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One pot synthesis using supported reagents system $KSCN/SiO_2$–RNH_3OAc/Al_2O_3: synthesis of 2-aminothiazoles and *N*-allylthioureas

Tadashi Aoyama,[a,*] Sumiko Murata,[a] Izumi Arai,[a] Natsumi Araki,[a] Toshio Takido,[a] Yoshitada Suzuki[b] and Mitsuo Kodomari[b]

[a]*Department of Materials and Applied Chemistry, College of Science and Technology, Nihon University, Kanda Surugadai, Chiyoda-ku, Tokyo 101-8308, Japan*
[b]*Department of Applied Chemistry, Shibaura Institute of Technology, Shibaura, Minato-ku, Tokyo 108-8548, Japan*

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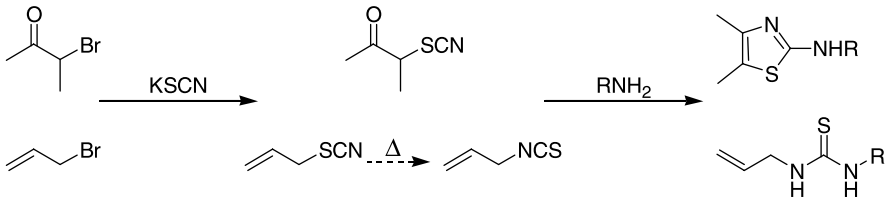
Abstract—A simple and efficient method has been developed for the synthesis of 2-aminothiazoles and *N*-allylthioureas from commercially available materials in one pot by using a supported reagents system, $KSCN/SiO_2$–RNH_3OAc/Al_2O_3, in which α-halo ketone reacts first $KSCN/SiO_2$ and the product, α-thiocyanatoketone, reacts with RNH_3OAc/Al_2O_3 to give the final product, 2-aminothiazoles, in good yield and allyl bromide reacts with $KSCN/SiO_2$ and the product, allyl isothiocyanate, reacts with RNH_3OAc/Al_2O_3 to give *N*-allylthiourea.

1. Introduction

Thiazoles and thioureas are very useful compounds in medicinal, drug and agricultural chemistry. For example, the aminothiazole ring system is a useful structural element in medicinal chemistry and has found broad application in drug development for the treatment of allergies,[1] hypertension,[2] inflammation,[3] bacterial infection[4] and HIV.[5] Symmetrical and unsymmetrical thioureas are an important class of compounds in agricultural and medicinal chemistry[6] and are also used as building blocks for the synthesis of both five and six membered heterocycles.[7] 2-Aminothiazoles are usually synthesized either by the condensation of α-halo ketones with monosubstituted thioureas or by the reaction of α-thiocyanatoketones with aromatic or aliphatic amine hydrochloride.[8] α-Thiocyanatoketones are prepared from the reaction of α-halo ketones with potassium thiocyanate. There are many procedures for the synthesis of symmetrical and unsymmetrical thioureas.[9–14] The most common method is the condensation of primary or secondary amines with isothiocyanates.[6,15] *N*-Allylthioureas are prepared from the reaction of allylisothiocyanate with amines. Allylic isothiocyanates are easily prepared from the reaction of potassium thiocyanate and allylic halides.[16] Thus, both 2-aminothiazoles and allylthioureas could be able to synthesize by using a same reaction process, thiocyanation and amination process (Scheme 1).



Scheme 1. Stepwise synthesis of aminothiazole and allylthiourea.

Keywords: Thiazoles; Thioureas; One pot process.
* Corresponding author. Tel./fax: +81 3 3259 0818; e-mail: aoyama@chem.cst.nihon-u.ac.jp

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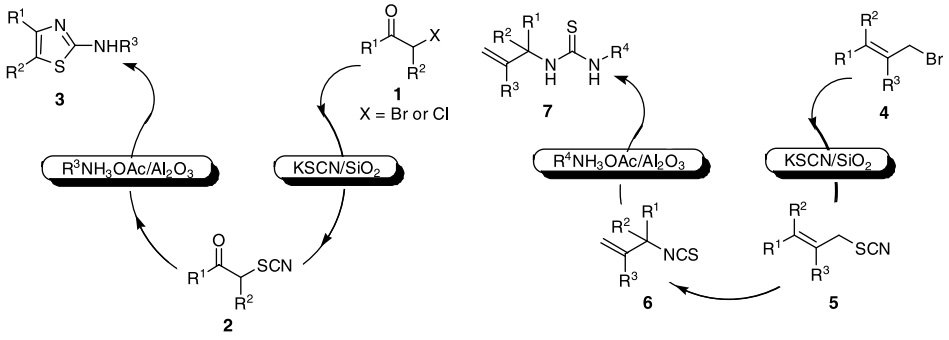


Scheme 2. One-pot synthesis of thiazoles and thioureas using supported reagents.

One-pot synthesis, which can carry out multi-step reactions or multiple reactions in one pot, is very attractive in organic synthesis. In traditional process, the reaction and the isolation of products have to be carried out more than once to synthesize the target compounds. One-pot process, however, can provide the target compounds in not only a single operation and with low cost but also in high total yield. Much effort has been devoted to the development of one-pot reaction process. One-pot synthesis using polymer or inorganic solid supported reagents is unique. Three different reaction stages are able to exist separately in the same vessel when three kinds of inorganic solid supported reagents are used.[17] Thus, synthesis of a compound, which is prepared stepwise in homogeneous solution could be possible in one-pot if each step in the multi-step reaction can be achieved using inorganic solid supported reagents. We have demonstrated the possibility of multi-step reactions in one-pot by using a couple of supported reagents, for example, $ZnCl_2/SiO_2$–K_2CO_3/Al_2O_3,[18a] $CuBr_2/Al_2O_3$–$KSCN/SiO_2$,[18b] $KSCN/SiO_2$–RNH_3OAc/Al_2O_3[18c,d] $CuBr_2/Al_2O_3$–Na_2CO_3/Al_2O_3[17] and Na_2CO_3/SiO_2–PPA/SiO_2.[18e] We described recently the highly efficient method for the one-pot synthesis of 2-aminothiazoles and *N*-allylthioureas from α-halo ketones and allylic halides by using a supported reagents system, silica gel-supported potassium thiocyanate ($KSCN/SiO_2$)-alumina-supported ammonium acetates (RNH_3OAc/Al_2O_3). In this paper, we report on the one-pot synthesis using the supported reagents system, $KSCN/SiO_2$–RNH_3OAc/Al_2O_3, in detail (Scheme 2).

2. Results and discussion

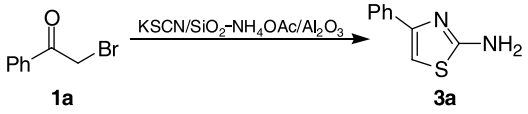
2.1. Determination of the optimum conditions

First, we optimized molar ratios of the reagents by using the reaction of phenacyl bromide (**1a**) as a model reaction (Table 1). A mixture of **1a** (1 mmol), $KSCN/SiO_2$ (1 mmol) and NH_4OAc/Al_2O_3 (2 mmol) in benzene was stirred at 80 °C for 6 h to gave the desired product **3a** in 44% yield along with large amount of **1a** (entry 1). Although twice amount of $KSCN/SiO_2$ was used under the same reaction conditions, the yield of **3a** did not increase. α-Thiocyanatoketone (**2a**) was formed as a main product (entry 2). The use of large amount of NH_4OAc/SiO_2 (6 mmol) gave **3a** in 75% yield along with acetic acid phenacyl ester, which was formed from the reaction of **1a** with NH_4OAc/Al_2O_3 (entry 3). When 5 mmol of $KSCN/SiO_2$ and 6 mmol of NH_4OAc/Al_2O_3 was used against 1 mmol of **1a**, **3a** was obtained in 83% yield (entry 4).

Next, various inorganic solids were tested to decide the most effective inorganic support for NH_4OAc. The results obtained were summarized in Table 2. Neutral alumina was the most effective inorganic support for NH_4OAc. The other inorganic solids tested gave a moderate yield of **3a**. When using magnesium oxide (MgO) as a support, **3a** was formed in a very low yield, and **2a** was obtained as a main product in 72% yield. Thus, we decided to use neutral alumina as a support for NH_4OAc.

The optimum amount of NH_4OAc loaded on Al_2O_3 was investigated (Table 3). When the loading ratio of

Table 1. Preparation of **3a** using $KSCN/SiO_2$–NH_4OAc/Al_2O_3



Entry	$KSCN/SiO_2$ (mmol)	NH_4OAc/Al_2O_3 (mmol)	Yield (%)[a]
1	1	2	44
2	2	2	46
3	3	6	75
4	5	6	83

[a] Isolated yield.

Table 2. Preparation of **3a** using various inorganic supported NH_4OAc

Support	SSA (m^2/g)[a]	pH	Yield (%)[b]
Neutral alumina	200	7.5	83
Acidic alumina	200	4.5	72
Basic alumina	200	10.0	58
Silica gel	450	5.5–7.0	47
MS-5A	400	11.0	67 (24)[c]
Magnesium oxide	70	11.1	17 (72)[c]

[a] Specific surface area.
[b] Isolated yield.
[c] Yield **2a**.

Table 3. Effect of loading ratio NH_4OAc/Al_2O_3

Entry	Loading ratio (mmol/g)	Yield of **3a** (%)[a]
1	0.5	32
2	1.0	83
3	2.0	45 (46)[b]
4	4.0	34 (60)[b]
5	6.0	40 (63)[b]

[a] Isolated yield.
[b] Yield of **2a**.

NH_4OAc/Al_2O_3 was over 2.0 mmol/g, the yield of **3a** was low and **2a** was formed. In these cases NH_4OAc/Al_2O_3 worked as well as NH_4OAc. The reaction using NH_4OAc/Al_2O_3 with a loading of 0.5 mmol/g also gave **3a** in low yield but **2a** was not detected. In this case, the reaction proceeded completely but **3a** was strongly adsorbed on the surface of alumina. When a mixture of **3a** (1 mmol) and alumina (12 g) was stirred in benzene for 6 h, trace amount of **3a** was in solution. When **3a** adsorbed on alumina was extracted with ethyl acetate, **3a** was recovered in 93% yield. NH_4OAc/Al_2O_3 with a loading of 1.0 mmol/g was the most effective for the reaction and was used in the subsequent reactions.

