation of dithiocarbamates[14] (or trithiocarbonate salt) with 2-halothiazolium[14] or 2-chloropyridinium salts;[15] (d) direct displacement by amines on 1,3-diphenylthiourea,[16a] nitrosothiourea,[16b] thiuram disulfide,[17] 1,1′-thiocarbonyldiimidazole[18] or azoles;[19] (e) reaction of substituted guanidines with hydrogen sulfide.[20] Although some of these methods are safer, avoiding toxic thiophosgene or isothiocyanates, they suffer from practical limitations involving harsh reaction conditions, multistep synthetic operations, difficult starting materials, lack of generality of reaction or overall poor yields.

Our efforts were therefore directed towards the development of more efficient and safer thiocarbonyl transfer reagents for thiourea synthesis. Since 1-(methyldithiocarbonyl)imidazole **1** and its *N*-methyl salt **2** are structurally similar to thiophosgene, we became interested in studying their synthetic application as potential thiophosgene equivalents and methyldithiocarbonyl transfer reagents. We have achieved the desired transformations and report in this paper the reaction of **1** and **2** with amines leading to useful syntheses of both symmetrical and unsymmetrical thioureas and methyl dithiocarbamates.

Results and Discussion

The 1-(methyldithiocarbonyl)imidazole **1** has been prepared earlier[21] by heating imidazole with dimethyl trithiocarbonate in the presence of triethylamine. While this work was in progress, the preparation of **1** based on the reaction of imidazole with carbon disulfide in the presence of sodium hydride in THF followed by alkylation with methyl iodide was reported.[22] The reagent **1** was subsequently utilized for *S*-methyl dithiocarbonylation of alcohols yielding xanthates in good yields.[22] We have subsequently followed the same method for the preparation of **1** except using DMSO instead of THF as the solvent. At this stage, it was envisaged that the corresponding quaternary salt **2** should be more reactive than **1** in its reaction with various nucleophiles. Thus when **1** was reacted with excess methyl iodide (4 equiv.) in refluxing

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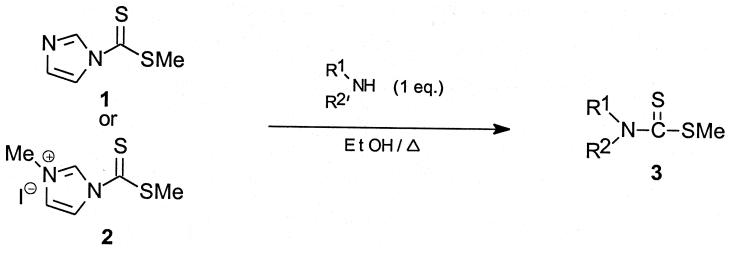


Scheme 1.

Table 1. Synthesis of methyl dithiocarbamates **3**

3	R^1	R^2	Reaction time (h) for reagent **1**	Yield (%)	Reaction time (h) for reagent **2**	Yield (%)
3a	$C_6H_5CH_2$	H	0.5	70	0.5	98
3b	C_6H_5	H	1.5	76	1.0	86
3c	4-$MeOC_6H_4(CH_2)_2$	H	1.0	75	0.75	90
3d	Allyl	H	3.0	76	2.0	86
3e	Cyclopropyl	H	6.0	80	4.0	97
3f	$EtCO_2CH_2$	H	6.0	80	4.0	93
3g	C_6H_5	Me	3.0	87	2.0	98
3h	Me	Me	6.0	81	4.5	94
3i	$-(CH_2)_2-O-(CH_2)_2-$		3.0	76	2.5	84

benzene the corresponding *N*-methyl-*N*′-(methyldithiocarbonyl)imidazolium iodide **2** was obtained in 95% yield as an orange crystalline solid. The structure of **2**, which was found to be more reactive than **1**, was established with the help of spectral and analytical data.

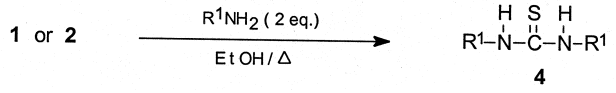
Synthesis of methyl dithiocarbamates 3

The reactivity of **1** and **2** towards various amines was next investigated. Thus when an equimolar mixture of **1** and benzylamine was refluxed in ethanol for 0.5 h, the reaction mixture afforded the corresponding methyl *N*-benzyldithiocarbamate **3a** in 70% yield (Scheme 1, Table 1) after work-up. However when the quaternary salt **2** was reacted with benzylamine under identical conditions, **3a** was obtained in an improved (98%) yield (Scheme 1, Table 1). Similarly the other aliphatic/aromatic primary and secondary amines were reacted with 1 equiv. of either **1** or **2** to afford the corresponding methyl dithiocarbamates **3b**–**i** (Table 1) in high yields. The yields of **3a**–**i** obtained from the quaternary salt **2** are much higher than those obtained from **1** (Table 1) and the products obtained were of higher purity.

A number of dithiocarbamates (dithiourethanes) exhibit important biological activities and are valuable analytical reagents[23] or synthetic intermediates in heterocyclic synthesis.[24] The most general method for the synthesis of methyl dithiocarbamates involves a lengthy two step procedure[25] using the reaction of amines with carbon disulfide in the presence of base followed by alkylation with methyl iodide. The other methods involve reaction of organolithium[26] or Grignard reagents[27] with tetramethylthiuram disulfide or aminolysis of tertiary alkyl xanthates.[23] Reaction of amines with diphenyl trithiocarbonate S,S-oxide[28] is also reported to give dithiocarbamates. However these methods have limited application and give poor yields of dithiocarbamates in many cases while trithiocarbonate S,S-dioxide is itself prepared from toxic thiophosgene. The above reaction thus provides a facile route to methyl dithiocarbamates from non-hazardous **1** and **2**.

Synthesis of symmetrical thioureas 4

When 2 equiv. of aniline were reacted with 1 equiv. of 1-(methyldithiocarbonyl)imidazole **1** or its salt **2** in refluxing ethanol, the reaction mixture after work-up afforded the corresponding 1,3-diphenylthiourea **4a** in 86

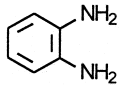
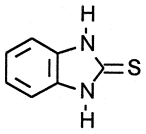
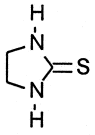
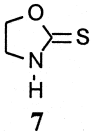


Scheme 2.

