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PII: S0040-4020(16)30410-0

DOI: 10.1016/j.tet.2016.05.025

Reference: TET 27752

To appear in: *Tetrahedron*

Received Date: 27 February 2016

Revised Date: 28 April 2016

Accepted Date: 9 May 2016

Please cite this article as: Halimehjani AZ, Martens J, Schlüter T, A one-pot three-component synthesis of dithiocarbamates starting from vinyl pyridines and vinyl pyrazine under solvent- and catalyst-free conditions, *Tetrahedron* (2016), doi: 10.1016/j.tet.2016.05.025.

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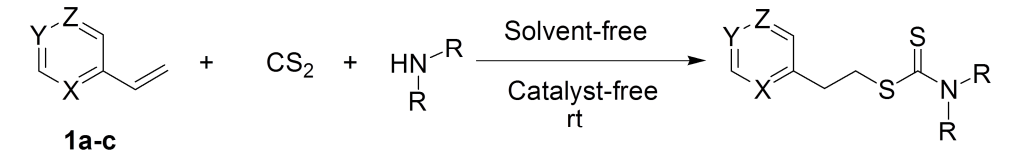

1a-c

1a: X=N and Y, Z=CH
1b: Y=N and X, Z=CH
1c: X, Z=N and Y=CH

29 examples
up to quantitative isolated yield

Tetrahedron

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A one-pot three-component synthesis of dithiocarbamates starting from vinyl pyridines and vinyl pyrazine under solvent- and catalyst-free conditions

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Dithiocarbamate
Solvent-free
Catalyst-free
Vinyl pyrazine
Vinyl pyridines

ABSTRACT

A novel and efficient one-pot three-component reaction for the synthesis of dithiocarbamates at room temperature under solvent– and catalyst–free conditions, starting from readily available amines, CS_2 and vinyl pyridines and vinyl pyrazine is reported. Excellent yield, green reaction conditions, and complete regioselectivity toward anti–Markovnikov adducts are particular advantages of this work.

1. Introduction

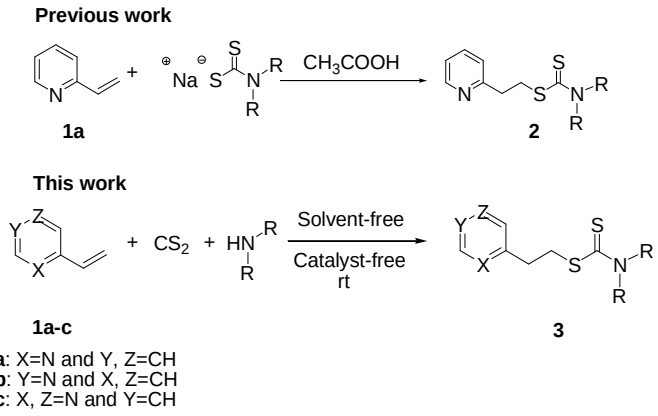
Multicomponent reactions (MCRs), without any doubt, provide one of the most efficient and effective methods in the sustainable and diversity–oriented synthesis of biologically active compounds.[1] Beside the famous MCRs reported to date, the design of novel MCRs with green procedures has attracted great attention from different branches of chemistry for the synthesis of novel materials. Performing the MCRs under solvent– and catalyst–free conditions is completely in agreement with the goals of green chemistry by reducing the pollution, decreasing handling and labor cost, and reducing the number of steps for producing the catalyst or removing the catalyst from the reaction media.[2]

Multicomponent reactions based on CS_2 provide an efficient tool for the synthesis of diverse of functional groups such as dithiocarbamates,[3] dithiocarbonates (xanthates),[4] trithiocarbonates,[5] dithioesters,[6] heterocycles,[7] etc.[8] Reaction of amines with CS_2 provides dithiocarbamic acids as intermediates, the analogues of carbamic acids in which both oxygen atoms are replaced by sulfurs, which are good mononucleophiles from their sulfur atom or a potential bisnucleophile from their sulfurs and nitrogen group.[9] Recently, several efficient procedures for the synthesis of dithiocarbamates have been developed by our group and others to overcome most of the drawbacks associated with the classical methods by using the direct condensation of amines, carbon disulfide, and various electrophiles such as alkyl halides,[10] *α,β*–unsaturated carbonyl compounds,[11] electron-rich alkenes such as ethyl vinyl ethers[12] and *N*–vinyl amides,[13] carbonyl compounds,[14] orthoformates[15a] and epoxides.[15] Compounds containing dithiocarbamate moieties have shown various biological activities as herbicides, fungicides, and pesticides in agriculture,[16] antitumor, anticancer and antibacterial activities in medicine,[17] as radio–pharmaceutical agents for medical imaging,[18] as ligands in coordination chemistry,[19] for sulfur vulcanization in rubber manufacturing,[20] radical chain transfer agents in reversible addition–fragmentation chain transfer (RAFT) polymerizations[21] and as intermediates in organic synthesis.[22] Due to the wide application of dithiocarbamates, the synthesis of these compounds with different substitution patterns at the thiol chain by a convenient and safe method has become a field of increasing interest in synthetic organic chemistry during the past few years.

2. Results and discussion

In continuation of our research toward the synthesis of novel dithiocarbamates and their applications in organic synthesis, herein we report an efficient, novel, and

environmentally benign procedure for the synthesis of dithiocarbamates via one-pot three-component reactions of amines, CS_2 and vinyl pyridines or vinyl pyrazine at room temperature under solvent– and catalyst–free conditions as outlined in Scheme 1.