Previously, we have reported that silica gel is effective support for KSCN and $KSCN/SiO_2$ is a useful reagent for transformation of alkyl halides to alkyl thiocyanates.[19]

This supported reagents system, $KSCN/SiO_2$–NH_4OAc/Al_2O_3, worked well for the thiocyanation and the amination in one pot, whereas in the case of the reaction using the unsupported reagents system or using the reagents system in which one reagent is supported on inorganic solid and the other is unsupported, the yields of products were lower than that in the reaction using the supported reagents system. **3a** was also synthesized by using stepwise reaction process, thiocyanation and amination process, and the total yield of **3a** was lower than that from the reaction using $KSCN/SiO_2$–NH_4OAc/Al_2O_3. The reaction of **1a** with $KSCN/SiO_2$ in benzene proceeded at 80 °C to give **2a** in quantitatively after 1.5 h. The reaction of **2a** with NH_4OAc/Al_2O_3 also occurred in benzene under similar conditions and afforded **3a** in 54% yield after 6 h. When the reaction using 0.1 mmol of **2a** and 6 mmol of NH_4OAc/Al_2O_3 was carried out under the similar conditions, **3a** was formed in 78% yield. This result suggests that the amination process successfully proceeds in the presence of a large excess of NH_4OAc. In one-pot process, **2a** formed from the reaction of **1a** and $KSCN/SiO_2$ reacts immediately with NH_4OAc/Al_2O_3, in which a large excess of NH_4OAc to **2a** is always present. Therefore the yield in one-pot synthesis is higher than that in stepwise process (see Table 4).

Table 4. Reaction of **1a** with various reagents systems[a]

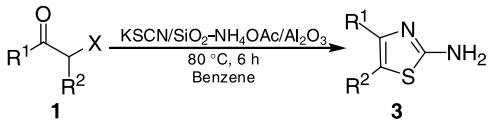
Reagents system	Yield of **3a** (%)[b]
KSCN–NH_4OAc	14
KSCN–NH_4OAc/SiO_2	31
$KSCN/SiO_2$–NH_4OAc	32
$KSCN/SiO_2$–NH_4OAc/Al_2O_3	83

[a] All reactions were carried out using **1a** (1 mmol), KSCN/(SiO_2) (5 mmol) and $NH_4OAc/(Al_2O_3)$ (6 mmol).
[b] Isolated yield.

2.2. Preparation of 2-aminothiazoles

As shown in Table 5, various α-halo ketones react with $KSCN/SiO_2$ and NH_4OAc/Al_2O_3 in one pot to afford the desired 2-aminothiazoles in moderate to high yields. When phenacyl chloride was used instead of phenacyl bromide, **3a** was obtained in 80% yield (Table 1, entry 4 vs Table 5, entry 1). The halo ketones in which, halogen is attached to the primary carbon and the benzylic carbon, afforded the corresponding 2-aminothiazoles in high yield (entries 1–5). On the other hand, in the reactions with the halo ketones having a halogen attached on the secondary carbon, the yields were low (entries 6–8). 2-Bromopropiophenone (**1g**) gave bis[2-(4-phenyl-5-methyl)thiazoyl] amine (**8g**) as a main product in 54% yield and expected **3g** in 46% yield (Scheme 3). Compound **8g** was resulted from the reaction of **2g** with **3g**.

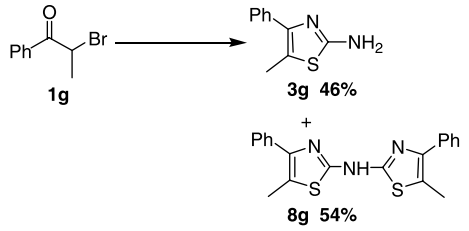
Table 5. One-pot synthesis of 2-aminothiazoles[a]



1 **3**

Entry	X	R^1	R^2	Product	Yield (%)[b]
1	Cl	C_6H_5	H	**3a**	80
2	Br	C_6H_5	C_6H_5	**3b**	87
3	Br	4-Me–C_6H_4	C_6H_5	**3c**	90
4	Br	4-Cl–C_6H_4	C_6H_5	**3d**	92
5	Cl	CH_3	H	**3e**	83
6	Cl	CH_3	CH_3	**3f**	58
7	Br	C_6H_5	CH_3	**3g**	46
8	Br	4-Cl–C_6H_4	CH_3	**3h**	74

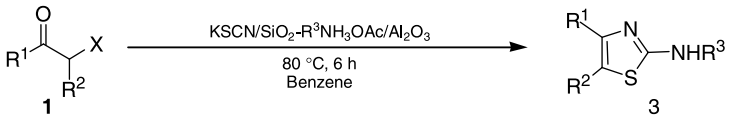
[a] All reactions were carried out using **1** (1 mmol), $KSCN/SiO_2$ (5 mmol) and NH_4OAc/Al_2O_3 (6 mmol).
[b] Isolated yield.



Scheme 3. Formation of **8g** from **1g**.

The reaction of various combinations of α-halo ketones and alkylammonium acetate were carried out. The results were shown in Table 6. The reaction of α-bromo propiophenone with various alkylammonium acetates gave the corresponding 2-alkylaminothiazoles in good to excellent yields. The yields of the products were not affected by the length of alkyl chain attached on an amine. When alicyclic ammonium acetate was used the yields were increased. The successful use of ethanolamine, 2-hydroxypropylamine and allylamine indicates that this procedure is unaffected by the presence of a functional group such as a C–C double bond and a hydroxyl group in an amine part. The reaction of 3-chloro-2-butanone with 2-hydroxyethylamino acetate and 2-hydroxypropylamino acetate gave unexpected compounds, 4,5-dimethyl-3-(2-hydroxyethyl)-1,3-thiazole-2(3*H*)-imine (**3′ao**) and 4,5-dimethyl-3-(2-hydroxypropyl)-1,3-thiazole-2(3*H*)-imine (**3′ap**), along with desired **3ao** and **3ap** (entries 33 and 34). We examined whether **3′** was formed from isomerization reaction of **3**. When **3ao** was stirred in benzene in the presence of $KSCN/SiO_2$ and RNH_3OAc/Al_2O_3 at 80 °C for 6 h, isomerization reaction

Table 6. One-pot synthesis of 2-alkylamino thiazoles from haloketones and various alkylammonium acetates[a]



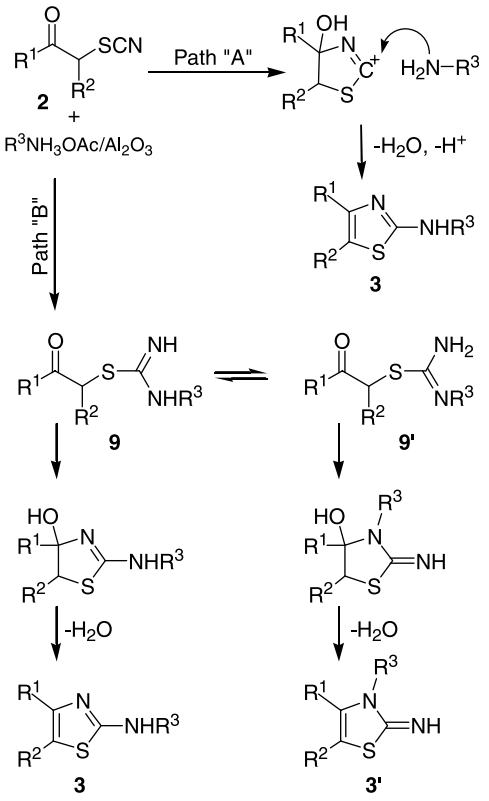
Entry	X	R^1	R^2	R^3	Product	Yield (%)[b]
1	Br	C_6H_5	CH_3	*n*-C_4H_9	**3i**	85
2	Br	C_6H_5	CH_3	*iso*-C_4H_9	**3j**	83
3	Br	C_6H_5	CH_3	*sec*-C_4H_9	**3k**	88
4	Br	C_6H_5	CH_3	$C_{10}H_{21}$	**3l**	87
5	Br	C_6H_5	CH_3	*cyclo*-C_5H_9	**3m**	92
6	Br	C_6H_5	CH_3	*cyclo*-C_6H_{11}	**3n**	88
7	Br	C_6H_5	CH_3	$CH_2C_6H_5$	**3o**	79
8	Br	C_6H_5	CH_3	$C_2H_4C_6H_5$	**3p**	83
9	Br	C_6H_5	CH_3	CH_2CHCH_2	**3q**	99
10	Br	C_6H_5	CH_3	C_2H_4OH	**3r**	60
11	Br	C_6H_5	CH_3	$CH_2CH(OH)CH_3$	**3s**	99
12	Br	C_6H_5	C_6H_5	*n*-C_4H_9	**3t**	65
13	Br	C_6H_5	C_6H_5	*iso*-C_4H_9	**3u**	80
14	Br	C_6H_5	C_6H_5	*sec*-C_4H_9	**3v**	69
15	Br	C_6H_5	C_6H_5	$C_{10}H_{21}$	**3w**	60
16	Br	C_6H_5	C_6H_5	*cyclo*-C_5H_9	**3x**	97
17	Br	C_6H_5	C_6H_5	*cyclo*-C_6H_{11}	**3y**	95
18	Br	C_6H_5	C_6H_5	$CH_2C_6H_5$	**3z**	88
19	Br	C_6H_5	C_6H_5	$C_2H_4C_6H_5$	**3aa**	86
20	Br	C_6H_5	C_6H_5	CH_2CHCH_2	**3ab**	94
21	Br	C_6H_5	C_6H_5	C_2H_4OH	**3ac**	62
22	Br	C_6H_5	C_6H_5	$CH_2CH(OH)CH_3$	**3ad**	96
23	Cl	CH_3	H	$CH_2C_6H_5$	**3ae**	80
24	Cl	CH_3	H	CH_2CHCH_2	**3af**	73
25	Cl	CH_3	H	C_2H_4OH	**3ag**	45
26	Cl	CH_3	H	$CH_2CH(OH)CH_3$	**3ah**	54
27	Br	C_6H_5	H	$CH_2C_6H_5$	**3ai**	82
28	Br	C_6H_5	H	CH_2CHCH_2	**3aj**	72
29	Br	C_6H_5	H	C_2H_4OH	**3ak**	39
30	Br	C_6H_5	H	$CH_2CH(OH)CH_3$	**3al**	53
31	Cl	CH_3	CH_3	$CH_2C_6H_5$	**3am**	46
32	Cl	CH_3	CH_3	CH_2CHCH_2	**3an**	55
33	Cl	CH_3	CH_3	C_2H_4OH	**3ao**	17 (7)[c]
34	Cl	CH_3	CH_3	$CH_2CH(OH)CH_3$	**3ap**	17 (4)[d]

[a] All reactions were carried out using **1** (1 mmol), $KSCN/SiO_2$ (5 mmol) and R^3NH_3OAc/Al_2O_3 (6 mmol).
[b] Isolated yield.
[c] Yield of 4,5-dimethyl-3-(2-hydroxyethyl)-1,3-thiazole-2(3*H*)-imine (**3′ao**).
[d] Yield of 4,5-dimethyl-3-(2-hydroxypropyl)-1,3-thiazole-2(3*H*)-imine (**3′ap**).

was not observed. Considerable mechanism was proposed in Scheme 4. The reaction between an intermediate, α-thiocyanatoketones, and RNH_3OAc/Al_2O_3 proceeds through two pathways. When the reaction proceeds with path A, only 2-aminated thiazoles are formed. If nucleophilic attack of an amine to the thiocyanato group occurs faster than cyclization of α-thiocyanatoketones (path B), an intermediate (**9**) are produced. In principle, both nitrogen atoms can attack the carbonyl carbon. It is known that the sp^2 nitrogen atom is a better base and nucleophile than the sp^3 nitrogen atom.[20] The ring closure provably occurs in a fast step, therefore 2-aminothiazoles are mainly produced in many cases.