Table 2. Synthesis of symmetrical disubstituted thioureas **4**

4	R^1	Reaction time (h) for reagent **1**	Yield (%)	Reaction time (h) for reagent **2**	Yield (%)
4a	C_6H_5	6.0	86	4.5	96
4b	$C_6H_5CH_2$	4.0	79	3.0	92
4c	$C_6H_5CH_2CH_2$	5.0	80	4.0	91
4d	4-$MeOC_6H_4(CH_2)_2$	6.0	75	4.0	89
4e	2-Pyridyl	6.0	70	4.5	80
4f	Allyl	5.5	75	4.0	90
4g	Me_3C	6.0	40	4.0	60
4h	$CH_3(CH_2)_{15}$	4.0	78	2.5	86
4i	Cyclohexyl	4.5	82	3.5	94
4j	Cyclopropyl	5.0	79	4.0	91

Table 3. Synthesis of heterocyclic thiones

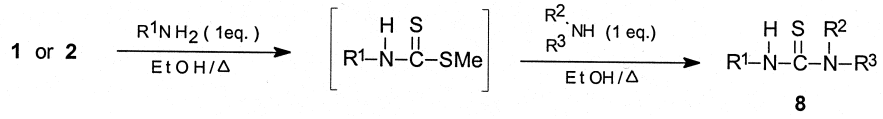
Entry	Amine	Product	Reaction time (h) for reagent **1**	Yield (%)	Reaction time (h) for reagent **2**	Yield (%)
1		 **5**	5.0	74	3.0	92
2		 **6**	4.0	77	2.5	90
3		 **7**	4.5	80	2.5	89

and 96% yields, respectively (Scheme 2, Table 2). Other acyclic or cyclic aliphatic and heteroaromatic primary amines also reacted with either **1** or **2** affording symmetrical *N*,*N*′-disubstituted thioureas **4b**–**j** in 40–82% and 60–94% yields, respectively. However, secondary amines like *N*-methylaniline and morpholine failed to give *N*,*N*′-tetra-subsituted thioureas under identical conditions and stoichiometry, and yielded only dithiocarbamates **3g** and **3i** in 87 and 76% yields, respectively.

The amines containing an additional nucleophilic group such as *o*-phenylenediamine, ethylenediamine and ethanolamine reacted with **1** or **2** in refluxing ethanol to give benzimidazoline-2-thione **5**, imidazolidine-2-thione **6**, oxazolidine-2-thione **7** in high yields (Table 3).

Synthesis of unsymmetrical di- and tri-substituted thioureas 8

We further explored the synthesis of unsymmetrical *N*,*N*′-di- and tri-substituted thioureas in a one pot sequence using either **1** or **2**. Thus an equimolar mixture of aniline and **1** was refluxed in ethanol for 1.5 h (monitored by TLC) followed by addition of benzylamine (1 equiv.). Reflux



Scheme 3.

Table 4. Unsymmetrical di- and tri-substituted thioureas **8**

8	R^1	R^2	R^3	Reaction time (h) for reagent **1**	Yield (%)	Reaction time (h) for reagent **2**	Yield (%)
8a	C_6H_5	$C_6H_5CH_2$	H	2.5	75	2.5	92
8b	C_6H_5	$C_6H_5(CH_2)_2$-	H	5.5	73	4.0	93
8c	C_6H_5	4-$MeOC_6H_4$	H	6.5	74	4.0	86
8d	C_6H_5	2-Pyridyl	H	6.0	89	3.5	91
8e	C_6H_5	Me	H	6.5	65	2.5	94
8f	C_6H_5	Cyclohexyl	H	6.5	65	4.5	82
8g	$C_6H_5CH_2$	Cyclohexyl	H	4.5	61	3.5	96
8h	C_6H_5	Me	Me	6.5	79	5.0	94
8i	$C_6H_5CH_2$	$-(CH_2)_5-$		6.5	87	5.5	96
8j	C_6H_5	$-(CH_2)_2-O-(CH_2)_2-$		6.0	88	4.0	90
8k	C_6H_5	H	H	4.5	66	3.0	94
8l	$C_6H_5CH_2$	H	H	5.0	66	3.0	84
8m	H	C_6H_5	CH_3	4.0	72	3.0	78
8n	H	$-(CH_2)_5-$		4.5	76	3.0	87

was maintained for 2.5 h, when all the *N*-phenyldithiocarbamate **3b** had been consumed (TLC). The reaction mixture afforded the corresponding *N*-benzyl-*N′*-phenylthiourea **8a** (Scheme 3, Table 4) in 75% yield after work-up. The other unsymmetrical *N*,*N′*-di- (**8b**–**g**) and tri-substituted (**8h**–**j**) thioureas were similarly obtained in 61–89% and 79–88% overall yields, respectively, by reacting **1** first with a primary amine followed by treatment with a second amine in a sequential manner (Table 4). The methodology could be extended further for the synthesis of mono (**8k**–**l**) and *N*,*N*-disubstituted (**8m**–**n**) thioureas by reacting **1** or **2** with ammonia and primary or secondary amines sequentially under identical conditions. As observed earlier, yields of thioureas **8a**–**n** were higher when the salt **2** was reacted with amines (Table 4).

In conclusion, we have successfully demonstrated the synthetic potential of 1-(methyldithiocarbonyl)imidazole **1** and its quaternary salt **2** as useful methyldithiocarbonyl and thiocarbonyl transfer reagents. A high yielding general synthesis of methyl dithiocarbamates, symmetrical and unsymmetrical mono-, di- and tri-substituted thioureas has been developed. The reaction represents a convenient and less hazardous procedure for the synthesis of a variety of thioureas with wide structural variations. We are further exploring other applications of these reagents **1** and **2** either as a thiophosgene equivalent or as methyldithiocarbonyl transfer reagents, which will be published later.