Scheme 1. A one-pot three-component synthesis of ditiocarbamates

A literature survey revealed that the reaction of dithiocarbamic acid salts with 2–vinylpyridine **1a** in acetic acid as solvent and promoter gave the corresponding dithiocarbamic acid esters as outlined in Scheme 1.[23] According to our experience in the field of dithiocarbamates, we hypothesized that while the reaction of an amine with CS_2 provides the dithiocarbamic acid as intermediate, it is acidic enough to activate the 2–vinylpyridine **1a** for nucleophilic attack. For this purpose, we investigated a one-pot three-component reaction of diethylamine, CS_2 and **1a** as a model reaction at room temperature under solvent– and catalyst–free conditions. We observed that a quantitative yield of **3a** was obtained. While the reaction gives similar yields in polar and nonpolar organic solvents (hexane, CH_2Cl_2, THF, acetone, DMF and methanol) and water, performing the reaction under solvent–free conditions was selected as optimum due to the simplicity and reaction rate. In addition, although the nucleophilicity of dithiocarbamate salts in basic media is more than under neutral conditions, the reaction of diethylamine with CS_2 and **1a** in basic media did not proceed. Furthermore, reaction of commercially available sodium diethyldithiocarbamate with **1a** under solvent-free condition gave no desired product.

With optimized conditions in hand, the scope of this reaction was investigated using different primary and secondary amines and vinyl containing compounds (Table 1). As shown in Table 1, primary aliphatic amines such as ethylamine, isopropylamine, butylamine, isobutylamine, allylamine, (*R*)–phenylethylamine, benzylamine and 4–methoxybenzylamine gave excellent yields. A primary amine containing a hydroxyl group, 3–aminopropanol, was applied in this reaction with excellent yield (entry 11). Dithiocarbamate **3q** derived from biologically active tryptamine[24] was prepared in excellent yield (entry 17). Propargylamine gave the corresponding product **3n** in good yield with 2-(2-(4,5-dihydro-5-methylenethiazol-2-ylthio)ethyl)pyridine **3n'** as an inseparable side product (**3n:3n'**, 86:14) and 24% of 4–methylene–thiazolidine–2–thione[25] (entry 14). Different secondary amines such as pyrrolidine, piperidine, morpholine, diethylamine, and diallylamine gave excellent yields. In addition, (*R*)–thiazolidine–4–carboxylic acid methyl ester as an ester of an unnatural amino acid gave 75% isolated yield (entry 18).

Reactions of aromatic amines with CS_2 usually do not proceed without a base. Surprisingly, we observed that aromatic amines can be successfully applied in this protocol with excellent yields (entries 15 and 27–29). The vinyl pyridine plays an additional role in this reaction as catalyst to promote the reaction of aromatic amines with CS_2. The structure of products was confirmed by IR, ^1H and ^{13}C NMR and HRMS analysis. In addition, the structure of compound **3e** was confirmed by single crystal X–ray diffraction and ORTEP representations are shown in Figure 1 (CCDC no. 1438807).

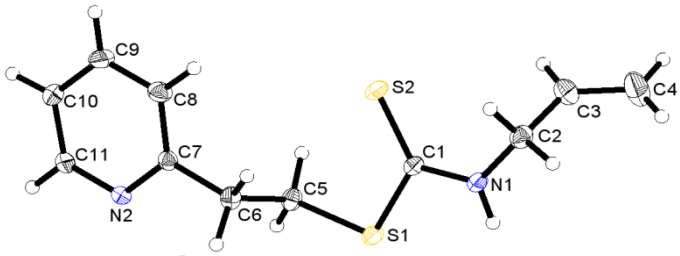
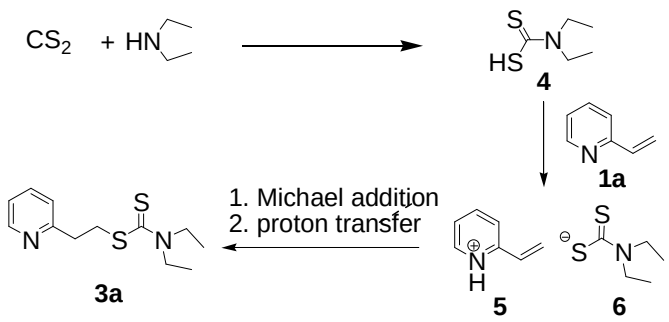


Figure 1. ORTEP image of X–ray crystal structure of **3e**.

2–Vinylpyridine, 4–vinylpyridine and 2–vinylpyrazine worked equally well in this protocol to give the corresponding dithiocarbamates with pyridine or pyrazinyl group in the structure. 1–vinylimidazole was also evaluated without any desired product formation (entry 30).

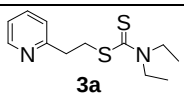
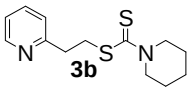
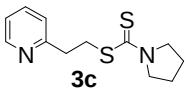
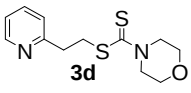
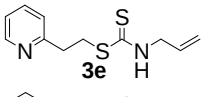
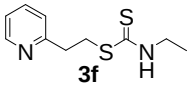
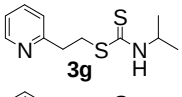
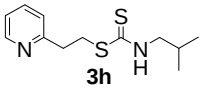
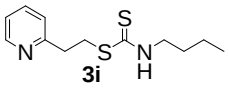
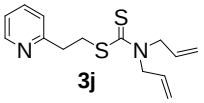
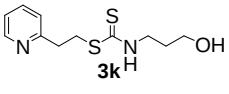
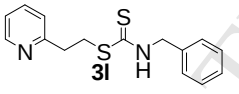
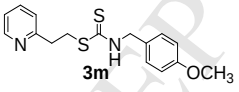
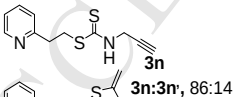
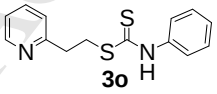
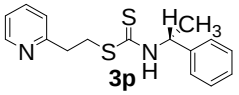
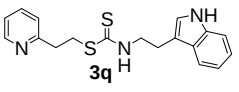
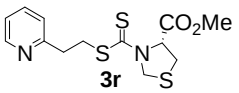
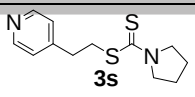
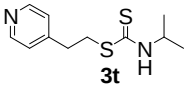
It has been well documented that the biological activity of a compound can be improved by increasing the number of dithiocarbamate moieties in the structure.[26] For this purpose, *bis* (dithiocarbamate) (entry 22) was prepared in 69% yield via the one–pot, pseudo–five–component reaction of 1,3–propanediamine, CS_2 and 4–vinylpyridine in solvent–free conditions at room temperature.