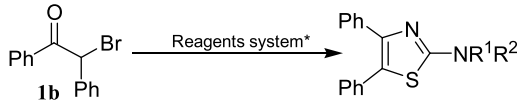
Schantl et al. have reported one-pot synthesis of 2-aminothiazoles in methanol.[21] However, the synthesis of *N*,*N*-disubstituted-2-aminothioureas by this method is sluggish and the yields are low. In contrast, our procedure gave *N*,*N*-disubstituted-2-aminothioureas in high yields. The results were summarized in Table 7. For instance the reaction of 2-bromo-2-phenyl benzophenone (**1b**) with $KSCN/SiO_2$ and alumina supported pyrrolidino acetate gave 4,5-diphenyl-2-pyrrolidino thiazole (**3aq**) in 89% yield. All of the *sec*-alicyclic ammonium acetate afforded the corresponding *N*,*N*-disubstituted-2-aminothiazoles in good yields. The reaction of **1b** with 2-hydroxy-*N*-methylethylamine salt gave **3at** in moderate yield. Dibutyl ammonium and di-*iso*-butyl ammonium acetate are soluble in benzene, thus, in the case of these amines an ammonium trifluoroacetate were used. **3au** and **3av** were also obtained in good yields from **1b**.

Kurz et al. have reported the synthesis of the aminothiazole derivatives from the reaction of α-thiocyanato malonic acid derivatives and hydroxylamines (Scheme 5).[22] We carried out the synthesis of similar compounds from α-bromo-α-methyl malonic acid diethyl ester by using a couple of supported reagents $KSCN/SiO_2$ and NH_4OAc/Al_2O_3. However, the expected compounds were not observed, and a small amount of thiocyanated compounds were detected. α-Bromo-α-methyl malonic acid diethyl ester did not react with $KSCN/SiO_2$ under similar conditions. Therefore our method could not be applicable for the halo



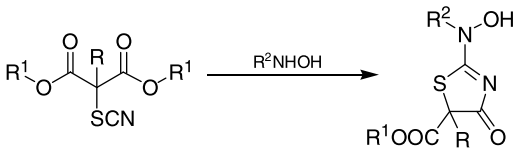
Scheme 4. Reaction path of 2-aminothiazoles.

Table 7. Preparation of 2-dialkylamino-4,5-diphenylthiazoles[a]



Product	Yield (%)[b]
3aq	89
3ar	94
3as	84
3at	65
3au	72[c]
3av	67[c]

[a] All reactions were carried out using **1b** (1 mmol), $KSCN/SiO_2$ (5 mmol) and $R^1R^2NH_2OAc/Al_2O_3$ (6 mmol).
[b] Isolated yield.
[c] Using a salt of trifluoroacetic acid.



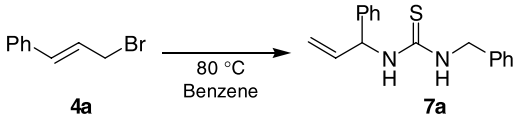
Scheme 5. Reaction of thiocyanato malonic acid derivatives and hydroxylamines.

ketone containing a halogen attached on the tertiary carbon.

2.3. Preparation of *N*-allylthioureas

The synthesis of *N*-allylthioureas using $KSCN/SiO_2$–NH_4OAc/Al_2O_3 system was also tried. In order to determine the optimum conditions for the synthesis of *N*-allylthioureas in fast and efficient way, molar ratios of the supported reagents and the reaction time were investigated (see Table 8). The reaction of cinnamyl bromide with $KSCN/SiO_2$ (5 mmol) and $BnNH_3OAc/Al_2O_3$ (6 mmol) in benzene at 80 °C for 3 h gave **7a** in 68% yield along with a small amount of dibenzylthiourea as a byproduct (entry 1). This dibenzylthiourea is presumed to result from the transamination of **7a** with benzylamine, which released from benzyl ammonium acetate. Transamination of *N*-benzoyl-*N′*-alkylthioureas with amines has been reported.[23] When 3 mmol of $BnNH_3OAc/Al_2O_3$ was used for the reaction, **7a** was yielded without dibenzylthiourea, and the reaction intermediate **5a** was observed in the reaction mixture (entry 2). When the reaction time was prolonged to 6 h, the yield of **7a** increased to 78% (entry 3). Using 1.5 mmol of $BnNH_3OAc/Al_2O_3$, the yield of **7a** decreased (entry 4). Thus, we decided to use 5 mmol of $KSCN/SiO_2$ and 3 mmol of $BnNH_3OAc/Al_2O_3$ against 1 mmol of allylic bromide for subsequent reactions.

Table 8. Preparation of **7a** using $KSCN/SiO_2$–$BnNH_3OAc/Al_2O_3$



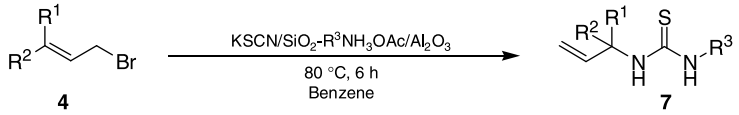
4a **7a**

Entry	$KSCN/SiO_2$ (mmol)	$BnNH_3OAc/Al_2O_3$ (mmol)	Time (h)	Yield (%)[a]
1	5	6	3	68
2	5	3	3	68
3	5	3	6	78
4	5	1.5	6	67

[a] Isolated yield.

Various combination of ammonium acetates and allylic bromides were used for the synthesis of *N*-allylthioureas. The results were summarized in Table 9. Various allylic bromides reacted with $KSCN/SiO_2$ and $BnNH_3OAc/Al_2O_3$ in one pot to afford the corresponding thioureas (entries 1–3). The reaction of crotyl bromide and of 1-bromo-3-methyl-2-butene gave the desired products **7c** and **7d** in excellent

Table 9. One-pot synthesis of *N*-allylthioureas from allylic bromides and various alkylammonium acetates[a]



Entry	R^1	R^2	R^3	Product	Yield (%)[b]
1	H	H	$CH_2C_6H_5$	**7b**	59
2	H	CH_3	$CH_2C_6H_5$	**7c**	92
3	CH_3	CH_3	$CH_2C_6H_5$	**7d**	94
4	H	C_6H_5	*n*-C_4H_9	**7e**	74
5	H	C_6H_5	*iso*-C_4H_9	**7f**	65
6	H	C_6H_5	*sec*-C_4H_9	**7g**	51
7	H	C_6H_5	CH_2CHCH_2	**7h**	60
8	H	C_6H_5	*cyclo*-C_5H_9	**7i**	50
9	H	C_6H_5	*cyclo*-C_6H_{11}	**7j**	70
10	H	C_6H_5	$C_2H_4C_6H_5$	**7k**	51
11	H	CH_3	*n*-C_4H_9	**7l**	89
12	H	CH_3	*iso*-C_4H_9	**7m**	82
13	H	CH_3	*sec*-C_4H_9	**7n**	88
14	H	CH_3	CH_2CHCH_2	**7o**	88
15	H	CH_3	*cyclo*-C_5H_9	**7p**	92
16	H	CH_3	*cyclo*-C_6H_{11}	**7q**	90
17	H	CH_3	$C_2H_4C_6H_5$	**7r**	89
18	CH_3	CH_3	*n*-C_4H_9	**7s**	79
19	CH_3	CH_3	*iso*-C_4H_9	**7t**	73
20	CH_3	CH_3	*sec*-C_4H_9	**7u**	62
21	CH_3	CH_3	CH_2CHCH_2	**7v**	71
22	CH_3	CH_3	*cyclo*-C_5H_9	**7w**	82
23	CH_3	CH_3	*cyclo*-C_6H_{11}	**7x**	85
24	CH_3	CH_3	$C_2H_4C_6H_5$	**7y**	92

[a] All reaction were carried out using **4** (1 mmol), KSCN/SiO_2 (5 mmol) and R^3NH_3OAc/Al_2O_3 (3 mmol).
[b] Isolated yield.

yields, respectively. Cinnamyl bromide and 1-bromo-2-methyl-2-butene were also converted into the corresponding *N*-allylthioureas in good yields under the same conditions. Allyl bromide was the most inactive among the allylic bromides used for the transformations. When cinnamyl chloride was used instead of cinnamyl bromide for the reaction, the yield of **7a** was lower than that of cinnamyl bromide. The reactions of allylic bromides and a series of alkylammonium acetate gave the corresponding thioureas, however, *tert*-butylammonium acetate did not give the desired thiourea. The yields of *N*-allylthioureas depended on the allylic bromides used. For instance, cinnamyl bromide gave the products in moderate yields, whereas, 2-bromo-3-methyl-2-butene gave the product in good to excellent yields. The yields seem to depend on the rate of the rearrangement from the thiocyanate into the isothiocyanate. A mixture of allylic bromides and KSCN/SiO_2 was stirred in benzene at 80 °C for 6 h, and then the ratio of the thiocyanate to the isothiocyanate in the solution was measured by ^{1}H NMR. The correlation, however, between the yield and the rate of the rearrangement was not observed. Further investigation is now in progress. Although Bergmann et al.[24] has reported that cinnamyl thiocyanate isomerizes without allyl rearrangement and cinnamyl isothiocyanate is formed instead of the anticipated α-phenyl isothiocyanate, in our reaction process cinnamyl thiocyanate rearranged into α-phenyl isothiocyanate, resulting thioureas (**7e–7k**) were 1-phenylallyl type compound.

In conclusion, various α-halo ketones and allylic bromides were converted into 2-aminothiazoles and *N*-allylthioureas in the presence of KSCN/SiO_2–RNH_4OAc/Al_2O_3. It is particularly noteworthy that this method does not need to handle of the isolation of reaction intermediate and this method may be applicable to laboratory scale and combinatorial synthesis of 2-aminothiazoles and *N*-allylthioureas.

3. Experimental

3.1. General

Melting points were determined on a Yanako Micro melting point apparatus or on a Büchi 535 or were uncorrected. Elemental analysis were performed on a Yanako CHN corder MT-5. NMR spectra were recorded on a JEOL JNM-GX400 or on a JEOL JNM-LA300 spectrometer. Tetramethylsilane ($\delta=0$) was used as an internal standard for ^{1}H NMR. Mass analysis were performed on an Agilent G1969 LC/MDS TOF. IR spectra were recorded on a HORIBA FT-710 or on a Thermo Electron Nicolet 380 spectrometer.