Experimental

General

Melting Points were obtained on a Thomas Hoover Capillary melting point apparatus and are uncorrected. IR spectra were recorded on Perkin Elmer 983 and Shimadzu 8201 PC spectrometers. ^{1}H NMR spectra were recorded on Bruker-ACF-300 and Jeol-LA-400 spectrometers in CCl_4, $CDCl_3$ or DMSO-d_6 using TMS as internal reference and the chemical shifts are reported in δ (ppm) relative to TMS. The coupling constants (*J*) are given in Hertz (Hz). Mass spectra were obtained on a Jeol JMS-D-300 and Finnigan Voyager-GC-8000 Mass spectrometers. Elemental analyses were carried out on Heraeus CHN-O-Rapid analyzer.

All reactions were conducted in oven-dried (120°C) glassware. All reactions were monitored by analytical TLC on glass plates coated with silica gel (Acme's) containing 13% calcium sulfate as binder and visualization of spots was accomplished by exposure to iodine vapor or by spraying with acidic potassium permanganate solution. Column chromatography was carried out using silica gel (Acme's 60–120 Mesh) and eluted with a mixture of hexane and ethyl acetate. Ethanol was dried over calcium oxide. All amines were distilled (or recrystallized in case of solids) before use.

Synthesis of 1-(methyldithiocarbonyl)imidazole 1

To a solution of imidazole (20.42 g, 0.3 mol) in dry DMSO (150 mL) was added sodium hydride (60%, 14 g, 0.35 mol) at room temperature under an atmosphere of nitrogen. After stirring for 0.5 h, carbon disulfide (18 mL, 0.3 mol) was added at 0°C. The reaction mixture was stirred for a further 0.5 h at room temperature then dimethyl sulfate (33 mL, 0.35 mol) was added. After 6 h, the reaction mixture was poured into crushed ice and extracted with chloroform (3×75 mL). The combined organic extracts were washed with water (2×100 mL), dried (anhydrous Na_2SO_4) and evaporated under reduced pressure to afford crude 1-(methyldithiocarbonyl)imidazole **1** which was purified by passing through a short silica gel column using hexane/ethyl acetate (80:20) as eluent to give a yellow viscous oil (45.50 g, 96%). IR and ^{1}H NMR spectra obtained were as reported earlier.[22]

Synthesis of 3-methyl-1-(methyldithiocarbonyl)-imidazolium iodide 2

To an ice cooled stirring solution of 1-(methyldithiocarbonyl)-imidazole **1** (15.8 g, 0.1 mol) in sodium dried benzene (200 mL), methyl iodide (25 mL, 0.4 mol) was added dropwise over 0.5 h. After complete addition of MeI, the reaction mixture was brought to room temperature then refluxed for 3 h. The orange colored crystals formed in the reaction were filtered and washed with dry benzene to give pure **2**; Orange crystals, yield 95% (28.5 g), mp 79–80°C (dec.); IR (KBr): 3066, 1642, 1611, 1582, 1178, 1088 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6–$CDCl_3$): δ 10.18 (s, 1H, –NC*H*=N), 8.43 (br s, 1H, HC=C), 7.95 (s, 1H, HC=C), 4.02 (s, 3H, NCH_3), 2.96 (s, 3H, SCH_3); MS (FAB) (*m*/*z*, %): 173 (M^+-127, 97); Anal. calcd for $C_6H_9N_2S_2I$ (300.18): C 24.01, H 3.02, N 9.33%; found: C 24.20, H 2.98, N 9.47%.

General procedure for the synthesis of methyl dithiocarbamates (3a–i)

To a solution (or suspension) of **1** (1.58 g, 0.01 mol) or its salt **2** (3.00 g, 0.01 mol) in absolute ethanol, the appropriate amine (0.01 mol) in 20 mL of absolute ethanol was added and the reaction mixture was refluxed for 0.5–6 h (monitored by TLC). Ethanol was removed under reduced pressure and the residue was poured into water, extracted with chloroform (3×25 mL), dried (anhydrous Na_2SO_4) and evaporated under reduced pressure to afford methyl dithiocarbamates which were passed through a silica gel column using hexane–ethyl acetate (97:3) as eluent to give pure products.

Methyl *N*-benzyldithiocarbamate (3a). 1.38 g, 70% (1.93 g, 98%);[43] Colorless crystals (hexane); mp 55–56°C (lit. mp 57°C);[29] as a mixture of *trans*–*cis* isomers[44] in the ratio of 17:3, the data for the minor isomer are given in square brackets; IR (KBr): 3260, 2914, 2832, 1600, 1495, 1374, 1168, 1036 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 [7.31] (br s, 1H, NH), 7.23–7.11 (m, 5H, ArH), 4.45 [4.26] (d, *J*=6.0 Hz, 2H, HNCH_2), [2.52] 2.49 (s, 3H, SCH_3); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ [201.53] 198.85, 136.02 [134.98], [128.65] 128.54, 127.86, [127.70] 127.56, [50.75] 49.97, [18.73] 18.00; MS (*m*/*z*, %): 197 (M^+, 98), 150 (25), 91 (79); Anal. calcd for $C_9H_{11}NS_2$ (197.33): C 54.78, H 5.62, N 7.10%; found: C 54.89, H 5.58, N 7.23%.

Methyl *N*-phenyldithiocarbamate (3b). 1.39 g, 76% (1.58 g, 86%); Colorless crystals (ether–hexane); mp 92–93°C

(lit. 94–95°C);[30] IR (KBr): 3116, 2918, 2808, 1502, 1325, 1031, 592 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.22 (br s, 1H, NH), 7.45–7.29 (m, 5H, ArH), 2.64 (s, 3H, SCH_3); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 201.50, 137.98, 129.29, 127.61, 125.24, 19.07; MS (*m*/*z*, %): 183 (M^+, 8), 57 (100); Anal. calcd for $C_8H_9NS_2$ (183.30): C 52.42, H 4.95, N 7.64%; found: C 52.67, H 5.18, N 7.78%.