A proposed mechanism for this reaction is given in Scheme 2. It is proposed that the initial event is the reaction of diethylamine with CS_2 to produce the corresponding dithiocarbamic acid **4** which then protonates the 2–vinylpyridine to afford **5**. Nucleophilic attack of the sulfur anion **6** on **5** results in formation of the corresponding product **3a**. Since the reaction of the corresponding sodium dithiocarbamate salt with vinylpyridine was not observed, the proposed mechanism shows that the acidic hydrogen of the dithiocarbamic acid is essential for the reaction.



Scheme 2. A proposed mechanism

Table 1 Diversity in the synthesis of dithiocarbamates

Entry	amine	Michael acceptor	Product	Yield (%)[a]
1	diethylamine		 **3a**	quant.[b, 27]
2	piperidine		 **3b**	quant.[b]
3	pyrrolidine		 **3c**	quant.[b]
4	morpholine		 **3d**	78%[b]
5	allylamine		 **3e**	quant.[b]
6	ethylamine		 **3f**	quant.[b]
7	isopropylamine		 **3g**	quant.[b]
8	isobutylamine		 **3h**	quant.[b]
9	butylamine		 **3i**	quant.[b]
10	diallylamine		 **3j**	quant.[b]
11	3-aminopropanol		 **3k**	quant.[b]
12	benzylamine		 **3l**	98%[b]
13	4-methoxybenzyl amine		 **3m**	quant.[b]
14	propargyl amine		 **3n** **3n:3n'**, 86:14 **3n'**	76%[b]
15	aniline		 **3o**	60%[c]
16	(*R*)-1-phenylethyl amine		 **3p**	quant.[b]
17	tryptamine		 **3q**	88%[c]
18	(*R*)-thiazolidine-4-carboxylic acid methyl ester		 **3r**	75%[c]
19	pyrrolidine		 **3s**	quant.[b]
20	isopropylamine		 **3t**	quant.[b]
21	pyrrolidine		**3u**	quant.[b]
22	1,3-propane diamine		**3v**	69%[c]
23	butylamine		**3w**	98%[b]
24	diethylamine		**3x**	quant.[b]
25	diethylamine		**3y**	91%[b]
26	butylamine		**3z**	95%[b]
27	4-methoxyaniline		**3aa**	93%[c]
28	4-methoxyaniline		**3ab**	95%[c]
29	4-methoxyaniline		**3ac**	95%[c]
30	pyrrolidine		**3ad**	0%

[a] Isolated yield. [b] isolated pure after work-up. [c] isolated by column chromatography.

3. Conclusion

In conclusion, a novel and environmentally benign procedure for the synthesis of dithiocarbamates from readily available amines, CS_2 and vinyl pyridines or vinyl pyrazine was developed. Performing the reaction under solvent– and catalyst–free conditions at ambient temperature, excellent yield, green reaction conditions, a simple work-up procedure and complete regiospecifity toward anti–Markovnikov adducts are the main advantages of this work which makes it a useful and attractive strategy in combinatorial chemistry.

4. Experimental

4.1. **General.** All reagents and solvents were analytically pure and were purchased from Merck or Fluka and used as received. Melting points were obtained on a melting apparatus of

Laboratory Devices and are uncorrected. IR spectra were recorded on a Bruker Tensor 27 spectrometer equipped with a "Golden Gate" diamond-ATR (attenuated total reflection) unit. ^{1}H and ^{13}C NMR spectra of isolated products were recorded on a Bruker AMX R 500 (measuring frequency: ^{1}H NMR = 500.1 MHz, ^{13}C NMR = 125.8 MHz) or a Bruker Avance III 500 (measuring frequency: ^{1}H NMR = 499.9 MHz, ^{13}C NMR = 125.7 MHz) in $CDCl_3$ or DMSO-d_6 solution. Mass spectra were obtained on a Waters Q-TOF Premier (ESI) spectrometer.

4.2. Typical procedure for the synthesis of dithiocarbamates

In a test tube equipped with a magnetic stir bar, 2-vinylpyridine (3 mmol, 0.323 mL) and carbon disulfide (4 mmol, 0.24 mL) were added. The mixture was cooled in an ice bath and diethylamine (3.3 mmol, 0.34 mL) was added dropwise. Then, the ice bath was removed and the mixture was stirred vigorously at room temperature for 6 h. In most of the cases, completion of the reaction can be simply observed by solidification of the reaction mixture. After completion, the reaction was quenched with 0.1 M aqueous $NaHCO_3$ solution (10 mL). In the case of solid compounds, the products were simply collected by filtration and washing with water. For oily compounds, the products were extracted with ethyl acetate (2×20 mL) and the combined organic layers were washed with water (20 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure to give the products in high purity. If needed, the products were purified by flash column chromatography (silica gel, ethyl acetate: petroleum ether; 3:7). In the case of *bis*dithiocarbamate (Table 1, entry 22), 3 mmol (0.25 mL) of 1,3-propanediamine was reacted with 6.5 mmol of 4-vinyl pyridine (0.7 mL) and 8 mmol (0.48 mL) of carbon disulfide. The products were characterized by their IR, ^{1}H and ^{13}C NMR spectra and HRMS analyses.

4.2.1. *2-(Pyridin-2-yl)ethyl diethylcarbamodithioate* (**3a**): Yellow viscous oil; IR (KBr) ν 1485, 1415, 1267, 1205, 1140, 985 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25-1.30 (6H, t, J= 7.4 Hz, $2CH_3$), 3.21 (2H, t, J= 7.8 Hz, CH_2), 3.68-3.76 (4H, m, NCH_2 and SCH_2), 4.04 (2H, t, J= 7.3 Hz, NCH_2), 7.15 (1H, t, J= 7.3 Hz, ArH), 7.28 (1H, d, J= 7.6 Hz, ArH), 7.61 (1H, t, J= 7.8 Hz, ArH), 8.55 (1H, t, J= 4.7 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.6, 12.4, 36.2, 37.4, 46.6, 49.4, 121.5, 123.3, 136.4, 149.2, 159.8, 195.4 ppm; HRMS (ES^+) calcd for $C_{12}H_{19}N_2S_2$ $(M+H)^+$ 255.0990, found 255.0985.