Preparation of KSCN/SiO_2. Silica gel [Wakogel C-200 (Wako Pure Chemical Ind. LTD), 25.70 g] was added to a solution of potassium thiocyanate (250 mmol, 24.30 g) in distilled water, and the mixture was stirred at room temperature for 0.5 h. The water was removed by rotary evaporator under reduced pressure, and the resulting reagent was dried in vacuo (10 mmHg) at 150 °C for 2 h.

Preparation of NH_4OAc/Al_2O_3. Alumina (ICN Biomedical N-Super 1, 9.23 g) was added to a solution of ammonium acetate (10 mmol. 0.77 g) in methanol, and the mixture was stirred at room temperature for 0.5 h. The methanol was

removed by rotary evaporator under reduced pressure, and the resulting reagent was dried in vacuo (10 mmHg) at room temperature for 2 h.

3.2. Typical procedure for the preparation of 2-aminothiazoles

A mixture of α-halo ketones (1 mmol), $KSCN/SiO_2$ (5 mmol, 1 g) and RNH_3OAc/Al_2O_3 (6 mmol, 6 g) was stirred in benzene (10 mL) at 80 °C for 6 h, and then the used supported reagents were removed by filtration. The filtrate was evaporated to leave crude product, which was purified by column chromatography.

3.2.1. 2-Amino-4-phenylthiazole (3a). Yellow needles. Mp 150–151 °C (hexane/ethyl acetate) (lit.[25] 150 °C). HR-MS (TOF-CI) Calcd for $C_9H_9N_2S$ (MH^+): 177.0486. Found: 177.0494. IR (KBr): 3436, 3115, 1598, 1518, 1342, 716 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.33 (2H, s), 6.71 (1H, s), 7.25–7.31 (1H, m), 7.35–7.40 (2H, m), 7.74–7.78 (2H, m).

3.2.2. 2-Amino-4,5-diphenylthiazole (3b). White solid. Mp 189–190 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{15}H_{13}N_2S$ (MH^+): 253.0799. Found: 253.0805. IR (KBr): 3423, 3273, 3060, 1631, 1543, 1529, 1336, 764, 696 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.25 (2H, s), 7.23–7.28 (8H, m), 7.44–7.47 (2H, m).

3.2.3. 2-Amino-4-(*p*-methylphenyl)-5-phenylthiazole (3c). Yellow solid. Mp 181–182 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{16}H_{15}N_2S$ (MH^+): 267.0955. Found: 267.0961. IR (KBr): 3433, 3255, 3059, 1622, 1525, 1504, 1331, 829, 760, 692 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 2.27 (3H, s), 7.06 (2H, d, $J=8.3$ Hz), 7.19 (2H, s), 7.20–7.32 (7H, m).

3.2.4. 2-Amino-4-(*p*-chlorophenyl)-5-phenylthiazole (3d). Yellow powder. Mp 188–189 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{15}H_{12}ClN_2S$ (MH^+): 287.0409. Found: 287.0408. IR (KBr): 3429, 3251, 3076, 1618, 1525, 1493, 1331, 841, 762, 694 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.24 (2H, s), 7.19–7.28 (7H, m), 7.37–7.41 (2H, m).

3.2.5. 2-Amino-4-methylthiazole (3e). Yellow oil. HR-MS (TOF-CI) Calcd for $C_4H_7N_2S$ (MH^+): 115.0329. Found: 115.0336. IR (neat): 3444, 3290, 1620, 1545, 1520, 1442, 1331, 787 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.13 (3H, s), 5.61 (2H, s), 5.96 (1H, s).

3.2.6. 2-Amino-4,5-dimethylthiazole (3f). Yellow solid. Mp 83–84 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_5H_9N_2S$ (MH^+): 129.0486. Found: 129.0485. IR (KBr): 3423, 3296, 1612, 1520, 1317, 877 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.10 (3H, s), 2.17 (3H, s), 4.92 (2H, s).

3.2.7. 2-Amino-5-methyl-4-phenylthiazole (3g). Brown crystals. Mp 115–116 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{10}H_{11}N_2S$ (MH^+): 191.0642. Found: 191.0635. IR (KBr): 3419, 3276, 3080, 1635, 1597, 1537, 1333, 773, 700 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.39 (3H, s), 4.95 (2H, s), 7.27–7.32 (1H, m), 7.37–7.42 (2H, m), 7.55–7.57 (2H, m).

3.2.8. Bis[2-(4-phenyl-5-methyl)thiazoyl] amine (8g). Yellow solid. Mp 128–129 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{20}H_{18}N_3S_2$ (MH^+): 364.0942. Found: 364.0945. IR (neat): 3199, 3055, 2932, 2857, 1587, 1533, 1445, 1311, 770, 697 cm^{-1}. ^1H NMR (400 MHz, DMSO): δ 2.45 (6H, s), 7.32–7.36 (2H, m), 7.44–7.48 (4H, m), 7.68–7.70 (4H, m), 12.04 (1H, s).

3.2.9. 2-Amino-4-(*p*-chlorophenyl)-5-methylthiazole (3h). Yellow needles. Mp 144–145 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{10}H_{10}ClN_2S$ (MH^+): 225.0253. Found: 225.0258. IR (KBr): 3437, 3261, 3107, 1624, 1541, 1487, 1335, 1092, 835 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.95 (3H, s), 5.22 (2H, s), 7.35 (2H, d, $J=8.4$ Hz), 7.49 (2H, d, $J=8.4$ Hz).

3.2.10. 2-Butylamino-5-methyl-4-phenylthiazole (3i). Brown oil. HR-MS (TOF-CI) Calcd for $C_{14}H_{19}N_2S$ (MH^+): 247.1268. Found: 247.1274. IR (neat): 3203, 3100, 2957, 2930, 1585, 1332, 773, 670 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.95 (3H, t, $J=7.3$ Hz), 1.41 (2H, sext, $J=7.3$ Hz), 1.63 (2H, quint, $J=7.3$ Hz), 2.40 (3H, s), 3.22 (2H, t, $J=7.3$ Hz), 5.47 (1H, s), 7.25–7.31 (1H, m), 7.36–7.40 (2H, m), 7.55–7.58 (2H, m).

3.2.11. 2-*iso*-Butylamino-5-methyl-4-phenylthiazole (3j). White crystals. Mp 123–124 °C (hexane/ethyl acetate). Anal. Calcd for $C_{14}H_{18}N_2S$: C, 68.25; H, 7.36; N, 11.37. Found: C, 68.24; H, 7.40; N, 11.49. HR-MS (TOF-CI) Calcd for $C_{14}H_{19}N_2S$ (MH^+): 247.1268. Found: 247.1275. IR (neat): 3199, 3106, 2951, 2865, 1590, 1464, 1432, 1330, 774, 696 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.96 (6H, d, $J=6.8$ Hz), 1.85–1.97 (1H, m), 2.40 (3H, s), 3.02 (2H, t, $J=6.3$ Hz), 5.30 (1H, s), 7.26–7.30 (1H, m), 7.37–7.40 (2H, m), 7.56–7.58 (2H, m).

3.2.12. 2-*sec*-Butylamino-5-methyl-4-phenylthiazole (3k). Brown oil. HR-MS (TOF-CI) Calcd for $C_{14}H_{19}N_2S$ (MH^+): 247.1268. Found: 247.1261. IR (neat): 3199, 3081, 2966, 2930, 2874, 1626, 1449, 1334, 770, 699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.96 (3H, t, $J=7.3$ Hz), 1.23 (3H, d, $J=6.3$ Hz), 1.55–1.66 (2H, m), 2.38 (3H, s), 3.30–3.39 (1H, m), 5.76 (1H, s), 7.26–7.30 (1H, m), 7.35–7.39 (2H, m), 7.55–7.57 (2H, m).

3.2.13. 2-Decylamino-5-methyl-4-phenylthiazole (3l). Brown oil. HR-MS (TOF-CI) Calcd for $C_{20}H_{31}N_2S$ (MH^+): 331.2207. Found: 331.2212. IR (neat): 3205, 3101, 3058, 2925, 2854, 1587, 1466, 1333, 773, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (3H, t, $J=7.1$ Hz), 1.24–1.33 (14H, m), 1.53–1.60 (2H, m), 2.38 (3H, s), 3.14 (2H, t, $J=7.1$ Hz), 5.82 (1H, s), 7.26–7.30 (1H, m), 7.35–7.40 (2H, m), 7.54–7.57 (2H, m).

3.2.14. 2-*cyclo*-Pentylamino-5-methyl-4-phenylthiazole (3m). Yellow solid. Mp 99–100 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{15}H_{19}N_2S$ (MH^+): 259.1268. Found: 259.1271. IR (neat): 3184, 3056, 2953, 2868, 1622, 1447, 1353, 769, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.46–1.70 (6H, m), 1.96–2.04 (2H, m), 2.39 (3H, s),

3.71–3.76 (1H, m), 5.68 (1H, s), 7.25–7.28 (1H, m), 7.35–7.39 (2H, m), 7.55–7.57 (2H, m).

3.2.15. 2-*cyclo*-Hexylamino-5-methyl-4-phenylthiazole (3n). Yellow crystals. Mp 97–99 °C (hexane/ethyl acetate). Anal. Calcd for $C_{16}H_{20}N_2S$: C, 70.55; H, 7.40; N, 10.28. Found: C, 70.71; H, 7.29; N, 10.49. HR-MS (TOF-CI) Calcd for $C_{16}H_{21}N_2S$ (MH^+): 273.1425. Found: 273.1433. IR (neat): 3171, 3079, 2925, 2851, 1577, 1447, 1333, 770, 694 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.18–1.44 (5H, m), 1.60–1.62 (1H, m), 1.73–1.78 (2H, m), 2.07–2.11 (2H, m), 2.40 (3H, s), 3.23–3.32 (1H, m), 4.92 (1H, d, J= 7.3 Hz), 7.26–7.30 (1H, m), 7.36–7.40 (2H, m), 7.56–7.59 (2H, m).

3.2.16. 2-Benzylamino-5-methyl-4-phenylthiazole (3o). White solid. Mp 152–153 °C (hexane/ethyl acetate) (lit.[26] 151–153 °C). HR-MS (TOF-CI) Calcd for $C_{17}H_{17}N_2S$ (MH^+): 281.1112. Found: 281.1107. IR (KBr): 3186, 1600, 1576, 1452, 1331, 777, 696 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.35 (3H, s), 4.33 (2H, s), 6.42 (1H, s), 7.22–7.36 (8H, m), 7.53–7.57 (2H, m).

3.2.17. 2-(2-Phenylethylamino)-5-methyl-4-phenylthiazole (3p). White crystals. Mp 118–119 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{18}H_{19}N_2S$ (MH^+): 295.1268. Found: 295.1278. IR (neat): 3186, 3085, 1581, 1493, 1433, 772, 691 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.41 (3H, s), 2.95 (2H, t, J=7.1 Hz), 3.51 (2H, dt, J=7.1, 5.9 Hz), 5.10 (1H, s), 7.22–7.34 (6H, m), 7.37–7.41 (2H, m), 7.56–7.59 (2H, m).