Methyl *N*-(4′-methoxyphenethyl)dithiocarbamate (3c). 1.81 g, 75% (2.17 g, 90%); Colorless crystals (chloroform–hexane); mp 58–59°C; as a mixture of *trans–cis* isomers in the ratio of 87:13, the data for the minor isomer are given in square brackets; IR (KBr): 3245, 2991, 1607, 1506, 1384, 1247, 936 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ [7.78] 7.29 (br s, 1H, NH), 7.10 (d, *J*=8.5 Hz, 2H, ArH), 6.88 (d, *J*=8.5 Hz, 2H, ArH), 3.95–3.90 [3.66–3.63] (m, 2H, C*H*$_2$NH), 3.77 (s, 3H, OCH_3), 2.89 (t, *J*=7.0 Hz, 2H, ArC*H*$_2$), [2.67] 2.61 (s, 3H, SCH_3); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ [201.58] 198.79, 158.27, 129.97, 129.55, 114.17, 55.14, 48.07 [47.35], [33.78] 33.14, [18.74] 17.93; MS (*m*/*z*, %): 241 (M^+, 37), 194 (6), 134 (100); Anal. calcd for $C_{11}H_{15}NOS_2$ (241.37): C 54.73, H 6.26, N 5.80%; found: C 54.52, H 6.18, N 5.92%.

Methyl *N*-allyldithiocarbamate (3d). 1.12 g, 76% (1.27 g, 86%); Light yellow viscous oil; as a mixture of *trans–cis* isomers in the ratio of 79:21, the data for the minor isomer are given in square brackets; IR (neat): 3225, 2916, 1637, 1495, 1370, 1318, 1255, 931 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ [7.88] 7.09 (br s, 1H, NH), 5.89–5.79 (m, 1H, CH_2=C*H*), 5.27–5.15 (m, 2H, CH=C*H*$_2$), 4.31 [4.14] (br s, 2H, CH_2), [2.76] 2.60 (s, 3H, SCH_3); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ [201.95] 199.10, 131.94 [131.04], [118.74] 118.19, 49.27 [48.45], [18.79] 18.09; MS (*m*/*z*, %): 147 (M^+, 71), 132 (59), 41 (53); Anal. calcd for $C_5H_9NS_2$ (147.27): C 40.78, H 6.16, N 9.51%; found: C 40.91, H 6.35, N 9.35%.

Methyl *N*-cyclopropyldithiocarbamate (3e). 1.18 g, 80% (1.43 g, 97%); Colorless crystals (chloroform–hexane); mp 67–68°C; as a mixture of *trans–cis* isomers in the ratio of 84:16, the data for the minor isomer are given in square brackets; IR (KBr): 3158, 2960, 1605, 1499, 1446, 1409, 1330, 967 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.44 (br s, 1H, NH), [3.48] 3.21 [br s, 1H, –C*H*$(CH_2)_2$], [2.75] 2.66 (s, 3H, SCH_3), 1.12–0.70 (m, 4H, CH(C*H*$_2)_2$); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 204.91, [29.79] 27.29, 19.01 [18.27], 8.17 [7.40]; MS (*m*/*z*, %): 147 (M^+, 82), 91 (78); Anal. calcd for $C_5H_9NS_2$ (147.27): C 40.78, H 6.16, N 9.51%; found: C 40.86, H 6.23, N 9.67%.

Methyl (*N*-carboethoxymethyl)dithiocarbamate (3f). 1.55 g, 80% (1.80 g, 93%); Colorless crystals (chloroform–hexane); mp 78–79°C; IR (KBr): 3273, 3210, 2977, 1722, 1641, 1522, 1413, 1304, 1258, 1220 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.53 (br s, 1H, NH), 4.46 (d, *J*=4.5 Hz, 2H, C*H*$_2$NH), 4.27 (q, *J*=7.0 Hz, 2H, OCH_2), 2.64 (s, 3H, SCH_3), 1.15 (t, *J*=7.0 Hz, 3H, CH_2CH_3); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 199.70, 168.90, 62.02, 48.29, 18.37, 14.13; MS (*m*/*z*, %): 193 (M^+, 66), 72 (100); Anal. calcd for $C_6H_{11}NO_2S_2$ (193.30): C 37.28, H 5.74, N 7.25%; found: C 37.08, H 5.96, N 7.36%.

Methyl *N*-methyl-*N*-phenyldithiocarbamate (3g). 1.72 g, 87% (1.93 g, 98%); Colorless crystals (chloroform–hexane); mp 79–80°C; IR (KBr): 2931, 1588, 1485, 1426, 1355, 1101, 955 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.49–7.40 (m, 3H, ArH), 7.25 (dd, *J*=7.2, 3.4 Hz, 2H, ArH), 3.77 (s, 3H, NCH_3), 2.57 (s, 3H, SCH_3); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 200.50, 144.86, 129.75, 128.96, 126.94, 46.00, 20.77; MS (*m*/*z*, %): 197 (M^+, 65), 150 (97); Anal. calcd for $C_9H_{11}NS_2$ (197.33): C 54.78, H 5.62, N 7.10%; found: C 54.67, H 5.68, N 7.29%.

Methyl *N*,*N*-dimethyldithiocarbamate (3h). 1.09 g, 81% (1.27 g, 94%); Colorless crystals (chloroform–hexane); mp 47–48°C (lit. mp 47°C);[27] IR (KBr): 3193, 2991, 2943, 1610, 1510, 1384, 1245, 1099, 933 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.56 (s, 3H, NCH_3), 3.38 (s, 3H, NCH_3), 2.64 (s, 3H, SCH_3); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 198.37, 45.36, 41.37, 20.46; MS (*m*/*z*, %): 135 (M^+, 6), 88 (100); Anal. calcd for $C_4H_9NS_2$ (135.25): C 35.52, H 6.71, N 10.36%; found: C 35.65, H 6.98, N 10.42%.

Methyl morpholine-4-carbodithioate (3i). 1.35 g, 76% (1.49 g, 84%); Colorless crystals (chloroform–hexane); mp 84–85°C (lit. mp 82.5–83.5°C);[31] IR (KBr): 2980, 2960, 2860, 1444, 1420, 1263, 1226, 1113, 1040, 999 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.12 (br s, 4H, $N(CH_2)_2$), 3.73 (t, *J*=7.4 Hz, 4H, $O(CH_2)_2$), 2.64 (s, 3H, SCH_3); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 198.79, 66.20, 50.80, 19.81; MS (*m*/*z*, %): 177 (M^+, 89), 86 (100); Anal. calcd for $C_6H_{11}NOS_2$ (177.30): C 40.65, H 6.25, N 7.90%; found: C 40.52, H 6.21, N 8.12%.