4.2.2. 2-(Pyridin-2-yl)ethyl piperidine-1-carbodithioate (**3b**): Yellow solid; m. p. 44.5-47 ^{o}C; IR (KBr) ν 1474, 1429, 1228, 1117, 1007, 984 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.71-1.74 (6H, m, $3CH_2$), 3.23 (2H, t, J= 7.3 Hz, CH_2), 3.73 (2H, t, J= 7.3 Hz, SCH_2), 3.88 (2H, brs, NCH_2), 4.32 (2H, brs, NCH_2), 7.14-7.17 (1H, m, ArH), 7.29 (1H, d, J= 7.8 Hz, ArH), 7.63 (1H, td, J= 7.6 and 1.9 Hz, ArH), 8.56 (1H, d, J= 4.9 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.3, 25.4, 25.9, 36.2, 37.5, 51.2, 52.8, 121.5, 123.3, 136.4, 149.3, 159.8, 195.5 ppm; HRMS (ES^+) calcd for $C_{13}H_{18}N_2S_2Na$ $(M+Na)^+$ 289.0809, found 289.0802.

4.2.3. 2-(Pyridin-2-yl)ethyl pyrrolidine-1-carbodithioate (**3c**): Light brown solid; m. p. 57-59 ^{o}C; IR (KBr) ν 1595, 1437, 1166, 1011, 949 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.95-2.01 (2H, m, CH_2), 2.05-2.10 (2H, m, CH_2), 3.21 (2H, t, J= 7.3 Hz, CH_2), 3.63 (2H, t, J= 7.0 Hz, SCH_2), 3.71 (2H, t, J= 7.8 Hz, NCH_2), 3.95 (2H, t, J= 7.0 Hz, CH_2N), 7.13-7.15 (1H, m, ArH), 7.28 (1H, d, J= 7.8 Hz, ArH), 7.62 (1H, td, J= 7.6 and 1.9 Hz, ArH), 8.56 (1H, d, J= 5.0 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.2, 26.0, 35.5, 37.6, 50.6, 54.9, 121.5, 123.3, 136.4, 149.2, 159.8, 192.6 ppm; HRMS (ES^+) calcd for $C_{12}H_{16}N_2S_2Na$ $(M+Na)^+$ 275.0653, found 275.0657.

4.2.4. 2-(Pyridin-2-yl)ethyl morpholine-4-carbodithioate (**3d**): Yellow solid; m. p. 75.3-77.5 ^{o}C; IR (KBr) ν 1583, 1408, 1229, 1109, 999, 767 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.24 (2H, t, J= 7.4 Hz, CH_2), 3.75-3.78 (6H, m, 2 OCH_2 and SCH_2), 3.98 (2H, brs, NCH_2), 4.35 (2H, brs, NCH_2), 7.15-7.18 (1H, m, ArH), 7.28 (1H, d, J= 7.8 Hz, ArH), 7.64 (1H, td, J= 7.6 and 1.9 Hz, ArH), 8.56 (1H, d, J= 4.9 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 36.0, 37.3, 50.8 (2C), 66.2 (2C), 121.6, 123.3, 136.4, 149.3, 159.6, 197.6 ppm; HRMS (ES^+) calcd for $C_{12}H_{16}N_2OS_2Na$ $(M+Na)^+$ 291.0602, found 291.0599.

4.2.5. 2-(Pyridin-2-yl)ethyl allylcarbamodithioate (**3e**): Yellow solid; m. p. 57-59 ^{o}C; IR (KBr) ν 3158, 1641, 1568, 1438, 1379, 1321, 1257, 1003, 919 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.25 (2H, t, J=7.8 Hz, CH_2), 3.64 (2H, t, J= 7.3 Hz, SCH_2), 4.42 (2H, t, J= 6.4 Hz, CH_2), 5.25-5.33 (2H, m, CH_2=), 5.91-5.99 (1H, m, CH=), 7.17 (1H, dd, J= 7.3 and 4.9 Hz, ArH), 7.28 (1H, d, J= 7.8 Hz, ArH), 7.63-7.67 (1H, m, ArH), 8.10 (1H, brs, NH), 8.56 (1H, d, J= 4.9 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 34.5, 38.1, 49.8, 118.7, 122.2, 123.9, 132.6, 137.1, 149.5, 159.7, 198.1 ppm; HRMS (ES^+) calcd for $C_{11}H_{14}N_2S_2Na$ $(M+Na)^+$ 261.0496, found 261.0499.

4.2.6. 2-(Pyridin-2-yl)ethyl ethylcarbamodithioate (**3f**): Yellow solid; m. p. 82-84 ^{o}C; IR (KBr) ν 3170, 1587, 1536, 1378, 1153, 1000, 955, 876 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (3H, t, J= 7.4 Hz, CH_3), 3.23 (2H, t, J= 7.3 Hz, CH_2), 3.64 (2H, t, J= 7.4 Hz, SCH_2), 3.74-3.83 (2H, m, NCH_2), 7.17 (1H, t, J= 6.4 Hz, ArH), 7.26 (1H, d, J= 7.8 Hz, ArH), 7.64 (1H, tt, J= 7.6 and 2.0 Hz, ArH), 7.82 (1H, brs, NH), 8.56 (1H, d, J= 4.9 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 34.5, 38.2, 42.5, 122.1, 123.8, 137.0, 149.6, 159.9, 197.4 ppm; HRMS (ES^+) calcd for $C_{10}H_{14}N_2S_2Na$ $(M+Na)^+$ 249.0496, found 249.0494.