3.2.18. 2-Allylamino-5-methyl-4-phenylthiazole (3q). Crystals. Mp 102–103 °C (hexane/ethyl acetate). Anal. Calcd for $C_{13}H_{14}N_2S$: C, 67.79; H, 6.13; N, 12.16. Found: C, 67.69; H, 6.05; N, 12.18. HR-MS (TOF-CI) Calcd for $C_{13}H_{15}N_2S$ (MH^+): 231.0955. Found: 231.0957. IR (KBr): 3194, 1645, 1589, 1421, 1331, 966, 914, 773, 703 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.38 (3H, s), 3.76 (2H, d, J= 4.4 Hz), 5.12–5.17 (1H, m), 5.22–5.29 (1H, m), 5.78–5.91 (1H, m), 6.05 (1H, s), 7.25–7.31 (1H, m), 7.38 (2H, t, J= 7.5 Hz), 7.56 (2H, d, J=7.5 Hz).

3.2.19. 2-(2-Hydroxyethylamino)-5-methyl-4-phenylthiazole (3r). Brown oil. HR-MS (TOF-CI) Calcd for $C_{12}H_{15}N_2OS$ (MH^+): 235.0905. Found: 235.0908. IR (neat): 3277, 3082, 2917, 2859, 1564, 1539, 1490, 1441, 1330, 1070, 773, 699 cm^{-1}. ^1H NMR (400 MHz, DMSO): δ 2.32 (3H, s), 3.28 (2H, q, J=5.9 Hz), 3.55 (2H, t, J= 5.9 Hz), 4.79 (1H, s), 7.26–7.30 (1H, m), 7.36–7.41 (3H, m), 7.55–7.58 (2H, m).

3.2.20. 2-(2-Hydroxypropylamino)-5-methyl-4-phenylthiazole (3s). White powder. Mp 92–93 °C (hexane/ethyl acetate). Anal. Calcd for $C_{13}H_{16}N_2OS$: C, 62.87; H, 6.49; N, 11.28. Found: C, 62.67; H, 6.47; N, 11.26. HR-MS (TOF-CI) Calcd for $C_{13}H_{17}N_2OS$ (MH^+): 249.1061. Found: 249.1059. IR (KBr): 3345, 3319, 3205, 1600, 1560, 1443, 1134, 1078, 771, 700 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.07 (3H, d, J=6.2 Hz), 2.31 (3H, s), 3.15 (2H, t, J=5.7 Hz), 3.75–3.87 (1H, m), 4.82 (1H, d, J=4.6 Hz), 7.27 (1H, t, J=7.3 Hz), 7.35–7.41 (3H, m), 7.55 (2H, d, J=7.2 Hz).

3.2.21. 2-Butylamino-4,5-diphenylthiazole (3t). White crystals. Mp 117–118 °C (hexane/ethyl acetate) (lit.[27] 117–118 °C). HR-MS (TOF-CI) Calcd for $C_{19}H_{21}N_2S$ (MH^+): 309.1425. Found: 309.1428. IR (KBr): 3203, 3097, 2983, 2954, 1585, 1436, 1334, 756, 694 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 0.90 (3H, t, J=7.2 Hz), 1.36 (2H, s, J=7.2 Hz), 1.56 (2H, q, J=7.2 Hz), 3.24 (2H, q, J= 6.8 Hz), 7.18–7.30 (8H, m), 7.37–7.40 (2H, m), 7.72 (1H, t, J=5.3 Hz).

3.2.22. 2-(*iso*-Butylamino)-4,5-diphenylthiazole (3u). White powder. Mp 115 °C (hexane/ethyl acetate). Anal. Calcd for $C_{19}H_{20}N_2S$: C, 73.99; H, 6.54; N, 9.08. Found: C, 74.00; H, 6.41; N, 9.14. HR-MS (TOF-CI) Calcd for $C_{19}H_{21}N_2S$ (MH^+): 309.1425. Found: 309.1429. IR (KBr): 3199, 3093, 2960, 2866, 1570, 1462, 1427, 1335, 758, 698 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 0.92 (6H, d, J= 6.6 Hz), 1.89 (1H, m), 3.07 (2H, t, J=5.7 Hz), 7.17–7.30 (8H, m), 7.36–7.40 (2H, m), 7.78 (1H, t, J=5.7 Hz).

3.2.23. 2-(*sec*-Butylamino)-4,5-diphenylthiazole (3v). White powder. Mp 93–94 °C (hexane/ethyl acetate). Anal. Calcd for $C_{19}H_{20}N_2S$: C, 73.99; H, 6.54; N, 9.08. Found: C, 74.12; H, 6.43; N, 9.17. HR-MS (TOF-CI) Calcd for $C_{19}H_{21}N_2S$ (MH^+): 309.1425. Found: 309.1434. IR (KBr): 3157, 3080, 2968, 2927, 2879, 1618, 1442, 1335, 756, 688 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 0.92 (3H, t, J= 7.3 Hz), 1.19 (3H, d, J=6.4 Hz), 1.45–1.66 (2H, m), 3.58–3.71 (1H, m), 7.20–7.31 (8H, m), 7.39–7.42 (2H, m), 7.63 (1H, d, J=7.7 Hz).

3.2.24. 2-Decylamino-4,5-diphenylthiazole (3w). White solid. Mp 57 °C (hexane/ethyl acetate). Anal. Calcd for $C_{25}H_{32}N_2S$: C, 76.48; H, 8.22; N, 7.14. Found: C, 76.58; H, 8.22; N, 7.17. HR-MS (TOF-CI) Calcd for $C_{25}H_{33}N_2S$ (MH^+): 393.2364. Found: 393.2368. IR (KBr): 3192, 3080, 3060, 2918, 2850, 1581, 1433, 1338, 758, 694 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 0.83 (3H, t, J=7.0 Hz), 1.23–1.30 (14H, m), 1.57 (2H, quint, J=6.8 Hz), 3.22 (2H, q, J= 6.8 Hz), 7.17–7.31 (8H, m), 7.35–7.39 (2H, m), 7.71 (1H, t, J=5.5 Hz).

3.2.25. 2-*cyclo*-Pentylamino-4,5-diphenylthiazole (3x). White powder. Mp 144 °C (hexane/ethyl acetate). Anal. Calcd for $C_{20}H_{20}N_2S$: C, 74.96; H, 6.29; N, 8.74. Found: C, 75.07; H, 6.32; N, 8.80. HR-MS (TOF-CI) Calcd for $C_{20}H_{21}N_2S$ (MH^+): 321.1425. Found: 321.1430. IR (KBr): 3192, 3080, 2947, 2868, 1562, 1441, 1338, 756, 696 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 1.51–1.61 (4H, m), 1.63–1.67 (2H, m), 1.89–1.94 (2H, m), 3.94 (1H, m), 7.17–7.30 (8H, m), 7.36–7.40 (2H, m), 7.76 (1H, d, J=6.5 Hz).

3.2.26. 2-*cyclo*-Hexylamino-4,5-diphenylthiazole (3y). White powder. Mp 154 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{21}H_{23}N_2S$ (MH^+): 335.1581. Found: 335.1581. IR (KBr): 3205, 3078, 2929, 2856, 1558, 1439, 1338, 756, 694 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 1.14–1.36 (5H, m), 1.54–1.57 (1H, m), 1.69 (2H, m), 1.96–1.99 (2H, m), 3.48 (1H, m), 7.16–7.29 (8H, m), 7.35–7.38 (2H, m), 7.67 (1H, d, J=7.5 Hz).

3.2.27. 2-Benzylamino-4,5-diphenylthiazole (3z). White powder. Mp 142 °C (hexane/ethyl acetate). Anal. Calcd for

$C_{22}H_{18}N_2S$: C, 77.16; H, 5.30; N, 8.18. Found: C, 77.18; H, 5.11; N, 8.21. HR-MS (TOF-CI) Calcd for $C_{22}H_{19}N_2S$ (MH^+): 343.1268. Found: 343.1271. IR (KBr): 3199, 3099, 2972, 2887, 1581, 1448, 760, 694 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 4.49 (2H, d, J=5.8 Hz), 7.12–7.41 (15H, m), 8.26 (1H, t, J=5.8 Hz).

3.2.28. 4,5-Diphenyl-2-(2phenethylamino)thiazole (3aa). White powder. Mp 137–138 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{23}H_{21}N_2S$ (MH^+): 357.1425. Found: 357.1427. IR (KBr): 3195, 3086, 1583, 1495, 1335, 758, 696 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 2.91 (2H, t, J=7.3 Hz), 3.49 (2H, q, J=6.8 Hz), 7.17–7.33 (13H, m), 7.39–7.42 (2H, m), 7.85 (1H, t, J=5.5 Hz).

3.2.29. 2-Allylamino-4,5-diphenylthiazole (3ab). White powder. Mp 131–132 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{18}H_{17}N_2S$ (MH^+): 293.1112. Found: 293.1122. IR (KBr): 3188, 3078, 2972, 2925, 1581, 1439, 1425, 1338, 1309, 964, 910, 760, 698 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 3.91 (2H, t, J=5.5 Hz), 5.13 (1H, dd, J=10.3, 1.5 Hz), 5.27 (1H, dd, J=17.0, 1.5 Hz), 5.86–5.99 (1H, m), 7.18–7.31 (8H, m), 7.36–7.39 (2H, m), 7.88 (1H, t, J=5.5 Hz).

3.2.30. 4,5-Diphenyl-2-(2-hydroxyethylamino)thiazole (3ac). White solid. Mp 91 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{17}H_{17}N_2OS$ (MH^+): 297.1061. Found: 297.1057. IR (KBr): 3311, 3199, 3107, 3016, 2924, 1572, 1444, 1336, 1068, 756, 694 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 3.36 (2H, q, J=5.7 Hz), 3.60 (2H, q, J=5.7 Hz), 4.83 (1H, t, J=5.4 Hz), 7.18–7.32 (8H, m), 7.37–7.41 (2H, m), 7.77 (1H, t, J=5.7 Hz).

3.2.31. 4,5-Diphenyl-2-(2-hydroxypropylamino)thiazole (3ad). White powder. Mp 111–112 °C (hexane/ethyl acetate). Anal. Calcd for $C_{18}H_{18}N_2OS$: C, 69.65; H, 5.84; N, 9.02. Found: C, 69.71; H, 5.72; N, 9.02. HR-MS (TOF-CI) Calcd for $C_{18}H_{19}N_2OS$ (MH^+): 311.1218. Found: 311.1215. IR (KBr): 3357, 3209, 3082, 2972, 1558, 1442, 1336, 1124, 1072, 758, 696 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 1.11 (3H, d, J=6.2 Hz), 3.21 (2H, t, J=5.7 Hz), 3.85 (1H, m), 4.83 (1H, d, J=4.8 Hz), 7.16–7.31 (8H, m), 7.35–7.39 (2H, m), 7.74 (1H, t, J=5.7 Hz).