General procedure for the synthesis of symmetrical thioureas (4a–j)

In a typical experiment, a solution (or suspension) of **1** (1.58 g, 0.01 mol) or **2** (3.00 g, 0.01 mol) and the appropriate amine (0.02 mol) in absolute ethanol (20 mL) was refluxed for 2.5–6.0 h (monitored by TLC). The excess solvent was evaporated under reduced pressure to give crystalline thioureas which were filtered and washed with ethanol. Analytically pure samples were obtained by crystallization from ethanol/water.

1,3-Diphenylthiourea (4a). 1.96 g, 86% (2.19 g, 96%); White solid (ethanol); mp 151–152°C (lit. mp 152–153°C);[10b] IR (KBr): 3394, 3211, 1649, 1542, 1456, 1340, 1236, 1020, 933 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 9.42 (br s, 2H, NH), 7.57–7.12 (m, 10H, ArH); ^{13}C NMR (100.4 MHz, DMSO-d_6): δ 179.62, 138.77, 128.10, 124.54, 123.69; MS (*m*/*z*, %): 228 (M^+, 77), 93 (100), 77 (79); Anal. calcd for $C_{13}H_{12}N_2S$ (228.31): C 68.39, H 5.30, N 12.27%; found: C 68.51, H 5.23, N 12.54%.

1,3-Dibenzylthiourea (4b). 2.02 g, 79% (2.36 g, 92%); white solid (ethanol); mp 146–147°C (lit. mp 145–147°C);[10b] IR (KBr): 3311, 3060, 2925, 2841, 1612, 1454, 1242, 1028, 821 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 7.94 (br s, 2H, NH), 7.34–7.22 (m, 10H, ArH), 4.67 (br s, 4H, –C*H*$_2$Ar); ^{13}C NMR (100.4 MHz, DMSO-d_6): δ 183.79, 139.23, 128.25, 127.21, 126.83, 50.00; MS (*m*/*z*, %): 256

(M^+, 70), 106 (100), 91 (88); Anal. calcd for $C_{15}H_{16}N_2S$ (256.38): C 70.27, H 6.29, N 10.93%; found: C 70.53, H 6.31, N 10.98%.

1,3-Diphenethylthiourea (4c). 2.28 g, 80% (2.58 g, 91%); White solid (ethanol–water); mp 91–92°C (lit. mp 90°C);[32] IR (KBr): 3256, 3049, 2928, 1556, 1489, 1310, 1133, 1000 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.31–7.20 (m, 10H, ArH), 5.82 (br s, 2H, NH), 3.61 (br s, 4H, HNCH_2), 2.83 (t, J=7.0 Hz, 4H, ArCH_2); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 181.74, 138.33, 128.79, 128.74, 126.76, 45.38, 35.12; MS (*m*/*z*, %): 284 (M^+, 81), 104 (100); Anal. calcd for $C_{17}H_{20}N_2S$ (284.43): C 71.79, H 7.09, N 9.85%; found: C 71.83, H 7.17, N 9.73%.

1,3-Di(4′-methoxyphenethyl)thiourea (4d). 2.58 g, 75% (3.06 g, 89%); Colorless solid (ethanol–water); mp 125–126°C (lit. mp 123–125°C);[33] IR (KBr): 3311, 3036, 2925, 2841, 1612, 1554, 1454, 1241, 1028, 821 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.12-7.06 (d, J=8.6 Hz, 4H, ArH), 6.83 (d, J=8.6 Hz, 4H, ArH), 5.76 (br s, 2H, NH), 3.69 (s, 6H, OMe), 3.59 (br s, 4H, HN–CH_2), 2.78 (t, J=7.0 Hz, 4H, ArCH_2); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 181.66, 158.46, 130.20, 129.73, 114.22, 55.29, 45.55, 34.20; MS (*m*/*z*, %): 344 (M^+, 93), 134 (99), 120 (97), 91 (34); Anal. calcd for $C_{19}H_{24}N_2O_2S$ (344.48): C 66.25, H 7.05, N 8.13%; found: C 66.42, H 7.27, N 8.35%.

1,3-Di(2′-pyridyl)thiourea (4e). 1.61 g, 70% (1.84 g, 80%); Colorless solid (ethanol–water); mp 153–154°C (lit. mp 152–153°C);[10b] IR (KBr): 3201, 3036, 1594, 1554, 1526, 1472, 1356, 938 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 9.78 (br s, 2H, NH), 8.87 (br s, 2H, ArH), 8.41 (d, J=6.0 Hz, 2H, ArH), 7.86–7.70 (m, 2H, ArH), 6.88 (br s, 2H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.96, 152.47, 138.61, 137.27, 118.19, 116.35; MS (*m*/*z*, %): 230 (M^+, 45), 137 (44), 94 (100); Anal. calcd for $C_{11}H_{10}N_4S$ (230.30): C 57.37, H 4.38, N 24.33%; found: C 57.62, H 4.19, N 24.51%.

1,3-Diallylthiourea (4f). 1.17 g, 75% (1.40 g, 90%); Colorless solid (ether–hexane); mp 48–49°C (lit. mp 47–49°C);[34] IR (CCl_4): 3284, 2993, 2849, 1640, 1417, 1325, 1062, 928 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.67 (br s, 2H, NH), 5.94–5.81 (m, 2H, CH=CH_2), 5.26–5.16 (m, 4H, CH_2=CH), 4.12 (br s, 4H, NCH_2); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 181.56, 133.07, 116.73, 46.55; MS (*m*/*z*, %): 156 (M^+, 24), 155 (24), 99 (74), 41 (100); Anal. calcd for $C_7H_{12}N_2S$ (156.25): C 53.81, H 7.73, N 17.93%; found: C 53.98, H 7.51, N 17.79%.

1,3-Di-*t*-butylthioourea (4g). 0.75 g, 40% (1.13 g, 60%); Colorless solid (ethanol–water); mp 128–129°C (lit. mp 129–131°C);[10b] IR (KBr): 3265, 2960, 1534, 1317, 1055 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.30 (br s, 2H, NH), 1.49 (br s, 18H, CH_3); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 180.01, 53.25, 29.61, 29.41; MS (*m*/*z*, %): 188 (M^+, 5), 57 (100); Anal. calcd for $C_9H_{20}N_2S$ (188.34): C 57.40, H 10.70, N 14.87%; found: C 57.54, H 10.88, N 14.76%.