4.2.7. 2-(Pyridin-2-yl)ethyl isopropylcarbamodithioate (**3g**): Yellow solid; m. p. 62.5-64 ^{o}C; IR (KBr) ν 3147, 1553, 1371, 1164, 991, 917 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30 (6H, d, J= 6.5 Hz, $2CH_3$), 3.21 (2H, t, J= 7.3 Hz, CH_2), 3.62 (2H, t, J= 7.3 Hz, SCH_2), 4.74-4.81 (1H, m, NCH), 7.16 (1H, dd, J= 7.8 and 5.0 Hz, ArH), 7.27 (1H, d, J= 7.8 Hz, ArH), 7.51 (1H, brs, NH), 7.64 (1H, td, J= 7.6 and 1.9 Hz, ArH), 8.56 (1H, dd, J= 5.0 and 1.9 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.1, 34.4, 38.2, 49.3, 122.1, 123.8, 137.0, 149.6, 159.9, 196.2 ppm; HRMS (ES^+) calcd for $C_{11}H_{17}N_2S_2$ $(M+H)^+$ 241.0828, found 241.0835.

4.2.8. 2-(Pyridin-2-yl)ethyl isobutylcarbamodithioate (**3h**): Yellow solid; m. p. 60-62 ^{o}C; IR (KBr) ν 3128, 1554, 1378, 1256, 1152, 1065, 1001, 887 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.00 (6H, d, J= 6.8 Hz, $2CH_3$), 2.02-2.10 (1H, m, CH), 3.22 (2H, t, J= 7.2 Hz, CH_2), 3.59-3.64 (4H, m, SCH_2 and NCH_2), 7.15-7.19 (1H, m, ArH), 7.25 (1H, d, J= 7.8 Hz, ArH), 7.64 (1H, td, J= 7.6 and 1.9 Hz, ArH), 7.88 (1H, brs, NH), 8.56 (1H, d, J= 4.9 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.5, 28.1, 34.5, 38.2, 54.9, 122.0, 123.8, 136.9, 149.6, 159.9, 197.9 ppm; HRMS (ES^+) calcd for $C_{12}H_{18}N_2S_2Na$ $(M+Na)^+$ 277.0809, found 277.0803.

4.2.9. 2-(Pyridin-2-yl)ethyl butylcarbamodithioate (**3i**): Yellow solid; m. p. 91-93 ^{o}C; IR (KBr) ν 3149, 1539, 1358, 1153, 1003, 920 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.97 (3H, t, J= 7.3 Hz, CH_3), 1.40-1.44 (2H, m, CH_2), 1.62-1.71 (2H, m, CH_2), 3.21 (2H, t, J= 7.1 Hz, CH_2), 3.63 (2H, t, J= 7.6 Hz, SCH_2), 3.74-3.78 (2H,

m, NCH_2), 7.17-7.19 (1H, m, ArH), 7.26 (1H, d, *J*= 7.8 Hz, ArH), 7.64 (1H, td, *J*= 7.6 and 1.6 Hz, ArH), 7.86 (1H, brs, NH), 8.56 (1H, d, *J*= 4.9 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 20.4, 30.8, 34.5, 38.2, 47.4, 122.1, 123.8, 136.9, 149.6, 159.9, 197.5 ppm; HRMS (ES^+) calcd for $C_{12}H_{19}N_2S_2$ $(M+H)^+$ 255.0984, found 255.0989.

4.2.10. 2-(Pyridin-2-yl)ethyl diallylcarbamodithioate (**3j**): Viscous pale yellow oil; IR (KBr) *v* 1643, 1593, 1470, 1435, 1228, 995, 928 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.24 (2H, t, *J*= 7.4 Hz, CH_2), 3.73 (2H, t, *J*= 7.7 Hz, SCH_2), 4.33 (2H, brs, NCH_2), 4.70 (2H, brs, NCH_2), 5.20-5.28 (4H, m, $2CH_2$=), 5.80-5.94 (2H, m, 2CH=), 7.15-7.17 (1H, m, ArH), 7.27 (1H, d, *J*= 7.8 Hz, ArH), 7.64 (1H, td, *J*= 7.6 and 1.9 Hz, ArH), 8.56 (1H, , *J*= 4.9 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 37.0, 37.7, 54.0, 56.8, 118.8, 119.0, 121.9, 123.7, 130.9, 131.5, 136.8, 149.8, 160.1, 198.3 ppm; HRMS (ES^+) calcd for $C_{14}H_{18}N_2S_2Na$ $(M+Na)^+$ 301.0809, found 301.0816.

4.2.11. 2-(Pyridin-2-yl)ethyl 3-hydroxypropylcarbamodithioate (**3k**): Viscous yellow oil; IR (KBr) *v* 3192, 1557, 1386, 1052, 1008, 910 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.90-1.96 (2H, m, CH_2), 3.23 (2H, t, *J*= 7.4 Hz, SCH_2), 3.50 (2H, t, *J*= 7.3 Hz, OCH_2), 3.82-3.88 (2H, m, NCH_2), 3.95-3.99 (2H, m, NCH_2), 7.18-7.20 (1H, m, ArH), 7.27 (1H, d, *J*= 7.8 Hz, ArH), 7.66 (1H, td, *J*= 7.6 and 1.8, ArH), 8.55 (1H, d, J= 4.9 Hz, ArH), 8.75 (1H, brs, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.7, 34.5, 38.3, 46.2, 61.3, 122.4, 124.1, 137.4, 149.4, 159.6, 197.1 ppm; HRMS (ES^+) calcd for $C_{11}H_{16}N_2OS_2Na$ $(M+Na)^+$ 279.0602, found 279.0599.

4.2.12. 2-(Pyridin-2-yl)ethyl benzylcarbamodithioate (**3l**): Colorless solid; m.p. 94-96 ^{o}C; IR (KBr) *v* 3156, 1553, 1433, 1006, 925 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.26 (2H, t, *J*= 7.1 Hz, CH_2), 3.64 (2H, t, *J*= 7.1 Hz, SCH_2), 4.96 (2H, d, *J*= 5.1 Hz, NCH_2), 7.12-7.41 (7H, m, ArH), 7.65 (1H, dt, *J*= 7.6 and 1.8 Hz, ArH), 8.19 (1H, brs, NH), 8.31 (1H, dd, *J*= 5.0 and 1.8 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 34.4, 38.1, 51.6, 122.1, 123.8, 128.5, 128.7, 129.3, 136.7, 137.0, 149.5, 159.6, 197.8 ppm; HRMS (ES^+) calcd for $C_{15}H_{16}N_2S_2Na$ $(M+Na)^+$ 311.0653, found 311.0652.