3.2.32. 2-Benzylamino-4-methylthiazole[28] (3ae). White solid. Mp 95–96 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{11}H_{13}N_2S$ (MH^+): 205.0799. Found: 205.0802. IR (KBr): 3201, 1589, 1468, 1450, 1360, 980, 731, 692 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.16 (3H, s), 4.44 (2H, s), 6.02 (1H, s), 6.39 (1H, s), 7.25–7.38 (5H, m).

3.2.33. 2-Allylamino-4-methylthiazole (3af). Brown oil. HR-MS (TOF-CI) Calcd for $C_7H_{11}N_2S$ (MH^+): 155.0642. Found: 155.0649. IR (neat): 3205, 1583, 1547, 1427, 1417, 922, 688 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 2.05 (3H, s), 3.83 (2H, d, J=5.0 Hz), 5.07–5.12 (1H, m), 5.18–5.25 (1H, m), 5.82–5.94 (1H, m), 6.14 (1H, s), 7.58 (1H, m).

3.2.34. 2-(2-Hydroxyethylamino)-4-methylthiazole (3ag). Brown oil. HR-MS (TOF-CI) Calcd for $C_6H_{11}N_2OS$ (MH^+): 159.0592. Found: 159.0590. IR (neat): 3280, 2947, 2918, 1562, 1541, 1067 cm^{-1}. ^1H NMR (400 MHz, DMSO): δ 2.01 (3H, s), 3.18 (2H, q, J=5.6 Hz), 3.44 (2H, t, J=5.6 Hz), 4.69 (1H, s), 6.05 (1H, s), 7.33 (1H, t, J=5.6 Hz).

3.2.35. 2-(2-Hydroxypropylamino)-4-methylthiazole (3ah). Yellow solid. Mp 71 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_7H_{13}N_2OS$ (MH^+): 173.0748. Found: 173.0748. IR (KBr): 3240, 1558, 1543, 1442, 1321, 1146, 1066, 690 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 1.04 (3H, d, J=6.2 Hz), 2.06 (3H, s), 3.10 (2H, t, J=5.7 Hz), 3.71–3.82 (1H, m), 4.77 (1H, d, J=4.7 Hz), 6.09 (1H, s), 7.38 (1H, t, J=5.7 Hz).

3.2.36. 2-Benzylamino-4-phenylthiazole (3ai). Yellow solid. Mp 98–99 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{16}H_{15}N_2S$ (MH^+): 267.0955. Found: 267.0956. IR (KBr): 3234, 2972, 1591, 1481, 1448, 1334, 712 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 4.45 (2H, s), 6.35 (1H, s), 6.66 (1H, s), 7.22–7.35 (8H, m), 7.77–7.80 (2H, m).

3.2.37. 2-Allylamino-4-phenylthiazole (3aj). Yellow crystals. Mp 73 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{12}H_{13}N_2S$ (MH^+): 217.0799. Found: 217.0797. IR (KBr): 3192, 1601, 1585, 1483, 1442, 1423, 926, 702, 671 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.86 (2H, m), 5.14–5.19 (1H, m), 5.25–5.32 (1H, m), 5.82–5.94 (1H, m), 6.26 (1H, s), 6.68 (1H, s), 7.24–7.30 (1H, m), 7.34–7.39 (2H, m), 7.56–7.80 (2H, m).

3.2.38. 2-(2-Hydroxyethylamino)-4-phenylthiazole (3ak). Brown oil. HR-MS (TOF-CI) Calcd for $C_{11}H_{13}N_2OS$ (MH^+): 221.0748. Found: 221.0749. IR (neat): 3282, 3116, 1556, 1051, 773, 706 cm^{-1}. ^1H NMR (400 MHz, DMSO): δ 3.35 (2H, q, J=5.6 Hz), 3.58 (2H, q, J=5.6 Hz), 4.78 (1H, t, J=5.6 Hz), 7.02 (1H, s), 7.23–7.26 (1H, m), 7.33–7.37 (2H, m), 7.64 (1H, t, J=5.6 Hz), 7.79–7.81 (2H, m).

3.2.39. 2-(2-Hydroxypropylamino)-4-phenylthiazole (3al). Yellow powder. Mp 104–105 °C (hexane/ethyl acetate). Anal. Calcd for $C_{12}H_{14}N_2OS$: C, 61.51; H, 6.02; N, 11.96. Found: C, 61.57; H, 5.94; N, 11.93. HR-MS (TOF-CI) Calcd for $C_{12}H_{15}N_2OS$ (MH^+): 235.0905. Found: 235.0905. IR (KBr): 3359, 3113, 1560, 1483, 1340, 1119, 943, 704 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 1.11 (3H, d, J=6.2 Hz), 3.24 (2H, t, J=5.6 Hz), 3.81–3.93 (1H, m), 4.85 (1H, d, J=4.6 Hz), 7.03 (1H, s), 7.26 (1H, t, J=7.2 Hz), 7.37 (2H, t, J=7.2 Hz), 7.65 (3H, t, J=5.6 Hz), 7.82 (2H, d, J=7.2 Hz).

3.2.40. 2-Benzylamino-4,5-dimethylthiazole[28] (3am). Brown powder. Mp 114–115 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{12}H_{15}N_2S$ (MH^+): 219.0955. Found: 219.0958. IR (KBr): 3199, 1593, 1468, 1454, 1354, 712 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 1.97 (3H, s), 2.08 (3H, s), 4.35 (2H, d, J=5.5 Hz), 7.18–7.39 (5H, m), 7.68 (1H, t, J=5.5 Hz).

3.2.41. 2-Allylamino-4,5-dimethylthiazole (3an). Brown needles. Mp 69 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_8H_{13}N_2S$ (MH^+): 169.0799. Found:

169.0797. IR (KBr): 3203, 3103, 1593, 1427, 1344, 1306, 1228, 966, 912, 704 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.11 (3H, s), 2.18 (3H, s), 3.83 (2H, d, $J=5.3$ Hz), 5.15–5.20 (1H, m), 5.26–5.33 (1H, m), 5.60 (1H, s), 5.84–5.98 (1H, m).

3.2.42. 2-(2-Hydroxyethylamino)-4,5-dimethylthiazole (3ao). Brown oil. HR-MS (TOF-CI) Calcd for $C_7H_{13}N_2OS$ (MH^+): 173.0748. Found: 173.0747. IR (neat): 3270, 2923, 2854, 1542, 1058, 822 cm^{-1}. ^1H NMR (400 MHz, DMSO): δ 1.96 (3H, s), 2.08 (3H, s), 3.19 (2H, q, $J=5.9$ Hz), 3.48 (2H, t, $J=5.9$ Hz), 4.74–4.92 (1H, m), 7.12 (1H, t, $J=5.1$ Hz).

3.2.43. 4,5-Dimethyl-3-(2-hydroxyethyl)-1,3-thiazole-2(3*H*)-imine (3′ao). White solid. Mp 176–177 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_7H_{13}N_2OS$ (MH^+): 173.0748. Found: 173.0742. IR (neat): 3170, 3092, 2961, 2925, 2878, 1655, 1502, 1444, 1402, 1057 cm^{-1}. ^1H NMR (400 MHz, DMSO): δ 1.94 (3H, s), 2.04 (3H, s), 3.58 (2H, q, $J=5.8$ Hz), 3.88 (2H, t, $J=5.8$ Hz), 4.85 (1H, t, $J=5.8$ Hz), 11.81 (1H, s).

3.2.44. 2-(2-Hydroxypropylamino)-4,5-dimethylthiazole (3ap). Brown oil. HR-MS (TOF-CI) Calcd for $C_8H_{15}N_2OS$ (MH^+): 187.0905. Found: 187.0897. IR (neat): 3250, 2961, 2923, 2857, 1562, 1454, 1410, 1375, 1085 cm^{-1}. ^1H NMR (400 MHz, DMSO): δ 1.03 (3H, d, $J=6.6$ Hz), 1.96 (3H, s), 2.07 (3H, s), 3.00–3.11 (2H, m), 3.70–3.78 (1H, m), 4.77 (1H, s), 7.13 (1H, t, $J=5.4$ Hz)

3.2.45. 4,5-Dimethyl-3-(2-hydroxypropyl)-1,3-thiazole-2(3*H*)-imine (3′ap). White powder. Mp 160–161 °C (hexane/ethyl acetate). Anal. Calcd for $C_8H_{14}N_2OS$: C, 51.58; H, 7.58; N, 15.04. Found: C, 51.49; H, 7.62; N, 14.98. HR-MS (TOF-CI) Calcd for $C_8H_{15}N_2OS$ (MH^+): 187.0905. Found: 187.0897. IR (neat): 3374, 3103, 2962, 2947, 2926, 2892, 1660, 1493, 1438, 1401, 1369, 1134, 936 cm^{-1}. ^1H NMR (400 MHz, DMSO): δ 1.05 (3H, d, $J=6.3$ Hz), 1.94 (3H, s), 2.03 (3H, s), 3.55 (1H, dd, $J=13.5$, 8.2 Hz), 3.89 (1H, dd, $J=13.5$, 4.0 Hz), 4.00–4.06 (1H, m), 4.79 (1H, d, $J=5.1$ Hz), 11.79 (1H, s).

3.2.46. 4,5-Diphenyl-2-pyrrolidinothiazole (3aq). Yellow solid. Mp 116–117 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{19}H_{19}N_2S$ (MH^+): 307.1268. Found: 307.1277. IR (KBr): 2914, 2852, 1599, 1560, 1495, 1331, 762, 700 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 1.94–2.00 (4H, m), 3.39 (4H, t, $J=6.5$ Hz), 7.17–7.30 (8H, m), 7.39–7.42 (2H, m).

3.2.47. 4,5-Diphenyl-2-piperidinothiazole (3ar). Yellow crystals. Mp 152–153 °C (hexane/ethyl acetate) (lit.[27] 152–153 °C). HR-MS (TOF-CI) Calcd for $C_{20}H_{21}N_2S$ (MH^+): 321.1425. Found: 321.1432. IR (KBr): 2933, 2852, 1600, 1541, 1495, 1444, 1329, 761, 698 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 1.61 (6H, m), 3.45 (4H, m), 7.20–7.33 (8H, m), 7.36–7.41 (2H, m).

3.2.48. 4,5-Diphenyl-2-morpholinothiazole (3as). White crystals. Mp 116–117 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{19}H_{19}N_2OS$ (MH^+): 323.1218. Found: 323.1226. IR (KBr): 2960, 2845, 1599, 1572, 1444, 1336, 1120, 762, 702 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 3.41 (4H, t, $J=4.8$ Hz), 3.72 (4H, t, $J=4.8$ Hz), 7.22–7.30 (8H, m), 7.39–7.42 (2H, m).