1,3-Dihexadecylthiourea (4h). 4.09 g, 78% (4.52 g, 86%); White solid (ethanol); mp 88–89°C; IR (KBr): 3072, 2953, 2912, 2848, 1570, 1338 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.68 (br s, 2H, NH), 3.39 (br s, 4H, NCH_2), 1.62–1.58 (m, 4H), 1.26 (br s, 52H), 0.88 (t, J=7.5 Hz, 6H); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 181.42, 44.39, 31.94, 29.75, 29.68, 29.59, 29.52, 29.37, 29.28, 29.01, 26.92, 22.70, 14.13; MS (*m*/*z*, %): 525 (M^++1, 10), 524 (M^+, 7), 491 (26), 250 (100); Anal. calcd for $C_{33}H_{68}N_2S$ (524.98): C 75.50, H 13.06, N 5.34%; found: C 75.42, H 13.13, N 5.28%.

1,3-Dicyclohexylthiourea (4i). 1.97 g, 82% (2.26 g, 94%); Colorless solid (ethanol–water); mp 179–180°C (lit. mp 179–180°C);[10b] IR (KBr): 3242, 3199, 2926, 2850, 1548, 1498, 1320, 1274, 1226 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.00 (br s, 2H, NH), 3.92 (br s, 2H, HNCH(CH_2–)$_2$), 2.04–2.00 (m, 4H), 1.77–1.60 (m, 6H), 1.44–1.16 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.80, 52.73, 32.76, 25.29, 24.63; MS (*m*/*z*, %): 240 (M^+, 80), 239 (78), 98 (94); Anal. calcd for $C_{13}H_{24}N_2S$ (240.41): C 64.95, H 10.06, N 11.65%; found: C 65.23, H 10.15, N 11.47%.

1,3-Dicyclopropylthiourea (4j). 1.23 g, 79% (1.42 g, 91%); Colorless crystals (ethanol); mp 130–131°C; IR (KBr): 3396, 3200, 2969, 2118, 1518, 1473, 1323, 1249, 1212, 900 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.53 (br s, 2H, NH), 0.86–0.85 (m, 4H), 0.69–0.65 (m, 6H); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 184.44, 29.67, 7.47; MS (*m*/*z*, %): 157 (M^++1, 64), 156 (M^+, 91), 56 (100), 41 (84); Anal. calcd for $C_7H_{12}N_2S$ (156.25): C 53.81, H 7.73, N 17.93%; found: C 53.92, H 7.67, N 18.18%.

General procedure for the synthesis of heterocycles 5–7

To a solution (or suspension) of **1** (1.58 g, 0.01 mol) or its salt **2** (3.00 g, 0.01 mol) in absolute ethanol (20 mL), the appropriate amine (*o*-phenylenediamine, ethylenediamine, ethanolamine) (0.01 mol) in 20 mL of absolute ethanol was added all at once. The reaction mixture was refluxed for 2.5–5 h (monitored by TLC). Excess ethanol was removed under reduced pressure to afford a solid mass which was crystallized from ethanol/water to give pure products.

2(1*H*)-Benzimidazolinethione (5). 1.11 g, 74% (1.38 g, 92%); Colorless solid (ethanol–water); mp 301–302°C (lit. mp 298°C);[35] IR (KBr): 3152, 1620, 1507, 1462, 1378, 1178, 742 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6–$CDCl_3$): δ 12.40 (br s, 2H, NH), 7.18–7.10 (m, 4H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6–$CDCl_3$): δ 167.99, 132.33, 122.14, 109.58; MS (*m*/*z*, %) 150 (M^+, 100), 91(69); Anal. calcd for $C_7H_6N_2S$ (150.21): C 55.97, H 4.03, N 18.65%; found: C 55.76, H 4.21, N 18.86%.

2-Imidazolidinethione (6). 0.79 g, 77% (0.92 g, 90%); Colorless solid (ethanol–water); mp 196–197°C (lit. mp 195–196°C);[10b] IR (KBr): 3247, 2918, 2850, 1572, 1471, 1363, 1028 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 7.96 (br s, 2H, NH), 3.35 (br d, J=8.0 Hz, 4H, CH_2); ^{13}C NMR (100.4 MHz, DMSO-d_6): δ 183.53, 43.96; MS (*m*/*z*, %): 103 (M^++1, 18), 102 (M^+, 100); Anal. calcd for $C_3H_6N_2S$ (102.16): C 35.27, H 5.92, N 27.42%; Found: C 35.34, H 5.89, N 27.51%.

2-Oxazolidinethione (7). 0.82 g, 80% (0.92 g, 89%); Colorless solid (ethanol); mp 97–98°C (lit. mp 98–99°C);[36] IR (KBr): 3211, 1525, 1397, 1169, 913 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.18 (br s, 1H, NH), 4.73 (t, J=9.0 Hz, 2H, CH_2), 3.85 (t, J=9.0 Hz, 2H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.26, 70.42, 44.19; MS (*m*/*z*, %): 104 (M^++1, 92), 103 (M^+, 100); Anal. calcd for C_3H_5NOS (103.15): C 34.93, H 4.89, N 13.58%; found: C 34.73, H 4.71, N 13.53%.

General procedure for the preparation of unsymmetrical thioureas (8a–n)

In a typical experiment, a solution (or suspension) of **1** (1.58 g, 0.01 mol), or its salt **2** (3.0 g, 0.01 mol), and a primary amine (0.01 mol) in absolute ethanol (30 mL) was refluxed for 0.5–1.5 h. After disappearance of the amine (monitored by TLC), a solution of the second amine (0.01 mol), or ammonia solution (25%, 1 mL), in ethanol (20 mL) was added. The reaction mixture was refluxed for the stated time, then worked up as described for symmetrical thioureas.

For the synthesis of **8m** and **8n** the reagent **1** or **2** was first reacted with ammonia solution (25%, 1 mL, 0.013 mol) at room temperature, followed by treatment with secondary amines (0.01 mol) and further refluxing in ethanol.