4.2.13. 2-(Pyridin-2-yl)ethyl 4-methoxybenzylcarbamodithioate (**3m**): Colorless solid; m.p. 87-88.5 ^{o}C; IR (KBr) *v* 3138, 1510, 1251, 1029, 910 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.22 (2H, t, *J*= 7.2 Hz, CH_2), 3.64 (2H, d, *J*= 7.2 Hz, SCH_2), 3.87 (3H, s, OCH_3), 4.88 (2H, d, *J*= 4.8 Hz, NCH_2), 6.90 (2H, d, *J*=8.6 Hz, ArH) 7.13-7.29 (4H, m, ArH), 7.65 (1H, td, *J*= 7.6 and 1.8 Hz, ArH), 8.05 (1H, brs, NH), 8.35 (1H, dd, *J*= 5.6 and 1.7 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 34.4, 38.1, 51.1, 55.8, 114.7, 122.1, 123.8, 128.7, 130.2, 137.0, 149.5, 159.7, 159.8, 197.6 ppm; HRMS (ES^+) calcd for $C_{16}H_{18}N_2OS_2Na$ $(M+Na)^+$ 341.0758, found 341.0746.

4.2.14. 2-(Pyridin-2-yl)ethyl prop-2-ynylcarbamodithioate (**3n**): Colorless solid; m.p. 96-100 ^{o}C; IR (KBr) *v* 3294, 3157, 2087, 1568, 1474, 1378, 1314, 1256, 1099, 1003, 931 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.38 (1H, t, *J*= 2.6 Hz, CH), 3.26 (2H, t, *J*= 7.1 Hz, CH_2), 3.65 (2H, t, *J*= 7.1 Hz, SCH_2), 4.55 (2H, dd, *J*= 4.8 and 2.6 Hz, NCH_2), 7.16-7.26 (2H, m, ArH), 7.66 (1H, td, *J*= 7.6 and 1.8 Hz, ArH), 8.51 (1H, brs, NH), 8.60 (1H, dd, *J*= 5.5 and 1.7 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.9, 36.4, 37.5, 73.0, 78.0, 121.8, 123.5, 136.8, 149.1, 159.1, 197.8 ppm; HRMS (ES^+) calcd for $C_{11}H_{12}N_2S_2Na$ $(M+Na)^+$ 259.0340, found 259.0333.

4.2.15. 2-(Pyridin-2-yl)ethyl phenylcarbamodithioate (**3o**): Colorless solid; m.p. 132-134.5 ^{o}C; IR (KBr) *v* 2692 (NH), 1594, 1493, 1352, 961, 696 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.14 (2H, t, *J*= 7.3 Hz, CH_2), 3.65 (2H, t, *J*= 7.4 Hz, SCH_2), 7.23-7.26 (2H, m, ArH), 7.31 (1H, d, *J*= 7.8 Hz, ArH), 7.37-7.41 (2H, m, ArH), 7.63 (2H, brs, ArH), 7.71 (1H, td, *J*= 7.6 and 1.9 Hz, ArH), 8.52 (1H, dd, *J*= 5.1 and 1.8 Hz, ArH), 11.65 (1H, brs, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.7, 36.5, 121.7, 123.1, 123.9, 126.0, 128.7, 136.5, 139.6, 149.0, 159.2, C=S (not observed) ppm; HRMS (ES^+) calcd for $C_{14}H_{15}N_2S_2$ $(M+H)^+$ 275.0677, found 275.0667.

4.2.16. 2-(Pyridin-2-yl)ethyl (R)-1-phenylethylcarbamodithioate (**3p**): Colorless solid; m.p. 97-99 ^{o}C; IR (KBr) *v* 3151, 1543, 1373, 1130, 1017, 953, 757, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.65 (3H, d, *J*= 6.9 Hz, CH_3), 3.21 (2H, t, *J*= 7.3 Hz, CH_2), 3.66 (2H, t, *J*= 7.2 Hz, SCH_2), 5.85-5.91 (1H, m, NCH), 7.14-7.42 (7H, m, ArH), 7.64 (1H, td, *J*= 7.6 and 1.8 Hz, ArH), 7.97 (1H, brs, NH), 8.43 (1H, d, *J*= 4.8 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 34.5, 38.1, 56.1, 122.1, 123.8, 126.9, 128.1, 129.2, 137.0, 142.0, 149.6, 159.8, 196.8 ppm; HRMS (ES^+) calcd for $C_{16}H_{18}N_2S_2Na$ $(M+Na)^+$ 325.0809, found 325.0817.

4.2.17. 2-(Pyridin-2-yl)ethyl 2-(1H-indol-3-yl)ethylcarbamodithioate (**3q**): Colorless solid; m.p. 103-105 ^{o}C; IR (KBr) *v* 3159, 1523, 1221, 1006, 945, 731, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.14-3.20 (4H, m, $2CH_2$), 3.58 (2H, t, *J*= 7.4 Hz, SCH_2), 4.06-4.10 (2H, m, NCH_2), 6.98-7.39 (6H, m, ArH), 7.58-7.67 (2H, m, ArH), 8.11 (1H, brs, NH), 8.43 (1H, dd, *J*= 5.0 and 1.6 Hz, ArH), 8.74 (1H, brs, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.0, 34.2, 37.6, 47.4, 111.4, 112.2, 118.7, 119.5, 121.8, 122.1, 122.3, 123.5, 127.3, 136.4, 136.8, 148.9, 159.4, 197.1 ppm; HRMS (ES^+) calcd for $C_{18}H_{19}N_3S_2Na$ $(M+Na)^+$ 364.0918, found 364.0919.