3.2.49. 4,5-Diphenyl-2-(*N*-methyl-2-hydroxyethylamino)thiazole (3at). White powder. Mp 69 °C (hexane/ethyl acetate). HR-MS (TOF-CI) Calcd for $C_{18}H_{19}N_2OS$ (MH^+): 311.1218. Found: 311.1215. IR (KBr): 3367, 2924, 2862, 1599, 1552, 1415, 1333, 754, 696 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 3.10 (3H, s), 3.53 (2H, t, $J=5.7$ Hz), 3.67 (2H, q, $J=5.7$ Hz), 4.86 (1H, t, $J=5.7$ Hz), 7.19–7.31 (8H, m), 7.39–7.42 (2H, m).

3.2.50. 2-(*N*,*N*-Dibutylamino)-4,5-diphenylthiazole (3au). Yellow oil. HR-MS (TOF-CI) Calcd for $C_{23}H_{29}N_2S$ (MH^+): 365.2051. Found: 365.2051. IR (KBr): 1600, 1545, 1495, 1444, 1336, 756, 696 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 0.98 (6H, t, $J=7.4$ Hz), 1.39 (4H, m), 1.69 (4H, m), 3.45 (4H, t, $J=7.4$ Hz), 7.15–7.30 (8H, m), 7.51–7.55 (2H, m).

3.2.51. 2-(*N*,*N*-Di-*iso*-butylamino)-4,5-diphenylthiazole (3av). Yellow oil. HR-MS (TOF-CI) Calcd for $C_{23}H_{29}N_2S$ (MH^+): 365.2051. Found: 365.2056. IR (KBr): 1601, 1541, 1495, 1442, 1336, 756, 696 cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 0.96 (12H, d, $J=6.6$ Hz), 2.24 (2H, m), 3.34 (4H, d, $J=7.5$ Hz), 7.25–7.37 (8H, m), 7.40–7.47 (2H, m).

3.3. Typical procedure for the preparation of *N*-allylthioureas

A mixture of allyl bromides (1 mmol), $KSCN/SiO_2$ (5 mmol, 1 g) and RNH_3OAc/Al_2O_3 (3 mmol, 3 g) was stirred in benzene (10 mL) at 80 °C for 6 h, and then the used supported reagents were removed by filtration. The filtrate was evaporated to leave crude product, which was purified by column chromatography.

3.3.1. 1-Benzyl-3-(1-phenylallyl)-thiourea (7a). White powder. Mp 80–81 °C (hexane/ethyl acetate). Anal. Calcd for $C_{17}H_{18}N_2S$: C, 72.30; H, 6.42; N, 9.92. Found: C, 72.21; H, 6.53; N, 10.10. HR-MS (TOF-CI) Calcd for $C_{17}H_{19}N_2S$ (MH^+): 283.1268. Found: 283.1273. IR (neat): 3266, 1549 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 4.55 (2H, s), 5.06–5.18 (2H, m), 5.54 (1H, s), 5.83–5.93 (1H, m), 6.30 (1H, s), 6.40 (1H, s), 7.08–7.26 (10H, m).

3.3.2. 1-Allyl-3-benzyl thiourea (7b). White solid. Mp 93 °C (hexane/ethyl acetate). Anal. Calcd for $C_{11}H_{14}N_2S$: C, 64.04; H, 6.84; N, 13.58. Found: C, 64.10; H, 6.94; N, 13.83. HR-MS (TOF-CI) Calcd for $C_{11}H_{15}N_2S$ (MH^+): 207.0955. Found: 207.0962. IR (neat): 3237, 1558 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 4.03 (2H, s), 4.65 (2H, s), 5.14–5.19 (2H, m), 5.76–5.86 (1H, m), 6.19 (1H, s), 6.37 (1H, s), 7.27–7.37 (5H, m).

3.3.3. 1-Benzyl-3-(1-methylallyl)-thiourea (7c). White solid. Mp 68–69 °C (hexane/ethyl acetate). Anal. Calcd for $C_{12}H_{16}N_2S$: C, 65.41; H, 7.32; N, 12.71. Found: C, 65.44; H, 7.44; N, 12.70. HR-MS (TOF-CI) Calcd for $C_{12}H_{17}N_2S$ (MH^+): 221.1112. Found: 221.1108. IR (neat): 3221, 1558 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.20 (3H, d, $J=6.8$ Hz), 4.42 (1H, s), 4.62 (2H, s), 5.02–5.10 (2H, m),

5.67–5.78 (1H, m), 6.08 (1H, s), 6.29 (1H, s), 7.23–7.30 (5H, m).

3.3.4. 1-Benzyl-3-(1,1-dimethylallyl)-thiourea (7d). White crystals. Mp 58–59 °C (hexane/ethyl acetate). Anal. Calcd for $C_{13}H_{18}N_2S$: C, 66.62; H, 7.74; N, 11.95. Found: C, 66.76; H, 7.85; N, 12.04. HR-MS (TOF-CI) Calcd for $C_{13}H_{19}N_2S$ (MH^+): 235.1268. Found: 235.1268. IR (KBr): 3267, 1545 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.35 (6H, s), 4.77 (2H, d, $J=5.1$ Hz), 5.13–5.22 (2H, m), 5.94 (1H, dd, $J=17.9$, 10.6 Hz), 6.26 (1H, s), 6.29 (1H, s), 7.22–7.29 (5H, m).

3.3.5. 1-Butyl-3-(1-phenylallyl)-thiourea (7e). White powder. Mp 77–78 °C (hexane/ethyl acetate). Anal. Calcd for $C_{14}H_{20}N_2S$: C, 67.70; H, 8.12; N, 11.28. Found: C, 67.60; H, 8.28; N, 11.26. HR-MS (TOF-CI) Calcd for $C_{14}H_{21}N_2S$ (MH^+): 249.1425. Found: 249.1425. IR (neat): 3264, 1545 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.87 (3H, t, $J=7.3$ Hz), 1.25 (2H, sext, $J=7.3$ Hz), 1.47 (2H, quint, $J=7.3$ Hz), 3.44 (2H, s), 5.24–5.31 (2H, m), 5.49 (1H, s), 5.88 (1H, s), 5.97–6.05 (1H, m), 6.30 (1H, s), 7.28–7.39 (5H, m).

3.3.6. 1-*iso*-Butyl-3-(1-phenylallyl)-thiourea (7f). White powder. Mp 92–93 °C (hexane/ethyl acetate). Anal. Calcd for $C_{14}H_{20}N_2S$: C, 67.70; H, 8.12; N, 11.28. Found: C, 67.40; H, 8.21; N, 11.49. HR-MS (TOF-CI) Calcd for $C_{14}H_{21}N_2S$ (MH^+): 249.1425. Found: 249.1421. IR (neat): 3266, 1552 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.81–0.84 (6H, m), 1.73–1.86 (1H, m), 3.29 (2H, s), 5.25–5.32 (2H, m), 5.42 (1H, s), 5.89 (1H, s), 5.97–6.05 (1H, m), 6.34 (1H, s), 7.29–7.39 (5H, m).

3.3.7. 1-*sec*-Butyl-3-(1-phenylallyl)-thiourea (7g). White powder. Mp 112–113 °C (hexane/ethyl acetate). Anal. Calcd for $C_{14}H_{20}N_2S$: C, 67.70; H, 8.12; N, 11.28. Found: C, 67.72; H, 8.27; N, 11.16. HR-MS (TOF-CI) Calcd for $C_{14}H_{21}N_2S$ (MH^+): 249.1425. Found: 249.1430. IR (neat): 3266, 1536 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.72 (1.5H, t, $J=7.4$ Hz), 0.90 (1.5H, t, $J=7.4$ Hz), 1.06 (1.5H, d, $J=6.3$ Hz), 1.15 (1.5H, d, $J=6.3$ Hz), 1.36–1.43 (1H, m), 1.44–1.57 (1H, m), 4.18 (1H, s), 5.24–5.34 (2H, m), 5.38 (1H, s), 5.59 (1H, s), 5.96–6.06 (1H, m), 6.20 (1H, s), 7.30–7.40 (5H, m).

3.3.8. 1-Allyl-3-(1-phenylallyl)-thiourea (7h). White powder. Mp 56–57 °C (hexane/ethyl acetate). Anal. Calcd for $C_{13}H_{16}N_2S$: C, 67.20; H, 6.94; N, 12.06. Found: C, 67.35; H, 6.91; N, 11.95. HR-MS (TOF-CI) Calcd for $C_{13}H_{17}N_2S$ (MH^+): 233.1112. Found: 233.1113. IR (neat): 3251, 1540 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 4.09 (2H, s), 5.09–5.14 (2H, m), 5.24–5.31 (2H, m), 5.61 (1H, s), 5.76–5.85 (1H, m), 5.96–6.05 (1H, m), 6.09 (1H, s), 6.40 (1H, s), 7.29–7.38 (5H, m).

3.3.9. 1-*cyclo*-Pentyl-3-(1-phenylallyl)-thiourea (7i). White powder. Mp 137–138 °C (hexane/ethyl acetate). Anal. Calcd for $C_{15}H_{20}N_2S$: C, 69.19; H, 7.74; N, 10.76. Found: C, 69.12; H, 7.89; N, 10.99. HR-MS (TOF-CI) Calcd for $C_{15}H_{21}N_2S$ (MH^+): 261.1425. Found: 261.1430. IR (neat): 3263, 1539 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.31–1.47 (2H, m), 1.54–1.63 (4H, m), 1.89–2.04 (2H, m), 4.31 (1H, s), 5.25–5.33 (2H, m), 5.58 (1H, s), 5.88 (1H, s), 5.98–6.07 (1H, m), 6.12 (1H, s), 7.30–7.40 (5H, m).

3.3.10. 1-*cyclo*-Hexyl-3-(1-phenylallyl)-thiourea (7j). White powder. Mp 136–137 °C (hexane/ethyl acetate). Anal. Calcd for $C_{16}H_{22}N_2S$: C, 70.03; H, 8.08; N, 10.21. Found: C, 69.78; H, 8.19; N, 10.28. HR-MS (TOF-CI) Calcd for $C_{16}H_{23}N_2S$ (MH^+): 275.1581. Found: 275.1578. IR (neat): 3250, 1541 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.01–1.18 (3H, m), 1.27–1.40 (2H, m), 1.54–1.63 (3H, m), 1.84–1.87 (1H, m), 1.97–1.99 (1H, m), 4.03 (1H, s), 5.25–5.32 (2H, m), 5.42 (1H, s), 5.77 (1H, s), 5.96–6.04 (1H, m), 6.25 (1H, s), 7.28–7.39 (5H, m).

3.3.11. 1-Phenetyl-3-(1-phenylallyl)-thiourea (7k). Yellow oil. HR-MS (TOF-CI) Calcd for $C_{18}H_{21}N_2S$ (MH^+): 297.1425. Found: 297.1429. IR (neat): 3260, 1545 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.70–2.82 (2H, m), 3.69 (2H, s), 5.07–5.14 (2H, m), 5.45 (1H, s), 5.82–5.90 (1H, m), 6.13 (1H, s), 6.59 (1H, s), 7.07 (2H, d, $J=6.8$ Hz), 7.15–7.29 (8H, m).