1-Benzyl-3-phenylthiourea (8a). 1.82 g, 75% (2.23 g, 92%); Colorless solid (ethanol–water); mp 165–166°C (lit. mp 162–164°C);[16a] IR (KBr): 3363, 3145, 2974, 1541, 1504, 1301, 1245, 1178, 1066, 970 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (br s, 1H, NH), 7.40–7.20 (m, 10H, ArH), 6.25 (br s, 1H, NH), 4.85 (d, J=5.4 Hz, 2H, C*H*$_2$Ar); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 180.78, 137.21, 136.07, 130.50, 128.65, 127.54, 125.10, 49.30; MS (*m*/*z*, %): 242 (M^+, 62), 106 (53), 91 (98); Anal. calcd for $C_{14}H_{14}N_2S$ (242.34): C 69.39, H 5.82, N 11.56%; found: C 69.45, H 5.91, N 11.77%.

1-Phenethyl-3-phenylthiourea (8b). 1.87 g, 73% (2.38 g, 93%); Colorless solid (ethanol); mp 106–107°C (lit. mp 106°C);[37] IR (KBr): 3371, 3021, 1536, 1494, 1350, 1263, 1000 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.77 (br s, 1H, NH), 7.34–6.97 (m, 10H, ArH), 5.95 (br s, 1H, NH), 3.89 (q, J=7.0 Hz, 2H, HNC*H*$_2$), 2.93 (t, J=7.0 Hz, 2H, CH_2); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 181.60, 138.47, 135.92, 130.13, 128.77, 127.19, 126.67, 125.19, 46.38, 34.84; MS (*m*/*z*, %): 256 (M^+, 84), 152 (81), 151 (100), 93 (88); Anal. calcd for $C_{15}H_{16}N_2S$ (256.38): C 70.27, H 6.29, N 10.93%; found: C 70.13, H 6.32, N 11.05%.

1-(4′-Methoxyphenyl)-3-phenylthiourea (8c). 1.91 g, 74% (2.22 g, 86%); Colorless solid (ethanol–water); mp 142–143°C (lit. mp 143°C);[38] IR (KBr): 3250, 2960, 2835, 1546, 1506, 1463, 1333, 1246, 1033 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 9.41 (br s, 2H, NH), 7.33–7.30 (m, 5H, ArH), 6.94–6.88 (m, 4H, ArH), 3.34 (s, 3H, OMe); ^{13}C NMR (100.4 MHz, DMSO-d_6): δ 180.19, 156.49, 139.39, 132.22, 128.36, 126.07, 123.64, 113.62, 55.20; MS (*m*/*z*, %): 258 (M^+, 14), 123 (73), 108 (100); Anal. calcd for $C_{14}H_{14}N_2OS$ (258.34): C 65.09, H 5.46, N 10.84%; found: C 65.12, H 5.53, N 10.97%.

1-(2′-Pyridyl)-3-phenylthiourea (8d). 2.04 g, 89% (2.08 g, 91%); Colorless solid (ethanol–water); mp 167–168°C (lit. mp 167°C);[39] IR (KBr): 3217, 1596, 1529, 1468, 1188, 1140 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 13.69 (br s, 1H, NH), 9.68 (br s, 1H, NH), 8.21 (d, J=4.8 Hz, 1H, ArH), 7.67–7.63 (m, 3H, ArH), 7.42–7.39 (m, 2H, ArH), 7.26–7.23 (m, 1H, ArH), 7.02–6.96 (m, 2H, ArH); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 178.66, 153.40, 145.45, 138.74, 129.40 128.59, 126.14, 125.00, 118.04, 112.65; MS (*m*/*z*, %): 229 (M^+, 84), 94 (98), 77 (63); Anal. calcd for $C_{12}H_{11}N_3S$ (229.31): C 62.85, H 4.84, N 18.32%; found: C 62.79, H 4.78, N 18.36%.

1-Methyl-3-phenylthiourea (8e). 1.06 g, 64% (1.56 g, 94%); Colorless solid (ethanol); mp 153–154°C (lit. mp 154–157°C);[16a] IR (KBr): 3252, 3157, 2985, 1522, 1364, 1256, 1035 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.21 (br s, 1H, NH), 7.44–7.22 (m, 5H, ArH), 6.08 (br s, 1H, NH), 3.13 (d, J=4.6 Hz, 3H, NCH_3); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 181.60, 136.31, 130.16, 127.24, 125.39, 32.06; MS (*m*/*z*, %): 167 (M^++1, 35), 166 (M^+, 100), 133 (50), 93 (99); Anal. calcd for $C_8H_{10}N_2S$ (166.25): C 57.80, H 6.06, N 16.85%; found: C 57.78, H 6.18, N 16.72%.

1-Cyclohexyl-3-phenylthiourea (8f). 1.52 g, 65% (1.92 g, 82%); Colorless solid (ethanol); mp 152–153°C (lit. mp 150–151°C);[16a] (KBr): 3311, 3240, 2929, 2854, 1554, 1452, 1292, 1190, 1064, 927 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.65 (br s, 1H, NH), 7.47–7.38 (m, 2H, ArH), 7.34–7.26 (m, 1H, ArH), 7.22–7.15 (m, 2H, ArH), 5.90 (br s, 1H, NH), 4.26 (br s, 1H, NHC*H*), 2.10–1.98 (m, 2H), 1.77–1.58 (m, 3H), 1.46–1.32 (m, 2H), 1.28–1.07 (m, 3H); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 184.61, 136.09, 130.25, 127.20, 125.09, 54.18, 32.75, 25.42, 24.70; MS (*m*/*z*, %): 234 (M^+, 62), 151 (72), 93 (100); Anal. calcd for $C_{13}H_{18}N_2S$ (234.36): C 66.62, H 7.74, N 11.95%; found: C 66.56, H 7.71, N 11.89%.

1-Benzyl-3-cyclohexylthiourea (8g). 1.51 g, 61% (2.38 g, 96%); Colorless solid (ethanol); mp 91–92°C (lit. mp 93–94°C);[40] IR (KBr): 3309, 3238, 2927, 2852, 1552, 1540, 1512, 1491, 1304, 1212, 1197 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.38–7.26 (m, 5H, ArH), 6.16 (br s, 1H, NH), 5.79 (br s, 1H, NH), 4.63 (br s, 2H, ArC*H*$_2$), 3.84 (br s, 1H, HNC*H*), 1.98–1.90 (m, 2H), 1.68–1.54 (m, 3H), 1.39–1.27 (m, 2H), 1.20–1.08 (m, 3H); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 180.59, 136.97, 128.95, 127.95, 127.56, 52.99, 48.43, 32.71, 25.33, 24.53; MS (*m*/*z*, %): 248 (M^+, 52), 106 (39), 91 (100); Anal. calcd for $C_{14}H_{20}N_2S$ (248.39): C 67.70, H 8.12, N 11.28%; found: C 67.67, H 8.04, N 11.19%.