4.2.18. (R)-Methyl 3-((2-(pyridin-2-yl)ethylthio)(thiocarbonyl))thiazolidine-4-carboxylate (**3r**): Viscous yellow oil; IR (KBr) *v* 1739, 1593, 1375, 1172, 996, 756 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.10-3.19 (3H, m, CH_2 and SCH_2 in ring), 3.29-3.41 (1H, m, SCH_2 in ring), 3.62-3.71 (5H, m, SCH_2 and OCH_3), 4.63 (1H, d, *J*= 9.2 Hz, NCH_2S), 4.84 (1H, d, *J*= 9.2 Hz, NCH_2S), 5.70 (1H, dd, *J*=7.2 and 3.2 Hz, NCH), 7.07 (1H, dd, *J*= 7.5 and 5.0 Hz, ArH), 7.15 (1H, d, *J*= 7.8 Hz,ArH), 7.54 (1H, td, 7.6 and 4.8 Hz, ArH), 8.47 (1H, d, *J*= 4.9 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 32.4, 36.4, 36.8, 51.2, 53.2, 68.4, 121.6, 123.2, 136.4, 149.3, 159.3, 169.0, 196.0 ppm; HRMS (ES^+) calcd for $C_{13}H_{16}N_2O_2S_3Na$ $(M+Na)^+$ 351.0272, found 351.0280.

4.2.19. 2-(Pyridin-4-yl)ethyl pyrrolidine-1-carbodithioate (**3s**): Yellow solid; m.p. 74-75.5 ^{o}C; IR (KBr) *v* 1597, 1415, 1168, 1009, 809 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.98-2.12 (4H, m, $2CH_2$), 3.04 (2H, t, *J*= 7.6 Hz, CH_2), 3.57 (2H, t, *J*= 7.6 Hz, SCH_2), 3.64 (2H, t, *J*= 6.9 Hz, NCH_2), 3.94 (2H, t, *J*= 7.0 Hz, NCH_2), 7.24 (2H, dd, *J*= 4.6 and 1.5 Hz, ArH), 8.54 (2H, d, *J*= 4.4 and 1.6 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.2, 26.0, 34.7, 36.0, 50.6, 55.0, 124.0, 148.9, 149.8, 191.9 ppm; HRMS (ES^+) calcd for $C_{12}H_{16}N_2S_2Na$ $(M+Na)^+$ 275.0643, found 275.0647.

4.2.20. 2-(Pyridin-4-yl)ethyl isopropylcarbamodithioate (**3t**): Yellow solid; m.p. 103-105 ^{o}C; IR (KBr) *v* 3148, 1604, 1556, 1376, 1168, 996, 802 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.21 (6H, d, *J*= 6.6 Hz, $2CH_3$), 2.92 (2H, t, *J*= 7.3 Hz, CH_2), 3.45 (2H,

t, *J*= 7.8 Hz, SCH_2), 4.64-4.71 (1H, m, NCH), 7.13 (2H, dd, *J*= 4.4 and 1.6 Hz, ArH), 7.49 (1H, brs, NH), 8.45 (2H, dd, *J*= 4.4 and 1.7 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 34.9, 35.0, 49.0, 124.1, 149.0, 149.6, 195.3 ppm; HRMS (ES^+) calcd for $C_{11}H_{16}N_2S_2Na$ $(M+Na)^+$ 263.0643, found 263.0647.

4.2.21. 2-(Pyrazin-2-yl)ethyl pyrrolidine-1-carbodithioate (**3u**): Brown solid; m.p. 64-66 °C; IR (KBr) *v* 1462, 1439, 1333, 1157, 1007, 945 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.97-2.11 (4H, m, $2CH_2$), 3.27 (2H, t, *J*= 7.2 Hz, CH_2), 3.63 (2H, t, *J*= 6.9 Hz, SCH_2), 3.73 (2H, t, *J*= 7.4 Hz, NCH_2), 3.95 (2H, t, *J*= 7.0 Hz, NCH_2), 8.44 (1H, d, *J*= 2.6 Hz, ArH), 8.52-8.54 (2H, m, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.2, 25.9, 34.7, 34.8, 50.6, 54.5 142.6, 144.1, 145.0, 155.5, 192.1 ppm; HRMS (ES^+) calcd for $C_{11}H_{16}N_3S_2$ $(M+H)^+$ 254.0786, found 254.0786.

4.2.22. Bisdithiocarbamate (**3v**): Colorless solid; m.p. 131 °C (decomposed); IR (KBr) *v* 3176, 1606, 1567, 1385, 1327, 1103, 1000, 953, 801 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.87-1.93 (2H, m, CH_2), 2.94 (4H, t, *J*= 7.1 Hz, $2CH_2$), 3.48 (4H, t, *J*= 7.3 Hz, $2SCH_2$), 3.61 (4H, t, *J*=7.2 Hz, $2NCH_2$), 7.29 (4H, dd, 4.4 and 1.6 Hz, ArH), 8.48 (4H, d, *J*= 4.3 and 1.7 Hz, ArH), 10.00 (2H, brs, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.2, 33.9, 34.1, 44.5, 124.0, 148.8, 149.5, 195.6 ppm; HRMS (ES^+) calcd for $C_{19}H_{24}N_4S_4Na$ $(M+Na)^+$ 459.0782, found 459.0786.

4.2.23. 2-(Pyridin-4-yl)ethyl butylcarbamodithioate (**3w**): Yellowish solid; m.p. 88-89.5 °C; IR (KBr) *v* 3170, 1606, 1562, 1381, 1150, 998, 919 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.97 (3H, t, *J*= 7.4 Hz, CH_3), 1.38-1.46 (2H, m, CH_2), 1.64-1.70 (2H, m, CH_2), 3.02 (2H, t, *J*= 7.3 Hz, CH_2), 3.53 (2H, t, *J*= 7.8 Hz, SCH_2), 3.75-3.79 (2H, m, NCH_2), 7.22 (2H, dd, *J*= 4.5 and 1.6 Hz, ArH), 7.80 (1H, brs, NH), 8.54 (2H, dd, *J*= 4.4 and 1.6 Hz, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.6, 19.9, 30.3, 35.0, 36.7, 47.2, 124.0, 148.9, 149.7, 196.7 ppm; HRMS (ES^+) calcd for $C_{12}H_{18}N_2S_2Na$ $(M+Na)^+$ 277.0809, found 277.0802.