3.3.12. 1-Butyl-3-(1-methylallyl)-thiourea (7l). Yellow oil. HR-MS (TOF-CI) Calcd for $C_9H_{19}N_2S$ (MH^+): 187.1268. Found: 187.1276. IR (neat): 3263, 1549 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.94 (3H, t, $J=7.5$ Hz), 1.32 (3H, d, $J=6.8$ Hz), 1.37 (2H, sext, $J=7.5$ Hz), 1.58 (2H, quint, $J=7.5$ Hz), 3.48 (2H, s), 4.55 (1H, s), 5.15–5.27 (2H, m), 5.81–5.89 (1H, m), 6.15 (2H, s).

3.3.13. 1-*iso*-Butyl-3-(1-methylallyl)-thiourea (7m). Colorless oil. HR-MS (TOF-CI) Calcd for $C_9H_{19}N_2S$ (MH^+): 187.1268. Found: 187.1269. IR (neat): 3264, 1549 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.94 (6H, d, $J=6.8$ Hz), 1.31 (3H, d, $J=6.8$ Hz), 1.90 (1H, m), 3.31 (2H, s), 4.66 (1H, s), 5.13–5.25 (2H, m), 5.81–5.90 (1H, m), 6.55 (2H, s).

3.3.14. 1-*sec*-Butyl-3-(1-methylallyl)-thiourea (7n). White powder. Mp 72–73 °C (hexane/ethyl acetate). Anal. Calcd for $C_9H_{18}N_2S$: C, 58.02; H, 9.74; N, 15.04. Found: C, 57.99; H, 10.04; N, 14.92. HR-MS (TOF-CI) Calcd for $C_9H_{19}N_2S$ (MH^+): 187.1268. Found: 187.1262. IR (neat): 3236, 1553 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.90–0.96 (3H, m), 1.17–1.20 (3H, m), 1.32 (3H, d, $J=6.6$ Hz), 1.50–1.62 (2H, m), 4.21 (1H, s), 4.42 (1H, s), 5.18–5.28 (2H, m), 5.80–5.89 (2H, m), 6.07 (1H, s).

3.3.15. 1-Allyl-3-(1-methylallyl)-thiourea (7o). Yellow oil. HR-MS (TOF-CI) Calcd for $C_8H_{15}N_2S$ (MH^+): 171.0955. Found: 171.0960. IR (neat): 3261, 1549 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.32 (3H, d, $J=6.8$ Hz), 4.13 (2H, s), 4.52 (1H, s), 5.17–5.27 (4H, m), 5.80–5.93 (2H, m), 6.09 (2H, s).

3.3.16. 1-*cyclo*-Pentyl-3-(1-methylallyl)-thiourea (7p). White powder. Mp 72–73 °C (hexane/ethyl acetate). Anal. Calcd for $C_{10}H_{18}N_2S$: C, 60.56; H, 9.15; N, 14.12. Found: C, 60.33; H, 9.18; N, 14.32. HR-MS (TOF-CI) Calcd for $C_{10}H_{19}N_2S$ (MH^+): 199.1268. Found: 199.1264. IR (neat): 3240, 1549 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.32 (3H, d, $J=6.6$ Hz), 1.45–1.52 (2H, m), 1.59–1.72 (4H, m), 2.00–2.05 (2H, m), 4.34 (1H, s), 4.60 (1H, s), 5.16–5.26 (2H, m), 5.82–5.90 (1H, m), 5.99 (1H, s), 6.13 (1H, s).

3.3.17. 1-*cyclo*-Hexyl-3-(1-methylallyl)-thiourea (7q). White powder. Mp 107–108 °C (hexane/ethyl acetate). Anal. Calcd for $C_{11}H_{20}N_2S$: C, 62.22; H, 9.49; N, 13.19. Found: C, 62.10; H, 9.77; N, 13.35. HR-MS (TOF-CI) Calcd for $C_{11}H_{21}N_2S$ (MH^+): 213.1425. Found: 213.1423. IR (neat): 3240, 1552 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.15–1.24 (3H, m), 1.32 (3H, d, $J=6.8$ Hz), 1.34–1.43 (2H, m), 1.59–1.71 (3H, m), 1.99–2.04 (2H, m), 4.03 (1H, s), 4.40 (1H, s), 5.18–5.28 (2H, m), 5.79–5.88 (1H, m), 5.86 (1H, s), 5.95 (1H, s).

3.3.18. 1-(1-Methylallyl)-3-phenetyl thiourea (7r). White powder. Mp 54–55 °C (hexane/ethyl acetate). Anal. Calcd for $C_{13}H_{18}N_2S$: C, 66.62; H, 7.74; N, 11.95. Found: C, 66.60; H, 7.87; N, 11.74. HR-MS (TOF-CI) Calcd for $C_{13}H_{19}N_2S$ (MH^+): 235.1268. Found: 235.1275. IR (neat): 3224, 1550 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.24 (3H, d, $J=6.8$ Hz), 2.88–2.92 (2H, m), 3.81 (2H, s), 4.20 (1H, s), 4.98–5.04 (2H, m), 5.64–5.72 (1H, m), 5.92 (1H, s), 6.09 (1H, s), 7.19–7.25 (3H, m), 7.28–7.33 (2H, m).

3.3.19. 1-Butyl-3-(1,1-dimethylallyl)-thiourea (7s). Yellow oil. HR-MS (TOF-CI) Calcd for $C_{10}H_{21}N_2S$ (MH^+): 201.1425. Found: 201.1425. IR (neat): 3258, 1545 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.93 (3H, t, $J=7.5$ Hz), 1.34 (2H, sext, $J=7.5$ Hz), 1.40 (6H, s), 1.54 (2H, quint, $J=7.5$ Hz), 3.56–3.61 (2H, m), 5.29–5.36 (2H, m), 6.02 (1H, s), 6.02 (1H, dd, $J=17.6$, 10.7 Hz), 6.14 (1H, s).

3.3.20. 1-(1,1-Dimethylallyl)-3-*iso*-butylthiourea (7t). White solid. Mp 48–49 °C (hexane/ethyl acetate). Anal. Calcd for $C_{10}H_{20}N_2S$: C, 59.95; H, 10.06; N, 13.98. Found: C, 59.94; H, 10.31; N, 13.89. HR-MS (TOF-CI) Calcd for $C_{10}H_{21}N_2S$ (MH^+): 201.1425. Found: 201.1418. IR (neat): 3234, 1533 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.92 (6H, d, $J=6.7$ Hz), 1.41 (6H, s), 1.89 (1H, m), 3.43 (1H, d, $J=6.7$ Hz), 3.44 (1H, d, $J=6.7$ Hz), 5.31–5.38 (2H, m), 6.04 (1H, dd, $J=17.7$, 10.6 Hz), 6.09 (1H, s), 6.14 (1H, s).

3.3.21. 1-*sec*-Butyl-3-(1,1-dimethylallyl)-thiourea (7u). Colorless oil. HR-MS (TOF-CI) Calcd for $C_{10}H_{21}N_2S$ (MH^+): 201.1425. Found: 201.1428. IR (neat): 3258, 1542 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.91 (3H, t, $J=7.3$ Hz), 1.17 (3H, d, $J=6.6$ Hz), 1.40 (3H, s), 1.40 (3H, s), 1.53 (2H, quint, $J=7.3$ Hz), 4.31–4.42 (1H, m), 5.29–5.37 (2H, m), 5.91 (1H, s), 6.03 (1H, dd, $J=17.7$, 10.6 Hz), 6.04 (1H, s).

3.3.22. 1-Allyl-3-(1,1-dimethylallyl)-thiourea (7v). White solid. Mp 55–57 °C (hexane/ethyl acetate). Anal. Calcd for $C_9H_{16}N_2S$: C, 58.65; H, 8.75; N, 15.20. Found: C, 58.59; H, 8.99; N, 15.11. HR-MS (TOF-CI) Calcd for $C_9H_{17}N_2S$ (MH^+): 185.1112. Found: 185.1118. IR (neat): 3246, 1545 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.43 (6H, s), 4.24–4.27 (2H, m), 5.14–5.21 (2H, m), 5.29–5.37 (2H, m), 5.83–5.93 (1H, m), 6.03 (1H, dd, $J=17.6$, 10.7 Hz), 6.10 (1H, s), 6.33 (1H, s).

3.3.23. 1-*cyclo*-Pentyl-3-(1,1-dimethylallyl)-thiourea (7w). White solid. Mp 66–67 °C (hexane/ethyl acetate). Anal. Calcd for $C_{11}H_{20}N_2S$: C, 62.22; H, 9.49; N, 13.19. Found: C, 62.24; H, 9.86; N, 13.03. HR-MS (TOF-CI) Calcd for $C_{11}H_{21}N_2S$ (MH^+): 213.1425. Found: 213.1429. IR (KBr): 3246, 1513 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.41 (6H, s), 1.44–1.49 (2H, m), 1.56–1.67 (4H, m), 1.97–2.05 (2H, m), 4.56–4.64 (1H, m), 5.29–5.36 (2H, m), 6.04 (1H, dd, $J=17.7$, 10.6 Hz), 6.12 (1H, s), 6.36 (1H, s).

3.3.24. 1-*cyclo*-Hexyl-3-(1,1-dimethylallyl)-thiourea (7x). White solid. Mp 97–99 °C (hexane/ethyl acetate). Anal. Calcd for $C_{12}H_{22}N_2S$: C, 63.67; H, 9.80; N, 12.37. Found: C, 63.39; H, 10.11; N, 12.21. HR-MS (TOF-CI) Calcd for $C_{12}H_{23}N_2S$ (MH^+): 227.1581. Found: 227.1575. IR (KBr): 3220, 1540 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.14–1.28 (2H, m), 1.36–1.47 (2H, m), 1.40 (6H, s), 1.54–1.65 (4H, m), 1.98–2.02 (2H, m), 4.18–4.27 (1H, m), 5.29–5.36 (2H, m), 6.02 (1H, dd, $J=17.7$, 10.6 Hz), 6.02 (1H, s), 6.04 (1H, s).

3.3.25. 1-(1,1-Dimethylallyl)-3-phenetyl thiourea (7y). White needles. Mp 70–71 °C (hexane/ethyl acetate). Anal. Calcd for $C_{14}H_{20}N_2S$: C, 67.70; H, 8.12; N, 11.28. Found: C, 67.52; H, 8.34; N, 11.35. HR-MS (TOF-CI) Calcd for $C_{14}H_{21}N_2S$ (MH^+): 249.1425. Found: 249.1417. IR (neat): 3254, 1551 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.24 (6H, s), 2.91 (2H, t, $J=6.6$ Hz), 3.91 (2H, dt, $J=6.6$, 5.4 Hz), 4.90–4.98 (2H, m), 5.76 (1H, dd, $J=17.7$, 10.6 Hz), 5.93 (1H, s), 6.22 (1H, s), 7.20–7.25 (3H, m), 7.29–7.33 (2H, m).

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