1,1′-Dimethyl-3-phenylthiourea (8h). 1.42 g, 79% (1.69 g, 94%); White solid (ethanol); mp 137–138°C (lit. mp 137–138°C);[16a] IR (KBr): 3271, 2927, 1598, 1494, 1375, 1253, 1137, 935 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.34–7.14 (m, 6H, ArH, NH), 3.28 (s, 6H, $(CH_3)_2$); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 182.57, 139.85, 128.64, 125.36, 124.54, 41.47, 41.39; MS (*m*/*z*, %): 180 (M^+, 59), 179 (38), 147 (48), 88 (69); Anal. calcd for $C_9H_{12}N_2S$ (180.27): C 59.97, H 6.71, N 15.54%; found: C, 60.01, H 6.90, N 15.61%.

***N*-Benzyl-1-piperidinethiocarbamide (8i).** 2.04 g, 87% (2.25 g, 96%); White solid (ethanol); mp 86–87°C (lit. mp

88°C);[41] IR (KBr): 3052, 2932, 1530, 1414, 1324, 1261, 1075 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.33–7.27 (m, 5H, ArH), 5.71 (br s, 1H, NH), 4.87 (d, J=6.4 Hz, CH_2), 3.78 (br s, 4H, CH_2), 1.64 (br s, 6H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 181.18, 138.20, 128.76, 128.04, 127.64, 50.30, 48.93, 25.45, 24.24; MS (*m*/*z*, %): 234 (M^+, 49), 219 (8), 143 (19); Anal. calcd for $C_{13}H_{18}N_2S$ (234.36): C 66.62, H 7.74, N 11.95%; found C 66.53, H 7.62, N 12.03%.

***N*-Benzyl-4-morpholinethiocarbamide (8j).** 1.95 g, 88% (2.00 g, 90%); Colorless solid (ethanol); mp 131–132°C (lit. mp 132°C);[16a] IR (KBr): 3193, 2946, 1592, 1529, 1331, 1221, 1110, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.48 (br s, 1H, NH), 7.33–7.09 (m, 5H, ArH), 3.77 (d, J=4.4 Hz, 4H, $H_2C–N–CH_2$), 3.69 (d, J=4.4 Hz, 4H, $H_2C–O–CH_2$); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 183.69, 139.89, 129.13, 125.16, 122.81, 66.01, 49.71; MS (*m*/*z*, %): 222 (M^+, 80), 135 (71), 86 (100); Anal. calcd for $C_{11}H_{14}N_2OS$ (222.31): C 59.43, H 6.35, N 12.60%; found: C 59.31, H 6.44, N 12.56%.

Phenylthiourea (8k). 1.00 g, 66% (1.43 g, 94%); White solid (ethanol–water); mp 153–154°C (lit. mp 154°C);[16a] IR (KBr): 3421, 3180, 2997, 1612, 1523, 1450, 1265, 1062, 962 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.40 (br s, 1H, NH), 7.46–7.24 (m, 5H, ArH), 6.26 (br s, 2H, NH_2); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 181.52, 136.37, 130.29, 127.77, 125.10; MS (*m*/*z*, %): 152 (M^+, 100), 119 (69), 93 (94); Anal. calcd for $C_7H_8N_2S$ (152.22): C 55.24, H 5.29, N 18.40%; found: C 55.35, H 5.36, N 18.61%.

Benzylthiourea (8l). 1.10 g, 66% (1.39 g, 84%); White solid (ethanol–water); mp 164–165°C (lit. mp 165°C);[2a] IR (KBr): 3345, 2878, 1573, 1435, 1234, 1148, 1042, 918 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.30–7.20 (m, 6H, ArH, NH), 6.13 (br s, 2H, NH_2), 4.60 (d, J=4.6 Hz, 2H, NCH_2); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 181.33, 136.65, 128.97, 128.01, 127.55, 48.66; MS (*m*/*z*, %): 166 (M^+, 16), 91 (100); Anal. calcd for $C_8H_{10}N_2S$ (166.25): C 57.80, H 6.06, N 16.85%; found: C 57.75, H 6.09, N 16.80%.

1-Methyl-1-phenylthiourea (8m). 1.20 g, 72% (1.29 g, 78%); White solid (ethanol); mp 107–108°C (lit. mp 107°C);[2a] IR (KBr): 3234, 2883, 1500, 1460, 1367, 1274, 1097, 999 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.23 (br s, 1H, NH), 7.44–7.40 (m, 2H, ArH), 7.34–7.22 (m, 3H, ArH), 6.02 (br s, 1H, NH), 3.13 (br s, 3H, NCH_3); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 181.56, 136.32, 130.16, 127.28, 127.22, 32.05; MS (*m*/*z*, %): 166 (M^+, 100); Anal. calcd for $C_8H_{10}N_2S$ (166.25): C 57.80, H 6.06, N 16.85%; found: C 57.69, H 6.11, N 16.78%.

Piperidine-1-thiocarbamide (8n). 1.09 g, 76% (1.25 g, 87%); Colorless solid (ethanol); mp 125–126°C (lit. 126–128°C);[42] IR (KBr): 3183, 2908, 1482, 1439, 1398, 1330, 1211, 946 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.86 (br s, 2H, NH_2), 2.75 (d, J=4.0 Hz, 4H, CH_2NCH_2), 1.48 (br s, 6H, $(CH_2)_3$); ^{13}C NMR (100.4 MHz, $CDCl_3$): δ 184.02, 47.02, 26.86, 24.95; MS (*m*/*z*, %): 144 (M^+, 19); Anal. calcd for $C_6H_{12}N_2S$ (144.24): C 49.97, H 8.38, N 19.42%; found: C 49.86, H 8.51, N 19.22%.

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