4.2.24. 2-(Pyridin-4-yl)ethyl diethylcarbamodithioate (**3x**): Pale yellow solid; m.p. 63-65 °C; IR (KBr) *v* 1603, 1494, 1417, 1276, 1202, 1008, 914 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30 (6H, t, *J*= 7.1 Hz, $2CH_3$), 3.02 (2H, t, *J*= 7.6 Hz, CH_2), 3.56 (2H, t, *J*= 7.8 Hz, SCH_2), 3.74 (2H, q, *J*= 7.1 Hz, NCH_2), 4.05 (2H, q, *J*= 7.1 Hz, NCH_2), 7.23 (2H, dd, *J*= 4.4 and 1.6 Hz, ArH), 8.54 (2H, dd, *J*= 4.4 and 1.6, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.6, 12.4, 34.6, 36.6, 46.7, 49.5, 124.0, 149.0, 149.8, 194.7 ppm; HRMS (ES^+) calcd for $C_{12}H_{18}N_2S_2Na$ $(M+Na)^+$ 277.0809, found 277.0805.

4.2.25. 2-(Pyrazin-2-yl)ethyl diethylcarbamodithioate (**3y**): yellow Oil; IR (KBr) *v* 1486, 1417, 1268, 1205, 1018, 912, 727 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.27-1.31 (6H, m, $2CH_3$), 3.28 (2H, t, *J*= 7.2 Hz, CH_2), 3.71-3.76 (4H, m, NCH_2 and SCH_2), 4.06 (2H, q, *J*= 7.2 Hz, NCH_2), 7.45 (1H, d, *J*= 2.6 Hz, ArH), 8.53-8.55 (2H, m, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.6, 12.4, 34.6, 35.4, 46.7, 49.5, 142.6, 144.1, 145.0, 155.5, 194.8 ppm; HRMS (ES^+) calcd for $C_{11}H_{18}N_3S_2$ $(M+H)^+$ 256.0942, found 256.0940.

4.2.26. 2-(Pyrazin-2-yl)ethyl butylcarbamodithioate (**3z**): Colorless solid; m.p. 79-81 °C; IR (KBr) *v* 3189, 1541, 1401, 1325, 1059, 1023, 922 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.95 (3H, t, *J*= 7.4 Hz, CH_3), 1.37-1.45 (2H, m, CH_2), 1.61-1.69 (2H, m, CH_2), 3.25 (2H, t, *J*= 7.1 Hz, CH_2), 3.68-3.79 (4H, m, SCH_2 and NCH_2), 7.28 (1H, brs, NH), 8.46 (1H, d, *J*= 2.4 Hz, ArH), 8.53-8.56 (2H, m, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.6, 19.9, 30.3, 33.8, 34.5, 47.1, 142.6, 144.1, 145.0, 155.2, 196.8 ppm; HRMS (ES^+) calcd for $C_{11}H_{18}N_3S_2$ $(M+H)^+$ 256.0937, found 256.0944.

4.2.27. 2-(Pyrazin-2-yl)ethyl 4-methoxyphenylcarbamodithioate (**3aa**): Cream solid; m.p. 94.5-97.5 °C; IR (KBr) *v* 3135, 1606, 1510, 1335, 1247, 1023, cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.27 (2H, t, *J*= 7.3 Hz, CH_2), 3.71 (2H, t, *J*= 7.2 Hz, SCH_2), 3.84 (3H, s, OCH_3), 6.92 (2H, m, ArH), 7.29 (2H, brs, ArH), 8.40 (1H, d, *J*= 2.6 Hz, ArH), 8.52-8.54 (2H, m, ArH), 9.40 (1H, brs, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 34.5, 34.7, 55.5, 114.4, 128.1, 142.6, 144.1, 144.9, 155.2, 158.9, two carbons were not observed ppm; HRMS (ES^+) calcd for $C_{14}H_{15}N_3OS_2Na$ $(M+Na)^+$ 328.0554, found 328.0560.

4.2.28. 2-(Pyridin-4-yl)ethyl 4-methoxyphenylcarbamodithioate (**3ab**): Cream solid; m.p. 111-113.5 °C; IR (KBr) *v* 2741 (NH), 1606, 1507, 1363, 1249, 1035, 974 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.04 (2H, t, *J*= 7.7 Hz, CH_2), 3.55 (2H, t, *J*= 7.7 Hz, SCH_2), 3.85 (3H, s, OCH_3), 6.85-7.50 (6H, m, ArH), 8.53-8.56 (2H, m, ArH), 9.70 (1H, brs, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 34.5, 35.8, 55.5, 114.3, 114.7, 124.0, 126.9, 148.9, 149.7, 158.5, C=S not observed; HRMS (ES^+) calcd for $C_{15}H_{16}N_2OS_2Na$ $(M+Na)^+$ 327.0602, found 327.0595.

4.2.29. 2-(Pyridin-2-yl)ethyl 4-methoxyphenylcarbamodithioate (**3ac**): Cream solid; m.p. 122-124 °C; IR (KBr) *v* 2500-3200 (NH), 1508, 1349, 1244, 992, 828 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.24 (2H, t, *J*= 7.4 Hz, CH_2), 3.69 (2H, t, *J*= 7.4 Hz, SCH_2), 3.84 (3H, s, OCH_3), 6.87-7.33 (6H, m, ArH), 7.63-7.68 (1H, m, ArH), 8.53-8.55 (1H, m, ArH), 9.34 (1H, brs, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 37.4, 55.4, 114.3, 114.8, 121.6, 123.4, 126.9, 136.4, 136.6, 149.2, 159.4, two carbons were not observed; HRMS (ES^+) calcd for $C_{15}H_{16}N_2OS_2Na$ $(M+Na)^+$ 327.0602, found 327.0607.

Acknowledgments

We are grateful to the Faculty of Chemistry of Kharazmi University for supporting this work. We also thank Dr. Marc Schmidtmann for X-ray analysis.

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